

Investigation of Cat and Dog Allergen Sensitivities in Childhood Asthma

Çocukluk Çağı Astımında Kedi ve Köpek Allerjen Duyarlılıklarının Araştırılması

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Cite this article as: Canitez Y, Taş G, Karalı Z. Investigation of cat and dog allergen sensitivities in childhood asthma. J Curr Pediatr. 2025;23(3):231-242



Abstract

Introduction: Cat and dog allergens are among the inhalant allergens that are important risk factors for the development of allergic diseases in childhood. In recent years, there has been an increase in the adoption of pets (cats, dogs, etc.) and their care at home. Therefore, we aimed to investigate the prevalence and associated characteristics of cat and dog allergen sensitization in asthmatic children aged 0-18 in our region.

Materials and Methods: 880 asthmatic pediatric patients (0-18 years old) who admitted to the Faculty of Medicine, Department of Pediatric Allergy and were diagnosed with asthma were included in the study. Sensitization of asthmatic pediatric patients to cat allergen, dog allergen, and other inhalant allergens (based on skin prick test results), gender, age, serum total IgE levels, and the presence of other concomitant allergic diseases were retrospectively analyzed.

Findings: The study's inclusion of 880 children diagnosed with asthma had a 39% female (n= 343), 61% male (n=537) distribution. The most common allergic disease associated with asthma was allergic rhinitis (n= 402, 44.9%). Sensitivity to at least one inhalant allergen (presence of atopy) was detected by skin prick tests in 55.7% (n=490). Sensitivity to cat allergen was detected in 8.3% (n=73). The distribution of sensitivity to cat allergen by age was as follows: 3.7% in the 0-3 age, 6.7% in the 4-6 age, 14.5% in the 7-12 age, 9.8% in the 13-18 age group. Sensitivity to dog allergen was found in 41(4.7%) children in the study population, with the distribution by age being: 2.4% in the 0-3 age, 2.7% in the 4-6 age, 8.7% in the 7-12 age, and 6.5% in the 13-18 age group. The rates of cat/dog sensitization were higher in boys but statistically significant difference was found only for dog allergens.

Conclusion: The prevalence of cat and dog allergies in asthmatic children in the Bursa region was found to be significantly high, requiring attention. The fact that cat and dog allergen sensitivities increase with age suggests that this situation should be taken into consideration in the follow-up of these patients and that patients should be re-evaluated in these respects as they age.

Öz

Giriş: Kedi ve köpek alerjenleri, çocukluk çağında alerjik hastalıkların gelişimi için önemli risk faktörleri olan inhalan alerjenler arasındadır. Son yıllarda evcil hayvan (kedi, köpek vs.) sahiplenerek evde bakma alışkanlıklarında artış gözlenmektedir. Bu nedenlerle bölgemizde 0-18 yaş astımlı çocuklarda kedi ve köpek alerjen duyarlılıklarının görülme sıklığının ve ilişkili özelliklerin araştırılması amaçlanmıştır.

Keywords

Child, asthma, cat, dog, allergen, sensitization

Anahtar kelimeler

Çocuk, astım, kedi, köpek, alerjen, duyarlılık

Received/Geliş Tarihi : 27.08.2025

Accepted/Kabul Tarihi : 02.10.2025

Published Date/

Yayınlanma Tarihi : 29.12.2025

DOI:10.4274/jcp.2025.91129

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Gereç ve Yöntem: Çalışmaya Tıp Fakültesi Çocuk Alerji Bilim Dalı'na başvuran ve astım tanısı konulan 880 astımlı çocuk hasta (0-18 yaş) dahil edildi. Astımlı çocuk hastaların kedi allerjisi, köpek allerjisi ve diğer inhalan alerjenlere duyarlılıkları (deri prick testleri sonuçlarına göre), cinsiyet, yaş, ve serum total IgE düzeyleri, eşlik eden diğer alerjik hastalıkların varlığı, retrospektif olarak incelendi.

Bulgular: Çalışmaya %39'u (n=343) kız, %61'i (n=537) erkek toplam 880 astım tanılı çocuk alındı. Astıma en sık eşlik eden alerjik hastalık alerjik rinit (n=402, %44,9) idi. Astımlı çocuklarda deri prik testleri ile en az bir inhalan alerjene duyarlılık durumu (atopi varlığı) %55,7 (n=490) oranında saptandı. Tüm çalışma popülasyonunda kedi alerjenine duyarlılık %8,3 (n=73) oranında saptandı. Kedi alerjenine duyarlılığın yaşlara göre dağılımı; 0-3 yaş grubunda %3,7, 4-6 yaş grubunda %6,7, 7-12 yaş grubunda %14,5, 13-18 yaş grubunda %9,8 oranlarında idi. Tüm çalışma popülasyonunda köpek alerjenine duyarlılık 41 (%4,7) çocukta bulundu, yaşlara göre dağılımı; 0-3 yaş grubunda %2,4, 4-6 yaş grubunda %2,7, 7-12 yaş grubunda %8,7, 13-18 yaş grubunda ise %6,5 oranlarında bulundu. Kedi ve/veya köpek allerjisi duyarlılığı saptanma oranlarının genel olarak yaş ile artma eğiliminde olduğu görülmüştür. Kedi ve/veya köpek duyarlılığı oranları erkek çocuklarda daha yüksek oranlarda idi, ancak sadece köpek allerjisi için istatistiksel anlamlı fark bulundu.

Sonuç: Bursa bölgesindeki astımlı çocuklarda kedi ve köpek allerjisi görülme oranlarının dikkate alınması gereken belirgin oranlarda bulunduğu saptandı. Kedi ve köpek alerjen duyarlılıklarının yaşla birlikte artması, bu hastaların takibinde bu durumun gözönünde tutulması ve hastaların bu açılardan yaş artışı ile birlikte tekrar değerlendirilmesi gerektiğini düşündürmüştür.

Introduction

Asthma is a chronic inflammatory disease of the airways characterized by reversible bronchoconstriction and is the most common chronic disease of childhood (1,2). Risk factors for asthma include genetic predisposition, atopic constitution, gender, obesity, and exposure to certain environmental factors. Allergens, viral infections, exercise, contact with irritants, and environmental air pollution can trigger symptoms (3,4).

Childhood asthma is primarily seen as allergic asthma, and various inhaled allergens play a significant role in asthma symptoms and flare-ups (5,6). Atopy refers to an immunological condition characterized by an individual's ability to produce specific immunoglobulin E (IgE) antibodies against allergens or to show positive sensitivity to the same allergens in a skin prick test (5,7,8). Since the IgE-mediated early-type hypersensitivity response is more pronounced in atopic individuals, the threshold value required for symptom development decreases when exposed to inhaled allergens (5). For this reason, atopy is considered one of the key determinants in both the onset of childhood allergic asthma and the increase in the frequency of flare-ups (9). Several studies have demonstrated that IgE sensitization to common aeroallergens, such as dust mites, pollen, and pet allergens, is associated with a more severe symptom profile, increased bronchial hyperactivity, and higher healthcare utilization in children with asthma (8-10). Approximately 50-80% of asthma in childhood is classified as the atopic asthma phenotype; however, it has been reported that this atopy rate can vary depending on many individual and environmental factors (11). The onset of atopy is a multidimensional process shaped by the immune system's response to allergens from early life, environmental exposure patterns, and genetic characteristics (9).

Animal allergens, particularly those from cats and dogs, are significant risk factors for the development of allergic diseases in childhood (12). Cat and dog allergens (e.g., *Fel d 1*, *Can f 1*) can be spread into the environment through passive transfer via the clothing, hair, or fur of pet owners, even if the individual does not own a pet or has not had direct contact with one. Therefore, allergen exposure can occur anywhere for individuals who are sensitive (13,14). Cat and dog allergens (e.g., *Fel d 1*, *Can f 1*) can be spread into the environment through passive transfer via the clothing, hair, or fur of pet owners, even if the individual does not own a pet or has not had direct contact with one. Therefore, allergen exposure can occur anywhere for individuals who are sensitive (13,14). It has been reported that among inhaled allergens, sensitivity to cats and, to a slightly lesser extent, dogs is increasingly recognized as an important inhaled allergen in childhood asthma (15).

The prevalence of cat and dog sensitivity in childhood asthma is an increasingly prominent issue due to rising pet ownership and the frequency of atopy. It is reported that sensitivity rates to pet allergens in developed countries range from 10% to 30% of the general population, with cat/dog sensitivity accounting for a significant portion of this (16,17). This sensitization is a significant risk factor for asthmatic children in terms of both disease onset and severity. Community-based studies have reported that sensitization to cat and dog allergens (particularly *Fel d 1* and *Can f 1*) affects up to 25% of children and adults (17). However, when focusing on children with asthma, this rate increases significantly. The KiGGS cohort study, conducted in Germany, assessed specific IgE levels to inhaled allergens in approximately 13,000 children aged three to 17 years. The prevalence of cat and dog sensitivities was found to be

around 33% and 41%, respectively, in children diagnosed with asthma. These rates were significantly lower in children without asthma (18). This study shows that children with asthma are significantly more likely to be sensitive to cats and dogs than the general pediatric population. According to the KiGGS data, over one-third of children with asthma in the 7-13 age group are sensitive to cats, and nearly half are sensitive to dogs. The rate is lowest in younger age groups and highest in adolescents (18). This situation suggests that exposure to animal allergens is chronic and that the rate of sensitization accumulates with increasing age and maturation of the immune system (11,18).

In addition to this information, it has been observed that in recent years, it has become increasingly common in Turkey to adopt pets (cats, dogs, etc.) and care for them at home (19,20). Approximately 17% of the Turkish population owned a cat or dog in 2019, and this rate is reported to have approached 20% by 2023 (21). The same study indicates that around 6,146,000 individuals in Turkey own cats or dogs (20). The significant effects of inhaled allergens, such as dust mites, cats, dogs, mice, cockroaches, and mold spores, on individuals with asthma and allergies are well known (22). Therefore, identifying potential allergens and taking the necessary precautions to avoid them is considered necessary in the management of childhood asthma (23).

Currently, there is a lack of information in the literature regarding the prevalence of cat and/or dog allergen sensitivity in asthmatic children in the Bursa region. For this reason, this study was designed to investigate the prevalence of sensitivity to cat and dog allergens, as well as other inhalant allergens, in children diagnosed with asthma who live in the Bursa region, and to examine related characteristics.

Materials and Methods

A total of 880 children between the ages of 0 and 18 who were diagnosed with asthma after applying to the Pediatric Allergy Department Outpatient Clinic at Bursa Uludağ University Faculty of Medicine between January 1, 2016, and June 30, 2019, were included in this retrospective study. The patients' gender, age at onset of asthma symptoms, additional allergic disease diagnoses, common allergens identified through skin prick (epidermal) tests, and serum total IgE levels were recorded. As a standard clinical routine, asthma diagnoses were made in all cases according to the GINA asthma diagnostic criteria (24,25).

Skin prick tests for allergens were performed and evaluated in the Pediatric Allergy Department Laboratory using ALK-Abello (Horsholm, Denmark) standard allergen

kits and disposable Stallerpoint plastic lancets (Stallergenes, Antony, France), in accordance with EAACI recommendations (26). In skin prick tests, allergens were applied to the volar surfaces of both forearms, ensuring they did not touch each other, in accordance with standard practice. A different single-use lancet was used for each allergen, and the allergen was applied to the epidermis at a depth of 1 mm. Edema of at least 3 mm compared to the negative control was considered a positive test result 15 to 20 minutes after allergen application (26). All inhaled allergens administered to asthmatic children included in the study are shown in Table 4.

The presence of sensitivity to allergens was defined as individual results. Cases in which at least one positive result (sensitivity) to common allergens was detected in skin prick tests were defined as atopic. Additionally, when defining the results, the "pets general" result was defined as positive if sensitivity to at least one of the cat or dog allergens was detected (Table 1 and Table 4). Similarly, the "mites general" result was defined as positive when sensitivity to at least one mite allergen (at least one of the allergens *Dermatophagoides pteronyssinus* or *Dermatophagoides farinae*) was detected. (Table 1 and Table 4). The same method was used to define "general results" for each of the other allergen groups ("grass pollens general", "cereal pollens general", "tree pollens general", "cereal pollens general", "fungal spores general") (Table 1 and Table 4). Immulite 2000 (Diagnostic Products Corporation, Los Angeles, CA, USA) test kits were used for serum total IgE measurements, and results were reported in IU/mL.

The normality of continuous variables was examined in the statistical analysis of the data using the Shapiro-Wilk test. Age, age at diagnosis, and total IgE level were expressed as median (minimum, maximum) values. Categorical data were presented as n (%), and the Pearson Chi-Square and Fisher's Exact tests were used to analyze categorical data. The Mann-Whitney U test was used to compare total IgE measurements between groups. Data analysis was performed using the IBM SPSS Statistics 25 program, with an α level of 0.05 for statistical comparisons.

Results

Of the children with asthma included in the study, 39% (343 children) were female, and 61% (537 children) were male. The median age at diagnosis was 8.42 years, with a range of 1.75 to 18 years. The median age of onset of asthma symptoms was 3 years (min-max: 1- 16.6 years) in girls and 2 years (min-max: 1 - 17 years) in boys. Asthma symptoms

have been found to show significant differences in age of onset according to gender, with slightly earlier onset in boys ($p<0.001$). Among children with asthma, the most common accompanying allergic diseases were, in order: allergic rhinitis (45.6%), allergic conjunctivitis (18.8%), atopic dermatitis (15.1%), and food allergy (6%).

In skin prick tests performed with common inhalant allergens, sensitivity to at least one inhalant allergen (presence of atopy) was detected in 55.7% ($n = 490$) of patients, while 44.3% ($n = 390$) were determined to be non-

atopic (no sensitivity to any inhalant allergen). The skin prick test results for cats, dogs, and other common inhalant allergens, categorized by patient age group, are presented in Table 1.

Among the entire study population of 880 children with asthma, cat allergen sensitivity was detected in 73 children (8.3%), and dog allergen sensitivity was detected in 41 children (4.7%). Among asthmatic children, sensitivity to cat allergens was higher than sensitivity to dog allergens in the entire study population and in all age groups (Table 1). When

Table 1. Results of allergen sensitivities detected by skin prick tests in the entire study population of children with asthma ($n=880$) and by age groups

	Ages 0-3 ($n=246$) n (%)	Ages 4-6 ($n=300$) n (%)	Ages 7-12 ($n=242$) n (%)	Ages 13-18 ($n=92$) n (%)	Total ($n=880$) n (%)
Pets general*	11 (4.5)	22 (7.3)	39 (16.1)	10 (10.9)	82 (9.3)
Cat	9 (3.7)	20 (6.7)	35 (14.5)	9 (9.8)	73 (8.3)
Dog	6 (2.4)	8 (2.7)	21 (8.7)	6 (6.5)	41 (4.7)
Mites general*	62 (25.2)	110 (36.7)	133 (55)	46 (50)	351 (39.9)
Grass pollens general*	22 (8.9)	39 (13)	82 (33.9)	47 (51.1)	190 (21.6)
Cereal pollens general*	14 (5.7)	35 (11.7)	67 (27.7)	43 (46.7)	159 (18.1)
Tree pollens general*	10 (4.1)	27 (9)	36 (14.9)	20 (21.7)	93 (10.6)
Weed pollens general*	11 (4.5)	22 (7.3)	37 (15.3)	21 (22.8)	91 (10.3)
Fungal spores general*	22 (8.9)	37 (12.3)	44 (18.2)	17 (18.5)	120 (13.6)

Data are presented as n (%).
General*: Presence of sensitivity to at least one allergen in this group

Table 2. Comparison of cat allergen sensitivity rates in children with asthma according to age groups

	Cat allergen sensitivities		p	Group comparisons
	Positive (+) n (%)	Negative (-) n (%)		
Group 1 (Ages 0-3) ($n=246$)	9 (3.7)	237 (96.3)	<0.001	Group 1- Group 2: $p=0.119$ Group 1- Group 3: $p<0.001$ Group 1- Group 4: $p=0.052$ Group 2- Group 3: $p=0.003$ Group 2- Group 4: $p=0.318$ Group 3- Group 4: $p=0.259$
Group 2 (Ages 4-6) ($n=300$)	20 (6.7)	280 (93.3)		
Group 3 (Ages 7-12) ($n=242$)	35 (14.5)	207 (85.5)		
Group 4 (Ages 13-18) ($n=92$)	9 (9.8)	83 (90.2)		

Table 3. Comparison of dog allergen sensitivity rates in children with asthma according to age groups

	Dog Allergen Sensitivities		p	Group Comparisons
	Positive (+) n (%)	Negative (-) n (%)		
Group 1 (Ages 0-3) ($n=246$)	6 (2.4)	240 (97.6)	0.002	Group 1-Group 2: $p=0.867$ Group 1- Group 3: $p=0.003$ Group 1- Group 4: $p=0.096$ Group 2- Group 3: $p=0.002$ Group 2- Group 4: $p=0.105$ Group 3- Group 4: $p=0.518$
Group 2 (Ages 4-6) ($n=300$)	8 (2.7)	292 (97.3)		
Group 3 (Ages 7-12) ($n=242$)	21 (8.7)	221 (91.3)		
Group 4 (Ages 13-18) ($n=92$)	6 (6.5)	86 (93.5)		

sensitivity rates to cat allergens are examined by age group, the lowest rates are found in the 0-3 age group, showing an upward trend up to the 7-12 age group, and slightly lower rates in the 13-18 age group compared to the 7-12 age group. Sensitivity rates to dog allergens also showed a similar trend to cat sensitivity, increasing with age (Table 1).

Other inhalant allergen sensitivities detected in children with asthma, in order of prevalence, were: sensitivity to mites, 39.9%, grass pollen sensitivity was 21.6%, cereal pollen sensitivity was 18.1%, fungal spore sensitivity was 13.6%, tree pollen sensitivity was 10.6%, and weed pollen sensitivity was 10.3% (Table 1). Among all inhaled allergens, mite sensitivities

Table 4. Comparison of the rates of sensitivity to cats, dogs, and other inhalant allergens in children with asthma according to gender.

	Girls (n=540) n (%)	Boys (n=340) n (%)	p
Pets general*	24 (7.1)	58 (10.7)	0.067
Cat	24 (7.1)	49 (9.1)	0.291
Dog	9 (2.6)	32 (5.9)	0.025
Mites general*	118 (34.7)	233 (43.1)	0.013
<i>D. pteronyssinus</i>	108 (31.8)	211 (39.1)	0.028
<i>D. farinae</i>	107 (31.5)	213 (39.4)	0.017
Grass pollens general*	65 (19.1)	125 (23.1)	0.157
Grasses mix	64 (18.8)	117 (21.7)	0.310
<i>Dactylis glomerata</i>	53 (15.6)	112 (20.7)	0.057
<i>Lolium perenne</i>	12 (3.5)	32 (5.9)	0.112
<i>Phleum pratense</i>	54 (15.9)	98 (18.1)	0.387
<i>Cynodon dactylon</i>	50 (14.7)	102 (18.9)	0.110
Cereal pollens general*	51 (15)	108 (20)	0.061
Pollens mix	14 (4.1)	32 (5.9)	0.241
<i>Secale cereale</i>	49 (14.4)	104 (19.3)	0.065
<i>Triticum sativum</i>	45 (13.2)	98 (18.1)	0.054
<i>Avena sativa</i>	41 (12.1)	94 (17.4)	0.032
Tree pollens general*	27 (7.9)	66 (12.2)	0.044
Trees mix	11 (3.20)	28 (5.2)	0.171
<i>Alnus glutinosa</i>	6 (1.8)	12 (2.2)	0.641
<i>Betula verrucosa</i>	8 (2.4)	19 (3.5)	0.329
<i>Olea europaea</i>	21 (6.2)	58 (10.7)	0.021
Weed pollens general*	29 (8.5)	62 (11.5)	0.161
Weeds mix	18 (5.3)	40 (7.4)	0.219
<i>Artemisia vulgaris</i>	17 (5)	25 (4.6)	0.802
<i>Plantago lanceolata</i>	24 (7.1)	55 (10.2)	0.114
<i>Parietaria officinalis</i>	8 (2.4)	18 (3.3)	0.403
Fungal spores general*	39 (11.5)	81 (15)	0.137
<i>Alternaria alternata</i>	32 (9.4)	78 (14.4)	0.028
<i>Cladosporidium herb.</i>	3 (0.9)	12 (2.2)	0.135
<i>Aspergillus fumigat.</i>	7 (2.1)	23 (4.3)	0.080

Data are presented as n (%).

General*: Presence of sensitivity to at least one allergen in this group

Table 5. Relationship between sensitivity to cat and dog allergens and serum total IgE

Allergens	Sensitivity	Total IgE level	p ^a
Pets general*	Negatif (n=798)	79.8 (1.0:5310)	<0.001
	Pozitif (n=82)	318 (2.0:3549)	
Cat	Negatif (n=807)	88.2 (2.0:5290)	<0.001
	Pozitif (n=73)	325 (2.5:3540)	
Dog	Negatif (n=839)	71.8 (1.0:5310)	<0.001
	Pozitif (n=41)	310 (2.0:3549)	

The data is presented as the median (minimum: maximum).
 General*: Presence of sensitivity to at least one allergen in this group
 a: Mann-Whitney U test

were the most frequently detected allergen sensitivities in all age groups. Sensitivity rates to inhaled allergens were lowest in the 0-3 age group, and generally increased with age (Table 1).

The prevalence rates of cat and dog allergen sensitivity in asthmatic children, categorized by age group, are presented in Tables 2 and 3. The prevalence rates of cat allergen sensitivity in asthmatic children generally increased with age, compared to the 0-3 age group (Table 2). It has been determined that the detection rates of cat allergen sensitivity generally show statistically significant differences across age groups ($p < 0.001$). When age groups were compared with each other, it was determined that the rate of sensitivity to cats among patients aged 7-12 was statistically significantly higher than in the 0-3 and 4-6 age groups ($p < 0.001$ and $p = 0.003$, respectively). On the other hand, it was determined that the sensitivity rates of patients aged 13-18 to cats were higher than those of the 0-3 and 4-6 age groups; however, no statistically significant difference was found ($p = 0.052$ and $p = 0.318$, respectively). Additionally, a comparison between the 7-12 age group and the 13-18 age group revealed no statistically significant difference in sensitivity rates between the groups ($p = 0.259$) (Table 2).

The prevalence rates of dog allergy sensitivity also tend to increase with age, generally compared to the 0-3 age group (Table 3). The prevalence rates of dog allergen sensitivity also tended to increase with age, generally higher in older age groups compared to the 0-3 age group (Table 3). It was determined that dog allergen sensitivity generally showed statistically significant differences across age groups ($p = 0.002$). When age groups were compared with each other, it was determined that the rates of sensitivity to dogs among patients in the 7-12 age group were statistically significantly higher than those in the 0-3 and 4-6 age groups ($p = 0.003$

and $p = 0.002$, respectively). In terms of dog allergen sensitivity, no statistically significant difference was found between the 7-12 age group and the 13-18 age group ($p = 0.518$) (Table 3).

The comparison of detection rates for inhalant allergen sensitivities by gender is presented in Table 4. Cat allergen sensitivity was found to be higher in males than in females; however, no statistically significant difference was detected between the two groups ($p = 0.291$). The prevalence of dog allergen sensitivity was found to be statistically significantly higher in males than in females ($p = 0.025$). For other inhalant allergens, sensitivity rates generally tended to be higher in male children than in female children. However, these differences were statistically significant for only a small number of allergens (Table 4). It was determined that sensitivity to house dust mites, *Dermatophagoides farinae*, and *Dermatophagoides pteronyssinus* was statistically significantly higher in males than in females ($p = 0.013$, $p = 0.028$, and $p = 0.017$, respectively). Additionally, sensitivity to *Avena sativa* grain pollen ($p = 0.032$), overall tree pollen sensitivity ($p = 0.044$), *Olea europaea* sensitivity ($p = 0.021$), and *Alternaria alternata* sensitivity ($p = 0.028$) were also found to be statistically significantly higher in males (Table 4).

Table 5 shows changes in serum total IgE measurements according to the presence of cat and dog allergen sensitivities. Total IgE levels were found to be statistically significantly higher in cases of sensitivity to cat or dog allergens than in cases where sensitivity to these allergens was negative. The presence of sensitivity to cat or dog allergens was also found to be associated with higher total IgE levels.

Discussion

This study examined the sensitivity rates to cat and dog allergens, as well as various inhalant allergens, in pediatric patients diagnosed with asthma. IgE-mediated sensitivity to cat and dog allergens (especially *Fel d 1* and *Can f 1*) in children with asthma is an important factor in both the onset of the disease and the frequency of symptom exacerbations (22,23). Data collected from a wide range of provinces across Turkey reveals that pet ownership is rapidly becoming widespread. A national survey of 519 cat and/or dog owners found that 82.9% of participants acquired their pet within the last 10 years, with the majority being cat owners (19). These data suggest that a significant portion of the current cat and/or dog population stems from relatively recent adoptions, and that there has been a notable proliferation in recent years (19).

Inhalant allergen sensitivity is one of the major risk factors for the development of asthma (9,11,22). The presence of atopy in children with asthma is one of the most important biological markers determining both the phenotype and clinical course of the disease (9). The emergence of atopy is a multidimensional process shaped by the immune system's response to allergens from early life, environmental exposure patterns, and genetic characteristics. According to the literature, approximately 50-80% of pediatric asthma can be classified under the atopic asthma phenotype; however, this rate varies depending on many individual and environmental factors (11,22). In this study, the prevalence of atopy (the presence of sensitivity to at least one inhaled allergen) was determined to be 55.7% in all asthmatic children in the study group based on skin prick tests with inhaled allergens. This rate is similar to research results reported from other regions in Turkey. In a 16-year study of pediatric patients aged 1-18 years diagnosed with asthma in Istanbul, the atopy rate was reported to be 61% (27) besides history and physical examination, many in vivo and in vitro laboratory tests are used. Skin prick test (SPT). In the Eastern Black Sea region, a study conducted on children aged 3-17 found that 35.9% of children with asthma had allergen sensitivity (28). The prevalence of atopy in children with asthma was reported as 60.3% and 61.1% in two separate studies conducted in Ankara province, and as 42.9% in Diyarbakır province (29,30,31). Other studies on the prevalence of inhalant allergen sensitivity (atopy) in children with asthma found rates of 41.2% and 72.5% in two separate studies in China (32,33) pediatric asthma is becoming more prevalent. Despite a growing body of evidence, there remains a significant unmet need for adequate management of childhood asthma. The Subspecialty Group of Respiratory Diseases of the Society of Pediatrics, the Chinese Medical Association, and the editorial board of the Chinese Journal of Pediatrics have recently updated the "Guidelines for diagnosis and optimal management of asthma in children," first published in 2008. Methods: This article reviews the major updates to the guidelines and covers the main recommendations for diagnosis, assessment, and treatment of pediatric asthma in China. Key regional data on epidemiology, clinical features, disease burden, knowledge among children and parents, and risk factors including pollution are provided to contextualize the recommendations. Results: The major updates to the guidelines include: (1. Studies conducted in different regions of Australia reported rates of 68-88%, while in England, the rate was reported as 44.1% (34,35). The prevalence of inhaled allergens and atopy in children with asthma may vary

depending on factors such as age, genetic characteristics, regional characteristics, climate, geographical characteristics, living conditions, and environmental characteristics, which in turn influence the variety and intensity of allergens to which they are exposed (11,22).

In our study, cat allergen sensitivity was generally found to be higher than dog allergen sensitivity in children with asthma across the entire study population and in all age groups (Table 1). It has been reported that cat allergies are generally more common than dog allergies in children with asthma, and that various immunological and environmental factors are among the possible reasons for this situation (36-38). Among the reasons that can lead to this situation, it is reported that the biophysical properties of the primary cat allergen *Fel d 1* are significant. *Fel d 1* binds to tiny particles, remains suspended in the air for a long time, easily adheres to textiles, and thus creates widespread environmental exposure through schools, nurseries, and public areas, even if there are no cats in the home (39). Similarly, the ease with which cat allergens attach to textiles and clothing increases passive transport, allowing cat allergens to be found everywhere and raising the risk of sensitization in children (36,37). Secondly, in cat and dog allergies, sensitization patterns and IgE levels differ. Specific IgE levels for cat allergy in asthmatic children were found to be higher than in patients with rhinitis alone, demonstrating that sensitization at this molecular level is more strongly associated with the asthma phenotype (12,39). Additionally, some epidemiological studies have reported that exposure to indoor cats is a more substantial risk factor for asthma, with a higher prevalence of asthma and asthma-like symptoms in children sensitive to cat allergens (37,38).

Cat (*Fel d 1*, *Fel d 4*) and dog (*Can f 1* and *6*) allergens are among the major inhalant allergens involved in the development of asthma and allergic rhinitis in childhood. Numerous studies have reported that sensitivity to these allergens varies according to age, geography, exposure to pets, and gender (40,41). This study found that cat and/or dog allergen sensitivity also showed statistically significant differences across age groups. In subgroup analyses, a marked increase in sensitivity was observed after the 0-3 age group, reaching the highest rates in the 7-12 age group and slightly lower rates in the 13-18 age group. Generally, sensitivity to inhaled allergens (atopy) tends to increase with age (18,42). It is also known that the duration and intensity of allergen exposure may play a role in the development of inhalant allergen sensitivity (11). Comparative studies conducted in various countries have shown that atopic sensitivity increases linearly as the allergen load increases (11,18,42).

In our country, the practice of keeping pets in homes has increased significantly over the last decade (19-21). If these trends continue, new studies conducted in the coming years may indicate whether allergen exposure rates will increase among 13-to 18-year-olds. If these trends continue, new studies conducted in the coming years may indicate whether allergen exposure rates will increase among 13-to 18-year-olds (43). A study conducted in Istanbul reported an increase in pet sensitivity with age among asthmatic children aged 1 to 18 (27). Additionally, a study conducted in China among asthmatic patients aged 5 to 65 found that sensitivity to cats and dogs increased with age (44). A study conducted in Boston on children with aeroallergen sensitivity found that sensitivity to cats and dogs increases with age (45). Based on these data, various factors, including allergen exposure, age, genetics, and environment, are thought to influence the rates of sensitization to cat and/or dog allergens (11).

This study found that the age at which asthma symptoms began differed significantly by gender among children with asthma, with symptoms typically starting slightly earlier in boys. The earlier onset of asthma symptoms in boys is consistent with well-established gender differences in asthma epidemiology. Studies have reported higher incidence and prevalence rates of asthma in boys during childhood, as well as an earlier age of onset (46-48). The prevalence of asthma and atopy rates is higher in males until school age. After adolescence, however, an increase in favor of females has been reported (48). It has been reported that this condition in male children at an early age may be related to their relatively narrower airway diameters, higher viral infection load, and earlier and stronger Th2 response (49-51). The higher incidence of lower respiratory tract infections and bronchiolitis episodes in male infants is another factor supporting the “early-onset asthma” phenotype with recurrent wheezing in early childhood (52). In contrast, it has been reported that the more favorable airway diameter/lung growth ratio in girls, along with the partially protective effect of sex hormones that modulate the Th2 response of the immune system during the prepubertal period, may contribute to symptoms appearing at a later age on average (53,54).

In the present study, we found that the rates of sensitization to inhalant allergens (cat, dog, mites, pollen, and mold spores) in children with asthma tended to be higher in boys than in girls. It has been reported that inhalant allergen sensitivity in children with asthma may generally show some differences based on gender (54-56). Epidemiological data show that inhalant allergen sensitivities are more

common in boys during early and middle childhood and in girls during adolescence and beyond (40,41,45,54-56). A study conducted in Boston on children with aeroallergen sensitivity reported that boys had significantly higher rates of sensitivity to all inhaled allergens compared to girls, particularly to dog and grass pollen (45). Additionally, in Sweden, serial measurements conducted in the BAMSE birth cohort between the ages of 4 and 24 reported that male gender is an independent risk factor for IgE sensitivity to both cat and dog allergens (40). This difference is believed to result from the development of the immune system, the interaction of hormonal processes with age, and the effects of environmental exposure on aging (54-56). Additionally, it has been reported that skin barrier integrity is lower in male infants and that this may play a critical role in sensitization during early life (56). Additionally, the higher incidence of viral infections such as respiratory syncytial virus and rhinovirus in boys in the first 3 age groups may increase allergen sensitivity by deepening epithelial damage (57). The 4-6 age group is a period when the immune system is still maturing. It has been reported that Th2 dominance is more prevalent in boys than in girls at this age. It has been noted that atopic sensitivity is notably higher in boys with indoor inhalant allergens (mites, mold spores) (40,58). At the same time, boys' greater behavioral exposure to outdoor allergens (pollen, fungal spores, etc.) may contribute to allergen sensitization. During the 7-12 age period, when gender differences are pronounced, it has been shown that total IgE levels in boys are significantly higher than in girls in this age group (40,55). With puberty, hormonal effects become more pronounced between the ages of 13-18. While the effect of estrogen in increasing mast cell activation can lead to an increase in allergic sensitivity in girls in the post-pubertal period; it has been suggested that the role of testosterone in suppressing airway inflammation may reduce sensitivity in boys (54,59). It has also been reported that atopic diseases may be seen at higher rates in girls after puberty compared to boys (54,59). For these reasons, gender differences in allergen sensitivity change during later adolescence. Some studies even report that girls catch up to boys, reaching higher rates of sensitivity (54,59).

In our study, when the inhalant allergen sensitivities observed in asthmatic children were examined individually, mites were the highest at 39.9%, followed by grass pollens at 21.6%, cereal pollens at 18.1%, and fungal spores at 13.6%. Depending on differences in climate conditions, vegetation, and living conditions between countries, as well as between regions within the same country, inhalant

allergen sensitivities may occur at varying rates (11). In a study conducted in the Mediterranean region of Turkey, the distribution of allergen sensitivities among children diagnosed with asthma was reported as follows: dust mites (66%), grass/grain pollen mixture (51.2%), and tree pollen mixture (50.9%) (60). A study conducted on children with asthma in Ankara reported that pollen sensitivity was the most common (32%), followed by sensitivity to mites (15.9%) (61). In another study conducted in Malatya, sensitivities were detected in children diagnosed with asthma and allergic rhinitis at rates of 48.9% for grass-cereal pollen mixture, 48.5% for weed-pollen mixture, and 40.2% for mites. (62). In another study conducted in Mersin, mites were reported at the highest rates in asthmatic children (*Dermatophagoides pteronyssinus* 67.9%, *Dermatophagoides farinae* 67.2%), followed by *Alternaria alternata* (19.4%) (63). In patients presenting with chronic cough in the Gaziantep region, skin prick test results showed that the most common positive reactions were to grass pollen (50.4%), mites (24.6%), and cereal pollen (23.3%), respectively (64). In Canada, sensitivities to dust mites (84.2%), cats (76.5%), and dogs (63%) were identified among cases of asthma and allergic rhinitis (65). In a study conducted in three separate regions in Australia, it was reported that mite sensitivity was again the most prominent factor (34). In our study, consistent with the literature in general, the highest level of mite sensitivity was detected, and it was thought that this situation could be related to the humid and temperate climate in our region, as well as living conditions. It is clear that the prevalence of atopy and the distribution of inhaled allergens in childhood asthma are multifactorial, shaped by a complex process involving age, genetic makeup, living conditions, geographical or regional characteristics, regional climate, environmental conditions, and allergen exposure load (11).

In the present study, sensitization rates to inhalant allergens other than cat and dog allergens were found to generally increase with advancing age. Similar results to those found in our study have been reported in numerous studies in the literature. A study of schoolchildren and adolescents in Korea found that pollen sensitivity increases with age (66). In a study conducted in Italy, where asthmatic children were divided into four groups-ages 1-3, 4-6, 7-9, and 10-17, it was found that pollen sensitivity increased with age (67). Similarly, a study conducted in Ankara on children aged 2-5, 6-11, and 12-18 found that pollen sensitivity increases with age (43). Additionally, a similar study conducted in Adana reported that pollen sensitivity in children increases with age (68). Age is one of the most significant factors in determining

atopy. While sensitivity to inhaled allergens is relatively low in the preschool period, IgE-mediated sensitivity to allergens such as pollen, mites, cats, and dogs increases significantly during school age and adolescence (42). The BAMSE and ISAAC cohorts show that the prevalence of atopy has increased significantly, particularly among children aged 6 to 14 years (42). In this study, allergic rhinitis was detected in 45.6% of children diagnosed with asthma among the allergic diseases accompanying asthma. Asthma and allergic rhinitis are two atopic diseases that often occur together in children because they have similar immunological mechanisms and environmental triggers (11,69). Studies have shown that between 40% and 60% of children diagnosed with asthma are also affected by allergic rhinitis (11,69). In this context, the finding that allergic rhinitis was detected in 45.6% of children with asthma in our study is consistent with the literature (11,69).

In this study, it was observed that total IgE levels were statistically significantly higher in asthmatic children with positive sensitivities to cat and dog allergens (consistent with the existing literature on this subject). It is known that total IgE can be influenced by factors such as race, genetics, environmental conditions, and the presence of other accompanying diseases (70,71). A direct correlation has been found between total IgE levels and asthma severity in patients with asthma (70). Total IgE, unlike specific IgE, reflects the entire IgE pool but is a highly nonspecific marker; nevertheless, numerous studies have shown that total IgE levels generally increase as the burden of inhalant allergen sensitivity increases (72,73). According to the results of studies in the literature, children with asthma who are sensitive to cat/dog extracts or their molecular components (*Fel d 1*, *Fel d 4*, *Can f 1*, *Can f 6*, etc.) tend to have higher total IgE, more pronounced eosinophilia, and more severe asthma symptoms than both healthy controls and asthmatics without pet (cat and/or dog) sensitivity (12,72,74-76). A study conducted in adult asthmatic patients in our country has found that skin prick test positivity for aeroallergens is associated with elevated total IgE levels (77). In another study conducted on children with asthma, a relationship was found between high total IgE levels and sensitivity to dust mites, pollen, and pet allergens, but no relationship was found with fungal allergens (78). Additionally, another multicenter study reported that the presence of sensitivity to *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*, cat, *Alternaria*, tree pollen mixture, and grass pollen mixture was associated with increased total IgE levels (79).

Study Limitations

The main limitation of our study was that it was retrospective and conducted in a single center. However, because the institution is a tertiary healthcare center to which all relevant patients in the Bursa region apply, and because the study was conducted on a large population, it was considered to contain reliable data on pediatric asthmatic patients living in the region.

Conclusion

Inhaled allergen sensitivities play a significant role in childhood asthma. It was determined that the incidence rates of cat and dog allergies in asthmatic children in the Bursa region are significant enough to warrant consideration and evaluation. Cat allergen sensitivity was found to be higher than dog allergen sensitivity in children with asthma across the total study population and in all age groups. This situation is thought to be related to various immunological mechanisms and differences in allergen sensitization patterns, as well as environmental factors. Cat allergies are likely more common than dog allergies due to the characteristics of cat allergens, greater exposure, and other reasons. The increase in sensitivity to cat and dog allergens with age suggests that this situation should be considered when following up with these patients and that they should be reevaluated in this regard.

Ethics

Ethics Committee Approval: Approval was received from the Medical Ethics Committee of Bursa Uludağ University Faculty of Medicine (decision numbered 2019-21/37).

Footnotes

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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