ORIGINAL ARTICLE

Skin Prick Test Reactivity to Common Aeroallergens among Allergic Rhinitis Patients

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Abstract

Objective: To identify the common aeroallergens causing allergy symptoms among the allergic rhinitis patients.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Immunology, Armed Forces Institute of Pathology (AFIP), Rawalpindi, from January to July 2016.

Methodology: Patients with a clinical diagnosis of allergic rhinitis were enrolled. Skin Prick Test (SPT) was performed on these patients using 12 common aeroallergens along with positive (histamine hydrochloride, 10 mg/ml) and negative (glycerin saline) controls. Results were recorded after 15 minutes, considering a wheal diameter ≥3 mm as positive. Chi-square test was used to compare frequencies; and p-value of less than 0.05 was considered significant.

Results: Out of 130 patients, 78 (60%) were males and 52 (40%) were females. The rate of sensitization to any allergen was 90%. One hundred and two (78%) were poly-sensitized to more than two allergens and 20% were sensitized to more than six allergens. Most common outdoor and indoor allergens were *Broussonetia papyrifera* (50.7%) and *Dermatophagoides farina* (42.3%), respectively. Dog epithelia and aspergillus were the least prevalent allergens (13.8% each).

Conclusion: This study highlighted an increased overall frequency of sensitization to any allergen and significance of tree and weed allergens; especially, *Broussonetia papyrifera* and *Cannabis sativa*. It also emphasized increased prevalence of skin reactivity to indoor allergen, *Dermatophagoides farina* in the city.

Key Words: *Allergy, Aeroallergens, Prevalence, Skin prick test, Allergic rhinitis.*

INTRODUCTION

Allergic rhinitis (AR) is a common immunological disorder; and worldwide 10-40% of the population is affected by this respiratory allergy.[1] It is characterized by sneezing, rhinorrhea (anterior and posterior), nasal congestion and/or nasal itching. A strong association between AR and other conditions like asthma, allergic conjunctivitis and sinusitis has been observed.[2] Asthma occurs in 25 to 50 percent of individuals with AR. Conversely, AR occurs in 75 to 90 percent of adult subjects with asthma.[3]

AR whether seasonal or perennial has a negative impact on quality of life by causing significant morbidity and economic expanse.[4]

Aeroallergens are notorious for their role in pathogenesis of AR. Identification of the most common aeroallergens causing respiratory allergies is critical in diagnosis and management of AR. Educating effective ways of aeroallergen avoidance to the patients, selecting a cost-effective panel of allergen extracts for skin prick test, and ensuring availability of selective vials of allergens for effective allergen immunotherapy strictly depend on the information about common culprit aeroallergens causing AR in a particular area.[5]

Literature review reveals different allergen sensitization profile in different regions of the world. When the pollen count of 9000 particles per cubic meter is considered record in some areas of United States, pollen count easily goes above 30,000 particles per cubic meter in Islamabad, accounting for maximum number of allergy patients dwelling the city when compared with other areas of the country. Information obtained from Allergy Clinic, PIMS, Islamabad disclosed that 360 patients attended the clinic on the same day, 14th March, 1996; and a state of emergency was declared as over 200 patients were waiting for oxygen mask within one hour.

As the prevalence of respiratory allergies has increased worldwide, mainly due to industrialization leading to environmental changes, a group of professionals and experts are of the opinion that pollen allergens are not the only cause of the prevalent allergies; rather the ascending rise in allergic diseases is equally associated with other environmental pollutants like dust mites, molds and animal dander.[6]

The rationale of this study was to look into the latest trends of allergic sensitization to aeroallergens in

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patients of AR dwelling in Islamabad city in order to formulate better strategies for management and prevention of AR. The objective of this study was to identify the common aeroallergens causing allergy symptoms among the allergic rhinitis patients.

METHODOLOGY

The study was conducted as a cross-sectional study on the patients with rhinitis symptoms, who were referred to Immunology Department of Armed Forces Institute of Pathology (AFIP), Rawalpindi, between January to July 2016. The Ethics Committee approved the study protocol and informed consent was obtained from all the patients.

A total of 130 patients were enrolled in the study. Inclusion criteria were patients having a problem with sneezing and runny or blocked nose in the absence of cold or flu in the past 12 months; not taking any medications for the symptoms, and without any history of specific immunotherapy.

A study questionnaire recording demographic data, smoking history, family history of allergic diseases, pattern of symptoms (seasonal/perineal) and comorbidities (asthma/rhino-conjunctivitis) was obtained from each patient. Active smoker was defined as a person who was smoking at a frequency of at least one cigarette a day or one cigarette a week for a period of one year.

Skin prick test was performed on all patients using 12 common aeroallergen extracts (Greerlabs, USA); and included two dust mites (*Dermatophagoides farina*e and *Dermatophagoides pteronyssinus*), mould mix (*Alternaria alternata, Cladosporium, Penicillium chrysogenum (notatum)*, Aspergillus mix (*A. amstelodami, A. flavus, A. fumigatus, A. nidulans, A. niger*), German cockroach (*Blattella germanica*), standardized cat hair (*Felis catus*), dog epithelia (*Canis sp.*), Dandelion (*Taraxacum officinale*), southern grass mix (Kentucky blue, Meadow Fescue, Orchard, Perennial Ryegrass, Redtop, Sweet Vernal, Timothy, Bermuda and Johnson), paper mulberry (*Broussonetia papyrifera*), ragweed mix (*Ambrosia trifida* and *Ambrosia artemisiifolia*) and cannabis (*Cannabis sativa*). Aeroallergens were selected based on the common plants of the city; and other allergens were identified by the consulting specialists examining the patients for complaints related to ear, nose and throat, based on history and examination.

Skin prick tests were performed by an immunologist accompanied by a nurse with expertise in emergency management of anaphylaxis and other allergic reactions. Allergen extracts were applied to the forearms of patients along with positive (histamine hydrochloride, 10mg/ml) and negative (glycerin saline) controls and epidermis was irritated using lancet. Results were recorded after 15 minutes, considering a wheal diameter ≥3 mm positive when compared with negative control. Venous blood was collected from 130 patients and serum was separated and stored at -20°C.

For total IgE levels in serum, ELISA was performed in duplicate on all the serum samples using commercial kit (DIPLUS, Canada). According to manufacturer, IgE level more than 100 IU/ml was considered elevated.

Microsoft excel was used to process and analyze data. Chi-square test was used to compare frequencies and independent sample t-test was used to compare means. A p-value of less than 0.05 was considered significant.

RESULTS

One hundred and thirty patients were evaluated for skin prick test against 12 allergens. Demographic characteristics of the patients are presented in Table I. The median duration of allergic rhinitis was 3.5 (0.5-20) years. Among 130 patients of allergic rhinitis, additional symptoms of allergic conjunctivitis were found in 52% (68) patients while 16.9% (22) of the patients had coexisting asthma along with allergic rhinitis. A positive family history of allergic diseases was found in 56.9% (74) patients while 28.6% (37) of the patients were active smokers. Among patients with positive skin prick test, seasonal pattern (symptoms restricted to particular season) was observed in 66% (86) of the patients while perennial pattern (everlasting symptoms) was seen in 34% (44).

Table I: Characteristics of patients with allergic rhinitis.

Characteristics	No. (%) of the cases
Total patients	130
Mean age (±SD)	38.32 (±12)
Gender:	
Male	78 (60%)
Female	52 (40%)
Median duration of allergic rhinitis (range)	3.5 years (0.5-20)
Active rhinoconjunctivitis	68 (52%)
Asthma	22 (16.9%)
Active smoker	37 (28.6%)
Family history	74 (56.9%)
Severity of disease:	
Mild	25.38%
Moderate	23.08%
Severe	51.54%
Seasonal	86 (66%)
Perennial	44 (34%)

Overall rate of sensitization to any allergen was around 90% (118), with 10% (12) of the patients showing no reaction to any of the tested allergens.

Out of all patients, 78% (102) were poly-sensitized (positive skin reaction to at least two allergens) and 20% (26) were sensitized to more than six allergens.

Among the patients with allergic rhinitis, *Broussonetia papyrifera*, *Dermatophagoides fariae* and *Cannabis*

sativa were the most prevalent allergens (50.7% (66), 42.3% (55) and 41.5% (54), respectively, (Table II).

Among indoor allergens, *Dermatophagoides farina* was the most common allergen (42.3%, n=55) followed by *Dermatophagoides pteronyssinus* (38.4%, n=50), *Blattella germanica* (26.1%,n=34) and *Felis catus* (25.3%, n=33). Dog epithelia (*canis sp.*) and Aspergillus made the least prevalent allergens (13.8%, n=18 each), (Table II).

Among outdoor allergens, *Broussonetia papyrifera* (50.7%, n=66) made the most prevalent allergen followed by *Cannabis sativa* (41.5%, n=54). Other common outdoor allergens included *Taraxacum officinale* (40%, n=52); grass mix (32.3%, n=42) and ragweed mix (32.3%, n=42).

Among weed pollens, *Cannabis sativa* made the most frequent allergen (41.5%, n=54) while ragweed was least prevalent (32.3%, n=42), (Table II).

Among patients with positive skin prick tests, mean and median numbers of positive reactions were 3.8 ±1.8 and 4 (IQR=1.8), respectively.

There were 78 (60%) males and 52 (40%) females evaluated for skin prick responses against aero-allergens. Mean age of men and women with positive reactions were 39.2 ±15.1 and 36.8 ±15, respectively. However, the differences were not significant (p=0.4). Except for cockroach (*Blattella germanica*), no statistically significant difference was observed in rate of sensitization to selected allergens between male and female patients (female *vs.* male; 38.4 *vs.* 17.9; p=0.009).

Table II: Prevalence of positive skin prick test to selected allergens and total IgE among patients with allergic rhinitis.

Aeroallergens		All patients	Sex		p-value
		(n=130)	Male	Female	(Male vs. Female)
Common name	Scientific name		(n=78)	(n=52)	
Mites	*Dermatophagoides farina*	42.3% (55)	41.0% (32)	44.2% (23)	0.7
Mites	*Dermatophagoides pteronyssinus*	38.4% (50)	37.1% (29)	40.3% (21)	0.7
Molds	*Alternaria alternata*				
Mix	*Cladosporium, Penicillium chrysogenum (notatum)*	23.8% (31)	21.7% (17)	26.9% (14)	0.5
Aspergillus mix	*A. amstelodami, A. flavus, A. fumigatus, A. nidulans, A. niger*	13.8% (18)	8.9% (7)	21.1% (11)	0.05
Cockroach	*Blattella germanica*	26.1% (34)	17.9% (14)	38.4% (20)	0.009
Cat hair	*Felis catus*	25.3% (33)	20.5% (16)	32.6% (17)	0.1
Dog epithelia	*Canis sp.*	13.8% (18)	15.3% (12)	11.5% (6)	0.5
Dandelion	*Taraxacum officinale*	40.0% (52)	44.8% (35)	32.6% (17)	0.2
Grass mix		32.3% (42)	34.6% (27)	28.8% (15)	0.5
Kentucky blue, Orchard	*Pao pratensis,*				
Perennial ryegrass	*Dactylis glomerata,*				
Timothy	*Lolium perenne,*				
Sweet vernal	*Phleum pretense,*				
Red top	*Anthoxanthum odoratum,*				
Meadow fescue	*Agrostis gigantean,*				
Bermuda, and	*Festuca pratensis,*				
Johnson	*Cynodon dactylon, and Sorghum halepense*				
Paper mulberry	Broussonetia papyrifera	50.7% (66)	53.2% (42)	46.5% (24)	0.4
Ragweed mix	Ambrosia trifida and Ambrosia artemisiifolia	32.3% (42)	34.6% (27)	28.8% (15)	0.5
Cannabis	Cannabis sativa	41.5% (54)	42.3% (33)	40.3% (21)	0.8
IgE (Mean±SD IU/ml)		213 ±238 IU/ml	263 ±264 IU/ml	136 ±161 IU/ml	<0.005

Table III: Prevalence of positive skin prick test to selected allergens among different age groups of allergic rhinitis patients.

Allergens	1-17 years (n= 8)	18-30 years (n= 35)	31-45 years (n= 49)	>46 years (n= 38)	p-value
Mites *D.farinae*	50.0% (4)	28.6% (10)	42.9% (21)	52.6% (20)	0.2
Mites *D.pteronyssinus*	50.0% (4)	22.9% (8)	40.8% (20)	36.0% (18)	0.1
Molds mix	25.0% (2)	25.7% (9)	16.3% (8)	38.7% (12)	0.4
Aspergillus	37.5% (3)	14.3% (5)	14.3% (7)	16.7% (3)	0.2
Cockroach	50.0% (4)	34.3% (12)	18.4% (9)	26.5% (9)	0.1
Cat hair	25.0% (2)	34.3% (12)	16.3% (8)	33.3% (11)	0.3
Dog epithelia	12.5% (1)	11.4% (4)	18.4% (9)	22.2% (4)	0.7
Dandelion	12.5% (1)	37.1% (13)	46.9% (23)	28.8% (15)	0.3
Grass mix.	37.5% (3)	31.4% (11)	24.5% (12)	38.1% (16)	0.4
Paper mulberry	62.5% (5)	42.9% (15)	46.9% (23)	34.8% (23)	0.4
Ragweed	12.5% (1)	31.4% (11)	36.7% (18)	28.6% (12)	0.6
Cannibis	62.5% (5)	45.7% (16)	40.8% (20)	24.1% (13)	0.5

The mean total IgE level was 213 ±46 IU/ml. The mean total IgE level in men was determined as 263 ±264 IU/ml which was higher than that of females 136 ±161 IU/ml and the difference was significant ($p < 0.05$), (Table II). Significantly, higher values of mean total IgE were observed in individuals with positive SPT when compared with IgE values of patients with negative SPT ($p < 0.01$).

There was no difference in the prevalence of positive skin prick test between younger and older patients with allergic rhinitis (Table III).

DISCUSSION

As aeroallergens are the main cause of triggering symptoms in patients with respiratory allergies and allergen avoidance constitutes an important aspect of management; therefore, defining most prevalent allergens has been subject of many studies carried out in different parts of the world. Patients from a particular area benefit a great deal from these studies as allergen panel for skin prick test and specific immunotherapy should be selected depending upon prevalent allergens causing allergies in that area.[5]

Our study revealed a higher rate of sensitization to any allergen (90.7%) which is higher than the results from other studies.[7]

Although, some communities are more affected by indoor allergens, pollens still make the most common allergens responsible for allergic rhinitis worldwide. Most important pollens causing allergies are different in different parts of the world; and meteorological parameters (wind, temperature, solar radiation, humidity, and rainfall) have a strong impact on pollen concentration.[8] Islamabad is well known for its high pollen count turning the spring season into allergy season with almost all hospital emergencies on red alert to provide relief to allergy patients. Paper mulberry pollen was pointed out as main culprit triggering allergy symptoms in local patients by NIH in early 1990s. However, a number of health professionals serving in the Federal government hospitals believed that an ascending rise in allergies in the city is equally caused by other environmental factors like dust and not solely by pollens.[6]

Likewise, skin prick test in patients of allergic rhinitis revealed a high incidence of plant pollen allergy and the most common was found to be paper mulberry (*Broussonetia papyrifera*) which is in accordance with other local studies.[9]

Cannabis (*Cannabis sativa*) 41.5% was most common sensitizing weed allergen in this study. In spite of prohibition of cultivation of cannabis by anti-narcotic law of Pakistan and campaigns by Capital Development Authority (CDA) to eradicate cannabis, it grows wildly in many areas of Islamabad, accounting for a large number of patients presenting to allergy clinics during fall.

Allergic sensitization to grass allergen in this study is 32.3%, which is less than reported in other studies from countries like Iran,[9] Netherlands,[10] and Germany,[11] but in agreement with other studies from UAE.[12]

Moreover, rate of sensitization to molds (*Alternaria alternata, Cladosporium, Penicillium chrysogenum*) was found to be 23.8%, which was higher than results of studies from Iran and Saudi Arabia but lower than studies from Sudan.[13] In this study, least prevalent mold was found to be aspergillus with 13.8% which was still higher than what was found in Saudi Arabia but much lower than results of studies from Sudan.[13]

Among indoor allergens, most prevalent allergen was found to be mites with *D. farinae* accounting for 41% and *D. pteronyssinus* accounting for 37.1%. Dust storms are common in Islamabad in the month of May and June; however, no data is available on effects of dust storms on public health, particularly respiratory allergies in this area. With consideration of humidity reaching as high as 90% in December and an average temperature remaining above 20°C from March to August in Islamabad, our results were to be expected and are supported by other studies carried out in Pakistan.[14] Higher rate of sensitization to dust mites has also been reported in other studies from humid regions like Thailand,[15] and Malaysia.[16] Unexpectedly, hot and dry regions like Kuwait,[17] and Qatar,[18] are also known for this particular allergy; and possible reason could be increased use of airconditioners that make the environment favorable for mites. Another possible explanation could be increased humidity in coastal cities of these countries that make them favorable for dust mite growth when compared with other cities of these countries.[19]

In the current study, sensitization rate to cat allergen was found to be 33.3%, which is in contrast to studies from USA and Japan which showed a higher rate of sensitization to cat allergens. A cultural trend of keeping cats as pets in countries like US and Japan is an obvious risk factor and can be offered as a possible explanation for this prevalence as high as 80% or above in local atopics.[20,21]

Likewise, sensitization against dog allergen which was 22.2% was lower than the prevalence reported from countries like US and Sweden once again referring to the fact that in countries like US more than 60% of the households keep pets and more than 161 million of these pets are dogs and cats.[22]

In this study, 78% of the patients were poly-sensitized to two or more allergens. Factors that lead to multi-allergen sensitization include genetics, environmental factor and cross-sensitization between botanically closed species sharing common allergenic epitopes.[23] In spite of using plant allergens that do not belong to closely related species; more than one third of the patients were

sensitized to more than six allergens, reflecting co-sensitization between allergens of different categories.

About 10% of the patients did not show skin response to any of the tested allergens. This is lower than some other studies that report 19%,[5] and 58%,[24] patients with negative SPT reactivity. Possible reasons for negative response to SPT include sensitivity of SPT less than 100% and the fact that patients were allergic to particular allergens that were not tested in the study, or not yet identified.

Except for cockroach (*Blattella germanica*), data analysis did not reveal statistically significant difference in rate of sensitization to selected allergens between male and female patients (Table II). Since cockroaches are among the most common pests in many homes, and usually at night they search for food in kitchen and rubbish bins, the possible explanation for increased sensitization in females could be frequent and prolonged exposure of ladies working in kitchens. In some studies from countries like Kuwait,[17] prevalence rate of sensitization towards outdoor allergens is higher in males than in females, as men usually spend more time outdoors; and therefore, they are more exposed to outdoor aeroallergens, when compared with females. However, the present study did not highlight any difference of sensitization to outdoor allergens between male and female patients.

No statistically significant difference was observed in rate of sensitization to selected allergens between younger and older patients with allergic rhinitis. The present findings differ from results of some of the studies,[17] which reveal higher prevalence of indoor allergens like mite and cockroach in young patients (Table III).

In this study, the mean total IgE in sera of allergic rhinitis patients was higher in male patients when compared with females and similarly patients with positive SPT have higher levels of total IgE as compared to patients with negative SPT. Possible explanation for increased IgE levels in males could be increased smoking trend in males and relatively increased exposure to outdoor aeroallergens keeping in mind the cultural trend of more working males as compared to their female counterparts. Apart from allergic diseases, elevated total IgE depends on several other factors; such as parasitic infestation, genetic background, smoking, diet and environmental pollution.[25]

CONCLUSION

The study revealed very common poly-sensitization among the residents of Islamabad. This work supports increased prevalence of paper mulberry and cannabis allergy among residents of Islamabad, once again reminding the Capital Development Authority (CDA) to eradicate cannabis weeds and paper mulberry trees. In addition to plant pollens, prevalence of indoor allergen is also rising among atopic residents of Islamabad. Furthermore, allergy diagnosis can be simplified by using a combination of only common aeroallergens (*e.g.*, cannabis, paper mulberry).

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