

Short communication

The association between atopy and asthma in a semirural area of Tanzania (East Africa)

Background: Atopy is consistently associated with asthma, except in a study in Africa. We assessed the association between atopy and asthma in women from a semirural area of Tanzania (East Africa).

Methods: All pregnant women delivering at the district hospital during a 1-year period were recruited ($n=658$, 60.6% of those selected). Asthma was investigated by a standard questionnaire and atopy by specific IgE (immunoglobulin E) antibodies to *Dermatophagoides pteronyssinus* (Der p 1) and cockroach.

Results: The prevalence of wheezing chest was 10.7%; of asthma, 3.5%. Levels of specific IgE of >0.35 kU/l (73%) and high levels of total IgE (62% higher than 1000 kU/l) were highly prevalent. Specific IgE antibody levels in sera were not associated with asthma (3.8% of women with negative specific IgE to any antigen had asthma in comparison to 4.0% of women with positive specific IgE; odds ratio [OR]=1.06, 0.35–3.22). Total IgE was not different between women with asthma and women without asthma ($P=0.36$).

Conclusions: In tropical regions, the association between allergy and asthma is complex, and specific IgE reactivity to environmental allergens may not be related to asthma.

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Key words: Africa; asthma; atopy; specific IgE;
total IgE.

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Accepted for publication 3 April 2000

There is abundant evidence linking exposure to environmental allergens, development of specific IgE reactivity, and asthma (1). This evidence has not been presented without dispute (2, 3) but has been largely accepted as the predominant paradigm (4). Because of the lack of definitive evidence, some authors have assessed the relation between exposure to aeroallergens and asthma in developing countries, where the markedly differing environment may offer opportunities for reassessing the role of aeroallergens. In a recent study in a rural area of Ethiopia (5), reactivity to environmental allergens was rare and negatively associated with asthma. The present study aimed to investigate the relationship between specific reactivity to aeroallergens and asthma among women from Ifakara, Tanzania (East Africa).

Material and methods

Design and subjects

Ifakara is a semirural area in southeast Tanzania. The present cross-sectional study included mothers of children participating in a trial of iron supplementation and malaria chemoprophylaxis, followed from delivery in four randomized groups for up to 3 years (6). Of the 1086 neonates at the district hospital of Ifakara during the years 1985–6, 832 were included in the trial. Among these, 658 mothers (79%) participated in the interview at 18 months. A second interview was performed when the children were 3 years old, and was answered by 520 mothers, 489 (74%) of whom had participated in the previous interview. The housing and environmental conditions of these women were those commonly found

in semirural Africa (i.e., most of the women working in agriculture, few smokers, small and crowded houses with earth floors, no ventilation, and no electricity).

Measurement of asthma

A questionnaire on history of asthma and environmental conditions, based on the AMICS questionnaire (7), was administered to mothers during the visit at 18 months. The questionnaire was translated into Swahili by a bilingual pediatrician from Ifakara Hospital and back-translated by another bilingual. Two trained fieldworkers carried out the interviews. A new questionnaire, including the respiratory symptoms questionnaire of the ECRHS (8), was undertaken at the visit at 3 years.

Atopy and allergens in dust

A sample of sera collected during delivery was stored at -20°C , and a 1-ml aliquot was used to measure IgE levels. Sera were available for 608 out of the 658 mothers (92.4%). Levels of total serum IgE and specific serum IgE against *Dermatophagoides pteronyssinus* (Der p 1) and cockroach were blindly measured by the CAP method (Kabi Pharmacia, Uppsala, Sweden), and the values were expressed in kU/l. We did a pilot study to determine the most common allergens out of a panel of nine (Der p 1, *D. farinae*, cockroach, cat, dog, timothy grass, *Cladosporium*, *Aspergillus*, and ragweed) in 10 adult asthmatics in Ifakara Hospital, and we found that only Der p 1 and cockroach were reactive in more than one patient; among the rest, only cat and *Aspergillus* were reactive in one subject. Similarly, in a study in Guinea-Bissau (West Africa), the predominant specific IgEs were against dust mite and cockroach (9). The laboratory did not quantify values higher than 2000 kU/l, and a value of 2001 kU/l was assigned. Dust samples were taken by a standard procedure (7) from children's mattresses (or stowma in 38% due to absence of mattress) in all houses. Only 128 samples were assayed due to budget restrictions. Selection of these samples was carried out at random among all collected dust samples. We used a standard household vacuum cleaner (1000 W, Rowenta) with battery, fitted with 8- μm filter paper (Whatman) in an ALK dust trap. Mattress covers were measured over the whole surface and vacuumed for the same duration. Environmental levels of Der p 1 and Fel d 1 were determined by enzyme-linked immunosorbent assay, as described elsewhere (7).

Definitions and statistical analysis

Wheezing was defined as a positive answer to the question, "Have you ever had a wheezing chest?" from the AMICS questionnaire, and current asthma was,

according to the ECRHS protocol (8), defined as a positive answer to at least one of the following questions of the short respiratory questionnaire:

- "Have you been woken by an attack of shortness of breath at any time in the last 12 months?"
- "Have you had an attack of asthma in the last 12 months?"
- "Are you currently taking any medicine (including inhalers, aerosols, or tablets) for asthma?"

Positive IgE in sera was taken as a titer higher than 0.35 kU/l. Logistic regression was used to assess the multivariate relation between asthma and specific and total IgE. Pearson correlation after a natural logarithmic transformation (due to right skew of variables) was carried out among specific and total IgE levels and levels of allergens in dust. Analyses were carried out with the Stata package (StataCorp, College Station, TX, USA). Statistical significance was viewed as P values lower than 0.05.

Results

The prevalence of ever wheezing was 10.7% and of current asthma 3.5% (Table 1). Positivity to specific IgE (73%) and total IgE (62% higher than 1000 kU/l) was high. Mean levels of allergens in dust were 2.21 and 0.30 $\mu\text{g/g}$ dust for Der p 1 and Fel d 1, respectively (22% and 3% of subjects had values higher than 2 $\mu\text{g/g}$, and 6% and 1% higher than 10 $\mu\text{g/g}$, respectively).

Neither specific IgE to either of the two allergens nor total IgE was associated with the presence of current asthma or wheezing chest ever (Table 2). Total IgE was higher in asthmatics, but the difference was not statistically significant, either when treated as a categorical variable (Table 2), or as a continuous variable ($P=0.36$).

Levels of allergen in dust were not consistently correlated with concentration of specific IgE (Table 3).

Table 1. Description of 608 women, symptoms and atopy

	<i>n</i>	(%)
Age in years (mean and range)	26	15–44
Wheezing chest, ever	65	(10.7%)
Current asthma	18	(3.5%)*
Total IgE in kU/l		
> 100 and $\leq$ 1000	205	(33.7%)
> 1000 and $\leq$ 2000 kU/l	188	(30.9%)
> 2000 kU/l	189	(31.1%)
Specific IgE Der p 1		
> 0.35 and $\leq$ 0.7 kU/l	69	(11.3%)
> 0.7 kU/l	228	(37.4%)
Specific IgE cockroach		
> 0.35 and $\leq$ 0.7 kU/l	60	(9.8%)
> 0.7 kU/l	351	(57.5%)
Atopy†	446	(73.3%)

* 18 out of 520 women.

† Any specific IgE > 0.35 kU/l.

Table 2. Association between atopy and asthma

	<i>n</i>	Wheezing chest, ever		Current asthma	
		%	OR (95% CI)	%	OR (95% CI)
Crude					
Specific IgE					
Negative‡	162	11.7%	1	3.8%	1
Only cockroach	149	11.4%	0.97 (0.48–1.94)	3.2%	0.84 (0.20–3.62)
Only Der p 1	36	8.3%	0.68 (0.19–2.44)	5.6%	1.50 (0.16–14)
Both	260	10.0%	0.82 (0.44–1.55)	4.3%	1.16 (0.34–4.12)
Atopy†	446	10.3%	0.86 (0.82–1.49)	4.0%	1.06 (0.35–3.22)
Total IgE in kU/l					
≤100‡	26	16.0%	1	0.0%	–
101–1000	205	7.8%	0.42 (0.12–1.37)	3.2%	–
1001–2000	188	11.2%	0.63 (0.20–2.04)	4.0%	–
>2000	189	12.6%	0.73 (0.22–2.30)	5.0%	–
≤1000‡	231	8.6%	1	2.9%	–
>1000	377	11.7%	1.43 (0.82–2.49)	4.5%	1.59 (0.49–5.20)
Multivariate‡					
Specific IgE to cockroach			0.87 (0.46–1.62)		0.71 (0.20–2.50)
Specific IgE to Der p 1			0.72 (0.40–1.29)		1.27 (0.36–4.61)
Total IgE >1000 kU/l			1.72 (0.92–3.21)		1.66 (0.45–6.17)

† Atopy defined as any specific IgE >0.35 kU/l.

‡ Reference group. In multivariate model are individuals with negative specific IgE and total IgE <1000 kU/l, adjusted by age.

OR: odds ratio; 95% CI: 95% confidence interval.

Levels of aeroallergens were not associated with asthma (odds ratio = 1.00, 95% CI = 0.30–3.30; and 0.70, 0.21–2.30, for Der p 1 and Fel d 1, respectively). There was a positive correlation between total IgE and specific IgE to Der p 1 and cockroach (Table 3). The geometric mean of total IgE was 102 kU/l in nonatopic mothers, 196 kU/l in mothers reactive to Der p 1, and 201 kU/l in mothers reactive to cockroach ($P < 0.01$).

Discussion

Specific IgE reactivity to environmental allergens, as well as levels of indoor dust, was not related to asthma in this semirural region of Africa. Only in rural areas of Ethiopia (5) has a lack of association with reactivity to environmental allergens been found, although atopy was rare in Ethiopia, whereas it was very common in our study.

IgE reactivity to common allergens has been strongly associated with asthma in most of the studies, involving all ages, carried out in the developed world (3), as well

as in Asia (10) and other parts of Africa (11). How to interpret the lack of association in our study is a matter for discussion. One explanation of the present results is that high levels of total IgE may saturate the IgE receptor and block access by the mast cells to specific IgE, thus suppressing the allergic response (12).

Another possibility is the presence of some degree of cross-reactivity between parasitic infection and Der p 1, given that parasitic infection may potentiate the allergic response to environmental allergens (13). However, cross-reactivity could explain present results only in the presence of negative confounding (i.e., a correlation between Der p 1 and parasites, and a negative association between parasites and asthma). Studies including individual measurements of parasitic infection did not find a negative association between parasites and asthma (14, 15). Therefore, the hypothesis of negative confounding due to cross-reactivity seems unlikely.

Total IgE levels, which were extremely high as in other parts of Africa (16), were not associated with wheezing or asthma. The role played by total IgE in asthma may involve mechanisms other than simply allergy. In tropical regions, specific IgE reactivity to parasites could contribute to the clinical symptoms of asthma (12) by nonallergic mechanisms. High levels of total IgE were probably due to IgE specific to parasites, and to nonspecific Th2/IL-4-dependent polyclonal IgE synthesis. Polyclonal synthesis can suppress allergic responses by reducing the production of specific IgE antibodies, an effect which may result in an inverse relationship between total and specific serum IgE levels (17). However, we did not find such an inverse relationship between specific and total IgE.

Table 3. Correlation between variables of atopy and allergen in indoor dust

	Coefficient†	
	IgE to Der p 1	IgE to cockroach
IgE to cockroach	0.47**	1
Total IgE	0.31**	0.38**
Der p 1 levels in dust	0.03	0.21*
Fel d 1 levels in dust	0.05	0.01

† Pearson correlation coefficient after natural logarithm transformation of all variables.

* $P < 0.05$; ** $P < 0.01$.

Levels of allergens in mattress dust were among the lowest reported (7). Levels of Der p 1 were higher than those reported in Germany by the Multicentre Allergy Study, but similar to those reported in Ashford (Kent, UK) and lower than those reported in Australia and New Zealand (7). Levels of Fel d 1 were much lower than those reported in the UK, and other countries (7).

A limitation of the present study was the cross-sectional design, which restricts the capacity to disentangle the temporal relationship among exposure, sensitization, and onset of the disease, especially as atopy and asthma were measured at different times. This is particularly important for dust allergens, the role of which in atopy and asthma, if any, would derive from earlier exposures. However, in the case of the association between atopy and asthma, we assume that IgE reactivity is constant over time. We have used two definitions of asthma, given the difficulty of measuring asthma by questionnaire in a developing country. Results were similar whatever the definition used, indicating that misclassification of diagnosis did not bias the results. The prevalence of asthma was similar to that reported by recent studies in Africa (18, 19).

Finally, mothers participating in the present study were not a random sample of all mothers in the region. Only 70% of all deliveries occurred in the hospital, and 23% of mothers who delivered in the hospital did not want to participate in the trial. In addition, there was a 21% loss between birth and the 18-month follow-up, mainly due to the death or severe anemia of the children (6). Overall, only 658 of the 1086 mothers delivering in the hospital (61%) participated. This probably reduced

the representativeness of the frequency of atopy and asthma observed, but it is unlikely to have produced a selection bias. The problem of a selection bias in the association between atopy and asthma depends on the losses between birth and the study of mothers at 18 months (21%). If the losses were related to the mothers' atopy or asthma, a bias could have occurred. However, it is unlikely to have occurred since most losses were due to the death or severe anemia of the children.

In conclusion, the present study provides IgE levels and their relation to asthma in a general population of a semirural area of Africa, while most of the current knowledge of atopy in human populations comes from studies in the developed world. Overall, specific IgE against environmental allergens was not related to asthma in this semirural region of Africa, at variance with the strong association observed in the developed world. In tropical locations with very high levels of the allergic phenotype, the association between allergy and asthma is complex, and environmental allergens may not play any role.

Acknowledgments

We thank the mothers and children who participated in this study for their generosity; all the professionals working at the Ifakara center, particularly the director Hassan Mshinda; John Aponte and Pere Joan-Ventura for their help in preparing the data set; and Paul Cullinan for his comments on the manuscript. This study was supported in part by grants from the Fondo Investigaciones Sanitarias, Madrid, Spain (FIS, no. 97/1220), and the Generalitat de Catalunya (CIRIT/GRQ96-9304, 97-SGR00079).

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