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Epidemiology of food allergy

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Abstract Food allergies are associated with considerable psychosocial stress and restrictions in quality of life. While parents often report food allergies in their children, studies show that the perceived prevalence is often higher than the actual diagnosed prevalence. Epidemiological studies show an increasing prevalence worldwide, with significant regional differences. In Europe, self-reported prevalence varies widely, from less than 1% to over 10%, depending on region, age and foods analysed. In North America and Northern Europe, peanut and egg allergies are more common, while shellfish and fish allergies dominate in Asia. Environmental factors, ethnicity, genetic predisposition, dietary habits and socioeconomic conditions play a significant role in the development and distribution of food allergies. These factors must be taken into account when developing prevention and treatment strategies.

Keywords Prevalence · Diagnosis · Sensitization · Dietary habits · Prevention

Introduction

The psychosocial stress caused by food allergies is considerable due to the associated reduction in quality of life. This represents a growing burden for families and society, and strategies for prevention, diagnosis and treatment are needed.

Epidemiological studies are crucial both for understanding the aetiology of food allergies and for developing evidence-based guidelines for the prevention and clinical management of food allergies. For example, epidemiological data from the late 1980s and 1990s indicated that delayed introduction of peanut resulted in a 10-fold prevalence of peanut allergy in children of Jewish descent in London compared to children in Israel, where peanut was consumed earlier and more frequently [1]. Subsequent intervention studies brought a paradigm shift in our scientific understanding of the pathogenesis and prevention of food allergy [2].

"Perceived" food allergy

The frequency of food allergies in children is often overestimated by their parents, which is partly due to a lack of knowledge or misinterpretation of the symptoms, but also to different diagnostic criteria for food allergies.

For example, in a US study, 30% of parents reported that their child had a food allergy. They were also asked how the diagnosis was made. Only one in five medically diagnosed food allergies was confirmed by oral challenge testing, in contrast, in 32% of cases this medical diagnosis was made without any further diagnostics [3].

A recent study of two large German birth cohorts (KUNO Kids and Ulm SPATZ Health Study) found that the point prevalence of parent-reported food allergy symptoms in children aged 1 and 2 years was 13.2 and 13.9% respectively [4].

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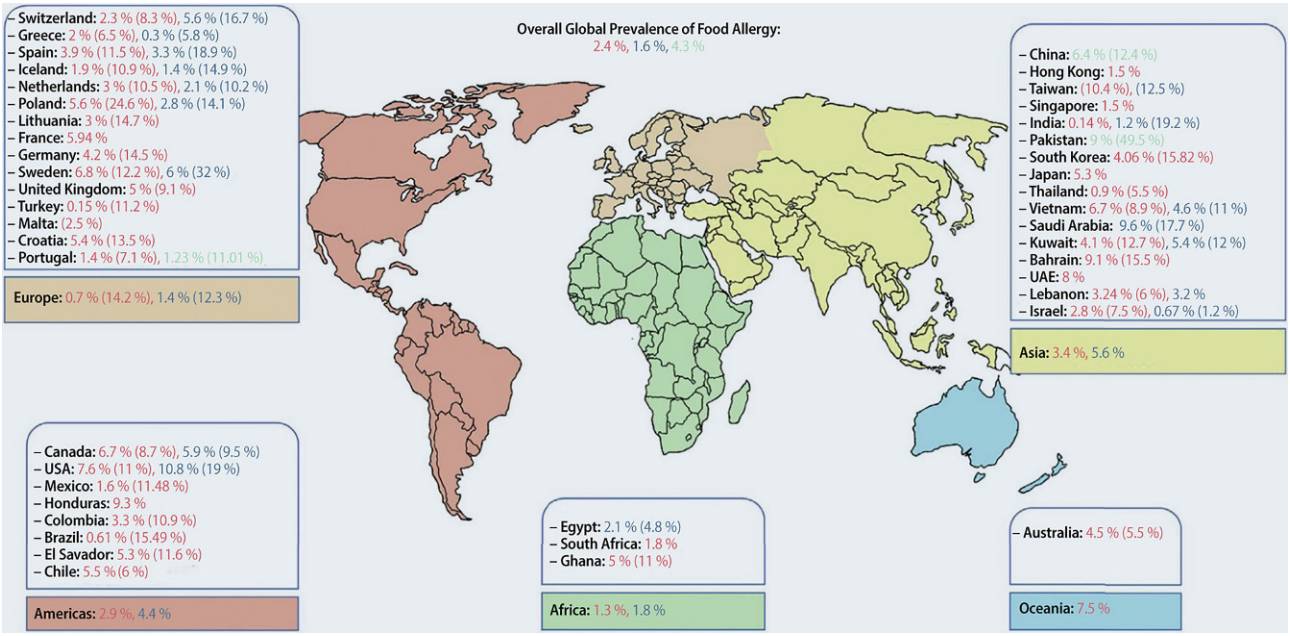

Fig. 1 Prevalence of food allergy (FA) around the world according to clinical diagnosis of FA (represented in bold) and self-reported FA (indicated between parentheses). Clinical diagnosis of FA is defined as physician-confirmed FA based on suggestive history and allergen-specific immunoglobulin E (IgE) evidenced by skin prick testing and/or measurement of specific IgE, or based on challenge-proven FA. Different age groups are represented in different colours (adult in blue; children in red; and all age groups, including adolescents, in green)

Actual food allergy worldwide

Childhood food allergies are increasing in prevalence and affect around 8% of children and 10% of adults in industrialised countries [5]. They show clear geographical differences (Fig. 1). They are also influenced by age, ethnicity, genetic predisposition, dietary habits and environmental factors.

In North America and Northern Europe, for example, peanut and hen's egg allergies are more common, while shellfish and fish allergies dominate in Asia [6].

In Europe, the prevalence of self-reported food allergies in school children varies considerably, from 6.5% in Athens to 24.6% in Lodz. The prevalence of food sensitisation ranges from 11.0% in Reykjavik to 28.7% in Zurich. In all centres, most food-sensitised persons have a primary food allergy. However, birch pollen-associated food allergies are common in Central and Northern Europe. Food allergies to milk and hen's egg occur frequently throughout Europe and to fish and shrimp mainly in the Mediterranean region and in Iceland. Peach, kiwi and peanut are important food allergens in most countries, as well as hazelnut, apple, carrot and celery in Central and Northern Europe and lentils and walnut in the Mediterranean region [7].

In southern Europe, on the other hand, allergies to lipid transfer proteins (LTP), which are found in peach and other foods, dominate. These allergies are often severe and can lead to systemic reactions [8].

A recent study from the USA, which analysed data from over 218,000 children, found that the cumulative incidence of IgE-mediated food allergies is 4.0%, with peanuts (1.9%), hen's egg (0.8%) and shellfish (0.6%) being the most common allergens [9].

In Australia, the HealthNuts study showed that the prevalence of food allergy confirmed by oral challenge testing at 1 and 4 years of age was 11.0 and 3.8%, respectively. At the age of 4 years, the prevalence of peanut allergy was 1.9%, hen's egg allergy 1.2% and sesame allergy 0.4%. By the age of 6 years, hen's egg allergy disappeared more frequently (89%) than peanut allergy (29%) [10].

The prevalence of hen's egg allergy was highest at the age of 1 year and decreased considerably at the age of 10 years (9.5 and 0.6% respectively). At the ages of 6 and 10 years, peanut was the most common food allergy (3.1 and 2.9%), followed by cashew allergy (2.8 and 2.6%). Peanut allergy only disappeared in 3.8% between the ages of 6 and 10 years, and cashew allergy also persisted between the ages of 6 and 10 years. Hen's egg was the third most common allergy at the age of 6 years (1.2%), while hazelnut was the third most common at the age of 10 years (0.8%). A definite wheat allergy was rare in both age groups (e.g. 0.04%), although the prevalence of possible wheat allergies suspected by parents was higher at 0.8%. A similar pattern was observed for cow's milk allergy. All other allergen triggers were rare and generally affected less than 0.5% of all food allergies between the ages of 6 and 10 years [10].

At the ages of 6 and 10 years, sensitisation to aeroallergens was more common than sensitisation to food. Overall, the prevalence of sensitisation to at least one

food decreased between the ages of 1 and 6 years and then remained stable between the ages of 6 and 10 years (10.1 and 11.2%). Peanuts and tree nuts were the most common triggers for food sensitisation between the ages of 6 and 10 years. The prevalence of sensitisation to peanuts, eggs and hazelnuts decreased between the ages of 6 and 10 years, while sensitisation to sesame and soy increased [11].

Factors associated with persistence of peanut allergy at 1 year of age were a positive peanut prick test of 8 mm or more, sensitisation to nuts and severe eczema with early onset. Factors at 1 year of age associated with persistence of hen egg allergy at 6 years of age were a positive prick test of 4 mm or greater, other (peanut and/or sesame) food sensitisation, allergy to baked hen egg and early onset severe eczema [12].

Grabenhenrich et al. [13] analysed the prevalence of food allergies in school children aged 6 to 10 years in eight European countries (Germany was not included). The study was based on a follow-up of a multicentre European birth cohort (EuroPrevall-iFAAM). In 16.2% of the total of 6105 children, parents reported allergic reactions after eating food. However, the results of the study showed that 1.4 to 3.8% of schoolchildren suffered from food allergies, based on the results of double-blind, placebo-controlled oral food challenge. The most common allergens were hazelnut and peanut.

A recent update on the prevalence of food allergies in children in Europe is provided by a systematic review and meta-analysis by Spolidoro et al. [14]: 76 of the 110 studies included were conducted in children. The results show that the lifetime prevalence of self-reported food allergies in children in Europe is 18.7%, while the point prevalence is 14.1%, lowest in Northern Europe and highest in Western Europe.

The point prevalence of sensitisation based on specific IgE is 18.4%, while skin prick test positivity is 4.5%, lowest in Southern Europe and highest in Western Europe.

In contrast, the point prevalence based on clinical history or positive food challenge to all foods from 2000–2021 is 2.7% and based on positive food challenge 0.7%. The prevalence was lowest in Southern Europe and highest in Northern Europe.

The same meta-analysis showed the following data for the eight major food allergies in all age groups for self-reported lifetime prevalence vs. prevalence confirmed by food challenge [15]: cow's milk 5.7% vs 0.3%, hen's egg 2.4% vs 0.8%, wheat 1.6% vs 0.1%, soya 0.5% vs 0.3%, peanut, 1.5% vs 0.1%, tree nuts 0.9% vs 0.04%, fish 1.4% vs 0.02% and shellfish 0.4% vs 0.1%.

Cow's milk, hen's egg, wheat and soya allergies or sensitisation were more common in children than in adults, while peanut, nut and shellfish allergies or sensitisation were more common in adults than in children. The observed result is consistent with the fact that cow's milk, hen's egg, wheat and soya allergies usually occur earlier in life and children tend to develop tolerance before adulthood. In contrast, fish and shellfish allergies develop later and, like peanut and nut allergies, tend to persist into adulthood.

Frequency of food allergies in Germany

The KiGGS study (Child and Adolescent Health Survey, 2003-2006) provided comprehensive data on sensitisation to inhalant and food allergens in children and adolescents in Germany. In the study, specific IgE antibodies against 20 common allergens, including 9 food allergens, were measured in 12,988 children aged 3–17 years. The distribution of food sensitisation showed that 40.8% of 3- to 17-year-olds were sensitised to at least one of the allergens tested. Sensitisation was more common in boys than in girls (45.0% vs. 36.4%). Younger children (3–6 years) showed lower sensitisation rates compared to older children and adolescents (7–17 years). Of all food allergens, the highest prevalence was recorded against peanut (10.6%), followed by apple, carrot and wheat (9.2–9.9%), as well as chicken egg white, milk protein and soya bean (5–6.3%). The most common food sensitisations in younger children (0–3 years) were cow's milk and hen's egg and in older children and adolescents (11–17 years) apple and carrots, the latter often in connection with cross-reactivity to pollen allergies [16].

The prevalence of food allergy confirmed by a double-blind, placebo-controlled food challenge was 4.2% in Germany in 2004, with 3.5% of children and adolescents having symptoms of food allergy and 0.7% having symptoms of nonallergic food hypersensitivity [17].

In the EuroPrevall birth cohort, which included over 12,000 infants from nine different European countries, 2% of infants in Germany were allergic to chicken eggs [18] and 0.5% to cow's milk [19]. A further 0.5% showed a non-IgE-mediated cow's milk allergy.

Data from more recent studies in Germany confirm a significantly lower prevalence of medically diagnosed food allergies in children aged 1 and 2 years compared to the self-reported prevalence, which was 2.4 and 2.7% in the KUNO Kids cohort and 2.3 and 3% in the SPATZ cohort. Overall, it was shown that the prevalence of food allergies in young children has remained stable over the last 10 years, but at a high level, with cow's milk and citrus fruits being common food allergens suspected by parents [4].

The most common foods that trigger anaphylaxis in children in Germany are peanut, cow's milk, cashew and hen's egg and in adults wheat flour, shellfish, hazelnut and soya [20].

Predisposing factors

The genetic influence on food allergy was confirmed in a meta-analysis. A family history of atopic dis-

eases, including asthma, eczema and allergic rhinitis, increases the risk of food allergies by a factor of 1.9 to 2.1 [21].

Filaggrin mutations are a risk factor for allergy to various foods (hen's egg, cow's milk, peanut, hazelnut, fish, soya, cashew, walnut and sesame) and particularly favour the persistence of hen's egg and cow's milk allergy beyond early infancy [22].

A recent systematic review and meta-analysis by Christensen et al. [23] confirmed the previous findings that the severity of atopic dermatitis (AD) in children has a strong influence on the prevalence of food sensitisation and food allergy. The prevalence of sensitisation and food allergy increased with the severity of AD and was 49.8% vs. 31.4% in children with a moderate-to-severe course.

Environmental factors play a significant role in the development of food allergies. The studies show that children in urban areas have a higher prevalence of food allergies than children in rural areas. For example, the prevalence of food allergies in children in urban areas in the USA is 9.8% compared to 6.2% in rural areas [24]. This is generally attributed to higher exposures to air pollution and indoor allergens and less contact with animals and nature. In rural areas, contact with farm animals and consumption of non-pasteurised milk may be protective [25, 26].

Dietary habits also vary regionally and influence the prevalence of food allergies. In countries where a Western diet with a high proportion of processed foods and low fibre content predominates, food allergies are more common. One possible explanation is the observation that this diet can negatively influence the microbiome and the immune response [27].

Socioeconomic factors are also decisive: children from lower-income households often have less access to diagnosis and treatment of food allergies. There are also differences in the prevalence and severity of food allergies between different ethnic groups. In the US, Asian, Hispanic and non-Hispanic black children have higher rates of food allergies compared to non-Hispanic white children [28]. A recent study in the US found that non-Hispanic white children and adults have the lowest rate of self-reported or parent-reported food allergies (9.5%) compared to Asian (10.5%), Hispanic (10.6%) and non-Hispanic black (10.6%) children and adults. An analysis of 60,000 Australian school children found that those born in Australia to Asian mothers were more than 2.5 times more likely to have a nut allergy at age 5 than non-Asian children. In contrast, children born in Asia who subsequently migrated to Australia had a significantly reduced risk. Migration from Asia after the early infant period appears to protect against the development of a nut allergy [29].

Non-IgE-mediated food allergies

Food protein-induced enterocolitis syndrome (FPIES) and eosinophilic diseases of the gastrointestinal tract (e.g. eosinophilic oesophagitis, EoE) pose a particular diagnostic challenge, as they are often misdiagnosed and incorrectly treated due to the sometimes delayed gastrointestinal manifestation and the lack of typical immediate allergic type symptoms.

The epidemiological data on FPIES are limited. Spanish and Japanese birth cohorts showed an incidence rate of 0.7 and 1.6% respectively. A population-based prevalence study in the USA published in 2019 estimated the lifetime FPIES prevalence in children at 0.5% and also showed a high rate of comorbidities such as IgE-mediated food allergies, asthma, allergic rhinitis and atopic dermatitis [30].

The triggers for acute FPIES depend on local dietary habits: in the USA it is cow's milk, soya, rice, in Australia rice, cow's milk and hen's egg, in Spain cow's milk followed by fish and hen's egg, in Italy and the UK fish, milk and in Greece fish, cow's milk and rice.

The most common trigger for acute FPIES in Germany was cow's milk, followed by fish, vegetables (e.g. potatoes, pumpkin), meat (e.g. beef) and cereals. Milk protein was the most common trigger for chronic FPIES [31].

In a recently published systematic review and meta-analysis of 25 studies up to December 2022, the prevalence of eosinophilic oesophagitis (EoE) in Europe varied widely. The increase in incidence across Europe over the last 30 years has been greater than the increase in the number of oesophagogastroduodenoscopies performed. In children, the highest incidence of EoE from regional studies was documented in Spain (15.4 per 100,000 person–years) and the lowest in Slovenia and the Netherlands (< 1.5/100,000). The most frequently reported comorbidities in children were erosive oesophagitis (41.8%), followed by asthma (31.3%), food allergies (25.6%), rhinitis (24.6%) and dermatitis (11.9%) [32].

Pollen-associated food allergies

Pollen-associated food allergies in children in Germany and Europe are common and increase with age. The prevalence varies depending on the region and is strongly influenced by sensitisation to specific pollen species such as birch.

Furthermore, there are differences in the prevalence of pollen-associated food allergies between rural and urban areas, e.g. sensitisation to hazelnut and birch pollen allergens is more common in urban areas among schoolchildren in Berlin.

A birth cohort study in Germany found that 1.9% of school-aged children had symptoms of hazelnut allergy, with half of these cases being due to a primary hazelnut allergy. In addition, 11.6% of children re-

ported symptoms of birch pollen allergy, and 0.6% had both birch pollen and hazelnut allergy symptoms [33].

Another study in Paris showed that sensitisation to birch pollen in asthmatic schoolchildren increased from 11.6% in the 1990s to 31% in the 2010s. This led to an increase in pollen-associated food allergies from 6 to 16%. Climate change and environmental factors could be responsible for this significant increase in allergic diseases [34].

Conclusion

The prevalence of food allergies in children has increased overall over the last 10 years, although there are significant regional differences. This represents a considerable burden for society and includes both the health effects, such as the risk of anaphylaxis, as well as the impairment of quality of life and the economic costs. Food allergies are most common in infants and young children, with a significant proportion of these allergies persisting into school age. Environmental factors, dietary habits and socioeconomic conditions significantly influence the regional distribution of food allergies in children. These factors must be taken into account when developing prevention and treatment strategies.

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