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PATTERNS OF SENSITIZATION TO FOOD AND INHALANT ALLERGENS AMONGST CHILDREN IN KENYA
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PATTERNS OF SENSITIZATION TO FOOD AND INHALANT ALLERGENS AMONGST CHILDREN IN KENYA

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ABSTRACT

Background: **Allergic disease is preceded by development of a sensitized state against allergens, characterized by production of allergen-specific immunoglobulin (sIgE) in serum.**
Objectives: **To determine the frequency and patterns of sensitivity to food and inhalant allergens among children.**
Methods**: A retrospective study conducted at Gertrudes Children's Hospital in Nairobi, Kenya. Laboratory data for sIgE antibodies for the period between January 2014 and December 2017 were retrieved and analysed. Serum sIgE ≥0.35 kU/L indicated sensitization. Descriptive statistics were used to summarize continuous data as median (interquartile range), and categorical data as absolute and relative (%) numbers.**
Results**: 642 sIgE test results were retrieved; 509 (79.3%) against food allergens and 133 (20.7%) against inhalant allergens. Median age of patients evaluated for food allergen sensitization was 3.0 (1 – 6) years; approximately half (50.7%) were males. 242 children (47.5%) were sensitized to at least one food allergen. The most frequently sensitizing foods were milk (17.5%), wheat flour (14.7%) and potato (12.6%). Median age of patients evaluated for inhalant allergen sensitization was 4.0 (2 – 8) years, with a slight preponderance of males (51.1%). 64 children (48.1%) were sensitized to at least one aeroallergen. The most frequently sensitizing aeroallergens were *Dermatophagoides pteronyssinus* (30.8%), *Dermatophagoides pteronyssinus* (24.8%) and grass pollen (12.8%).**
Conclusions: **Milk, wheat, potato, house dust mites and grass pollen were the most common food and aeroallergens encountered among children at a private children's hospital in Kenya. Further studies are needed to clarify the relationship between serum sIgE levels and clinical manifestations of allergic disease locally.**

INTRODUCTION

The prevalence of allergies among children is increasing worldwide. Allergic sensitization is a requirement for the development of allergic disease and is characterized by the production of specific IgE (sIgE) against allergens, that is detectable in serum[1]. The initial assessment of patients with suspected allergic disease includes a detailed clinical history and physical examination, which guide subsequent investigations. The identification of specific allergic triggers is then performed through *in vivo* tests such as skin prick testing (SPT) or laboratory-based *in vitro* assays[2,3]. These tests identify a sensitized state by measuring allergen specific IgE, and the information obtained is used, in the context of the patient's clinical manifestations, to guide allergy treatment by identification of the triggering allergens so that they may be avoided or eliminated.

Laboratory-based *in vitro* allergen-specific IgE is a widely available and commonly requested test that is perfomed on serum, and the results are quantified in units (IU/mL) to reflect the concentrations of sIgE. This quantitative reporting allows for better prediction of the likelihood of clinical reaction following exposure to that particular allergen in a specific individual[4]. Advantages of the allergen sIgE serology tests over SPTs include the lack of interference from antihistamines and wide availability; while the disadvantages include delayed results, high cost and the need to obtain a blood sample. Comparative studies have shown that serum sIgE tests and SPT have relatively similar diagnostic properties, and both have good sensitivity for detection of allergic sensitization[3,4].

Local data on patterns of allergy sensitization in children is not readily available. The aim of this study was to determine the patterns of sensitization to food and inhalant allergens among children seen at a private hospital in Kenya. Specifically, we aimed to determine the proportion of sensitized children among those tested for allergen specific IgE, and to determine the most frequent food and inhalant allergens leading to sensitization.

METHODS

Retrospective data on allergen-specific IgE testing among children aged 0-13 years between 1 January 2014 and 31st December 2017 at Gertrudes Children's Hospital (GCH) was collected anonymously from the laboratory database. GCH is the largest exclusively paediatric hospital in east and central Africa. It is a private facility that mainly serves the urban Nairobi population. Specific IgE in serum (RIDA qLine® Allergy kit) is the most commonly used test to evaluate allergy sensitization in children at GCH. The test kit consists of two separate panels, a food panel comprising 23 food allergen extracts and an aeroallergen panel comprising 20 inhalant allergen extracts. Allergen specific IgE was reported as a value between 0.1 and 100 kU/L, with allergen sensitization defined as the presence of allergen sIgE >0.35 kU/L. Results are graded according to the radioallergosorbent (RAST) classes 0-6 that allow for prediction of risk of developing allergic symptoms after exposure to an allergen. These classes correspond to serum levels of sIgE. The study was approved by the GCH Ethics and Scientific Review Committee.

Descriptive statistics were used to summarize, and present continuous data as median (interquartile range) and categorical data as absolute and relative (%) numbers. Chi-square test or, when appropriate, Fischer's exact test were used to compare differences between groups. For all analyses, p values of <0.05 were considered statistically significant.

RESULTS

A total of 642 laboratory results of serum samples tested for sIgE between January 2014 and December 2017 were retrieved and analysed. Of these, 509 (79.3%) sera were tested against food allergens, while 133 (20.7%) were tested against inhalant allergens. Clinical data on allergic manifestations or allergic disease was available for only 8.8% (n = 45) and 18% (n = 24) of those tested for sensitivity to food and inhalant allergens respectively.

The baseline characteristics of the 509 children evaluated for food allergen sensitization are shown in Table 1. Majority of the children were aged between 1 and 6 years, and approximately half were males. The male children were slightly younger than females, with a mean age of 3.8 $\pm$ 3.3 years, and median (IQR) of 3.0 (1, 5) years compared to a mean of 4.5 $\pm$ 3.9 years, and median (IQR) of 3.0 (1, 7) years among females; (p = 0.05).

Table 1

Baseline characteristics of children tested for food allergen sensitization

Characteristics	***n* = 509, (%)**
Age, years	
Median (IQR)	3.0 (1, 6)
Sex	
Male	258 (50.7)
Female	251 (49.3)
Overall sensitized (sIgE positive)	242 (47.5)
Monosensitized (1food allergen)	79 (32.6)
Polysensitized (>1 food allergen)	163 (67.4)

Overall, 242 children (47.5%) were sensitized to at least one food allergen. Of the sensitized children, majority had sIgE to more than one food allergen. Most of the sensitized children were younger than 3 years old (Table 2), with a decrease in sensitization rates with increasing age.

Table 2

Food allergen sensitization rates according to age

Age group, years	***n* = 242, (%)**
0 – 3	126 (52.1)
4 – 9	86 (35.5)
10 – 13	30 (12.4)

The most frequently sensitizing foods were milk (17.5%), wheat flour (14.7%), potato (12.6%), peanut (12%), hazelnut (11.4%), egg white (10.4%), casein (10.2%) and sesame seed (10%). The least sensitizing foods were the poultry meat mix (0%), gluten (2.7%), meat mix (3.6%), carrot and soya bean (5.3% each) and almond (5.9%). Table 3 shows the frequencies of sensitization to individual food allergens.

Table 3

Sensitization rates against individual food allergens

Food allergens		**sIgE positive** ***n*** **= 509, (%)**
F17	Hazelnut	58 (11.4)
F13	Peanut	61 (12.0)
F20	Almond	30 (5.9)
F2	Milk	89 (17.5)
F1	Egg white	53 (10.4)
F75	Egg yolk	33 (6.5)
F78	Casein	52 (10.2)
F79	Gluten	3 (2.7)
F31	Carrot	27 (5.3)
F25	Tomato	48 (9.4)
F3	Cod	31 (6.1)
F23	Crab	44 (8.6)
F33	Orange	44 (8.6)
F49	Apple	36 (7.1)
F4	Wheat flour	75 (14.7)
F5	Rye meal	45 (8.8)
F10	Sesame seed	51 (10.7)
F14	Soya bean	28 (5.3)
FX25	Poultry meat mix	0 (0.0)
FX26	Meat mix	4 (3.6)
F16	Walnut	36 (9.1)
F35	Potato	50 (12.6)
F85	Celery	38 (9.6)

The baseline characteristics of the 133 children evaluated for inhalant allergen sensitization are listed in Table 4. Majority of the children were aged between 2 – 8 years, and males were slightly more than females. The males were significantly younger than females, with a mean age of 4.2 $\pm$ 3.3 years, and median (IQR) of 3.0 (2, 6.3) years compared to a mean of 5.5 $\pm$ 4.0 years, and median (IQR) of 5.0 (2, 8) years among females; (p = 0.04).

Table 4

Baseline characteristics of children tested for inhalant allergen sensitization

Characteristics	***n*** **= 133, (%)**
Age, years	
Median (IQR)	4.0 (2, 8)
Sex	
Male	68 (51.1)
Female	65 (48.9)
Overall sensitized (sIgE positive)	64 (48.1)
Monosensitized (1aeroallergen)	16 (25)
Polysensitized (> 1 aeroallergen)	48 (75)

Overall, 64 children (48.1%) were sensitized to at least one inhalant allergen. Of the sensitized children, majority had sIgE to more than one inhalant allergen. Most of the sensitized children were aged between 4 and 9 years old, as shown in Table 5.

Table 5

Inhalant allergen sensitization rates according to age

Age group, years	***n* = 64, (%)**
0 – 3	24 (37.5)
4 – 9	27 (42.2)
10 – 13	13 (20.3)

The most frequent inhalant allergens were *Dermatophagoides pteronyssinus* (30.8%), *Dermatophagoides farinae* (24.8%), grass pollen (12.8%), plantain (11.3%) and *Penicillum notatum* (10.5%). The least sensitizing inhalant allergens were rabbit (3.8%), cat, horse, hamster and *Alternaria alternata* (4.5% each). Table 6 shows the frequencies of sensitization to individual inhalant allergens.

Table 6

Sensitization rates against individual environmental allergens

Inhalant allergens		**sIgE positive** ***n* = 133, (%)**
D1	*Dermatophagoides pteronyssinus*	41(30.8)
D2	*Dermatophagoides farinae*	33 (24.8)
T2	Alder	11 (8.3)
T3	Birch	10 (7.5)
T4	Hazel	8 (6.0)
T7	Oak	11 (8.3)
GX	Grass pollen	17 (12.8)
G12	Rye pollen	11 (8.3)
W6	Mugwort	11 (8.3)
W9	Plantain	15 (11.3)
E1	Cat	6 (4.5)
E3	Horse	6 (4.5)
E5	Dog	10 (7.5)
E6	Guinea pig	7 (5.3)
E84	Hamster	6 (4.5)
E82	Rabbit	5 (3.8)
M1	*Penicillum notatum*	14 (10.5)
M2	Cladosporium	9 (6.8)
M3	Aspergillus fumigatus	8 (6.0)
M6	*Alternaria alternata*	6 (4.5)

DISCUSSION

This study provides local data on the spectrum of allergens and patterns of allergic sensitivity among children at an urban private hospital setting in Kenya. Five hundred and nine children were evaluated for allergen-sIgE levels against 23 food allergen extracts, while 133 were evaluated for sIgE against 20 inhalant allergens. Despite lack of documentation of allergic symptoms on the test requisitions for most of the children, it is assumed that the basis of testing was to confirm or rule out sensitization due to clinical features suggestive of allergy.

Using sIgE levels, we showed that sensitization to allergens among this selected group of children is relatively high. Sensitization to food allergens was found in 47.5% of the children, while sensitization to inhalant allergens was found in 48.1% of the children evaluated. However, high levels of sIgE to allergens does not always correlate with the presence of clinical reactivity or allergy; this 'false sensitization' may be caused by several factors, including development of tolerance towards the allergens, cross-reactivity between food and aeroallergens, and in tropical countries, the presence of concurrent helminthic or parasitic infections[5]. Interpretation of sIgE tests should therefore be performed in consideration of clinical manifestations.

A high proportion of sensitized children in our study were sensitized against more than one allergen (67.4% and 75% for food and inhalant allergens respectively). This is in keeping with other studies which show that atopic individuals are usually sensitized to many allergens simultaneously. Sensitization to multiple allergens (polysensitization) may increase the risk and severity of allergic morbidities by causing a synergistic effect in aggravation symptoms among those with clinical manifestations.

Polysensitization, as seen in this study, may also occur due to IgE cross-reactivity between different allergens that have a similar structure, giving rise to positive results that are not clinically relevant[6]. Differentiation of cross-reactivity between biologically related allergens and a true sensitization may be difficult. Some of the cross-reactivity may be due to the presence of cross-reactive carbohydrate derivatives (CCDs); these are carbohydrate epitopes present on some protein allergens, to which antibody may bind. Incorporation of a CCD-blocking agent in the assay reduces false positive results caused by anti-CCD IgE.

Newer methods of *in vitro* allergy testing help to resolve issues of cross-reactive antibodies by using allergens that have been characterized by their molecular structure; in these cases, specific epitopes are used for testing, as opposed to whole allergen extracts, to identify sensitization to species-specific allergen components; a practice known as component-resolved diagnostics (CRD). CRD can be used in polysensitized patients as a second-line test to differentiate genuine sensitizations from cross-reactivity.

Majority of the children evaluated for food allergen sensitization in our study were aged 1 to 6 years, of whom the most frequently sensitized were younger than 3 years old; while most of those evaluated for inhalant allergen sensitization were slightly older, 2 to 8 years, of whom the most frequently sensitized were in the age bracket of 4 - 9 years. These findings are in keeping with other studies which show that foods are common allergens in early childhood but are replaced by inhalant or environmental allergens as the children grow[7].

The most frequent sensitizations involved milk (17.5%), wheat (14.7%) and potato (12.6%).

Cow's milk is a common food allergen globally, and our findings mirror those reported elsewhere; 19.9% in the United States[8] with even higher rates in South Africa (27%)[9].

The rates of wheat sensitization in our study were slightly lower than those described in Iran, at 18.3%[10], but higher than South Africa at 6%[9]. Globally, the prevalence of clinically relevant wheat allergy among children is not well described, but it is estimated to be less than 1%, and most children outgrow it by 16 years of age[11]. Similar to our study, high levels of sensitization to potato have been reported in Zimbabwe (16%)[12]. Potato is a widely available and consumed food locally, and we are unaware of documented reports of severe allergic reactions in people exposed to potatoes, which implies possible tolerance or cross-reactivity of sIgE antibodies.

Peanut was a frequently sensitizing food, at 12%, closely matching other reports (13.04% in the United States)[13]; this rate is much lower than that reported in South African children (44%), although the South African study was conducted among a highly selected population of children with documented atopic dermatitis[14]. Other commonly sensitizing foods were hazelnut (11.4%), egg (10.4%), casein (10.2%) and sesame (10%). Egg allergens are frequent globally, with varying sensitization rates of 0-54%[15]; however, allergic manifestations usually resolve as the children grow older[16].

The least sensitizing foods in our study included poultry (0%), gluten (2.7%), meat (3.6%), carrot (5.3%), soya (5.3%) and almond (5.9%). Of the three children sensitized to gluten, only one had sIgE to wheat; this may be explained by cross-reactivity of IgE to wheat albumin or globulins with the glutens. Sensitization to meat animal protein among children is not well described, and other studies have reported similarly low rates of sensitization; 1.6-4% for pork, 1.4-3.3% for chicken, and 1.72-2.5% for beef meat[17]. Of note is that allergen mixes were used to screen for sensitization to chicken and beef meat. These allergen mixes have been shown to be relatively labile and insensitive compared to testing against the specific allergen. A negative test to an allergen mix in the presence of a strong history of an allergic response therefore does not exclude sensitization. Soy protein is not a common allergen in children, and our findings are comparable to those from studies conducted elsewhere, with a sensitization rate 4.1% or less[17]. Higher rates of sensitization to soya have been reported in South Africa, 9%[9].

The most frequent inhalant allergen sensitizations involved house dust mites (*Dermatophagoides pteronyssinus*, 30.8% and *Dermatophagoides farinae,* 24.8%), similar to findings from other regions. Dust mites are common indoor allergens found in beddings, carpets and upholstery. The mite, its secretions and excretions are all potential allergens that float in the air and can be inhaled to induce respiratory allergic symptoms[18]. *D. pteronyssinus* commonly occurs in humid regions and cross-reacts with *D. farinae*, that is found more commonly in drier areas. Damp conditions within the household may predispose to dust-mite infestations.

Grass and weed pollens (plantain), were the next frequently sensitizing aeroallergens, at 12.8% and 11.3% respectively. These are outdoor allergens, and the rates found in our study were much lower than those reported elsewhere, at 23 - 39.2%[19,20]. Among the moulds, the most frequently sensitizing allergen in our population was *Penicillum notatum* (10.5%). Studies from other geographic regions report *Alternaria alternatum* as the most commonly sensitizing mould, with varying rates of sensitization from 27.3 – 89%[19,21]. *Alternaria* is primarily an outdoor mould, while *Penicillum* is an indoor allergen. Indoor infestations of moulds require spaces with moisture. Our findings on sensitization to inhalant allergens suggest that indoor allergens are more frequent than outdoor allergens, in our setting.

A notable limitation to this study was the lack of clinical information for majority of the tested subjects, which does not allow us draw

conclusions on the association between sensitization and allergic symptoms.

CONCLUSION

Almost half the children sent for allergy testing had sensitization against food and aeroallergens at a private children's hospital in Kenya. Food allergy sensitization was mainly in children under the age of 3 years while aeroallergen sensitization was more common in the 4 - 9-year age group. Allergic sensitization to milk, wheat, potato, house dust mites and grass pollen were the most common food and aeroallergens encountered

This study provides preliminary data on a wide range of commonly sensitizing food and inhalant allergens among children in Kenya. Further studies should clarify the presence of allergic disease among sensitized patients in our setting, to know the truly allergic proportion of sensitized patients and the association of these allergen sources with allergic disease.

REFERENCES

1. Fiocchi A, Pecora V, Petersson CJ, Dahdah L, Borres MP, Amengual MJ, et al. Sensitization pattern to inhalant and food allergens in symptomatic children at first evaluation Allergology and Immunology. Ital J Pediatr . 2015;41(1):1–9. http://dx.doi.org/10.1186/s13052-015-0204-9

2. Sicherer SH, Wood RA. Allergy testing in childhood: using allergen-specific IgE tests. Pediatrics. 2012 Jan;129(1):193–7.

3. Williams P, Sewell WAC, Bunn C, Pumphrey R, Read G, Jolles S. Clinical immunology review series: an approach to the use of the immunology laboratory in the diagnosis of clinical allergy. Clin Exp Immunol. 2008 Jul;153(1):10–8.

4. Bernstein IL, Li JT, Bernstein DI, Hamilton R, Spector SL, Tan R, et al. Allergy diagnostic testing: an updated practice parameter. Ann Allergy Asthma Immunol. 2008 Mar;100(3 Suppl 3):S1-148.

5. Vieths S, Scheurer S, Ballmer-Weber B. Current understanding of cross-reactivity of food allergens and pollen. Ann N Y Acad Sci. 2002 May;964:47–68.

6. Schmitz R, Ellert U, Kalcklösch M, Dahm S, Thamm M. Patterns of Sensitization to Inhalant and Food Allergens – Findings from the German Health Interview and Examination Survey for Children and Adolescents. Int Arch Allergy Immunol. 2013;263–70.

7. Chiu CY, Huang YL, Tsai MH, Tu YL, Hua MC, Yao TC, et al. Sensitization to food and inhalant allergens in relation to atopic diseases in early childhood: A birth cohort study. PLoS One. 2014;9(7):3–9.

8. Warren CM, Jhaveri S, Warrier MR, Smith B, Gupta RS. The epidemiology of milk allergy in US children. Ann Allergy, Asthma Immunol. 2013 May 1;110(5):370–4. https://doi.org/10.1016/j.anai.2013.02.016

9. Gray CL, Levin ME, Zar HJ, Potter PC, Khumalo NP, Fenemore B, et al. Food allergy in South African children with atopic dermatitis. Curr Allergy Clin Immunol. 2014;25:572–9.

10. Hosseini S, Shoormasti RS, Akramian R, Movahedi M, Gharagozlou M, Foroughi N, et al. Skin Prick Test Reactivity to Common Aero and Food Allergens among Children with Allergy. Iran J Med Sci. 2014 Jan;39(1):29–35.

11. Keet CA, Matsui EC, Dhillon G, Lenehan P, Paterakis M, Wood RA. The natural history of wheat allergy. Ann Allergy Asthma Immunol. 2009 May;102(5):410–5.

12. Sibanda E. Increasing trend of sensitization to food and inhalant allergen sources in Zimbabwe. Curr Allergy Clin Immunol. 2013;26(4):214–9.

13. Kumar R, Tsai H-J, Hong X, Liu X, Wang G, Pearson C, et al. Race, Ancestry, and Development of Food-Allergen Sensitization in Early Childhood. Pediatrics. 2011 Oct 1;128(4):e821 LP-e829. http://pediatrics.aappublications.org/content/128/4/e821.abstract

14. Gray CL, Levin ME, Toit G. Ethnic differences in peanut allergy patterns in South African children with atopic dermatitis. Curr Allergy Clin Immunol. 2015;26(8):721–30.

15. Rona RJ, Keil T, Summers C, Gislason D, Zuidmeer L, Sodergren E, et al. The prevalence of food allergy: a meta-analysis. J Allergy Clin Immunol. 2007 Sep;120(3):638–46.

16. Sicherer SH, Wood RA, Vickery BP, Jones SM, Liu AH, Fleischer DM, et al. The Natural History

of Egg Allergy in an Observational Cohort. J Allergy Clin Immunol. 2014;133(2):492–9.
17. González G, Alejandra V, González G, Díaz AM, Fernández K, Rivera MF. Prevalence of food allergens sensitization and food allergies in a group of allergic Honduran children. Allergy, Asthma Clin Immunol. 2018;1–7. https://doi.org/10.1186/s13223-018-0245-x
18. Lin H, Lin R, Li N. Sensitization rates for various allergens in children with allergic rhinitis in Qingdao, China. Int J Environ Res Public Health. 2015;12(9):10984–94.
19. Ahmed H, Ospina MB, Sideri K, Vliagoftis H. Retrospective analysis of aeroallergen ' s sensitization patterns in Edmonton , Canada. Allergy, Asthma Clin Immunol. 2019;1–6. https://doi.org/10.1186/s13223-019-0320-y
20. Verini MU, Rossi N, Verrotti A, Pelaccia G, Nicodemo A, Chiarelli F. Sensitization to environmental antigens in asthmatic children from a central Italian area. Sci Total Environ. 2001;63–9.
21. Kołodziejczyk K, Bozek A. Clinical Distinctness of Allergic Rhinitis in Patients with Allergy to Molds. Heffler E, editor. Biomed Res Int. 2016;2016:3171594. https://doi.org/10.1155/2016/3171594