

## The relationship between the results of skin prick test and the pulmonary symptoms in patients with allergic rhinitis symptoms

*Allerjik rinit semptomları olan hastalarda deri prik testi sonuçları ile akciğer semptomları arasındaki ilişki*

Melike Demir<sup>1</sup>, Gülistan Karadeniz<sup>1</sup>, Emre Günbey<sup>2</sup>, Hayriye Karabulut<sup>3</sup>

<sup>1</sup> Keçiören Eğitim ve Araştırma Hastanesi Göğüs Hastalıkları Kliniği, Ankara

<sup>2</sup> Ondokuz Mayıs Üniversitesi Tıp Fakültesi, Kulak Burun Boğaz Anabilim Dalı, Samsun

<sup>3</sup> Gazi Üniversitesi Tıp Fakültesi, Kulak Burun Boğaz Anabilim Dalı, Ankara

### Özet

**Amaç:** Deri prik testi sonuçları ve akciğer semptomlarının sıklığı arasındaki ilişkiyi incelemek ve allerjik rinit semptomları bulunan hastalarda hangi allerjenlerin akciğer semptomlarıyla daha yakın ilişkili olduğunu araştırmaktır.

**Yöntem:** Rinit semptomları ile başvuran ve deri prik testi yapılan 1343 hasta çalışmaya dahil edildi. Öksürük, nefes darlığı ve hırıltılı solunum akciğer semptomları olarak kabul edildi. Deri prik testi ve akciğer semptomları arasındaki ilişki araştırıldı.

**Bulgular:** 1343 hastadan 449'unda deri prik testi negatif, 894'ünde pozitif idi. En sık akciğer semptomlarının öksürük (%52.9) ve nefes darlığı (%45.2) olduğu gözlemlendi. Akciğer semptomları allerjik grupta (%70.8) allerjik olmayan gruba (%29.2) göre anlamlı oranda daha fazlaydı (p=0.021). Akciğer semptomu olan ve olmayan gruplar karşılaştırıldığında allerjen dağılımı ve sayıları yönünden anlamlı fark izlenmedi.

**Sonuç:** Akciğer semptomları olan hastalarda olmayanlara göre deri prik testi anlamlı oranda daha yüksek bulundu. Allerjik rinitli hastalarda allerjen dağılımı ile akciğer semptomları arasında ilişki bulmadık.

**Anahtar Kelimeler:** Allerjik rinit, deri prik testi, öksürük, astma, hırıltılı solunum.

### Abstract

**Objective:** To investigate the relationship between skin prick test results and the frequency of pulmonary symptoms and to discover which allergens are more commonly associated with the pulmonary symptoms in patients with allergic rhinitis symptoms.

**Method:** 1343 patients who presented with rhinitis symptoms and underwent the skin prick test were included in the study. Coughing, shortness of breath and wheezing were considered as pulmonary symptoms. The relationship between the skin prick test results and the pulmonary symptoms were investigated.

**Results:** Of the 1343 patients, skin prick test was negative in the 449 and positive in the 894 of the patients. It was observed that the most frequent pulmonary symptoms were coughing (52.9%) and shortness of breath (45.2%). Pulmonary symptoms were significantly high in the allergic patients (70.8%) compared to the non-allergic group (%29.2) (p=0.021). No significant differences were detected between the patient groups with and without pulmonary symptoms in terms of distribution and count of allergens.

**Conclusion:** A positive skin prick test occurred significantly high in patients with pulmonary symptoms compared to the patients without pulmonary symptoms. We did not find a relationship between the distribution of allergens and the pulmonary symptoms in patients with allergic rhinitis.

**Keywords:** Allergic rhinitis, skin prick test, coughing, asthma, wheezing.

### Introduction

Allergic rhinitis (AR) is a common disease seen in the 10-20 % of society with frequencies differing by region (1, 2). AR is classified according to periods of symptoms known as perennial (whole year/ongoing) and seasonal and is defined as persistent rhinitis when symptoms occur >4 days/week and >4 consecutive weeks (3,4). The relation between AR and asthma has been known for years (4). AR is a risk factor for developing asthma and can eventually lead to the development of asthma (5). The risk of developing asthma is 3-fold higher in patients with AR compared to

the normal population (4). While asthma symptoms develop in 38% of the patients with AR, nasal symptoms are seen in 78% of patients with asthma (6). The relationship between AR and asthma can be explained by three mechanisms. The first mechanism is known as the nasobronchial reflex, while the second one is characterized by inflammatory cells and mediators entering into the nasal airway by postnasal flow. The third mechanism occurs by inflammatory mediators entering the lungs through the systemic circulation via absorption (6, 7). The proteins activated and



secreted from eosinophils cause damage to bronchial epithelial cells in patients with AR. Moreover, it has been shown that bronchial hyperactivity could occur in patients with AR who have no symptoms of asthma (8). Pulmonary symptoms can be seen in patients with AR without asthma; however, these symptoms can be indicative of asthma risk in patients with AR.

The aim of this study was to investigate the relationship between the distribution of allergens and the frequency of pulmonary symptoms in patients with a prediagnosis of AR and to compare the skin prick test results of the patients with pulmonary symptoms and without pulmonary symptoms.

**Table 1.** Distribution of interior environment allergens according to gender (\* Statistically significant)

Interior environment allergens	Female (%)	Male (%)	p	Total (%)
<i>D. Farinae</i>	23.4	18.8	0.134	22
<i>D. Pteronyssinus</i>	49.4	29.7	0.0001*	43.5
<i>Alternaria</i>	11.1	7.1	0.117	9.9
<i>Aspergillus</i>	5.5	5	0.86	5.4
<i>Cladosporium</i>	7.2	6.3	0.177	6.9
<i>Cockroach</i>	35.3	30	0.162	33.7
<i>Cat hair</i>	7.4	4.2	0.11	6.4
<i>Dog hair</i>	17.2	12.7	0.09	16.2
<i>Barn door fowl</i>	8.7	0.8	0.0001*	6.3

## Patients and Methods

Patients that were pre-diagnosed for allergic rhinitis and scheduled for a follow-up visit after a skin prick test performed in the allergy laboratory of Kecioren Training and Research Hospital between January 2008 - December 2011, were included into the study. Age, gender, drugs use, living environment, education levels, and occurrence of nasal, ocular, or pulmonary symptoms were asked of each patient. AR was diagnosed according to the results of a physical examination, nasal endoscopy, and skin prick test exams. The presence of sneezing, runny, stuffy, or itchy nose, serous secretions in the nasal cavity during endoscopic examination, pale nasal mucosa, and presence of concha with edema

(pale or purple) were considered to be allergic symptoms.

Alyostal ST-IR (Stallegenes S.A.France) standard allergen extracts were used for the skin prick test. Antihistamine drugs were stopped 10 days prior to the skin prick test, antidepressant drugs were stopped 20 days prior to the skin prick test and H2-receptor blockers were withdrawn 24 hours before testing. Allergen extracts that were taken in standard doses and placed in Quick test applicators with 8 distinct edges were applied onto the skin after having cleaned the ventral side of a patient's forearm with alcohol. The results were evaluated 15 minutes later. Histamine hydrochloride was used as a positive control and isotonic NaCl was used as a negative control. The validity criterion for the test was deemed acceptable when the positive control was >3 mm and the negative control was <3mm. Skin reaction response to the allergen with an induration of 3 mm or higher in diameter was accepted as a positive reaction (3). Thirty of the most common allergen extracts with negative and positive controls were applied onto the skin of a patient's forearm using a total of 4 applicators for the skin prick test. Two house dust mites, three fungal spores, one insect, three animal epithelia, fifteen pollen and seven food allergens were utilized in the skin prick test.

**Table 2.** Distribution of exterior environment allergens according to gender (\* Statistically significant)

Exterior environment allergens	Female (%)	Male (%)	p	Total (%)
<b>Tree mix 1</b>	46.2	25.6	0.0001*	40
<b>Tree mix 2</b>	23.4	15.4	0.007*	21.1
<b>Cereals mix</b>	36.3	45.5	0.011*	39
<b>Grass pollens</b>	42.4	45.5	0.417	43.3
<b>Wheat pollens</b>	42.6	51.7	0.014*	45.3
<b>Grass mix</b>	24.4	18.1	0.044	22.5
<b>Olea europea</b>	40	24.2	0.0001*	35.2
<b>Populus alba</b>	16.1	14.6	0.611	15.7
<b>Salix caprea</b>	11.1	9.5	0.55	10.6
<b>Pinus sylvestris</b>	13.2	9.3	0.150	12.1
<b>Meadow grass</b>	43	47.3	0.264	44.3
<b>Vernal grass</b>	38.1	41.2	0.405	39
<b>Mugwort</b>	24.1	16.4	0.012*	21.8
<b>Nettle</b>	44.1	20.6	0.0001*	37



The files from a total of 2050 patients were investigated retrospectively. Patients with previously diagnosis of chronic asthma, chronic obstructive pulmonary disease, hypertension, diabetes mellitus, anemia, heart disorders, autoimmune disorders, depression, anxiety disorders and thyroids disorders were excluded from the study. After screening patients that met the exclusion criteria, 1343 patients were included in the study. The pulmonary symptoms (coughing, shortness of breath, wheezing) of the patients were queried. Patient demographics, clinical symptoms and results of the skin prick test were investigated.

Patients with AR and NAR were compared in terms of pulmonary symptoms. In addition, patients with pulmonary symptoms and without pulmonary symptoms were compared in terms of skin prick test results. Patients with pulmonary symptoms included those with pulmonary symptoms who had at least one of the following: coughing, shortness of breath or wheezing. Statistical analysis was done by using the SPSS program, version 15.0. A one sample Kolmogorov-Smirnov test was used to determine the suitability of the data to a normal distribution. Independent sample t tests between groups were used for parametric measurements and Wilcoxon and Mann Whitney U tests were used for nonparametric measurements. A p-value < 0.05 was considered statistically significant for these tests.

## Results

Of the 1343 patients, skin prick test was negative in the 449 (NAR) and positive in the 894 (AR) of the patients. In the NAR group, 263

(58.6%) of the subjects were female and 186 (41.4%) were male. The group consisting of patients with AR had 628 (72.2%) females and 266 (29.8%) males ( $p < 0.05$ ). There was no significant difference in terms of disease period and age of initial onset of disease between the NAR and AR groups. The mean age of patients in the NAR group was  $32.3 \pm 11.4$  years (range 16-72 years) and  $32.2 \pm 10.7$  years (range 16-69 years) for the patients with AR. The age of initial onset of symptoms was  $26.2 \pm 12$  years (range 7-62 years) in the NAR group and  $26 \pm 11.4$  years (range 1-66 years) in the AR group ( $p < 0.05$ ). The highest frequency of consultation occurred in the month of June for patients with AR (17.4%) and also for the NAR subjects (13.1%). The month with the lowest frequency of consultation was February (5.3%) for patients with AR and April (4.9%) for the NAR group.

A positive skin prick test occurred at a significantly higher frequency in the group with pulmonary symptoms (70.8%) compared to the group without pulmonary symptoms (29.2%) ( $p = 0.021$ ). No significant differences were detected between two groups when the distribution and count of allergens was analyzed. The frequency of coughing and shortness of breath was significantly higher in patients with AR compared to the NAR ( $p = 0.01$  and  $0.03$ , respectively, Figure 1). The mean number for allergen sensitivity was  $6.2 \pm 4.7$  in patients with AR. The ratio of shortness of breath was 48.2% in females and 38.1% in males with AR and the difference was significant ( $p < 0.05$ ). There was no significant difference between the genders in terms of coughing and wheezing symptoms.

**Table 3:** Periods of pulmonary symptoms throughout year (AR: Allergic rhinitis, NAR: Nonallergic rhinitis, \* statistically significant)

Symptom	AR		NAR		p value
	Seasonal	Perennial	Seasonal	Perennial	
Shortness of breath	25.7%	74.3%	14%	86%	0.002*
Coughing	38.4%	61.6%	35.2%	64.8%	0.43
Wheezing	30.5%	69.5%	22.8%	77.2%	0.19



**Table 4.** The relationship between the pulmonary symptoms (coughing, shortness of breath and wheezing) and the distribution of allergens (AR: Allergic rhinitis, \* statistically significant)

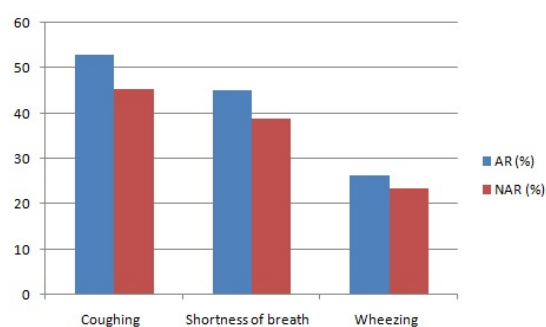
Type of allergen	Pulmonary symptoms		p
	Seasonal AR %	Perennial AR %	
Tree mix 2	31.1	20.2	0.03*
Cereals mix	60.2	29.2	< 0.0001*
Grass pollens	60.2	32.9	< 0.0001*
Populus alba	25.3	12	0.003*
Meadow grass	57	34.9	< 0.0001*
Vernal grass	58	28.9	< 0.0001*
Mugwort	32	15.5	0.001*
Egg white	12.3	3.8	0.011*
Egg yolk	7.4	2.3	0.038*
Wheat	65	33.5	< 0.0001*

Wheat pollen allergy in 405 (45.3%) patients, meadow grass allergy in 396 (44.3%) patients, and D. Pteronyssinus allergy in 389 (43.5%) of the 894 patients with AR was determined. Among the allergens, only D. Pteronyssinus was significant with 49.4% of females and 29.7% of males ( $p=0.0001$ ) being allergic. Distribution of interior and exterior environment allergens according to gender are presented in Table 1 and 2. All patients were questioned about the months when they experienced rhinitis symptoms and classified according to periods of symptoms known as perennial (whole year/ongoing, had symptoms for more than 4 months at a time or all year) and seasonal and is defined as persistent rhinitis when symptoms occur >4 days/week and >4 consecutive weeks (4). The patients were determined to have seasonal AR if they had AR symptoms in the spring for at least 2 consecutive years. The interval of symptoms seen throughout one year is shown in Table 3 and the relationship between pulmonary symptoms and the distribution of allergens is shown in Table 4.

### Discussion

It has been determined from our study that among the patients consulted with rhinitis symptoms, 52.9% experienced coughing and 45.2% reported shortness of breath. It was also determined that coughing and shortness of breath were significantly higher in the AR group compared to the control group. The

most frequently allergens were wheat pollens, meadow grass, and D. Pteronyssinus, respectively. The frequency of pulmonary symptoms was higher in the AR group compared to the control group.

**Figure 1.** Incidence of pulmonary symptoms in allergic and non-allergic rhinitis groups (AR: Allergic rhinitis, NAR: nonallergic rhinitis)

It was shown that the most frequent pulmonary symptom was coughing, with a rate of 52.9%, while the second most frequently experienced pulmonary symptom was shortness of breath with a rate of 45.2%. Harmanci et al. had determined that most incidences of pulmonary symptoms involved coughing (89.2%) and shortness of breath (81%) in patients with AR who were consulted to the pulmonary disease outpatient clinic with a positive skin prick test and a diagnosis of asthma and/or rhinitis (9,10). Moreover, Edis et al. had reported in their study that the most frequently reported symptoms were shortness of breath (65.3%) and coughing (63.8%) (6).

Talay et al. determined that the most reported symptom their patients experienced was shortness of breath as well (93%) (11).

Pulmonary symptoms occurred in 70.8% of patients in the AR group, while 29.2% of control group patients had pulmonary symptoms ( $p<0.05$ ). Progression risk of bronchial hyper-reactivity (BHR) and asthma were increased in patients with AR (8). The pulmonary symptoms seen at higher frequencies in patients with AR compared to controls may be precursors for BHR and asthma (11). In our study, 894 (66.6%) of 1343 patients were found to have a positive skin prick test. In the study published by Eriksson and Holmen, a positive skin prick test was found in 44% of 7009 patients with asthma and rhinitis (12). Edis et al. determined that a positive skin prick test occurred in 59.7% of patients consulted with pulmonary symptoms (6). It was found that the incidence of positive skin prick tests with basic inhaled allergens occurred in 51.9 % of allergic patients in Ankara and around the Ankara region (13). It has been determined that the highest incidence occurred in wheat pollen allergen with 45.3% in the first range, followed by meadow grass allergen with 44.3% in the second range and *D. Pteronyssinus* allergen with 43.5% in the third range of the skin prick test results. The sensitivity responses to mites occurred most frequently (63%) in patients with chronic AR in Hong Kong (14). A study conducted on the presence of mites in house dust in different regions of Turkey showed that the density of house dust mites were higher in shore regions, with a ratio of 46-86%, than the middle of Anatolia (15). One of our studies made in the Kecioren district of Ankara showed that sensitivity to house dust mites was less than tree, grass and meadow pollens (16). It was determined in this study, similar to the previous study, that the sensitivity to mites was much less than pollen. In accordance with climate properties and due to the intensive wheat production and low humidity of our region, wheat and grass pollens are the more common allergens in our study. It was found in a study that the response to *D. Pteronyssinus* was much higher in females than males in a domestic environment. Sonmez et al. showed

that the response to house dust mites was not specific to a certain gender (17). It was found in a study made by Bertelsen et al. that the response to house dust mites was much higher in females compared to males (18). It was thought that the sensitivity was higher in females because female patients mainly work in household environments which cause them to be in contact with house dust mites more than males.

The mean age of the patients with AR was 16-69 years ( $32.2\pm 10.7$ ) in our study. The allergic rhinitis ratio is usually decreased by age (19). Richard et al. reported significant decreases in the allergic rhinitis ratio at initiation of the disease in people ages 45 or over (20). A significant relationship in our study was found between grain, grass pollens, meadow grass, spring grass, wheat pollens and shortness of breath in patients with AR ( $p<0.0001$ ). In our study, although coughing symptoms occurred most frequently in patients with AR, a significant relationship between shortness of breath symptoms and pollen was also determined.

In our study, a positive skin prick test occurred at a significantly higher frequency in the group with pulmonary symptoms compared to the group without pulmonary symptoms in patients who presented with rhinitis symptoms. We did not find a relationship between the distribution of allergens and the pulmonary symptoms in patients with allergic rhinitis. We recommend to investigate the relationship of pulmonary symptoms and distribution of allergens in patients with allergic rhinitis in the future studies including bronchial provocation tests and long term follow-up.

## References

1. Bauchau V, Durham SR. Epidemiological characterization of the intermittent and persistent types of allergic rhinitis. *Allergy*. 2005; 60:350-3.
2. Bousquet J, Van Cauwenberge P, Khaltaev N. Aria Workshop Group; World Health Organization. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol*. 2001;108 (5 Suppl):S 147-334.





3. Van Hoecke H, Vandeplass G, Acke F, Thas O, De Sutter A, Gevaert P, Van Cauwenberge P, Dhooge I. Dissemination and implementation of the ARIA guidelines for allergic rhinitis in general practice. *Int Arch Allergy Immunol.* 2014;163(2):106-13.
4. Feng S, He Q, Fan Y, Mi J, Guo L, Hong H, Li H. Nasal endoscopic findings and nasal symptoms in patients with asthma: A clinical study from a rhinological perspective. *Allergol Immunopathol (Madr).* 2014 Mar 21. pii: S0301-0546(14)00025-1. doi: 10.1016/j.aller.2013.10.005.
5. Baser S, Ozkurt S, Topuz B, Kiter G, Karabulut H, Akdag B, Evyapan F. Peak expiratory flow monitoring to screen for asthma in patients with allergic rhinitis. *J Investig Allergol Clin Immunol.* 2007;7(4):211-5.
6. Corren J. Allergic rhinitis and asthma: how important is the link? *J Allergy Clin Immunol.* 1999; 9(2):781-6.
7. Corren J. The impact of allergic rhinitis on bronchial asthma. *J Allergy Clin Immunol.* 1998;101(2):352-6.
8. Kokuludag A, Erdem N, Erdinc M, Terzioğlu E, Sebik F. Nonspecific Bronchial Hyperactivity in Patients with Allergic Rhinitis And its Relationship with Serum Eosinophilic Cationic Protein. *Ege Journal of Medicine.* 2000;39(3):193-8.
9. Topal O, Erbek SS, Erbek S, Cakmak O. Epidemiological characteristics, distribution of allergens, and symptom severity in patients with perennial allergic rhinitis, living in Konya region. *The Turkish Journal of Ear Nose and Throat.* 2008;18(4):227-31.
10. Harmancı E, Us T, Ozdemir N, Akgun Y, Aydınlı A, Mutlu S. The relationship between skin prick tests and serum specific ige which is determined by chemiluminescence method in the diagnosis of respiratory system allergies. *The Turkish Respiratory Journal.* 2000; 2:31-5.
11. Talay F, Kurt B, Tug T. The Comparison of Clinical Characteristics and Pulmonary Functions of Allergic and Non-Allergic Asthma Patients. *Duzce Medical Journal.* 2008;3:15-20.
12. Eriksson NE, Holmen A. Skin prick tests with standardized extracts of inhalant allergens in 7099 adult patients with asthma or rhinitis: cross-sensitizations and relationships to age. sex. month of birth and year of testing. *J Investig Allergol Clin Immunol.* 1996; 6:36-46.
13. Kalpaklıoğlu AF. Cockroach sensitivity in inner-city allergic patients in Turkey. *Turkish Respiratory Journal.* 2001;2:17-20.
14. Yuen AP, Cheung S, Tang KC, Ho WK, Wong BY, Cheung AC, et al. The skin prick test results of 977 patients suffering from chronic rhinitis in Hong Kong. *Hong Kong med J.* 2007;13:131-6.
15. Ciftci İH, Cetinkaya Z, Atambay M, Kiyildi N, Aycañ OM, Daldal N. House dust mite fauna in western Anatolia. Turkey. *Korean J Parasitol.* 2006;44:259-64.
16. Karabulut H, Karadag AS, Acar B, Demir M, Babademez MA, Karasen RM. The evaluation of skin prick test results in Ankara Kecioren area according to Meteorologic and demografik features. *KBB Forum.* 2009; 8(3): 46-54.
17. Sonmez TG, Caliskan S. Prevalence of house dust mite allergy in cases with Atopic disease symptoms in Kocaeli province, Turkey. *Bulletin of Microbiology.* 2009;43:309-12.
18. Bertelsen RJ, Instanes C, Granum B, Lodrup KC, Hetland G, Carlsen KH, et al. Gender differences in indoor allergen exposure and association with current rhinitis. *Clinical & Experimental Allergy.* 2010;40(9):1388-97.
19. Jones N. Allergic rhinitis: etiology, predisposing and risk factors. *Rhinology.* 2004;42: 49–56.
20. Richards S, Thornhill D, Roberts H, Harries U. How many people think they have high fever and what they do about it. *Br J Gen Pract.* 1992; 42:284-6.

