ORIGINALA ARTICLE
Iran J Allergy Asthma Immunol
April 2018; 17(2):123-133.

IgE Sensitization to Inhalant Allergens and Its Association with Allergic Diseases in Adults

Raheleh Shokouhi Shoormasti[1], Mohammad Reza Fazlollahi[1], Anoshirvan Kazemnejad[2], Behnoosh Tayebi[1], Fatemeh Nadali[3,4], Maryam Sharif Shoushtari[1,5], Shamim Khandan Alamdari[1], Majid Moslemi[4], Masoud Movahedi[6], Adriano Mari[7], Zahra Pourpak[1], and Mostafa Moin[1,6]

[1] *Immunology, Asthma, and Allergy Research Institute, Tehran University of Medical Sciences, Tehran, Iran*
[2] *Department of Biostatistics, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran*
[3] *Hematology and Blood Banking Department, School of Allied Medical Sciences, Tehran University of Medical Sciences, Tehran, Iran*
[4] *Blood Transfusion Organization Research Center, Tehran, Iran*
[5] *Department of Biology, Science and Research Branch, Islamic Azad University, Tehran, Iran*
[6] *Department of Immunology and Allergy, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran*
[7] *Associated Centers for Molecular Allergology, CAAM, Rome, Italy*

Received: 10 July 2017; Received in revised form: 21 August 2017; Accepted: 29 August 2017

ABSTRACT

Allergic sensitization to inhalant allergens could be considered as a predictor in allergic diseases. The objective of this study was to assess IgE-mediated sensitization to inhalant allergens in allergic and non-allergic adults as well as the evaluation of its association with allergic diseases.

This cross-sectional study was conducted from 2013 to 2016 in 604 allergic and 102 non-allergic adults selected from blood donor volunteers in Tehran, Iran. After taking informed consent, a standard questionnaire was filled to determine asthma, allergic rhinitis and/or conjunctivitis and atopic dermatitis in participants. Specific IgE assay to common inhalant allergens was performed for all subjects. Logistic regression analysis was used to evaluate the impact of IgE sensitization on allergic diseases. A total of 371(61.4%) allergic subjects and 41(40.2%) non-allergic patients were males.

The weeds (especially saltwort) and grasses (particularly meadow fescue and ryegrass) were identified as the most common inhalant allergens. The prevalence of IgE sensitization to trees, weeds, and grasses was higher in subjects with allergic rhino-conjunctivitis and trees sensitization was a significant factor in them [OR=2.32, 95% CI (1.58-3.41)]. IgE sensitization to any inhalant allergens could be a predictor for allergic rhinitis, conjunctivitis and rhino-conjunctivitis in adults [OR=2.20, 95% CI (1.54-3.15], [OR=1.81, 95% CI (1.28-2.54)] and [OR=2.55, 95% CI (1.72-3.78)], respectively. With an increase in the sum of specific IgE concentrations, the prevalence of allergic conjunctivitis and rhino-conjunctivitis also increased.

Corresponding Authors: Zahra Pourpak, MD, PhD;
Immunology, Asthma, and Allergy Research Institute, Tehran University of Medical Sciences, Tehran, Iran. Tel: (+98 21) 6691 9587, Fax: (+98 21) 6642 8995, E-mail: pourpakz@sina.tums.ac.ir

Adriano Mari, MD;
Associated Centers for Molecular Allergology, CAAM, Rome, Italy.
Tel: (+39 338) 88 373 52, E-mail: adriano.mari@caam-allergy.com

Published by Tehran University of Medical Sciences (http://ijaai.tums.ac.ir)

Our results showed the association between positive specific IgE and its concentration with some allergic diseases which could help physicians to prevent such diseases by recognizing and treating them, particularly in individuals with a positive family history of allergic diseases.

Keywords: Allergen; Allergic diseases; IgE; Inhalant; Sensitization

INTRODUCTION

Environmental changes, the transformation of human lifestyle and changes in urbanization patterns could have given rise to the spread of atopic diseases in the past decades. Increasing temperatures and pollination periods lead to changes in the rate of inhalant allergens.[1]The most important inhalant allergens consist of pollens (trees, grasses, and weeds), house dust mites, molds and animal danders.[2]

Allergic sensitization is attributed to the presence of allergen-specific Immunoglobulin E in the blood. The IgE sensitization is not always concordant with allergic symptoms.[3] Increase in the rate of inhalant allergens due to the aforementioned reasons[1]and individuals' exposure, especially those who are atopic, may result in further allergic sensitizations.[4] Some studies have reported IgE sensitization as a predictor in emerging and preceding some allergic diseases.[5] Multiplex allergen-specific IgE panels evaluate allergen-specific IgE against several allergens at the same time. These multiplex panels are used for different age groups and regions[6] providing invaluable findings to determine allergic sensitization patterns, the etiology, prevention and management of allergic diseases.[7] A 25-50% prevalence of inhalant allergen sensitization has been reported in different countries, especially in developed countries.[5] According to previous studies, the difference in IgE sensitization pattern has been reported among countries, cities and overall, different geographical locations.[8]

Limited studies have been conducted regarding IgE sensitization in allergic adults of Tehran city especially applying in vitro methods. It has been performed some studies regarding the common allergens in other provinces of Iran.[9-11] The performance of these studies in different locations and update these information in different durations could be helpful for physicians, patients and researchers.

With respect to different sensitization patterns in various geographical regions and their importance in allergic diseases, the objective of this study was the assessment of IgE sensitization paradigms to inhalant allergens in adults using the specific panel as well as the prediction of their effect in different allergic symptoms.

MATERIALS AND METHODS

Participants

We performed this cross-sectional study on blood donor adult volunteers referred to Blood Transfusion Organization and students of Tehran University of Medical Sciences from September 2013 to April 2016. The individuals aged 18 to 45 years living in Tehran for a minimum duration of last one year, were included in this study. A total of 2569 subjects participated in this study. A validated standard questionnaire was filled out for participants to assess their allergic symptoms.[12] The questionnaire included demographic information, clinical symptoms of asthma, allergic rhinitis, conjunctivitis (AC), atopic dermatitis (AD), family history of atopic diseases and smoking habits. A total of 604 subjects with allergic symptoms (allergic group) including the subjects with asthma symptoms (wheezing, dyspnea, cough, asthma attack, asthma medication)[13,14], allergic rhinitis (sneezing, nasal itching, stuffy nose, runny nose), conjunctivitis (ocular itching, watering and redness of eye)[15] and atopic dermatitis symptoms (itching, generalized dry skin, flexural involvement and visible eczema)[16] and 102 subjects without any allergic symptoms (non-allergic group) were entered the study.

Informed consent was obtained from all subjects. The ethics approval of this study was given by the Ethics Committee of Immunology, Asthma, and Allergy Research Institute, Tehran University of Medical Sciences (No. 412/280).

Definitions

In this study, the classification of allergic diseases (including asthma, allergic rhinitis, allergic conjunctivitis and atopic dermatitis) was performed based on following definitions.

Having "wheezing with dyspnea" in last 12 months[13,14] and "nasal and eye allergic symptoms stemmed from pollen or animals" in last 12 months[15] was considered as the definition of asthma, allergic rhinitis, and conjunctivitis, respectively. Moreover, diagnosis of atopic dermatitis was performed based on UK Diagnostic Criteria for Atopic Dermatitis[16]as mentioned in the previous study.[12].

The positive specific IgE to one and more than one allergen was defined as "Any Allergen Sensitization".

The positive specific IgE to one and more than one trees, grasses and trees were defined as "Any Pollen Sensitization".

Specific IgE Assay

Three milliliters of blood was taken from allergic and non-allergic participants. Serum was separated and stored at -70℃. Multiplex assay for specific IgE (qline Allergy, R-Biopharm, Germany) was performed for 20 inhalant allergens. The allergens consisted of grasses (Bermuda grass, timothy grass, ryegrass, meadow fescue), weeds (mugwort, Russian thistle or saltwort, dandelion, white goosefoot), trees (plane tree, ash, cypress, olive, poplar) as outdoor allergens; cat, dog, house dust mites and cockroach as indoor allergens and molds (*Alternaria alternata, Aspergillus fumigatus*).

Qline Allergy is a multiplex test on nitrocellulose membrane test to measure the specific IgE. In the first phase, 400 µL of serum was added to the membrane. After 30 minutes of incubation, the strips were washed. Then 400 µL of antibody was added and after incubation and washing, 400 µL of the anti-IgE conjugate was added. Finally, after 20 minutes of incubation and washing, strips were incubated with the substrate for 15 minutes. Following washing and drying the panels, qline strip was read by the scanner. Five standards were applied in each panel. Allergen-specific IgE concentration is reported in IU/mL. The test result was considered positive if the concentration of specific IgE was ≥0. 35 IU/mL.

Statistical Analysis

Statistical analysis of data was done by IBM SPSS software version 20. The frequency and percent of categorical data were calculated. Quantitative variables were reported as mean and Standard Deviation (SD). The normality of quantitative variables was determined using one sample Kolmogorov-Smirnov test. Simple logistic regression and multiple logistic regressions were used to predict the impact of independent variables on outcome variable (allergic diseases). This analysis was performed in two status (unadjusted and adjusted). The variables including age, sex, smoking status and family history were considered as confounder variables. Odds Ratio (OR) and 95% confidence Interval (CI) were calculated for stating the association between allergic sensitization and allergic diseases. Prism 5 (Graphpad Software Inc., La Jolla, CA, USA) software was used to draw the graph.

RESULTS

Study participants were classified in two groups: allergic (n=604) and non-allergic (n=102) subjects. A total of 371 (61.4%) allergic subjects and 41 (40.2%) non-allergic patients were male. The mean age of the allergic and non-allergic subjects was 29.71±7.28 and 26.27± 8.03 years. The frequencies of different allergic symptoms were as follows: asthma (16.4%), allergic rhinitis (70%), conjunctivitis (42.7%) and atopic dermatitis (11.4%).

Three hundred seventy-nine (62.7%) allergic participants showed sensitization to any inhalant allergen. Table 1 depicts demographic and clinical data as well as the prevalence of IgE sensitization to inhalant allergens in allergic and non-allergic groups. Sensitization to outdoor inhalant allergens was much higher than indoor allergens. The most commonly inhalant allergens in allergic subjects were saltwort, meadow fescue, ryegrass and plane tree (Figure 1) while saltwort, plane tree, and white goosefoot were the most common frequent sensitization in the non-allergic group.

The most common mono-sensitizations were to saltwort and house dust mites.

Table 2 summarizes the prevalence of different inhalant allergens according to sex and age groups. With a rise in age, the percentage of sensitization to at least one allergen dwindled, though, was not statistically significant. Although sensitization to most allergens was higher in males, we found no significant difference between allergen sensitization regarding sex (except for meadow fescue).

The prevalence of positive specific IgE to any allergen, trees, grasses, weeds, and mites was evaluated in different seasons (spring, summer, fall, and winter).

The frequency of IgE sensitization to any allergen, trees, grasses, and mites was higher in spring compared to other seasons but only allergic sensitization to trees and seasons were statistically significant (p=0.003).

Table 3 presents the number and percentage of inhalant allergens in allergic subjects according to different allergic disorders. As Table 3 shows, the sensitization to most inhalant allergens especially outdoor allergens was higher in subjects with allergic rhino-conjunctivitis (ARC) rather than other disorders. Furthermore, sensitization to indoor allergens specifically animals and mites were higher in subjects with asthma and atopic dermatitis.

The positive specific IgE to any allergen, trees, weeds, and grasses was higher in subjects with allergic conjunctivitis and allergic rhino-conjunctivitis compared to other disorders. Positive specific IgE to at least one inhalant allergen could be an independent predictor for allergic rhinitis, conjunctivitis and rhino-conjunctivitis in the logistic regression analysis [OR=2.29, 95% CI (1.54-3.43], [OR=1.81, 95% CI (1.26-2.60)] and [OR=2.55, 95% CI (1.72-3.78)]. In addition to allergic sensitization, family history of allergy and age was significantly associated with allergic rhinitis, allergic conjunctivitis, and allergic rhino-conjunctivitis (Table 4). The accompanying allergic sensitization to any inhalant allergen and positive family history of allergy was an important risk factor for allergic conjunctivitis and allergic rhinoconjunctivitis and especially allergic rhinitis.

Interestingly, sensitization to house dust mites and tree sensitization were a significant predictor for allergic rhinitis [OR=3.25, 95% CI(1.31,8.03) and allergic conjunctivitis [OR=2.19, 95% CI (1.50-3.19)], respectively.

In a regression model, after entering all the data about inhalant allergens, age, gender, family history and smoking status as independent variables, it was noticed that age and gender were significantly associated with asthma. In another model, meadow fescue, saltwort, house dust mites, age and family history were significantly associated with allergic rhinitis. In the third model, the role of plane tree, age and family history were significant in allergic conjunctivitis. In addition, acacia and sex remained as a significant predictor in subjects with atopic dermatitis.

Table 1. The demographic data, clinical symptoms and allergic sensitization in allergic and non-allergic subjects

		Allergic Subjects N (%)	Non-allergic Subjects N (%)
Questionnaire based- data	Frequency	604	102
	Male/Female	371/233	41/61
	Family History	285(49.7)	17(20.2)
	Active Smoking	99(17.1)	6(6.4)
	Asthma	99(16.4)	-
	Allergic Rhinitis	420(70)	-
	Allergic Conjunctivitis	256(42.7)	-
	Allergic Rhinoconjunctivitis	215(36)	-
	Atopic dermatitis	69(11.4)	-
IgE Sensitization	Any Allergen	379(62.7)	27(26.5)
	Indoor	16(2.6)	3(2.9)
	Outdoor	269(44.5)	20(19.6)
	Indoor + Outdoor	94(15.6)	4(3.9)
	Mono	114(18.9)	11(10.8)
	Multi	265(43.9)	16(15.7)
	Weeds	296(49)	21(20.6)
	Trees	176(29.1)	12(11.8)
	Grasses	211(34.9)	9(8.8)
	Trees + Grasses + Weeds	121(20)	5(4.9)
	Mites	54(8.9%)	3(2.9)
	Animals	61(10.1)	4(3.9)
	Molds	8(1.3)	-
	Cockroach	14(2.3)	-

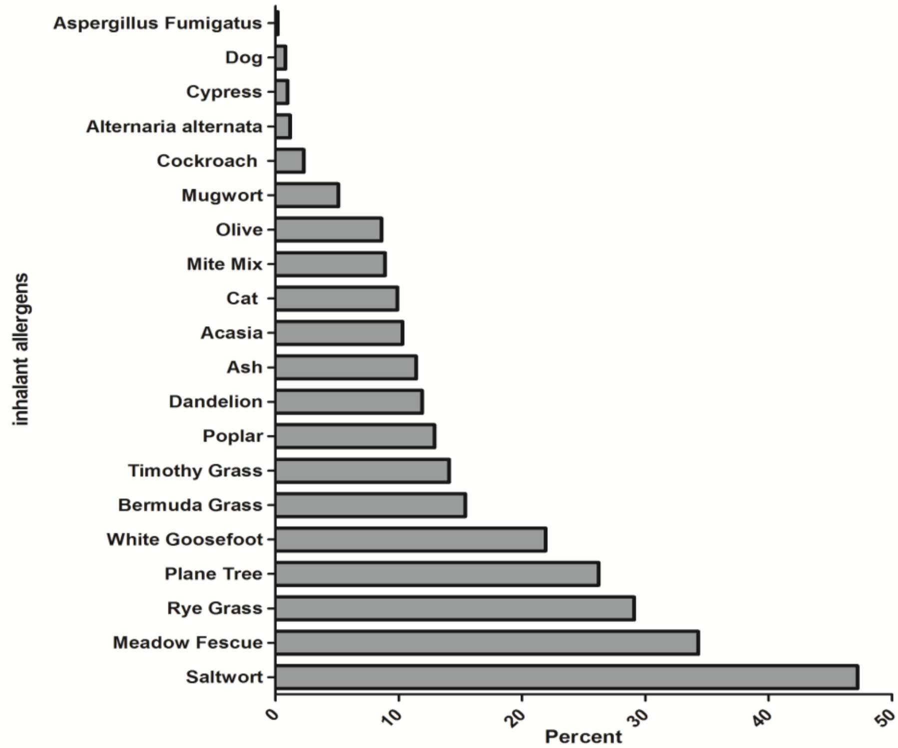

Figure 1. The most common inhalant allergens in allergic subjects

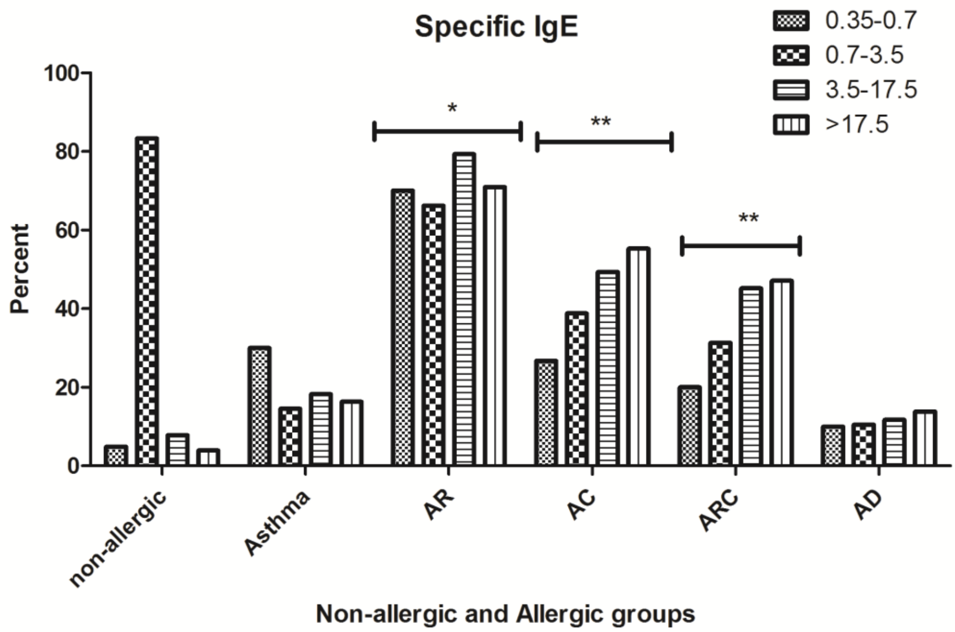

Figure 2. The relationship between the sum of specific IgE concentration (IU/mL) and different allergic diseases; AR (Allergic Rhinitis), AC (Allergic Conjunctivitis), ARC (Allergic Rhinoconjunctivitis), AD (Atopic Dermatitis). *p<0.05, ** p<0.01.

Table 2. The prevalence of sensitization to inhalant allergens in allergic subjects according to sex and age groups

Allergens	Sex				Age Groups			
	Allergic subjects N (%)	Male N (%)	Female N (%)	*p* value	18-25 y N (%)	26-35 y N (%)	36-45 y N (%)	*p* value
Any Allergen	379(62.7)	242(65.2)	137(58.8)	0.11	129(65.8)	167(64)	79(56.4)	0.18
Weeds	296(49)	191(51.5)	105(45.1)	0.12	109(55.6)	125(47.9)	58(41.4)	0.03*
Trees	176(29.1)	115(31)	61(26.2)	0.20	63(32.1)	74(28.4)	39(27.9)	0.60
Grasses	211(34.9)	139(37.5)	72(30.9)	0.09	66(33.7)	98(37.5)	47(33.6)	0.61
Bermuda grass	93(15.4)	64(17.3)	29(12.4)	0.11	28(14.3)	49(18.8)	16(11.4)	0.12
Timothy grass	85(14.1)	58(15.6)	27(11.6)	0.16	28(14.3)	39(14.9)	18(12.9)	0.85
Ryegrass	176(29.1)	118(31.8)	58(24.9)	0.06	58(29.6)	82(31.4)	36(25.7)	0.49
Meadow fescue	207(34.3)	139(37.5)	68(29.2)	0.03*	66(33.7)	95(36.4)	46(32.9)	0.73
Mugwort	31(5.1)	20(5.4)	11(4.7)	0.71	15(7.7)	9(3.4)	7(5)	0.13
White goosefoot	132(21.9)	88(23.7)	44(18.9)	0.16	50(25.5)	50(19.2)	32(22.9)	0.26
Saltwort	285(47.2)	186(50.1)	99(42.5)	0.06	104(53.1)	120(46)	58(41.4)	0.09
Dandelion	72(11.9)	46(12.4)	26(11.2)	0.64	31(15.8)	22(8.4)	18(12.9)	0.05
Plane tree	158(26.2)	103(27.8)	55(23.6)	0.25	58(29.6)	65(24.9)	35(25)	0.48
Ash	69(11.4)	42(11.3)	27(11.6)	0.92	28(14.3)	26(10)	15(10.7)	0.33
Cypress	6(1)	4(1.1)	2(0.9)	0.79	3(1.5)	0	3(2.1)	0.08
Olive	52(8.6)	29(7.8)	23(9.9)	0.38	20(10.2)	21(8)	11(7.9)	0.66
Acacia	62(10.3)	42(11.3)	20(8.6)	0.28	23(11.7)	20(7.7)	19(13.6)	0.13
Poplar	78(12.9)	54(14.6)	24(10.3)	0.12	34(17.3)	26(10)	18(12.9)	0.06
Mites mix 1	54(8.9)	37(10)	17(7.3)	0.26	14(7.1)	28(10.7)	12(8.6)	0.40
Aspergillus fumigatus	1(0.2)	1(0.3)	-	0.42	0.0	1(0.4)	0	0.52
Alternaria alternata/tenuis	7(1.2)	5(1.3)	2(0.9)	0.58	5(2.6)	2(0.8)	0	0.07
Cat	60(9.9)	35(9.4)	25(10.7)	0.60	22(11.2)	30(11.5)	8(5.7)	0.14
Dog	5(0.8)	1(0.3)	4(1.7)	0.05	3(1.5)	2(0.8)	0	0.31
Cockroach	14(2.3)	9(2.4)	5(2.1)	0.82	2(1)	8(3.1)	4(2.9)	0.32

*$p<0.05$, Mites mix (Dermatophagoides pteronyssinus, Dermatophagoides farina), y (years)

Table 3. The prevalence of inhalant allergens in allergic subjects according to different allergic diseases

Allergens		Asthma N=99 N (%)	Allergic Rhinitis N=420 N (%)	Allergic Conjunctivitis N=256 N (%)	Allergic Rhinoconjunctivitis N=215 N (%)	Atopic Dermatitis N=69 N (%)
IgE Sensitization	Any allergen	57(57.6)	287(68.3)	180(70.3)	162(75.3)	44(63.8)
	Indoor	6(6.1)	12(2.9)	5(2.3)	5(2.3)	2(2.9)
	Outdoor	36(36.4)	202(48.1)	126(49.2)	116(54)	29(42)
	Indoor + Outdoor	15(15.2)	73(17.4)	49(19.1)	41(19.1)	13(18.8)
	Mono	13(13.1)	81(19.3)	43(16.8)	38(17.7)	11(15.9)
	Multi	44(44.4)	206(49)	137(53.5)	124(57.7)	33(47.8)
	Weeds	45(45.5)	222(52.9)	141(55.1)	126(58.6)	37(53.6)
	Trees	27(27.3)	135(32.1)	99(38.7)	88(40.9)	19(27.5)
	Grasses	35(35.4)	162(38.6)	108(42.2)	96(44.7)	24(34.8)
	Trees + Grass + Weeds	20(20.2)	91(21.7)	67(26.2)	58(27)	13(18.8)
	Any pollen	51(51.5)	274(65.2)	174(68)	157(73)	42(60.9)
	Mites	9(9.1)	46(11)	25(9.8)	25(11.6)	7(10.1)
	Animals	14(14.1)	43(10.2)	29(11.3)	22(10.2)	8(11.6)
	Molds	1(1)	5(1.2)	3(1.2)	2(0.9)	1(1.4)
	Cockroach	2(2)	10(2.4)	4(1.6)	4(1.9)	2(2.9)

Table 4. Logistic regression analysis of asthma, allergic rhinitis, conjunctivitis, rhinoconjunctivitis and atopic dermatitis according to IgE sensitization status

Independent Variables	Asthma: *p* value, Unadjusted OR (95% CI)	Asthma: *p* value, Adjusted ‡ OR (95% CI)	Allergic Rhinitis: *p* value, Unadjusted OR (95% CI)	Allergic Rhinitis: *p* value, Adjusted ‡ OR (95% CI)	Allergic Conjunctivitis: *p* value, Unadjusted OR (95% CI)	Allergic Conjunctivitis: *p* value, Adjusted ‡ OR (95% CI)	Allergic Rhinoconjunctivitis: *p* value, Unadjusted OR (95% CI)	Allergic Rhinoconjunctivitis: *p* value, Adjusted OR (95% CI)	Atopic Dermatitis: *p* value, Unadjusted OR (95% CI)	Atopic Dermatitis: *p* value, Adjusted OR (95% CI)
Any Allergen	NS	NS	<0.001 2.20 (1.54-3.15)	<0.001 2.29 (1.54-3.43)	0.001 1.81 (1.28-2.54)	0.001 1.81 (1.25-2.60)	<0.001 2.46 (1.70-3.56)	<0.001 2.55 (1.72-3.78)	NS	NS
Any Pollen	NS	NS	<0.001 2.14 (1.50-3.05)	<0.001 2.18 (1.46-3.25)	<0.001 1.88 (1.34-2.64)	<0.001 1.89 (1.32-2.70)	<0.001 2.54(1.74-3.60)	<0.001 2.60 (1.77-3.82)	NS	NS
Any Grass	NS	NS	0.004 1.77 (1.20-2.61)	0.006 1.83 (1.19-2.84)	0.001, 1.78 (1.26-2.50)	0.005 1.67 (1.17-2.40)	<0.001 1.95 (1.37-2.76)	0.001 1.88 (1.30-2.71)	NS	NS
Any Trees	NS	NS	0.02 1.60 (1.07-2.40)	0.05 1.55 (0.98-2.44)	<0.001, 2.22 (1.55-3.18)	<0.001 2.19 (1.50-3.19)	<0.001 2.35 (1.64-3.38)	<0.001 2.32 (1.58-3.41)	NS	NS
Any Weeds	NS	NS	0.004 1.68 (1.18-2.39)	0.005 1.76 (1.18-2.62)	0.007, 1.56 (1.13-2.17)	0.006 1.63 (1.15-2.30)	<0.001 1.85 (1.1-2.60)	<0.001 2.01 (1.40-2.87)	NS	NS
Any Indoor Allergen	NS	NS	0.04 1.64 (1.00-2.69)	0.07 1.61 (0.94-2.77)	NS	NS	NS	NS	NS	NS
Any Allergen and Positive Family history	NS	NS	<0.001 3.13 (1.99-4.91)	<0.001 3.17 (1.99-5.06)	<0.001 2.07 (1.45-2.95)	<0.001 1.99 (1.39-2.86)	<0.001 2.57 (1.80-3.70)	<0.001 2.50 (1.73-3.69)	NS	NS

NS= Not Significant, ‡ Adjusted for age, sex, smoking, and family history of allergic diseases

In the logistic regression analysis in different age groups, IgE sensitization to any allergen and any pollen was significantly associated with allergic rhinitis and rhino-conjunctivitis in the two age groups of 25-35 and 35-45 years.

As figure 2 illustrates, the relationship between specific IgE concentration and the prevalence of non-allergic and allergic disorders in subjects was evaluated. We found a significant relationship between the sum of specific IgE concentration and allergic rhinitis (p=0.04), allergic conjunctivitis (p=0.001) and rhino-conjunctivitis (p=0.004). As the specific IgE increased, the prevalence of allergic conjunctivitis and rhino-conjunctivitis increased as well.

DISCUSSION

The results of this study demonstrated that atopic sensitization to inhalant allergens was reflected in more than 60% of allergic adults. The IgE sensitization to weeds and grasses pollens was the most frequent among inhalant allergens. Regarding our findings, allergic sensitization to inhalant allergens could be a predictor for allergic diseases particularly allergic rhinitis, conjunctivitis, and rhinoconjunctivitis. The higher concentration of specific IgE was related to higher prevalence of allergic disorders mainly allergic conjunctivitis and rhinoconjunctivitis.

Sensitization to any inhalant allergen was found in 62.7% of allergic adults. The men showed higher sensitization compared to women albeit it was not meaningful. In similar studies conducted in Europe[17] and Sub-Saharan Africa,[5] the prevalence of allergic sensitization to at least one allergen was lower than that of our study. Also, in this study, the allergic sensitization in non-allergic subjects was detected to be 26.5%. This result shows that there are sensitized subjects without any allergic symptoms. Kerkhof et al

Published by Tehran University of Medical Sciences (http://ijaai.tums.ac.ir)

reported that 43% of individuals sensitized to aeroallergens showed no clinical symptoms. It could result from low exposure to inhalant allergens in these individuals[18] and IgE production to cross reactive carbohydrate determinants (CCD).[19] In a study in the European community, 32.3 to 41.8% of the general population (with and without allergic symptoms) showed atopic sensitization.[20] Moreover, specific IgE was not detected in the serum of 38.3% of allergic individuals in this study. It could arise from the presence of IgE locally, IgE sensitization to other unidentified allergens,[20] non-IgE mediated reactions,[18] different methods for assessment of specific IgE, source, and quality of allergens[21] and sensitization to different plant species. Also, applying the customized regional panel of allergens especially pollen allergens could reduce false negative sensitization.[22]

The specific IgE assay to inhalant allergens showed weeds (especially saltwort) and grasses (particularly meadow fescue and ryegrass) as the most common inhalant sensitizers. The literature review showed similar and different results with this study. In line with this study, numerous sensitization to saltwort (*Salsola kali*) has been reported by Assarzadegan et al in Iran.[9] In a recent paper in Canada, most common prick test reactions were cat dander, grasses and birch allergens.[23] In another study in sub-Saharan Africa, sensitization to mites wasin the highest rate.[5] Based on the results of a multicenter study in Europe, grass mix, house dust mites and cats were reported among the most common aeroallergens.[17] Some environmental factors such as the weather change and pollutants may affect the aeroallergen concentration and as a result their sensitization patterns in different regions.[24] Interestingly, cats were identified as the most common indoor allergen among allergic subjects (especially asthma) of this study. It could be caused or exacerbated by an increase in the popularity of pet keeping, especially keeping cats, by Iranian households.

Multi sensitization to respiratory allergens was seen in 43.9% allergic and 16.3% non-allergic subjects. Some studies found a significant association between higher frequency of multi sensitization in allergic disorders and their severity.[25] Interestingly, in our study, subjects with allergic rhino-conjunctivitis showed the highest prevalence of poly-sensitization rather than other diseases (57.7%). It is noteworthy that some multi sensitizations stem from cross-reactivity molecules[22] and cross reactive carbohydrates[19] and their exact evaluation utilizing molecular techniques are needed.[22]

The highest prevalence of atopic sensitization was observed in the age group 18-25 years and decreased with an increase in age, though insignificantly. In another study by Salo, the highest prevalence of IgE sensitization was related to age groups between 10 to 39 years of age.[26] According to some studies, the association of IgE sensitization to inhalant allergens with age groups is significant especially in childhood and early adulthood.[26] In contrast, allergic sensitization to inhalant allergens was considered as a predictor for subjects with allergic rhinitis, conjunctivitis, and rhinoconjunctivitis in age groups 25-35 and 35-45 years, while regression analysis of allergic sensitization with asthma and atopic dermatitis subjects showed no significant association in age groups of this study. Similar to our study, in the study of Warm et al, IgE sensitization was considered as an important factor in allergic rhinitis patients in the age group of 22-40 years rather than in asthmatic patients.[27]

The results revealed that sensitization to outdoor allergens was higher in allergic rhinoconjunctivitis, allergic rhinitis and conjunctivitis patients rather than asthma and atopic dermatitis patients while participants with asthma showed higher sensitization to indoor allergens, especially animal allergens. In another study by Hosseini et al, skin prick test positivity to trees and house dust mite was higher in asthmatic children.[28] In line with the present study, a multicenter study in China represented more frequency and association of outdoor and indoor allergens in intermittent allergic rhinitis and asthma severity, respectively.[29] According to our knowledge, allergic sensitization in patients with allergic conjunctivitis has been evaluated in limited studies. We found IgE sensitization to trees allergens was significantly associated with allergic conjunctivitis.

Based on the results of this study, 63.8% of subjects with atopic dermatitis were sensitized to any inhalant allergens. According to the literature review, the role of environmental allergens (especially pollen, animal dander, and house dust mites) in developing and exacerbating of atopic dermatitis is considerable and are bought up as triggers in worsening this disease in adult patients.[30]

In the present study, allergic sensitization to any allergen especially pollen allergens was considered as a risk factor for allergic rhinitis, allergic conjunctivitis, and allergic rhino-conjunctivitis while we did not find

Published by Tehran University of Medical Sciences (http://ijaai.tums.ac.ir)

any association between allergic sensitization to any inhalant allergen and other allergic diseases including asthma and atopic dermatitis in allergic adults of this study. Our finding regarding allergic rhinitis is consistent with Warm et al study.[27] In controversy to our study, some studies showed allergic sensitization as a significant factor in asthma.[31] The results of Vidal et al study revealed the association between IgE sensitization to allergenic molecules of mites (including Der p 1 and Der p 2) and asthma in patients with allergy to house dust mites.[32] This discrepancy between studies could result from a limited range of age group in the present study compared to that of the Sweden study. On the other hand, the lower association between allergic sensitization and asthma could be attributed to other factors (such as obesity, air pollution, and smoking tobacco) rather than allergic sensitization in developing and increasing the asthma prevalence.[27] As the findings of this study showed, in a logistic regression model, the age and gender remained as the significant predictors in asthma patients while in addition to age and family history, allergic sensitization to meadow fescue, Russian thistle, and house dust mites was considered as risk factors of allergic rhinitis.

Regarding the study findings, increasing the specific IgE concentration against aeroallergens revealed a positive relationship with the frequency of some allergic disorders. In a study by Olivieri et al, they found a meaningful association between the level of specific IgE and the use of medicines and referral to a physician resulted from respiratory disorders.[33]In another study by Marinho et al, the increasing specific IgE concentration is associated with the risk of current rhinitis and current rhinoconjunctivitis in children at 5 years of age.[34] It could be concluded that concentration of specific IgE is useful in the evaluation of allergic diseases.

The prevalence of allergic sensitization in different seasons displayed that sensitivity to any inhalant allergen, tree and grass pollens and mites was higher in spring than other seasons but it was statistically significant just for trees sensitization. It is interesting that the prevalence of IgE sensitization to trees and grasses was higher in summer and mites in fall and winter in the previous study.[35] The dissimilarity in precipitation, temperature, air pollution in different years could be the reasons of alteration in pollen count and as a result different sensitization.[36]

Despite acceptable concordance between skin prick test and in vitro tests for most inhalant allergens,[37] one limitation could be that performing skin prick test as a sensitive evaluation is impossible or is very difficult with a high number of allergens in a huge number of participants who were referred for blood donation. Also, the region of birth was not determined in this study. More studies are required to examine the role of the region of birth as a possible factor in current sensitization to allergens in adults. One of the limitations of this study was the limited number of allergens in this diagnostic panel as an in vitro test. Also, the determination of cross-reactivity between allergens and CCD marker was impossible using this panel. More studies are under evaluation as the next step of the current investigation the results of which will be reported in the future articles.

The sensitivity prevalence to pollen allergens (mainly weeds and grasses) were demonstrated in allergic adults. The presence of specific IgE to inhalant allergens and their concentration were significantly associated with current allergic rhino-conjunctivitis, rhinitis, and conjunctivitis in adults. This could help physicians prevent such diseases by recognizing and treating them, particularly in individuals with a positive family history of allergic diseases. It seems that in asymptomatic individuals with a high concentration of specific IgE, further studies are required to determine the precautious measures needed to prevent the situation from evolving from sensitization to disease.

ACKNOWLEDGEMENTS

This study has been supported by Immunology, Asthma, and Allergy Research Institute, Tehran University of Medical Sciences and Iran Ministry of Health and Medical Education. We thank Prof. Maritta Kilpelainen to permit us to use the questionnaire of allergic rhinitis and allergic conjunctivitis. We would like to appreciate the staffs of Iran Blood Transfusion Organization and Mrs. Zahra Ebadi for their outstanding cooperation.

REFERENCES

1. Jalbert I, Golebiowski B. Environmental aeroallergens and allergic rhino-conjunctivitis. Curr Opin Allergy Clin Immunol 2015; 15(5):476-81.
2. Bousquet J, Khaltaev N, Cruz A, Denburg J, Fokkens W, Togias A, et al. Allergic rhinitis and its impact on asthma

(ARIA) 2008. Allergy 2008; 63(s86):8-160.

3. Haftenberger M, Laußmann D, Ellert U, Kalcklösch M, Langen U, Schlaud M, et al. Prevalence of sensitisation to aeroallergens and food allergens. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 2013; 56(5-6):687-97.
4. Gomes Camara Camacho I. Inhalant Allergens in Portugal. Int Arch Allergy Immunol 2017; 172(2):67-88.
5. Mbatchou Ngahane BH, Noah D, Nganda Motto M, Mapoure Njankouo Y, Njock LR. Sensitization to common aeroallergens in a population of young adults in a sub-Saharan Africa setting: a cross-sectional study. Allergy Asthma Clin Immunol 2016; 12:1.
6. Pawankar R, Canonica G, Holgate S, Lockey R, Blaiss M. The World Allergy Organization (WAO) White Book on Allergy(Update 2013).
7. Sakashita M, Hirota T, Harada M, Nakamichi R, Tsunoda T, Osawa Y, et al. Prevalence of allergic rhinitis and sensitization to common aeroallergens in a Japanese population. Int Arch Allergy Immunol 2010; 151(3):255-61.
8. Wang W, Huang X, Chen Z, Zheng R, Chen Y, Zhang G, et al. Prevalence and trends of sensitisation to aeroallergens in patients with allergic rhinitis in Guangzhou, China: a 10-year retrospective study. BMJ Open 2016; 6(5):e011085.
9. Assarehzadegan M-A, Shakurnia A, Amini A. The most common aeroallergens in a tropical region in Southwestern Iran. World Allergy Organ J 2013; 6(1):1-7.
10. Farrokhi S, Gheybi MK, Movahed A, Tahmasebi R, Iranpour D, Fatemi A, et al. Common aeroallergens in patients with asthma and allergic rhinitis living in southwestern part of Iran: based on skin prick test reactivity. Iran J Allergy Asthma Immunol 2015; 14(2):133-8.
11. Fereidouni M, Farid Hossini R, Assarehzadegan MA, Jabberi Azad F, Varasteh A. skin prick test reactivity to common aeroallergens among allergic rhinitis patients in Mashhad,Iran. allergo et immunopathol 2009; 37(2):73-9.
12. Shokouhi Shoormasti R, Pourpak Z, Fazlollahi MR, Kazemnejad A, Nadali F, Ebadi Z, et al. The prevalence of Allergic Rhinitis, Allergic Conjunctivitis, Atopic Dermatitis and Asthma among Adults of Tehran. In Press 2017.
13. Available from: http://www.ecrhs.org/Quests.htm.
14. Sistek D, Tschopp JM, Schindler C, Brutsche M, Ackermann-Liebrich U, Perruchoud AP, et al. Clinical diagnosis of current asthma: predictive value of respiratory symptoms in the SAPALDIA study. Swiss Study on Air Pollution and Lung Diseases in Adults. Eur Respir J 2001; 17(2):214-9.
15. Kilpelainen M, Terho EO, Helenius H, Koskenvuo M. Validation of a new questionnaire on asthma, allergic rhinitis, and conjunctivitis in young adults. Allergy 2001; 56(5):377-84.
16. Williams HC, Burney PG, Hay RJ, Archer CB, Shipley MJ, Hunter JJ, et al. The U.K. Working Party's Diagnostic Criteria for Atopic Dermatitis. III. Independent hospital validation. Br J Dermatol 1994;131: 406–16..
17. Newson RB, van Ree R, Forsberg B, Janson C, Lotvall J, Dahlen SE, et al. Geographical variation in the prevalence of sensitization to common aeroallergens in adults: the GA(2) LEN survey. Allergy 2014; 69(5):643-51.
18. Kerkhof M, Schouten JP, De Monchy JG. The association of sensitization to inhalant allergens with allergy symptoms: the influence of bronchial hyperresponsiveness and blood eosinophil count. Clin Exp Allergy 2000; 30(10):1387-94.
19. Falak R, Sankian M, Ketabdar H, Moghadam M, Varasteh A. The role of Anti-CCD antibodies in grape allergy diagnosis. Rep Biochem Mol Biol 2013; 1(2): 74-81.
20. Bousquet PJ, Castelli C, Daures JP, Heinrich J, Hooper R, Sunyer J, et al. Assessment of allergen sensitization in a general population-based survey (European Community Respiratory Health Survey I). Ann Epidemiol 2010; 20(11):797-803.
21. Matricardi PM, Kleine-Tebbe J, Hoffmann HJ, Valenta R, Hilger C, Hofmaier S, et al. EAACI Molecular Allergology User's Guide. Pediatr Allergy Immunol 2016; (27 Suppl 23):1-250.
22. Migueres M, Davila I, Frati F, Azpeitia A, Jeanpetit Y, Lheritier-Barrand M, et al. Types of sensitization to aeroallergens: definitions, prevalences and impact on the diagnosis and treatment of allergic respiratory disease. Clin Transl Allergy 2014; 4:16.
23. Lok SD, Davis BE, Cockcroft DW. Prevalence of allergen sensitization in 1000 adults in Saskatchewan. Allergy Asthma Clin Immunol 2017; 13:9.
24. D'Amato G, Baena-Cagnani CE, Cecchi L, Annesi-Maesano I, Nunes C, Ansotegui I, et al. Climate change, air pollution and extreme events leading to increasing prevalence of allergic respiratory diseases. Multidiscip Respir Med 2013; 8(1):12.
25. Ciprandi G, Cirillo I. Monosensitization and polysensitization in allergic rhinitis. Eur J Intern Med 2011; 22(6):e75-9.

26. Salo PM, Arbes SJ, Jr., Jaramillo R, Calatroni A, Weir CH, Sever ML, et al. Prevalence of allergic sensitization in the United States: results from the National Health and Nutrition Examination Survey (NHANES) 2005-2006. J Allergy Clin Immunol 2014; 134(2):350-9.
27. Warm K, Hedman L, Lindberg A, Lotvall J, Lundback B, Ronmark E. Allergic sensitization is age-dependently associated with rhinitis, but less so with asthma. J Allergy Clin Immunol 2015; 136(6):1559-65.
28. Hosseini S, Shoormasti RS, Akramian R, Movahedi M, Gharagozlou M, Foroughi N, et al. Skin Prick Test Reactivity to Common Aero and Food Allergens among Children with Allergy. Iran J Med Sci 2014; 39(1):29-35.
29. Li J, Huang Y, Lin X, Zhao D, Tan G, Wu J, et al. Influence of degree of specific allergic sensitivity on severity of rhinitis and asthma in Chinese allergic patients. Respir Res 2011; 12:95.
30. Akdis CA, Akdis M, Bieber T, Bindslev-Jensen C, Boguniewicz M, Eigenmann P, et al. Diagnosis and treatment of atopic dermatitis in children and adults: European Academy of Allergology and Clinical Immunology/American Academy of Allergy, Asthma and Immunology/PRACTALL Consensus Report. Allergy 2006; 61(8):969-87.
31. Ronmark EP, Ekerljung L, Mincheva R, Sjolander S, Hagstad S, Wennergren G, et al. Different risk factor patterns for adult asthma, rhinitis and eczema: results from West Sweden Asthma Study. Clin Transl Allergy 2016; 6:28.
32. Vidal C, Lojo S, Juangorena M, Gonzalez-Quintela A. Association Between Asthma and Sensitization to Allergens of Dermatophagoides pteronyssinus. J Investig Allergol Clin Immunol 2016; 26(5):304-9.
33. Olivieri M, Heinrich J, Schlunssen V, Anto JM, Forsberg B, Janson C, et al. The risk of respiratory symptoms on allergen exposure increases with increasing specific IgE levels. Allergy 2016; 71(6):859-68.
34. Marinho S, Simpson A, Soderstrom L, Woodcock A, Ahlstedt S, Custovic A. Quantification of atopy and the probability of rhinitis in preschool children: a population-based birth cohort study. Allergy 2007; 62(12):1379-86.
35. Shokouhi Shoormasti R, Pourpak Z, Fazlollahi MR, Shabani A, Kazemnejad A, Ebadi Z, et al. Determination of the most common indoor and outdoor allergens in 602 patients with allergic symptoms by specific IgE local panel. Iran J Allergy Asthma Immunol 2017; 16(4):298-306.
36. Ariano R, Canonica GW, Passalacqua G. Possible role of climate changes in variations in pollen seasons and allergic sensitizations during 27 years. Ann Allergy Asthma Immunol 2010; 104(3):215-22.
37. Cox L, Williams B, Sicherer S, Oppenheimer J, Sher L, Hamilton R, et al. Pearls and pitfalls of allergy diagnostic testing: report from the American College of Allergy, Asthma and Immunology/American Academy of Allergy, Asthma and Immunology Specific IgE Test Task Force. Ann Allergy Asthma Immunol 2008; 101(6):580-92.