Original Article

Identification of IgE-Mediated Food Allergy and Allergens in Older Children and Adults with Asthma and Allergic Rhinitis

Raj Kumar[1], Dolly Kumari [2,3], Prakriti Srivastava[1], Vishal Khare[1], Hena Fakhr[1], Naveen Arora[2], S.N. Gaur[1] and B.P. Singh[2]

Vallabhbhai Patel Chest Institute[1], University of Delhi, Delhi; Institute of Genomics and Integrative Biology (CSIR)[2], Delhi and Dr B.R. Ambedkar Centre for Biomedical Research[3], University of Delhi, Delhi, India

ABSTRACT

Background and objective. Prevalence of immunoglobulin (Ig) E-mediated food allergy is primarily reported for certain pediatric populations and adults. The present study was aimed to investigate the relative prevalence of food allergy and allergens in older children and adults with asthma and allergic rhinitis.

Methods. Patients (12-62 years) were screened using standard questionnaire and skin prick-test (SPT) with common foods and aeroallergens. Specific IgE level was determined by enzyme linked immunosorbent assay (ELISA) and allergy was established by blinded food challenges.

Results. Of 1860 patients screened, 1097 (58.9%) gave history of food allergy. Of the history positive patients skin tested (n=470), 138 (29.3%) showed a marked positive reaction to food extracts. Rice elicited positive SPT reaction in maximum number of cases 29 (6.2%) followed by blackgram 28 (5.9%), lentil 26 (5.5%), citrus fruits 25 (5.3%), pea 18 (3.8%), maize 18 (3.8%) and banana 17 (3.6%). The SPT positive patients showed elevated specific IgE levels (range: 0.8-79 IU/mL) against respective food allergens than normal controls (0.73 IU/mL, mean±2SD). Food allergy was confirmed in 21/45 (46.6%) of the patients by blinded controlled food challenges. The prevalence of food allergy was estimated to be 4.5% (2.6%-6.34%) at 95% confidence interval (95% CI) in test population (n=470). Sensitisation to food was significantly associated with asthma ($p=0.0065$) while aeroallergens were strongly related to rhinitis ($p<0.01$).

Conclusions. Food allergy is estimated to be 4.5% in adolescents and adults with asthma, rhinitis or both. Rice, citrus fruits, blackgram and banana are identified as major allergens for inducing allergic symptoms.

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Key words: Asthma, Rhinitis, Food allergy, Skin prick test, Enzyme linked immunosorbent assay, Double-blind, placebo-controlled food challenge.

INTRODUCTION

Recent estimates suggest that IgE-mediated food allergy affects 6% to 8% children and 3% to 4% adults imparting great clinical and social burdens.[1-4] Food allergy commonly manifests as adverse reactions of the gastrointestinal tract and the skin, including atopic dermatitis, acute urticaria and sometimes life-threatening anaphylaxis. However, the role of foods as triggers of asthma and rhinitis is less clear. Food-induced symptoms occur in approximately 2% to 29% of children and about less than 1% of adults with asthma.[5] Food sensitisation in early infancy could lead to the development of respiratory allergy and is a significant risk factor for asthma in 10% to 53% of cases.[6-8] Allergic rhinitis has also become a frequent respiratory manifestation affecting 20% of food allergic population.[8-10]

The epidemiology of food allergy is influenced by genetic, cultural and geographical dietary influences. Severe and fatal reactions can occur at any age but those at greatest risk are adolescents and young adults with asthma and a known food allergy to peanut, tree nut, fruits, milk, wine, vegetables and/or seafood.[11] The foods most commonly causing breathlessness are hazelnut in Norway, Sweden, and Germany, fruits in Iceland, Belgium, Ireland, and Italy, and peanut in the USA.[11]

India represents one-seventh of the world population with diverse culture and dietary habits

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Correspondence and reprint requests: Dr Raj Kumar, Professor and Head, Department of Respiratory Allergy and Applied Immunology, Vallabhbhai Patel Chest Institute, University of Delhi, Delhi 110 007, India; Phone: 91-11-27667102, 27667667, 27667441, 27666182; Fax: 91-11-27666549; E mail: rajkumar_27563@yahoo.co.in

but little is known about the prevalence of food allergy in this subcontinent. Recent studies[12-15] in India suggest a considerable increase in the prevalence of bronchial asthma (3.9%-11.6%) than reported earlier. Allergy to foods might further aggravate the symptoms, however, the knowledge is limited to a few studies. Food such as egg, milk, cereals and legumes, commonly induce IgE-mediated reactions in children and adult population in the country.[16-18] The present study was undertaken to investigate the relative prevalence of food allergens which cause IgE-mediated reactions in older children and adults with asthma, allergic rhinitis or both. Attempt was also made to determine associations between asthma and/or allergic rhinitis and IgE mediated food allergy.

MATERIAL AND METHODS

Study Population

Study population included older children and adults (n=1860) (mean age 30±12 years; range 12-62 years) with asthma and allergic rhinitis or both. The patients of respiratory allergy (history) included in the study during 2003-05 for their allergy diagnosis and treatment at out-patient department, Viswanathan Chest Hospital, V.P. Chest Institute, Delhi. Of these, 936 (50.3%) were males. The subjects were screened for food allergy using a detailed questionnaire which was used earlier for survey of food allergic cases at Asthma and Allergy Research Unit, Department of Medicine, University of Western Australia.[19] The questionnaire also included the patient's details relevant to dietary habits in Indian subcontinent. In all of them, a detailed history was recorded and radiographs of chest and paranasal sinuses, spirometry and blood analysis were performed. The diagnosis of asthma and rhinitis were ascertained as per the American Thoracic Society (ATS) guidelines[20] and Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines.[21] The food allergens were selected for testing based on the survey of 100 cases on a trial basis prior to the start of the study. Few more food items were later included depending on the requirement for respective patient(s). The study protocol was approved by the Human Ethics Committee of the Institute and written consent was obtained from patients and non-allergic volunteers (n=50).

Out of the total cases included, 332 (17.8%) suffered with bronchial asthma, 106 (5.7%) with rhinitis and 1422 (76.5%) had both the symptoms. Of these, 1097 (58.9%) (526 males; 47.9%) gave a history of food allergy. Allergic reactions were frequently reported after consumption of curd in 894 (48.1%) cases, rice in 816 (43.9%), citrus fruits in 655 (35.2%), banana in 502 (27.0%), milk in 221 (11.9%) and blackgram in 180 (9.7%) cases. Non-vegetarians experienced most allergic reactions with eggs 50 (2.7%) followed by chicken 279 (1.5%) and fish 224 (1.2 %) in our test population.

Laboratory Studies

Diagnosis of food allergy was made by skin prick test (SPT), specific IgE estimation by enzyme linked immunosorbent assay (ELISA) and oral food challenge. The details of patient's characteristics and diagnostic testing plan followed in the present study is shown in figure.

Skin prick test and sera collection. Food and aeroallergens extracts (50% glycerinated) were procured from Antigen Laboratory, Institute of Genomics and Integrative Biology, Delhi. The SPTs were performed with common food and inhalant allergens from pollens, fungi and insects. Histamine diphosphate (5mg/mL) and phosphate buffer saline (PBS) were used as positive and negative controls, respectively. A drop of the extract was placed on the volar aspect of the forearm and the skin was pricked by a 26 1/2" G sterile needle. Skin tests were graded after 20 minutes. The SPT reactions with wheal-diameter that was 3mm or greater than the reading in the negative control were considered as a "marked positive reaction".

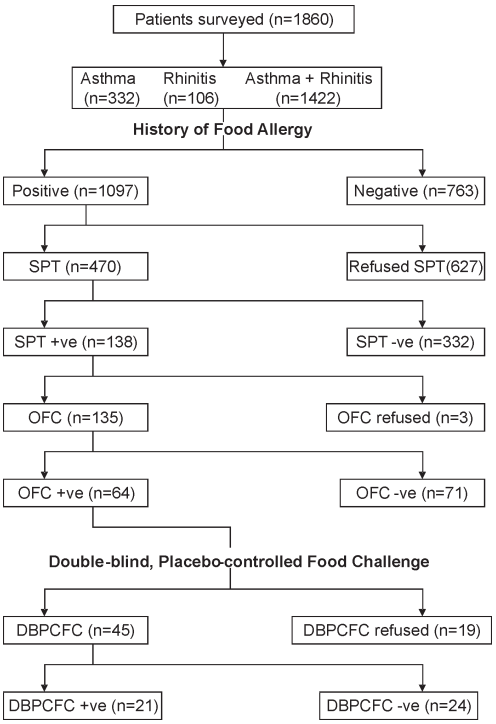

Figure 1. Flow-chart describing the steps involved in patient's selection and testing in the present study.

SPT=Skin prck test; OFC=Open food challenge; DBPCFC= Double-blind placebo-controlled food challenge; +ve= Positive; -ve=Negative

Blood was collected from SPT positive patients with a history of food allergy and from 50 normal individuals with negative SPTs. Serum was separated and used for immunoassay.

Specific IgE estimation. Specific IgE in patient's sera was determined by ELISA as described by Voller *et al*.[22] Briefly, one microgram food extract (protein) in carbonate buffer (1µg/100µL per well) was coated in microtiter plate (Nunc, USA) overnight at 4 °C and blocked with 3% defatted milk for three hours at 37 °C. The plate was washed with PBS-Tween 20 (0.05%) and incubated with diluted (1:10 v/v) hypersensitive patient's sera overnight at 4 °C. Normal human sera (NHS) were used as control. The plate was washed and incubated with anti-human IgE-horse radish peroxidase 1:1000 v/v (Sigma, St.Louis, MO) for three hours at 37 °C. Colour was developed with addition of ortho-phenylene diamine. The reaction was stopped after 20 minutes by adding 5N sulphuric acid and absorbance was read at 492nm. Mean±2SD of normal controls was taken as cut-off for ELISA positive results.

Open food challenges (OFC). The food challenges were carried out in patients showing history of food allergy, positive SPT and or elevated specific IgE in the serum.

For OFC, the patients were given 2g to 60g of suspected food(s) and kept under observation. The symptoms, such as breathlessness, cough, sneezing, rhinorrhea, vomiting and urticaria, appeared after OFC was recorded. Spirometric evaluation including forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), ratio of FEV_1/FVC, peak expiratory flow rate (PEFR) was done before and after OFC and the fall in FVC and FEV_1 was also recorded.

For double-blind, placebo-controlled food challenge (DBPCFC), the placebo and the active test food were prepared without any perceivable sensory differences between them.[23] The patients were given 2g to 40g of active test food. Pulmonary function testing was done before and after the intake of placebo and active test food. Neither the patient nor the technician making recordings were aware about ingredients of placebo or active test food. Patients who developed symptoms, such as breathlessness, cough, sneezing, rhinorrhea, vomiting, urticaria and/or significant reduction in FEV_1 (>15%-20%) were scored as positive.[24] Patients were kept under observation for at least three hours and in case of appearance of the severe symptoms, the patients were admitted and administered appropriate medication. In case of anaphylactic reaction, the patients were given injection of epinephrine, nebulised with salbutamol and ipratropium bromide.

Statistical Analysis

Prevalence rate was calculated at 95% confidence interval (CI). Kappa test was done to assess the degree of agreement between SPT, and specific IgE results. Kappa value, k='0' indicates no agreement between test and outcome, k='1' indicated perfect agreement; k<0.4 indicated poor agreement, k=0.4-0.7 indicated fair to good agreement, and k>0.7 indicated excellent agreement. The relation between risk factors and food sensitisation was performed by univariate analysis using Chi-square test and odds ratio (OR) and its 95% CI. A p-value less than 0.05 was considered significant.

RESULTS

Food Allergen Sensitisation in Population with Asthma, Rhinitis or Both

Skin prick tests with food and aeroallergen extracts could be performed on 470/1097 history positive cases with asthma, rhinitis or both. Patients with asthma with rhinitis showed maximum positive SPT reactions followed by bronchial asthma and allergic rhinitis. Of 470 patients skin tested, 138 (29.3%) exhibited positive reactions to one or more food(s). Rice elicited marked positive SPT reaction in maximum 29 (6.2%) cases followed by blackgram 28 (5.9%), lentil 26 (5.5%), citrus fruits 25 (5.3%), pea 18 (3.8%), maize 18 (3.8%) and banana 17 (3.6%). Coconut, soybean, wheat, potato, almond, cheese, radish, tomato, carrot, cashew nut, and cauliflower showed positive SPT in 1.9% to 1.3% cases. Among non-vegetarian foods, fish elicited positive SPT in 13 (2.8%) patients, whereas only eight (1.7%) and three (0.6%) cases showed a positive SPT with chicken and egg, respectively.

Skin Reactivity with Inhalant Allergen Extracts

Among food sensitised cases (history and SPT positive), 49/138 (35.5%) patients also showed a positive SPT to one or more pollen extracts. The pollen extracts of *Amaranthus spinosus* (n=14), *Imperata cylindrica, Prosopis juliflora* (n=8 each), *Ehretia laevis* and *Artemisia scoparia* (n=7 each) elicited marked positive SPT in some food allergic cases. A majority of the food sensitised patients (52.1%) were SPT positive to insect allergens while only 14.7 % showed positivity with fungal extracts. Precisely, positive SPT with food coexisted with positive SPT to insects extracts, viz. *Periplaneta americana* (n=51), *Spodoptera litura* (n=24), *Culex quinquefasciatus* (n=23) and *Musca domestica* (n=17) extracts.

Evaluation of Risk Factors for Respiratory Diseases

A positive SPT elicited by allergen with a wheal diameter that was 3mm or greater than that of negative control was defined as sensitisation. Risk factors, namely, sex and allergen sensitisation were evaluated for respiratory allergic diseases, viz, asthma, rhinitis or both (Table 1). A significant male preponderance was observed in prevalence of allergic asthma (OR, 1.8 [1.32-2.36 at 95% CI]; p<0.05) and or asthma with rhinitis (OR, 1.7 [1.3-2.2 at 95% CI]; p=0.0001). Sensitisation to food allergens was significantly associated with asthma alone (OR, 1.7 [1.2-2.6 at 95% CI]; p=0.05). But food sensitivity was significantly less common in cases of asthma associated with rhinitis (OR 0.6 [0.4-0.9 at 95% CI]; p<0.05). There was a significant association of pollen sensitisation and rhinitis, (OR, 5.5 [2.8-10.8], p<0.0001). However, sensitisation with pollens was less common in patients of asthma with rhinitis (Table 1).

(p=0.0078), *Brassica campestris* pollens (p=0.234) and *Culex quinquefasciatus* (p=0.0409) whereas sensitisation to citrus fruits was significantly related to *Aspergillus fumigatus* (p=0.02). Pea sensitisation showed significant correlation with *Imperata cylindrica* pollen (p=0.0489). Sensitivity to maize (corn) correlated significantly with *Artemisia scoparia* (p=0.0272), *Imperata cylindrica* (p=0.0156) pollens and *A. fumigatus* fungus (p=0.02) whereas sensi-tisation to banana showed significant correlation with sensitivity to *Amaranthus spinosus* (p=0.0435) and *A. scoparia* pollens (p=0.002). Skin reaction to lima bean demonstrated significant correlation with *A. scoparia* (p=0.0448) and *B. campestris* pollens (p=0.0279). Sensitisation to fish significantly correlated with pollens (n=4), namely *Amaranthus spinosus, A. scoparia, Brassica campestris* and *Prosopis juliflora* pollens. Food allergens, however, did not show statistically significant correlation with insect allergens, namely *Periplanata americana* (cockroach), *Spodoptera litura* (moth) and *Musca domestica* (house fly).

Table 1. Evaluation of risk factors for respiratory allergy, *viz.* asthma, rhinitis and asthma with rhinitis

Variables/Risk Factors		No. of Patients	Respiratory Allergy					
			Asthma	Odds Ratio	Rhinitis (95 % CI)	Odds Ratio (95 % CI)	Asthma + Rhinitis	Odds Ratio (95 % CI)
Sex	Male	619	144	1.77 (1.32-2.36)	36	0.94 (0.58-1.5)	495	1.71 (1.31 -2.22)
	Female	614	90	1.00	38	1.00	430	1.00
	p-value		p=0.0001		p=0.7827		p< 0.0001	
Food sensitisation	Yes	138	38	1.74 (1.16-2.61)	7	0.82 (0.37 to 1.82)	93	0.65 (0.45 -0.96)
	No	1095	196	1.00	67	1.00	832	1.00
	p-value		p=0.0065		p=0.6258			p=0.028
Pollen sensitisation	Yes	56	9	0.81 (0.39 - 1.68)	13	5.53 (2.83 to 10.83)	34	0.5 (0.29-0.86)
	No	1177	225	1	61	1	891	1.00
	p-value		p=0.5702		p<0.0001			p=0.0114
Fungal sensitisation	Yes	23	4	0.9 (0.3-2.66)	5	4.59 (1.66 to 12.74)	14	0.51 (0.22 - 1.19)
	No	1210	230	1.00	69	1.00	921	1.00
	p-value		p=0.8447		p=0.0013			p=0.1135
Insect sensitisation	Yes	147	13	0.38 (0.21 - 0.68)	23	3.76 (2.22 to 6.37)	112	1.07 (0.72 -1.61)
		1086	221	1.00	51	1.00	813	1.00
	p-value		p=0.0008		p<0.0001			p=0.7269

CI=Confidence interval

Correlations between sensitisation to aeroallergens and 10 common foods were analysed (Table 2). Sensitisation to rice showed some correlation with *Artemisia scoparia* pollen while blackgram (*Phaseolus mungo*) showed significant correlation with *Artemisia scoparia* pollen (p<0.05). Sensitisation to lentil correlated significantly with *Artemisia scoparia*

Specific IgE Estimation

Specific IgE was determined in sera of patients showing marked positive SPT (n=138) to food extracts. Of 260 tests done with patient's serum samples against different foods, 176 (67.7%) demonstrated ELISA positive results. Elevated

Table 2. Correlation between aeroallergens and common food sensitisers in respiratory allergy

	Rice	Blackgram	Lentil	Citrus Fruits	Pea	Maize	Banana	Lima bean	Peanut	Fish
Amaranthus spinosus										
Pearson r	0.3443	0.3107	**0.6384**	0.4051	0.2108	0.2887	**0.5101**	0.4889	0.08313	**0.7579**
P value	0.1917	0.2416	**0.0078**	0.1196	0.4332	0.2781	**0.0435**	0.0546	0.7595	**0.0007**
Artemisia scoparia										
Pearson r	0.8135	**0.9848**	0.4901	-0.09587	0.02941	**0.9192**	**0.9861**	**0.8871**	-0.04583	**0.9861**
P value	0.0939	**0.0023**	0.402	0.8781	0.9626	**0.0272**	0.002	**0.0448**	0.9417	**0.002**
Brassica campestris										
Pearson r	0.3721	0.6657	0.8217	0.4311	0.2847	0.6877	0.7338	0.8079	0.5509	0.9683
P value	0.4111	0.1026	0.0234	0.3934	0.5361	0.0877	0.0605	0.0279	0.1999	0.0015
Ehretia laevis										
Pearson r	-0.2236	-0.04834	-0.3536	0.8315	-0.1387	0.1534	0.1581	0.2646	-0.5669	0.2887
P value	0.7177	0.9385	0.5594	0.1685	0.824	0.8055	0.7995	0.6671	0.3189	0.6376
Imperata cylindrica										
Pearson r	0.4378	0.3222	-0.2469	0.1127	**0.5783**	**0.6768**	0.4159	0.1882	-0.04432	-0.04432
P value	0.1547	0.307	0.4392	0.7274	**0.0489**	**0.0156**	0.1788	0.5794	0.8912	0.8912
Prosopis juliflora										
Pearson r	0.4175	0.5472	-0.02052	0.1127	-0.1398	0.3777	0.4154	0.533	-0.1873	**0.6448**
P value	0.2299	0.1016	0.9551	0.7727	0.7001	0.2819	0.2325	0.1127	0.6043	**0.0441**
Aspergillus fumigatus										
Pearson r	0.2445	0.488	0.9258	**0.98**	0.4115	**0.98**	0.8584	0.9189	0.9258	0.9117
P value	0.7555	0.512	0.0742	**0.02**	0.5885	**0.02**	0.1416	0.0811	0.0742	0.0883
Periplaneta americana										
Pearson r	0.2875	-0.1513	0.12	-0.1052	0.3144	-0.04838	-0.1208	-0.07929	0.3119	0.1344
P value	0.1234	0.4333	0.5351	0.5801	0.0907	0.8032	0.525	0.677	0.0934	0.479
Spodoptera litura										
Pearson r	-0.06825	-0.5805	0.1115	0.2781	-0.4826	-0.2755	-0.3525	-0.4227	0.2229	0.282
P value	0.8978	0.227	0.8335	0.5937	0.3323	0.5972	0.4932	0.4037	0.6712	0.5883
Musca domestica										
Pearson r	0.01656	-0.3463	-0.5385	0.06195	0.3063	0.009169	-0.2326	-0.1079	0.3843	0.06749
P value	0.9719	0.4467	0.2123	0.895	0.5041	0.9844	0.6157	0.8179	0.4519	0.8857
Culex quinquefasciatus										
Pearson r	-0.01897	-0.01897	**0.7273**	0.57	0.5429	-0.2917	0.1186	-0.2114	0.6788	-0.1331
P value (two-tailed)	0.9644	0.9644	**0.0409**	0.1402	0.1644	0.4833	0.7797	0.6153	0.0642	0.7533

Data with significant correlation are marked in bold face; Pearson r=Pearson's correlation co-efficient.

specific IgE (0.80-79 IU/mL) was observed in 135 patients' samples to one or more food than normal controls 0.78 IU/mL (≥ mean±2 SD). The SPT results demonstrated substantial agreement with specific IgE data (k=0.773), showing k greater than 0.7 for most of the allergens excluding banana (k= 0.55) and curd (k=0.39). Maximum number of patients showed elevated specific IgE against blackgram (n=22) followed by rice and lentil (n=19 each), citrus fruits (n=16), maize (n=12), lima bean, French bean, mustard and pea (n=11 each).

Open Food Challenges

Altogether 135 patients with positive SPT and ELISA, consented for OFC with respective food(s). Of the 184 oral OFCs, 85 (46.2%) were assessed positive in 64 individuals (Table 3). Twenty-one patients showed positive reaction to more foods on OFC. The most common foods with positive OFC were rice followed by citrus fruits, banana, curd and blackgram. Of the 33 cases tested with citrus fruits, 15 (45.5%) gave positive OFC; followed by banana 10/24 (41.6%), curd 9/22 (40.9%) rice 21/52 (38.5%) and blackgram 6/16 (37.5%) respectively. The OFC was positive with pea, peanut, milk, french bean, maize, cauliflower, cashew nut, egg and mustard in one to three patients. The common reactions after the OFC were breathlessness, rhinorrhea, abdominal cramps, nausea, vomiting, diarrohea, itching in mouth or redness, throat pain, choking sensation in throat and/or urticaria. Symptoms appeared within 5 to 30 minutes of the OFC.

Double-blind, Placebo-controlled Food Challenge

In 45 patients, 52 double-blind food challenges were performed with their consent. Of these, 21/45 (46.6%) of patients showed a positive reaction in the DBPCFC to one or more foods. Five patients showed sensitis-ation with multiple foods. Ten patients with positive OFC were assessed negative in DBPCFC. The most common foods with positive challenges were rice and blackgram (n=6 each) followed by citrus fruits (n=5) and banana (n=2). Curd, peanut, cauliflower, chickpea, potato, pea and almond showed positive blinded challenge in one patient each (Table 3). Most of the patients complained for

breathlessness or wheezing (n=16), cough and itching in mouth and choking sensation in throat (n=6 each) sneezing and runny nose (n=2 each). Gastrointestinal discomfort in three patients and skin rashes in two patients were additional symptoms observed after the challenge. Two patients sensitive to rice and blackgram, respectively experienced severe systemic reaction and were managed with pharmacologic treatment in emergency ward.

and likelihood ratios for positive and negative test results were 1.5 and 0.0, respectively. Analysis of the data indicated good negative predictive value (1 at 95% CI, 0.8668-1) than positive predictive value (0.35 at 95% CI, 0.2534-0.4629) for OFC test.

DISCUSSION

Studies on IgE-mediated food allergy and allergens are primarily focused on general paediatric or adult

Table 3. Results of food challenge tests, namely open food challenge (OFC) and double-blind, placebo-controlled food challenge (DBPCFC) carried out on asthma and rhinitis patients

Allergens	OFC Results		DBPCFC Results		SPT Wheal Size Range (mm)	Specific IgE Range (IU/mL)
	Patients Tested (n=135)	Patients Positive (n=64)	Patients Tested (n=45)	Patients Positive (n=21)		
Rice	52	21	16	6	4-7	0.8-10.0
Citrus fruits	33	15	7	5	6-9	1.9-16.3
Banana	24	10	6	2	3-6	1.8-4.5
Curd	22	9	3	1	3-8	0.8-4.5
Blackgram	16	6	6	6	5-12	0.98-79.0
Pea	6	3	2	1	7-18	0.96-27.2
Peanut	5	3	1	1	6-15	0.8-68.3
Milk	3	3	3	0	3-6	1.6-13.8
French bean	6	2	nd	nd	7-11	2.4-43.0
Maize	3	2	nd	nd	3-7	1.3-14.3
Cauliflower	3	2	2	1	3-6	4.8
Egg	2	2	nd	nd	3-6	1.0-32.4
Mustard	2	1	1	0	5-8	4.5
Potato	2	1	1	1	5-6	3.3
Soybean	1	1	1	0	8	3.3
Almond	1	1	1	1	9	6.4
Chickpea	1	1	1	1	13	4.9
Tomato	1	1	1	1	6	5.7
Wheat	1	1	nd	nd	6	3.0
Total tests	**184**	**85**	**52**	**27**		

SPT=Skin prick test; IgE=Immunoglobulin E; nd=Not done

Estimation of Food Allergy

Of 1860 respiratory allergy patients, 1097 gave history of food allergy, whereas 763 (41.0%) patients showed no history of allergen sensitisation. Of 1097 history positive patients, 470 (42.8%) could be evaluated by SPT, ELISA and OFC tests. History of food allergy was confirmed in 21(4.5%) patients by DBPCFC. The prevalence of food allergy was estimated to be 4.5% ([2.6-6.3] at 95% CI), in the test population (n=470).

The pre-test and post-test probability was calculated based on OFC test. The change in pre-test and post-test probability was 0.26 and 0.35, respectively. The pre- and post-test odds were 0.36 and 0.54

population. These reports suggest that foods play an important role in exacerbation and continuance of respiratory manifestations.[5-10] But the true prevalence of IgE-mediated food allergy in the population with respiratory allergy is unknown. The present study was undertaken to identify the prevalence of IgE-mediated food allergy and allergens in the adolescent and adult population with asthma, rhinitis and/or both.

Various foods have been implicated as trigger factors in different geographical regions.[1-4] Rice is detected as an important allergen in Thailand (ranked 4th), Japan (5th) and Indonesia (6th).[25] Chickpea and blackgram are reported as major food allergens from India and lentil from Mediterranean countries.[18,26,27] In the present study, rice elicited

marked positive SPT in (6.2%) maximum cases may be due to its high consumption by Indian population. Blackgram, a legume was the second most common offender afflicting sensitisation in 5.9% cases. Many patients also showed sensitisation to other legumes, such as lentil, pea, lima bean, French bean, chickpea etc, because legumes are important source of dietary proteins in India. Peanut and soybean, which rank among the top eight food allergens in US and Europe,[1, 4] exhibited positive skin reactions in only 2% to 3% of our patients. Citrus fruits proved third important offender in our test population. Higher sensitisation to citrus fruits has also been observed in different population of Germany and Finland.[2,3,28]

Food sensitisation (positive SPT or raised specific IgE) is reported to be highly prevalent in subjects with atopic manifestations (25%) than in the general population.[28, 29] Previously in a group of patients with life-threatening asthma, 52.6% had positive SPT or elevated specific IgE to foods.[8] Food sensitisation is considered as an important risk factor for respiratory allergy.[6-10] Wang *et al*[9] reported that sensitivity to soy, wheat, peanut, fish and egg was significantly correlated with sensitisation to some aeroallergens. The similar trend was also observed in other studies where food sensitisation strongly correlated with aeroallergen sensitisation.[7, 8, 25, 30] In the present study, 29.3% of asthma and rhinitis cases showed marked positive SPT (sensitisation) to one or more foods. It has been observed in the present study that sensitisation to food allergen (potential food allergy) was significantly associated with asthma, whereas inhalant allergens (pollen, fungal and insects) were strongly related to rhinitis. Positive SPT reaction to food with coexisting pollen and other indoor allergens was observed in our patients. This may be due to cross-reactivity or co-sensitisation. The results suggest that concommitant sensitisations to food with pollen and insect may enhance the risk of asthma and rhinitis or contribute towards exacerbation of symptoms. The synergistic action of these factors may influence the development and progression of atopic manifestations.

Clinical diagnosis of food allergy relies on history, SPT, specific IgE estimation and DBPCFCs.[24] Previously, elevated specific IgE was observed in 45% of asthma and 9% to 20% of rhinitis patients.[9,10] Diagnostic decision points for specific IgE to predict symptomatic food allergy were established, but predicted probabilities varied among different foods and populations studied.[31] In the present study, food allergic cases (DBPCFC positive) showed marked positive SPT reaction and significantly elevated specific IgE levels (2.3-79 IU/mL) against rice, citrus fruits, blackgram, lentil, mustard, French bean and lima bean. Blinded challenges with suspected foods were positive in 21/45 (46.6%) of patients demonstrating high specific IgE to respective food(s). Out of 184 OFCs performed in 135 patients, 85 (46.2%) demonstrated positive reaction to different foods, namely rice (n=21), citrus fruits (n=15), banana (n=10), curd (n=9), blackgram (n=6), pea, peanut, milk (n=3 each), French bean, maize, cauliflower, egg (n=2 each) and others.

In the present study, sensitisation to food was observed in 138/470 (29.3%) of patients by SPT and food allergy was confirmed in 4.5% cases by DBPCFCs. The discrepancy in self-reported food reactions (11.0%-65.5%), food sensitisation (4.9%-21.0%) and challenge proven allergy symptoms (1.1%-3.5%) has also been observed in earlier studies.[2-4,28,32-34] This may be due to strong tendency of people to casually relate any discomfort with ingested foods. Besides, the processing of the recipe of the active test food may have led to reduced allergenicity.

Food allergy affects family, social activities, stress level, meal preparation, school attendance and activity scores.[35] The advantage of the present study is that it has generated valuable knowledge about food allergens and allergy in older children and adults with asthma, rhinitis/or both in the country. It emphasises the need for accurate diagnosis by food challenges to prevent individuals being on unnecessarily restricted diets leading to malnutrition. However, the diagnosis of food allergy is tricky in Indian population because of diverse dietary habits, and different meal preparations. But the timely detection of suspected food allergen(s) can help in developing avoidance strategy for the better management of the disease. The limitation of the present study is that we could not get consent for DBPCFCs from a large number of OFC positive or negative patients. Hence, we could not calculate positive or negative predictive values for specific IgE and SPT in reference to DBPCFC's outcomes. Positive-predictive values for specific IgE derived by standard method offer clue about level of sensitisation, similar to absolute value of specific IgE given in the present study. However, positive-predictive values do not describe the true clinical reactivity of patient that requires OFC. Further, there may be referral bias since the patients selected for the present study are the referred cases to a tertiary care hospital (VPCI, Delhi).

CONCLUSIONS

In the present study, prevalence of food allergy is estimated to be 4.5% of adolescent and adults with asthma, rhinitis or both with rice, citrus fruits, blackgram and banana as common offending food allergens. More studies are recommended taking large population of patients to establish the diagnostic decision points for major food allergens in the country.

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