Trends of sensitization to aeroallergens in patients with allergic rhinitis and asthma in Bursa City, South Marmara Sea Region of Turkey

Background and aim: Allergic rhinitis (AR) and asthma are the most common allergic disorders worldwide. Aeroallergens are critical causative factors in the pathogenesis of these disorders and sensitization to aeroallergens differs in various countries and regions. Identification of the most common aeroallergen sensitization is crucial in the diagnosis and management of AR and asthma. We examined the distribution of aeroallergen sensitizations detected by skin prick tests (SPTs), in adult patients with AR and/or asthma in Bursa City.

Materials and methods: Five hundred forty-five patients who underwent a SPT and were diagnosed with rhinitis and/or asthma in Uludag University Faculty of Medicine, Department of Immunology and Allergic Diseases outpatient clinic from March 2018 to August 2018 were retrospectively evaluated. SPTs with standard extracts including house dust mites, pollens, moulds, animal dander and latex were performed on patients.

Results: In the present study, a total of 545 patients included, most of the patients (270; 49.5%) were between 30 and 49 years of age. The prevalence of atopy was 57.9%. The most common aeroallergens detected in the SPT were Dermatophagoides farinae (50%) and D. pteronyssinus (44%), followed by grass-rye mix (43%), grass mix (38.6%), olive (33.2%) and wheat (32.3%). The sensitization to olive pollen was higher in mild asthma (52%), sensitization to D. farinae was higher in patients with mild-moderate asthma (54.5%, 54.2%) (p <0.05).
**Conclusions:** Our study revealed that house dust mite (HDM) was the most common sensitizing aeroallergen in patients with AR and asthma while pollens were the most common allergen in patients with only AR. The sensitization to grass and olive pollen were higher in mild asthma than moderate and severe. Regional allergy panels may provide important clinical clues for characteristics and course of allergic diseases.

**Key words:** Aeroallergen, asthma, allergic rhinitis, Bursa, Turkey
1- Introduction

The prevalence of allergic rhinitis (AR) and asthma has risen significantly over the last two decades [1]. Prevalence of respiratory allergies (AR, asthma) was documented as 12–20% worldwide [2]. AR is the most common atopic disease and affects more than 500 million people around the world [3]. Furthermore, 300 million people worldwide suffer from asthma, and it is projected to increase to 400 million by the year 2025 [4]. In particular, increasing industrialization and air pollution are considered as leading causes of high prevalence of AR and asthma [5,6].

The aetiology of AR and asthma are complex resulting from genetics [7,8] and interacting environmental factors [9,10]. Allergic sensitization to aeroallergens is a major risk factor for developing an allergic disease and optimal management of allergic disease requires the identification of the allergic sensitivities of the patient [11]. The common allergens include house dust mites (HDMs), grasses, trees, weed pollens, animal dander and moulds [5].

Turkey is a bridge between Europe and Asia, surrounded by the Marmara Sea, Black Sea and Mediterranean on three sides. In Turkey, the prevalence of AR and asthma varies between 11.4-22.7% and 2-17%, respectively in adult patients based on regional prevalence [4,12-17]. Depending on considerable variety of climates, aeroallergen spectra and disease prevalence rates differs in distinct regions of Turkey. There is only one research which revealed the aeroallergen sensitivity of patients with asthma in Bursa. Bursa is located in the southeast of the Marmara Sea and Northwest of Turkey [18] at an altitude of 100 m (328 feet) above sea-level, with an average relative humidity of 69%. Because the humidity rate of Bursa province is above 50%, it facilitates the growth of mites in indoor environments.
Avoiding exposure to an allergen is the best way to prevent the disease. Our study aims to find out the prevalence of various allergens leading to AR and/or asthma through skin prick test (SPT) in Bursa City, Turkey.

2- Methods

This retrospective clinical study was conducted in the Department of Immunology and Allergic Diseases, Uludag University Medical Faculty Hospital, Bursa, Turkey. The study was approved by the institutional ethics committee of Uludag University (identification 2019/20).

2.1. Subjects

The medical records of 545 adult patients who were diagnosed with rhinitis and/or asthma and lived in Bursa City were analysed. AR and asthma were diagnosed and classified based on Allergic Rhinitis and their impacts on Asthma (ARIA) and the Global Initiative for Asthma (GINA) guidelines, respectively. Asthma severity was classified as mild/moderate/severe according to medication use that level of treatment as defined in GINA mild(step 1-2), moderate (step 3), severe (step 4-5 ) [19]. We reviewed the medical records of all patients presented to our department from March 2018 to August 2018.
2.2. Skin prick tests

The SPT was conducted using a standard commercial extract panel (Alk - Abello, Lincoln Diagnostics, Dallas, TX, USA), consisting of 17 aeroallergens (Grass mix, grass-rye mix, weed mix, birch, trees mix, olive, oak, wheat, cat, dog, latex, *Dermatophagoides pteronyssinus, D. farinae, Acarus siro, fusarium, Alternaria, cockroach*). SPT was performed according to the international guidelines as a single-test on two forearms with lancets and standardized allergens by the same trained nurse. Histamine hydrochloride (10 mg/ml) and 0.9% saline were applied as positive and negative controls, respectively. The wheel diameter was measured after 20 min and reported in ‘mm’. A skin reaction of ≥3 mm than that produced by the negative control on the SPT was considered as a positive reaction.

2.3. Analysis

The data were analysed using the Statistical Package for Social Sciences (SPSS) version 21 software (IBM Corp., Armonk, NY, USA). Chi-square, independent T test and Mann–Whitney U test were used to examine and compare the relationship between the characteristics of the sample. A p-value of less than 0.05 was considered statistically significant.
3- Results

3.1. Study population

A total of 545 patients (407 female and 138 male) were enrolled in this study. The median age was 41 (min 18, max 82 years). Most of the patients (270; 49.5%) were in the age group of 30–49 years (Table). Three hundred sixteen of the patients (57.9%) were found to be sensitized to at least one of the 17 aeroallergen extracts tested. One hundred sixty-seven of sensitized patients (52.8%) had AR without asthma, 135 of sensitized patients (42.7%) had AR with asthma, 14 of sensitized patients (4%) had only asthma.

3.2. Prevalence of aeroallergen sensitization

The most frequent aeroallergen we determined in the SPT was mites (D. farinae 50%; D. pteronyssinus 44%), followed by grass-rye mix 43%, grass mix 38.6%, olive (33.2%), wheat pollen (32.3%), storage mite (Acarus siro) (26.3%), tree pollens (23.7%), weed pollen (22.5%), birch pollen (22.2%), oak (20.3%), cockroach (19.9%), Fusarium (14.6%), dog (12.7%), cat (12%), Alternaria (12%), latex (10.8%) (Figure 1).
3.3. Gender and allergen sensitization

Females showed higher test positivity rate for grass-rye mixes, weeds, olive pollen and cats compared to males (p = 0.047, p = 0.017, p = 0.034 and p = 0.049, respectively). No significant difference observed between genders for the remaining allergens.

3.4. Age groups and allergen sensitization to pollens

We classified patients into three groups according to age cutoff points commonly used in the medical literature (18–29, 30–49, 50+ years old). There was a significant difference among groups for grass-rye mix, grass mix, wheat allergen sensitivity rate. The sensitization rates to the grass-rye mix were 32.4%, 55.1% and 12.5% for subjects in 18–29 years, 30–49 years and 50+ years, respectively. We found a significant association between sensitization to grass-rye mix and the age groups of the subjects (p = 0.001). The sensitization rates against grass were higher in the 30–49 years group (53.3%), than 18–29 years group (33.6%) and 50+ (13.1%), (p = 0.001). The prevalence of sensitization to wheat was also higher in 30–49 years (55.9%) than 18–29 years group (33.3%) and 50+ (10.8%) (p = 0.001).

3.5. Asthma and/or allergic rhinitis and common allergen sensitization

In asthma patients with AR, the most frequent aeroallergens were mites (*D. pteronyssinus* 52.6%; *D. farinae* 51.3%) followed by grass-rye mix (41.5%), grass mix (38.5%), olive pollen (31.1%), storage mite (28.1%), wheat pollen (28.1%), cat (11.2%) and dog (14.1%) sensitizations were rare.
In patients with only AR, the most frequent aeroallergen was grass-rye mix (52.8%), followed by mites (*D. farinae* 44.3%; *D. pteronyssinus* 40.1%), grass mix (39.5%), olive pollen (36.5%), wheat pollen (36.5%), weed pollen (25.1%), storage mite (25.1%). Latex (8.4%) and *Alternaria* (9%) were rare.

In patients with only asthma, the most frequent aeroallergens were grass mix (28.6%), birch (28.6%), oak (28.6%), cockroach (28.6%); followed by grass-rye mix (21.4%), storage mite (21.4%), *D. farinae* (21.4%), wheat pollen (21.4%), tree pollen (21.4%). Cat, latex, *Alternaria* sensitization were not seen (0%) (Figure 2).

**3.6. Asthma severity and common allergen sensitization**

Our study showed an association between sensitization to four aeroallergens (grass-rye mix, grass mix, olive pollen, *D. farinae*) and asthma severity. The sensitization rates to the grass-rye mix were 36%, 58.8% and 29.8% for subjects in mild, moderate and severe asthma, respectively. The sensitization rates against grass were higher in mild asthma (60%) than moderate (52.9%) and severe (29.8%), (p = 0.01). The sensitization to olive pollen was higher in mild asthma (52%), sensitization to *D. farinae* was higher in patients with mild-moderate asthma (54.5%, 54.2%) (p = 0.04) (Figure 3).

**4- Discussion**

AR and asthma are leading causes of morbidity over the world, and the prevalence of these diseases is continuously increasing related to growing environmental pollution [3,6].
Identification of allergens that trigger factors in AR and asthma is the initial step, and the treating physician should be aware of geographical distribution and prevalence of aeroallergens in a particular area [20]. The SPT is an easy and quick tool for IgE-mediated allergy diagnosis. As far as we know, this is the first reported study to investigate the aeroallergen distribution in adult subjects with AR and/or asthma in the southeast of the Marmara Sea, Northwest of Turkey.

Turkey, a country having lands both in Asia and Europe, consists of many different geographic features and climates. Turkey is surrounded by sea in three directions, having a rainy climate in the north, Mediterranean climate in western and southern regions, and cold and rough climate in eastern and inner parts. Western and north-western parts are industrialized [15]. This geographical and climatic differences result in varying aeroallergen spectra and subsequently to different sensitization rates to these aeroallergens [6]. Bursa is an industrialized city with three million inhabitants, situated at 41°11’ N, 29°04’ E in north-western Turkey at an altitude of about 100 m above sea-level, and located on a plain flanked by Mount Uludag to the south and the Samanli Range to the north [21].

In our study, 316 patients had a positive reaction to SPT. House dust mites (HDMs were the most prevalent sensitizing aeroallergens (D. pteronyssinus, 50%; D. farinae, 44%) followed by pollen (grass-rye mix 43%, grass mix 38.6%, olive 33.2%, wheat 32.3%, trees mix 23.7%, weeds 22.5%, birch 22.2%, oak 20.3%), storage mites (26.3%), cockroach (19.9%), moulds (Fusarium 14.6%, Alternaria 12%), epithelia (dog 12.7%, cat 12%). There is remarkable variability in aeroallergen distribution among countries, even among regions within the same country [4]. In general, HDM sensitization is more common in tropical countries such as Malaysia and Singapore [22]. However, pollens are the most sensitizing
aeroallergens in Europe [23]. Allergic sensitization to mites has been studied in different regions of Turkey. Studies in Turkey have reported sensitization rates to D. pteronyssinus and D. farinae rates as 72.5% and 63.7% in Düzce [24], 62.2% and 51.3% in Eskişehir [25], 25.3% and 29.3% in Istanbul [26], 22.4% and 21.5% in Isparta [27]. A previous study that included various regions of Turkey, showed that the presence of mites was related to an increase both in mean temperature (>15 °C) and in humidity (≥40%) as well as low altitude (<300 m) [28]. In our study, high sensitization to HDMs was expected due to the regional geography with 69% humidity and location at an altitude of 100 m (328 feet) above sea-level.

Our study showed more prevalent sensitivity to grass-rye mixes, weeds, olive pollen, cats among women. Conversely, other studies from Kuwait and China showed a higher prevalence rate of sensitization towards outdoor allergens in males [29, 30]. No convincing clarifications have been given for this gender differences. There is no evidence to suggest that sex leads to differential exposure to aeroallergens [29].

Looking at the age distribution of the allergen groups, sensitization to grass-rye, grass and wheat were seen more frequently in patients between 30 and 49 years. We found no difference in sensitization to other aeroallergens according to age groups. A previous study from Kuwait indicated age-dependent sensitization to the HDM D. microceras, which had a higher prevalence rate in the 45+ years age group [29]. Other studies from Turkey and other countries found no difference in the prevalence of positive SPT between younger and older patients with AR [26, 27, 31].

HDM sensitization associated with the risk of rhinitis and asthma in children and adults has been shown by several researchers [32,33]. Allergic responses to HDM is associated with
airway hyperresponsiveness and it is the most important indoor allergen for asthma [34–37]. A previous study from Bursa and other studies showed high sensitization to HDM in asthma patients [5, 17, 32, 38]. In accordance with the literature, we found high HDM sensitivity in asthmatic patients. Related to the regional geography with high humidity and temperature, sensitization to indoor allergens was expected.

Looking at the association between asthma severity and allergen sensitivity, olive and grass sensitization was higher in mild asthma. 24.4% of olive trees in Turkey are located in the Marmara region. 37.4% of the olive trees in the Marmara region are in Bursa. In addition, the most grown fruit in the province is olive [39]. Therefore, sensitization to olive tree is expected. \textit{D. farinae} sensitization was higher in mild and moderate asthma. Grass-rye sensitization was higher in moderate asthma. A study from Kuwait indicated a high frequency of severe asthma with patients sensitized to Cladosporium, Aspergillus and Alternaria. A study from Saudi Arabia showed higher asthma severity correlation with the degree of sensitization to \textit{D. pteronyssinus} and \textit{D. farinae}.

For patients with only AR, the most frequent aeroallergen was the grass-rye mix, followed by mites, grass mix and olive. In this regard, our results are consistent with some previous studies, which indicated grass pollens as the most common allergen in patients with AR [26, 29, 40, 41]. On the other hand, some of the previous studies from many countries showed HDMs are common aeroallergens in patients with AR [4, 5, 31, 40–42]. This appears to be a geographical variation. Our findings correlated with the climate of Bursa, which is characterized by dry and warm summers and wet and cold winters. The climate in Bursa allows many plants to grow, flower, produce and release pollen grains into the atmosphere at any time of the year. The number of pollen grains increases from February to April and
reaches its maximum level in May [21]. Grass pollen which is the most dominant aeroallergen in May and June causes great problems to individuals with pollen allergy [21,43].

5- Conclusion

The most frequent aeroallergen we determined in the SPT was mites, followed by pollens, cockroach, mold, animal dander ad latex. Our study showed high HDM sensitization in patients with asthma and AR; on the other hand, sensitization to pollens was most common in patients with only AR. Furthermore, olive sensitive patients had mild asthma, and mite-sensitive patients had mild to moderate severity. Identification of allergens is an essential step in the diagnosis of respiratory allergic disease. Specific allergy panels based on regional differences in patterns of sensitizations can provide cost-effective screening of sensitized patients and better management of disease with environmental allergen control.
Table. Distribution of age, gender and diagnosis according to SPT positivity.

Figure 1. Distribution of allergen sensitization of population

Figure 2. Distribution of allergen sensitization according to diseases

Figure 3. Distribution of allergen sensitization according to asthma severity
References


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<tr>
<td>Male</td>
<td>92</td>
<td>40</td>
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</table>

**Table.** Distribution of all the patients, and patients with positive and negative SPT according to age, gender and diagnosis.

*SPT* skin prick test
Figure 1. Distribution of allergen sensitization of the study population
**Figure 2.** Distribution of allergen sensitization according to diseases

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Figure 3. Distribution of allergen sensitization according to asthma severity
Declaration of interest

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