

INCREASING TREND OF SENSITISATION TO FOOD AND INHALANT ALLERGEN SOURCES IN ZIMBABWE

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ABSTRACT

Diseases that result from allergic reactions are common worldwide. Their frequency and associated triggers are rarely documented in Africa. We have summarised the findings of an audit of 981 laboratory test results of patients attending a specialist allergy clinic in Harare, Zimbabwe. The majority of the patients were children or young adults. The serological tests correlated well with skin-prick test findings. The test panels included 11 inhalants (house-dust mites, pollen, animal hair and moulds) and 22 food-allergen sources, including egg, milk, grains, nuts, fruits and vegetables. Serological reactivity to allergen sources was found in all age groups tested. A steep increase in the numbers of allergic patients was noted among those born in the last 30 years, while the number of people with moderate to severe allergic diseases doubled with each subsequent decade from 1980 to 2010.

The most significant inhalant-allergen sources were house-dust mites and pollen. House-dust mite sensitisation exceeded 50% in some age groups. Sensitisation to *Dermatophagoides pteronyssinus* was more prevalent than sensitisation to *D. farinae*. Grass-pollen allergy was more frequently diagnosed than allergy to tree and weed pollen, and was found in 30% of patients in certain age groups. The numbers of people with food-allergen sensitisation were lower than those with house-dust mite or pollen allergy. The most prominent food-allergen sources were potato (16%) and peanuts (15%).

This study confirms the persistence of inhalant allergic diseases in Zimbabwe and reports the increasing prevalence of food allergy. It is also shown that in some cases (peanut, potato) sensitisation does not translate to clinical manifestations of disease.

INTRODUCTION

The allergens that cause asthma and rhinitis in Zimbabwe have been sporadically studied since the 1970s.^{1,2} There has been a recent resurgence of interest in allergy with researchers highlighting the existence and profile of allergen sources in selected target populations.^{3,4} The few available reports indicate a general increase in the prevalence of respiratory allergies and their association with asthma, allergic rhinitis, conjunctivitis and dermatitis. There are no reports of sensitisation to food allergen sources. The care of patients with allergic diseases is fragmented. Patients with allergic conditions are first seen by family practitioners and then referred to organ-based specialists. These include but are not limited to paediatricians, internists, ear, nose and throat (ENT) surgeons, dermatologists and ophthalmologists. One specialist, a clinical immunologist, also attends to patients with allergic conditions.

This brief paper on allergies in Zimbabwe is derived from the observations made in one specialist centre, the Asthma, Allergy and Immune Dysfunction Clinic (AAIC). Patients of all ages who have been filtered through the referral system attend this clinic. Patients have allergic rhinitis, asthma, dermatitis, conjunctivitis, urticaria, angio-oedema, and

autoimmune and immunodeficiency diseases. There is an on-site laboratory that provides allergy testing and other laboratory tests.

METHODS

CLINICAL ASSESSMENT

A detailed case history is obtained using a semi-structured questionnaire. The questionnaire is designed to determine the target organs, severity and periodicity of the symptoms. The section on nasal symptoms probes the presence or absence of nasal blockage, rhinorrhoea and the associated ear, throat and ocular manifestations of nasal allergy. The section on lower respiratory tract allergy probes the presence or absence of dyspnoea, cough, wheeze and the need and frequency of accessing the services of accident and emergency units on account of respiratory discomfort. The skin allergy part of the questionnaire likewise focuses on the type, distribution, characteristics (pruritic/non-pruritic) and age of onset of suspected skin allergy. A family predisposition to atopy is also captured in the history. The questionnaire enables the attending physician to focus on the most probable target organs and to order relevant investigations. Allergic rhinitis is the commonest finding, asthma the second and dermatitis the third. The remainder

of conditions occur less frequently. A clinical evaluation is conducted and when indicated skin-prick testing is offered. A skin-prick test panel including some 50 food and inhalant allergen extracts is available. Some patients may require laboratory testing.

CLINICAL INVESTIGATIONS

Patients are offered skin-prick testing to panels of allergen sources that are relevant to their symptoms. Skin-prick test wheal diameters exceeding 3 mm are scored as reactive. Negative saline and positive histamine controls are included in each skin-prick test panel.

LABORATORY PROCEDURES

The laboratory determines the presence of allergen specific IgE antibodies using a modified Western blotting method Euroimmun, (Lubeck Germany). The test panel was the Euroline (Euroimmun) allergy profile (DP 3712-1601 E) membrane strip impregnated with allergen extracts. Reactivities against a tested allergen extract are scored semiquantitatively as negative (-) or positive. Positive scores were weak (=/-), moderate (+), high (++) or very high (+++). The kits are presented in the format of standard panels that include up to 27 allergen epitopes (Table I). It is

not possible to selectively test for individual allergens using this method. The consequence of this is that a large number of allergens, including those that would have been suspected on the basis of the clinical examination, are tested.

PATIENTS' INCLUSION

We reviewed the serology results of 1 000 sequential subjects who were tested for allergies at the AAIC between 2007 and 2011. All the subjects had been referred to the allergy clinic on the basis of clinical suspicion of allergy. The allergologist likewise had retained a level of suspicion that informed his decision to refer the patients for laboratory allergy testing. Although some of the patients would have been offered targeted skin-prick testing as well, only the Western blot results were included in the analysis. The rationale for this selection was the reproducibility of the Western blot test and the relative absence of interference from concomitantly administered medicines including antihistamines. In addition the test panel includes a broader range of allergen sources. The selected patients were therefore considered a better reflection of the sensitisation pattern in this population.

RESULTS

Results of 981 allergy patients were included. The remainder may have reports indicating inadequate samples or other challenges that the laboratory may have faced in processing their samples. The analysis distinguishes between patients with sensitisation and those reported negative. Although the test kit measures the allergen specific IgE antibodies semiquantitatively with a range from weak to very high, there is no attempt to grade the concentrations of allergen specific IgE. It is recognised that the concentrations of allergen specific antibodies may not correlate with the degree of clinical response or skin testing when challenged with a specific allergen. Since the focus was on sensitisation, all sensitised individuals were included.

AGE DISTRIBUTION

The 981 patients included in the study were born between 1932 and 2011. Although the numbers in each age bracket varied, the trend showed a clear increase in the number of younger people with allergies. A near logarithmic increase in the numbers of people with allergies is observed for the 1980 to 2012 birth cohorts (Fig. 1). The number of subjects born between 1939 and 1949 was relatively low. Statistical assessment of these age groups was challenging. Therefore, the inhalant-allergen sources causing sensitisation in patients born between 1949 and 2010 for the respective groups are summarised.

Table I. Food-allergen sources included in the test panel

Food-allergen sources	Inhaled allergen sources
f1 egg white	gm2 grass pollen
f25 egg yolk	t3 tree pollen
f3 codfish	w6 mugwort
f2 milk	d1 <i>D. pteronyssinus</i>
f76 alpha-lactalbumin	d2 <i>D. farine</i>
f77 beta-lactoglobulin	e1 cat
f78 casein	e2 dog
e204 BSA/BSA	e3 horse
f4 wheat flour	m2 <i>Cladosporium</i>
f9 rice	m3 <i>Aspergillus</i>
f14 soya bean	m6 <i>Alternaria</i>
f23 shrimp	
f13 peanut	
f17 hazelnut	
f20 almond	
f31 carrot	
f35 potato	
f49 apple	
f5 rye flour	
fs5 celery	
f23 crab	
f25 tomato	
f84 kiwi	

BSA - bovine serum albumin

INHALANT-ALLERGEN SOURCES
HOUSE-DUST MITES

The most frequent source of sensitisation to inhaled allergens was house-dust mites. Sensitisation was noted to the house-dust mites *Dermatophagoides pteronyssinus* and *D. farinae* (Table II). Rates of sensitisation increased progressively with age. More than half the patients in the age groups 10-19, 30-39 and 40-49 years were sensitised. The overall trend was one of an upward trajectory of sensitisation rates with decreasing age. Sensitisation was predominantly to *D. pteronyssinus*. More than two-thirds of house-dust mite sensitised subjects were dually sensitised to both *D. pteronyssinus* and *D. farinae*, with the incidence of *D. farinae* sensitivity less among all age groups. There were isolated cases of monosensitisation to *D. farinae*. House-dust mite sensitisation was principally associated with symptoms of allergic rhinitis (Fig. 2) and asthma.

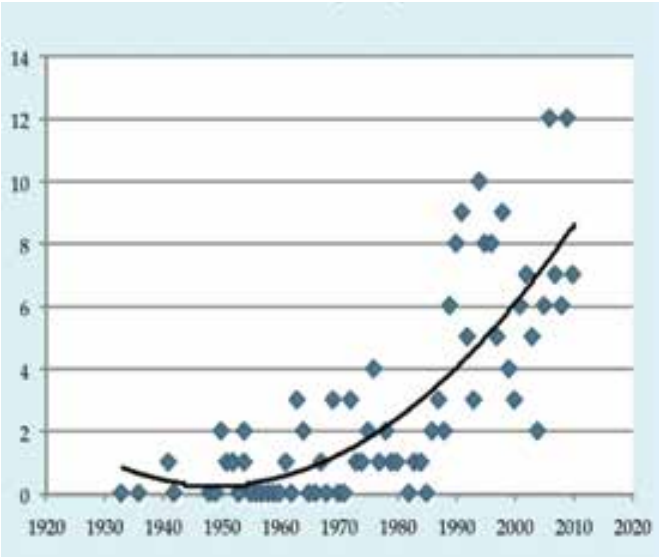


Fig. 1. Number of patients (%) with any allergy (ingested or inhaled) plotted by year of birth (n=981).

POLLEN

Pollen was the second commonest group of allergens (Table II), including grass, tree and weed pollen. The frequency of pollen sensitisation was higher in younger than in older patients. Patients born between 1990 and 1999 were sevenfold more likely to be sensitised to grass pollen than those born between 1960 and 1969. The age gap roughly reflects the generational difference in age between a parent and child. The lowest numbers of grass pollen sensitised patients were in the older age groups. The numbers increased with decreasing ages, peaking in the 10-19-year age group and dipping slightly in the under-9-year age groups, suggesting perhaps that they are yet to seek treatment. Pollen sensitisation was associated with asthma, allergic rhinitis and conjunctivitis (Fig. 3)

ANIMAL HAIR

Laboratory tests were performed to determine allergen specific IgE to animal hair and dander (Table III). The selected sources were cat, dog and horse. The order generally represents the frequency of exposure to animal hair and dander. Age stratified sensitisation to the



Fig. 2. The allergic salute of a patient with rhinitis.

Table II. Age distribution of patients with house-dust mite and grass-pollen sensitisation in different age groups*					
	<i>D. pteronyssinus</i>	<i>D. farinae</i>	Grass	Tree	Mugwort
0-9 years (n=116)	36.2	27.6	25	17.2	17.2
10-19 years (n=98)	52	41.8	35.7	27.6	15.3
20-29 years (n=48)	19.4	15.3	35.7	27.6	15.3
30-39 years (n=45)	53.3	40	25	17.2	17.2
40-49 years (n=35)	51.4	34.3	15.5	11.1	6.7

*The figures are percentages of all the patients with serological evidence of allergy.



Fig. 3. Allergic conjunctivitis.

respective allergen sources showed an increasing trend relative to the year of birth. Sensitisation to cat and dog doubled with each decade. Only four subjects born between 1940 and 1959 were sensitised to cat-, dog- or horse-derived allergens. Sensitisation to cat allergen was more frequent than that to dog and horse allergens.

MOULDS

The patients were sensitised to *Cladosporium*, *Aspergillus* and *Alternaria* (Table III). The percentage of *Cladosporium*-sensitised individuals ranged from 0% to 4.1% in the age groups between 0 and 49 years. Corresponding percentages for *Aspergillus* were between 4% and 14%. The rates of sensitisation were highest in the youngest age groups. The trend of mould sensitisation was upward.

Figure 4 summarises sensitisation to inhaled allergens.

FOOD ALLERGY

The test panel included egg, fish, milk, grains, nuts, vegetables and fruits (Table I). Allergic reactivity was observed in all the food allergen groups and across age groups. The most frequent sensitisation was to potato (16%) and peanut (15%). The frequency of sensitisation to the remainder of allergen sources was below 10%. Sensitisation to shrimp was very infrequent (0.2%)

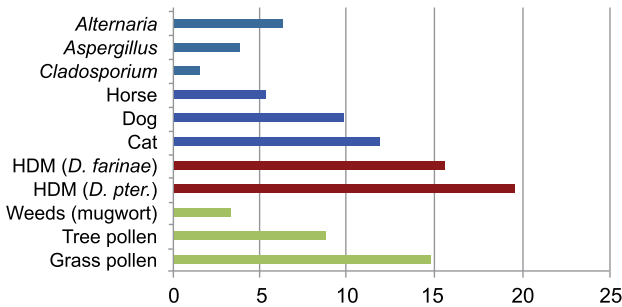


Fig. 4. Sensitisation to inhaled-allergen sources in Zimbabwe.

NUTS

Patients were sensitised to peanut, hazelnut and almond. Peanut sensitisation was highest (15%), with 8% sensitised to hazelnut and only 2% to almond. The striking observation was that despite the high level of sensitisation to peanuts, there are no severe manifestations of peanut allergy. Peanut sensitisation in this population is therefore not associated with serious manifestations of allergy.

GRAINS

Sensitisation to wheat, rice, rye and soya was detected in the patient population. Sensitisation to soya (9%) and rice (9%) was more frequent than sensitisation to wheat (7%). Sensitisation to rye was least frequent (2.6%). Sensitisation to the edible grains was associated with skin manifestations of allergy (dermatitis/urticaria) as well as to gastrointestinal symptoms.

EGG

Allergy to egg was a predominantly paediatric presentation (Fig. 5). The majority of patients with detectable allergen specific IgE antibodies to egg were below the age of 5 years. Sensitisation to egg white (7.3%) was twice as frequent as sensitisation to egg yolk (3.5%). The clinical symptom complex associated with egg sensitisation included infantile eczema (Fig. 6).

Table III. Sensitisation to three examples of animal hair and inhaled moulds in different age groups.*

	Cat	Dog	Horse	Cladosporium	Aspergillus	Alternaria
0-9 years (n=116)	15.5	25	8.6	1.7	14.6	6.9
10-19 years (n=98)	27.6	24.5	14.3	4.1	11.2	16.3
20-29 years (n=48)	27.5	24.5	14.3	1	4.1	7.1
30-39 years (n=45)	15.5	25	8.6	2.2	11.1	6.7
40-49 years (n=35)	28.9	24.4	8.9	0	5.7	5.7

*The figures are percentages of all the patients with serological evidence of allergy.

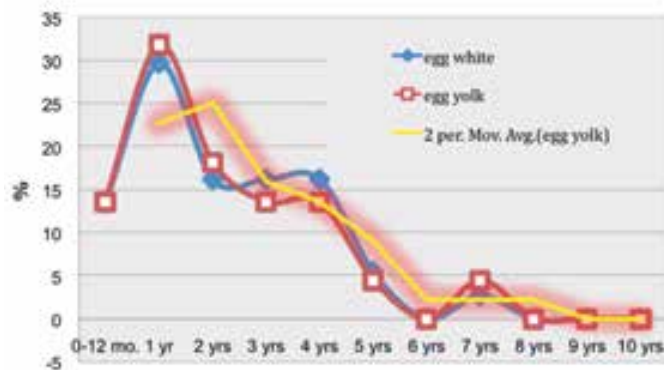


Fig. 5. Sensitisation to egg allergen sources by age.



Fig. 6. Dermatitis. Perioral hyperpigmentation and eczema of the wrists.

CODFISH AND SHRIMP

The test panel included codfish and shrimp. These allergen sources are relatively infrequent in this landlocked country. Patients sensitised to shrimp were invariably sensitised to house-dust mites as well, raising the possibility of cross-reactivity.

MILK

The immunoblots were embedded with the milk allergen extracts milk, alpha-lactalbumin, beta-lactoglobulin, casein and bovine serum albumin (BSA). Sensitisation to any of the milk allergens was reported in only 2.7% of the almost 1 000 patients, making this an unusual allergen source in this population.

VEGETABLES AND FRUITS

The rates of sensitisation to potato were the highest among food-allergen sources. The laboratory evidence of sensitisation poorly correlated with clinical disease. Carrot sensitisation on the other hand was less frequent but more

commonly implicated in urticaria. Apple sensitisation was associated with the oral allergy syndrome and gastrointestinal manifestations.

Figure 7 summarises the food allergens.

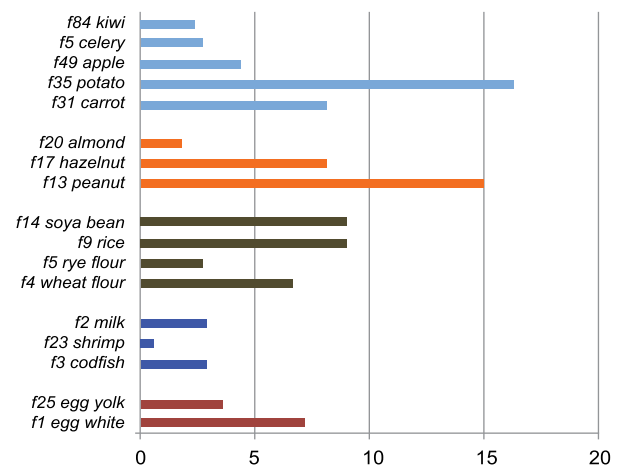


Fig. 7. Summary of food-allergen sensitisation (%) (note high sensitisation to potato and peanut).

DISCUSSION

This paper summarises the results of an audit review of the profile of allergic sensitisation in 981 patients who attended the AAIC, a specialist referral centre in Harare, Zimbabwe. The patients were clinically evaluated and offered skin-prick tests and, if indicated, laboratory testing. Medical practitioners in private practice primarily referred all the patients to the AAIC. The need for referral suggests that the symptoms could have been more severe than can be managed at the level of general practitioners and other physicians. There is also a possibility that only those patients who could afford consultation at both primary care physician and specialist levels were referred. These considerations should be borne in mind when the representativeness of the overall findings is assessed. Caution should also be exercised in extrapolating disease prevalence from the evidence of allergen sensitisation. The laboratory test panel is an immunoblot strip with a standard allergen panel. It does not permit selective testing of clinically suspected allergen sources. Some of the tests offered would not have been suspected from the history or examination. Notwithstanding the fact that the patients had relatively more severe disease and could afford private health care, they are all drawn from the same community. The air they inhale and the food they eat differs minimally from that inhaled or ingested by their neighbours.

The allergen sensitisation patterns are therefore a reasonable representation of allergen sources and should provide a credible panorama of sensitisation patterns in Zimbabwe. The demographic distribution shows that the allergy burden affects young adults and children. There is an increase in sensitisation to food-allergen sources. An exponential increase in allergen sensitisation was observed in patients born after 1980. The number of people with allergic diseases doubled each decade from approximately 2% in 1980, 4% in 1990, 6% in 2000 to approximately 8% in 2010 (Fig. 1). If the trajectory stays on this course, allergic diseases will surpass HIV infection rates within the next 10 years. Unfortunately there is limited evidence of preparations to address the emerging epidemic. Policy makers could once again be taken by surprise!

The panel of allergen sources tested included previously described inhalant- and food-allergen sources.⁵ Allergy to the respiratory sources manifests as respiratory allergy (asthma, rhinitis and conjunctivitis). The predominant inhalant allergen was house-dust mites. Although sensitivity to both *D. pteronyssinus* and *D. farinae* was detected, the former predominated. House-dust mite allergy is implicated in rhinitis, asthma and conjunctivitis. The high levels of sensitisation to house-dust mites confirmed earlier reports from Zimbabwe^{1,2} and a more recent report by Rujeni *et al.*⁶ who studied a cohort of schistosome-infected individuals.

The second commonest allergen source was pollen. Sensitisation to grass pollen was more prevalent than that to tree or weed pollen. A seasonal pattern of sensitisation was observed. Presentation with grass pollen sensitisation peaked during the second half of the rainy season (February to April). Allergy to moulds (*Cladosporium*, *Aspergillus* and *Alternaria*) was infrequent but appeared to be associated with more severe respiratory symptoms than allergy to pollen. This pattern of sensitisation and the corresponding disease severity is similar to what was observed and reported by Ordman¹ in 1972.

Unlike for respiratory allergy, there are very few reports on food allergy in Zimbabwe. It appears that food allergy has been rare and has not warranted research efforts. This report is the first to present evidence of sensitisation to a large range of food-allergen sources. Food allergy is implicated in eczema and atopic dermatitis syndromes. Some food-allergen sources, such as peanuts, are associated with severe symptoms including anaphylaxis and death.⁷ High levels of sensitisation to potato (16%) and peanut (15%) allergen sources are reported. The two food sources are widely available and liberally consumed. There

are no reports of severe allergic reactions in people exposed to the allergens. In respect of peanut allergy, not a single case of peanut-allergy-induced anaphylaxis was reported. This raises questions regarding the correlation between laboratory evidence of allergy (to peanuts) and clinical observations. Similar observations have been made by Amoah *et al.*⁸ in Ghana. In collaboration with researchers in Vienna, Austria and Stockholm, Sweden, we investigated the apparent contradiction between the reports in the literature and our observation of apparent tolerance to peanut allergens. We were able to show that the IgE antibodies recognised peanut allergens such as Ara h 2, 3, 6, 9, as well as cross-reactive carbohydrate determinants. Further studies of our patients are under way. The predominantly paediatric nature of allergy to egg components was confirmed. The majority of egg-allergic patients were under the age of 5 years. These patients appear to outgrow egg allergy.

CONCLUSION

We investigated nearly 1 000 adult and paediatric patients with allergic diseases. There is a marked increase in allergen sensitisation in young adults and children. House-dust mites remain the commonest inhaled allergen source. The mites are strongly associated with respiratory and ocular allergy. High levels of sensitisation to potato and peanut allergens were observed. There was no apparent clinical correlation between sensitisation to peanut or potato and disease. The findings in respect of food allergy show that they constitute an emerging epidemic. The interpretation of the clinical relevance of sensitisation may be different from what has been observed in Europe and North America. Resources should be allocated to support the investigation and management of this emerging epidemic.

Declaration of conflict of interest

The author declares no conflict of interest.

REFERENCES

1. Ordman D. Seasonal respiratory allergy in Bulawayo, Rhodesia: the pollen and fungus factors. *S Afr Med J* 1972;46(48):1898-1901.
2. Cookson JB, Merrett J, Merrett TG. Identification of allergen-specific IgE antibodies in the sera of African asthmatics. *Clin Allergy* 1976;6(4):395-398.
3. Kambarami RA, Marechera F, Sibanda EN, Chitiyo ME. Aero-allergen sensitisation patterns amongst atopic Zimbabwean children. *Cent Afr J Med* 1999;45:144-147.
4. Sibanda EN. Inhalant allergies in Zimbabwe: a common problem. *Int Arch Allergy Immunol* 2003;130:2-9.
5. Westritschnig K, Sibanda E, Thomas W, et al. Analysis of the sensitization profile towards allergens in Central Africa. *Clin Exp Allergy* 2003;33(1):22-27.
6. Rujeni N, Nausch N, Bourke CD, et al. Atopy is inversely related to schistosome infection intensity: a comparative study in Zimbabwean villages with distinct levels of *Schistosoma haematobium* infection. *Int Arch Allergy Immunol* 2012;158(3):288-298.
7. Sicherer SH. Epidemiology of food allergy. *J Allergy Clin Immunol* 2011; 127:594-602.
8. Amoah AS, Obeng BB, Larbi IA, et al. Peanut-specific IgE antibodies in asymptomatic Ghanaian children possibly caused by carbohydrate determinant cross reactivity. *J Allergy Clin Immunol* 2013;132(3):639-647.