

RESEARCH ARTICLE

Food IgE-Sensitization in Respiratory Allergic Patients in Jakarta

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Abstract

Food allergy and respiratory allergy may co-exist in atopic person. Although both conditions can worsen allergic symptoms, food allergen sensitization has not gain much attention in clinical studies. The aim of this study is to evaluate food IgE sensitization in respiratory allergic patients. This was a cross-sectional study in patients with a history of respiratory allergy in Jakarta, on September to December 2016. Adult asthmatic patients aged 19-60 years were invited to undergo serum specific IgE testing at the Allergy and Immunology Clinic, Cipto Mangunkusumo Hospital, Jakarta. Patients were included if they showed at least one positive skin prick test with environmental allergens. Quantitative determination of specific IgE in serum was carried out by multiple allergosorbent test. Serum specific IgE levels of more than 0.35 kU/L or Class 1 was considered positive. A total of 100 subjects were eligible for analysis; 76% were women. Patients mean age was 38.8 ± 12.1 (range 19-59) years old; 62% of the patients have both asthma and allergic rhinitis. There are 46% patients with at least one positive food-IgE sensitization. The most common sensitization was to shrimp (17%), followed by fruit-mix (14%), goat milk (13%), crab (13%), potato (13%), soybean (11%), and strawberry (11%). Significant difference of IgE sensitization was found between house dust mites and crab or shrimp and between cockroach and crab or shrimp. In conclusion food-IgE sensitization in respiratory allergic patients is common. The most common allergens were shrimp, fruit-mix, goat milk, crab, and potato.

Key words: asthma; allergic rhinitis; food IgE-sensitization; food allergy; serum food-specific IgE

Sensitisasi IgE Makanan pada Pasien Alergi Saluran Napas di Jakarta**Abstrak**

Alergi makanan dan alergi saluran napas dapat timbul bersamaan pada orang dengan atopi. Meskipun kedua kondisi dapat memperburuk gejala alergi, sensitisasi alergen makanan belum mendapatkan banyak perhatian dalam studi klinis. Tujuan penelitian ini adalah mengevaluasi sensitisasi IgE makanan pada pasien alergi saluran napas. Penelitian cross-sectional ini dilakukan pada pasien dengan riwayat alergi saluran napas di Jakarta, pada bulan September - Desember 2016. Pasien asma dewasa berusia 19-60 tahun dilakukan tes IgE spesifik serum di Poli Alergi Imunologi Penyakit Dalam RS dr. Cipto Mangunkusumo, Jakarta. Pasien diikutkan dalam penelitian jika menunjukkan setidaknya satu tes tusukan kulit positif dengan alergen lingkungan. Penentuan kuantitatif IgE spesifik dalam serum dilakukan dengan multiple allergosorbent test. Tingkat IgE spesifik serum lebih dari 0,35 kU/L atau kelas 1 dianggap positif. Sebanyak 100 subjek memenuhi syarat untuk analisis; 76% adalah perempuan. Rerata usia $38,8 \pm 12,1$ (kisaran 19-59) tahun; 62% pasien memiliki asma dan rinitis alergi. Terdapat 46% pasien dengan setidaknya satu sensitisasi IgE makanan positif. Sensitisasi yang paling umum adalah udang (17%), diikuti oleh buah-campuran (14%), susu kambing (13%), kepiting (13%), kentang (13%), kedelai (11%), dan stroberi (11%). Perbedaan signifikan dari sensitisasi IgE ditemukan antara tungau debu rumah dan kepiting atau udang dan antara kecoa dan kepiting atau udang. Disimpulkan sensitisasi IgE-makanan pada pasien alergi di saluran napas sering terjadi. Alergen yang paling umum adalah udang, buah-buahan, susu kambing, kepiting, dan kentang.

Kata kunci: asma; rinitis alergi; sensitisasi IgE-makanan; alergi makanan; serum IgE spesifik makanan.

Introduction

Adverse reaction or hypersensitivity to a specific food can be categorized as food allergy (allergic hypersensitivity) or food intolerance (non-allergic hypersensitivity).¹ In food allergy subgroup, adverse reaction occurred through immunologic mechanism to a food allergen, whether IgE-mediated or not.²

In IgE-mediated food allergy, there are food-specific IgE antibodies within the mast cells and basophils, which become activated when food allergens bind to them and cause histamine release.³ Asthma and food allergy may co-exist and having both conditions may increase allergic symptoms and fatal allergic reactions.⁴ Food allergy can also trigger respiratory symptoms and occupational asthma.^{5,6} Prevalence of food allergy is increasing worldwide, especially among infants and children.^{7,8} It is estimated to occur in 2-10% of the population.⁹ The prevalence of food allergy in adults is not clearly known. Food allergy in adults may reflect the persistence of food allergy in childhood or de novo sensitization to food allergens after childhood.¹⁰ Prevalence of food allergy in Indonesian population is not clearly known. Data from a pediatric clinic found that among 42 atopic dermatitis patients, there were sensitization to white egg (31%), cow's milk (23.8%), chicken (23.8%), yolk egg (21.4%), nuts (21.4%), and wheat (21.4%).¹¹ Although rare, anaphylaxis triggered by food allergen has been reported in Jakarta.¹²

Food sensitization can be confirmed by using IgE antibody testing, either *in vivo* using skin prick test (SPT) or *in vitro* using immunoassay test.¹³ Food-specific IgE levels are helpful in detecting IgE-mediated food allergy. Combination of SPT and specific IgE levels is recommended to diagnose food allergy.¹⁴ However, food allergy diagnosis should be established by a relevant clinical history and then confirmed by food challenge test.

Immunoassays to measure serum IgE levels have just been recently introduced in Indonesia. Diagnostic studies are still underway among adult patients with respiratory allergy. Compare to the standard SPT panel with limited allergens, the serum IgE panel is more comprehensive because it may accommodate 40-60 allergens in one test. The wide array of allergenic proteins tested in serum IgE immunoassay gave opportunity

to evaluate potential allergens that may trigger allergic symptoms. Knowing potential allergens in these patients may provide opportunity for better prevention program. Therefore, the aim of this study was to evaluate the pattern of food-specific IgE sensitization among adult patients with asthma and/or allergic rhinitis.

Methods

Study Design and Subjects

This was a cross-sectional study in patients with a history of respiratory allergy in Jakarta, Indonesia on September to December 2016. Adult asthmatic patients aged 19-60 years were invited to undergo serum specific IgE testing at the Allergy and Immunology Clinic, Cipto Mangunkusumo Hospital, Jakarta. Asthma diagnosis and severity was assessed using *Global Initiative on Asthma* (GINA) 2015 criteria and spirometry. Ethical approval was granted by the Ethical Committee of Medical Research, Faculty of Medicine, Universitas Indonesia. Patients were included if they showed at least one positive SPT with environmental allergens (Stallergens, SA, France), which included 19 allergens i.e. egg, peanut, soy, sardine, tuna, shrimp, crab, cocoa, Aspergillus mix, Candida, Alternaria, grass mix, cat, dog, guinea pig, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Blomia tropicalis*, and cockroach.

Specific IgE Measurement

Quantitative determination of circulating allergen specific IgE in serum was carried out by immunoblot method known as multiple allergosorbent (MAST) assays (AlleisaScreen® Panel 44 Food, Mediwiss Analytic, Germany). Serum specific IgE levels of more than 0.35 kU/L or Class 1 were considered positive. There were 26 food allergens in the food panel tested.

Results

A total of 100 subjects were enrolled in this study, 76% were women. Patients' mean age was 38.8 ± 12.1 years old, ranging from 19 to 59 years old. Majority of patients (62%) had both asthma and allergic rhinitis. Skin prick testing showed house dust mites (HDM) as a predominant allergen (89%) among the subjects, with *B. tropicalis* as the most common allergen (Table 1).

Table 1. Characteristics of The Study Subjects (n=100)

Characteristics	n	%
Gender		
Female	76	76
Male	24	24
Diagnosis		
Asthma	20	20
Asthma and allergic rhinitis	62	62
Allergic rhinitis	18	18
Major atopy by SPT		
<i>B. tropicalis</i>	76	76
<i>D. pteronyssinus</i>	70	70
<i>D. farinae</i>	69	69
Food-IgE sensitization by SPT		
Shrimp	35	35
Whole egg	33	33
Crab	29	29
Peanut	27	27
Tuna	26	26
Sardine	25	25
Cacao	22	22
Soybean	20	20

There are 46% patients showed food-IgE sensitization to at least one food allergen. The most common food-IgE sensitization was shrimp (17%), followed by fruit-mix (14%), goat milk (13%), crab (13%), potato (13%), soybean (11%), and strawberry (11%). Ten percent of the study subjects showed IgE-sensitization to lamb meat, wheat flour, nut mixture, and mushroom (Table 2).

Table 2. Distribution of Food Allergen IgE-sensitization (n=100)

Allergen	n	%
Egg white	5	5
Egg yolk	9	9
Milk	4	4
Goat milk	13	13
Cacao	9	9
Soybean	11	11
Chicken	6	6
Lamb meat	10	10
Beef	9	9
Sea fish mix	7	7
Salmon	6	6
Crab	13	13
Shrimp	17	17
Seafood mix	5	5
Strawberry	11	11
Pineapple	7	7
Fruit mix	14	14
Tomato	8	8
Potato	13	13
Celery	9	9
Wheat flour	10	10
Gluten	6	6
Peanut	7	7
Nut mixture	10	10
Baker's yeast	6	6
Mushroom	10	10

There was significant difference between HDM and crab or shrimp IgE-sensitization. Crab IgE-positive was significantly associated with positive *D. farinae* and *B. tropicalis*, while shrimp IgE-positive was strongly associated to all HDMs tested (Table 3). Significant difference was also found between cockroach and crustacean (crab or shrimp) IgE sensitization (Table 4).

Table 3. The Association between HDM and Crab or Shrimp IgE-Sensitization

Food IgE	<i>Der p</i>			<i>Der f</i>			<i>Blo t</i>		
	Yes (n=62)	No (n=38)	<i>P</i>	Yes (n=48)	No (n=52)	<i>P</i>	Yes (n=58)	No (n=42)	<i>P</i>
Crab									
Yes	10 (16.1%)	3 (7.9%)	0.360 [#]	10 (20.8%)	3 (5.8%)	0.025 [^]	12 (20.7%)	1 (2.4%)	0.007 [^]
No	52 (83.9%)	35 (92.1%)		38 (79.2%)	49 (94.2%)		46 (79.3%)	41 (97.6%)	
Shrimp									
Yes	16 (25.8%)	1 (2.6%)	0.003 [^]	14 (29.2%)	3 (5.8%)	0.002 [^]	15 (25.9%)	2 (4.8%)	0.006 [^]
No	46 (74.2%)	37 (97.4%)		34 (70.8%)	49 (94.2%)		43 (74.1%)	40 (95.2%)	

[#]Fisher's exact test, [^]Chi-square test, *Der p*: *D. pteronyssinus*, *Der f*: *D. farinae*, *Blo t*: *B. tropicalis*

Table 4. The Association between Cockroach and Crustacean IgE-sensitization

Food IgE	Bla g		p
	Positive (n=58)	Negative (n=42)	
Crab			
Yes	6 (27.3%)	7 (9.0%)	0.024 [^]
No	16 (72.7%)	71 (91.0%)	
Shrimp			
Yes	9 (40.9%)	8(10.3%)	0.002 [#]
No	13 (59.1%)	70 (89.7%)	

[#]Fisher's exact test, [^]Chi-square test

Discussion

This study is the first evaluation of food IgE-sensitization in patients with respiratory allergy in Indonesia. Results of serum IgE testing should be cautiously interpreted in relation with the clinical history.¹⁵ Although positive result of a specific IgE could mean allergy, clinical history must be considered when establishing diagnosis.¹⁶ Our study subjects were patients with respiratory allergy. Although food allergy may co-exist, we did not evaluate their clinical history in relation to food allergens and a diagnosis of food allergy was not established among them.

In this study, IgE-sensitization to at least one seafood allergen tested was 25%. Shrimp and crab are the most common seafood allergens. Crustacean shellfish allergy is common in Asian adults and includes allergy to shrimp, crab, crawfish and lobster. In Singapore, the common food hypersensitivity to crustaceans by skin prick testing was to shrimp (21.7%), crab (16.2%), and lobster (8.1%).¹⁷ Shellfish allergy is also predominant in Asian children.¹⁸ Interestingly, about 6-7% of the study subjects were sensitized to salmon and sea fish mix. Salmon is not native to Indonesian sea; they are imported fish and can be easily found in many restaurants in Jakarta. As comparison, epidemiology data showed that fish allergy is very low in Southeast Asia (0.26-2.5%).¹⁹

Sensitization to fruit-mix allergens ranked the second in our study subjects. Allergy to fruits and vegetables differs among geographical areas. Common fruits that have been reported to cause fruit allergy in Europe include apple, peach, kiwi, musk melon, grape, cherry, strawberry, banana, mango and pomegranate.²⁰ Vegetables have also been reported to cause allergy, which include celery, asparagus, avocado, bell pepper, cabbage, carrot, fennel, lettuce, potato, pumpkin, turnip and

zucchini.²¹ Fruit allergy in Japan was only 6% from all type of food allergies.²² Sensitization to potato was unexpected since it is not a staple food for Indonesian people. Allergy to a root vegetables like potato are rarely reported, though severe reactions could occur especially in children.^{23,24} The major allergenic protein in potato is patatin (Sol t 1).²⁵ High-sensitization to potato in our study subjects may reflect the change of eating pattern towards the western diet, which is commonly served in fast-food restaurants throughout Jakarta.

Sensitization to goat's milk was surprisingly higher than cow's milk. Food product containing goat's milk might be increasingly present in the diet and serve as hidden allergens in processed food. The allergenic proteins for goat's milk allergy are caseins, such as α S₁-, α S₂- and β -casein, but not whey proteins.²⁶ Other protein that could trigger IgE-mediated reactions in goat's milk is a 14 kDA protein corresponded to α -lactalbumin.²⁷ Allergy to goat's milk in person tolerant to cow's milk may be caused by IgE binding to caprine β -casein (β cap) without binding to bovine β -casein (β bov) despite 91% similarity of its amino acid sequences.²⁸

Soybean (*Glycine max*) is an important food source in Indonesian diet as it is the major ingredient in tempeh, tofu, and soybean sauce. Severe allergy to soybean may be caused by a sensitization to the soybean major storage proteins, i.e. Gly m 5 or Gly m 6.²⁹ Among people with birch pollen allergy, there is also a potential cross reactivity of Bet v 1 (birch pollen allergen) to the soybean allergen Gly m 4.³⁰

There are some limitations in our study. First, positive results were not confirmed by clinical history and double-blind food challenge. Subjects were not patients with symptoms of food allergy; rather they are atopic individuals with asthma or allergic rhinitis. Therefore, positive results could only be interpreted as sensitization of the allergens tested. Second, this study was not aimed for diagnostic purposes. Positive results of serum IgE testing can be caused by cross-reactivity between protein allergens. The crustacean seafood sensitization showed strong associations with HDM or cockroach. Tropomyosin is the major allergen in crustacean allergies that involved in muscle contraction in invertebrate animals. It is found in crustaceans as well as molluscs (e.g. squid, snail, mussels) and insects.³¹ It is reported that their tropomyosins share a high homology to house dust mites' tropomyosins.³² There are 81% amino acid sequence homology between prawns and HDMs, and 82% homology between prawns and

cockroach.³³ It is not surprising that cross-reactivity can occur between HDM and shellfish.³⁴

Conclusion

Food-IgE sensitization in respiratory allergic patients is common. Five most common allergens were shrimp, fruit-mix, goat milk, crab, and potato. Although food allergy diagnosis cannot be established, these findings are helpful in identifying potential food sensitization among the patients and to design prevention program.

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