

EDITORIAL

Risk factors for the development of egg allergy: progress to date and future directions

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A dramatic increase in prevalence of food allergy has been observed in several developed countries over the last 10–15 years, making it an evolving public health challenge (1–5). Estimates of 6–8% have been reported for the prevalence of food allergy among children (1,2). Given that the increasing prevalence of asthma and allergic rhinitis was first observed around 50 years ago and may now have peaked in some settings (6), the recent emergence of food allergy has led some authors to suggest that we may be entering the ‘second wave’ of the allergy epidemic (3). The difference in the timing of emergence of asthma and allergic rhinitis, on the one hand, and food allergy, on the other hand, has led to suggestions that different risk factors may be at play (1,3).

Among infants and young children, egg allergy is the second most common food allergy after cow’s milk allergy (7–9). Although potential risk factors have been reported for food allergy in general (4, 5, 10), to date, no population-based study has investigated risk factors specific for the development of egg allergy. The study by Koplin et al. (11) investigating environmental and demographic risk factors for the development of egg allergy in infancy is therefore a welcome contribution to this evidence base. Involving the study of over 5000 12-month infants sampled from the general population, egg allergy was established using initial screening for allergen-specific IgE sensitization and, if present, confirmed using the gold standard of an oral food challenge.

The authors found that ownership of a dog at home and having older siblings were associated with a decreased risk of egg allergy, but that a family history of allergy and having a parent born in East Asia were associated with increased risk of egg allergy. Cesarean section delivery, use of antibiotics, attendance to day care, and maternal age were not associated with egg allergy. While in one sense these results are to be expected as these factors have also been noted in previous studies regarding food allergy and other allergic diseases (12), the study is a welcome development for its large sample size and being the first population-based study that has utilized the more objective oral food challenge to confirm the presence of egg allergy.

There are, however, a number of methodological issues arising from this study that warrant further consideration both in relation to the interpretation of these results and also for informing the development of future studies. Firstly, the study design was cross-sectional, with data on the exposures of interest being collected in retrospect. Consequently, because information on the risk factors and the outcome was assessed at the same time, it is inherently difficult to conclude

on the temporal relationship between the factors investigated and the development of egg allergy. The issue of reverse causality is a potentially important source of bias in cross-sectional epidemiologic investigations. The authors attempted to justify their retrospective collection of data on the risk factors by pointing to the possibility that families of potentially allergic children may modify certain lifestyle factors perceived as being important to the outcome, but this line of argument is misdirected. It is well known that, in establishing a causal relationship, a prospective framework, whereby the assessment of exposure data precedes the onset of the outcomes of interest, provides much stronger evidence than other study designs and this approach should, if possible, therefore always be pursued. There are several methods to handle the issue of outcome-related modification of exposures, and these should be explored where research teams consider this to be a potential risk. Therefore, future studies investigating the risk factors for the development of egg allergy will strengthen the evidence base by employing prospective study designs. In so doing, it must be appreciated that egg allergy has its origins early in life; thus, efforts should also be made to collect comprehensive information on potential risk factors prenatally, antenatally, as well as at birth and very early in life.

Secondly, the study was also primarily exploratory in nature (i.e. there was no prior hypothesis on the particular risk factors of interest); hence, further studies are now needed to confirm the putative role of the observed factors in the development of egg allergy during infancy.

Thirdly, it should be noted that a range of potential risk and confounding factors of interest were not considered in the present analysis. These include socioeconomic variables (e.g. income, education, and occupation), variables describing the home environment (e.g. dampness, mold, or other chemicals), season of birth, and being born in farming household or not. A recent review of studies investigating the role of diet in the development of asthma and allergy in children identified inadequate handling of potential confounding as a limitation to the evidence provided in these studies (13). A follow-up study to that review has proposed a comprehensive set of factors to take into account in future studies in order to enhance this evidence base (14).

Although the authors made robust attempts in their statistical analysis, considering the exploratory nature of the study, a less conservative statistical approach would have been welcomed, particularly the alpha significant level ($P = 0.1$) used to select variables into the final multivariable

model. An alpha level of $P < 0.20$ has been recommended in this type of setting, as factors may show their significance in the presence of others (15). The use of stepwise statistical techniques for variable selection would have also helped here in order to establish the most important factors, while at the same time excluding the less important ones.

Overall, the present study is a bold call to more rigorous investigations into the environmental factors that may be causing the increasing prevalence of egg allergy in particular and, more generally, food allergy. The authors have demonstrated that such investigation can be carried out not just among children selected based on allergic risk, but also in population-based studies. Most importantly, the authors have demonstrated that the less objective methods of establishing food allergy (particularly parental or self-reported surveys) can be overcome by utilizing oral food challenge, which is the gold standard of establishing food allergy in infancy and childhood. This work should therefore encourage research teams that similar studies can be mounted in other parts of the world for the study of both egg and other food allergies. However, further studies are required to confirm the putative roles of the factors observed in this study in the development of egg allergy, and this evidence base will be enhanced if future studies employ prospective study designs, and consider factors at the prenatal, antenatal, and postnatal stages of life in order to establish the temporal relationship between the

factors of interest and food allergy. This will also provide greater certainty in establishing the causal nature of the relationship between risk factors and the development of food allergy (16).

Contributorship

AS conceived the idea for this article, which was drafted by BN and then revised in light of critical feedback from AS. Both authors approved the final submitted version of the manuscript.

Conflict of interests

None known.

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