FOOD ALLERGY EPIDEMIC – IS IT ONLY A WESTERN PHENOMENON?

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ABSTRACT

The incidence and prevalence of allergic disease such as asthma, eczema and allergic rhinitis is widely reported to have increased over the past few decades, particularly in the developed world. Patient and public awareness of food allergy is also increasing. While most of the medical literature around food allergy focuses on the western world, there is also an increasing amount of evidence that food allergy (FA) is prevalent outside of the developed world. The true prevalence and morbidity of FA in the developing world is largely unknown. A literature review of the worldwide incidence of FA was undertaken with emphasis on the paediatric age group, for developing areas in Asia, Latin America and Africa to assess whether or not the ‘food allergy epidemic’ is a western phenomenon. We found that there are too few data using food challenges, the accepted gold standard, for the diagnosis of true FA to come to any conclusions either about the current prevalence of FA or whether it is rising. Robust, population-based studies are needed to establish the true burden of disease.

A food allergy (FA) is an adverse immune response to a food protein. This may be IgE-mediated (either primary or related to a cross-reacting pollen), or non-IgE-mediated. FA is distinct from other adverse responses to food, such as food intolerance, pharmacological reactions, and toxin-mediated reactions. The term food hypersensitivity (FHS) combines allergy and intolerance. While allergy tests can confirm IgE sensitisation, a double-blind placebo-controlled food challenge may be required to verify the diagnosis.

Cross-sectional studies, such as the International Study of Asthma and Allergies in Children (ISAAC) have confirmed that atopic diseases represent a major health problem in many countries, and that the rates of respiratory allergy such as allergic rhinitis and asthma have risen over time in many developed countries. The prevalence of FA is widely believed to have risen alongside this, although evidence for this is relatively limited. IgE-mediated FAs are most prevalent during childhood, affecting between 6% and 8% of children in the UK and USA.1 The majority of food-induced allergic reactions in young children in the UK and USA are due to cow’s milk protein, egg, peanuts and tree nuts. Wheat and soy cause IgE-mediated FA less frequently. With increasing age, peanuts and tree-nut allergies persist more often than cow’s milk and egg allergies, and they are associated with significant morbidity and mortality.2,3

The strongest evidence of an increase in FA over time relates to peanut allergy, where studies suggest a clear increase in prevalence in both the UK and the USA. Two studies, using similar methodology, conducted by Sicherer and colleagues at 5-year intervals, were very revealing.4 In 1997, a national random digit-dial phone survey was used to determine the prevalence of peanut and tree nut allergy in the USA. The follow-up study, conducted in 2002, showed that the rate of peanut and tree nut allergies had not increased significantly in adults but the reported prevalence of peanut allergies in children had doubled in the 5 years between the surveys.

Grundy and team, in a study on the Isle of Wight, also compared two comparable cohorts over time (6 years).5 Of all 2 878 children born between September 1994 and September 1996, 1 273 completed questionnaires, and of those, 1 246 had skin-prick tests (SPTs) at the age of 3–4 years. Those with positive SPT responses to peanut were subjected to oral peanut challenges, unless there was a history of immediate systemic reaction. These results were compared with an earlier, comparable cohort of 1 456 children from the same geographic area 6 years earlier (January 1989 to February 1990). The aim was to determine any change in the prevalence of peanut sensitisation and reactivity in early childhood. The authors found a 2-fold increase in reported peanut allergy (0.5% [6/1 218] to 1.0% [13/1 273]), but the difference was non-significant (p = 0.2). Peanut sensitisation increased 3-fold, with 41 (3.3%) of 1 246 children sensitised in 1994 to 1996 compared with 11 (1.1%) of 981 sensitised in the earlier cohort (p = 0.001). Overall, 18 (1.5%) of 1 246 children were considered to have symptomatic peanut allergy.

Subsequent studies in Canada6 also showed a high prevalence of peanut allergy in schoolchildren, and Australian data from childcare centres in the ACT and Central Sydney Area Health Service showed while allergies to proteins in milk, eggs and seafood have remained steady, peanut allergies increased by 50% between 2003 and 2006, and cashew allergies, while less common overall, increased a staggering five times.7 There also appears to be an increasing number of reactions reported to novel allergens such as sesame8 and kiwi fruit.9

Although FAs appear to be on the rise, a scarcity of data on their prevalence makes it difficult for governments and health services to react. Collecting prevalence data relating to FA is extremely challenging. The most robust studies require careful evaluation of each patient, with any allergy confirmed with double-blind, placebo-controlled food challenges. Such studies, on a population scale, require significant resources and thus most researchers have opted for a questionnaire-based approach. Unfortunately, questionnaire-based studies greatly overestimate the prevalence of FHS. The reported perceived prevalence of FHS using questionnaires varies from 3.24% to 34.9%.10

In a recent review by Venter et al.,11 of the prevalence and cumulative incidence of FHS in the first 3 years of
life in the UK between 2001 and 2002, it was concluded that there was no evidence of increased FHS in an unselected population over time when compared with a similar USA study 20 years previously. The study of a birth cohort of 969 children at 1, 2, and 3 years concluded that by the age of 3 years, 5-6% of children suffer from FHS, based on food challenges and a good clinical history. They also found large discrepancies between reported and true FHS in young children but were able to demonstrate that the true prevalence of FHS decreases with age, as is expected given the tendency of milk and egg allergy to resolve in childhood. There is a lack of such robust data available from developing countries.

This article considers the evidence that FA is already an established entity outside of the developed world, where data suggest it is a major public health concern, although it is unclear whether it is a growing one.

FOOD ALLERGY IN ASIA

Most of the world’s population lives in Asia. However, there is a paucity of adequate data on the prevalence and clinical features of FA in this region, and specifically of large, well-designed studies using robust diagnostic methods. This problem is exacerbated by large population sizes with diverse racial, cultural and socio-economic means and language. Asia is also unique as its range of different cultures and eating habits result in unique FAs. The most common cause of food-induced anaphylaxis is a cohort of children from Singapore, for example, is bird’s nest (27%), followed by egg and milk (11% combined). However, in recent years, data on the prevalence of FA in some countries in Asia have been published.

Epidemiology

The true prevalence of FA in the general population in Asia is uncertain. Estimates from Chinese studies range from 4.98% in the Sheng-Li oil fields of northeast China to 16.4% in a study of large-scale, unselected rural Chinese cohorts of twins in Anqing. The latter percentage represented those diagnosed by SPT and therefore reflects sensitisation rather than true clinical allergy. This study found FA was more common among children than among adults and was more prevalent among children in their first few years, in keeping with western data. A study using a parent-reported questionnaire among a large cohort of Chinese preschool children in Hong Kong reported a prevalence rate of parent-reported FA and parent-reported, doctor-diagnosed FA of 8.1% and 4.6%, respectively. This study has also shown parent-reported FA was less frequent among those born in mainland China, and who have subsequently moved to Hong Kong, than those born and raised in Hong Kong.

In the late 1990s, a parent-reported questionnaire of children from Singapore estimated the prevalence of FA to be 4-5%. Around the same time, a Korean study using a self-reported questionnaire in a huge cohort of children reported a lifetime prevalence of 10.9%. In keeping with other urban-rural comparisons, there was a slightly higher prevalence in the capital Seoul (12.4%) compared with provincial cities (10.1%). Similarly variable FA prevalence was noted in other Asian countries: as high as 5.5% in a cohort of Japanese children and as low as 1.2-1.7% in Israeli infants as assessed by detailed questionnaire and SPTs.

A cross-sectional study of 656 children of 6 months to 6 years of age in Thailand showed a prevalence of 6.25% in children less than 6 years based on a parent-reported questionnaire survey versus the 0.45% established through SPT and food challenge. This illustrates the discrepancy between reported and medically diagnosed allergy, adding to the difficulties in comparison between existing data.

Table I lists country-specific prevalence studies.

Table I. Country-specific prevalence of food allergy in children

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Country</th>
<th>Age (years)</th>
<th>Allergen</th>
<th>Prevalence (%)</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wang</td>
<td>1044</td>
<td>China</td>
<td>General</td>
<td>General</td>
<td>4.98</td>
<td>Questionnaire</td>
</tr>
<tr>
<td>Kim</td>
<td>2118</td>
<td>China</td>
<td>General</td>
<td>General</td>
<td>25.3</td>
<td>SPT</td>
</tr>
<tr>
<td>Leung</td>
<td>3287</td>
<td>Hong Kong</td>
<td>2-7</td>
<td>General</td>
<td>8.1/4.6</td>
<td>Parents / doctors</td>
</tr>
<tr>
<td>Lee B</td>
<td>6404</td>
<td>Singapore</td>
<td>5-12</td>
<td>General</td>
<td>4.5</td>
<td>Parent-reported</td>
</tr>
<tr>
<td>Lee S</td>
<td>25000</td>
<td>Korea</td>
<td>6-12</td>
<td>General</td>
<td>10.9</td>
<td>Self-reported</td>
</tr>
<tr>
<td>Fukiwake</td>
<td>456</td>
<td>Japan</td>
<td>0-6</td>
<td>General</td>
<td>5.5</td>
<td>Questionnaire</td>
</tr>
<tr>
<td>Dalal</td>
<td>&gt;9000</td>
<td>Israel</td>
<td>0-2</td>
<td>General</td>
<td>1.2-1.7</td>
<td>Questionnaire + SPT</td>
</tr>
<tr>
<td>Santadusit</td>
<td>656</td>
<td>Thailand</td>
<td>6 mo-6 yrs</td>
<td>General</td>
<td>6.25</td>
<td>Questionnaire</td>
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<tr>
<td>Santadusit</td>
<td>656</td>
<td>Thailand</td>
<td>6 mo-6 yrs</td>
<td>General</td>
<td>0.45</td>
<td>SPT + food challenges</td>
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<tr>
<td>Marrugo</td>
<td>3099</td>
<td>Colombia</td>
<td>Children &amp; adults</td>
<td>General</td>
<td>14.9</td>
<td>Self-reported</td>
</tr>
<tr>
<td>Bozzola</td>
<td>944</td>
<td>Argentina</td>
<td>Adults</td>
<td>General</td>
<td>5.1</td>
<td>Phone survey</td>
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<td>Naspitz</td>
<td>457</td>
<td>Brazil</td>
<td>1-12</td>
<td>Fish/egg</td>
<td>29.5/24.4</td>
<td>SPT in atopic children</td>
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<tr>
<td>Naspitz</td>
<td>457</td>
<td>Brazil</td>
<td>1-12</td>
<td>Fish/egg</td>
<td>11.3/4.8</td>
<td>SPT in children</td>
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<tr>
<td>Martinez</td>
<td>408</td>
<td>Chile</td>
<td>8 mo-15 yrs</td>
<td>Egg, milk, beef/peanut</td>
<td>7/1.1</td>
<td>SPT</td>
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<tr>
<td>Madrigal</td>
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<td>Mexico</td>
<td>Children</td>
<td>General</td>
<td>3.7</td>
<td>Survey</td>
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<td>Avila-Castañón</td>
<td>1419</td>
<td>Mexico</td>
<td>1-17</td>
<td>Fish/cow’s milk</td>
<td>12/7.7</td>
<td>SPT</td>
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<tr>
<td>Karabus &amp; Motala</td>
<td>400</td>
<td>South Africa</td>
<td>Children</td>
<td>Peanut/egg white</td>
<td>35/30</td>
<td>SPT in children with atopic dermatitis &amp; food elimination challenge</td>
</tr>
</tbody>
</table>

SPT = skin-prick test
Food as a trigger for anaphylaxis

Recent studies describing patterns of anaphylaxis show that food is an important cause of severe allergic reactions in Asia. Unlike the USA, Australia and the UK, peanut and tree nuts are rarely the cause of allergic reactions in the region.28

The mortality rate from FAs is 0.006 individuals per 100 000 children in the UK,29 while 150-200 individuals die from FAs every year in the USA. 30 Related studies of anaphylaxis in Asia are few, although the overall incidence of anaphylaxis appears to be low. Common food allergens causing anaphylaxis are milk, eggs, wheat, peanuts, and soybeans.31

FOOD ALLERGENS IN ASIA

Many food allergens are similar in both Asian and western communities. Hen’s egg, cow’s milk, wheat and to a lesser degree peanuts are known to be allergens.32 However, some differences, related in part to dietary exposure as well as the existence of geographically specific and unique food allergens, are apparent. Figure 1 highlights common country-specific food allergens, but it is important to note that comparison of specific food prevalence is made difficult as a result of the heterogeneity in the types of studies, age groups examined and definition and diagnosis of FA.3,13,19-21,23,24,26,27,33-36

In Japan, the most common allergens causing anaphylaxis were milk, eggs, wheat, peanuts, and soybeans, followed by sesame and buckwheat.33 Using a questionnaire survey in Korean children with atopic eczema, it was found that the most common food allergens were egg, milk, fish and seafood in 6-12-year-old children, and seafood, peach, milk, egg and fish in 12-15-year-old children.34 In Singapore, a cross-sectional study involving 75 atopic children aged under 3 years showed the prevalence of food sensitisation was highest for cow’s milk (45.9%) and egg white (38.7%).35 Unusual food allergens in Asian populations include silkworm pupa – a traditional Chinese food.36 Oil-fired pupa, water-boiled pupa and ground pupa powder are eaten for their nutritional value. It was reported that each year in China, over 1 000 patients suffer anaphylactic reactions after consuming silkworm pupa, foreign tourists among them.37 Buckwheat allergy has been described in China, Japan and Korea because it is used to make noodles, cakes and biscuits, and is consumed in large quantities, particularly in Japan, where it is used to make Soba noodles.38,39 Bird’s nest appears to be the most common cause of food-induced anaphylaxis among Singaporean children.28 It has been documented that the reaction is IgE-mediated and that the major allergen is a 66 kDa glycoprotein.40 Chestnut is frequently consumed in Korea, and represented the third most common food allergen as diagnosed by SPT among adults and children in Korea.41 Royal jelly is produced by worker bees as food for their larvae, and reports of asthma exacerbations and anaphylaxis to it have come from Hong Kong42 and Australia.43 Sesame is a major food allergen in Israel and is introduced early into the diet of children in this country, while chickpea is a staple food in India and is introduced into the child’s diet at an early age and has been reported as a cause of anaphylaxis.42

The relevance of food sensitisation, especially in atopic children, can be difficult to establish. Several Asian countries have reported rates of food sensitisation among atopic children below 5 years of age. The percentages and patterns vary depending on the geography and dietary exposures. In Northern China, around a third of atopic children were sensitised to each of milk and egg, while the study in Taiwanese children with atopic dermatitis suggested high rates of sensitisation to shrimp (62.7%), followed by egg white and milk (both 49.2%) and then peanut (35.6%).13 Unfortunately, as patients sensitised to food allergens are commonly clinically tolerant, these data tell us relatively little about the true prevalence of clinical allergy.

ALLERGENS IN LATIN AMERICAN COUNTRIES

Several studies have described the occurrence of self-reported reactions to food and many evaluations have been conducted to assess the frequency of sensitisa-

![Fig. 1. World map showing range of food allergens in order of decreasing frequency in specific developing countries](image-url)
tions by means of SPT and IgE assays, yet the precise prevalence of FA in Latin American countries is not known.21,43

In Colombia, a large cross-sectional study was conducted in children and adults in a randomised selection in Cartagena City. Questions covered personal and family history of allergies and FA. The overall prevalence of self-reported FA was 14.9%. Fruit/vegetables (41.8%), seafood (26.6%), and meats (20.8%), were the most reported allergens and the most frequently reported symptoms were skin (61.4%), gastrointestinal (29.1%), and respiratory reactions (8.6%).21

In Argentina, self-reported FA in adults via phone survey was estimated at 5.1% (n = 48/944).22

In Brazil, Naspitz et al.23 determined total and specific IgE serum levels to inhalant and food allergens (RAST, UniCAP – Pharmacia) among children attending an allergy clinic and age-matched controls. In this study a RAST ≥ class 1 was considered as positive (R+). Both the levels of total IgE and the frequency of R+ were significantly higher among atopic subjects (79%) compared with controls (26%). Although R+ to aeroallergens were more frequently reported, sensitisations to food allergens like fish (29.5 and 13.3%, p < 0.05), egg (24.4 and 4.8%, p < 0.05), cow’s milk (23.1 and 3.2%, p < 0.05), wheat (20 and 8.1%, p < 0.05), peanuts (14 and 4.8%, p < 0.05), soya (11.8 and 4.8%, p < 0.05), and com (10.6 and 4.8%, p < 0.05) were found in allergic children and controls respectively.23

In Chile, 408 allergic children between 8 months and 5 years of age were skin-prick tested for common allergens. House-dust mite predominated but sensitisation to cow’s milk, egg and beef was 7% each in children younger than 3 years old. For children between 3 and 5 years old, milk, seafood, peanut (1.1%) and soya were the most common food allergens. Soya (5.9%) and interestingly, orange (3.1%), were the most common sensitisations to foods in children older than 5 years old.24

In Mexico, a prospective observational survey of mothers from three different nurseries looked for adverse reactions to foods. The diagnosis of FA was based on the patient’s history, and when it was necessary, food exclusion and food challenges were performed. The diagnoses were: lactose intolerance (1.7%), allergy to eggs (0.6%), carrots (0.3%), food additives (0.6%), sausages and ham (0.3%). A 3.7% prevalence of adverse reactions to food was found in this population.25 Another study, reviewing the clinical records of allergic children for SPT results for food allergens noted that 50% of the children were sensitised to only 1 food allergen, 25% to 2 and 3% to more than 6. Fish, milk, seafood, soya, beans, orange, onion, tomato, chicken, nuts and strawberry were responsible for 58% of the total of sensitisations. Fish (12%) and cow’s milk (7.7%) were the most common.26

Figure 2 compares the available SPT data for fish and egg allergy in three Latin American countries.23,26

AFRICA

There is a dearth of paediatric FA data in the literature from African countries. However, there are some useful data from South Africa, including a prospective descriptive study of all children attending a Cape Town allergy clinic over a 2-month period in 2008. Karabus and Motala27 analysed data from 400 children including: age at presentation, sex, ethnic group and clinical diagnosis. Laboratory data included: total IgE, CAP-RAST, SPTs and elimination-challenge testing. The data are shown in Figure 3. In patients with FA there was a high prevalence of peanut allergy. In patients under the age of 3 years, the most common food allergens were egg, peanut and milk. In children over 3 years, peanut is the most common food allergen followed by egg and milk. Interestingly, potato is an emerging FA that may play a role in difficult-to-treat atopic eczema - studies are in progress to evaluate this. Another study looking at peanut allergy in Xhosa children in Cape Town44 showed that, despite a 5% rate of peanut sensitisation, none of the children was peanut allergic (prevalence 0%: 95% CI 0.0-2.4%). The reasons for this are under examination and are likely to be related, in part, to cultural differences in diet and peanut exposure in the Xhosa population.

There are very limited relevant data from other African countries.

Fig. 2. Fish and egg allergy prevalence in Latin American children based on skin-prick test data.
it remains very difficult to establish the true extent of the problem. By relying on patient-reported questionnaire data or objective data from allergy tests, without confirmatory provocation challenges, we are unable to draw firm conclusions either regarding current prevalence of FA or a change over time. Robust studies using gold standard diagnostic methods are costly and time-consuming but will be the only way health services can truly estimate disease burden. Novel FAs that are found in varying geographical locations are also of importance especially as exotic foods are increasingly imported from one part of the world to another.

REFERENCES


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Comprehensive references and bibliographic information are provided for various studies and reports related to allergic reactions, food allergy, and related health issues. The text includes contributions from multiple authors and institutions, reflecting a diverse range of research perspectives and methodologies. The references cover a broad spectrum of topics, including epidemiological studies, allergic reactions among infants, and the prevalence of food allergy in various populations.

The references emphasize the importance of understanding the mechanisms behind allergic reactions, the impact of food allergies, and the strategies for managing and preventing adverse outcomes. The text underscores the need for continued research and collaboration among healthcare professionals, policymakers, and the public to address the challenges posed by allergic conditions.