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The most common allergens according to skin prick test: The role of wheal diameter in clinical relevancy

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Abstract

The skin prick test (SPT) could be applied as a useful in vivo method for the detection of sensitization in epidemiological and diagnostic studies if the wheal size is ideally evaluated. We focused on SPT wheal size to identify sensitization pattern to common inhalant and food allergens. In this cross-sectional study, SPT results were obtained from a total of 972 allergic patients. Common allergen extracts for SPT were selected according to the type of allergic diseases, and the geographical pattern. SPT with food allergens was performed for patients with atopic dermatitis (AD) and chronic urticaria (CU). A total of 461 male (47.4%) and 511 female (52.6%) participated in this study (median age: 31 years). The majority of individuals were affected with allergic rhinitis (AR) (n = 624) and asthma (n = 224); while 129 and 67 patients suffered from AD and CU, respectively. The most common aeroallergens were Russian thistle (52.1%) and lamb's quarter (50.7%) with the largest wheal diameter. The wheal size of lamb's quarter was significantly different between patients with asthma and AR ($P < .001$). In addition, a significant difference was detected in wheal diameter in response to the Russian thistle between patients with AR and AD ($P = .001$). Shrimp (23.6%) and Peanut (22.5%) caused the most common food sensitization in patients with AD and CU. Having in mind the most common weed pollens including the Russian thistle and lamb's quarter, preventive strategies, such as, removing unwanted weeds or preventing them from growing, avoidance, and specific immunotherapy may be crucial for better disease control.

KEYWORDS

allergens; prevalence, skin prick test, wheal size

1 | INTRODUCTION

Allergic sensitization is the first phase of immune reactions for inducing allergic diseases. Different factors, such as, genetics, environment,

and age are crucial in the induction of these sensitizations.¹ Due to the increasing prevalence of allergic sensitization in communities, accurate identification of causal allergens with validated methods is necessary for further immunotherapy and allergen avoidance in susceptible individuals.² An inexpensive, rapid, reproducible, and precise method will be helpful in the diagnosis of affected patients.³ Skin prick test (SPT) is a standard in vivo screening procedure for the

Abbreviations: allergic rhinitis, (AR); atopic dermatitis, (AD); chronic urticaria, (CU); skin prick test, (SPT).

evaluation of IgE-mediated hypersensitivity. The most important applications of SPT include diagnosis of immediate type 1 hypersensitivity, specific Immunotherapy, and screening of sensitization patterns in epidemiologic studies.^{4,5} This test is based on an indirect measurement of antigen-specific IgE binding to FcεRI on mast cells.⁶ Epidermal deposition of allergens will result in local reactions including wheal and flare.⁷ Wheal is developed as a result of the linkage of histamine and their receptors and accordingly plasma extravasation around extract exposure. This test could present helpful and valuable documents if performed by expert specialists.⁸

SPT has several advantages including cheapness, being rapidly performed with minimal invasiveness, acceptable diagnostic sense if performed with dexterity and in a standardized routine.⁴ While a good correlation has been reported for positive SPTs and physician-diagnosed AR, statistical analysis raised controversies regarding the correlation of asthma and AD with food allergy.⁹ Although a positive SPT or allergic sensitization is not always equal to a clinical setting, it could increase the occurrence of further possible clinical symptoms.¹⁰ Concerning the European GA2LEN skin prick test study, there is a significant relationship between SPT wheal size and clinical symptoms.⁹

Identification of common sensitizers and evaluation of wheal size in response to SPT can help individuals; especially those with a history of allergy and/or asthma for further avoidance strategies. This study aimed to determine the most common allergens and evaluate SPT wheal diameter in allergic patients to identify sensitization patterns.

2 | METHODS

After obtaining informed consent and ethical approval from the ethics and research committee of Immunology, Asthma, and Allergy Research Institute (IAARI) and taking informed written consents from all the participants, a total of 972 patients with allergic symptoms who were referred to Asthma and Allergy Center, Tehran Medical Sciences, Branch of Academic Center for Education, Culture, and Research (ACECR), from April 2013 to February 2015 were included in this study. Demographic data, type of allergic diseases, and SPT wheal diameter were recorded. Common allergen extracts for SPT (Greer) were selected according to the type of allergic diseases, and the geographical pattern of living place. The SPT and its interpretation were performed by two expert allergists who were blind to the study. The guidelines of the European Academy of Allergy and Clinical Immunology (EAACI) were applied for performing and interpreting the SPT.⁴ The positive and negative controls were histamine (10 mg/mL) and normal saline, respectively. The wheal diameter ≥ 3 mm from negative control was considered as a positive result.¹¹

Data were analyzed using the SPSS software (version 18, Inc. Chicago) and Graphpad Prism 5 (graphpad software inc., La Jolla, California). A normality test was performed for quantitative variables. Median with Inter Quartile Range (IQR) (Q3-Q1) was reported for age and wheal size of SPT. The variables, such as, sex, age groups, and kind of allergic disease were considered as categorical variables. The frequencies of the positive SPT to different aero and food allergens

were reported by count and percentage. Chi-square test was used to evaluate the relationship between gender and different allergens positivity. The difference of wheal size to allergens was evaluated among different allergic diseases using the Kruskal-Wallis test and Mann-Whitney test. To evaluate the correlation between two quantitative variables, Pearson correlation test was applied.

3 | RESULTS

The median age of patients was 31 years (IQR = 14). A total of 461 males (47.4%) and 511 females (52.6%) participated in this study. The physician diagnosis of these subjects was as follows: allergic rhinitis (AR) (n = 624), asthma (n = 224), atopic dermatitis (AD) (n = 129), and chronic urticaria (CU) (n = 67). The frequency of allergic diseases based on age groups is shown in Figure 1. Accordingly, the frequency of allergic diseases was dissimilar in different decades of life. The highest frequency of asthma was found in individuals aged between 41 and 50 years and those less than 10 years; while AR mostly affected the patients in the third and fourth decades of life. The frequency of AD showed a decrease with age; being more prevalent in those below the age of 10 years. The highest frequency of CU was detected over 50 years of age.

Among the total of patients, 80.2% (n = 780) showed allergic sensitization to at least one allergen. Among them, the frequency of mono-sensitization and poly-sensitization was 5.3% (n = 41) and 94.7% (n = 739), respectively. Sensitivity to at least one allergen was significantly higher in men aged 11 to 20 years compared with women in the same age group ($P = .001$). Accordingly, the percentage of positive SPT to at least one allergen in patients aged less than 18 years was 76.3%. Furthermore, the highest frequency of sensitivity to at least one allergen was shown in patients with CU and AR. Additionally, evaluation of the frequency of allergens between genders indicated that male participants showed a higher prevalence of aeroallergen sensitizations and this difference was significant in terms of sensitization to plane tree ($P = .001$) and all types of grasses ($P < .01$).

As shown in Figure 2, the frequency of sensitization to allergens is different from allergic disorders. Sensitization to weed and tree pollens was more common in patients with asthma and AR; while individuals with AD and CU showed significant sensitization to mites and molds. The results of SPT revealed that 75% (n = 733) of all the participants were sensitized to inhalant allergens. Among pollens, weeds were reported as the most common allergens in allergic patients of this study (57.1%). Additionally, the most common aeroallergens in patients less than 18 years were grass (46.9%), weeds (46%), and trees (44.3%); while weeds (59.2%), trees (56.8%), and grasses (51.8%) were reported as the common aeroallergens in patients more than 18 years old. Among patients with AD and CU, sensitization to food and aeroallergens were 14.2% and 22.1%, respectively. Reaction to both groups of allergens was detected in 42.6% of participants. In addition, 36.6% of participants were sensitized with all three pollens types (trees, weeds, and grass).

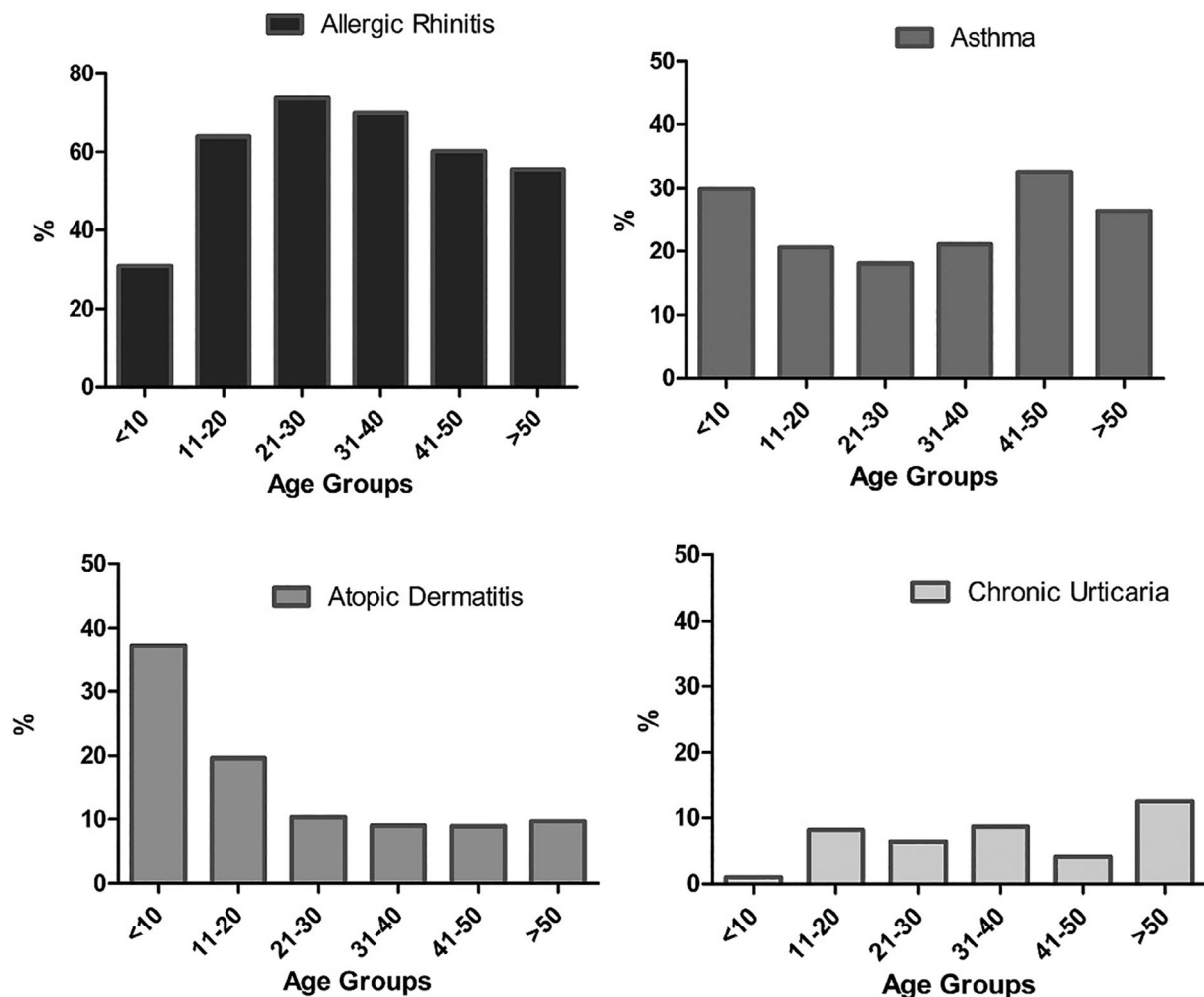


FIGURE 1 The pattern of allergic diseases (Asthma, AR, AD, and CU) in different age groups

Table 1 presents the percentage of common aero and food allergens. Russian thistle (52.1%) and lamb's quarter (50.7%) were the most common sensitizers among inhalant allergens; while shrimp (23.6%) and peanut (22.5%) were the most common food allergens among patients with AD and CU.

The median (IQR) skin prick wheal diameter to common allergens in patients with different allergic diseases is shown in Figure 3. To sum up, the Russian thistle and Lamb's quarter resulted in the largest wheal diameter. As the results represented, wheal size of lamb's quarter was significantly different between patients with asthma (median = 5 mm) and AR (median = 6 mm) ($P < .001$). In addition, a significant difference was detected in wheal diameter in response to Russian thistle allergen between patients with AR (median = 10 mm) and AD (median = 7 mm) ($P = .001$). Interestingly, the overall largest wheal size was found in response to Meadow fescue allergen among the patients with CU. The second large wheal size was detected in response to the Russian thistle allergen in individuals affected with AR.

There was a significant correlation between the wheal size of SPT to Russian thistle and the frequency of AR ($P = .03$) and AD ($P = .003$). Moreover, a significant correlation was explored between *Dermatophagoides pteronyssinus* (DP) and the frequency of AD ($P = .02$).

A significant cross-sensitization has been observed between some allergens. Russian thistle and Lams's quarter were the most common allergens with a strong cross-sensitization. From other cases in our study, we can imply probable cross-reactivity between DP and DF, Meadow fescue and Timothy grass or meadow fescue, and Ryegrass.

According to the clinical relevant cutoff of European GA2LEN skin prick test study for some allergens, such as, plane (>7 mm), mugwort (>5 mm), cockroach (>7 mm), cat (>7 mm), and Alternaria (>8 mm)⁹, our study showed that the frequency of sensitization to plane, mugwort, cockroach, cat, and Alternaria decreased from 35.7% to 5.4%, from 33.1% to 7.9%, from 24.9% to 1.4%, from 23.3% to 4.8%, and from 10.6% to 0.3%, respectively.

4 | DISCUSSION

According to our findings, 80.2% of patients had a positive skin test for at least one allergen. Russian thistle (*Salsola kali*) and lamb's Quarter (*Chenopodium album*) were the most common aeroallergens with the largest wheal diameter; while shrimp and peanut were the most common food allergens among patients affected with AD and CU.

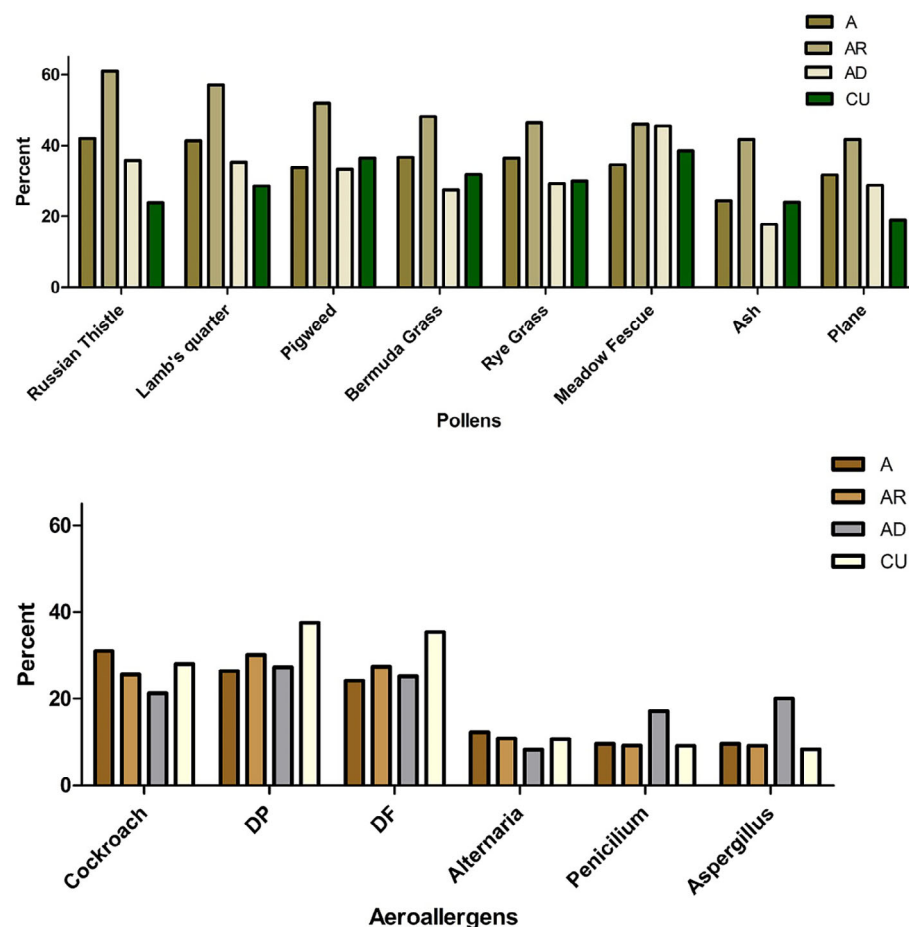


FIGURE 2 The frequency of common aeroallergens in patients with different Allergic diseases. A (asthma), AR (allergic rhinitis), AD (atopic dermatitis), and CU (chronic urticaria)

Some SPT-influencing factors include age, gender, simultaneous medications, and seasonal variability, and differences in choosing the body region, the distance between each skin pricks, and the SPT lancet.^{12,13} In the present study, we tried to decrease the confounding factors by executing the test with professional individuals; similarly performing the SPT.

In our study, the percentage of sensitization to at least one allergen was similar in both genders with some differences among certain age groups. Accordingly, positive SPT results were highly obtained in male individuals aged 11 to 20 years, and female participants aged 41 to 50 years. These findings are not compatible with Arbes et al. study.¹⁴ The percentage of positive SPT to at least one allergen in patients aged less than 18 years showed a highlighted increase compared with the previous study by Bousquet et al. (76.3% vs 58.1%).⁸ The pattern of sensitization to several allergens especially outdoor allergens has changed. In this regards, the most common aeroallergens in patients less than 18 years were trees (26%), *Alternaria* (26%), and weeds (23.6%) as reported by Hosseini et al.;¹⁵ while our results revealed that grass was the most common aeroallergen in the same subgroup of patients. In parallel with our findings, Loureiro G et al. reported grass sensitivity as the most common aeroallergen in patients aged less than 15 years living in Portugal.¹⁶

Our results revealed that although there is no significant relationship between the sensitivity to indoor and outdoor allergens among males and females, sensitivity to some outdoor allergens was

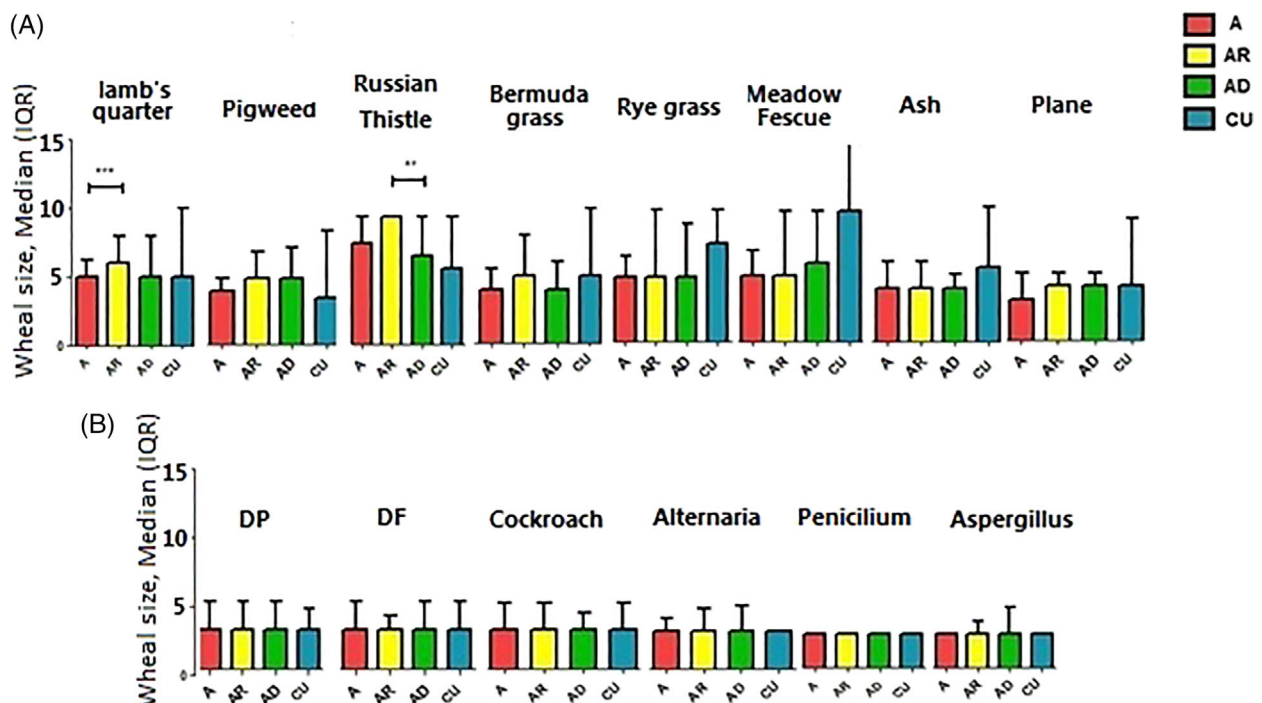
significantly higher in males compared with females. This can result from different levels and exposure duration with allergens and the difference in immune response between men and women.¹⁷

An interesting aspect in evaluating food and inhalant allergens is polysensitization and cross-reactivity such as the cross-reaction between *Salsola kali* (Russian Thistle) from the Amaranthaceae family and *Chenopodium album* (Lamb's Quarters) from the Chenopodiaceae family.¹⁸ In a recent meta-analysis performed by our team, *Salsola kali* was the most common aeroallergens in southwestern and northeastern areas of Iran, while house dust mite was more prevalent in northern and southern coastal areas.¹⁹ Another meta-analysis on food allergens revealed that in patients with atopic dermatitis, egg white and wheat were the most and least frequent food allergens.²⁰

In the study of Hosseini et al, milk, hen's egg, wheat, walnuts, and peanuts were reported as the most common food allergens¹⁵; while our results in patients with AD and CU under 18 years revealed that egg yolk and egg white were the most frequent allergens. In Gupta's study in the United States, the most common food allergens included peanuts, cow's milk, and shellfish.²¹ In Europe, allergies to milk and eggs were most common in children; while peanut, tree nuts, fish, and shellfish had a high frequency in adults.²² In our study, shrimp and peanut sensitization were more common in adults. Despite the low consumption of shrimp in our country, it was the most common food allergen in our study. It could be because of cross-reaction between

TABLE 1 The frequency of allergic sensitization to common inhalant and food allergens. The allergic sensitization to food allergens are reported in patients with atopic dermatitis and chronic urticaria

Inhalant allergens	Number	Sensitization ≥ 3 mm N (%)	Food allergens	Number	Sensitization ≥ 3 mm N (%)
Russian thistle	862	449(52.1)	Shrimp	89	21(23.6)
Lamb's quarter	793	402(50.7)	Peanut	142	32(22.5)
Rough pigweed	552	265(48)	Almond	129	25(19.4)
Meadow fescue	618	263(42.6)	Sesame	157	27(17.2)
Bermuda grass	587	250(42.6)	Curry	60	10(16.7)
Rye grass	791	332(42)	Soya	153	23(15)
Ash	679	247(36.4)	Hazelnut	103	14(13.6)
Plane	789	282(35.7)	Cinnamon	36	8(22.2)
Mugwort	532	176(33.1)	Pepper green	40	5(12.5)
<i>Dermatophagoides pterosynissus</i>	940	286(30.4)	Chocolate	49	8(16.3)
Timothy grass	307	91(29.6)	Onion	82	14(17.1)
<i>Dermatophagoides Farinae</i>	934	261(27.9)	Peach	72	9(12.5)
Poplar	506	137(27.1)	Fish	144	19(13.2)
Cockroach	762	190(24.9)	Tomato	166	25(15.1)
Cat	855	199(23.3)	Pepper	127	18(14.2)
Mosquito	568	142(25)			
Alternaria	781	83(10.6)	Wheat flour	78	8(10.3)
Aspergillus	694	65(9.4)	Egg white	131	13(9.9)
Penicilium	688	62(9)	Cow's milk	134	11(8.2)
Feather	869	105(12.1)	Egg yolk	57	11(19.3)

**FIGURE 3** A, Pollen-specific wheal size in different allergic diseases. B, Wheal size of skin prick test to cockroach, mites, and molds allergens in different allergic diseases. A (asthma), AR (allergic rhinitis), AD (atopic dermatitis), and CU (chronic urticaria)**<0.01, ***<0.001

shrimp and mites or cockroaches. These allergen sources have a cross-reactive protein named tropomyosin that could cause positive SPT for each of these three allergens.²³

The European GA2LEN skin prick test study⁹ has considered different clinical-relevant cut off points for some allergens. These cut off points may increase the clinical relevance and help the allergists in choosing the appropriate allergens for immunotherapy according to wheal size.

To the best of our knowledge, this is the first study to evaluate sensitization in a large number of participants; using SPT in Tehran. Despite all the promising findings, this study has some limitations. In addition, the results of SPT were not compared with in vitro techniques to evaluate the accuracy of the procedure.

Since the wheal diameter determines the results of SPT, more precise strategies should be developed to obtain accurate results. According to our findings, weeds, followed by trees are the most common allergens; causing allergic symptoms. These symptoms may vary based on resident region, geographical plant distribution, gender, climate, age groups, and diet. Finding the allergic pattern and the prevalent allergens may pave the road for further preventive strategies. Restricting the growth of unwanted plants, avoidance of being exposed to allergenic weeds, and immunotherapy methods may help control the symptoms in allergic individuals.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

AUTHOR CONTRIBUTION

Raheleh Shokouhi Shoormasti, Conception & design, analysis and interpretation and drafted the manuscript. Maryam Mahloujirad, Acquisition and interpretation and critically revised the manuscript. Nastaran Sabetkish, Acquisition and interpretation and critically revised the manuscript. Anoushirvan Kazemnejad, Analysis and interpretation and critically revised the manuscript. Vahid Ghobadi Dana, Acquisition and interpretation and critically revised the manuscript. Behnoosh Tayebi, Acquisition and interpretation and critically revised the manuscript. Javid Morad Abbasi, Acquisition and interpretation and critically revised the manuscript. Homa Sadri, Acquisition and interpretation and critically revised the manuscript. Mohammad Reza Fazlollahi, Conception & design, acquisition and interpretation and drafted the manuscript. Zahra Pourpak, Conception & design, acquisition and interpretation and drafted the manuscript. Mostafa Moin, Conception & design, acquisition and interpretation and drafted the manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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