Helminth infections, allergic disorders and immune responses: studies in Indonesia

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Chapter 5

The performance of ISAAC questionnaires and SPT/serology to assess clinical allergy in Indonesian school children with different socioeconomic status

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Abstract

In order to allow international comparisons of allergic disorders and the identification of possible risk factors, reliable diagnostic criteria, that are applicable to developing countries and to subjects with varying socioeconomic status, are needed. To assess the performance of currently available tools in an Indonesian population, the current study was conducted in children aged 7-13 years in an urban area in Makassar, covering 262 children from low- and 330 from high-socioeconomic status (SES) schools. Administered questionnaires modified from ISAAC and translated into Bahasa Indonesia were completed by parents and skin prick test (SPT) positivity as well as specific IgE to mite and cockroach were measured.

The prevalence of wheezing, runny nose, itchy rash in the last 12 months as reported by parents was significantly higher in low-SES school compared to high-SES school, but when the question whether a health worker (HW) had diagnosed the symptoms as asthma, rhinitis allergy or dermatitis allergy was considered, no differences between the low and high-SES schools were found. There was indeed a low agreement between parent reported and HW diagnosed allergic symptoms. The prevalence of SPT positivity to allergens was different from the prevalence of symptoms, being significantly lower in the low-SES school compared with high-SES. The objective parameters such as SPT positivity and specific IgE to allergens had overall a better predictive value for the allergic symptoms in the high-SES than in the low-SES school.

These data indicate that data from questionnaires have to be interpreted with some caution taking into account the varying performance of the questionnaires in developing countries that may strongly depend on socioeconomic status and educational level of the population studied

Introduction

The International study of asthma and allergies in childhood (ISAAC) has revealed that allergic diseases are increasing in many parts of the world such as Taiwan [342], Norway [343], Sweden [344], Poland [345], Croatia [346], Korea [347], Hongkong [348] and Germany [349]. In some western countries asthma and allergies have reached alarming proportions, affecting up to one-third of the children [214]. The prevalence of allergy in developing countries is lower than those in developed ones, however, there are great differences between urban and rural areas of Asia [165;166;350] and Africa [169;170;249;351] with urban areas showing prevalences that come close to those estimated in the western situation. Although genetic makeup plays an important role in the outcome of allergic disorders [191], it does not explain the great differences between developed and developing countries, nor between rural and urban communities, yet it is important to realize that gene by environment interaction could have a pronounced effect on disease outcome in these different settings [352].

In order to allow international comparisons to be made and the identification of possible risk factors for allergic disorders, a combination of objective methods and questionnaires are needed. Diagnosis of allergy based on questionnaires (parent/self-answered) has been used to measure the prevalence of allergy in children. Some investigators rely on parent/self-answered questions [353-355], while others advocate the use of the question "doctor diagnosed allergic disease" for epidemiological studies of allergy [356;357]. Due to a great variation in interpretation of allergy, ISAAC periodically improves the diagnostic criteria of these disorders [358-360]. However, in non-English speaking countries some of the routinely administered questionnaires may not perform well and outcomes of studies are to be interpreted with some caution [361]. Skin prick testing as well as specific IgE to allergens are two objective methods that can be used to determine atopic status, to predict the risk of having clinical allergy or to strengthen the diagnosis of allergy made on the basis of questionnaires.

The prevalence of allergic disorders was studied in two elementary schools in Makassar, Indonesia, one attended by children from families with low-SES and another by children from high-SES families. Clinical allergy was determined by questionnaires based on ISAAC and translated into Bahasa Indonesia that were completed by parents. The relationship between allergic symptoms and two objective measures of atopy, SPT positivity and allergen-specific IgE, was studied.

Material and methods

Study area and population

The study was conducted in two elementary schools in Makassar, the capital of South Sulawesi, Indonesia. One school was attended by children from families with low-SES (SD Cambaya), which 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 whose breadwinner mostly worked as a fisherman, menial laborer, or some that were skilled, but low ranking jobs. The high-SES school (SD Mangkura) was located in the centre of the city, about 7 km from the low-SES. The houses of these children were spread in different parts of the city and had good sanitary facilities. The children were transported 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 an agreement letter if they agreed for their child to participate in the study. Only children who returned the signed agreement letters were included in the study. The study was approved by the ethics committee of the Faculty of Medicine, Hasanuddin University, Indonesia.

ISAAC questionnaire

The questionnaire used was translated into Bahasa Indonesia in the same order as the ISAAC questionnaire. Because the questions were to be answered by parents, the core questionnaire that was used in this study was the questionnaire for children age 6-7 years old. The questions given regarding for wheezing and asthma as follow: 1) has your child ever had wheezing or whistling in the chest at any time in the past?; 2) has your child had wheezing or whistling in the chest in the last 12 months?; 3) how many attacks of wheezing has your child had in the last 12 months?; 4) in the last 12 months, how often, on average, has your child's sleep been disturbed due to wheezing?; 5) in the last 12 months, has wheezing ever been severe enough to limit your child's speech to only one or two words at a time between breaths?; 6) has your child ever had asthma?; 7) in the last 12 months, has your child's chest sounded wheezy during or after exercise?; and 8) in the last 12 months, has your child had a dry cough at night, apart from a cough associated with a cold or chest infection?

The questions given regarding for **rhinitis allergy** as follow: 1) has your child ever had a problem with sneezing, or a runny, or blocked nose when he/she did not have a cold or the flu?; 2) in the past 12 months, has your child had a problem with sneezing, or a runny, or blocked nose when he/she did not have a cold or the flu?; 3) in the past 12 months, was this nose problem accompanied by itchy-watery eyes?; 4) in which of the past 12 months did this nose problem occur?; 5) in the past 12 months, how much did this nose problem interfere with your child's daily activities?; 6) has your child ever had hayfever?.

The questions given regarding for **dermatitis allergy (eczema)** as follow: 1) has your child ever had an itchy rash which was coming and going for at least six months?; 2) has your child had this itchy rash at any time in the last 12 months?; 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 the ankles, under the buttocks, or around the neck, ears or eyes?; 4) has this rash cleared completely at any time during the last 12 months?; 5) in the last 12 months, how often, on average, has your child been kept awake by this itchy rash?; 6) has your child ever had eczema?.

In order to let the parents give a reliable answer, the ISAAC questionnaires were modified when it translated into Bahasa Indonesia: 1) question number 1 and 6 in core questions of wheeze/asthma if it translated into Bahasa Indonesia have the similar meaning (wheezing/whistling and asthma), therefore we changed the question number 6 to be 'has your child ever been diagnosed by doctor to had asthma?'; 2) in Indonesia hayfever is not a common term and only very people know it, therefore to be clear we changed the question number 6 in rhinitis core questions to be 'has your child ever been diagnosed by doctor as rhinitis allergy?'; 3) in Bahasa Indonesia eczema is the term that used not

only for dermatitis allergy (atopic dermatitis) but also for another skin chronic diseases caused by fungal and parasite infections like micosis and scabies, therefore we changed the question number 6 in the core questions of dermatitis allergy (eczema) to be 'has your child ever been diagnosed by doctor as dermatitis allergy?'; 4) in the core questions of dermatitis allergy we also added the option of 'no idea' to the question number 4, but then this question was excluded from analysis because 82% parents chose 'no idea' as the answer of this question. The changes (1,2 and 3) we made above were also aimed to confirm that the symptoms of allergy that observed by parent is the one that also diagnosed as allergy by doctor. However, health worker (HW) instead of doctor diagnosed symptom was utilized because parents in low-SES school use the term nurse and physician interchangeably

The questionnaires were also designed to obtain information on the SES of the parents by asking them about their job and their level of formal education. The questionnaires were checked and re-checked by two medical students from Hasanuddin University.

Skin prick test

SPT was performed if children were free from any medication for at least 7 days. SPT reactivity for aeroallergens was tested with extracts of *Dermatophagoides pteronyssinus*, and *Blatella germanica* preparation (HAL Allergen Laboratories, the Netherlands). Histamine chloride (10mg/ml) was used as the positive control and allergen diluent as the negative control (HAL Allergen Laboratories, The Netherlands). SPT was done on the volar side of the child's lower arm, using separate skin prick lancets. The wheal size for each child was measured after 15 minutes. Skin prick reactivity was considered positive if the longest diameter of the wheel size plus the diameter perpendicular to it divided by two, was at least 3 mm [362]. The same investigator performed the SPT for all children in the study.

Allergen specific-IgE

Serum level of mite- and cockroach-IgE was determined by radio allergosorbent test (RAST) as described previously [363]. Briefly, 50 µl sera were 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, Netherlands) directed to human IgE, was added. After overnight incubation and washing, bound radioactivity was measured. The outcomes were expressed as % binding. To convert these values into IU/ml, the results were plotted to a non-linear regression curve of chimaeric monoclonal IgE antibody dilution series against the major house-dust-mite allergen, *Der p 2*, and Sepharose-coupled mite extracts [304]. The cut off of the assay was 0.3 IU/ml and subjects were considered to have high levels of specific-IgE when the value was more than 1.0 IU/ml.

Statistical analysis

Standard statistical analyses were performed in SPSS for windows version 10. The prevalence of clinical allergy, SPT and specific-IgE between low-SES school and high-SES compared using Pearson *chi-square*. Statistic agreement between parent-answered questionnaire and HW confirmed diagnosis was estimated using the kappa statistic. Kappa value of 1 indicates perfect agreement, whereas kappa value of 0 indicates there is no agreement. Binary logistic regression adjusted with sex, age and interaction of sex and age was used to study the association between clinical allergy and SPT as well as specific-IgE to mite and cockroach. Odds ratios (OR) > 1 indicate a positive association of variable and the outcome, whereas an OR < 1 indicates a negative association. Outcomes of statistical tests were considered significant when two tailed p-values were smaller than 0.05.

Results

Responses to questionnaires: prevalence of allergic symptoms, SPT positivity and specific IgE to aeroallergens.

In total, nine hundred and seventeen parents and their children from low-SES and high-SES schools agreed to participate in the study. Of the 917, 262 of 497 (53%) from low-SES and 330 of 420 (79%) from high-SES schools completed the questionnaires. As shown in table 1, ever wheeze, wheezing in the last 12 months, ever runny nose, runny nose problem in the last 12 months, ever itchy rash and itchy rash in the last 12 months was significantly higher in low-SES compared to high-SES school. However, when questions regarding symptoms diagnosed by a HW were considered, there were no significant differences in allergic symptoms between the two schools. No differences of the symptoms of asthma (wheeze at rest, exercise wheeze, night wheeze, night cough and severe wheeze) were found between the two schools. While itchy-watery eyes and rhinitis interfering daily activity in nose problem were significantly higher in high-SES school compared to low-SES, children in low-SES were more often awake at night due to itchy rash. Not like ever wheeze, ever rhinitis and ever dermatitis, the symptoms of allergy observed by parent in the last 12 month were always accompanied by one or more symptoms that follow the question number 2 in each core questions, therefore we used these recent allergy symptoms as well as the symptoms that were confirmed by HW as allergic disorders indicators for further analysis.

There were considerable differences in the level of agreement between parent reported and HW diagnosed symptoms in low- and high-SES schools. Much lower values were obtained in low-SES school (kappa values for wheeze in the last 12 months and asthma, 0.61; for runny nose in the last 12 months and rhinitis allergy, 0.19; for itchy rash in the last 12 months and dermatitis allergy, 0.29). In the high-SES school there was a good

Questions:	Low-SES school	High-SES school	p
Core question of wheezing and asthma:			
1. has your child ever had wheezing or whistling in the chest at any time in the past?	20% (53/262)	10% (33/330)	<0.01
2. has your child had wheezing or whistling in the chest in the last 12 months?	13% (34/262)	7.6% (23/330)	<0.05
6. has your child ever been diagnosed by doctor to had asthma?	6.1(16/262)	7(23/330)	ns
If you answer yes to question number 2, in the last 12 months:			
3. how many attacks of wheezing has your child had	61.8% (21/34)	64.0% (16/25)	ns
1) None	32.4% (11/34)	32.0% (18/25)	
2) 1-3	5.9% (2/34)	4.0% (1/25)	
3) 4-12	0%	0%	
4) >12			
4. how often, on average, has your child's sleep been disturbed due to wheezing?			
1) Never woken with wheezing	14.7% (5/34)	28.0% (7/25)	ns
2) <1/week	85.3% (29/34)	72.0% (18/25)	
3) >1/week	0 %	0 %	
5. has wheezing ever been severe enough to limit your child's speech to only one or two words at a time between breaths?	26.5% (9/34)	24.0% (6/25)	ns
7. has your child's chest sounded wheezy during or after exercise?	29.4% (10/34)	32.0% (8/25)	ns
8. has your child had a dry cou gh at night, apart from a cough associated with a cold or chest infection?	34.2% (13/34)	52.0% (13/25)	ns
Core question of rhinitis allergy :			
1. has your child ever had a problem with sneezing, or a runny, or blocked nose when he/she did not have a cold or the flu?	67.9%(178/262)	41.2% 136/330)	<0.01
2. in the past 12 months, has your child had a problem with sneezing, or a runny, or blocked nose when he/she did not have a cold or the flu?	41.2%(108/262)	26.4% (87/330)	<0.01
6. has your child ever be en diagnosed by doctor as rhinitis allergy.	6.9% (18/262)	9.4% (31/330)	ns
If you answer yes to question number 2, in the last 12 months:			
3. has this nose problem accompanied by itchy -watery eyes?	16.7% (18/108)	28.7% (25/87)	<0.05
4. The question was excluded from analysis	-	-	-
5. how much this nose problem interfere your child daily activity?			
1) Not et all	33.3% (36/108)	17.2% (15/87)	<0.05
2) A little	50.0% (54/108)	65.0% (57/87)	
3) A moderate amount	12.0% (13/108)	14.9% (13/87)	
4) A lot	4.6% (5/108)	2.3% (2/87)	
Core question of dermatitis allergy (eczema):			
1. has yo ur child ever had an itchy rash which was coming and going for at least six months?	33.2% (87/262)	20.3 % 67/330)	<0.01
2. has yo ur child had this itchy rash at any time in the last 12 months?	18.3% (48/262)	10.05 (33/330)	<0.01
6. has your child ever been diagnosed by doctor as dermatitis allergy?.	8.4% (22/262)	6.1% (20/330)	ns
If you answer yes to question number 2, in the last 12 months:			
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 the ankles, under the buttocks, or around the neck, ears or eyes?	100%	100%	ns
4. has this rash cleared completely	54.2% (26/48)	45.5% (15/33)	ns
5. has your child been kept awake by this itchy rash?	75.0% (36/48)	33.3% (11/33)	<0.01

Table 1: The prevalences of allergy symptoms reported by parents in low- and high-SES schools. The difference of prevalences was tested using Pearson c*hi-square*.
statistically significant if p<0.05
ns: non significant

agreement between parent reported wheeze in the last 12 months and HW diagnosed asthma (kappa value 0.95) but considerably lower agreement for rhinitis allergy (kappa value 0.45) and dermatitis allergy (kappa value 0.45).

Prevalence (%)	Low- SES school (n=262)	High-SES school (n=330)	p
SPT positivity (%)			
D. pteronyssinus	2.3	10.3	<0.01*
B. .germanica	4.2	10.3	<0.01*
Any aeroallergen	5.7	16.4	<0.01*
Specific-IgE > 1 IU/ml(%)~			
D. pteronyssinus	16.8	20.3	0.31
B. germanica	14.3	2.2	<0.01
Any aeroallergen	24.6	20.7	0.29
Continous variable (GM and IQR)			
Mite IgE (IU/ml)~	0.35(0.15-0.64)	0.45(0.15-0.81)	0.19
Cochroach IgE (IU/ml)~	0.37(0.15-0.55)	0.20(0.15-0.22)	<0.01*

Table 2. The prevalence of SPT and the prevalence as well as the level of specific-IgE to aeroallergen in children from low-and high-SES schools. The difference of prevalence was tested using Pearson *chi-square* and Mann-Whitney test for the continuous variables.
* Statistically significant p<0.05
~ Available sera

The prevalences of SPT positivity were different from questionnaire based symptoms. Prevalence of SPT positivity to house dust mite (HDM) and cockroach was significantly lower in the low-SES school compared to high-SES. Despite the higher SPT positivity to HDM in high-SES school, IgE to mite was equivalent in the two schools and despite the higher SPT to cockroach in the high-SES school, IgE to cockroach was significantly higher in low-SES school compared to the high-SES school (table 2).

Association between specific IgE, SPT positivity and allergic symptoms reported by parents

In both schools, the positive response to wheezing in the last 12 months was associated with SPT positivity to one of the aeroallergens. When SPT positivity to each allergen was analyzed separately, only skin reactivity to mite was associated with an increased risk of wheezing (table 3); this association was only seen in the high-SES school. None of the objective parameters measured (SPT nor specific IgE) were associated with runny nose in the last 12 months in the two schools. The itchy rash in the last 12 months, was associated with some of the objective parameters but in the high-SES school only.

Association between specific IgE, SPT positivity and allergic symptoms diagnosed by a HW

When the questions of allergic diseases diagnosed by HW were analyzed and related to the objective parameters, in both schools, SPT positivity was a risk factor for asthma (Table 4). In contrast to runny nose in the last 12 months, the HW diagnosed

A. Low-SES school

	Wheezing		Runny nose		Itchy rash	
	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p
SPT	3.51(1.05-11.38)	0.04*	0.92(0.32-2.69)	0.89	0.77(0.09-6.23	0.81
Specific-IgE	1.53(0.54-3.64)	0.33	0.73(0.40-1.36)	0.32	0.97(0.33-2.88	0.96
Mite-SPT	3.24(0.54-19.34)	0.2	0.27(0.03-2.35)	0.23	0.94(0.11-8.39)	0.72
Mite-IgE	2(0.76-5.25)	0.16	0.83(0.31-1.32)	0.22	1.66(0.55-5.11)	0.36
Cockroach-SPT	2.67(0.65-11.02)	0.17	1.19(0.35-4.01)	0.78	1.1(1.13-9.12)	0.93
Cockroach-IgE	1.32(0.46-3.79)	0.61	0.7(0.33-1.49)	0.36	0.85(0.24-3.23)	0.84

B. High-SES school

	Wheezing		Runny nose		Itchy rash	
	OR (95%CI)	p	OR (95%CI)	p	OR (95%CI)	p
SPT	2.82 (1.13-6.00)	0.02*	1.48 (0.79-2.78)	0.22	2.55 (1.13-5.73)	0.02*
Specific-IgE	1.82 (0.66-5.04)	0.25	1.31 (0.66-2.53)	0.41	2.44 (1.04-5.71)	0.04*
Mite-SPT	3.20 (1.17-8.78)	0.02*	1.56 (0.74-3.34)	0.23	1.25 (0.41-3.81)	0.69
Mite-IgE	1.85 (0.67-5.12)	0.24	1.36 (0.71-2.61)	0.36	2.51 (1.10-5.67)	0.03*
Cockroach-SPT	1.25 (0.35-4.46)	0.73	1.37 (0.64-2.94)	0.42	3.40 (1.39-8.32)	<0.01*
Cockroach-IgE	3.14 (0.33-29.69)	0.32	0.56 (0.06-4.93)	0.6	1.97 (0.22-17.79)	0.54

Table 3. The odds ratio and 95% confidence intervals for the association of skin prick test positivity to aeroallergens, specific- and total-IgE antibodies with allergic symptoms reported by parents in low-SES(A) and high-SES (B) schools.
* Statistically significant $p<0.05$

rhinitis allergy was associated with SPT positivity in both schools. In the low-SES, SPT positivity to cockroach was associated with rhinitis allergy whereas in the high-SES school both cockroach and HDM positivity was associated with increased risk of rhinitis allergy. For dermatitis allergy, again in contrast to last 12 months itchy rash, HW diagnosed dermatitis allergy was more often associated with the objective parameters.

Percentage of clinical allergic cases attributable to atopy

The proportion of allergic cases that are attributable to atopy can be estimated by the population attributable risk [364]. As seen in table 5, in low-SES school, the percentage of asthma, rhinitis and dermatitis allergy cases diagnosed by HW that is attributable to atopy was lower compared to high-SES school. In both schools asthma and rhinitis have higher percentages attributable to SPT positivity than specific-IgE positivity. For dermatitis allergy the percentages attributable to SPT positivity and specific IgE were almost similar, but in low-SES school the percentages were lower compared to high-SES school.

A. Low-SES school

	Asthma		Rhinitis allergy		Dermatitis allergy	
	OR (95%CI)	**p**	**OR (95%CI)**	**p**	**OR (95%CI)**	**p**
SPT	4.40 (1.09-17.78)	0.04*	3.95 (0.99-15.74)	0.05*	1.72 (0.52-5.73)	0.37
Specific-IgE	1.54 (0.44-5.40)	0.50	0.60 (0.16-2.20)	0.45	1.87 (0.91-3.81)	0.09
Mite-SPT	3.11 (0.34-28.60)	0.31	0.97 (0.35-3.01)	0.76	0.94 (0.11-8.39)	0.96
Mite-IgE	2.71 (0.745-9.80)	0.13	0.61 (0.13-2.82)	0.53	2.42 (1.10-5.30)	0.03*
Cockroach-SPT	3.75 (0.73-19.16)	0.11	6.04 (1.44-25.26)	0.01*	2.72 (0.76-9.80)	0.12
Cockroach-IgE	0.52 (0.06-4.16)	0.53	0.34 (0.04-2.67)	0.30	1.44 (0.61-3.38)	0.40

B. High-SES school

	Asthma		Rhinitis allergy		Dermatitis allergy	
	OR (95%CI)	**p**	**OR (95%CI)**	**p**	**OR (95%CI)**	**p**
SPT	3.33 (1.301-8.48)	0.01*	4.63 (2.11-10.17)	<0.01*	3.88 (1.49-10.06)	<0.01*
Specific-IgE	2.22 (0.77-6.38)	0.14	3.00 (1.26-7.28)	0.01*	2.95 (1.03-8.42)	0.04*
Mite-SPT	3.72 (1.33-10.43)	0.01*	3.71 (1.51-9.13)	<0.01*	2.37 (0.74-7.62)	0.14
Mite-IgE	2.25 (0.78-6.46)	0.13	3.11 (1.29-7.48)	0.01*	3.05 (1.07-8.72)	0.04*
Cockroach-SPT	1.42 (0.39-5.16)	0.59	3.72 (1.51-9.14)	<0.01*	3.27 (1.10-9.72)	0.03*

Table 4. The odds ratio and 95% confidence intervals for the association of skin prick test to aeroallergens, specific- and total-IgE antibodies with clinical manifestation of allergies confirmed by health worker in liw-SES (A) and high-SES (B) schools.
* Statistically significant $p<0.05$

A. Asthma

	Asthma (-)		Asthma (+)		Relative	% of cases attributable to SPT+	Asthma (-)		Asthma (+)		Relative	% of cases attributable to Sp-IgE+
	N	SPT+(%)	N	SPT+(%)	risk		N	Sp-IgE+(%)	N	Sp-IgE+(%)	risk	
Low-SES school	246	4.88	16	18.75	4.50	13.11	222	24.77	12	33.33	1.52	10.88
High-SES school	307	14.98	23	34.78	3.03	22.12	248	20.16	18	33.33	1.98	15.18

B. Rhinitis

	Rhinitis allergy (-)		Rhinitis allergy (+)		Relative	% of cases attributable to SPT+	Rhinitis allergy (-)		Rhinitis allergy (+)		Relative	% of cases attributable to Sp-IgE+
	N	SPT+(%)	N	SPT+(%)	risk		N	Sp-IgE+(%)	N	Sp-IgE+(%)	risk	
Low-SES school	244	4.92	18	16.67	3.87	11.59	217	25.81	17	17.65	0.62	9.59
High-SES school	299	13.71	31	41.93	4.54	30.85	242	19.01	24	41.67	3.04	25.55

C. Dermatitis allergy

	Dermatitis allergy (-)		Dermatitis allergy (+)		Relative	% of cases attributable to SPT+	Dermatitis allergy (-)		Dermatitis allergy (+)		Relative	% of cases attributable to Sp-IgE+
	N	SPT+(%)	N	SPT+(%)	risk		N	Sp-IgE+(%)	N	Sp-IgE+(%)	risk	
Low-SES school	240	5.83	22	4.5	0.77	1.21	215	25.12	19	26.31	1.06	1.23
High-SES school	310	14.84	20	40	3.83	29.51	250	19.6	16	43.75	3.19	28.33

Table 5. Percentage of asthma (A), rhinitis allergy (B) and dermatitis allergy (C) cases attributable to skin prick test (SPT) and specific-IgE (Sp-IgE) positivity to aeroallergens in low- and high-SES schools.

Discussion

Socioeconomic status may influence prevalence of allergic disorders in the world as reported by ISAAC committee who indicated that the countries in the lowest quartile of GNP per capita have the lowest median positive responses to all the questions on symptoms of asthma, rhinitis and eczema [365]. A study done in schoolchildren aged 13-14 years attending 30 schools in socio economically diverse areas of Cape Town reported a trend for wheezing and allergic rhinitis symptoms to increase in a low to high-SES gradient [366;367]. Here in Makassar, an urban area of Indonesia, by using the ISAAC questionnaire we found a higher prevalence of allergic symptoms in low-SES compared to high-SES schoolchildren. However, the difference disappeared when the prevalence of symptoms confirmed by health worker was considered. The fact that we did not find a lower prevalence of allergic symptoms in the low-SES school, unlike data from Cape Town, might be due to the performance of the ISAAC questionnaire adapted for our study. The translation into Bahasa Indonesia might not perform well enough; the terms to describe wheeze, runny nose or itchy rash might not be accurate, there are no ISAAC questionnaires in Bahasa Indonesia that have been back translated.

Few studies have addressed the performance of ISAAC questionnaire in general population surveys in developing countries, most such studies have been performed in western countries. The asthma component of the ISAAC written questionnaire has been reported to be reproducible, adequate and able to differentiate between asthmatics and controls in Tasmania [368] and together with ISAAC video is thought to provide a strong tool to assess asthma prevalence as shown in a study of 475 adolescents in four secondary schools with mixed ethnic backgrounds [186] in Sidney. The rhinitis component of ISAAC core questions has a high positive predictive value in detecting atopy among children with symptoms, although it seemed less sensitive when it was used to detect atopy in a general population of children [369]. A modification of the UK diagnostic criteria for atopic dermatitis, which performed well not only in the UK [370] but also in Romanian population [371], was incorporated into ISAAC questionnaire. However, when tested in a developing country, Ethiopia, the written ISAAC questionnaire answered by parents indicated a prevalence of atopic dermatitis that was ten times less than if it was diagnosed by a doctor [254].

Each question in the English ISAAC questionnaire has been put in an order to first identify whether the parent has ever observed the symptoms, the occurrence of the symptoms in the last several months, the severity of the symptom and finally whether the symptoms are part of the clinical manifestations of allergy. However, as we have explained in material and methods, some questions were modified; whether these modification have affected the performance of the questionnaire needs to be investigated.

Altogether, there was poor agreement between the symptoms as reported by the parent and symptoms confirmed by HW, with the exception of wheezing in the past 12 months and asthma confirmed by HW (kappa value of 0.95) in the high-SES school. This value was only 0.61 in the low-SES school. For runny nose/rhinitis allergy and itchy rash/ dermatitis allergy, the agreement in low-SES school was particularly poor (0.29 and 0.19, respectively) and although slightly higher in high-SES school (for both 0.45) still remained disappointing. The poor agreement might result from the fact that several diseases that are highly prevalent, especially in the low-SES school, might have allergy-like symptoms difficult to differentiate from real allergy by parents. For instance, wheezing caused by viral and bacterial infections is known to be high in developing countries [372] and may be related to malnutrition, low maternal education, crowding, number of siblings, and exposure to tobacco smoke which are mostly found in low-SES families [373]. In addition, differentiation of allergic rhinitis from rhinitis caused by an infection is not simple since watery nose caused by microbial infections is highly prevalent in developing countries [372]. Similarly, skin disorders caused by bacterial, parasitic, fungal and arthropods are often seen in developing countries and along with lack of skin care may result in chronic skin disorders which may be difficult to distinguish from itchy-skin rash caused by allergy. One may argue that infections caused by viruses and bacteria are always accompanied by fever. However, during chronic infections, especially in tropical areas fever is sometimes not very obvious, which may make it difficult for a parent to recall whether the symptom was accompanied by fever or not. In addition, the educational background of the parents who answered the questionnaire is very likely to play a role in the performance of the test to identifying symptoms accurately. The low education level of parent in from low-SES school may also explain the lower response rate to questionnaires in this school compared to high-SES school.

When there is a large discrepancy between doctor diagnosed and parent-reported allergic symptoms [254] the need for objective parameters increases. Here we investigated the association between objective parameters of allergy and parent-reported as well as HW diagnosed symptoms of allergy. In both schools SPT positivity was a risk factor for wheezing reported by parents and for HW diagnosed asthma. However, there was a poor associations between SPT positivity/specific IgE and other symptoms reported by parents, and although this improved when HW diagnosed symptoms were considered, the most frequent associations were found in the high-SES school. Calculation that measured how much asthma, rhinitis allergy and dermatitis allergy was attributable to SPT and specific IgE, confirmed that in general these tests indicated a higher percentages of attributable cases in the high-SES compared with the low-SES school, but the values were lower in our study than that reported from a developed country such as USA, New Zealand, Sweden, Germany and Finland which found percentage of asthma cases attributable to

SPT in children to be 30%, 34%, 40%, 51% and 57%, respectively (reviewed by Pierce in [364]). The lower values in our study could either be due to the relative poor performance of the questionnaires or to the fact that sensitization or positive skin reactivity to allergens less often leads to clinical allergy in our population [364].

Conclusion

It is clear that questionnaires need to be carefully assessed in distinct geographical areas of the world where cultural and socioeconomic differences may modify responses. In urban areas of Indonesia the use of HW diagnosed data regarding allergy symptoms should be considered when embarking on epidemiological studies; especially when populations with low socioeconomic status are the focus of the study. A positive association between parent-reported wheezing in the last 12 months and HW diagnosed asthma as well as its association with SPT positivity indicates that for children aged 7-13 years, this question may enable studies to get an estimate of the prevalence of asthma. Although sensitization or positive skin reactivity to allergens does not automatically translate into clinical allergy, objective parameters such as SPT and specific-IgE, could be used to at least have a better estimation of allergic symptoms in populations with low-SES and education.