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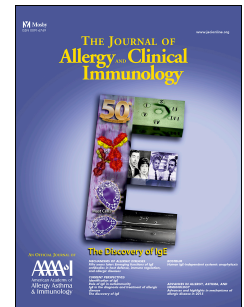
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Food Allergy in the developing world

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Food allergy (FA) in the developing world was once thought to be rare, but emerging epidemiological data in the recent decade has shown otherwise. This could be attributed to previous under-recognition or under-reporting of FA prevalence; alternatively, it could reflect steadily increasing prevalence of FA in parallel with rising economic growth. Here we review the epidemiology of food allergy in the developing world.

Epidemiology

There is a paucity of reliable data regarding food allergy (FA) in most developing countries (1). Many countries have data on surrogate measures of FA such as self-reported reactions and/or sensitisation (allergen-specific IgE; sIgE) to one or more foods rather than challenge-proven FA. Although we know food sensitization (FS) correlates poorly with clinical FA, such surrogate measures offer some understanding of disease characteristics in the absence of robust data on FA.

Prevalence data for food allergy confirmed by oral food challenges

Over the past 5 years, there have been 2 reports of challenge-proven FA prevalence in South Africa. An earlier study amongst children with atopic dermatitis found high rates of FS (66%) and challenge-proven FA (40%) (2), comparable to reported prevalence in the West. Overall, 24% of patients were peanut allergic including 15% (9/59) of Xhosa patients versus 38% (15/40) of mixed race patients ($p = 0.01$), suggesting that ethnic or lifestyle differences played a role (3). Ara h 2 was found to have a significantly lower predictive value for peanut allergy in Xhosas (53%) versus mixed race patients (93%), highlighting that internationally-derived 95% PPVs for peanut allergy might not apply in different ethnic groups.

Another South African study examined FA prevalence in an unselected diverse population from Cape Town by means of skin prick test (SPT) and open incremental oral food challenge (OFC). Forty-nine participants (9.6%; 95% CI 7.0-12.1%) were sensitized (SPT wheal $\geq 3\text{mm}$) to at least 1 of the 7 foods tested (4); and challenge-proven IgE-mediated FA to any food was 2.5% (95% CI 1.2-3.9), similar to prevalence from the developed world (1). Co-morbid allergic rhinitis, eczema and asthma were also noted to be strongly associated with FS and IgE-mediated FA (4).

Food allergy confirmed by IgE sensitization & self-reporting

The recent EuroPrevall study evaluating 12,000 adults aged 20–54 years living in South India found that only 1.2% had self-reported adverse symptoms to food together with sIgE to a food. However, sensitization rates were reported at up to 26.5% for many foods, which is higher than what has been described for many countries in North America or Europe (5).

In a cross-sectional survey of Ghanaian school children, up to 11% of 1,407 children reported adverse reactions to foods, of whom 5% showed sensitization by SPT (6). Food sensitization by SPT was 4.4% in rural versus 5.9% in urban children, but FS by sIgE was significantly higher in rural as compared to urban children (24% vs 8.5%), with higher median levels of sIgE which could not be explained by the presence of helminth infections.

Time trends of food allergy prevalence

Data on time trends in food allergy prevalence is only available from one developing country – China, a developing country with rapid urbanization. Two cross-sectional studies were

performed 10 years apart (1999 and 2009) using the same methodology examining the prevalence of sensitization and challenge-proven food allergy amongst infants aged 0-24 months at the same hospital clinic in Chongqing, China (7). The rate of sensitization to any food was 9.9% in 1999 and increased to 18% 10 years later. FA prevalence also increased significantly from 3.5% in 1999 to 7.7% in 2009 ($P=0.017$), with egg and cow's milk being the most common food allergens. In contrast to the West, peanut allergy remained rare in Chongqing.

In 2007, amongst 151 South African Xhosa-adolescents, 5% were reported to have peanut sensitization (PS) with none being peanut-allergic (PA) (peanut allergy prevalence 0%; 95% CI-0.0-2.4%) (8). In 2013-2014, Basera et al. reported an OFC-confirmed PA rate of 1.6% in Xhosa-children and a PS rate of 4.5% (4), suggesting a rising trend for FA at least in a select ethnic group in urban South Africa.

Hospital admissions for food anaphylaxis

Another proxy measure to aid understanding of food allergy epidemiology is hospital admission for food induced anaphylaxis. From July 2008 to June 2010, fifteen Latin American countries identified 634 patients (29.2%) aged <18 years who presented with systemic allergic reactions of whom 23.3% had identified foods as triggering agents (9). A systematic review and meta-analysis of studies examining the incidence of anaphylaxis caused by FA included studies from Brazil and Israel (10). Out of the 240 fatal food anaphylaxis episodes described, only 12 and 4 cases were from Brazil and Israel respectively, with the rest reported from the developed countries (E1,E2).

Risk factors for development of food allergy

Gene-environment interactions are important in determining risk of food allergy. Environmental exposures in early life play a major role in development of FA and are considered to be responsible for the recent rise in FA prevalence in Western countries. A recent report from the *Institute of Medicine* suggests that FA in the developed world may still be on the rise (E3). Factors associated with a shift to an urbanised lifestyle such as reduced microbial exposure, antibiotic use, changes in diet, reduced UV exposure and vitamin D insufficiency have all been implicated. Economic growth in developing countries can be expected to result in improved living conditions and a more urbanised lifestyle that will likely be associated with a similar rise in food allergy over time.

In addition to environmental factors, there is preliminary evidence that ethnicity may play a role in determining risk for food allergy. Amongst the 1-year-old Australian infants recruited to the HealthNuts study, those with parents of East Asian ethnicity had a 3-fold higher risk of food allergy compared to infants with Caucasian parents (E4). Furthermore, children with Asian-born mothers who were born in Australia were more likely to have nut allergy (aOR 2.67; 95%CI 2.28, 3.27) than non-Asian children born in Australia, whereas children with East-Asian parents who were born in Asia and subsequently migrated to Australia were at decreased risk of nut allergy (aOR 0.1; 95%CI 0.03, 0.31) (E5). These findings suggest that genetic factors associated with Asian heritage may confer an increased risk of food allergy that is only revealed when exposed in early life to environmental factors typical of the Western lifestyle. If this is correct, food allergy prevalence in developing countries with predominantly East Asian populations will likely increase with continued economic growth and adoption of the Westernized lifestyle. Similarly, in New Zealand, Pacific Islanders have higher anaphylaxis admission rates than other ethnic groups (E6). In the United States,

African American children (95% CI, 1.5-2.7%) have a higher rate of increase in food allergy than Caucasian children (95% CI, 0.4-1.6%) (E7). These findings may predict increased rates of food allergy in Asia and Africa with increasing urbanization.

Conclusion

The available data on food sensitization and challenge-proven diagnosis suggest an increasing prevalence of FA in several regions of the developing world (China, Africa). The Healthnuts study showed higher rates of FA in Asians who were born in Australia when compared with the Caucasian population; whereas rates in those born in Asia then arriving in Australia later are lower than rates observed for the local Caucasian population. This suggests that genetic predisposition has previously been masked by environmental protective factors; however, with increasing economic growth and adoption of Westernized lifestyle in these developing regions, there is likely to be a dramatic increase in food allergy prevalence. The prevalence may even exceed Western rates of food allergy. It is imperative to conduct robust studies to confirm FA prevalence and time trends in order to understand the likely demand on health services. Moreover, studies to examine risk factors relevant in these regions will be essential in order to develop targeted prevention strategies.

Table 1. Epidemiology studies of food allergy in developing countries

COUNTRY	YEAR OF STUDY	STUDY METHODOLOGY	ATOPY ASSESSMENT		PREVALENCE OF FA
			sIgE	SPT	
China	1999	Cross-sectional prevalence study involving children aged 0–24 months underwent SPT. FA was reported by parents and later confirmed with oral food challenge ^[7]	N/A	9.9%	3.5% (any food)
	2009	Same study was performed 10 years later using the same methodology and same age group (0–24 months) in the same clinic ^[7]	N/A	18%	7.7% (any food)
South Africa	2013-2014	Cross-sectional study involving 544 randomly selected children aged 12 to 36 months old from the childcare education facilities (CCFs) in the Cape Town metropolis. Participants were assessed by questionnaires, SPT & OFC ^[4]	N/A	9.6%	2.5%
	2010-2012	100 children (aged 6 months to 10 years) with moderate-to-severe AD were randomly selected from a dermatology clinic at the Red Cross Children's Hospital in Cape Town. Participants underwent allergy questionnaires, SCORAD assessment, SPT, sIgE testing & OFC ^[2,3]	66% (SPT or sIgE)		40%
India	2005-2010	588 subjects (236 cases and 352 controls) ranging from 20–54 years living in South India participated in a case-control study involving a detailed questionnaire and sIgE estimation for 24 common foods ^[5]	26.5%	N/A	1.2% (any food)
Ghana	2006-2008	Cross-sectional survey involving 1,604 Ghanaian schoolchildren aged between 5 and 16 years old recruited from 6 rural and 3 urban schools. Participants were assessed by questionnaires, SPT and sIgE ^[6]	35%	5%	11% (any food) (2.9% positive IgE to the reported allergic food)

N/A- data not available

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