Helminth infections and allergies in Ghana

Amoah, A.S.

Author: Amoah, Abena Serwaa
Title: Helminth infections and allergies in Ghana
Issue Date: 2014-11-11

chapter 3

Food allergy in Ghanaian schoolchildren: data on sensitization and reported food allergy

Benedicta B. Obeng[1,2], Abena S. Amoah[2], Irene A. Larbi[2], Maria Yazdanbakhsh[1], Ronald van Ree[3], Daniel A. Boakye[2] and Franca C. Hartgers[1]

Affiliations:

[1]Leiden University Medical Center, Parasitology, Leiden, the Netherlands;
[2]Noguchi Memorial Institute for Medical Research, Parasitology, Accra, Ghana;
[3]Academic Medical Center, Experimental Immunology and Otorhinolaryngology, Amsterdam, the Netherlands

- International Archives of Allergy and Immunology 2011; 155(1):63-73 -

Abstract

Background: Epidemiological data on food allergy are scarce in African countries. We studied the prevalence of food sensitization in Ghanaian schoolchildren.

Methods: Children (5–16 years; n = 1714) from 9 Ghanaian schools were given parental consent to participate in the study. Adverse reactions and food consumption were determined by a questionnaire and atopy by skin prick testing (SPT) to peanut and 6 fruits. Subjects with positive SPTs were considered cases (n = 43) and matched with at least 1 control (n = 84), using age, sex, and school as matching criteria. Serum samples from case-control sets were analyzed for specific IgE (sIgE) to foods that elicited a positive SPT response in cases.

Results: Overall, 11% of 1407 children reported adverse reactions to foods, and 5% of 1431 children showed a positive SPT reaction mostly directed against peanut and pineapple (both 2%). Although there was a positive association between adverse reactions and SPT responses to any food allergen in the urban children (adjusted OR = 3.6, 95% CI 1.2–10.8), most of the reported adverse reactions were not in children showing an SPT reaction to the specific food item. Specific IgE sensitization was very variable for the different foods, ranging from 0 to 100% in cases, and from 0 to 25% among controls. High IgE levels for a food item significantly increased the risk of SPT positivity to any food item in the urban, but not in the rural, schoolchildren.

Conclusions: Specific foods were identified to be allergenic in Ghana. We show a good association between SPT and sIgE in urban, but not in rural, schoolchildren. However, there was no clear association between reported adverse reactions to food and SPT or sIgE.

Key words:

Food allergy, Immunoglobulin E, schoolchildren, skin prick test, Africa

Introduction

Adverse reactions to foods are caused by several different mechanisms which could be metabolic, toxicological, or immunological in nature, or they are due to microbial contamination of the food. Food allergy is mediated by immunological mechanisms including IgE-mediated hypersensitive reactions to ingested food. The adverse reactions involved in classical IgE-mediated food allergy range from mild irritation to more severe life-threatening reactions involving the cutaneous, gastrointestinal, respiratory and cardiovascular systems. Unlike other adverse reactions to foods, food allergies are restricted to individuals who have previously been sensitized. Susceptibility to food allergy is thought to result from a combination of a genetic predisposition to allergic sensitization and exposure to food allergens [1, 2].

Food allergies are an increasing public health concern with a reported prevalence of up to 8% in young children and of 3–4% in adults in the United States, United Kingdom and Europe [3-6]. In 2008, Venter *et al*. [7] found the cumulative incidence of food hypersensitivity in 3-year-olds to be 6%; according to the authors, this indicated that the incidence of food allergy had not changed much since the study by Bock *et al*. [8] in 1987. However, earlier reports had indicated an increase in the prevalence of peanut allergy [9, 10].

Compared with other forms of allergy, such as allergy to aeroallergens, food allergy has been less extensively studied and is thus less understood. A 2004 study by Isolauri *et al*. [11] demonstrated that sensitization to dietary allergens had not followed the same consistent increase observed with sensitization to aeroallergens over several decades. Knowledge from studies on aeroallergens cannot always be applied to food allergens due to the different exposure and priming routes. Also, the reported prevalence and incidence of food allergy varies widely between locations and between assessment methods. Several studies rely on questionnaire data to assess the prevalence of food allergy [12, 13]. However, this would often include reports of other adverse reactions besides food allergy because questionnaire data are more sensitive to cultural and biased perceptions on allergy. In 2002, Woods *et al*. [14] showed that reported adverse reactions to food were an overestimation of food allergy as determined by objective methods like skin prick testing (SPT). A 2004 study by Roehr *et al*. [15] showed that the prevalence of reported perceived allergic symptoms to food was 38.4% compared to 4.2% confirmed clinically by blinded and controlled oral food challenges. This trend has also been observed in a number of other studies [7, 16].

Even when objective parameters are measured, estimation of food allergies is difficult. Individuals with elevated food allergen specific IgE (sIgE) antibodies do not always show clinical symptoms of food allergy or skin test reactivity. This has been partly explained by the cross-reactivity between airborne allergens and food allergens [17]. A recent study reported that sensitization to wheat and soy in school-aged children was mostly secondarily due to pollen sensitization [18]. In addition, while quantitative measurements of IgE antibodies to some foods like milk and eggs have been found to be useful for the evaluation of food hypersensitivity, they have shown limited value for others like wheat and soybeans [19, 20]. The double-blind placebo-controlled food challenge (DBPCFC) is the gold standard for determining food allergy. However, it can only be performed in a proper clinical setting under expert supervision and is therefore difficult to apply in epidemiological studies, especially when experience with DBPCFC is limited or even absent. The apparent complexity of the mechanisms which underlie food allergy development further complicates the study of food allergy. In terms of studying the risk factors that govern the development of food allergy, several dietary factors in early childhood have been suggested to play a role, including the duration of exclusive breastfeeding and the age at which the infant is introduced to formula milk and complementary solid foods. However results have been inconclusive [21-23].

These limitations of the study of food allergy are particularly evident with regard to the absence of information from low-income countries, particularly in Sub-Saharan Africa. Few studies on immigrant subjects suggest that food allergy is not exclusive to natives of countries in the northern hemisphere. A particular example is a study comparing food intolerances and allergies between native Italian children and immigrant children from Africa, which showed that adverse food reactions were also a problem in immigrant African children [24]. Dias *et al*. studied food allergy among Caucasian and non-Caucasian children (including Blacks, Asians, and children of mixed race) presenting at an allergy clinic [25]. They found that the non-Caucasian children had a lower mean age at which the first food-allergic reaction occurred, had a higher average number of food allergens per child, and constituted the greater proportion of patients at the allergy clinic when compared to the general paediatric clinic. Taken together, these results highlight the need for more studies within Africa and in other parts of the world where food allergy studies are limited.

We examined the extent of reactivity to a set of food allergens in a population of schoolchildren in Ghana, West Africa. Furthermore, we studied the reported symptoms of food allergy, the serum levels of food sIgE, and the relationship with skin test reactivity. We also explored how early life factors, socioeconomic status (SES), helminth infections, and allergy to aeroallergens are related to having a positive skin reaction to food allergens.

Methods

Study Design

We conducted a matched case-control analysis on sensitization to food allergens within a cross-sectional study of allergic disorders in Ghana. The relationship between SPT using fresh foods and sIgE sensitization to those same foods, eating patterns, and reported adverse reactions to foods were examined in this subpopulation. The study was approved by the Institutional Review Board of the Noguchi Memorial Institute for Medical Research, Ghana. Written or verbal parental consent confirmed by a signature or thumbprint were obtained for each child before we commenced with the study.

Study area and subjects

This was a cross-sectional study to assess the problem of food allergy in Ghana. It was conducted in the Greater Accra Region of Ghana between longitudes 000.35377° W and 000.42752° E and latitudes 005.72647° N and 005.53550° S. The study period was from March 2006 to March 2008. The study participants, aged between 5 and 16 years, were recruited from 3 urban and 6 rural schools which had been invited to take part in the study and had agreed. These included rural schools in Pantang (in the Ga district) and in Anyamam, Goi, Toflokpo, Agbedrafor, and Koluedor in the Dangme East district. The main income-generating activities in these rural areas are farming and fishing. The urban schools were located in the capital, Accra, in the suburbs of Madina and Achimota. Generally, activities in the urban area are more diverse and reported occupations vary from vocations like dressmaking and hairdressing, through teaching, to highly specialized jobs such as lawyers and medical doctors. Participation rates were not different between urban and rural areas (36.4% and 34.7%, respectively).

Skin prick test

Skin test reactivity to allergens was tested using the standard protocol [26]. Allergens included a commercial preparation of peanut (Alk-Abelló, Madrid, Spain), as well as fresh apple, banana, mango, orange, pawpaw, and pineapple from the local market for prick-to-prick testing [26]. These foods were selected based on availability and because they required no preparation before consumption. The allergen milk was not included since it is expensive in Ghana and only constitutes a small component of the Ghanaian diet. Soy is mostly used in infant-weaning foods which did not fall into our age range, while shellfish is also eaten in small quantities. Histamine chloride (10 mg/ml) was used as the positive control and the allergen diluent as the negative control (both controls from Alk-Abelló, Madrid, Spain). Skin prick tests were conducted on the volar side of the lower arm (avoiding the flexural and wrist areas) of the subjects using 1 mm standardized lancets. A skin reaction was considered positive when the average of the longest wheal diameter (D1) and its perpendicular length (D2) was ≥3 mm [27] for the test allergen and histamine and that to the negative control was <3 mm. Atopy was defined as a positive reaction to any of the food allergens tested.

Definition of cases and controls

Cases were defined as subjects who were SPT positive to any of the tested foods. Subjects who showed a negative response to the histamine-positive control (average wheal diameter <3 mm) were excluded. Each case was matched with at least one control of the same sex and age (± one year) from the same school. Controls were negative to all food allergens tested, with a diameter of 0 mm (complete absence of a wheal). Of the 71 atopic subjects in the cross-sectional population, 43 could be matched for age, sex, and school with at least one control based on the availability of blood samples for

IgE determination. Thirty-eight cases were successfully matched with 2 controls each, 4 cases were matched with single controls, and 1 case with 4 controls.

Questionnaire

We administered a questionnaire based on the International Study of Asthma and Allergies in Childhood (www.isaac.auckland.ac.nz) Phase II module (see thesis appendix) to the parents or guardians of the subjects to gather the demographic and socioeconomic characteristics of our study population, establish the risk factors associated with the development of various allergic orders, and investigate the reported symptoms of these allergic disorders. The questionnaire also included questions from the EuroPrevall study on the symptoms of adverse reactions to food (www.europrevall.org). The questionnaire was administered to the study participants by trained interviewers that were fluent in the local language of the participants. It included questions on early-life factors like breastfeeding duration, premature birth, birth weight, and day care attendance in the first 2 years of life, as well as daily and weekly food consumption patterns, observed adverse reactions to foods, and the amount of money spent monthly on food.

Food allergen sIgE

Food allergen sIgE antibodies against apple, banana, mango, orange, pawpaw, peanut, and pineapple were determined using ImmunoCAP™ (Phadia AB, Uppsala, Sweden) on serum samples from cases and controls. Antibody levels ≥0.35 kU/L were considered positive for allergic sensitization. In cases with multiple positive skin test reactions, sIgE for the different foods eliciting the responses was expressed as the total mean IgE per subject for comparison with cases with a single SPT response.

Parasitological examinations

Each subject provided one stool sample for the determination of the presence of intestinal helminth eggs using the Kato-Katz technique [28] with 25 mg of stool. The urine filtration method [29] was employed on single 10 ml urine samples from each subject to detect *Schistosoma haematobium* (urinary schistosomiasis) eggs. Urine samples were filtered using a nylon nucleopore filter (pore size 12 μm) in a swin-lok filtration device (Nucleopore, USA), and specimen slides were read by microscopy.

Statistical analysis

All data was entered into a Microsoft Access 2003 database. Analyses were performed using SPSS version 14.0 software while graphs were generated with Excel 2003 and GraphPad Prism version 5. The descriptive data are presented as frequencies, percentages, medians, and ranges. To test for significant associations between the measured variables and being a case, conditional logistic regression was performed using the Cox regression analysis option in SPSS. To ensure that the results of the adjusted conditional logistic regression were not erroneous due to collinearity, we checked the correlation between the covariates and put them in the model only if the coefficient of correlation was less than 80% and if the measures of tolerance and the variance inflation factor did not indicate collinearity. We displayed the relative risk estimate as odds ratios (ORs) with 95% confidence intervals. Nonparametric tests were used to explore differences in sIgE levels among cases and controls because IgE data were not normally distributed.

Results

Prevalence of food allergy in the cross-sectional survey

The total number of participants with parental consent was 1714. The prevalence of reported adverse reactions assessed by the questionnaire in 1407 subjects was 11.0% in the total sample, 13.2% (of 897) in rural children, and significantly lower in urban children, i.e. 7.6% (of 510); $p = 0.004$. However, reported reactions to pineapple and kontomire (cocoyam leaves) opposed this general trend and were significantly higher in urban children ($p < 0.01$). The relevant food items to which adverse reactions were reported are given in Figure 1a. The nature of the adverse reactions is summarized in Figure 1b, with diarrhoea and vomiting being the most frequent symptoms of adverse reactions in general. While symptoms involving tingling or swelling of the mouth, lips, and throat were significantly more frequent in urban subjects, all other symptoms reported were more frequent in rural subjects.

Skin reactivity to the 7 food allergens is presented in Table 1 as specific prevalence per food allergen and as overall sensitization to food. The specific foods which elicited the highest frequencies of skin reactivity were peanut (2.0%) and pineapple (2.0%). Banana and apple elicited very few positive reactions (0.4 and 0.3%, respectively) as shown in Table 1. A total of 71 subjects showed a positive skin reaction to any food allergen; 52 (73.2%) of these subjects were sensitized to single foods only. Among rural children, 4.4% had a positive SPT reaction to a food allergen compared to a prevalence of 5.9% among urban children. Furthermore, the proportion with multiple SPT positive results was 1.1% and 1.7% in rural and urban children, respectively, and the differences between rural and urban subjects were not statistically significant.

Pineapple and peanut ranked second and third (after beans) as foods to which adverse reactions were reported, and they induced the most positive SPT of all foods tested. A positive SPT response to any of the foods tested was positively associated with having a reported adverse response to any food (adjusted OR = 2.0, 95% CI 1.0–3.9) but this association was significant only in the urban subjects (adjusted OR = 3.6, 95% CI 1.2–10.8) (Table 2). For the specific food items, 4 out of 25 urban children (16.0%) with a positive SPT response to food had an adverse reaction to the specific food item, whereas this was only true for 2.9% in the rural children (1 out of 34). This difference, however, was not statistically significant.

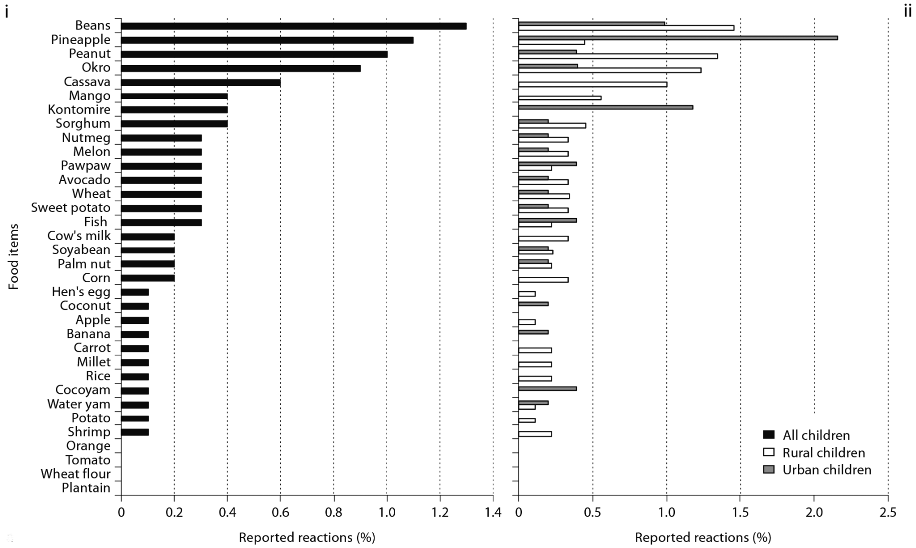

Figure 1a: Cross-sectional prevalence of reported adverse food reactions

Cross-sectional prevalence of reported adverse food reactions (n = 1407) to specific foods in all children (i) and in urban compared to rural subjects (ii). Significant urban versus rural differences were observed for pineapple and kontomire ($p < 0.01$) as well as for cassava ($p < 0.05$).

For peanut, the urban versus rural difference was borderline ($p < 0.10$).

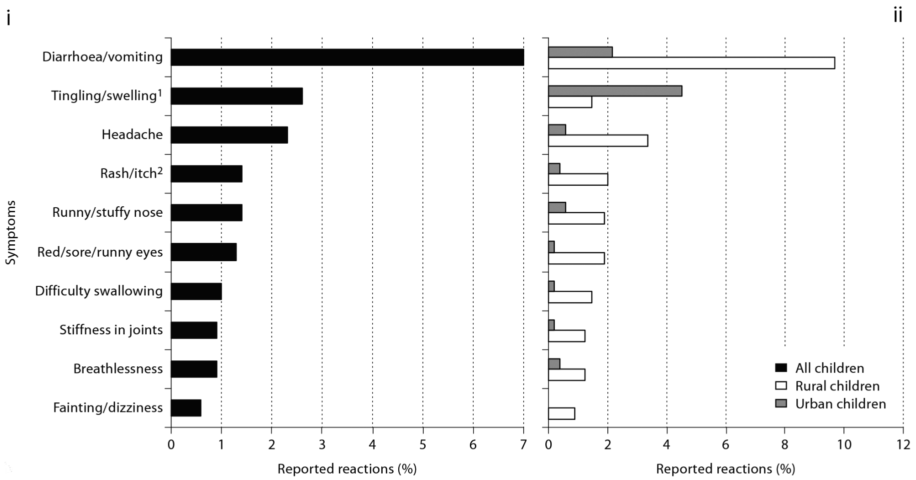

Figure 1b: Cross-sectional prevalence of symptoms of reported adverse food reactions

Cross-sectional prevalence of symptoms of reported adverse food reactions in all children (i) and in urban compared to rural subjects (ii).

[1] Tingling/swelling = swelling of the mouth, lips or throat

[2] Rash/itch = itching of the skin including nettle sting-like rash

Significant urban-rural differences were observed for diarrhoea/vomiting ($p < 0.001$), tingling/swelling, headache and red/sore/runny eyes ($p < 0.01$) as well as for rash/itch and difficulty swallowing ($p < 0.05$).

Table 1: Cross-sectional prevalence of food allergy by SPT

Food	Rural (n=906)	Urban (n=525)	Total (n=1431)
Peanut	18 (2.0)	11 (2.1)	29 (2.0)
Pineapple	16 (1.8)	12 (2.3)	28 (2.0)
Pawpaw	7 (0.8)	8 (1.5)	15 (1.0)
Orange	8 (0.9)	6 (1.1)	14 (1.0)
Mango	4 (0.4)	7 (1.3)	11 (0.8)
Banana*	1 (0.1)	5 (1.0)	6 (0.4)
Apple	2 (0.2)	2 (0.4)	4 (0.3)
Multiple foods	10 (1.1)	9 (1.7)	19 (1.3)
Any food	40 (4.4)	31 (5.9)	71 (5.0)

* P-value < 0.05 for the difference in prevalence between urban and rural subjects. Values are presented as n (%).

Table 2: Associations between SPT and reported adverse reactions to foods in a cross-sectional survey.

		Adverse reactions N (%)		
Area (N)	Any food SPT	No	Yes	Adjusted OR (95% CI)
Rural (813)	-	679 (96.0)	100 (94.3)	1
	+	28 (4.0)	6 (5.7)	1.5 (0.6 to 3.9)
Urban (409)	-	356 (94.7)	28 (84.8)	1
	+	20 (5.3)	5 (15.2)	**3.6 (1.2 to 10.8)**
Total (1222)	-	1035 (95.6)	128 (92.1)	1
	+	48 (4.4)	11 (7.9)	2.0 (1.0 to 3.9)*

Adjusted odd ratios are corrected for age, sex and school. ORs with p <0.05 are in bold and *p <0.10.

Table 3 shows the daily consumption of the foods that were tested in the SPT for the urban and rural children, separately. Consumption of orange, peanut, and banana was the most prevalent among all children (above 25%). With the exception of apple, all the other tested foods were more widely eaten among rural children than among urban children.

Measures of atopy in cases and controls

We looked for at least 1 matched control subject for each case, based on age, sex, school, and the presence of data for sIgE. This resulted in 43 cases and 84 controls. In Figure 2, we show that sIgE antibody levels were generally higher in cases than in controls. Moreover, while cases had up to 100% IgE sensitization (orange), the maximum proportion of sensitized subjects observed in controls was 25% (orange and banana). Apple was an exception, with none of the cases being sensitized. Generally, 72% of cases

Table 3: Daily consumption of the 7 foods items in the SPT

Food	Rural N (%)	Urban N (%)	Total N (%)
Orange	511 (57.3)	257 (50.7)	768 (54.9)
	892	507	1399
Pawpaw	130 (14.6)	30 (6.0)	160 (11.5)
	893	497	1390
Mango	297 (33.3)	82 (16.5)	379 (27.3)
	892	498	1390
Peanut	413 (46.3)	62 (12.2)	475 (34.0)
	892	507	1399
Apple	13 (1.5)	34 (6.7)	47 (3.4)
	894	505	1399
Banana	318 (35.6)	119 (23.5)	437 (31.2)
	894	506	1400
Pineapple	149 (16.7)	49 (9.8)	198 (14.2)
	894	500	1394

Daily consumption refers to consumption on 'most days'.
Values are presented as n (%) and total count.

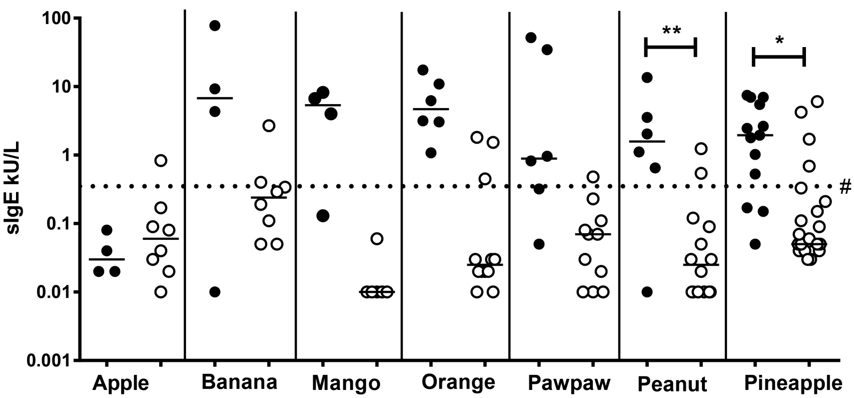

Figure 2: Median food specific IgE antibody levels in cases and controls
Median food specific IgE antibody levels in cases and controls per food item. Cases (closed symbols) had higher specific IgE levels than did matched controls (open symbols). * $p < 0.01$ and ** $p < 0.05$ by $\chi 2$ analysis. # 0.35 kU/L cut-off for IgE sensitization.

had positive sIgE responses to the specific food they reacted to in the SPT, compared to 16% of controls. This is reflected in an increased overall risk of having a positive SPT with an OR of 2.3 (95% CI 1.3–4.1) per unit increase (kU/L) in an sIgE level (OR adjusted for age, histamine wheal size, and skin reactivity to the aeroallergens cockroach and mite).

In Table 4 we show that cases who had multiple positive SPT responses (multi-atopics) had significantly higher median levels of food sIgE when compared with cases with single responses (p = 0.012, Mann-Whitney U test). All multi-atopics were sIgE-sensitized above the 0.35 kU/L cut-off to at least 1 of the relevant food items, compared to the single atopic cases with 61.3% sIgE sensitization ($p \leq 0.02$, χ^2 test). The single atopic cases without sIgE sensitization were not different in age, gender, wheal size per allergen, rural or urban location, or helminth infection compared to those with elevated sIgE levels.

Examining the possible differences between urban and rural children, we observed that controls from rural schools had a higher proportion of sIgE sensitization (24%) compared to controls from urban schools (8.5%), and they had significantly higher median levels of sIgE (Table 4). As a result, the odds of being a case predicted by the level of sIgE was much greater in the urban subjects (crude OR = 16.9, 95% CI 1.4–167.7) compared to rural subjects (crude OR = 3.4, 95% CI 1.0–11.0). Since helminth infections are associated with high IgE levels, we evaluated whether the higher levels of sIgE in the rural children were due to current helminth infections. However, the difference in sIgE levels between urban and rural children could not be explained by the presence of detectable helminth infections mainly in the rural children.

Regarding adverse food reactions, cases reported a higher prevalence (20%) compared to controls (9%), though this did not reach statistical significance in the matched analysis. The frequency of adverse reactions varied from a one-time event

Table 4: Specific IgE sensitization ≥0.35kU/L in controls and cases

		N	sIgE ≥0.35kU/L n (%)	Median sIgE kU/L and (range)	P-value: χ2 test[1]	P-value: #MWU/ KW Test[2]
Positive SPT	Controls (none)	84	13 (15.5)	0.05 (0 - 6.03)		
	Cases with:					
	At least one	43	31 (72.1)	2.04 (0.01 - 66.45)		
	Single	31	19 (61.3)	1.11 (0.01 - 52.00)	0.02	0.012
	Multiple	12	12 (100)	6.38 (0.56 - 66.45)		
Rural/Urban Category	Controls in:					
	urban areas	47	4 (8.5)	0.03 (0-2.69)	0.07	0.002
	rural areas	37	9 (24.3)	0.09 (0.01- 6.03)		
	Cases in:					
	urban areas	24	18 (75)	1.87 (0.01 - 66.45)	0.63	0.74
	rural areas	19	13 (68.4)	2.48 (0.01 - 30.05)		

[1]χ^2 test for proportion of sIgE sensitization;
[2]Mann-Whitney U / Kruskal-Wallis tests for IgE levels between single and multiple SPT cases as well as between urban and rural subjects in cases and controls.

to a frequency of over 4 times. The 3 subjects with frequencies over 4 times were all cases (8.6% of 35), compared to none of the 67 controls.

It is difficult to assess the prevalence of a positive SPT in the subjects with a claimed adverse response since we only tested 7 potential food allergens in the SPT. However, if we only consider the subjects with an adverse reaction to any of the food items that were tested in SPT, there were 11 out of 153 subjects (7.2%) with a positive SPT.

Very few children with a positive IgE response also presented adverse symptoms related to the specific food item. Only 3 out of 102 children for which both IgE and questionnaire data were available had adverse symptoms to the food to which they had a positive IgE titre (1 for pawpaw and 2 for pineapple).

Lifestyle Factors and SPT Reactivity to Food Allergens

Table 5 shows the effect of questionnaire-derived food consumption variables on the outcome of being a case. Although reported daily eating patterns were similar between cases and controls for most foods, we saw a significantly higher proportion of daily consumption of ice cream or yoghurt among cases (crude OR 4.2, 95% CI 1.1–15.6, p = 0.04). The same tendency was observed for daily rice consumption, though this did not reach statistical significance. The daily consumption of palm oil, on the other hand, was significantly lower among cases (crude OR 0.3, 95% CI 0.1–0.9, p = 0.04). None of the questionnaire-derived variables was independently associated with being a case after mutual adjustment.

The following reported early-life factors were not associated with being a case: premature birth, duration of exclusive breastfeeding, crèche or nursery attendance in the first 2 years of life, or the family's monthly expenditure on food. Body mass index (a surrogate for nutritional status) and current parasitic infections with malaria or helminths (hookworm, *Ascaris lumbricoides*, *Trichuris trichiura* or *S. haematobium*) were not associated with being a case. These results are shown in online supplementary Table S1.

Table 5: Associations between daily food habits and positive SPT for food.

Eating habit factors	N=89	Controls N=56	Cases N= 33	Crude OR (95% CI)	Adjusted OR (95% CI)
Daily consumption of dairy[1]	-	49 (87.5%)	24 (72.7%)	1.0	1.0
	+	7 (12.5%)	9 (27.3)	**4.2 (1.1 to 15.6)**	3.8 (0.9 to 16.3)*
Daily consumption of rice	-	28 (50%)	10 (30.2%)	1.0	1.0
	+	28 (50%)	23 (69.7%)	2.5 (0.9 to 6.5)	1.8 (0.6 to 5.1)
Daily consumption of palm oil	-	30 (53.6%)	26 (78.8%)	1.0	1.0
	+	26 (46.4%)	7 (21.1%)	0.3 (0.1 to 0.9)	0.3 (0.1 to 1.0)*

The adjusted odd ratios are corrected for age and all other variables,
ORs with $p < 0.05$ are in bold and *$p < 0.10$
[1]Dairy refers specifically to ice cream or yoghurt.

Discussion

We assessed, for the first time in West Africa, the prevalence of allergic sensitization to local food allergens in children and how this relates to reported adverse reactions to foods in a school-based study. In contrast to the difference in prevalence between urban (with a higher prevalence of mite SPT in children from private schools) and rural (with a higher prevalence of cockroach SPT) children that we observed in this population (Obeng *et al.*, manuscript in preparation), the prevalence of a positive SPT for food allergens was similar in urban and in rural children. Although we observed an overall tendency of an association between reported adverse reactions and SPT, this was significant only in urban children, and when specific food items were considered the association disappeared; this was probably due to lower statistical power. However, we have shown that there was a good agreement between the SPT and IgE antibody levels to specific foods in Ghanaian children, with a very strong association in urban children.

The overall prevalence of 5% skin test reactivity to any food in our population and between 0.3% and 2% for the specific food allergens is similar to and in some instances higher than reports from studies in other parts of the world [30]. The prevalence of reported adverse symptoms to peanut that we observed (1.5%) was a bit lower than that reported for children of similar age groups in the UK (1.9% for 6-year-old children, 1.8% for 11-year-old children, and 2.5% for 15-year-old children). Similarly, the percentage of children with a positive skin test for peanut was slightly lower in our study population (2.0%) compared to children in the UK (2.6–3.7%) [16, 31]. The prick-to-prick method allowed the testing of local foods, which would otherwise have been impossible with commercial extracts due to the poor sensitivity of such preparations. The panel of food allergens tested was selected from the local market and, with the exception of apple, they all form part of the regular Ghanaian diet. Our panel was limited to fresh fruits, aside from the commercial peanut extract, because they were readily available and did not require any previous preparation or cooking before consumption. Thus, it was easy to test the allergens in the same state as they are eaten. The strength of our study lies in its matched case-control design adjusting for demographic and environmental covariates which could be associated with atopy.

Even though in this study the panel of allergens included only 1 of the 8 major food allergens internationally recognized (peanut), it showed that other local foods may be of equal importance given the similar prevalence of sensitization to pineapple and peanut that we have found in this study. Dias *et al*. [25] found an increased prevalence of allergy to novel foods (i.e., foods which are not regularly used in food allergy test panels) like kiwi, legumes, and sesame, and they proposed that these may cause allergy mostly in the non-Caucasian population of the UK. Comparing skin test reactivity with IgE levels further demonstrated the importance of pineapple as an allergen as it showed the strongest association with sIgE antibody levels among cases stratified by specific food. None of the cases with a positive SPT to apple had elevated IgE levels. This is interesting because it reflects other findings that have described differences between specific foods in the predictive value of food sIgE antibody levels for allergy [19]. It may also be due to the fact that apples are relatively new and less important in the diet of this population. It is also possible that sensitization to apple is due to cross-reactivity with another allergen either from a local pollen or from another food. It is not unlikely that this putative cross-reactive allergen is presented in the SPT but not in the CAP assay.

We also observed that the proportion of helminth infections was similar between cases and controls. This is important given that helminth infections are associated with an expansion of B cells producing IgE. Studies on atopy in Gabon have shown high mite sIgE levels in helminth-infected subjects who did not show skin reactivity to mites [32]. In our study, we observed among controls that helminth infection was associated with increased IgE levels to the tested foods. Also, controls from rural schools had significantly higher median sIgE levels than did controls from urban schools, an observation which could be explained by the prevalence of helminth infections in the rural schools. Limiting our analyses to rural subjects did not show current infection to be significantly associated with IgE levels in controls, suggesting that the general observation of higher IgE in rural controls could be due to a history of helminth infection.

Cross-reactivities between inhalant allergens and the plant food allergens used in our study have been reported to involve the protein profilin, a pan-allergen ubiquitously expressed in eukaryotic cells [33, 34]. In a recent study by Asero *et al*. [35], pollen-allergic patients who had a positive skin test reaction to date palm profilin were all sensitized to grass, and half of them had food allergy with oral symptoms. The offending foods included pineapple, citrus fruit, and banana. Similar results were reported earlier by Reindl *et al*. [36], when IgE reactivity to profilin was associated with adverse reactions to pineapple and banana. Previous data from Ghanaian schoolchildren showed a low prevalence, i.e. 0.3%, for grass pollen allergy (unpublished data). However, extracts from local flora would have to be included to be able to test the cross-reactivity to plants and/or trees prevalent in this region. Thus, our results with a prevalence of 5% could reflect sensitization specific to these tested plant foods and possibly independent of profilin or profilin sensitization via another local allergen.

Our results showed a higher proportion of multi-atopic cases with IgE sensitization to the specific foods eliciting skin reactivity than in cases atopic to single foods. Future studies could focus on the multi-atopic subjects to determine if being sensitive to some principal or ubiquitous allergen results in reactions to multiple food allergens. This would not only be useful in the management of food allergies resulting in symptoms, but would also prevent unnecessary dietary restrictions. It is also possible that a general allergic susceptibility could cause one to develop sensitization to a series of important inhalant and food allergens, which might be supported by our observation of a positive association between histamine wheal size (data not shown) and having a positive skin reaction to food allergens or aeroallergens; this finding has been previously reported by Van Gysel *et al*. [37] and de Bilderling *et al*. [38].

We also showed that the patterns of consumption of food were generally similar in cases and controls. However, the daily use of palm oil was significantly higher in controls while the daily consumption of ice cream, reflecting a less traditional but more contemporary diet as well as a higher SES, was higher in cases. Palm oil use may be associated with more traditional cooking which could prevent atopy. Though food consumption could be influenced by socioeconomic differences, the amount of money spent by the family monthly (a surrogate SES variable) or body mass index were not associated with being a case. In a recent study in schoolchildren in South Africa, an urban diet was associated with a positive SPT to aeroallergens, but there were no data on SPT to food [39].

We found a positive association between reported adverse reactions and skin test reactivity in the urban children, but only 20% of the subjects matched for the specific food item. It is known that reported food allergy reactions are not always reliable as indicators for food allergy and, indeed, reports from previous studies have indicated discrepancies between the reported perceived symptoms of food allergy and the results of clinical testing [EuroPrevall centres, van Ree, personal communication [7, 16]. The reported adverse reactions could indeed include intolerances and dislikes but, on the whole, they included food items internationally recognized as problematic common food allergens like egg, fish, and peanut. Notably, the reported symptom of tingling/itching of the mouth and/or lips, a reaction expected to be indicative of food allergy, was more frequently found in subjects with a food sensitization (positive SPT), although numbers were quite low (8.5% in SPT positive subjects vs. 2.3% in SPT negative subjects). Particularly interesting was the fact that avoidance of offending foods by subjects reporting an adverse reaction was indicated by 50% of the subjects, both in cases and in controls. The reason for this may be the absence of severe reactions to the foods. Reported adverse reactions were mainly gastrointestinal and respiratory in nature. While early-life factors like breastfeeding duration and birth weight are reported to be related to the development of allergy [40], we found no such association in this study; this could be due to small numbers.

This study provides timely information on the type and prevalence of sensitization to plant food allergens, the reported perceived symptoms of food allergy, and the relationship of these conditions with other lifestyle factors generally reported to be associated with allergy. Our results show that IgE-mediated food atopy is important in Ghana, potentially to a similar extent as in Europe and America. We also showed that in addition to peanut, a recognized major food allergen, pineapple is an important local allergen which merits further study in Ghanaian and foreign populations. Our study also shows that, similar to previous studies, perceived adverse reactions are not always reflected in SPT results and IgE antibody titres. These findings highlight the importance of further research into food allergy in Ghana and Africa as a whole. It will be useful in the future to look at the prevalence of the major food allergens documented in the US and Europe for a comparison with the local allergens. Such studies could also analyze the role of cross-reactivity and employ a more stringent gold standard of diagnosis like the DBPCFC to allow the determination of true clinical food allergy.

Acknowledgements

Our thanks go to Dr. Paul van Rijn (HAL Allergy B.V., The Netherlands) and to Dr. Domingo Barber (Alk-Abelló, Spain) for providing the SPT material. We also thank Dr. Montserrat Fernández-Rivas for her advice regarding the allergens and SPT. The authors wish to acknowledge Professor Michael D. Wilson, Professor Kwabena M. Bosompem, and the technicians of the department of Parasitology of the Noguchi Memorial Institute for Medical Research (NMIMR) for their assistance with the fieldwork and parasitological diagnosis. We are also indebted to the community leaders and head teachers of all the schools involved in this study for their invaluable assistance. This study was funded by WOTRO grant WB 93-443, the GLOFAL project (FOOD-CT-2005-517812), and the EUROPREVALL project (FOOD-CT-2005-514000).

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Supplementary Material

Table S1: Associations between Lifestyle factors and positive SPT for food

Factors		Controls	Cases	Crude OR (95% CI)	Adjusted OR (95% CI)
Premature birth	-	57 (98.3%)	32 (94.1%)	1.0	1.0
	+	1 (1.7%)	2 (5.9%)	3.6 (0.3 to 40.8)	2.4 (0.1 to 71.6)
Exclusive breastfeeding for at least 3 months	-	25 (39.1%)	10 (29.4%)	1.0	1.0
	+	39 (61.9%)	24 (70.6%)	1.5 (0.6 to 3.8)	1.7 (0.4 to 6.5)
Day care attendance during first 2 years of life	-	47 (77.0%)	22 (62.9%)	1.0	1.0
	+	14 (23.0%)	13 (37.1%)	2.0 (0.8 to 4.9)	1.6 (0.4 to 1.0)
Expenditure on food per month (above median)	-	27 (28.2%)	17 (53.1%)	1.0	1.0
	+	29 (51.8%)	15 (46.9%)	0.8 (0.3 to 2.0)	0.5 (0.2 to 1.8)
Any helminth infection #	-	55 (76.4%)	27 (77.1%)	1.0	1.0
	+	17 (23.6%)	8 (22.9%)	1.0 (0.4 to 2.5)	0.9 (0.2 to 3.5)
Malaria infection	-	66 (79.5%)	33 (78.6%)	1.0	1.0
	+	17 (20.5%)	9 (21.4%)	1.1 (0.4 to 2.6)	0.8 (0.2 to 3.5)
BMI below normal $	-	64 (77.1%)	35 (81.4%)	1.0	1.0
	+	19 (22.9%)	8 (18.6%)	0.8 (0.3 to 1.9)	0.3 (0.1 to 1.9)

The adjusted odd ratios are corrected for age and all other variables.
Infection with any of the helminths: *S. haematobium*, *A. lumbricoides, T. trichiura* or hookworm.
$ Weight categories are as described in Hogewoning AA *et al. British Journal of Dermatology.* 2009; 161 (2): 475-7.
Odds ratios with $p < 0.05$ are in bold.


NET WEIGHT 50 KGS
ORIGIN : THAILAND
PROD. OCTOBER 2011
EXP. OCTOBER 2013