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RESEARCH

WHAT ARE THE DIFFERENCES BETWEEN ELDERLY AND NON-ELDERLY ASTHMA PATIENTS?

Abstract

Introduction: Previous studies have shown that diagnostic delay increases the severity of asthma in elderly populations. Addressing the disease characteristics in elderly patients may prevent delayed diagnosis and allow for better asthma control.

Materials and Method: Data of 160 asthma patients who had regular checkups in the last year were collected from a tertiary university hospital. Patients were divided into two groups: non-elderly (aged <60 years) and elderly (aged ≥60 years). Demographic characteristics, comorbidities, and clinical and functional parameters were documented.

Results: Most patients were non-elderly (68.1%) and never smokers (83.1%). Mean age at diagnosis and mean duration of asthma were higher in the elderly group; most elderly patients had late-onset asthma (p<0.05). Ratio of patients with a smoking history was lower, comorbidity rates were higher, and more patients were overweight in the elderly group (p<0.05). Fewer elderly patients had aeroallergen sensitization, polysensitization, or allergic rhinitis (p <0.05). Mean number of hospitalizations was higher, ad ratio of patients with good asthma symptom control was lower in the elderly group (p <0.05). In the elderly group, the ratio of the mean forced expiratory volume in the first second to the forced vital capacity and forced expiratory flow at 25%–75% of forced vital capacity were lower (p <0.05).

Conclusion: In elderly patients, asthma control was poorer and the rates of late-onset asthmatics (90.2%) and never-smoker asthmatics (92.2%) were higher. Despite the lower atopy rate (45.1%), the sensitization pattern was similar to that in younger patients.

Key Words: Asthma; Aged; Age at onset

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ARAŞTIRMA

YAŞLI VE YAŞLI OLMAYAN ASTIMLI HASTALAR ARASINDAKİ FARKLILIKLAR NELERDİR?

Öz

Giriş: Yapılan çalışmalar, yaşlı nüfusta astım tanısındaki gecikmenin hastalığın ciddiyetini artırdığını göstermiştir. Yaşlılarda bu hastalığın özelliklerinin gösterilmesi tanı gecikmesini önleyerek daha iyi astım kontrolü sağlayacaktır.

Gereç ve Yöntem: Son bir yıldır üçüncü basamak üniversite hastanesine düzenli kontrol başvuruları olan 160 astım hastasının verileri toplandı. Hastalar yaşlı olmayan (<60 yaş) ve yaşlı (≥60 yaş) olmak üzere iki grupta incelendi. Demografik özellikleri, ek hastalıkları, klinik ve fonksiyonel parametreleri kaydedildi.

Bulgular: Hastaların çoğunluğunu yaşlı olmayanlar (%68.1) ve hiç sigara içmemişler oluşturuyordu (%83.1). Ortalama tanı yaşı, ortalama astım süresi yaşlı grupta daha yüksekti ve yaşlı hastalarda geç-başlangıçlı astım çoğunluktaydı (p<0.05). Yaşlı grupta sigara içme öyküsü daha azdı, ek hastalık yüzdesi daha yüksekti ve aşırı kilolu hastalar çoğunluktaydı (p<0.05). Yaşlı grupta solunumsal allerjen duyarlılığı, çoklu allerjen duyarlılığı ve allerjik riniti olanların sıklığı daha düşüktü (p<0.05). Ortalama hastane yatış sayısı yaşlı grupta daha fazlaydı ve astım kontrol testine göre kontrol altında olanların oranı yaşlı grupta daha azdı (p<0.05). Yaşlılarda birinci saniye zorlu ekspirasyon volümünün zorlu vital kapasiteye oranının ve zorlu ekspirasyon ile volümlerin % 25 ila %75'inin atıldığı perioddaki akım hızının ortalamaları daha düşüktü (p<0.05).

Sonuç: Yaşlılarda astım kontrolü daha zayıftı ve geç-başlangıçlı astım hastalarının (%90.2) ve hiç sigara içmemişlerin (%92.2) yüzde değerleri daha yüksek bulundu. Daha düşük atopi yüzdesine rağmen (%45.1), duyarlılık dağılımı yaşlı olmayanlara benzer saptandı.

Anahtar Sözcükler: Astım; Yaşlı; Başlangıç yaşı

INTRODUCTION

Asthma is a common chronic respiratory disease affecting 1%–18% of the population of various countries (1). In Turkey, its prevalence has been determined to be between 2% and 10% in adults (2). Asthma was mainly considered a childhood disease in the past, but this belief has changed after the publication of studies proving that late-onset or even long-standing asthma is highly frequent among the elderly population. Worldwide studies have shown that in elderly populations, the prevalence of asthma ranges from 4.5% to 12.7% (3). There are very limited data specifically stating the asthma prevalence among Turkey's elderly population (4).

Although studies in developed countries have used ≥65 years as the age requirement for "elderly" individuals, current data from the World Health Organization (WHO) and United Nations have classified those aged ≥60 years as elderly, particularly in developing countries (5). Turkey consists of approximately 8.5 million people aged ≥60 years; this number accounts for approximately 11% of the country's population and is expected to increase to 14% by 2025 (6). Therefore, additional studies should be conducted for detecting problems among the elderly population and for finding solutions.

Studies have found that the rates of misdiagnosis or underdiagnosis of asthma are high in elderly populations. In addition, the rates of non-atopic asthma, severe asthma-related symptoms, and comorbid diseases are higher in elderly patients than in younger patients (7,8). Because asthma in the elderly is highly under- or misdiagnosed and thus undertreated, we evaluated and compared the demographic and clinical characteristics of our elderly asthmatic patients with those of non-elderly patients in this study. A recent review suggested the term "geriatric asthma" instead of "asthma in the elderly," because the latter phrase only describes the occurrence of the disease in this age range (7). Accordingly, our study compared geriatric asthmatics with younger asthmatics; however, we preferred to use both terms at appropriate places in our article. The contribution of these data to the literature would lead to a better understanding of the geriatric asthmatic population's characteristics, which is important for avoiding the significant diagnostic delay in this group.

MATERIALS AND METHOD

Study population

This study was conducted at a tertiary university hospital located in the eastern Black Sea region of Turkey, which has the most dense elderly population in our country. We retrospectively evaluated the data from asthma follow-up medical records of patients who were diagnosed with asthma according to the Global Initiative for Asthma (GINA) guidelines (1) and who had been admitted to the outpatient asthma clinic of the adult immunology and allergic diseases department at the hospital between June 2013 and January 2016. All the asthma patients included in our study had been regularly followed for at least the previous year.

Clinical variables

From the medical records, the asthma patients' sociodemographic (gender, age, employment status, body mass index (BMI), comorbid diseases, and smoking history), asthma history (age at asthma diagnosis), asthma-related conditions (aeroallergen sensitivity/atopy, sinonasal polyposis, allergic rhinitis, and drug allergies), clinical progression of asthma (asthma symptom control, number of controller medications, and hospital/emergency department admissions) and pulmonary function test (PFT) result data were obtained.

Aeroallergen sensitivity was determined according to the skin prick test, which was performed for a common panel of inhalant allergens, including *Dermatophagoides pteronyssinus* and *Dermatophagoides farinea*

(house dust mites), *Aspergillus, Alternaria, Cladosporium* and *Penicillium* (molds), cat and dog animal dander, latex, pollens from grass, trees and weeds, and cockroaches (Allergopharma Reinbek, Germany). Positive and negative controls were histamine (10 mg/mL) and phenolated glycerol-saline, respectively. All tests were performed on the volar surface of the patients' forearms using prick lancets. Reactions were measured after 15 min. A test was considered positive if it produced a wheal with a mean diameter (mean of maximum and 90° midpoint diameters) of >3 mm greater than the saline control. Atopy was defined as the presence of clinically relevant history and a positive skin test response to at least one inhalant allergen.

For evaluating asthma symptom control, GINA assessment of asthma control in adults was used (1). The four related questions are as follows. In the past 4 weeks, has the patient (1) experienced daytime asthma symptoms more than twice/week? (yes/no), (2) experienced any night waking due to asthma? (yes/no), (3) needed a symptom reliever more than twice/week? (yes/no), and (4) experienced any activity limitation due to asthma? (yes/no). Questions were asked to patients via face-to-face interviews. Based on the answers to these questions, the level of asthma symptom control was classified as well-controlled (absence of any "yes" answer), partly controlled (1–2 "yes" answers), or uncontrolled (3–4 "yes" answers).

PFTs were performed at rest in a sitting position using a pulmonary spirometer (CareFusion, Germany, 234 GmbH). The best of three attempts was recorded. Bronchodilator response was assessed by comparing the pre- and post-bronchodilator forced expiratory volume in the first second (FEV1). An FEV1 increase of >200 mL and 12% of the baseline value was accepted as a positive bronchodilator response. Reversibility of airflow limitation was measured after the administration of 400 µg of salbutamol.

Information on potential confounders

Smoking status was recorded as never smoker, former smoker, or current smoker. Those who had smoked >100 cigarettes in their lifetime and had smoked in the last 28 days were classified as current smokers; those who had smoked >100 cigarettes in their lifetime but had not smoked in the last 28 days were classified as former smokers; and those who had smoked <100 cigarettes in their lifetime and were not currently smoking were classified as never smokers. The number of pack-years (packs smoked per day × years as a smoker) was also recorded. A history of comorbidities (present/absent) was defined as a positive answer to questions regarding physician-diagnosed diabetes, hypertension, cerebrovascular disease, pulmonary disease, ischemic heart disease, and other diseases. The employment status of each patient at the time of data analysis was categorized as housewife, student, and others, according to most commonly observed jobs in the study population. Height and weight was measured while wearing light clothes and no shoes. BMI was calculated as the weight divided by the square of the height and was categorized according to the following criteria recommended by the WHO: underweight (<18.5 kg/m^2), normal range (≥18.5–25 kg/m^2), overweight (≥25–30 kg/m^2), and obese (≥30 kg/m^2). Polysensitization was defined as sensitization to at least two structurally different aeroallergens according to skin prick test. The presence (or absence) of sinonasal polyposis, allergic rhinitis, and drug allergies was evaluated based on a reliable history and endoscopic examination performed at the ear–nose–throat department. Lifetime hospitalization and emergency department visits related to asthma exacerbation were reported as number of visits.

Statistical analysis

Patients were evaluated in two groups: <60 years (non-elderly asthmatics) and ≥60 years (elderly asthmatics). For data analysis, Statistical package for the social sciences (SPSS) version 20 was used. Categorical variables are expressed as absolute and relative frequencies, whereas quantitative

variables are expressed as mean and standard deviation. To evaluate the relationship between independent variables (demographic variables, asthma history, asthma clinical course, PFT) and dependent variables (non-elderly asthmatics, elderly asthmatics) Pearson's *chi* square test was used for categorical variables and for numerical variables independent samples *t* test was used. The associations were considered significant at $p<0.05$.

Ethics

Ethical approval for the study was obtained from the institutional ethical committee.

RESULTS

In total, 160 asthma patients' data were analyzed in the study. The mean age of the patients was 49.7 ± 16.4 (16–82) years, with female predominance (126 patients, 78.8%). Age distribution and detailed demographic data of the patients are shown in Figure 1 and Table 1, respectively. Most patients were younger than 60 years (109, 68.1%), and only 31.9% of patients were aged ≥ 60 years. In the univariate analysis of demographic characteristics, the proportions of female patients, housewives, obese patients, never smokers, and patients with at least one comorbidity were higher in the elderly group ($p<0.05$), whereas the proportion of male patients was only higher in the non-elderly group ($p<0.05$; Table 1). In the elderly group, the mean FEV1 to forced vital capacity (FEV1/FVC) ratio and forced expiratory flow at 25%–75% of FVC (FEF25%-75%) were lower ($p<0.05$); however, there was no statistically significant difference in the mean FEV1% predicted (Table 1).

Table 1. Demographic characteristics of the study group.

	The whole group n=160	Non-elderly asthmatics n=109 (68.1%)	Elderly asthmatics n=51 (31.9%)	p
Male gender, n (%)	34 (21.2)	28 (25.7)	6 (11.8)	**0.04**
Age, year, mean±sd	49.7±16.4 (16-82)	40.8±11.2 (16-59)	68.7±6.9 (60-82)	**<0.0001**
Employment status (Housewife), n (%)	107 (66.9)	63 (57.8)	44 (86.93)	**0.001**
Overweight (BMI ≥30 kg/m²), n (%)	78(48.7)	45 (41.2)	33 (64.7)	**0.001**
Prevalence of comorbidity, n (%)	91 (56.9)	46 (42.2)	45 (88.2)	**<0.0001**
Never smokers, n (%)	133 (83.1)	86 (78.9)	47 (92.2)	**0.03**
Smoking pack.year, mean±sd	2.78±7.84	3.12±7.22	2.05±9.06	**>0.05**
FEV_1 % predicted, mean±sd	94.3±23.6	95.9±20.0	90.8±30.1	**>0.05**
FEF_{25-75} % predicted, mean±sd	69.0±29.9	73.0±29.0	60.4±30.2	**0.01**
FEV_1/FVC, mean±sd	76.3±9.0	77.6±8.74	73.3±9.25	**0.006**

Table 2. Asthma history and asthma related conditions of the patients.

	The whole group n=160	Non-elderly asthmatics n=109 (68.1%)	Elderly asthmatics n=51 (31.9%)	p
Age at asthma diagnosis,y, mean±sd (min 5, max 75)	41.3±15.1	35.2±11.9	54.3±12.8	**<0.0001**
Late onset (≥40 years), n (%)	86 (53.8)	40 (36.7)	46 (90.2)	**<0.0001**
Disease duration, y, mean±sd	8.5±9.16	5.74±4.95	14.3±12.7	**<0.0001**
Aeroallergen sensitization (positive skin prick test), n (%)	105 (65.6)	82 (75.2)	23 (45.1)	**<0.0001**
Polysensitization, n (%)	76 (72.4)	65 (79.3)	11 (47.8)	**0.003**
Sinonasal polyposis, n (%)	26 (16.3)	13 (11.9)	13 (25.5)	**0.03**
Allergic rhinitis, n (%)	128 (80.0)	99 (90.8)	29 (56.9)	**<0.0001**
Drug allergy, n (%)	10 (6.3)	7 (6.4)	3 (5.9)	**0.8**

Table 3. Clinical outcomes of the study group.

	The whole group n=160	Non-elderly asthmatics n=109 (68.1%)	Elderly asthmatics n=51 (31.9%)	p
Well asthma symptom control, n(%)	96 (60.0)	89 (81.6)	7 (13.7)	**<0.0001**
Lifetime hospitalisation, mean ±sd	0.76±3.02	0,27±1,02	1.82±5.01	**0.002**
≠ Lifetime ≥1 hospitalisation, n (%)	29 (18.1)	11 (10.0)	18 (35.2)	**<0.0001**
Lifetime emergency visits, mean ±sd	2.57±7.12	2.17 ±5.2	3.43±1.0	0.3
≠ Lifetime ≥1 emergency visits, n(%)	58 (36.2)	36 (33.0)	22 (43.1)	0.2
≠ Controller medication, mean ±sd	2.17±0.73	2.17±0.71	2.17±0.76	0.9
≠ Systemic corticosteroid use in lifetime, mean ±sd	2.22±6.27	1.94±5.02	2.82±8.38	0.4
≠ Patients on omalizumab	12 (7.5)	10 (9.1)	2 (3.9)	0.3

The asthma history and asthma-related conditions of the participants are listed in Table 2. In the univariate analysis, the mean age at asthma diagnosis, mean disease duration, rate of late-onset asthma (at ≥40 years of age) and rate of patients with SNP were higher in the elderly group, whereas the number of atopic, polysensitized patients and patients with allergic rhinitis was higher in the non-elderly group (Table 2). Additionally, the most commonly sensitized allergens were house dust mites, molds, and pollens in both groups (Figure 2).

Table 3 shows the clinical outcomes of the disease in all patients. In the univariate analysis, a lower rate of well-controlled asthma, higher mean lifetime hospitalizations, and ever hospitalization in lifetime were determined in the elderly group ($p<0.05$).

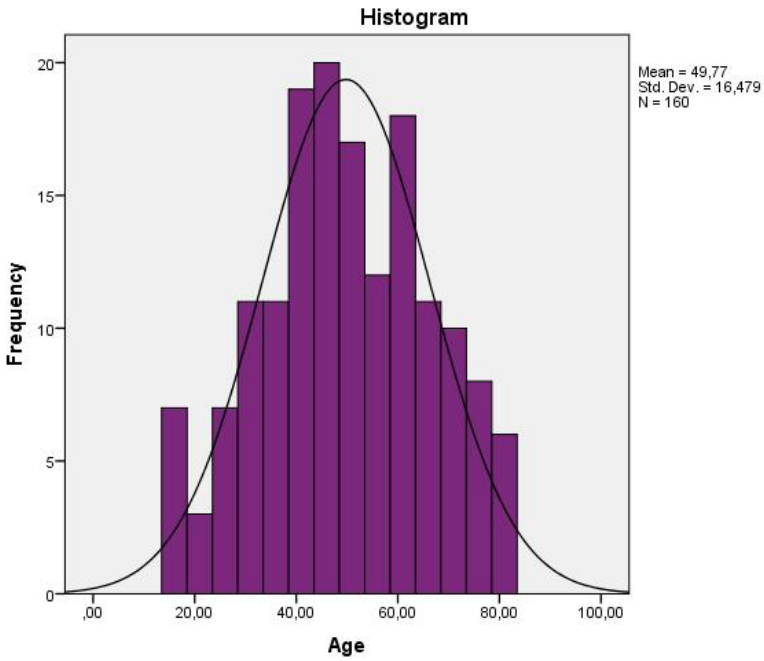

Figure 1. Age distribution of the patients.

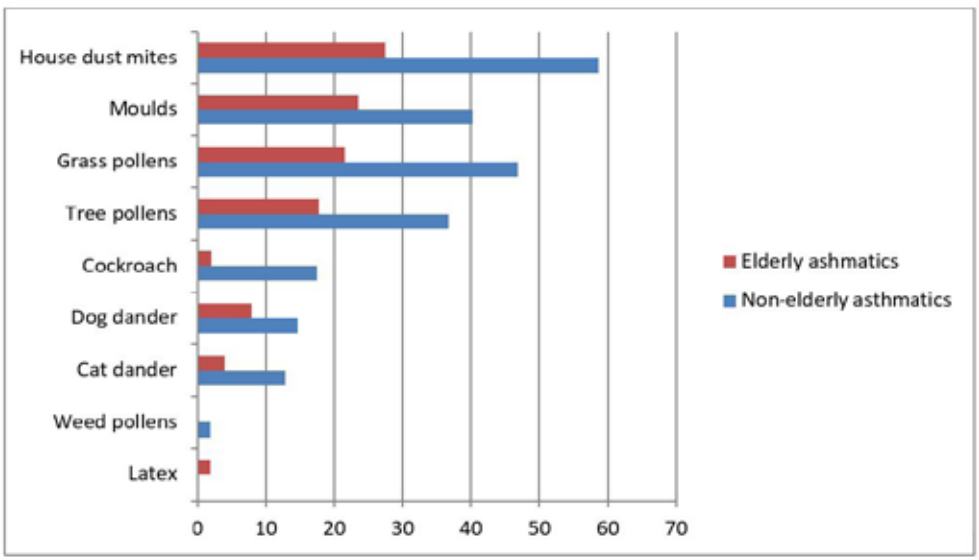

Figure 2. Distribution of aeroallergen sensitivity in percentages according to the age groups.

DISCUSSION

Previous studies have reported that an asthma diagnosis does not directly affect mortality (8); therefore, the life expectancy of individuals with and without asthma does not differ (3,9). Asthma treatment and monitoring require follow up for decades. However, due to certain barriers, such as comorbid diseases and uncertainty regarding the best testing methods, in the elderly population, it is difficult to even diagnose and properly treat the disease. Other barriers that have been reported in studies are both patient-related and clinician-related. The reduced perception or under-reporting of symptoms, difficulties in performing PFTs, insufficient understanding of the disease, poor adherence to therapy and follow up, poor inhaler technique, polypharmacy and increased risk of drug interactions, poor nutrition, sedentary life, and weight gain are patient-related factors; failure to recognize asthma due to comorbid conditions, misclassification as chronic obstructive pulmonary disease (COPD), and lack of knowledge regarding disease progression due to the exclusion of elderly age groups from population-based studies are classified as clinician-related factors (3,10). Accordingly, in this study, we evaluated and compared the characteristics of elderly asthma patients with those of a younger age group to better address the differences.

Our results showed that in our study population, older asthma patients accounted for 31.9%. Furthermore, older asthmatics differed in both demographic and clinical characteristics from younger asthmatics. Regarding demographic characteristics, the proportions of female patients, obese patients, never smokers, and patients with at least one comorbidity were higher among older asthmatics. Regarding clinical characteristics, the rate of late-onset asthma, mean age at asthma diagnosis, and number of patients with SNP were higher and the proportions of atopic patients and patients with allergic rhinitis were lower in the older group, despite almost half of them being sensitive to at least one aeroallergen. Asthma symptom control was poorer and the mean number of hospitalizations in lifetime and rate of hospitalization at least once in lifetime were higher in older asthmatics. Among PFT parameters, the mean rate of FEV1/FVC and FEF 25%-75% predicted were lower in the older group.

These findings exhibited both similarities to and differences from previous related studies. For example, Park et al. reported that older asthmatics' accounted for 26% of all asthma patients in their study; similarly, in our study that rate was 31.9%. However, in the same study, the female and male ratio was equal in the elderly population (11), but in our study, the rate of male patients in the elderly group was significantly lower. This result could be due to both higher underdiagnosis rates and less number of follow-up visits among male asthmatics than among female asthmatics at our institution. Asthma patients similar to those in our study are usually referred from other clinics or hospitals after being diagnosed by a pulmonologist or internal medicine specialist. It is possible that elderly male asthmatics were misdiagnosed as having COPD, coronary artery disease, heart failure, or other age-related conditions. In previous studies, it has been pointed out that patients and physicians commonly attribute asthma-like symptoms to other conditions (3), and a misdiagnosis of COPD is most commonly noted (12). Because even healthy elderly individuals have decreased FEV1/FVC due to the physiological changes of aging (such as increased stiffness of the chest wall, reduced respiratory muscle function, and decline of airway elasticity), they also exhibit decreased FEV1/FVC, leading to a misdiagnosis of COPD (13). As a result of these physiological changes, FEV1/FVC and FEF25%–75% were significantly lower in our older group, but FEV1 did not significantly differ between the older and younger groups, unlike that in previous studies (11,14). This difference may be explained by our department's position. It is a tertiary care unit and most patients are referred by clinicians

from other clinics due to a difficulty in controlling asthma-related symptoms, even among younger patients. Another reason for this result could be the age distribution of our study population; most patients were aged between 40 and 55 years (Fig. 1). Previous studies that have reported differences between younger and older patients' PFT results have compared individuals younger than 40 years with those older than 65 years (15,16), whereas we grouped all of our asthmatic patients aged<60 years into the "non-elderly" category.

The higher rates of comorbidities and obesity were similar to previous studies' findings (14,17). In the elderly, due to the high prevalence of comorbidities, depression, a sedentary lifestyle, and a decreased metabolism rate cause weight gain and obesity. Obesity has been suggested as a risk factor for asthma, especially among older women (18). In our study, the rate of obese patients was significantly higher in the elderly group. Moreover, 86.9% of them were housewives and 88.2% of them had comorbid diseases. These findings may suggest that the sedentary life of the elderly group could be a reason for high obesity rates.

In our study, the number of late-onset asthmatics whose age at diagnosis was ≥40 years, was significantly higher in the elderly group (90.2% vs. 36.7%). Disease duration was also significantly longer in older asthmatics (14.3 years vs. 5.7 years). In geriatric patients, asthma may persist from childhood or start in adult life, which is known as late-onset asthma. Late-onset asthma is less atopic in nature and progresses with more severe symptoms (19). However, in our study it was difficult to exactly define whether the late-onset patients had truly late-onset asthma or simply asthma that was recognized late. The importance of this difference has been stated in a previous report: "the 'missed' asthmatic patient with long-standing undertreated asthma is more likely to develop irreversible airflow obstruction" (20). From this point of view, based on the higher FEV1% values, we can speculate that the elderly asthmatics were mostly late-onset cases.

Atopy is an important contributor to asthma in older adults. Nonetheless, as expected, the proportions of atopic patients and polysensitized patients in the elderly group were lower than those in the younger group, despite almost half of the patients in the elderly group having aeroallergen sensitivity. The most common allergens were house dust mites, molds, and pollens in both groups. It is generally accepted that antigen-specific IgE sensitization decreases with age (3), and for many years asthma in older patients was characterized as non-atopic or intrinsic (9). However, over the past two decades, it has been reported that atopy is not uncommon among elderly asthmatics (3). Rogers et al. found the atopy rate in an asthma clinic to be 60% in patients aged > 65 years, and cockroach sensitization was the most prevalent at 47% (21). Huss et al. found that 74.6% of participants aged > 65 years tested positive for at least one allergen in a battery of common airborne allergens (22). In our elderly group, the atopy rate was 45.1%; therefore, skin tests in the elderly could be a good tool for managing asthma.

The number of patients with well-controlled asthma symptoms was significantly lower among the elderly group: 13.7% versus 81.6%. Furthermore, the mean number of hospitalizations and presence of previous hospitalizations was higher in the elderly group ($p<0.05$). In previous studies, older asthmatics exhibited a difficulty with asthma control (23), resulting in more hospitalizations and near-fatal asthma events (24). Bavbek et al. have also found advanced age to be a factor associated with severe asthma in Turkish patients (25). Some of the factors associated with the worse symptom control and severe asthma in the elderly are comorbid conditions, increased drug interactions, poor adherence to treatment recommendations, higher rates of obesity, less atopic nature of the disease, higher rates of late-onset asthma, and longer disease duration (3). Most of these characteristics were also present in our older asthmatic population, and the more severe disease progression among

the elderly in our study population may be related to such factors.

Strengths and limitations

A distinct strength of this study is that all participants were real-life asthma patients. Diagnoses were more accurate in this study than in studies that are population based and include patients with self-reported asthma diagnoses. However, the retrospective study design is a limitation. For comparing the clinical progression between elderly and non-elderly asthmatics, studies with a larger number of patients should be designed to better record the course of the disease in both groups.

In conclusion, this study revealed not only demographic and clinical differences between older and younger asthmatics but also revealed that aeroallergen sensitivity cannot be ignored, albeit to a lesser extent in the older group. Additionally, the results indicated a potentially high rate of underdiagnosis among male elderly asthmatics in our geographical location. However, it should be considered that these results cannot be generalized to all populations. We hope that the results of the current study will trigger further multicenter studies with larger sample sizes to define more generalized differences in the characteristics of elderly asthmatics' in our country.

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