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ALLERGIC DISORDERS AND SOCIO-ECONOMIC STATUS: A STUDY OF SCHOOL CHILDREN IN AN URBAN AREA OF MAKASSAR, INDONESIA

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ABSTRACT

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 positivity is more frequent 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.

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] has clearly shown how important the influence of environmental factors is on the expression of allergic disorders.

The worldwide 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 center in Java. A study which was conducted in 10 centers in India reported a large variation in the prevalence of asthma in the different centers (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 center in a developing country where large differences in SES and life style 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.

METHODS

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 laborers, 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 (Figure S1).

Questionnaires

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 (supplementary questionnaire 1-3), 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 anti-histamine, anti-asthmatic or corticosteroid drugs for at least 7 days prior to the testing. SPT reactivity to aeroallergens was tested with extract of *Dermatophagoides pteronyssinus* (house dust mite (HDM); HAL Allergen BV, Leiden, The Netherlands) and *Blattella germanica* (cockroach; Lofarma, Milan, Italy). Histamin chloride (10 mg/ml) was used as the positive control and allergen diluents as the negative control. SPT was done on the volar side of the child's lower arm, using separate skin prick test. The results for each child were measured after 15 minutes. Skin prick reactivity was determined to be positive if the longest diameter plus the diameter perpendicular of wheal 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 µl 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 were plotted to non-linear 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 hours 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 analyzed using IBM Statistical Package for Social Sciences (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 (± 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 chi-square tests, while comparisons of continuous data were analyzed by using Student *t*-tests. Specific IgE (s-IgE) and total IgE were normalized by log-transformation to obtain normally distributed data. Logistic regression was used to analyze 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 (β) 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 $P < 0.05$.

RESULTS

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 (Figure 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 (Figure 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 (≥ 3 mm) to histamine (Table 1). There were no differences in age and sex distribution between the histamine-negative population (N = 133 in high-SES and N = 77 in low-SES) and the histamine-positive population (high-SES: 216 children, high-SES: 197 children). The prevalence of positive 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 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 2a). 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 2b).

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

	High-SES		Low-SES		
	N	**Result**	**N**	**Result**	***P*-value**
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	
Helminth infection (N, n%)					
Any intestinal helminth	340	76 (22.4)	271	245 (90.4)	**<0.001**
Ascaris lumbricoides	340	20 (5.9)	271	208 (76.8)	**<0.001**
Trichuris trichiura	340	65 (19.1)	271	236 (87.1)	**<0.001**
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**
Dermatophagoides pteronyssinus	216	34 (15.7)	197	6 (3.0)	**<0.001**
Blattella germanica	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
B. germanica (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**

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*.

Table 2. Association between potential risk factors and clinical symptoms of allergic diseases in (a) high- and (b) low-SES schools^

		Wheeze		Eczema	
	N	***n* (%)**	**OR [95% CI]**	***n* (%)**	**OR [95% CI]**
(a)					
Parental job					
Low	8	0		0	
High	327	25 (7.6)	-	33 (10.1)	-
Parental education					
Low	117	5 (4.3)	reference	10 (8.5)	reference
High	217	20 (9.2)	2.27 [0.83-6.23]	23 (10.6)	1.27 [0.58-2.76]
Smoker inside the house					
No	162	10 (6.2)	reference	18 (11.1)	reference
Yes	173	15 (8.7)	1.44 [0.63-3.31]	15 (8.7)	0.76 [0.37-1.56]
Pet inside house					
Low	282	24 (8.5)	reference	28 (9.9)	reference
High	53	1 (1.9)	0.21 [0.03-1.56]	5 (9.4)	0.94 [0.35-2.57]
z-BMI∞	335	-0.10 ± 1.37§	0.86 [0.63-1.17]	-0.10 ± 1.37§	**1.31 [1.02-1.69]***
Number of siblings					
< 3	205	14 (6.8)	reference	19 (9.3)	reference
3+	130	11 (8.5)	1.26 [0.55-2.87]	14 (10.8)	1.18 [0.57-2.45]
Any intestinal helminth					
Negative	254	21 (8.3)	reference	28 (11.0)	reference
Positive	76	4 (5.3)	0.62 [0.20-1.85]	5 (6.6)	0.57 [0.21-1.53]
A. lumbricoides					
Negative	310	24 (7.7)	reference	31 (10.0)	reference
Positive	20	1 (5.0)	0.63 [0.08-4.89]	2 (10.0)	1.00 [0.22-4.51]
T. trichiura					
Negative	265	21 (7.9)	reference	29 (10.9)	reference
Positive	65	4 (6.2)	0.76 [0.25-2.30]	4 (6.2)	0.53 [0.18-1.58]
HDM SPT					
Negative	301	19 (6.0)	reference	29 (9.6)	reference
Positive	34	6 (17.6)	**3.18 [1.17-8.62]***	4 (11.8)	1.25 [0.41-3.80]
Cockroach SPT					
Negative	301	22 (7.3)	reference	25 (8.3)	reference
Positive	34	3 (8.8)	1.23 [0.35-4.34]	8 (23.5)	**3.40 [1.39-8.29]****

Table 2. *Continued*

		Wheeze		Eczema	
	N	***n* (%)**	**OR [95% CI]**	***n* (%)**	**OR [95% CI]**
(b)					
Parental job					
Low	222	34 (15.3)		45 (20.3)	reference
High	42	0	-	3 (7.1)	0.30 [0.09-1.02]
Parental education					
Low	255	34 (13.3)		47 (18.4)	reference
High	9	0	-	1 (11.1)	0.55 [0.07-4.53]
Smoker inside the house					
No	76	10 (13.2)	reference	14 (18.4)	reference
Yes	188	24 (12.8)	0.97 [0.44-2.13]	34 (18.1)	0.98 [0.49-1.95]
Pet inside house					
Low	223	28 (12.6)	reference	41 (18.4)	reference
High	41	6 (14.6)	1.19 [0.46-3.09]	7 (17.1)	0.91 [0.38-2.21]
z-BMI∞	264	-0.79 ± 1.25[§]	0.88 [0.66-1.17]	-0.79 ± 1.25[§]	1.17 [0.90-1.51]
Number of siblings					
< 3	93	13 (14.0)	reference	15 (16.1)	reference
3+	171	21 (12.3)	1.26 [0.55-2.87]	33 (19.3)	1.24 [0.64-2.43]
Any intestinal helminth					
Negative	21	2 (9.5)	reference	4 (19.0)	reference
Positive	241	32 (13.3)	1.45 [0.32-6.54]	44 (18.3)	0.95 [0.30-2.96]
A. lumbricoides					
Negative	58	4 (6.9)	reference	10 (17.2)	reference
Positive	204	30 (14.7)	2.33 [0.78-6.90]	38 (18.6)	1.10 [0.51-2.37]
T. trichiura					
Negative	30	3 (10.0)	reference	6 (20.0)	reference
Positive	232	31 (13.4)	1.39 [0.40-4.85]	42 (18.1)	0.88 [0.34-2.30]
HDM SPT					
Negative	258	32 (12.4)	reference	47 (18.2)	reference
Positive	6	2 (33.3)	3.53 [0.62-20.06]	1 (16.7)	0.90 [0.10-7.87]
Cockroach SPT					
Negative	253	31 (12.3)	reference	44 (17.4)	reference
Positive	11	3 (27.3)	2.69 [0.68-10.66]	4 (36.4)	2.71 [0.76-9.67]

^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). OR: Odds ratio, CI: Confidence intervals. The statistically significant results are given in bold. $^{*}P < 0.05$, $^{**}P < 0.01$

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; $P < 0.001$), and skin 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 an 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

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

		Any SPT		HDM SPT		Cockroach SPT	
	N	n	OR [95% CI)	n	OR [95% CI)	n	OR [95% CI)
(a)							
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]

Table 3. *Continued*

		Any SPT		HDM SPT		Cockroach SPT	
	N	n	OR [95% CI)	n	OR [95% CI)	n	OR [95% CI)
Ascaris lumbricoides							
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]
Trichuris trichiura							
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)							
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]

Table 3. *Continued*

		Any SPT		HDM SPT		Cockroach SPT	
	N	n	OR [95% CI)	n	OR [95% CI)	n	OR [95% CI)
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]
Ascaris lumbricoides							
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]
Trichuris trichiura							
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). OR: Odds ratio, CI: Confidence intervals. The statistically significant results are given in bold. ***$P < 0.001$. *$P < 0.05$.

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

	Clinical symptom of allergy in the past 12 months		Skin prick test reactivity	
	HDM adj. OR [95% CI]	**Cockroach adj. OR [95% CI]**	**adj. OR [95% CI]**	**adj. OR [95% CI]**
(a)				
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]**		
Specific IgE to HDM			6.19 [3.40-11.28]***	
Specific IgE to cockroach				5.68 [2.13-15.18]***
(b)				
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. OR: Odds ratio. CI: Confidence intervals. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$

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 reported 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 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 a livestock farm protected against atopy and allergic symptoms[34]; however, significant heterogeneity effects have also been reported across Europe[35].

Both helminth parasites and allergens 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* infection was much lower, infection with this parasite was not significantly associated with 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 sIgE to cockroach were higher in children infected with *T. trichuria* 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, which 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 the 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, socio-economic 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 determined 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.

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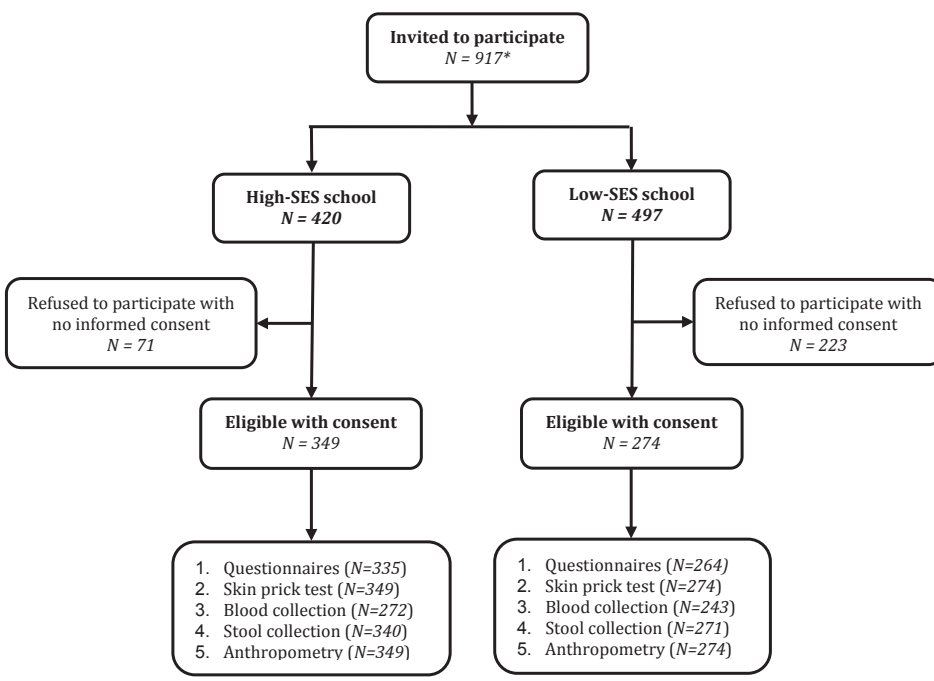
SUPPLEMENTARY FIGURE



* children from third to sixth grades of elementary school
N, number
SES, socio-economic status

Figure S1. Flow chart of the study. *The flow chart showing participation at each school and the measurements collected.*

SUPPLEMENTARY TABLE

Table S1. Association between potential risk factors of allergy and specific or total IgE in (a) high- and (b) low-SES schools^

		IgE to HDM#		IgE to *B. germanica*			Total IgE	
	N	geometric mean [95% CI]	β (95% CI)	geometric mean [95% CI]	β (95% CI)	N	geometric mean [95% CI]	β (95% CI)
(a)								
Parental job								
Low	6	0.47 [0.08-2.73]	reference	0.18 [0.07-0.50]	reference	6	538.0 [51.4-5635.3]	reference
High	261	0.27 [0.21-0.36]	-0.25 (-1.05-0.55)	0.08 [0.06-0.09]	-0.38 (-0.99-0.23)	261	1351.5 [1087.6-1679.3]	0.39 (-0.24-1.02)
Parental education								
Low	96	0.22 [0.14-0.37]	reference	0.09 [0.06-0.12]	reference	96	1177.7 [829.1-1672.8]	reference
High	171	0.31 [0.22-0.43]	0.14 (-0.10-0.39)	0.07 [0.06-0.10]	-0.09 (-0.28-0.10)	171	1413.6 [1072.5-1863.1]	0.08 (-0.12-0.28)
Smoker inside the house								
No	133	0.29 [0.19-0.45]	reference	0.07 [0.05-0.09]	reference	132	1160.2 [865.1-1556.0]	reference
Yes	134	0.26 [0.18-0.36]	-0.05 (-0.29-0.18)	0.09 [0.07-0.12]	0.12 (-0.06-0.31)	135	1505.9 [1094.6-2071.8]	0.11 (-0.07-0.30)
Pet inside house								
No	226	0.28 [0.20-0.38]	reference	0.07 [0.06-0.09]	reference	226	1390.6 [1091.9-1771.0]	reference
Yes	41	0.27 [0.14-0.50]	-0.01 (-0.33-0.32)	0.10 [0.07-0.15]	0.14 (-0.11-0.39)	41	1008.9 [634.3-1604.8]	-0.13 (-0.39-0.13)
z-BMI	272	-0.16 ± 1.34$	0.08 (-0.01-0.17)	-0.15 ± 1.34$	0.02 (-0.05-0.09)	272	-0.15 ± 1.35$	0.00 (-0.07-0.07)
Number of siblings								
< 3	165	0.24 [0.17-0.33]	reference	0.07 [0.05-0.09]	reference	164	1153.9 [868.9-1532.3]	reference
3+	107	0.33 [0.20-0.52]	0.13 (-0.11-0.37)	0.10 [0.07-0.13]	0.15 (-0.03-0.33)	108	1550.9 [1119.9-2147.9]	0.13 (-0.06-0.32)

Table S1 Continued

		IgE to HDM#		IgE to *B. germanica*			Total IgE	
	N	geometric mean [95% CI]	β (95% CI)	geometric mean [95% CI]	β (95% CI)	N	geometric mean [95% CI]	β (95% CI)
Any intestinal helminth								
Negative	205	0.29 [0.21-0.39]	reference	0.07 [0.06-0.10]	reference	205	1338.8 [1044.0-1716.8]	reference
Positive	62	0.24 [0.13-0.45]	-0.06 (-0.34-0.22)	0.09 [0.06-0.14]	0.09 (-0.13-0.30)	62	1275.4 [814.5-1997.0]	-0.01 (-0.23-0.21)
Ascaris lumbricoides								
Negative	250	0.28 [0.21-0.37]	reference	0.08 [0.06-0.10]	reference	250	1365.4 [1086.9-1715.4]	reference
Positive	17	0.25 [0.10-0.59]	-0.04 (-0.53-0.44)	0.06 [0.02-0.19]	-0.13 (-0.50-0.24)	17	839.3 [498.2-1414.0]	-0.20 (-0.59-0.18)
Trichuris trichiura								
Negative	215	0.29 [0.21-0.39]	reference	0.07 [0.06-0.09]	reference	215	1312.0 [1032.7-1666.8]	reference
Positive	52	0.23 [0.11-0.46]	-0.09 (-0.39-0.21)	0.09 [0.06-0.14]	0.10 (-0.13-0.33)	52	1373.6 [817.3-2308.4]	0.03 (-0.21-0.27)
(b)								
Parental job								
Low	198	0.27 [0.22-0.34]	reference	0.33 [0.28-0.38]	reference	194	12675.9 [10678.9-15046.5]	reference
High	37	0.14 [0.07-0.28]	**-0.31 (-0.56--0.06)***	0.26 [0.18-0.39]	-0.12 (-0.28-0.04)	37	9850.5 [6339.9-15305.0]	-0.14 (-0.32-0.04)
Parental education								
Low	228	0.25 [0.21-0.31]	reference	0.32 [0.28-0.37]	reference	224	12087.3 [10279.4-14213.2]	
High	7	0.06 [0.00-1.00]	**-0.63 (-1.18--0.09)***	0.20 [0.06-0.63]	-0.20 (-0.55-0.14)	7	15306.6 [4706.0-49785.6]	0.10 (-0.30-0.51)
Smoker inside the house								
No	68	0.23 [0.15-0.36]	reference	0.34 [0.26-0.45]	reference	68	12507.6 [9120.2-17153.2]	
Yes	167	0.25 [0.19-0.32]	0.02 (-0.18-0.23)	0.31 [0.26-0.36]	-0.04 (-0.17-0.09)	163	12037.7 [9997.2-14494.5]	-0.02 (-0.17-0.14)

Table S1 Continued

		IgE to HDM[#]		IgE to *B. germanica*			Total IgE	
	N	geometric mean [95% CI]	β (95% CI)	geometric mean [95% CI]	β (95% CI)	N	geometric mean [95% CI]	β (95% CI)
Pet inside house								
No	199	0.24 [0.19-0.31]	reference	0.31 [0.26-0.35]	reference	196	11647.7 [9732.1-13940.4]	reference
Yes	36	0.25 [0.17-0.38]	0.01 (-0.25-0.26)	0.39 [0.28-0.54]	0.08 (-0.08-0.24)	35	15593.4 [11418.2-21295.5]	0.11 (-0.08-0.30)
z-BMI	243	-0.80 ± 1.24[§]	0.06 (-0.02-0.13)	-0.80 ± 1.24[§]	0.04 (-0.01-0.09)	240	-0.80 ± 1.24[§]	0.02 (-0.04-0.07)
Number of siblings								
< 3	86	0.28 [0.19-0.40]	reference	0.31 [0.25-0.39]	reference	84	12430.6 [9623.6-16056.3]	reference
3+	157	0.23 [0.17-0.30]	-0.09 (-0.28-0.11)	0.31 [0.26-0.37]	0.00 (-0.12-0.12)	156	11463.0 [9392.3-13990.2]	-0.04 (-0.18-0.11)
Any intestinal helminth								
Negative	20	0.27 [0.14-0.51]	reference	0.23 [0.14-0.37]	reference	19	8009.1 [4576.8-14015.1]	reference
Positive	215	0.24 [0.19-0.30]	-0.01 (-0.31-0.29)	0.33 [0.28-0.38]	0.16 (-0.03-0.35)	212	12639.7 [10699.0-14932.4]	0.23 (0.00-0.45)*
Ascaris lumbricoides								
Negative	52	0.29 [0.20-0.41]	reference	0.30 [0.23-0.40]	reference	51	11839.7 [8225.2-17042.7]	reference
Positive	183	0.23 [0.18-0.30]	-0.07 (-0.28-0.15)	0.32 [0.28-0.38]	0.05 (-0.09-0.18)	180	12270.6 [10264.0-14669.5]	0.04 (-0.12-0.20)
Trichuris trichiura								
Negative	28	0.20 [0.09-0.43]	reference	0.21 [0.14-0.31]	reference	27	7874.6 [5019.0-12354.8]	reference
Positive	207	0.25 [0.20-0.31]	0.11 (-0.15-0.38)	0.34 [0.29-0.39]	0.21 (0.05-0.38)*	204	12896.7 [10879.3-15288.2]	0.23 (0.04-0.43)*

^association based on univariate linear model. [§]Mean and standard deviation. The total population examined [N). [#]IgE to *Dermatophagoides pteronyssinus* [HDM). β (beta): estimate regression coefficients. CI: Confidence intervals. The statistically significant results are given in bold. *$P < 0.05$.

SUPPLEMENTARY QUESTIONNAIRES

The International Study of Asthma and Allergies in Childhood (ISAAC) core questionnaires

2

1. Core questionnaire for wheezing and asthma (all questions are about problems which occur when this child DOES NOT have cold or the flu)

No	Question	Answer
1	Have you ever had wheezing or whistling in the chest at any time in the past?	[ ] Yes [ ] No If no skip to Q6
2	Have you had wheezing or whistling in the chest in the last 12 months?	[ ] Yes [ ] No If no skip to Q6
3	How many attacks of wheezing have you had in the last 12 months?	[ ] None [ ] 4-12 [ ] 1-3 [ ] > 12
4	In the last 12 months, how often, on average, has your sleep been disturbed due to wheezing?	[ ] Never woken with wheezing [ ] Less than one night per week [ ] One or more nights per week
5	In the last 12 months, has wheezing ever been severe enough to limit your speech to only one or two words at a time between breaths?	[ ] Yes [ ] No
6	Have you ever had asthma? Diagnosed by a doctor	[ ] Yes [ ] No
7	In the last 12 months, has your chest sounded wheezy during or after exercise?	[ ] Yes [ ] No
8	In the last 12 months, have you had a dry cough at night, apart from a cough associated with a cold or chest infection?	[ ] Yes [ ] No
9	If yes for question number 6, what is the name of medicine that Doctor gave	
10	Has any member of your family ever had asthma?	[ ] Yes [ ] No [ ] No idea
11	If you answered "yes" to question 10, indicate relationship to you (*tick all that apply*)	[ ] Father [ ] Mother [ ] Brother or Sister [ ] Mother's family _____ [ ] Father's family_____

2. Core questionnaire for allergic rhinitis (all questions are about problems which occur when this child DOES NOT have a cold or the flu)

No	Question	Answer
1	Have you ever had a problem with sneezing or a runny or blocked nose (nose problem) without cold or the flu?	[ ] Yes [ ] No If no skip to Q6
2	In the past 12 months, have you had a problem with sneezing, or a runny, or blocked nose when you DID NOT have a cold or the flu?	[ ] Yes [ ] No If no skip to Q6
3	In the past 12 months, has this nose problem been accompanied by itchy-watery eyes?	[ ] Yes [ ] No
4	In which of the past 12 months did this nose problem occur? (Please tick any which apply)	[ ] Jan [ ] Mei [ ] Sep [ ] Feb [ ] Jun [ ] Oct [ ] Mar [ ] Jul [ ] Nov [ ] Apr [ ] Aug [ ] Dec [ ] Rainy season [ ] Dry season [ ] Anytime [ ] No idea
5	In the past 12 months, how much did this nose problem interfere with your daily activities?	[ ] Not at all [ ] A Moderate [ ] A little [ ] A lot
6	Have you had a doctor diagnosed rhinitis allergy / hay fever?	[ ] Yes [ ] No
7	If yes for question number 6, what is the name of medicine that Doctor gave	
8	Has any member of your family ever had rhinitis allergy / hay fever?	[ ] Yes [ ] No
9	If you answered "yes" to question 8, indicate relationship to you (*tick all that apply*)	[ ] Father [ ] Mother [ ] Brother or Sister [ ] Mother's family _____ [ ] Father's family_____

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3. Core questionnaire for eczema (show the pictures to the subject)

No	Question	Answer
1	Have you ever had an itchy rash which was coming and going for at least six months?	[ ] Yes, picture number_____ [ ] No If no skip to Q6
2	Have you had this itchy rash at any time in the last 12 months?	[ ] Yes [ ] No If no skip to Q6
3	Has this itchy rash at any time affected any of the following places: The folds of the elbows, behind the knees, in front of ankles, under the buttocks or around the neck, ears or eyes?	[ ] Yes [ ] No
4	Has this rash cleared completely at any time during the past 12 months?	[ ] Yes [ ] No
5	In the last 12 months, how often, on average, have you been kept awake by this itchy rash?	[ ] Never in the past 12 months [ ] Less than one night per week [ ] One or more nights per week
6	Have you had Doctor diagnosed dermatitis allergy/eczema?	[ ] Yes [ ] No
7	If yes for question number 6, what is the name of medicine that Doctor gave	----------
8	Has any member of your family ever had had allergy eczema?	[ ] Yes [ ] No
9	If you answered "yes" to question 8, indicate relationship to you (*tick all that apply*)	[ ] Father [ ] Mother [ ] Brother or Sister [ ] Mother's family _____ [ ] Father's family_____

3.1 Modification in Indonesian version of ISSAC Questionnaire for eczema

No	Before	Questions of eczema	Answer
1	Modify from Q1	Have you ever had skin problem that occur more than once in the same location?	1. Yes 2. No, **You don't need to continue**
2	Modify from Q6	Have your skin problem been diagnosed by doctor/nurse as dermatitis allergy?	1. Yes 2. No
Additional	SHOW ECZEMA PICTURE		
3	Modify from Q1	Have you ever had itchy skin problem that look like in the picture?	1. Yes 2. No
4	Modify from Q3	Which area	Fossa cubiti Fossa poplitea Fossa Axiller Inguinale Dorsum pedis Dorsum palmar Another area ……
5	Q2	In the last 12 month have you ever had the symptoms?	1. Yes 2. No, **You don't need to continue**.
6	Q4	In the last 12 month, did your skin disorders completely disappear?	1. Yes 2. No
7	Modify from Q5	In the last 12 month how many times you weak at night due to itchy of your skin disorders	1. 1-3 x/ year 2. 4-12 x/year 3. >12x/year