

Association Between Food Allergy and Childhood Asthma: So Close and Yet So Far!

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The concept of food allergy/sensitization among children with asthma is a touchy topic for families as well as physicians. Many parents (and even physicians) restrict certain foodstuffs in affected children based on perceived association with symptoms and/or the traditional Indian concept of ‘hot’ and ‘cold’ foods. These days, physicians often order easily available (albeit expensive) allergy tests, and advise omission of items based on the reports. Such trends are observed in other countries also. However although about 20% children consume restricted diets, objective confirmation of food allergy (based on elevated specific IgE levels and food challenge) is present in less than 5% [1]. An older study from our institution also demonstrated poor correlation between parental perception of food allergy (with consequent dietary restrictions) and responses to food challenge [2]. Similarly, another study from south India showed a stark discordance between people reporting adverse effects with ingestion of brinjal (about 9%), positive skin prick test to brinjal extract (4.3%), and allergen specific IgE (0.8%) [3]. Further, about 2% of people surveyed had no symptoms on consumption, but skin prick test was positive. In fact, there is often discordance between results of food challenge tests and measurement of specific antibodies [4], and also among different methods for measuring antibodies [5]. Such data downplaying a relationship between food consumption and asthma symptoms and/or exacerbations, are countered by observations supporting a link between food allergy and other allergic conditions such as asthma, allergic rhinitis and atopic dermatitis. These studies

include associations between allergic symptoms and food consumption and/or relief in symptoms with modification(s) in diet [6, 7]. There is also evidence from multi-ethnic settings that there may be racial (perhaps genetic) differences in the prevalence of food allergy [8] as is the case with asthma. Despite these diverse pieces of evidence, a clear cause-and-effect relationship between food consumption and asthma symptoms has not been described. Against this backdrop, the systematic review by Zhou et al. published in this journal [9] throws further light on the matter.

The systematic review was undertaken to explore the prevalence of asthma (O = Outcome) among children (P = Population), with food allergy (E = Exposure), using primary and secondary research studies (S = Study design). However, the authors did not state the comparison appropriately. Rather than comparing food allergy (Exposure/ Risk factor) vs. no food allergy (C = Comparison), they stated a comparison between asthma and non-asthma.

The appropriate study designs for addressing the research question would be (i) comparison of asthma incidence between cohorts of children with and without food allergy, (ii) case-control studies examining food allergy as a risk factor for asthma, (iii) cross-sectional comparisons of children with and without food allergy to estimate asthma prevalence, and (iv) cohort/cross-sectional studies documenting food allergy prevalence among asthmatic children. However the last of these would require comparison against food allergy prevalence in the local population, derived through other studies. Rather than pursuing these lines of inquiry separately, Zhou et al. combined various approaches and clubbed all types of studies together.

Two electronic databases (Pubmed and EMBASE) were searched for published studies. The authors specified the search terms, search date, and search method. They also undertook additional searches of the reference lists of included

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studies. However, there is no information on language restriction. Notably the Cochrane Library was not searched. Although the search appears comprehensive, it is unclear if this was complete, as one apparently eligible Indian study by Kumar et al. [10] was not included. The authors omitted to include a Table of Excluded studies, hence completeness of literature searching could not be assessed. It is also interesting that the authors excluded 25 studies from a short-list of 32, yet included 8 (and not 7) in the systematic review! There was also no attempt to identify ongoing studies and/or unpublished data. A quality assessment tool was used, categorising each study as Good, Fair, or Poor in terms of methodological quality.

The research questions of the 8 included studies were quite different. Four of these [11–14] were based on the ISAAC questionnaire to determine the prevalence of asthma/wheezing, with a few additions to study ‘food allergy’. In contrast, one study [15] prospectively followed a small cohort of 80 infants admitted with wheezing, to determine the prevalence of asthma and food allergy at school age. Another was a serial follow-up of a Danish birth cohort till 6 y of age to determine the timing and pattern of sensitization to various antigens [16]. Yet another was a case-control study comparing food allergy among children with (and without) asthma [17]. Only one study [18] examined the prevalence of current asthma among children with and without food allergy. Besides these design differences there was dissimilarity among the studies in terms of demographic characteristics such as age, gender, ethnicity, etc.; and also more important issues such as outcomes evaluated, definitions of food allergy, and method of diagnosing/labelling asthma. For these reasons, it can be argued that it may be inappropriate to pool data from the 8 studies.

Inexplicably, four of the eight included studies [12, 14, 15, 17] are not included in the list of references [9].

Some of these methodological limitations preclude detailed analysis of the reported results. In general, there appears to be increased prevalence of food allergy (or rather food sensitization) among children with asthma (compared to those without asthma). Likewise, perhaps children with food allergy/sensitization are more likely to have asthma (at present or later).

What are the clinical implications of these data? At our institution’s Allergy and Asthma Clinic, although about 30% of several thousand asthmatic children (over a 15 y period) report symptom exacerbation/triggering with consumption of one or more foodstuffs, we neither restrict food items from diet, nor routinely test for food allergy. Families are advised to consider restricting specific food items (one at a time) only if there is (i) consistent response, *i.e.* each consumption is associated with symptoms, (ii) symptoms occur within minutes to hours after consumption, and (iii) a brief 2–4 wk trial of omission results in significant clinical improvement. More recently, many families present to the Clinic with test reports

suggesting allergy/hypersensitivity to multiple food items. Several of these children have discordance between test reports and parental perception of food allergy and/or asthma symptom exacerbation. Some reports are also positive for items that children have never consumed. These phenomena could be explained partly by cross-reactivity between antigens present in different foodstuffs [19–21], as well as cross-reactivity between food antigens and non-food compounds [22, 23]. It could also happen because the offending antigen is present in a food additive (such as coloring agents, flavoring agents, etc) rather than the food item itself [24]. Such observations also raise questions about the method of allergen testing and/or interpretation of findings. For these reasons, we do not advocate restriction of any food item based on test reports alone. Of course, it should be recognized that most asthmatic children in our setting may not have an atopic basis; hence food (and other allergen) sensitization may play a lesser role than in societies where atopy and allergy are dominant.

In conclusion, there are pointers to a relationship between food allergy/sensitization and asthma, although a causal link is yet to be demonstrated.

Compliance with Ethical Standards

Conflict of Interest None.

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