



## ORIGINAL ARTICLE

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## Ragweed (*Ambrosia artemisiifolia*) is the most important seasonal allergen in the Black Sea Region

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### Abstract

**Background:** Allergic rhinitis and allergic asthma are respiratory tract diseases predominantly triggered by allergens such as pollens, house dust mite, mold etc. The prevalence of respiratory allergens varies according to geographic location. Ragweed (*Ambrosia artemisiifolia*), a prevalent weed particularly in South America and Europe, is being investigated for its sensitization frequency in the Black Sea region of our country. This study aims to evaluate ragweed and other allergens associated with respiratory allergic diseases in this region and determine their disease frequency.

**Materials and methods:** A retrospective analysis was performed on patients diagnosed with allergic rhinitis, conjunctivitis, and asthma who attended the Immunology and Allergy outpatient clinic at Samsun Training and Research Hospital between 2017 and 2024. Data from 3,000 diagnosed patients were examined.

**Results:** Of the 3,000 patients, 2,124 (70%) were female and 876 (30%) were male. All patients were diagnosed with allergic rhinitis, while conjunctivitis was observed in 2,300 patients (76%), and asthma was diagnosed in 1,382 patients (46.6%). The most frequently detected allergen was house dust mite (75%). Ragweed pollen was identified as the most common cause of seasonal allergic rhinitis (15%). Moreover, ragweed pollen was found to be the allergen associated with the highest risk of asthma development (p-value:  $6.69 \times 10^{-52}$ ).

**Conclusion:** Ragweed pollen allergy is common in our region, and the allergenicity load is high. The sensitization rate may increase over time. If the prevalence is determined accurately, appropriate preventive measures and treatments can be developed.

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## Introduction

Allergic rhinitis and allergic asthma are allergic diseases of the respiratory tract. Allergic rhinitis is the most common cause of rhinitis other than infection. It may be associated with allergic conjunctivitis (80%) and asthma (18-40%).<sup>1</sup> Allergic rhinitis is also present in 90-95% of allergic asthma patients.<sup>1,2</sup> Rhinorrhea, nasal congestion, postnasal drip, sneezing, and intranasal itching are the most common symptoms. The duration of symptoms, whether symptoms are accompanied by fever and pain, whether nasal discharge is bilateral, whether symptoms increase with animal contact in open air or in a closed environment, and the color of nasal discharge are questions that guide diagnosis. Bilateral transparent nasal discharge, painless, fever-free, symptoms lasting at least 2 weeks favor allergic rhinitis. Bilateral eye itching, watering, and redness are symptoms of conjunctivitis, whereas cough without phlegm accompanied by shortness of breath are symptoms of asthma.<sup>1-3</sup> Patients with a preliminary diagnosis of allergic rhinoconjunctivitis and/or asthma based on these findings are diagnosed by detecting the allergen with skin prick test and specific immunoglobulin-E (IgE), and based on physical examination.<sup>4</sup> In the skin prick test, induration of more than 3 mm after dropping the allergen onto the skin is considered positive.<sup>5</sup> Specific IgE is measured using the immunoCAP method, which is preferred because it has higher specificity.<sup>6</sup>

The severity of the disease is determined by whether the patient's symptoms continue throughout the year or seasonally, how many days per week the symptoms occur, how long they last during the day, and whether the symptoms are present at night.<sup>3,4</sup> There is a standard approach for the severity of rhinitis in the recommendations of the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines<sup>4</sup> and the Global Initiative for Asthma Guidelines (GINA) for asthma.<sup>7</sup> According to GINA, asthma is stratified into treatment steps depending on the dose required to achieve and maintain adequate symptom control.

Pollens are the most common allergens in seasonal allergic rhinitis, while house dust mites, cats, dogs, and mushrooms are the most common allergens in perennial allergic rhinitis. Patients who are sensitized to more than one allergen are considered polysensitized.<sup>8</sup>

Respiratory allergen causes vary depending on geographic location. All climates can be seen in our country due to its location. The effectiveness of allergens is also affected by climate, temperature, and altitude.<sup>9,10</sup> Ragweed (*Ambrosia artemisiifolia*), from the Asteraceae family, is a common weed found especially in South America and Europe. It is also found in Asia and Australia. It is an important cause of seasonal allergic rhinitis and asthma in America and Europe and has a high allergenic effect.<sup>11-13</sup> Climate change, increased land use, and air pollution are estimated to increase the spread and allergenicity of ragweed.<sup>13</sup> There are studies investigating respiratory allergen sensitization in our country focusing on sensitization with weed mixtures, but ragweed alone has not been evaluated.<sup>14-19</sup> It is not known in which regions and how frequently ragweed sensitization occurs in our country. Our study aimed to evaluate allergens, especially ragweed, for respiratory allergic diseases in the Black Sea region and to determine the disease frequency.

## Materials and Methods

Records of 3,000 patients diagnosed with allergic rhinitis, conjunctivitis, and asthma at Samsun Training and Research Hospital Immunology and Allergy outpatient clinic (2017-2024) were reviewed. Only patients over 18 years old were included. Nonallergic rhinitis conditions like vasomotor and senile rhinitis were excluded. Disease severity and detected allergens for each patient were documented. The severity of rhinitis and asthma was assessed according to ARIA guidelines. This assessment is presented in Table 1. The severity and treatment of asthma were assessed according to GINA.

In the skin prick test, *Dermatophagoides farinea* (D. farinea), *Dermatophagoides pteronyssinus* (D. pteronyssinus), *Acaris ciro*, Grass mix, Tree mix 1-2, Hazel, *Olea europaea*, ragweed, *Cupressus orizanica*, *Alternaria alternata*, *Aspergillus*, *Cladosporium*, *Penicillium*, Cat, Dog, *Chenopodium album*, *Plantago lanceolata*, *Artemisia vulgaris*, *Parietaria officinalis*, *Fraxinus excelsior*, *Populus alba*, *Salix caprea*, *Cynodon dactylon*, *Lolium perenne*, *Festuca pratensis*, *Holcus lanatus*, *Ulmus scabra*, *Robinia pseudoacacia*, Latex, *Betula alba*, *Quercus robur*, *Acer pseudoplatanus*, *Platanus orientalis*, and *Ulmus scabra* were evaluated. Solutions from Alergofarma and ALK companies were used in prick tests. The allergens to be tested were applied to the skin along with positive (histamine) and negative (saline) controls. After approximately 15-20 minutes, the test sites were examined. An induration and erythema with a diameter of 3 mm or greater was considered positive. Specific IgE was evaluated by the immunoCAP method. According to the instructions in the analysis kit package insert, results above 0.35 kUA were considered positive.

In the patient analyses, those sensitized to only one allergen were recorded as monosensitized, while those sensitized to two or more allergens were recorded as polysensitized. Patients with only pollen sensitization were evaluated as having seasonal respiratory tract disease;

**Table 1** Severity evaluation of allergic rhinitis and asthma according to the Allergic Rhinitis and its impact on asthma guidelines.

Severity	Symptoms
Intermittent	<4 days a week or <4 consecutive weeks
Persistent	>4 days a week and For >4 consecutive weeks
Mild	None of the following are present: Sleep disturbance Impairment of daily activities, leisure, and/or sport Impairment of work or school
Moderate-severe	One or more of the following are present: Sleep disturbance Impairment of daily activities, leisure, and/or sport Impairment of work or school

patients with house dust mite, mold, cat, and dog sensitization were evaluated as having perennial respiratory tract disease, provided their clinical presentations were compatible. The diagnosis was made in patients with compatible clinical findings and a positive skin prick test and/or specific IgE.

All data were recorded and analyzed using Microsoft Excel and SPSS programs. Simple calculations were performed using Excel and SPSS. The chi-square test was used for statistical analysis. For our study, an application was submitted to the Ethics Committee of Samsun Training and Research Hospital on 09.07.2019, and approval was received with decision number TUEK67-2019BADK/13-99. Informed consent was obtained from every patient.

## Results

A total of 3,000 patients participated in the study; 2,124 (70%) were female and 876 (30%) were male. All patients were diagnosed with allergic rhinitis. Conjunctivitis was present in 2,300 (76%) of the patients, and 1,382 (46.6%) were diagnosed with asthma. The average age of the participants was 37.2 years (range, 18-66). The demographic characteristics are detailed in Table 2.

Monosensitization was observed in 42.5% (n = 1,275) of the cohort. Among these, 80% (n = 1,023) were sensitized to *D. farinae* and *D. pteronyssinus*, 8% (n = 235) to ragweed, 4% (n = 120) to grass mix, 4% (n = 118) to *Artemisia*, 2% (n = 60) to *Cupressus*, and 2% (n = 58) to hazelnut pollen.

Polysensitization was detected in 57.5% (n = 1,774) of the group. The number of patients experiencing solely seasonal symptoms was 598 (20%). Perennial symptoms with seasonal exacerbations were reported by 1,379 (46%) patients.

The following sensitizations were identified in the 598 seasonally polysensitized patients: sensitization to ragweed (*Ambrosia*) was detected in 156 (26%), grass mix in 121 (20%), *Cupressus* in 87 (15%), *Artemisia* in 69 (11.5%), *Plantago* in 60 (10%), hazel in 43 (7%), *Chenopodium* in 34 (6%), and *Olea* (olive tree) in 28 (4%) patients.

The following sensitizations were identified in the 1,379 perennial and seasonally exacerbated polysensitized patients: house dust mites were detected in 1,237 (89%), ragweed in 55 (3.8%), grass mix in 48 (3.4%), *Cupressus* in 39 (2.8%), *Artemisia* in 6 (0.4%), and others in 32 (2.3%). The data are presented in Table 3 and illustrated in Figure 1.

Based on these findings, house dust mites and ragweed pollen were found to be associated with asthma.

A total of 446 patients were identified with ragweed sensitization. Among them, 235 were monosensitized, 156 were co-sensitized with other pollen allergies, and 55 were co-sensitized with perennial allergies and other pollens. Allergic rhinoconjunctivitis was present in all 446 patients, while 48 experienced only allergic rhinitis. Asthma was diagnosed in 312 patients. Ragweed-sensitized asthma patients who were monosensitized were controlled with step 3-4 treatment according to the GINA treatment protocol. Symptom control was achieved with moderate-to-high doses of inhaled corticosteroids in combination with beta-2 agonists. Symptoms typically commenced in August and concluded in October; 70% of patients experienced symptoms for 1-2 months. The severity of rhinitis symptoms was classified as severe in 85% of the patients.

Sensitization rates among patients with asthma (n = 1,382) were observed as follows: house dust mite monosensitization was found in 567 patients, ragweed monosensitization in 167 patients, hazelnut monosensitization in 14 patients, and mixed grass pollen monosensitization in 15 patients. Seasonal polysensitization was identified in 196 patients, and both perennial and seasonal polysensitization were detected in 423 patients. The findings are presented in Table 3.

## Discussion

Ragweed pollen was the most frequently detected allergen after house dust mite in allergic rhinitis, conjunctivitis, and asthma in this study. House dust mite allergy was identified at a notably high rate (75%). This was followed by sensitization to ragweed (15%), grass (9.5%), *Artemisia* (6.4%), *Cupressus* (6%), *Plantago* (4.7%), and hazel pollen (4.6%). Sensitization to house dust mites and ragweed pollen increases the risk of asthma. The risk was found to be higher for ragweed pollen compared to house dust mites. *Plantago* and *Artemisia* pollen did not appear to contribute to the development of asthma. Additionally, no statistically significant association was observed between asthma and grass pollen, *Cupressus*, or hazel tree pollen. Statistical analysis could not be performed for cat and dog dander, *Aspergillus*, *Alternaria*, and olive tree pollen due to the low number of sensitized individuals.

There was a statistically significant association between ragweed sensitization and asthma (p-value =  $9.46 \times 10^{-28}$ , i.e.,  $p < 0.05$ ). No significant association was found between asthma and other pollen sensitizations (*Cupressus*-asthma analysis p-value = 0.275,  $p > 0.05$ ; grass mix-asthma analysis p-value = 0.337,  $p > 0.05$ ). House dust mites are the most common cause of allergic respiratory diseases and are associated with asthma (p-value =  $6.69 \times 10^{-52}$ ,  $p < 0.05$ ). In this region, one out of every four patients sensitized to ragweed develops clinical asthma. The pollen season lasts for approximately three months, during which asthma symptoms may begin concurrently with rhinitis symptoms. These symptoms can be mistaken for a lower respiratory tract infection.

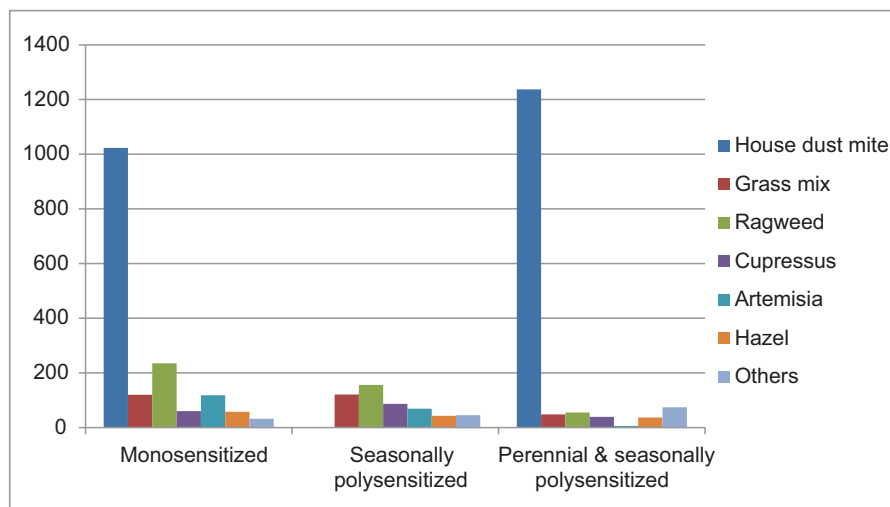
We evaluated our study as a retrospective analysis. Under normal circumstances, component-resolved

**Table 2** Demographic characteristics.

	Female	Male
Number of Patients	2124 (70%)	876 (30%)
Average Age	36	38
Allergic rhinitis	2124	876
Allergic rhinoconjunctivitis	1520(71%)	780 (89%)
Allergic asthma	940 (44%)	442 (50%)
Monosensitized	863 (40%)	412 (47%)
Polysensitized seasonal	297 (14%)	49 (5%)
Polysensitized perennial & seasonal	964 (45%)	415 (47%)

**Table 3** Allergens and clinic data.

Allergens	Patient number	Rhinitis Patient number	Conjunctivitis Patient number	Asthma(mild) Patient number	Asthma(severe) Patient number	Allergen-asthma relationship p-value
House dust mite Monosensitized	2260 75.3% (1023)	2260	1716	1216 (567)	4	$6.69 \times 10^{-52}$ (p:<0.05)
Grass mix Monosensitized	287 9.5% (120)	287	225	124 (15)		0.337 (p:>0.05)
Ragweed Monosensitized	446 15% (235)	446	348	312 (167)		$9.46 \times 10^{-28}$ (p:< 0.05)
Cupressus Monosensitized	186 6% (60)	186	137	78 -		0.275 (p:>0.05)
Plantago Monosensitized	142 4.7% (130)	142	106	22 -		$1.3410^{-13}$ (p:< 0.05)
Artemisia Monosensitized	193 6.4% (118)	193	143	-		
Hazel Monosensitized	138 4.6% (58)	138	95	65 (14)		0.87 (p:>0.05)
Others: cat, dog, olea, <i>Aspergillus</i> , <i>alterneria</i> etc.	164 5.4%	164	124	32		

**Figure 1** Sensitization rates according to allergens.

diagnostics could not be performed because they are not covered by government reimbursement and have not yet been indicated for use in every patient for diagnosis. Conducting component analysis in this study would have helped identify the specific components with the highest allergenicity. However, since our study was retrospective

in design, this was not feasible. This represents a limitation of our study. Ragweed components, in particular, do not exhibit cross-reactivity with other pollens. Cross-reactions exist among species within the genus *Ambrosia*, which belongs to the Asteraceae family and includes at least 51 identified species. Therefore, we believe that our study

accurately reflects the association between ragweed sensitization and asthma, as well as its comparison with other pollens.

However, it was the most common cause of seasonal allergic rhinitis in this region. *Ragweed (Ambrosia artemisiifolia)*, one of the seasonal respiratory allergens worldwide, is a pollen with very high allergenicity.<sup>20</sup> It is an aggressive pollen, and its spread is increasing worldwide.<sup>13</sup> *Ambrosia artemisiifolia* is an important cause of seasonal allergic rhinitis in North America and European countries. It can become a significant health problem because its rate of spread is high.<sup>21</sup> In Europe and the United States, ragweed sensitization has been reported at varying rates depending on the region, ranging from 10% to 30%.<sup>13</sup> A study conducted in Africa found a prevalence of 8%, while in Egypt, it was reported to be 34% (22,23).

We could not find any studies investigating the prevalence and disease frequency of ragweed pollen in our country. Therefore, our knowledge regarding its increasing prevalence is limited; however, this study demonstrated that ragweed exhibits high allergenicity, as evidenced by a high rate of sensitization among atopic individuals and an associated risk of asthma.

Treatment steps for allergic respiratory tract diseases are as follows: allergen avoidance, treatments to suppress allergic respiratory symptoms (antihistamines, nasal steroids, montelukast, inhaled steroids, inhaled beta-2 agonists), and immunotherapy. With immunotherapy, respiratory diseases may improve, or their severity may decrease.<sup>8</sup> This study found that ragweed sensitization is high in the Black Sea region of our country. Given its high allergenic potential, such studies are increasingly important for the development and production of immunotherapies. Further research is necessary to explore the frequency of sensitization in various regions.

The limitation of our study is its single-center design and the absence of component analysis.

## Conclusion

Ragweed pollen allergy is also present in our country. The frequency of sensitization may increase over time. If its prevalence is accurately determined, appropriate precautions and treatments can be developed.

## Acknowledgment

Our study has not been published before and an application was made to the Ethics Committee of Samsun Training and Research Hospital in 09.07.2019 and approval was received with the decision number TUEK67-2019BADK/13-99. All data informed consent for every patient was recorded.

## Authors Contribution

Aksakal S. designed all aspects of the study. Arslan NG was involved in referring patients and reviewing and editing the manuscript.

## Conflict of Interest

The authors declare no potential conflicts of interest with respect to research, authorship and/or publication of this article.

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