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Aeroallergen sensitization and associated comorbid diseases of an adult Filipino population with allergic rhinitis

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ABSTRACT

Background: There is a large global variation in sensitization patterns to aeroallergens due to differences in climate, urbanization, and lifestyle. Knowledge of the most common inhalant allergens is important for appropriate prevention and management of allergic rhinitis (AR).

Objective: This study aims to provide data on aeroallergen sensitization patterns and associated comorbid diseases of adult Filipinos with AR.

Methods: Medical records of adult Filipinos seen in an Otolaryngology-Allergy Clinic from January 2011 to 2016 were reviewed. Inclusion criteria used was presence of clinically defined AR and positive skin test to at least one aeroallergen in the test panel. Demographics, comorbid conditions, and results of skin prick test were determined. Standard descriptive statistics were used for analysis.

Results: One hundred ninety-one adult patients were included in this study. Mean age was 38.8 years, and majority lived in an urban area (71.2%). Most patients exhibited polysensitization (97.4%). All exhibited sensitization to indoor and 86.9% to outdoor allergens. The most common indoor allergens were *Dermatophagoide*s *pteronysinus* (97.4%), *Dermatophagoide*s *farinae*, (95.8%), cockroach (80.1%), and molds (72.8%). Bermuda (67%), Johnson grass (58.7%), and Acacia (58.2%) were the most common outdoor allergens. Urticaria (18.8%), dermatitis (16.8%), and asthma (11.5%) were the most common associated comorbid disease. Twelve percent of patients had more than one associated comorbid disease. Asthma + urticaria followed by asthma + dermatitis were the most common comorbid combinations. One patient had three comorbid diseases: asthma + urticaria + rhinosinusitis.

Conclusion: Compared to earlier studies, aeroallergen sensitization patterns of Filipinos remain unchanged. This study also identifies for the first time, the associated comorbid diseases of AR in this population. Understanding these factors can guide treatment strategies to reduce disease burden.

Keywords: Aeroallergen sensitization; Allergic rhinitis; Allergic rhinitis comorbidity; Filipinos; Skin prick test

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INTRODUCTION

The skin prick test (SPT) is a standard diagnostic technique in clinical practice used for investigation of sensitization in IgE-mediated allergic disease such as allergic rhinitis (AR), asthma, urticaria, atopic eczema, food, and drug allergy. It utilizes the presence and degree of cutaneous reactivity as surrogate marker for sensitization of target organs. It is helpful in cases when diagnosis is uncertain, when empiric treatment fails, or when targeted therapy for specific allergens is needed [1]. There is a large global variation in sensitization patterns due to differences in climate, urbanization, and lifestyle. Knowledge of the most common inhalant allergens in the local setting is important for appropriate prevention and management of AR. Data on sensitization patterns among Filipinos is available for the 1970's and 1990's. However, changes in economic conditions, level of industrialization, and lifestyle in the last 2 decades can affect prevailing circulating aero-allergens and consequently, sensitization patterns. This study aims to provide data on sensitization patterns to aeroallergens and the associated comorbid diseases of an adult Filipino population with AR.

MATERIALS AND METHODS

This study was approved by the Institutional Scientific and Ethical Review Boards of St. Luke's Medical Center (RPC-105-12-15). A retrospective chart review of Filipinos, aged 20 years and older, referred to an Otolaryngology-Allergy Clinic during the study period January 2011 to 2016 was done. Inclusion criteria for subjects were presence of symptoms of clinically defined AR and positive SPT to at least one aeroallergen in the test panel. Clinically, AR was defined as presence of 2 or more of the following symptoms: watery rhinorrhea, nasal obstruction, sneezing, or nasal/ocular pruritus for more than 1 hour per day within the last 6 months. From the records, the following data were extracted: demographics, location of residence (urban/rural), AR symptoms, comorbid conditions, and results of SPT. Comorbid conditions were determined based on available laboratory results (pulmonary function test, sinus X-rays, or videoendoscopy reports), referring physician's diagnosis, or patient's recall of their physician's diagnosis. Recorded comorbid conditions were either being currently treated at the time of referral or had been treated in the past by the referring physician.

The SPT was performed on the volar side of the forearm and results were read after 15 minutes. Mean wheal diameter was determined by measuring the largest diameter and its perpendicular diameter and dividing the sum by two. A positive test was defined as a mean wheal diameter of 3 mm greater than the negative control. Antihistamine medications of patients were stopped 1 week before performance of SPT. The test panel used consisted of the following allergen extracts: *Dermatophagoides pteronyssinus* (Greer Laboratories Inc., Lenoir, NC, USA), *Dermatophagoides farina* (Greer Laboratories Inc., Lenoir, NC, USA), *Blomia tropicalis* (NUS, Singapore), cockroach (Greer Laboratories Inc., Lenoir, NC, USA), molds (Greer Laboratories Inc., Lenoir, NC, USA), dog (HollisterStier, Spokane, WA, USA), cat (HollisterStier, Spokane, WA, USA), mouse (Greer Laboratories Inc., Lenoir, NC, USA), Bermuda (Greer Laboratories Inc., Lenoir, NC, USA), Acacia (Greer Laboratories Inc., Lenoir, NC, USA), Johnson grass (Greer Laboratories Inc., Lenoir, NC, USA), Pigweed (Greer Laboratories Inc., Lenoir, NC, USA), Feather mix (HollisterStier, Spokane, WA, USA), kapok (Greer Laboratories Inc., Lenoir, NC, USA). Positive control histamine and negative control diluent were sourced from HollisterStier (Spokane, WA, USA).

Standard descriptive statistics were used to determine frequency and percentage for categorical variables. Mean and standard deviation were determined for continuous variables. Data was encoded on Microsoft Office Excel 2007 (Microsoft, Redmond, WA, USA) and analyzed using IBM SPSS Statistics ver. 20.0 (IBM Co., Armonk, NY, USA).

RESULTS

A total of 191 adult patients were included in this study. Mean age was 38.8 years (median, 38; standard deviation, 13.07), and most lived in an urban area (71.2%). Most patients exhibited polysensitization (97.4%). All patients exhibited sensitization to indoor and 86.9% to outdoor allergens (Table 1). The most common indoor allergens were house dust mites (HDM) *D. pteronyssinus* (97.4%) and *D. farinae* (95.8%), followed by cockroach (80.1%) and molds (72.8%). Bermuda (67%), Johnson grass (58.7%), and Acacia (58.2%) were the most common outdoor allergens (Table 2). No statistically significant association was found between type of home and sensitization to indoor or outdoor allergens.

Table 1. Patient demographics and characteristics (n = 191)

Characteristic	Value
Sex	
Female	124 (64.9)
Male	67 (35.1)
Age (yr)	
Female	38.1 ± 13.04
Male	40.1 ± 13.13
Residence location	
Urban	136 (71.2)
Rural	55 (28.8)
Type of aeroallergen	
Indoor	191 (100)
Outdoor	161 (86.9)
Type of sensitization	
Monosensitization	5 (2.6)
Polysensitization	186 (97.4)

Values are presented as number (%) or mean ± standard deviation.

Table 2. Frequency of most common aeroallergens

Type of aeroallergen	Percentage
Indoor	
<i>Dermatophagoides pteronyssinus</i>	97.4
<i>Dermatophagoides farinae</i>	95.8
Cockroach	80.1
Molds	72.8
<i>Blomia tropicalis</i>	60.8
Dog	59.8
Cat	59.5
Mouse	30.9
Outdoor	
Bermuda	67.0
Johnson grass	58.7
Acacia	58.2
Pigweed	57.9
Feather mix	39.5
Kapok	32.5

Table 3. Frequency of comorbid diseases

Comorbid disease	No. (%)
Sinusitis	17 (8.9)
Asthma	22 (11.5)
Urticaria	36 (18.8)
Dermatitis	32 (16.8)
Food allergy	10 (5.2)
Angioedema	8 (4.2)
Drug allergy	5 (2.6)
Otitis media	6 (3.1)

Urticaria (18.8%), dermatitis (16.8%), and asthma (11.5%) were the most common comorbid diseases associated with AR (Table 3). Twelve percent (23 of 191) of patients had more than one associated comorbid disease; the most common combinations among these patients were asthma + urticaria followed by asthma + dermatitis. One patient had 3 comorbid diseases, namely, asthma + urticaria + rhinosinusitis. No statistically significant association was found between either sex or type of home and comorbid conditions.

DISCUSSION

Sensitization to aeroallergens

Globally, HDM are common sensitizing aeroallergens in patients with AR. In the adult population of Southeast Asian countries, HDM sensitization is reported to be 80% for Malaysia, 33.3%–68.5% for Singapore, and 64.7% for Thailand [2-4]. In Vietnam, where sensitization to mites is common in both rural and urban areas, specific rates for HDM *D. pteronyssinus* are men 16.5%, women 10.6% and for *D. farinae*, men 15.3% and women 6.3% [5].

The earliest published study in the Philippines on sensitization patterns reports HDM (87%), cockroach (41%), mold spores (37%), cat dander (36%), kapok (35%), and dog dander (32%) as the most common aeroallergens [6]. A more recent study reports HDM sensitization to be 33.3%–47.1% [7]. Our results show that HDM continue to be leading indoor allergens for Filipinos. However, our rates of greater than 90% are among the highest reported for the region. This can be attributed to our study population which consists of patients seen in a specialty clinic. The hospital catchment for referrals comes mainly from the surrounding highly urbanized areas where HDM sensitization is likely to be high.

Sensitization to *B. tropicalis* in highly urbanized Metro Manila is reported to be 85% [8]. In our study population of urban and rural dwellers, the prevalence rate of 60.8% is consistent with reported rates of 68.9% in Singapore but much higher than Vietnam's rates (men, 27.7%; women, 18.7%) [3, 5]. In our study, 60.8% of patients with a positive test for *Blomia* also exhibit sensitization to *Dermatophagoides*. In tropical countries like those in the Southeast Asian region, the codominant presence of both *Dermatophagoides* and *Blomia* species in the environment is reported to be the cause of a wide range of mite sensitization among atopic individuals [9].

Cockroach sensitization also continues to remain high in the list of sensitizing indoor allergens for Filipinos. In general, for Southeast Asian nations, AR is associated with cockroach sensitization [5, 10]. However, our rates for cockroach sensitization are much higher than Vietnam where rates are 13.1% in the adult population [5]. The difference may be

attributed to our study population, which consisted of symptomatic and treatment seeking patients seen in a specialty clinic, compared to the randomly selected study respondents in the Vietnam study.

Grass is reported to be the predominant outdoor allergen in earlier Philippine studies [11]. Our results show that grass continues to be the most common outdoor allergen in the country. Other Southeast Asian countries with published sensitization results for grass in the adult population show much lower rates than the Philippines. Thailand reports rates of only 21% for Johnson grass and 17% for Bermuda grass [12].

There is a high prevalence of polysensitization (97.4%) in our study. A review of published literature on sensitization reports that 51% – 81% of patients with allergies are polysensitized [13]. Specifically, among atopic patients, 74.3% of those with respiratory allergies are polysensitized [14]. The risk of AR is also reported to increase with the number of sensitizations [15]. Our high rates of polysensitization can be attributed to our study population of patients with active clinical allergic nasal symptoms.

Common comorbid conditions of AR

In our study, the most common comorbid diseases are urticaria, dermatitis, and asthma. Asthma as a comorbid condition in patients with AR is associated with poorer control, greater exacerbations, and increased emergency visits [16, 17]. Among Asian populations, AR and asthma are the most common reported comorbid diseases. In a study on respiratory diseases in Taiwan, AR and asthma were the most frequently reported comorbid diseases with rates of 14.1% [18]. For Korea, AR + asthma rates are 16.1% [19] while in Thailand, rates of AR + asthma are 18.5% [20]. Among Malaysian patients with AR, 28.8% have concomitant asthma [21].

Presentation of asthma and/or AR is reported to be strongly associated with HDM sensitization in tropical urban settings [3]. HDM are the main sensitizing allergens among adult asthmatics in Singapore and Malaysia [20, 21]. In Thailand, 40.8% to 51.1% of patients with allergic airway disease test positive for HDM [22, 23]. In Vietnam, AR but not asthma is associated with mite sensitization. All patients with asthma in our study exhibit sensitization to HDM.

Atopic dermatitis is postulated to be the initial phase of the so called allergic march. Prevalence is reported to be 2%–10% in adults; it is reported to be increasing in industrialized countries. The role of sensitization to inhalant allergens in atopic dermatitis is unclear. An international consensus on mite sensitization concludes that there is evidence HDM are involved in the pathogenesis of AD but the definite association needs to be established [24].

Among the various types of urticaria, the acute form is often IgE mediated. In acute urticaria, histamine is the key mediator in the activation of superficially situated mast cells in the skin. Currently, the signaling mechanisms for mast cell activation for most urticaria are not clearly established. Furthermore, various studies show that in addition to release of histamine from underlying mast cells, other features are present, such as upregulation of adhesion molecules and altered cytokine expression in both involved and uninvolved skin. This suggests that the pathophysiology of urticaria is complex [25, 26]. In the Southeast Asian region, urticaria and its associations with other IgE mediated diseases are largely underexplored. A Thai study reports that 20.4% of patients with urticaria have concomitant AR. Furthermore, 34.9% of

patients with chronic idiopathic urticaria test positive to mites [27]. All urticaria patients in our study test positive to at least one HDM species. The clinical relevance of HDM sensitivity to urticaria symptoms among our patients is, at this time, unclear and unknown.

In general, Filipinos regardless of their symptom severity, are not likely to seek consultation for AR [28]. The patients who seek consult at a specialty clinic are likely to have complicated or uncontrolled disease that is perceived to require specialized treatment and/or management. This may explain the high number (12%) of our patients who have more than one comorbid disease associated with AR. Although urticaria is the most common single comorbid condition, asthma remains the most common disease in combination with other IgE mediated diseases for our patients with AR. This finding suggests the applicability of the united airway concept to our population.

Although studies on aeroallergen sensitization in the Philippines are scarce, our results are consistent with earlier studies that show HDM as common sensitizing indoor allergens among Filipinos with AR. Similarly, the finding of grass as the most common sensitizing outdoor allergen is consistent with these early studies. Our results suggest that the most common indoor and outdoor sensitizing aeroallergens for Filipinos with AR may not have significantly changed.

Our study identifies, for the first time, the associated comorbid diseases of AR in a Filipino population. Knowledge of these conditions can guide therapeutic interventions and strategies to reduce the disease burden of AR. However, due to the study design and nature of the study population, our study has certain limitations. The diagnosis of co-morbid conditions is based on a retrospective chart review. Laboratory examinations are not always available to confirm/validate patients' recall of their comorbid diseases. Also, patients referred to specialty centers are likely to have more severe, uncontrolled, complicated disease or multiple coexisting comorbid conditions which can result to selection bias. Therefore, we recommend that other studies with greater sample size and respondents from less specialized clinics/hospitals be done to confirm the applicability of our results to the general population of Filipinos with AR.

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