Pollen Serum Specific IgE Sensitization in Respiratory Allergic Patients in Jakarta, Indonesia

Iris Rengganis[1], Agus J. Susanto[2]

[1] Department of Internal Medicine, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia.
[2] Department of Internal Medicine, Faculty of Medicine, University of Sebelas Maret - Moewardi Hospital, Surakarta, Indonesia.

Corresponding Author:
Iris Rengganis, MD., PhD. Division of Allergy and Clinical Immunology, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital. Jl. Salemba Raya No. 4, Jakarta 10430, Indonesia. email: irisrengganis@yahoo.com.

ABSTRAK

Latar belakang: *serbuk sari dari pohon-pohon atau rerumputan di Indonesia mempunyai penyebaran sepanjang masa akibat iklim tropisnya. Meskipun demikian, alergi serbuk sari belum diteliti dengan baik. Penelitian ini bertujuan untuk menilai profil sensitisasi serbuk sari IgE pada pasien dengan alergi pernapasan di Jakarta.* ***Metode:*** *penelitian ini adalah penelitian potong lintang pada pasien dengan riwayat alergi pernapasan di Jakarta, Indonesia yang dilaksanakan antara bulan September dan Desember 2016. Pasien asma dewasa berusia 19-60 tahun diundang untuk menjalani pemeriksaan serum IgE spesifik di Klinik Alergi dan Imunologi, Rumah Sakit Cipto Mangunkumo, Jakarta. Pasien diikutsertakan dalam penelitian bila mereka menujukkan setidaknya satu hasil positif pada pemeriksaan uji tusuk kulit (prick test) terhadap alergen-alergen lingkungan. Penentuan kuantitatif kadar IgE spesifik dalam serum dilakukan dengan pemeriksaan menggunakan multiple allergosorbent (MAST) assays (Polycheck Allergy®, Biocheck GmbH, Munster, Jerman). Kadar IgE spesifik dalam serum yang melebihi 0,35 kU/L atau Kelas 1 dianggap positif.* ***Hasil:*** *sejumlah 106 kasus memenuhi syarat untuk dianalisis; 81 (76.4%) di antaranya adalah wanita. Usia rata-rata pasien adalah 38,8 (12,1) tahun (kisaran usia 19-59 tahun). Sekitar 59,4% pasien mempunyai asma sekaligus rinitis alergi. Terdapat 9 (8,5%) pasien dengan hasil positif untuk sensitisasi serbuk sari IgE; 8 di antaranya menunjukkan sensitisasi terhadap setidaknya 2 serbuk sari. Sensitivitas terhadap serbuk sari gulma goosefoot ternyata paling tinggi (5,7%), diikuti oleh serbuk sari gandum hitam (4,7%), serbuk sari pisang raja (4,7%) dan serbuk sari tanaman wall pellitory (4.7%) dan serbuk sari rumput Bermuda (3,8%).* ***Kesimpulan:*** *meskipun sebagian besar serbuk sari yang diuji bukan merupakan tumbuhan asli di Indonesia, beberapa pasien menunjukkan sensitisasi IgE spesifik. Orang dengan alergi yang berencana bepergian ke daerah endemik tempat asal serbuk sari yang relevan perlu diberi saran. Panel alergen serbuk sari dari tanaman lokal sangat dinantikan.*

Kata kunci: *asma, rinitis alergi, sensitisasi IgE, alergi pernapasan, alergen serbuk sari.*

ABSTRACT

Background: *pollens from trees or grasses in Indonesia have a perennial distribution due to the tropical climate. However, pollen allergy has not been well studied. This study aimed to evaluate the profile of pollen IgE sensitization in respiratory allergic patients in Jakarta.* ***Methods:*** *this was a cross-sectional study in patients with a history of respiratory allergy in Jakarta, Indonesia between September and 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 (MAST) assays (Polycheck Allergy®, Biocheck GmbH, Munster, Germany). Serum specific IgE levels of more than 0.35 kU/L or Class 1 was considered positive. ***Results:*** *a total of 106 cases were eligible for analysis; 81 (76.4%) were women. Patients' mean age was 38.8+12.1 (range 19-59) years old. 59.4% of patients have both asthma and allergic rhinitis. There are 9 (8.5%) patients positive for IgE-pollen sensitization; 8 among them showed sensitization to at least 2 pollens. Sensitivity to goosefoot pollen is the highest (5.7%), followed by rye pollen (4.7%), plantain pollen (4.7%), wall pellitory pollen (4.7%), and Bermuda grass pollen (3.8%).* ***Conclusion:*** *although most pollens tested are not originated from native plants to Indonesia, a small number of patients showed specific IgE-sensitizations. Allergic persons planning to travel to the endemic areas of the relevant pollen should be advised. A panel of pollen allergens from local plants is highly desired.*

Keywords: *asthma, allergic rhinitis, IgE-sensitization, respiratory allergy, pollen allergens.*

INTRODUCTION

Respiratory allergy (allergic asthma and rhinitis) is common in Indonesia, which is caused by complex interactions among genetic and environmental factors.[1,2] The allergic reaction is usually mediated by immunoglobulin E (IgE) following an exposure to environmental allergens, including pollen.[3] The IgE sensitization can be confirmed by using IgE antibody testing, either in vivo using skin prick test (SPT) or in vitro using immunoassay test.[4] The multiple allergosorbent (MAST) assay is now gaining popularity due to its practical use and lower cost than the singleplex assay. Concordance rates of MAST assays with SPT were reported around 79-100%.[5]

Positive IgE sensitization, either by SPT or serology, does not prove any allergic disease without relevant clinical history and other definitive testing. However, knowing the pattern of IgE sensitization in allergic individual would be valuable information for future prevention. Environmental control to reduce or to prevent contact with allergens is still the mainstay of allergic disease management.[6,7]

Pollen allergy has not been well studied in Indonesia, although sensitization does occur in the community.[8] The distribution of pollen allergen differs between areas, climates and vegetation.[9] In addition, pollen exposure has a complex relationship with clinical symptoms.[10,11] Until recently, the available test to confirm pollen allergy in Indonesia is by the skin prict test (SPT) only. Commercial reagents for SPT usually use pollen from mixed grass because it is an important cause of allergic reaction and symptoms of respiratory allergy.[12,13] Alternatively, pollen protein extract can be used for skin testing.[14,15]

Pollens from trees or grasses in Indonesia have a perennial distribution due to the tropical climate. However, pollen allergy has not been well studied. Since the introduction of serum specific IgE testing in Indonesia, more pollen allergens can be tested using the manufacturer's standard inhalant panel test. Evaluation of IgE sensitization profile of pollen allergens in allergic patients could be used in the future management plan and preventive strategy for the patients. Moreover, IgE sensitization profile will provide basic information to design specific immunotherapy when it is available in Indonesia. Therefore, the objective of this study was to evaluate the profile of pollen IgE sensitization in respiratory allergic patients in Jakarta based on a multiplex assay.

METHODS

This is a cross-sectional study in patients with a history of respiratory allergy in Jakarta, Indonesia between September and 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 had no contraindication to underwent skin prick testing (SPT) and showed at least one positive result 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. Grass mix allergens consisiting of bent grass, Bermuda grass (Cynodon dactylon), bromus, cocksfoot, meadow fescue, meadow grass, oat grass, rye-grass, sweet vernal grass, timothy, wild oat, and Yorkshire fog. There are no exclusion criteria in this study.

Ethical approval was granted by the Ethical Committee of Medical Research, Faculty of Medicine, University of Indonesia with Letter No. 796/UN2.F1/ETIK/2016.

Procedure

All patients have been previously diagnosed as having respiratory allergy, either as allergic asthma or rhinitis. Patients underwent skin prick test (SPT) to confirm their atopy. Patients who met all inclusion criteria proceed to specific IgE measurement.

Specific IgE Measurement

Quantitative determination of specific IgE in serum was carried out by immunoblot method known as multiple allergosorbent (MAST) assays (Polycheck Allergy®, Biocheck GmbH, Munster, Germany) and Biocheck Imaging Software. A 5-mL vein blood was withdrawn from each patient and was centrifuge to obtain the serum. Allergen cassette was washed and added with 250 µL of start solution. After 60 seconds of incubation, 200 µL of patients' sera were added. Incubation was done on shaker for 60 minutes and washed 6 times. Then the anti-IgE was added and was incubated for 45 minutes on shaker. After washing, 250 µL of enzyme tagged conjugate were added and incubated for 20 minutes. Finally, 250 µL luminescent reagent was added and incubated for another 20 minutes. The results were scanned and read with Biocheck Image Software as class 0-6. Serum specific IgE level of more than 0.35 kU/L or Class 1 was considered positive. There were 18 pollen allergens in the inhalant panel tested, i.e. cypress pollen, hazel pollen, white ash pollen, oak pollen, olive pollen, birch pollen, rye pollen, cultivated oat pollen, Kentucky blue grass pollen, Timothy grass pollen, cultivated wheat pollen, cocksfoot pollen, Bermuda grass pollen, plantain pollen, goosefoot pollen, mugwort pollen, ragweed pollen, wall pellitory pollen.

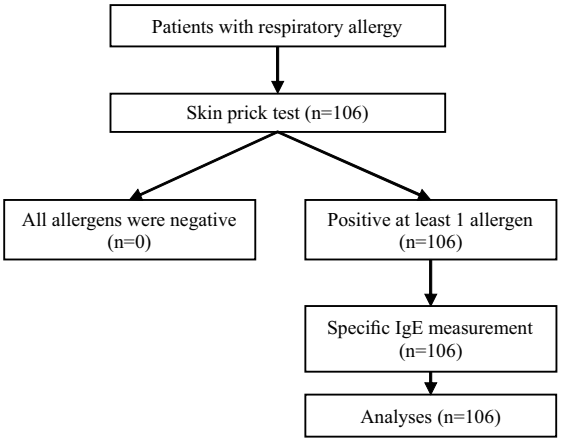

Figure 1. Recruitment of the study subjects

Tabel 1. Characteristics of the study subjects (n=106)

Variables	n (%)
Gender	
- Female	81 (76.4)
- Male	25 (23.6)
Diagnosis	
- Asthma	25 (23.6)
- Asthma and allergic rhinitis	63 (59.4)
- Allergic rhinitis	18 (17.0)
Asthma severity (n=88)	
- Intermitten	29 (33.0)
- Persistent	59 (67.0)
Major atopy by skin prick test	
- House doust mites allergens	93 (87.7)
- Food allergens	5 (4.7)
- Cockroach	3 (2.8)
- Mould	3 (2.8)
- Animal epithelia	2 (1.9)

Statistical Analysis

Demography data and asthma severity were presented descriptively. The profile of specific pollen IgE sensitization were described as frequency and percentage

RESULTS

One hundred and six subjects were enrolled in this study. Eighty-one of them (76.4%) were

Table 2. Distribution of pollen allergen IgE-sensitization

	No. Allergen	n (%)
1.	Cypress pollen	2 (1.9)
2.	Hazel pollen	1 (0.9)
3.	White ash pollen	1 (0.9)
4.	Oak pollen	3 (2.8)
5.	Olive pollen	2 (1.9)
6.	Birch pollen	2 (1.9)
7.	Rye pollen	5 (4.7)
8.	Cultivated oat pollen	3 (2.8)
9.	Kentucky blue grass pollen	3 (2.8)
10.	Timothy grass pollen	3 (2.8)
11.	Cultivated wheat pollen	3 (2.8)
12.	Cocksfoot pollen	3 (2.8)
13.	Bermuda grass pollen	4 (3.8)
14.	Plantain pollen	5 (4.7)
15.	Goosefoot pollen	6 (5.7)
16.	Mugwort pollen	2 (1.9)
17.	Ragweed pollen	2 (1.9)
18.	Wall pellitory pollen	5 (4.7)

women. Patients' mean age was 38.8 (12.1) years old, ranging from 19 to 59 years old. Majority of patients (59.4%) had both asthma and allergic rhinitis (**Figure 1**). SPT showed house dust mites as a predominant allergen (87.7%) among the subjects (**Table 1**). Sensitivity to grass mix pollen using SPT was found in 11 (10.4%).

There are 9 (8.5%) patients positive for pollen IgE-sensitization; 8 among them showed sensitization to at least 2 pollens. The highest number of polysensitization was 17 pollens in one patient, followed by 15 pollens found in another one. Sensitivity to goosefoot pollen is the highest (5.7%), followed by rye pollen (4.7%), plantain pollen (4.7%), wall pellitory pollen (4.7%), and Bermuda grass pollen (3.8%). Sensitivity to other pollens was below 3% (**Table 2**).

Seven of the 9 patients with pollen IgE-sensitization showed also sensitivity to HDM by SPT; the other two were sensitized to food and mould allergens. None of the patients had pollen monosensitization.

DISCUSSION

In this study, the prevalence of pollen IgE sensitization was 8.5%. However, type of pollen varied greatly and included all the 18 pollens tested. Interestingly, most of the pollens tested here are not native to Indonesia. The top 5 pollen sensitizations in our study were goosefoot, plantain, wall pellitory, rye grass, and Bermuda grass.

Goosefoot weed (Chenopodium spp) is originated from Europe but now can be found throughout the world. It is the most prevalent sensitizing pollens in Kuwait, where the plant was imported and cultivated to "green" the deserts.[16] Significant sensitization has also been found in other desert areas in Saudi Arabia, United Arab Emirates and Sudan due to imported plants.[17] In Iran, pollen of white goosefoot (Chenopodium album) is the most common pollen allergen and is associated with the severity of allergic rhinitis (90.4% vs. 9.6%; p=0.035 in persistent vs. intermittent allergic rhinitis patients).[18]

Plantain (Plantago lanceolata) weed is native to Europe and Asia, but currently can be found anywhere in the world. Plantain pollen is usually common in temperate regions and is an important cause of respiratory allergy, particularly in North America, Australia and Europe.[19,20]

Wall pellitory (Parietaria officinalis) is a common weed around the Mediterranean and along the west coast of Europe to the north in central England. Its pollen has been known to induce asthma, allergic rhinitis and allergic conjunctivitis.[21,22]

Allergy to grass pollens has been extensively studied in temperate climates but it has now recognized as important inhalant allergen all over the world.[23] Allergenic grass pollens of the Poaceae family are the most frequently found, which include three subfamilies, i.e. the temperate Pooideae (e.g. Timothy grass, ryegrass and cocksfoot), subtropical Chloridoideae (e.g. Bermuda grass) and Panicoideae (e.g. Bahia grass). Timothy and ryegrass pollens are the most clinically predominant pollen allergen worldwide.[24,25] Data from subtropical and tropical areas showed different pattern. In Singapore, SPT results from 1,000 rhinitis allergic patients found three outdoor allergenic pollens, i.e. Bahia grass (23.1%), mugwort (17.4%) and Bermuda grass (17.3%).[26] Subtropical grass pollens seems to be more important allergen sources than temperate

grass pollens.[23]

Previous study using pollen allergen extract and SPT in Jakarta found that the most common pollen in allergic patients was cogon grass pollen (20.3%).[27] Cogon grass is not cultivated but grows easily everywhere and is considered an invasive weed.[28] Another important allergen was acacia pollen that is found in 16% of allergic patients as well as healthy subjects. Acacia tree (Acacia auriculiformis) is native to Australia, Indonesia, and Papua New Guinea.[29]

Pollen allergy differs geographically and depend on the native plantation in particular area or regions. For instance, the most common pollen allergy in Europe is grass pollen but the type of grass differs among vegetational areas.[9] Tree pollens are also important allergens in Europe; the most common allergenic tree pollens are birch (Betula) in North, Central, and Eastern Europe; olive (Olea europaea) and cypress (Cupressus) in the Mediterranean regions.[9] Different profile was observed in desert areas which found the highest sensitization to indigenous pollens were Chenopodium murale in Sudan, Salsola imbricate and Prosopis juliflora in Riyadh, Saudi Arabia.[17] In Iran, tree pollens from Chenopodium album, Russian thistle and ash tree are the commonest allergens,[30] while in Japan, pollen from Japanese cedar and Japanese cypress are the most common cause of rhinitis allergy.[31]

Sensitivity to environmental allergens is not similar among individuals. Some people are sensitized only after high and long-time exposure and some others can show wide sensitivity to many low dose allergens. Responsiveness to allergens is genetically determined, but allergic symptoms can only manifest in atopic persons when there is continuous exposure to an allergen, which is sufficient to elicit reaction and clinical symptoms.[32,33]

This study provided the first information of pollen IgE sensitization among respiratory allergic patients using a panel of multiple allergens. It showed that pollen allergens may have a role in eliciting allergic symptoms. However, there were several limitations in this study. First, the allergens tested was not specifically developed from native pollens of Indonesian local plants. Second, positive results were not confirmed by SPT as the gold standard to diagnose allergy; thus, positive results in this study could only mean IgE sensitization not allergy. Third, the clinical implication of this IgE sensitization was not assessed as all patients showed also sensitization to other group of allergens as showed by the positive SPT.

CONCLUSION

Pollen IgE-sensitization is found in a small percentage of respiratory allergic patients although most of the pollen sources are not native plants to Indonesia. This finding is particularly useful for allergic persons planning to travel to the endemic areas of the relevant pollen. A panel of pollen allergens from local plants is highly needed in the future.

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