

EuroPrevall cohort study and its application in Asia

Alessandro Fiocchi

Epidemiologic data show a constant increase in food allergy prevalence among Western populations. Following this trend, is an increase in hospitalization for food allergies, particularly among children. United Kingdom (UK) surveys revealed highly significant growth in food allergy admissions, from 5 to 26 per million people, from 1990 to 2004, with even higher rates for children, a nearly seven-fold increase from 16 to 107 per million.¹

Current estimates of the prevalence of food allergies vary widely between different populations and studies. However, these apparent differences may in large part reflect non-uniformity in study designs, populations and data analysis and interpretation. Other possible sources of heterogeneity include variability in epidemiology survey response and participation rates, length of initial questionnaires, use of a second stage assessment (eg, questionnaire followed by telephone interview), and having several prevalence estimates (eg, point, period and accumulative) in a cohort study. Technical issues such as use of oral food challenge, variability in the cut-offs for positive skin-prick test (SPT) and immunoglobulin E confirmation, and differences in allergens also confound conclusive determination of food allergy prevalence rates.

These problems were highlighted in a meta-analysis of 51 original studies from 24 countries, which produced markedly varying results depending on the assessment method used (Table 1).² Notwithstanding considerable variation in the results of studies of food allergenicity, a large randomized telephone survey in 10 European countries, showed cow milk to be the most often reported food allergy in children and the second most common one in adults.³

From Department of Child and Maternal Medicine University of Milan Medical School at the Melloni Hospital, Milan, Italy

“Prevalence of allergic disease in Asia is likely to increase to similar levels to those seen in the West.”

Alessandro Fiocchi

The EuroPrevall birth cohort study on food allergy

The European Union (EU) funded EuroPrevall birth cohort study is a multidisciplinary project involving nine EU countries (Table 2),⁴ that was set up to resolve such discrepancies, specifically, to: provide comprehensive information and authoritative estimates of the prevalence of food allergy across European countries; detect regional differences in the prevalence and risk factors of food allergy; determine whether food allergy is less prevalent in developing countries on the basis of lifestyle-related factors (eg, hygiene, diet, pollution, susceptibility to infections); quantify the socio-economic burden and costs of food allergy.

EuroPrevall participating centers recruited 12,049 infants and their families, who were followed-up for 24 months. To ensure consistency in reporting and data analysis, the study used double-blind placebo-controlled food challenge, which is

Table 1. Varying prevalence estimates of food allergies in 24 countries²

Assessment method	Proportion of overall population hypersensitive (%)					
	Any food	Peanut	Cow milk	Egg	Fish	Shellfish
Self-report	13.0	0.8	3.0	2.0	0.8	0.2
IgE-positive	5.0	3.8	3.0	2.0	0.3	
SPT	13.0	3.0	1.0	0.6	0.8	2.7
IgE & SPT	3.0	1.2	0.7	1.0	0.3	0.7
DBPCFC	3.0		0.8	0.7	0.4	0.2

IgE, immunoglobulin E; SPT, skin-prick test; Double-blind placebo-control food challenge

Table 2. EuroPrevall study centers

Country	City
Germany	Berlin
Greece	Athens
Iceland	Reykjavik
Italy	Milan
Lithuania	Vilnius
Netherlands	Amsterdam
Poland	Lodz
Spain	Madrid
United Kingdom	Southampton

the gold-standard food allergy diagnostic criterion, coupled with a standardized questionnaire to gather information on reported food hypersensitivity of infants, parents, and siblings; nutrition and supplements during pregnancy; received medications; mode of delivery; socio-demographic background; and environmental exposures.⁴

EuroPrevall baseline data showed that self-reports of ever having adverse reactions to food were considerably more common in mothers from Germany (30%), Iceland, UK and the Netherlands (all 20–22%), compared to those from Italy (11%), Lithuania, Greece, Poland and Spain (all 5–8%). Prevalence estimates of parental asthma, allergic rhinitis and/or eczema were highest in the northwest (Iceland, UK), followed by west (Germany, the Netherlands), south (Greece, Italy, Spain) and lowest in central and east Europe (Poland, Lithuania). More than 17% of Spanish and Greek children were exposed to tobacco smoke in utero, compared to only 8–11% for other countries. The cesarean section rate was highest in Greece (44%) and lowest in Spain (<3%). Country-specific differences were found for antibiotic use, pet ownership, type of flooring and babies' mattresses.⁵ Future publications will relate these data to the actual food allergy incidences, and will include country differences, sensitivity and challenge-confirmed allergy to foods as hen egg, cow milk, wheat, peanuts, soy, and fish, and development of tolerance to these foods at 24-month follow-up. A previous prospective study, reported the mean duration of cow milk allergy to be 27 months after diagnosis.⁶

Food allergy prevalence in Asia

Asia has the fastest growing populations in the world. Socio-economic growth in the developing countries from this region remains strong as they become more urbanized and industrialized, with the consequence that the prevalence of allergic disease in Asia is likely to increase to similar levels to those seen in the West. Comparison of cross-sectional data collected in 1999 and again in 2009 at the same clinic in Chongqing, China, showed a two-fold increase in the prevalence of food allergy, from 3.5 to 7.7% ($p = 0.017$), and SPT sensitization, from 9.9% to 18.0% ($p = 0.02$).⁷

Despite earlier attempts to gauge the burden of food allergy in Asia, for example, the Global View of Food Allergy (GLOFAL) study, its true prevalence remains unclear. Current epidemiological data derive from certain countries with keen medical professionals and local allergy organizations; data from Thailand, Israel and Korea, show the general prevalence rate of self-reported food allergy to range from 1.2% to 6.5%.^{8–10} Higher prevalence was reported in Hong Kong, where parent-reported food allergy was 8.1% of pre-schoolers, while parent-reported, doctor-diagnosed food allergy was 4.6%.¹¹ The top-ranking allergy-inducing foods comprised shellfish, egg, peanut, beef, cow milk, and tree nuts. Moreover, cases of parent-reported food allergy were higher in children born and raised in Hong Kong than in those born in mainland China.¹¹ While geography and lifestyle certainly affect food allergy trends, maternal atopic dermatitis and Autumn birth have also been reported to influence the development of food allergy in Korea.¹² Cow milk was the second most common food allergen in Japan, Korea, and China and the third most common in Thailand. It is second only to egg as a primary cause of anaphylactic shock in Japan.¹³

The EuroPrevall birth cohort study clearly indicates that a wide range of factors influence the development of food allergy; these include geographic, environmental, demographic and economic determinants. Since EuroPrevall covered only limited areas in Europe, its findings may not necessarily apply to Asia; therefore, any policies based on this study should be implemented carefully. The results of further Asian birth cohort studies are eagerly awaited.

References

1. Gupta R, Sheikh A, Strachan D, Anderson H. Time trends in allergic disorders in the UK. *Thorax*. 2007;62:91-6.
2. Rona R, 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;120:638-46.
3. Steinke M, Fiocchi A, Kirchlechner V, Ballmer-Weber B, Brockow K, Hischenhuber C, et al. Perceived food allergy in children in 10 European nations. A randomised telephone survey. *Int Arch Allergy Immunol*. 2007;143:290-5.
4. Keil T. The multinational birth cohort of EuroPrevall: background, aims and methods. *Allergy*. 2010;65:482-90.
5. McBride D, Keil T, Grabenhenrich L, Dubakiene R, Drasutiene G, Fiocchi A, et al. The EuroPrevall birth cohort study on food allergy: baseline characteristics of 12,000 newborns and their families from nine European countries. *Pediatr Allergy Immunol*. 2012;23:230-9.
6. Fiocchi A, Terracciano L, Bouygue GR, Veglia F, Sarratud T, Martelli A, et al. Incremental prognostic factors associated with cow's milk allergy outcomes in infant and child referrals: the Milan Cow's Milk Allergy Cohort study. *Ann Allergy Asthma Immunol*. 2008;101:166-73.
7. Chen J, Hu Y, Allen KJ, Ho M, Li H. The prevalence of food allergy in infants in Chongqing, China. *Pediatr Allergy Immunol*. 2011;22:356-60.
8. Santadusit S. Prevalence of adverse food reactions and food allergy among Thai children. *J Med Assoc Thai*. 2005;88:S27-32.
9. Dalal I. Food allergy is a matter of geography after all: sesame as a major cause of severe IgE-mediated food allergic reactions among infants and young children in Israel. *Allergy*. 2002;57:362-5.
10. Lee S. Prevalences of symptoms of asthma and other allergic diseases in Korean children: a nationwide questionnaire survey. *J Korean Med Sci*. 2001;16:155-64.
11. Leung T, Yung E, Wong Y, Lam C, Wong G. Parent-reported adverse food reactions in Hong Kong Chinese pre-schoolers: epidemiology, clinical spectrum and risk factors. *Pediatr Allergy Immunol*. 2009;20:339-46.
12. Kim J, Chang E, Han Y, Ahn K, Lee S. The incidence and risk factors of immediate type food allergy during the first year of life in Korean infants: a birth cohort study. *Pediatr Allergy Immunol*. 2011;22:715-9.
13. Sackesen C, Assaad A, Baena-Cagnani C, Ebisawa M, Fiocchi A, Heine RG, et al. Cow's milk allergy as a global challenge. *Curr Opin Allergy Clin Immunol*. 2011;11:243-8.