

# Allergic disorders and socio-economic status: a study of schoolchildren in an urban area of Makassar, Indonesia

F. Hamid<sup>1,2</sup>, S. Wahyuni<sup>3</sup>, A. van Leeuwen<sup>4</sup>, R. van Ree<sup>5</sup>, M. Yazdanbakhsh<sup>2</sup> and E. Sartono<sup>2</sup>

<sup>1</sup>Department of Microbiology, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia, <sup>2</sup>Department of Parasitology, Leiden University Medical Center, Leiden, The Netherlands, <sup>3</sup>Department of Parasitology, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia, <sup>4</sup>Department of Immunopathology, Sanquin Research, Amsterdam and <sup>5</sup>Department of Experimental Immunology and Department of Otorhinolaryngology, Academic Medical Center of the University of Amsterdam, Amsterdam, The Netherlands

## Clinical & Experimental Allergy

### Summary

**Background** In urban centres of developing countries, there is great variation in socio-economic status (SES) and lifestyle; however, little information is available on allergic disorders in groups with high- or low-SES within the same urban area.

**Objective** To determine the prevalence of allergic disorders and investigate risk factors related to them among high- and low-SES schoolchildren in Makassar, the capital city of South Sulawesi, Indonesia.

**Method** This cross-sectional study was performed in 623 children originating from high- ( $N = 349$ ) and low-SES ( $N = 274$ ) schools. Information on reported allergic symptoms and potential factors associated with allergic disorders was obtained by questionnaire. Specific IgE and skin prick test (SPT) reactivity were determined against aeroallergens [*Dermatophagoides pteronyssinus* (HDM) and cockroach]. Total IgE and helminth infections were also assessed.

**Result** The prevalence of SPT to any aeroallergens was significantly higher in high-SES than in low-SES school (25% vs. 8%,  $P < 0.001$ , respectively). However, specific IgE against cockroach and total IgE were significantly lower in high- than in low-SES children. Allergic symptoms were reported more often in low- compared to high-SES children. Specific IgE to aeroallergens significantly increased the risk of SPT positivity to the same aeroallergen in the high-, but not in the low-SES children. In the high- but not in low-SES, there was a significant positive association between SPT to HDM and wheeze. Similarly, cockroach skin reactivity and elevated BMI increased the risk of eczema in the high-SES children only.

**Conclusion and Clinical Relevance** Skin prick test is higher in high-SES, whereas IgE and allergic symptoms are higher in low-SES children. Specific IgE is a risk factor for being SPT-positive, and SPT positivity is a risk factor for allergic symptoms but only in children of high- and not low-SES school. Therefore, the socio-economic status of a child might affect the diagnosis of allergic disease in a developing country.

**Keywords** allergy, atopy, helminths, IgE, risk factors, socio-economic status

Submitted 4 August 2014; revised 6 January 2015; accepted 3 February 2015

### Correspondence:

Firdaus Hamid, Department of Microbiology, Faculty of Medicine, Hasanuddin University, Jl. Perintis Kemerdekaan KM. 10 Tamalanrea, 90245 Makassar, Indonesia and Department of Parasitology L4-Q, Leiden University Medical Center, Albinusdreef 2, 2333 ZA Leiden, The Netherlands.

E-mails: f.hamid@lumc.nl and firdaus.hamid@gmail.com

Cite this as: F. Hamid, S. Wahyuni, A. van Leeuwen, R. van Ree, M. Yazdanbakhsh and E. Sartono, *Clinical & Experimental Allergy*, 2015 (45) 1226–1236.

### Introduction

It has long been known that allergic diseases cluster within families, and this is likely to be due to genetic predisposition. However, environmental factors may modulate expression of allergic disorders. A higher prevalence of allergies in developed countries compared to developing ones [1], and the great differences in

prevalence between urban and rural populations particularly in developing [2–6] but also in developed countries [7–9] have clearly shown how important the influence of environmental factors is on the expression of allergic disorders.

The world-wide International Study of Asthma and Allergies in Childhood (ISAAC) has reported that Indonesia is one of the countries with low prevalence of allergy

in the world [1]. However, this study reported data from only one centre in Java. A study which was conducted in 10 centres in India reported a large variation in the prevalence of asthma in the different centres (ranging from 3% to 17%), indicating that the information on allergic disorders in Indonesia reported by the published ISAAC study may not be representative of the whole country.

Several factors related to western lifestyle such as increase in exposure to outdoor pollutants [10], increased indoor allergen load [11], altered diet [12, 13] and changes in exposure to infection/microbial products [14, 15] have been hypothesized to explain the increase in allergic disorders. Socio-economic status (SES) also can affect allergic disorders, as studied in affluent countries [16–18]. However, there are not many studies addressing the pattern of allergic disorders within an urban centre in a developing country where large differences in SES and lifestyle are seen.

To investigate this, we initiated a study in two schools with different socio-economic backgrounds (high- and low-SES school) in an urban area of Makassar, South Sulawesi, to measure the prevalence of atopy and reported clinical allergy. Data on several factors such as parental education, parental occupation, the presence of smokers in house, pets in house, nutritional status and helminth infections were collected to determine how these factors influence the allergic phenotype.

## Method

### *Study area and design*

The study was conducted in two elementary schools in Makassar, the capital city of South Sulawesi, Indonesia. Data were collected between October and December 2005. One school was attended by children from families with low-SES (SD Cambaya), and was located at the periphery of the city, near a port. The children from this school lived in the surrounding area and came from families with low education level who mostly worked as fishermen, menial labourers, or some that were skilled, but working in low-ranking jobs. The high-SES school (SD Mangkura) was located in the city centre, about 7 km from the low-SES school. The houses of these children were spread in different parts of the city and had good sanitary facilities. The children went to school by private vehicles or by a school bus.

A month prior to the start of the study, the parents of children in both schools from third to sixth grades were sent a letter informing them of the study and asking them to sign a letter if they agreed for their child to participate in the study. Only children who returned the signed letters were included in the study. The study was approved by the ethical committees of Faculty of Medicine, Hasanuddin University, Makassar, Indonesia

(ref:0147/H4.8.4.5.31/PP36-KOMETIK/2005). In total, 274 children from the low-SES and 349 from high-SES were included in the study.

### *Questionnaire*

Reported clinical symptoms of allergy were obtained by questionnaire. Clinical symptoms of asthma, allergic rhinitis and atopic dermatitis (eczema) in the previous 12 months were assessed using a modified ISAAC questionnaire (Questionnaire 1–3, Data S1), which had been translated into Bahasa Indonesia. Children were identified to have asthma symptoms (wheeze) if wheezing was reported in the past 12 months by parents or guardian. Rhinitis was defined by a positive response to the questions, 'In the past 12 months, has your child had a problem with sneezing or a runny or a blocked nose and has this nose problem been accompanied by itchy-watery eyes?'. Eczema in the past 12 months was determined by a positive response to the questions, 'Has your child had one or more skin problems accompanied by an itchy rash in the previous 12 months?'

An additional questionnaire was applied to obtain data on parental education, parental occupation, the number of siblings and pet contact inside the house as well as smokers in the house. Parental occupation was classified into 2 groups of low- and high-skill jobs. Educational levels were categorized as: 'low' for illiterate, elementary school or high school and 'high' for academic/university and above. The questionnaire was administered to the parents or guardians of children.

### *Skin prick testing*

Skin prick test (SPT) was performed if children were free from antihistamine, anti-asthmatic or corticosteroid drugs for at least 7 days prior to the testing. SPT reactivity to aeroallergens was tested with extract of *Dermaphagoides pteronyssinus* [house dust mite (HDM); HAL Allergy BV, Leiden, the Netherlands] and *Blattella germanica* (cockroach; Lofarma, Milan, Italy). Histamine chloride (10 mg/mL) was used as the positive control and allergen diluents as the negative control. SPT was carried out on the volar side of the child's lower arm, using separate skin prick test. The results for each child were measured after 15 min. Skin prick reactivity was determined to be positive if the longest diameter plus the diameter perpendicular of weal size divided by two was at least 3 mm. Body height and weight were also measured.

### *Specific and total IgE*

Serum level of mite- and cockroach-IgE was determined by radio allergosorbent test (RAST) as described previously [19]. Briefly, 50 µL serum was incubated

overnight with 1.5 mg of Sepharose-coupled allergen in a final volume of 300  $\mu$ L PBS, 3% BSA, 0.1% Tween-20. After washing away non-bound serum components, radiolabelled sheep antibodies (Sanquin, Amsterdam, the Netherlands) directed to human IgE were added. After overnight incubation and washing, bound radioactivity was measured. The outcomes were expressed as % binding. To convert these values into IU/mL, the result was plotted to nonlinear regression curve of chimeric monoclonal IgE antibody dilution series against the major house dust mite allergen, Der p 2 and Sepharose-coupled mite extracts.

The levels of total IgE were measured by ELISA in the Netherlands as described previously [20, 21]. The results were expressed as International Units (IU/mL).

#### Parasitological examination

The children were asked to fill a pot carefully using wooden spatula without water or urine contamination. The time of stool passed had to be recorded, and the stool had to be stored in a cool area if it stayed overnight in the house before delivery to school. Only stools that arrived in the laboratory not more than 12 h after passage were examined. The eggs from intestinal helminth such as *Ascaris lumbricoides*, *Trichuris trichiura* and hookworm were quantified using the Kato-Katz methods [22].

#### Statistical analysis

The collected data were analysed using IBM Statistical Package for Social Sciences (IBM SPSS Statistics for Windows; IBM Corp., Armonk, New York, USA) version 20. We investigated potential factors for allergic disorders separately for each school. Age-standardized z-scores of body mass index (z-BMI) were calculated according to WHO references values [23]. Descriptive data were expressed as means ( $\pm$  standard deviations), frequency (percentage of collected data) and geometric means [95% confidence intervals (CI)]. Prevalence rates were calculated and compared for different schools using Pearson's chi-square tests, while comparisons of continuous data were analysed by using Student's *t*-tests. Specific IgE (s-IgE) and total IgE were normalized by log-transformation to obtain normally distributed data. Logistic regression was used to analyse the associations between the potential factors and development of SPT and reported clinical symptoms of allergy in the past 12 months. Linear regression was used for analysis of continuous outcomes which provided estimated regression coefficients ( $\beta$ ) and their corresponding 95% CI. In multivariate analysis, we included age and sex as *a priori* confounders, as well as other variables that were significant in univariate analyses. All statistical tests were considered significant at  $P < 0.05$ .

## Result

### Characteristics of study participants

Among 917 children invited to the study, 71 (7.7%) refusals came from high-SES whereas 223 (24.3%) were from low-SES (Fig. S1). One of the reasons could have been illiteracy, but we have no data on this. Thus, a total of 349 children from the high-SES and 274 children from the low-SES school were included in the study (Fig. S1). Children were slightly younger in the high-SES compared to the low-SES school (mean age 9.05 vs. 9.92 years;  $P < 0.001$ ), whereas sex distribution was similar in both schools (Table 1). This slight age difference did not affect the results, as repeating the analysis after matching the study population for age, revealed identical results for the outcomes reported in this study. Occupation and education of the parents were homogeneous within the schools but very different between schools: in the high-SES school, 98% and 65% of parents had a high-skill occupation and high education, respectively; whereas in the low-SES school, 84% (230/274) of parents had a low-skill occupation and almost all parents had low education (97%, 255/264) (Table 1).

Almost all children (90%) from low-SES school were infected with at least one species of helminth compared to 22% in high-SES school (Table 1). The most common helminth infections were *T. trichiura* (87% in low-SES and 19% in high-SES) and *A. lumbricoides* (low-SES: 77%, high-SES: 6%). The prevalence of hookworm infection was very low (9 of 611, 1.5%); therefore, hookworm infection was excluded from further analysis.

### Prevalence of reported symptoms, skin prick test and IgE

The prevalence of reported wheeze in the previous 12 months was lower in the high-SES (7.5%) compared to the low-SES school (12.9%) as were the prevalence of reported symptoms of eczema (9.9% in high-SES school and 18.2% in low-SES school) and allergic rhinitis (26.6% vs. 41.3%,  $P = 0.001$ , respectively) in the past 12 months (Table 1).

For analysis of skin reactivity to aeroallergens, we included only children with a positive skin test ( $\geq 3$  mm) to histamine (Table 1). There were no differences in age and sex distribution between histamine-negative population ( $N = 133$  in high-SES and  $N = 77$  in low-SES) and histamine-positive population (high-SES: 216 children, high-SES: 197 children). The prevalence of SPT was higher in the high-SES school compared to low-SES school; any aeroallergen (25% vs. 8.1%,  $P < 0.001$ , respectively), HDM (15.7% vs 3%,  $P < 0.001$ , respectively) and cockroach (16.2% vs 6.1%,  $P = 0.001$ , respectively). In contrast, the levels of sIgE to cockroach as well as total IgE were significantly lower in the high-SES than

Table 1. Characteristics of population and allergic disorders in high- and low-socio-economic status (SES) schools

	High-SES		Low-SES		P-value
	N	Result	N	Result	
Age years (mean, SD)	349	9.05 ± 1.22	274	9.92 ± 1.62	< 0.001
Sex (N, %)					
Male	162	46.4	145	52.9	0.11
Female	187	53.6	129	47.1	
Parental job (N, %)					
Low skill	8	2.3	230	83.9	< 0.001
High skill	341	97.7	44	16.1	
Parental education (N, %)					
Low	117	35.0	255	96.6	< 0.001
High	217	65.0	9	3.4	
Smoker inside the house (N, %)					
No	162	48.4	76	28.8	< 0.001
Yes	173	51.6	188	71.2	
Pet inside house (N, %)					
No	294	84.2	232	84.7	0.88
Yes	55	15.8	42	15.3	
z-BMI (mean, SD)	349	-0.08 ± 1.39	274	-0.80 ± 1.24	< 0.001
Number of siblings (N, %)					
> 3	214	61.3	99	36.1	< 0.001
3+	135	38.7	175	63.9	
Clinical symptoms of allergy in the past 12 months (N, n%)					
Wheeze	335	25 (7.5)	264	34 (12.9)	0.027
Rhinitis	335	89 (26.6)	264	109 (41.3)	< 0.001
Eczema	335	33 (9.9)	264	48 (18.2)	0.003
Skin prick test reactivity (N, n,%)					
Any skin prick test reactivity	216	54 (25.0)	197	16 (8.1)	< 0.001
<i>Dermatophagoides pteronyssinus</i>	216	34 (15.7)	197	6 (3.0)	< 0.001
<i>Blatella germanica</i>	216	35 (16.2)	197	12 (6.1)	0.001
Specific IgE and Total IgE (geometric mean, 95% CI)					
House dust mite* (IU/mL)	272	0.27 (0.21–0.36)	243	0.24 (0.20–0.30)	0.55
<i>B. germanica</i> (IU/mL)	272	0.08 (0.07–0.10)	242	0.31 (0.27–0.36)	< 0.001
Total IgE (IU/mL)	272	1267.6 (1024.8–1568.0)	240	12925.9 (10834.6–15420.9)	< 0.001
Helminth infection (N, n,%)					
Any intestinal helminth	340	76 (22.4)	271	245 (90.4)	< 0.001
<i>Ascaris lumbricoides</i>	340	20 (5.9)	271	208 (76.8)	< 0.001
<i>Trichuris trichiura</i>	340	65 (19.1)	271	236 (87.1)	< 0.001

The number of positives (*n*) of the total population examined (*N*).

The statistically significant results are given in bold.

SD, standard deviation; z-BMI, z score of Body Mass Index; CI, Confidence intervals.

\*IgE to *D. pteronyssinus*.

in the low-SES. There were no differences in the levels of HDM sIgE between the two schools (Table 1).

#### Potential risk factors associated with reported clinical symptoms of allergy in the past 12 months

In the high-SES school, reported wheeze in the previous 12 months was significantly associated with SPT reactivity to HDM [odds ratio (OR), 3.18; 95% CI, 1.17–8.62; *P* = 0.023]. Skin reactivity to cockroach (OR, 3.40; 95% CI, 1.39–8.29; *P* = 0.007) and z-BMI (OR, 1.31; 95% CI, 1.02–1.69; *P* = 0.032) were positively associated with an increased risk for reported clinical symptoms of eczema

in the past 12 months (Table 2). However, we found no association between rhinitis and potential risk factors measured in the high-SES school (data not shown).

In the low-SES school, none of the exposures assessed were significantly associated with risk for reported clinical symptoms of allergy (Table 2).

#### Potential risk factors associated with skin prick test reactivity

In high-SES school, skin reactivity to HDM was positively associated with high levels of sIgE to HDM (OR, 6.03; 95% CI, 3.34–10.88; *P* < 0.001), whereas skin

Table 2. Association between potential risk factors and clinical symptoms of allergic diseases in high- and low-SES schools†

	High-SES				Low-SES			
	Wheeze		Eczema		Wheeze		Eczema	
	N	n (%)	OR [95% CI]	n (%)	N	n (%)	OR [95% CI]	n (%)
Parental job								
Low	8	0	–	0	222	34 (15.3)	–	45 (20.3)
High	327	25 (7.6)	–	33 (10.1)	42	0	–	3 (7.1)
Parental education								
Low	117	5 (4.3)	Reference	10 (8.5)	255	34 (13.3)	Reference	47 (18.4)
High	217	20 (9.2)	2.27 [0.83–6.23]	23 (10.6)	9	0	–	1 (11.1)
Smoker inside the house								
No	162	10 (6.2)	Reference	18 (11.1)	76	10 (13.2)	Reference	14 (18.4)
Yes	173	15 (8.7)	1.44 [0.63–3.31]	15 (8.7)	188	24 (12.8)	0.97 [0.44–2.13]	34 (18.1)
Pet inside house								
No	282	24 (8.5)	Reference	28 (9.9)	223	28 (12.6)	Reference	41 (18.4)
Yes	53	1 (1.9)	0.21 [0.03–1.56]	5 (9.4)	41	6 (14.6)	1.19 [0.46–3.09]	7 (17.1)
z-BMI‡	335	-0.10 ± 1.37§	0.86 [0.63–1.17]	-0.10 ± 1.37§	264	-0.79 ± 1.25§	0.88 [0.66–1.17]	-0.79 ± 1.25§
Number of siblings								
> 3	205	14 (6.8)	Reference	19 (9.3)	93	13 (14.0)	Reference	15 (16.1)
3+	130	11 (8.5)	1.26 [0.55–2.87]	14 (10.8)	171	21 (12.3)	1.26 [0.55–2.87]	33 (19.3)
Any intestinal helminth								
Negative	254	21 (8.3)	Reference	28 (11.0)	21	2 (9.5)	Reference	4 (19.0)
Positive	76	4 (5.3)	0.62 [0.20–1.85]	5 (6.6)	241	32 (13.3)	1.45 [0.32–6.54]	44 (18.3)
<i>A. lumbricoides</i>								
Negative	310	24 (7.7)	Reference	31 (10.0)	58	4 (6.9)	Reference	10 (17.2)
Positive	20	1 (5.0)	0.63 [0.08–4.89]	2 (10.0)	204	30 (14.7)	2.33 [0.78–6.90]	38 (18.6)
<i>T. trichiura</i>								
Negative	265	21 (7.9)	Reference	29 (10.9)	30	3 (10.0)	Reference	6 (20.0)
Positive	65	4 (6.2)	0.76 [0.25–2.30]	4 (6.2)	232	31 (13.4)	1.39 [0.40–4.85]	42 (18.1)
HDM SPT								
Negative	301	19 (6.0)	Reference	29 (9.6)	258	32 (12.4)	Reference	47 (18.2)
Positive	34	6 (17.6)	3.18 [1.17–8.62]*	4 (11.8)	6	2 (33.3)	3.53 [0.62–20.06]	1 (16.7)
Cockroach SPT								
Negative	301	22 (7.3)	Reference	25 (8.3)	253	31 (12.3)	Reference	44 (17.4)
Positive	34	3 (8.8)	1.23 [0.35–4.34]	8 (23.5)	11	3 (27.3)	2.69 [0.68–10.66]	4 (36.4)

†Association based on univariate logistic model.

‡Increase in risk of clinical symptoms of allergy for an increasing of each unitary in the tested variable.

§Mean and standard deviation.

\*The number of positives (*n*) of the total population examined (*N*). The statistically significant results are given in bold. \**P* < 0.05, \*\**P* < 0.01.

OR, odds ratio, CI, confidence intervals; HDM, house dust mite; SES, socio-economic status; SPT, skin prick test.

reactivity to cockroach was positively associated with high levels of sIgE to cockroach (OR, 5.64; 95% CI, 2.18–14.63;  $P < 0.001$ ) (Table 3a).

In the low-SES school, higher z-BMI was associated with SPT reactivity to cockroach. However, no significant association was found between skin reactivity and sIgE (Table 3b).

#### *Potential risk factors associated with total and allergen-specific IgE*

None of the measured potential risk factors were associated with total IgE or sIgE to aeroallergens in the high-SES school (Table S1a).

In the low-SES school, having parents with high-skill occupation ( $\beta = -0.31$ ;  $P = 0.014$ ) or high education ( $\beta = -0.63$ ;  $P = 0.023$ ) was associated with lower levels of sIgE to HDM. Levels of sIgE to cockroach as well as total IgE ( $\beta = 0.21$ ;  $P = 0.012$ ;  $\beta = 0.23$ ;  $P = 0.021$ , respectively) were significantly higher in children with *T. trichiura* infections (Table S1b).

#### *Multivariate analysis*

In high-SES school, skin reactivity to HDM was independent predictor of reported wheeze in the past 12 months (adjusted OR, 3.21; 95% CI, 1.17–8.78;  $P = 0.023$ ) while eczema was independently associated with positive skin reactivity to cockroach as well as high z-BMI. Analysis of skin reactivity adjusted for confounding factors revealed that skin reactivity to HDM remained positively associated with sIgE to HDM (adjusted OR, 6.19; 95% CI, 3.40–11.28;  $P < 0.001$ ) while skin reactivity to cockroach remained positively associated with sIgE to cockroach (adjusted OR, 5.68; 95% CI, 2.13–15.18;  $P < 0.001$ ) (Table 4).

In low-SES school, multivariate analysis revealed that high z-BMI was still associated with cockroach SPT reactivity (adjusted OR, 1.74; 95% CI, 1.02–2.96;  $P = 0.041$ ; Table 4) and having parents with high-skill occupation was still associated with having low levels of sIgE to HDM (adjusted  $\beta = -0.28$ ;  $P = 0.030$ ). Following adjustment with age and sex, infection with *T. trichiura* remained positively associated with high levels of sIgE to cockroach (adjusted  $\beta = 0.22$ ;  $P = 0.011$ ) as well as total IgE (adjusted  $\beta = 0.23$ ;  $P = 0.022$ ).

#### **Discussion**

This study has investigated allergic disorders in high- and low-SES school children living in the same urban centre of a developing country, namely Makassar, Indonesia. We observed the prevalence of skin prick test reactivity to aeroallergen was higher in high-SES

compared to the low-SES school. Conversely, the prevalence of reported allergic symptoms, IgE to cockroach as well as total IgE were higher in low-SES compared to high-SES school children. In the high-SES school, high sIgE to aeroallergens increased the risk of skin reactivity to the same aeroallergens, and moreover, skin reactivity to HDM increased the risk of reported wheeze. In contrast to the findings among the high-SES children, in the low-SES school, sIgE did not significantly increase the risk of being SPT-positive and SPT was not a significant risk factor for clinical symptoms of allergy. Studies in children among 22 countries worldwide found large variation in the prevalence of allergic symptoms and atopic sensitization among populations and also reported that the association between atopic sensitization and clinical symptoms of asthma increased with economic development [7]. The latter would be in line with our observation that in high-SES sensitization is linked to clinical symptoms whereas in low-SES, this is not the case.

Most studies on the association between BMI and allergic disorders in children are in high-income countries [24–26] while little is known on this association in children from low-to-middle income countries. Among high-SES school children in this study, we also found that skin reactivity to cockroach and BMI were positively associated with the increased risk of eczema. There are to our knowledge, no published reports on the association between eczema and cockroach sensitization while a similar trend for association between eczema and BMI has been reported by Yao et al. [27].

The fact that the prevalence of wheeze, allergic rhinitis and atopic eczema symptoms was lower in high-SES school children was opposite to the finding from a previous study conducted in children attending 30 schools in socio-economically diverse areas of Cape Town, South Africa, which reported that the prevalence of asthma, recent wheeze and allergic rhinitis increased from lowest to highest SES [28, 29]. One of the possibilities to consider is that certain viral infections, which might be associated with allergy-like symptoms and difficult to differentiate from real allergy by parents, were more prevalent in the low-SES children of the current study [30, 31].

High parental education and occupation, which are part of the indicators of high-SES, have been reported to be associated with atopy [32, 33]. Here, we found no association between skin prick test reactivity or report clinical symptoms of allergy and parental education nor with parental occupation, most likely due to homogeneity of these variables in each of high- and low-SES schools in our setting.

We could not find any association between allergic outcome measured and exposure to tobacco smoke or

Table 3. Association between potential risk factors of allergy and skin reactivity in (a) high- (b) low-SES school†

	N	Any SPT		HDM SPT		Cockroach SPT	
		n (%)	OR [95% CI]	n (%)	OR [95% CI]	n (%)	OR [95% CI]
<b>(a)</b>							
Parental job							
Low	3	0	–	0	–	0	–
High	213	54 (25.4)	–	34 (16.0)	–	35 (16.4)	–
Parental education							
Low	68	14 (20.6)	Reference	11 (16.2)	Reference	10 (14.7)	Reference
High	140	39 (27.9)	1.49 [0.74–2.98]	23 (16.4)	1.02 [0.46–2.23]	24 (17.1)	1.20 [0.54–2.68]
Smoker inside the house							
No	105	31 (29.5)	Reference	20 (19.0)	Reference	17 (16.2)	Reference
Yes	104	22 (21.2)	0.64 [0.34–1.20]	14 (13.5)	0.66 [0.31–1.39]	17 (16.3)	1.01 [0.49–2.11]
Pet inside house							
No	184	50 (27.2)	Reference	32 (17.4)	Reference	32 (17.4)	Reference
Yes	32	4 (12.5)	0.38 [0.13–1.15]	2 (6.3)	0.32 [0.07–1.39]	3 (9.4)	0.49 [0.14–1.71]
z-BMI‡	216	–0.09 ± 1.40§	1.10 [0.88–1.37]	–0.09 ± 1.40§	1.10 [0.85–1.43]	–0.09 ± 1.40§	0.93 [0.71–1.21]
Number of siblings							
> 3	123	27 (22.0)	Reference	17 (13.8)	Reference	18 (14.6)	Reference
3+	93	27 (29.0)	1.45 [0.78–2.70]	17 (18.3)	1.39 [0.67–2.91]	17 (18.3)	1.30 [0.63–2.70]
Any intestinal helminth							
Negative	165	46 (27.9)	Reference	28 (17.0)	Reference	28 (17.0)	Reference
Positive	44	8 (18.2)	0.57 [0.25–1.33]	6 (13.6)	0.77 [0.30–2.00]	7 (15.9)	0.93 [0.37–2.29]
<i>A. lumbricoides</i>							
Negative	201	53 (26.4)	Reference	33 (16.4)	Reference	34 (16.9)	Reference
Positive	8	1 (12.5)	0.40 [0.05–3.32]	1 (12.5)	0.73 [0.09–6.11]	1 (12.5)	0.70 [0.08–5.89]
<i>T. trichiura</i>							
Negative	170	46 (27.1)	Reference	28 (16.5)	Reference	28 (16.5)	Reference
Positive	39	8 (20.5)	0.70 [0.30–1.62]	6 (15.4)	0.92 [0.35–2.41]	7 (17.9)	1.11 [0.45–2.76]
Specific IgE to HDM	164	–	–	–	6.03 [3.34–10.88]***	–	–
Specific IgE to cockroach	164	–	–	–	–	–	5.64 [2.18–14.63]***
<b>(b)</b>							
Parental job							
Low	163	13 (8.0)	Reference	5 (3.1)	Reference	9 (5.5)	Reference
High	34	3 (8.8)	1.12 [0.30–4.15]	1 (2.9)	0.96 [0.11–8.47]	3 (8.8)	1.66 [0.42–6.47]
Parental education							
Low	183	14 (7.7)	Reference	5 (2.7)	Reference	10 (5.5)	Reference
High	6	1 (16.7)	2.41 [0.26–22.12]	1 (16.7)	7.12 [0.70–72.72]	1 (16.7)	3.46 [0.37–32.49]
Smoker inside the house							
No	51	5 (9.8)	Reference	2 (3.9)	Reference	5 (9.8)	Reference
Yes	138	10 (7.2)	0.72 [0.23–2.21]	4 (2.9)	0.73 [0.13–4.12]	6 (4.3)	0.42 [0.12–1.44]
Pet inside house							
No	170	15 (8.8)	Reference	5 (2.9)	Reference	12 (7.1)	–
Yes	27	1 (3.7)	0.40 [0.05–3.14]	1 (3.7)	1.27 [0.14–11.30]	0	–
z-BMI‡	197	–0.80 ± 1.26§	1.55 [0.99–2.43]	–0.80 ± 1.26§	1.14 [0.59–2.21]	–0.80 ± 1.26§	1.73 [1.03–2.92]*
Number of siblings							
> 3	69	8 (11.6)	Reference	2 (2.9)	Reference	6 (8.7)	Reference
3+	128	8 (6.2)	0.51 [0.18–1.42]	4 (3.1)	1.08 [0.19–6.05]	6 (4.7)	0.52 [0.16–1.67]
Any intestinal helminth							
Negative	17	1 (5.9)	Reference	1 (5.9)	Reference	1 (5.9)	Reference
Positive	178	15 (8.4)	1.47 [0.18–11.88]	5 (2.8)	0.46 [0.05–4.20]	11 (6.2)	1.05 [0.13–8.70]
<i>A. lumbricoides</i>							
Negative	43	1 (2.3)	Reference	1 (2.3)	Reference	1 (2.3)	Reference
Positive	152	15 (9.9)	4.60 [0.59–35.85]	5 (3.3)	1.43 [0.16–12.57]	11 (7.2)	3.28 [0.41–26.12]
<i>T. trichiura</i>							

Table 3 (continued)

	N	Any SPT		HDM SPT		Cockroach SPT	
		n (%)	OR [95% CI]	n (%)	OR [95% CI]	n (%)	OR [95% CI]
Negative	23	1 (4.3)	Reference	1 (4.3)	Reference	1 (4.3)	Reference
Positive	172	15 (8.7)	2.10 [0.26–16.70]	5 (2.9)	0.66 [0.07–5.90]	11 (6.4)	1.50 [0.18–12.21]
Specific IgE to HDM	171		–		2.70 [0.61–11.91]		–
Specific IgE to cockroach	171		–		–		3.13 [0.66–14.92]

†Association based on univariate logistic model.

‡Increase in risk of skin prick reactivity for an increasing of each unitary in the tested variable.

§Mean and standard deviation.

The number of positives (n) of the total population examined (N). The statistically significant results are given in bold. \*\*\*P < 0.001; \*P < 0.05. OR, odds ratio; CI, confidence intervals; HDM, house dust mite; SES, socio-economic status; SPT, skin prick test.

Table 4. Multivariate models for association between potential risk factors and clinical symptoms of allergy or skin reactivity in high- and low-SES schools†

	Clinical symptom of allergy in the past 12 months			
	Wheeze		Eczema	
	Adjusted OR [95% CI]	Adjusted OR [95% CI]	Adjusted OR [95% CI]	Adjusted OR [95% CI]
High-SES				
z-BMI‡		1.38 [1.06–1.78]*		
SPT HDM [reference : negative]	3.21 [1.17–8.78]*			
SPT cockroach [reference : negative]		3.81 [1.53–9.52]**		
sIgE to HDM			6.19 [3.40–11.28]***	
sIgE to cockroach				5.68 [2.13–15.18]***
Low-SES				
z-BMI‡				1.74 [1.02–2.96]*

†Multivariate model adjusted with age and sex.

‡Increase in risk of clinical symptoms of allergy or skin prick reactivity for an increasing of each unitary in the tested variable.

The statistically significant results are given in bold. \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001.

OR, odds ratio; CI, confidence intervals; HDM, house dust mite; SES, socio-economic status; SPT, skin prick test.

having pets at home which is similar to the findings is a study of rural and urban of Ecuador [3]. Although studies in Germany showed that being born and raised on livestock farm protected against atopy and allergic symptoms [34]; however, significant heterogeneity effects have also been reported across Europe [35].

Helminth parasites, such as allergies, are associated with Th2 immune responses characterized by the increased production of Th2 cytokines and with specific as well as polyclonal IgE [36]. In this study, total IgE levels were 10 times higher in the low-SES than in the high-SES school. In low-SES school, the levels of total IgE were significantly higher in children infected with *T. trichiura* where the prevalence of this infection was 87.1%. In the high-SES school where the prevalence of *T. trichiura* was much lower, infection with this parasite was not significantly associated with the increased

levels of total IgE, suggesting that levels of total IgE in low-SES school are likely to be the consequence of higher transmission of *T. trichiura* and other helminth such as *A. lumbricoides* which was also prevalent in low-SES school. In line with this, a study by Blackwell et al. [37] showed that in rural Ecuador and Bolivia, total IgE increased with increasing helminth positivity and decreased in parallel with reduction of helminth infestation [38].

Interestingly, the levels of cockroach sIgE were higher in children infected with *T. trichiura* in the low-SES school. Additionally, in the same school, we found that having parents with high-skill occupation significantly reduced sIgE levels to HDM, this might be because high-skill occupation means less exposure to helminths. It is also possible that IgE antibodies generated to helminth antigens might cross-react with allergens [39, 40] as was shown by a recent study among

Ghanaian children, which demonstrated that high levels of IgE to peanut were strongly associated with helminth infection [41].

In multivariate analysis of data from high-SES school, we found that the levels of sIgE to aeroallergens are strongly associated with the skin reactivity to the same aeroallergens. This is consistent with several studies which found a good agreement between SPT and sIgE in developed [42–44] and in an urban area of developing country [45]. However, no significant association was observed in the low-SES which is in line with our previous study conducted in a rural area of Indonesia where a dissociation between sIgE levels to aeroallergens and skin prick test to the same allergens was found [2]. These data show that despite living in the same city, socioeconomic differences might result in different association between sIgE and SPT reactivity.

The strength of this study is the relatively large number of children examined that lived in the same area. Weaknesses were cross-sectional design and the use of questionnaires to obtain information on clinical symptoms of allergic disease. The assessment of clinical symptoms of allergy by questionnaire could under or overestimate the real cases of allergic diseases. The other limitation of our current study was that the participant response rate particularly in low-SES was lower than in high-SES school, probably due to illiteracy but we have no data on this. In addition, in the low-SES school, the numbers of children with positive SPT were lower and therefore our studies of associations involving SPT might be underpowered. Confounding factors included in the study were limited; therefore, it is possible that we missed important potential confounding factors. The presence of helminth infection was deter-

mined by single Kato-Katz, which might miss light infections.

In conclusion, there are large differences between children from high- and low-SES schools in an urban area of Indonesia with respect to allergic disorders and factors that influence allergic outcomes. There is high IgE in low-SES but low SPT, while reported symptoms of allergy are higher in low-SES children. Our data also provide evidence that specific IgE is a risk factor for being SPT-positive and SPT positivity is a risk factor for allergic symptoms but only in children of high-SES and not low-SES school. Therefore, one needs to consider SES when testing for allergic disorders in cities in developing countries.

### Acknowledgements

This study was funded by the European Commission (Glofal, FP6-2003-FOOD-2-B). FH has received an EA-ACI (the European Academy of Allergy and Clinical Immunology) Exchange Research Fellowship 2012 and a scholarship from the Directorate General of Higher Education (DIKTI) 2013 of the Ministry of Education Culture of the Republic of Indonesia. The authors thank Paul van Rijn at HAL Allergy BV (Leiden, the Netherlands) for providing SPT reagents for the study. We also thank Christine and Hasni for their laboratory assistance. This study would not been possible without enthusiastic cooperation of children, their parents and teachers.

### Conflict of interest

The authors declare no conflict of interest.

### References

- 1 The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet* 1998; 351:1225–32.
- 2 Hamid F, Wiria AE, Wammes LJ *et al.* Risk factors associated with the development of atopic sensitization in Indonesia. *PLoS ONE* 2013; 8: e67064.
- 3 Cooper PJ, Chico ME, Rodrigues LC *et al.* Risk factors for atopy among school children in a rural area of Latin America. *Clin Exp Allergy* 2004; 34:845–52.
- 4 Davey G, Venn A, Belete H, Berhane Y, Britton J. Wheeze, allergic sensitization and geohelminth infection in Butajira, Ethiopia. *Clin Exp Allergy* 2005; 35:301–7.
- 5 Nyan OA, Walraven GE, Banya WA *et al.* Atopy, intestinal helminth infection and total serum IgE in rural and urban adult Gambian communities. *Clin Exp Allergy* 2001; 31:1672–8.
- 6 Perzanowski MS, Ng'ang'a LW, Carter MC *et al.* Atopy, asthma, and antibodies to *Ascaris* among rural and urban children in Kenya. *J Pediatr* 2002; 140:582–8.
- 7 Weinmayr G, Weiland SK, Bjorksten B *et al.* Atopic sensitization and the international variation of asthma symptom prevalence in children. *Am J Respir Crit Care Med* 2007; 176:565–74.
- 8 Wong GW, Chow CM. Childhood asthma epidemiology: insights from comparative studies of rural and urban populations. *Pediatr Pulmonol* 2008; 43:107–16.
- 9 Priftanji A, Strachan D, Burr M *et al.* Asthma and allergy in Albania and the UK. *Lancet* 2001; 358:1426–7.
- 10 Kim KH, Jahan SA, Kabir E. A review on human health perspective of air pollution with respect to allergies and asthma. *Environ Int* 2013; 59:41–52.
- 11 Morgan WJ, Crain EF, Gruchalla RS *et al.* Results of a home-based environmental intervention among urban children with asthma. *N Engl J Med* 2004; 351:1068–80.
- 12 Chen R, Hu Z, Seaton A. Eating more vegetables might explain reduced asthma symptoms. *BMJ* 2004; 328:1380.
- 13 Hooper R, Calvert J, Thompson RL, Deetlefs ME, Burney P. Urban/rural

- differences in diet and atopy in South Africa. *Allergy* 2008; **63**:425–31.
- 14 Yazdanbakhsh M, Kremsner PG, van Ree R. Allergy, parasites, and the hygiene hypothesis. *Science* 2002; **296**:490–4.
  - 15 von Mutius E. Infection: friend or foe in the development of atopy and asthma? The epidemiological evidence. *Eur Respir J* 2001; **18**:872–81.
  - 16 Basagana X, Sunyer J, Kogevinas M *et al.* Socioeconomic status and asthma prevalence in young adults: the European Community Respiratory Health Survey. *Am J Epidemiol* 2004; **160**:178–88.
  - 17 Jansson SA, Protudjer JL, Arnlind HM *et al.* Socioeconomic evaluation of well-characterized allergy to staple foods in adults. *Allergy* 2014; **69**:1241–7.
  - 18 Thakur N, Martin M, Castellanos E *et al.* Socioeconomic status and asthma control in African American youth in SAGE II. *J Asthma* 2014; **51**:720–8.
  - 19 Aalberse RC, Koshte V, Clemens JG. Immunoglobulin E antibodies that crossreact with vegetable foods, pollen, and Hymenoptera venom. *J Allergy Clin Immunol* 1981; **68**:356–64.
  - 20 Hamid F, Wiria AE, Wammes LJ *et al.* A longitudinal study of allergy and intestinal helminth infections in semi urban and rural areas of Flores, Indonesia (ImmunoSPIN Study). *BMC Infect Dis* 2011; **11**:83.
  - 21 Wiria AE, Prasetyani MA, Hamid F *et al.* Does treatment of intestinal helminth infections influence malaria? Background and methodology of a longitudinal study of clinical, parasitological and immunological parameters in Nangapanda, Flores, Indonesia (ImmunoSPIN Study). *BMC Infect Dis* 2010; **10**:77.
  - 22 Katz N, Chaves A, Pellegrino J. A simple device for quantitative stool thick-smear technique in Schistosomiasis mansoni. *Rev Inst Med Trop Sao Paulo* 1972; **14**:397–400.
  - 23 WHO Multicentre Growth Reference Study Group. *WHO Child Growth Standards: length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: methods and development*. Geneva: World Health Organization, 2006: 312.
  - 24 Tanaka K, Miyake Y, Arakawa M, Sasaki S, Ohya Y. U-shaped association between body mass index and the prevalence of wheeze and asthma, but not eczema or rhinoconjunctivitis: the ryukyus child health study. *J Asthma* 2011; **48**:804–10.
  - 25 Fitzpatrick S, Joks R, Silverberg JI. Obesity is associated with increased asthma severity and exacerbations, and increased serum immunoglobulin E in inner-city adults. *Clin Exp Allergy* 2012; **42**:747–59.
  - 26 Bruske I, Flexeder C, Heinrich J. Body mass index and the incidence of asthma in children. *Curr Opin Allergy Clin Immunol* 2014; **14**:155–60.
  - 27 Yao TC, Ou LS, Yeh KW, Lee WI, Chen LC, Huang JL. Associations of age, gender, and BMI with prevalence of allergic diseases in children: PATCH study. *J Asthma* 2011; **48**:503–10.
  - 28 Mercer MJ, Joubert G, Ehrlich RI *et al.* Socioeconomic status and prevalence of allergic rhinitis and atopic eczema symptoms in young adolescents. *Pediatr Allergy Immunol* 2004; **15**:234–41.
  - 29 Poyser MA, Nelson H, Ehrlich RI *et al.* Socioeconomic deprivation and asthma prevalence and severity in young adolescents. *Eur Respir J* 2002; **19**:892–8.
  - 30 Cashat-Cruz M, Morales-Aguirre JJ, Mendoza-Azpiri M. Respiratory tract infections in children in developing countries. *Semin Pediatr Infect Dis* 2005; **16**:84–92.
  - 31 Heymann PW, Carper HT, Murphy DD *et al.* Viral infections in relation to age, atopy, and season of admission among children hospitalized for wheezing. *J Allergy Clin Immunol* 2004; **114**:239–47.
  - 32 Forastiere F, Agabiti N, Corbo GM *et al.* Socioeconomic status, number of siblings, and respiratory infections in early life as determinants of atopy in children. *Epidemiology* 1997; **8**:566–70.
  - 33 Cooper PJ, Chico ME, Rodrigues LC *et al.* Reduced risk of atopy among school-age children infected with geohelminth parasites in a rural area of the tropics. *J Allergy Clin Immunol* 2003; **111**:995–1000.
  - 34 Von Ehrenstein OS, von Mutius E, Illi S, Baumann L, Bohm O, von Kries R. Reduced risk of hay fever and asthma among children of farmers. *Clin Exp Allergy* 2000; **30**:187–93.
  - 35 Ege MJ, Frei R, Bieli C *et al.* Not all farming environments protect against the development of asthma and wheeze in children. *J Allergy Clin Immunol* 2007; **119**:1140–7.
  - 36 Yazdanbakhsh M, van den Biggelaar A, Maizels RM. Th2 responses without atopy: immunoregulation in chronic helminth infections and reduced allergic disease. *Trends Immunol* 2001; **22**:372–7.
  - 37 Blackwell AD, Gurven MD, Sugiyama LS *et al.* Evidence for a peak shift in a humoral response to helminths: age profiles of IgE in the Shuar of Ecuador, the Tsimane of Bolivia, and the U.S. NHANES. *PLoS Negl Trop Dis* 2011; **5**: e1218.
  - 38 Flohrs K, Bruske I, Thiering E, Rzehak P, Wichmann HE, Heinrich J. Temporal changes in total serum immunoglobulin E levels in East German children and the effect of potential predictors. *Int Arch Allergy Immunol* 2012; **158**:27–34.
  - 39 van Ree R. Carbohydrate epitopes and their relevance for the diagnosis and treatment of allergic diseases. *Int Arch Allergy Immunol* 2002; **129**: 189–97.
  - 40 Acevedo N, Sanchez J, Erler A *et al.* IgE cross-reactivity between *Ascaris* and domestic mite allergens: the role of tropomyosin and the nematode polyprotein ABA-1. *Allergy* 2009; **64**:1635–43.
  - 41 Amoah AS, Obeng BB, Larbi IA *et al.* Peanut-specific IgE antibodies in asymptomatic Ghanaian children possibly caused by carbohydrate determinant cross-reactivity. *J Allergy Clin Immunol* 2013; **132**:639–47.
  - 42 Ollert M, Weissenbacher S, Rakoski J, Ring J. Allergen-specific IgE measured by a continuous random-access immunoanalyzer: interassay comparison and agreement with skin testing. *Clin Chem* 2005; **51**:1241–9.
  - 43 Onell A, Hjalte L, Borres MP. Exploring the temporal development of childhood IgE profiles to allergen components. *Clin Transl Allergy* 2012; **2**:24.
  - 44 Ro AD, Saunes M, Smidesang I *et al.* Agreement of specific IgE and skin prick test in an unselected cohort of two-year-old children. *Eur J Pediatr* 2012; **171**:479–84.
  - 45 Obeng BB, Amoah AS, Larbi IA *et al.* Food allergy in Ghanaian schoolchildren: data on sensitization and reported food allergy. *Int Arch Allergy Immunol* 2011; **155**:63–73.

### Supporting Information

Additional Supporting Information may be found in the online version of this article:

**Figure S1.** Flow chart of the study.

**Table S1a.** Association between potential risk factors

of allergy and specific or total IgE in high-SES school<sup>a</sup>.

**Table S1b.** Association between potential risk factors of allergy and specific or total IgE in low-SES school<sup>a</sup>.

**Data S1.** The International Study of Asthma and Allergies in Childhood (ISAAC) core questionnaires.