

RESEARCH ARTICLE

Food allergy in children with asthma and its correlation with level of asthma control

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Abstract

Background: There is paucity of regional data regarding food allergy among children with asthma.

Objectives: To estimate the proportion of children with asthma who have food-related respiratory symptoms and to correlate it with (a) skin prick test (SPT) results and (b) level of asthma control.

Methodology: This cross-sectional study involved children with asthma, aged ≥ 6 years attending the childhood asthma clinic in a tertiary care hospital, in the southern part of India from July 2017 to July 2019. Basic demography and clinical details were recorded. In subjects with a history of food allergy, skin prick test (SPT) was done using AllergoSPT according to guidelines recommended by British Society of Allergy and Clinical Immunology (BSACI). Asthma control was assessed using asthma control test (ACT) and childhood ACT questionnaires.

Results: Of the total 305 children included, the most commonly reported allergen was banana (45%, $n = 137$). The predominant symptom reported was wheezing (54%). SPT was positive in 76 children (24.9%). Level of asthma control (P value $< .01$), family history of atopy (P value $< .01$), and age at introduction of complementary foods (P value $< .01$) were significantly associated with food allergy.

Conclusion: Presumed food allergy is seen in one-fourth of children with asthma and significantly affects symptom control in them.

KEYWORDS

asthma control, children, food allergy

1 | INTRODUCTION

Food allergen sensitization is recognized as an important modifiable risk factor for asthma exacerbation.¹ Food-induced anaphylaxis is also an important cause of acute severe/life-threatening asthma exacerbation.² Although food allergens can vary across regions depending upon socio-cultural characteristics and availability of particular food in

the locality, globalization and increased social movement can bring people in contact with food from other countries or cultures and could be a reason for finding the increasing prevalence of food allergy in communities in which they had been considered rare in the past.^{3,4} Regional data regarding common food allergens and its effect on asthma symptom control are scarce and limited to a few geographic locations at present.⁵ Relying on patient-reported food allergy alone is

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an unreliable way of diagnosing food allergy and the scientific community is divided, on whether to do allergy testing in children with food allergy or not, with some vehemently opposing it and some others carrying out these tests in an indiscriminate manner. Therefore, there is a need for well-conducted robust studies in academic institutes to address this issue.

2 | OBJECTIVES

The primary objectives of our study were (a) to find out the proportion of children with asthma who have food-induced respiratory allergy symptoms and to correlate it with skin prick test (SPT) results, (b) to study the correlation of food allergy with level of asthma control. The secondary objective was to describe the factors associated with food allergy in children with asthma.

3 | MATERIALS AND METHODS

This was a cross-sectional study done between July 2017 and July 2019 at our hospital. The study was approved by our institute's post-graduate research monitoring committee and institute ethics committee for human studies (JIP/IEC/2017/0293). Our study population consisted of people belonging predominantly to South Indian Tamil-speaking ancestry and a rural background. Children 6 years and above regularly attending the childhood asthma clinic with clinical/spirometry evidence of asthma were included for the study after obtaining informed written consent from parent and assent from child (8 years and above). Children who had eczema, who were on drugs that can interfere with interpretation of SPT, those with brittle asthma, or those with acute exacerbation were excluded from the study. The sample size required was 83 in each group assuming a error of 5%, power of 80%, expected proportion of uncontrolled asthma as 20% and 40% among those without and with food allergy, respectively. However, we were able to recruit 76 cases and 229 controls. Basic demographics, clinical and treatment details were collected from the parents. For the diagnosis of food allergy, a history of symptoms attributable to a particular type of food along with SPT positivity for that particular food was considered as food allergy. The procedure of SPT was carried out as per the guidelines laid down by the British Society of Allergy and Clinical Immunology (BSACI) and emergency drugs and equipment to deal with the rare possibility of anaphylaxis were kept ready. A drop (10 μ L) of the suspected food allergen was placed on the forearm and a sterile lancet was used to prick the skin through the drop without causing bleeding. The allergen drops, including test allergens and positive and negative controls, were placed at a distance of 2 cm from each other to avoid cross reaction and were marked with an alphabet for identification. Twenty minutes after the prick, the site was examined for wheal and flare response and compared with positive and negative control. The test was considered as positive if a wheal greater than 3 mm, measured with a transparent scale, was produced, and reported as negative if there was no wheal

and flare or if it was 3 mm or lesser. Children with reported food allergy symptoms and SPT positivity were diagnosed as having food allergy to that particular food. Antigens (AllergoSPT), procured from Merck, were used for SPT. Asthma control was defined based on childhood asthma control test C-ACT/ACT scores. Children having a score of 20 or more were labeled as well controlled, those with 16 to 19 were labeled as partially controlled, and those with 15 or less were labeled as poorly controlled.

3.1 | Statistical analysis

Kolmogorov-Smirnov test was used to check the normality of data. Significance for continuous non-normal data was assessed using Mann-Whitney test and proportions using chi square test. For correlation, Spearman's correlation coefficient was used. SPSS version 23 was used for analysis.

4 | RESULTS

Of 307 children aged 6 years or above seen in asthma clinic during the study period, 305 were included for the study. Of 305, 167 children reported symptoms of food allergy. Out of whom, 76 children had SPT positivity (Figure 1). The median age of the study population was 10 years with an interquartile range (IQR) of 8 to 12. The majority were boys (67%), residing in rural areas (60%) and belonging to class 4 socioeconomic status (52%). The median BMI of the study population was 15.2, with an IQR of 14 to 16. In 223 (73.1%) children, breast feeding alone was continued till 6 months followed by addition of complementary feeds after 6 months. In 82 (26.9%) children, complementary feeds were started before 6 completed months of age. The median age of diagnosis of asthma was 7 years with an IQR of 5 to 9. The majority had mild persistent asthma (48.5%), were on rotahalers (89%), used the device correctly (96%), and were compliant to therapy (Table 1). The common symptoms attributable to food allergy

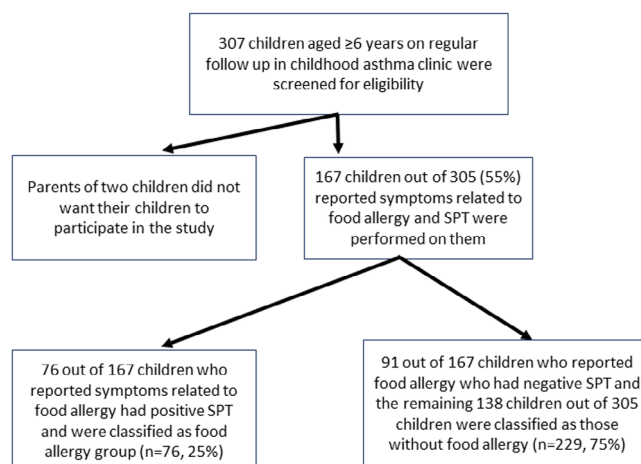


FIGURE 1 Study flow diagram

TABLE 1 Clinical characteristics of the study population

S No	Clinical characteristics		n (%)
1	Age at diagnosis (years)	Median (IQR)	7 (5.9)
2	Gender	Male	204 (66.9)
		Female	101 (33.1)
3	Background	Rural	184 (60.3)
		Urban	121 (39.7)
4	Socioeconomic Class (Modified B.G. Prasad's classification)	Class I	1 (3)
		Class II	27 (8.9)
		Class III	98 (32.1)
		Class IV	159 (52.1)
		Class V	20 (6.6)
5	Severity of asthma at diagnosis	Intermittent	88 (28.9)
		Mild persistent	148 (48.5)
		Moderate persistent	66 (21.6)
		Severe persistent	3 (1)
6	Duration of treatment (years)	Median (IQR)	2 (1.4)
7	Medication used	SABA alone	2 (0.7)
		SABA + Low dose ICS	135 (44.3)
		SABA + Low dose ICS + LTRA	12 (3.9)
		SABA+ Medium dose ICS	156 (51.1)
8	Type of device	Metered Dose Inhaler	35 (11.5)
		Rota haler	270 (88.5)
9	Use of technique	Correct	293 (96.1)
		Incorrect	12 (3.9)
10	Compliance	Good	299 (98)
		Poor	6 (2)

TABLE 2 Perceived food allergens

Allergens	n (%)
Banana	137 (44.9)
Grapes	108 (35.4)
Citrus	103 (33.8)
Milk	33 (10.8)
Watermelon	18 (5.9)
Chocolate	14 (4.6)
Pomegranate	13 (4.3)
Egg	12 (3.9)
Tomato	12 (3.9)
Peanut	8 (2.6)
Mutton	4 (1.3)
Others (Mango, Spinach, Jackfruit)	6 (1.96)

Note: Multiple responses possible for an individual patient.

were wheezing (54%), cough (19%), rhinorrhea (19%), and sneezing (7%). Oral allergy syndrome was seen in <1%. The common food substances perceived to be allergens are given in Table 2. For children

TABLE 3 Relationship between perceived food allergy and SPT positivity

Food allergens	Perceived food allergy (n)	SPT positivity n (%)
Banana	137	50 (36.4)
Citrus	102	20 (19.6)
Grapes	108	20 (18.5)
Cow's milk	33	9 (27.2)
Hen's egg	12	6 (50)
Peanut	8	4 (50)
Mutton	4	2 (50)

Note: Multiple responses possible for an individual patient.

with perceived food allergy, SPTs were done for the particular food that they reported allergy to and the proportion of SPT positivity to each food was noted. Hen's egg, peanut, and mutton had higher proportion of SPT positivity, followed by banana, cow's milk, and citrus fruits (Table 3). The Spearman's correlation for perceived food allergy and SPT was found to be 0.389 (P value < .01), indicating a moderate correlation. On comparing food allergy with symptom control, it was

TABLE 4 Food allergy and asthma control

Food allergy	Well controlled n (%)	Partially controlled n (%)	Poorly controlled n (%)	P value
Present	24 (12.2)	35 (47.3)	17 (48.6)	<.01*
Absent	172 (87.8)	39 (52.7)	18 (51.4)	

*Chi-squared test.

TABLE 5 Factors associated with food allergy

S No	Variable		Food allergy absent n (%)	Food allergy present n (%)	P value
1	Severity at diagnosis	Intermittent	74 (32.3)	14 (18.4)	.014*
		Mild persistent	111 (48.5)	37 (48.7)	
		Moderate or Severe persistent	44 (19.2)	25 (32.9)	
2	Age at introduction of complementary food	Median (IQR)	6 (5,6)	6 (6,7)	<.01 [#]
3	Family history of atopy	Present	52 (22.7)	36 (47.4)	<.01*
		Absent	177 (77.3)	40 (52.6)	
4	Asthma control test (ACT) scores	Median (IQR)	22 (20,24)	18 (16,21)	<.01 [#]

*Chi-squared test.

[#]Mann-Whitney test.

found that a greater number of children who did not have food allergy had well-controlled symptoms (Table 4). On analyzing factors associated with food allergy, it was found that children with food allergy had more moderate to severe persistent asthma, had significantly lower C-ACT/ACT scores, were introduced to weaning foods later, and had higher proportion of familial atopy (Table 5).

5 | DISCUSSION

We used SPT to diagnose food allergy in children, which is a reliable way of diagnosing food allergy as it has a high positive predictive value. When compared with a 2% to 3% prevalence of food allergy in the general population, one-fourth of children with asthma were found to have presumed food allergy in our study.⁶ This proportion is similar to that reported by Liu et al,⁷ Kumar et al,⁸ and Rona et al.⁹ Wheezing, cough, rhinorrhea, and sneezing were the common symptoms noted in our study, indicating that bronchospasm and allergic rhinitis are the common presenting features of food allergy in children with asthma. Oral allergy syndrome was exceedingly rare, and history of food-induced anaphylaxis was absent in our cohort. This contrasts with Bock et al's study in which fatalities have been reported due to anaphylaxis.¹⁰ Associated cutaneous or gastrointestinal symptoms were not reported by the participants in our study. This is in contrast to the findings of Cafarelli et al, in which they found that gastrointestinal symptoms such as diarrhea, vomiting, and abdominal pain were common manifestations of food allergy in children with asthma.¹¹ Fruits (banana, citrus, and grapes) were the common allergens reported by our patients as opposed to rice, legumes, banana, and citrus by Kumar et al's study, brinjal, prawn, banana, spinach, and egg were found to be the common allergens sensitizing children less than 16 years of

age according to Mandal et al, and pea nut, cow's milk, and hen's egg by Rance et al and Krogulska et al's study.^{8,12-14} Cross-reactivity between fruits and pollen might be a reason for patients reporting a higher prevalence of food allergy to fruits in our study. Though banana and other fruits were the major self-reported antigens, less than half of those who reported food allergy to these foods had SPT positivity. However, other allergens such as hen's egg, mutton, and peanut had a higher concordance between perceived food allergy and SPT positivity, even though the overall prevalence of allergy to these foods was low. Children with food allergy had higher proportion of uncontrolled asthma in our study, which was similar to the findings of Calamelli et al and Krogulska et al's study.^{6,14} From our study, we find that food allergy was associated with moderate to severe persistent asthma. This was similar to Wang et al's study in which hospitalization due to asthma and higher need for steroids were seen in children with food allergen sensitization.¹⁵ From our study, we also find that the timing of weaning food introduction and family history of atopy were significantly associated with food allergy, which was similar to Calamelli et al, Graif et al, and Al Ahamaddi et al's study.^{6,16,17}

6 | STRENGTHS AND LIMITATIONS

The strength of our study is that we screened more than 300 children with asthma to find out food allergy in them. Ours is probably one of the very few studies from this region looking at the problem of food allergy in children with asthma.

The limitations of our study include an inability to achieve a sample size of 83 in the food allergy group; we could enroll only 76 children who had food allergy by history and SPT. We also did not enquire about the source of fruits consumed (imported or locally grown). We did not test for cocoa, soy, pomegranate, and watermelon, even though

some children reported symptoms in relation to their intake due to difficulty in procuring those antigens. We also did not do a prick-prick test for the above food as we did not anticipate it. We did not do spirometry as a part of this study, but most children under follow-up have had spirometry done in the past. A double-blind placebo-controlled food challenge is the gold standard for diagnosing food allergy, but we could not do it due to time and resource constraints. Since ours is a hospital-based study, referral bias could be one of the reasons for finding a higher proportion of children with asthma who have presumed food allergy. Further community-based studies may be needed to find out the true prevalence of food allergy among children with asthma in the community.

7 | CONCLUSION

To conclude, we find presumed food allergy to be relatively common in children with asthma, quite contrary to popular belief. Perceived food allergy shows only a moderate correlation with SPT and cannot be relied upon in isolation to diagnose food allergy. Food allergy affects symptom control significantly and is associated with a family history of atopy and timing of complementary food introduction. However, our conclusions should be interpreted with caution in view of the limitations mentioned above.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

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All authors have read and approved the final version of the draft.

The corresponding author Venkatesh Chandrasekaran had full access to the data and takes complete responsibility for the integrity of the data and accuracy of data analysis.

TRANSPARENCY STATEMENT

The corresponding author, Venkatesh Chandrasekaran, affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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