

Original Article

Sensitization to Food and Aeroallergens in Patients with Asthma, Allergic Rhinitis, Eczema and Urticaria

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ABSTRACT

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Keywords

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Background and Aims: Allergic disorders such as asthma, urticaria, eczema, and allergic rhinitis are common worldwide, and allergens are the most common etiology and exacerbating factors. So, This study aimed to find the allergens in these patients with skin prick tests.

Materials and Methods: All the allergic cases referred to an allergic clinic in the north of Iran were visited by an allergist and clinical immunologist. Based on patient history, physical examination, and diagnosis, we select food allergens and aeroallergens. A standard skin prick test was performed on all patients, and all data was then analyzed SPSS 20.

Results: Two thousand one hundred and twenty-eight cases entered the study with a mean age of 27.65 ± 15.52 years old. 1235 (58.04%) females and 893 males (41.96%) participated in this study. Prevalence of allergic rhinitis, asthma, urticaria, and eczema were 717 (33.7%), 611 (28.8%), 550 (25.8%), and 250 (11.7%), respectively. The most common aeroallergens were *Dermatophagoides farinae* (75.9%), *Dermatophagoides pteronyssinus* (65.4%), feather (56.1%), and *Candida* (51.1%), respectively, in all patients. The most common food allergens were egg white (31.1%), cacao (29.7%), and egg yolk (28.9%), respectively, in all cases.

Conclusion: Both aeroallergens and food allergens were the most common in all allergens by skin prick test. Therefore, it is important to find the relationship between sensitization and allergy.

Introduction

The prevalence of allergic disorders has increased in the past decades. The exact etiology is unknown, but genetic and environmental factors contribute to this. In urban areas, the prevalence of allergic rhinitis, asthma, and eczema was 28.5%, 12.2%, and 15%, respectively, in students of guidance schools. The prevalence of asthma, allergic rhinitis, and eczema was 12%, 17%, 6% in elementary school [1, 2]. In a rural area, the prevalence of asthma was 19% and 29.9% in elementary school and guidance school students, respectively. 9.9% and 18.1% of primary and guidance school students were diagnosed with allergic rhinitis, respectively. Eczema was 6.1% and 5.5% prevalent in elementary school and guidance school students, respectively [3].

Review studies in Iran showed that the overall prevalence of asthma was 2.7% and 3.5% in children aged 6-7 and 13-14 years, respectively. Wheezing in the previous year was recorded in 7.6% and 10.7% in children aged 6-7 and 13-14 years, respectively. Prevalence of eczema was 5.98% and 6.52% in children aged 6-7 years and 13-14 years, respectively [4, 5]. Although allergic disorders do not negatively affect the Intelligence quotient (IQ), these diseases have high burdens on the patients, their families, and their country [6-8].

Aeroallergens have an important role in the exacerbation of allergic diseases. Indoor allergens such as mites, cockroaches, molds, pets, pollutions, and outdoor allergens such as

pollens, animals, fungus, and pollutions can induce and exacerbate allergic disorders.

The prevalence of allergens varies in different world areas depending on geographic conditions such as climate (dry, cold, warm, moderate), culture, and others [6, 7]. Skin prick test (SPT) and serum immunoglobulins levels assay such as Radio Allergo Sorbent Test or ImmunoCAP are used to detect allergens. Although ImmunoCAP is usually more sensitive than skin prick test, overall, skin prick test is more suitable and correlates with allergen-specific immunoglobulin (Ig)E against more aeroallergens [9, 10]. Oral food challenges are the standard gold test for food allergy. In the future, the probability of molecular-based allergy diagnostics will play an important role in treating allergic disorders. Detection of allergens helps avoid treatment and, in some patients, induces allergen-specific immunotherapy [11-13]. This study aimed to detect the prevalence of aeroallergens and food allergens in allergic patients, including asthma, allergic rhinitis, urticarial, and eczema.

Materials and Methods

This is a cross-sectional descriptive study. Allergists and clinical immunologists visited all allergic cases referred to an allergic clinic in the north of Iran. Besides, asthma was diagnosed according to the Global Initiative for Asthma (GINA) protocol [14]. Allergic rhinitis was diagnosed based on allergic rhinitis and its impact on asthma initiative

[15]. Atopic dermatitis was diagnosed based on modified Hanifin-Rajka criteria by the American Academy of Dermatology [16]. The duration of this study was from 2012 to 2019. Patients were six months to 65 years old. Based on history, physical examination, and diagnosis, we select some allergens. A standardized skin prick test was performed on all patients.

Seventy allergens were used that were produced by Staller genes company (French). All patients were tested by skin prick test on the forearm with positive (histamine) and negative (normal saline) controls. Distance between extracts was 2 cm. All tests were read after 15 minutes. A positive test was considered when the induration was greater than 3 mm compared to the negative control. The number of allergens was selected based on disease and history. Data were recorded in a questionnaire and SPSS version 20. Exclusion criteria were consuming any antihistamines five days prior to the test, local skin disorders such as ulcer, urticaria, eczema, and others, positive history of anaphylaxis six weeks prior and later, and positive dermographism. This study was approved by the Ethics Committee of Mazandaran University of medical sciences (Sari, Iran).

Statistical analysis

Collected data were analyzed using SPSS version 20 software by appropriate statistical procedures such as descriptive-analytic statistics, including central tendency, distribution, and dependency on the variables

obtained from the research questionnaire. To compare qualitative data, the chi-squared test and, if necessary, Fisher's exact test was performed, and a t-test was used to compare quantitative data. $P < 0.05$ was considered statistically significant.

Results

Out of 2128 allergic patients, 1235 cases (58%) and 893 (42%) were female and male, respectively, with the mean age of 27.65 ± 15.52 years (age range from six months to 65 years old). Asthmatic patients were more common (33.7%) and eczema cases were the least (11.7%). Above the age of 41 years old were common (22.93%) and less than 10 years old were the least (12.78%). Allergic rhinitis was more common ages between 21-30 years old. Asthma was more common ages between 11-20 years old. Urticarial and eczema were common ages more than 41 years old (Table 1). Positive SPT was more common in female (23%) than male (17%) but not significant (Table 2). *Dermatophagoides farinae*, *dermatophagoides pteronyssinus* and feather were more common aeroallergens in all allergic disorders (Table 3). Egg white, egg yolk, Banana and cereals were more common in urticarial patients. Egg white, cereals and egg yolk were common in the allergic rhinitis. In the asthmatic patients, egg yolk, hazel nut and chicken were common. Cereals, egg white, cacao and banana were common in eczema (Table 4). Positive SPT was more common ages 11-20 years old (Table 5).

Table 1. Age distribution of allergic disorders

Age	Allergic rhinitis	Asthma	Urticarial	Eczema	Total
	N (%)	N (%)	N (%)	N (%)	N (%)
≤ 10 years	78 (11.8)	112 (18.3)	65 (11.8)	17 (6.8)	272 (12.78)
11–20	150(20.9)	155 (25.4)	108 (19.6)	64 (25.6)	477 (22.41)
21-30	177 (24.7)	132 (21.6)	104 (18.9)	44 (17.6)	457 (21.47)
31-40	169 (23.6)	99 (16.2)	112 (20.4)	54 (21.6)	434 (20.39)
≥ 41	143 (19.9)	113 (18.5)	161 (29.3)	71 (28.4)	488 (22.93)
Total	717 (33.7)	611 (28.7)	550 (25.8)	250 (11.7)	2128 (100)

Table 2. The distribution of skin prick tests according to the gender

Gender	Skin prick test		Total N (%)
	Positive N (%)	Negative N (%)	
Female	490 (23)	745 (35)	1235 (58)
Male	365 (17)	528 (25)	893 (42)
Total	855 (40)	1273 (60)	2128 (100)

Table 3. The most common aeroallergen in allergic patients

Disorder\allergens	DF	DP	Cockroach	Feather	Cat	Dog	Candida	AA	Penicillium	Cladosporium
Urticarial	77.3	65.6	52.2	55.5	43.8	41.6	53.5	46.7	41.8	43.8
Allergic rhinitis	76.2	64.6	53.3	58.2	46.2	35.3	48.5	43.5	44.2	43.2
Asthma	74.5	63.7	48.4	55.2	45.3	38	48.4	46.2	39.1	44.8
Eczema	76	71.6	52.4	54	48.4	47.6	59.6	50.8	42.8	47.6

DF= *Dermatophagoides farinae*; DP= *Dermatophagoides pteronyssinus*; AA= *Alternaria alternate*. Note: Aspergillosis with 40.6% in allergic rhinitis and latex with 39% in asthma was more common.

Table 4. The most common food allergens in allergic patients

Disorder\ allergens	Egg white	Egg yolk	Hazel nut	Banana	Cacao	Carrot	Chicken	Cereals	kiwi	Apple
Urticarial	37.8	35.3	20.2	36.4	36.9	34.5	32.7	36.2	33.6	19.4
Allergic rhinitis	27.5	24.7	22.9	20.5	22.7	21.1	14.6	26.1	16.4	22.2
Asthma	18.9	25	23.9	23.6	19.7	20.1	23.7	20.6	18.7	19.8
Eczema	40	36.8	35.6	37.2	39.2	35.2	25.6	42.8	35.6	21.5

Note: Potato (50.29%), rice (29.2%) and tomato (23.9%) were more common in asthmatic patients.

Table 5. Skin prick test results according to age

Ages	Total %	Positive%	Negative %
6 months to 10years	12.8	6.1	6.7
11-20 years old	22.5	10.2	12.3
21-30 years old	21.5	8.2	13.3
31-40 years old	20.4	7.1	13.3
> 40 years old	22.8	8.7	14.2

Discussion

Outdoor and indoor allergens are important risk factors in inducing and exacerbating allergic diseases. Some studies showed that children with severe asthma tend to report higher allergic sensitization [17, 18]. Sensitivity to allergens does not necessarily mean the patient has allergic diseases and does not cause clinical manifestations. Allergen sensitizations were variable in different areas of the world [19]. This variability depends on geographic conditions such as humidity, warm and dry weather, culture, and genetics [10, 12, 19]. When exposure to pollen and food allergens happens, most patients know that their symptoms worsen but not with fungal agents. Our study showed that at least 40% of patients had positive skin prick tests, which was more common in males (23%) than females (17%). The prevalence of SPT- positive in our study is similar to Nabavi et al.'s study (35%) but less common than Mesdaghi et al. (65%), Ahmadiashar et al. (84%), Arshi et al. (97%), Akbari et al. (85%), Gharegozlo et al. (95%), Feridoni et al. (81%), Khazaei et al. (73%), Kashef et al. (62%), Farhoudi et al. (68%), Mohammadi et al. (86%), Farid et al. (66%), Assarehzadegan et al. (85%), Mahboubi Oskouei et al. (97%) and Hosseini et al. (58%) [20-33].

This variability is due to sampling size, allergen extracts selection, operators, geographic conditions, and genetic factors. The prevalence of allergic disorders was similar in all age groups except in the "under ten years old" age group, which showed less common positive SPT.

Allergic rhinitis was the most common, followed by asthma, urticarial, and atopic dermatitis. These results proved similar to Khazaei and Movahedi's studies [34, 26]. Farid's study performed in Dubai, UAE, showed the same results [30].

In total, *Dermatophagoides farinae* (75%), *Dermatophagoides pteronyssinus* (65%), feather (56%), *Candida* (51%) were the most common allergens in our study due to warm weather and high humidity. It is similar to Khazaei's study (mite = 86%, feather = 75%) in Sistan-Balochistan Province with warm and dry weather. The reason is using air conditioners and spending more time indoor [26]. However, in other studies, pollen sensitization was more common due to dry and warm weather, including Movahedi's [weeds (57%), grass (34%) and tree (28%)]; Kashef's (weeds (70%), grass (59%), tree (52%)); Arshi's (weeds 87%); Farhoudi's (weeds was more common: herbaceous II 62%, sycamore 57%, chenopodium 53%); Oskouei's (Russian thistle 50%, Ash 37%, grass mix 29%, tree mix 22%) [22, 27, 28, 32, 34]. No significant difference of aeroallergens has been observed in different seasons, even though the prevalence of aeroallergens was more common in summer [32]. Tree mix (26%), *Alternaria* (26%), weeds mix (23.6%), and *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus* (22.9%) were more common in Tehran [33]. Pollen's sensitization was more common in spring and summer [33]. The lowest prevalence of Pollen sensitization was in

individuals fewer than three years old [33]. Hosseini's study showed that cockroach, grass, and weeds in spring, *Dermatophagoides pteronyssinus* and *Alternaria* in summer, tree mix and weed mix in autumn, *Dermatophagoides farinae*, weeds mix, and tree mix in winter were more common [33]. According to reports, mites (*Dermatophagoides farinae*, and *Dermatophagoides pteronyssinus*) can also have a high incidence in dry and humid climates [9, 19, 26, 33, 37]. One of the reasons for the mite outbreak in the dry air is the use of water coolers.

In a study done in Dubai, the overall mites sensitization was more common, which is inconsistent with our study results indicating that *Dermatophagoides pteronyssinus* (68%), *Dermatophagoides farinae* (22%), *Alternaria* (7%), and Timothy (3%) were more common, respectively [30].

Food allergy made up half of the aeroallergens in our study. We showed that white egg (31.1%), cacao (29.7%), and yolk egg (28.9%) were more common. Surprisingly, milk sensitization was less common in our study (8.9%). We did not find a reason for it. The most common food sensitizations; in Khazaei et al.'s study were egg (30.33%), walnuts (29.16%), and cow's milk (21.46%), that cow's milk allergy was more common than our study [26]. Milk (21.7%), eggs (20%), wheat (18.3%), and walnuts (17.1%) were the most common in allergic patients in Tehran. In this study, the prevalence of food allergens under three years was more common. Contrary to our study, milk allergy was the most common sensitization [33].

Fungal sensitization was recorded in 45% of our cases. *Candida*, *Alternaria* and *cladosporium* were the most common. It is more common than Ahmadiashar (<15%) with more aspergillosis, Akbari (11-22%) with more Cladosporium and Kashef with more mixed fungus (8%) but less than Khazaei (50%), and Nabavi with more *Alternaria* (35%), [21, 23, 26, 27, 35]. However, another study in the same area by Hedayati et al., who evaluated antifungal serum specific IgE in Sari, showed that *Alternaria* (20%) and *Cladosporium* (19%) were more common [36]. Fungal sensitization in our study was more common than in Hedayati's study [36].

Alternaria (5%), *Aspergillus* (2.4%), *Penicillium* (0.5%), and *Cladosporium* (0.2%) were the most common fungal allergens in a study performed in Mashhad (in the northeast of Iran). The prevalence of fungus sensitization was less common than in our study [32]. The study showed that fungal sensitization was more common in summer and autumn [32]. The prevalence of pollens, mites, and molds was significantly more prevalent in children over five years old [27]. In a study conducted in Tehran, *Alternaria* sensitization was as high as 26% and more common in springtime (32.4%) and the least in autumn (14.7%) [33].

Overall, in our study, positive SPT in all age groups was between 20 to 23%, except for those under the age of 10 (12.8%). Based on these studies, there is sensitivity to fungi in all seasons, and all regions of Iran are involved. Most common fungal allergens include *Alternaria*, *Aspergillus*, *Penicillium*, *Cladosporium*, and *Candida*, which can cause allergic

reactions in allergic patients. Aeroallergens include *Dermatophagoides farinae* (77.3%), *Dermatophagoides pteronyssinus* (65.6%), feather (55.5%), and *Candida* (53.5%) were the most common in our urticarial patients. In another study by Ghaffari et al. on chronic urticarial patients, aeroallergen sensitization was 15%. *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* were more common (36%) than pollen (Timothy, Bermuda, Maple, and Nettle) (2.5%) [37]. Russian thistle, grass mix, and ash were the most common aeroallergens in patients with urticarial in Mashhad (Iran) [32].

Alternaria, *Aspergillus*, and *Penicillium* were most common in urticaria patients in Mashhad (northeast of Iran) [32]. In the present study, *Candida*, *Alternaria*, *Cladosporium*, and *Penicillium* were the most common in chronic urticarial patients.

In another study by Ghaffari et al., the fungal sensitization (*Alternaria* and *Aspergillus*) was 2.5% which was less common than the present study. The reason might be that the previous study was done with a smaller sample size [37]. Food allergens, including egg whites (37.8%), cacao (36.9%), banana (36.4%), and cereals (36.2%) were more common in our urticarial patients.

Allergic rhinitis was more common between the ages of 10 to 40 years in our study but in Kashef's study, allergic rhinitis had increased with age [27]. Aeroallergens include *Dermatophagoides farinae* (76.2%), *Dermatophagoides pteronyssinus* (64.6%), feather (58.2%), and *Candida* (48.5%) were the most common in our allergic rhinitis

patients. In a previous study conducted by the same author, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, cockroach, and feather were the most common in allergic rhinitis patients (prevailing 25.3%, 22.9%, 17.4%, and 4.7%, respectively). In allergic rhinitis and asthma patients put together, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, cockroach, and feather were the most common allergen (prevailing 32.6, 23.3, 10.9, and 7%, respectively) [38].

Pazoki et al. reported that pollen, mites, animal dander, and fungus sensitization were 54.20, 46.66, 18.78, and 17.37% prevalent in Tehran [39]. Mite and fungal sensitization can be common in dry and cold or dry and warm weather like Tehran and Zahedan [26, 39]. Total positive SPT was 86.7 % in allergic rhinitis patients, showing no significant difference between intermittent and persistent allergic rhinitis [29]. In the south of Iran, pollen sensitization was more common in all ages with allergic rhinitis (Weeds 75%, grass 64% and tree 56%) due to dry and cold weather. In this study, mites (22.7%) and molds (8.3%) sensitization were less common than our study. The pollen, mite, and mold sensitization frequency did not differ significantly between age groups [27]. Gharegozlo et al. showed 98.7% positive SPT in children with allergic rhinitis, which is more common than our study [24].

Arshi et al. showed that the prevalence of positive SPT for pollen was 87%, and Lambs Quarter was more common (74%). The pollen sensitization did not differ among genders (22). In Farhoudi's study, pollen sensitization

was more common (55-60%), but mites sensitization was less common (DP (19%), *Dermatophagoides farinae* (18%)) in allergic rhinitis patients [28]. Weeds, trees, grasses, mites, and cockroaches were more common, respectively, in allergic rhinitis patients in Ahwaz (Iran) [31]. In Hosseini's study in Tehran, *Dermatophagoides farinae*, tree mix, and *Dermatophagoides pteronyssinus*, aeroallergen sensitization was common in allergic rhinitis [33]. The findings of this study are very similar to our study, despite having different weather conditions, and this finding is inconsistent with other studies conducted in Tehran [22, 28].

Aspergillus, *Cladosporium*, *Alternaria*, and *Penicillium* sensitization was 12, 11, 10.7, and 8.3 percent respectively in Semnan (Iran) allergic rhinitis patients. There was no difference between genders and location (urban or rural). *Alternaria* was significantly more common above 50 years old than other fungal species [31], but in our study, *Candida*, *Penicillium*, *Alternaria*, and *Cladosporium* were more common in allergic rhinitis patients. In our previous study, ASP and *Alternaria* were 2.8% and 1.6%, respectively in allergic rhinitis and asthma patients. Moreover, *Alternaria* and *Aspergillus* were 10.9 and 4.7% [38].

Cephalosporium acremonium, *Penicillium* Mix, *Alternaria* Mix, and *Aspergillus fumigatus* were more common in allergic rhinitis patients in Ahvaz City. There is no significant difference between fungus sensitization and the type of allergic rhinitis (seasonal and perennial) [31]. *Alternaria*, *Aspergillus*, *Penicillium*, and *Cladosporium* were more

common in allergic rhinitis patients in Mashhad [32].

Food allergens, including white egg (27.5%), barely (25.9%), wheat (26.9%) were more common in our allergic rhinitis patients. In another study, food sensitization was low in allergic rhinitis (5.3% for pepper and peanut).

Aeroallergens including *Dermatophagoides farinae* (76 %), *Dermatophagoides pteronyssinus* (71.6%), *Candida* (59.6%), and feather (54%) were more common in our eczema patients. Russian thistle, grass mix, and ash were the most common aeroallergens in patients with atopic dermatitis in Mashhad (Iran) [32]. Only *Alternaria* was positive in eczema patients in Mashhad of Iran [32]. Food allergens include cereals (42.8%), egg whites (40%), cacao (39.2%) was more common in our eczema patients.

Aeroallergens include *Dermatophagoides farinae* (74.5%), *Dermatophagoides pteronyssinus* (63.7%), feather (55.2%), and *Candida* along cockroach (48.4%) was more common in our asthma patients. Children with asthma had 93% positive SPT in a Tehran research study [24]. Farhoudi et al. showed the prevalence of aeroallergens in children with asthma in Tehran and Karaj cities include trees 33%, *Dermatophagoides pteronyssinus* 31%, grasses 26%, weeds 23%, and feather 20%. Interestingly, *Dermatophagoides pteronyssinus* was relatively more common despite the dry and warm weather in these two cities [40]. Most of those who were positive SPT were born in the winter. Of course, we remembered that increase of eosinophil was more common in asthmatic patients with cockroach sensitization ($p < 0.02$) [40]. In Farhoudi's study, pollen

sensitization was more common (55-60%), but mites sensitization was less common (*Dermatophagoides pteronyssinus* 19%, *Dermatophagoides farinae* 18%) in asthmatic patients [28].

In a previous study by the same author, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, feather, and cockroach allergens were the most common (26.6%, 26.6%, 16.5%, and 12.7%, respectively). In allergic rhinitis and asthma patients put together, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, cockroach, and feather were the most common allergens (prevailing 32.6, 23.3, 10.9, and 7%, respectively) [38]. In Hosseini's study in Tehran, tree mix, weed mix, and *Dermatophagoides farinae* were the most common aeroallergen sensitizations in asthmatic patients [33].

Alternaria (14.5%), *Cladosporium* (13.2%), *Aspergillus* (12.7%), and *Penicillium* (12.7%) sensitization was more common in children with asthma in Semnan city of Iran. There was no significant relationship between fungal sensitization with age, gender, atopy, and location. Admission frequency, asthma severity, and disease duration were associated with positive fungal sensitization numbers [41], but *Candida*, *Alternaria*, *Cladosporium*, and *Penicillium* sensitization was more common in all of our patients, respectively. In our previous study, *Alternaria* and *Aspergillus* were 2.8% and 0.0%. In allergic rhinitis and

asthma patients put together, *Alternaria* and *Aspergillus* were 10.9 and 4.7%, respectively [38]. Other studies showed a relationship between fungal sensitization, especially *Alternaria* and respiratory diseases, and more frequent asthma attacks [42, 43]. Food allergens include potato (50.29%), rice (29.2%), and egg (25.7%) was more common in our asthma patients.

Conclusion

Aeroallergens and food allergens sensitization have a relatively high prevalence in patients with allergic disorders. Airborne allergens are more prevalent. In our region, mite sensitization was more prevalent due to hot and humid weather. Egg whites, Cacao, Banana, and cereals were more common in our urticarial patients. *Dermatophagoides farinae*, *dermatophagoides pteronyssinus*, feather, and *Candida* were the most common in our Asthma, allergic rhinitis, and atopic dermatitis patients. Potato, rice, and egg were more common in our asthma patients. Other studies are needed to evaluate the association of these allergens with the disease and its severity.

Conflict of Interest

No conflict of interest relevant to the present work is declared by all authors.

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