



CLINICAL STUDY

CLINICAL CHARACTERISTICS AND COMORBID DISEASES OF PEDIATRIC PATIENTS WITH ALLERGIC RHINITIS IN SIVAS

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SUMMARY

Objective: Our study aimed to evaluate the clinical features and accompanying comorbid diseases of children diagnosed with allergic rhinitis (AR) in Sivas.

Material and Methods: The medical records of 874 children (aged 0 to 18 years) diagnosed with allergic rhinitis between March 2019 and February 2020, were retrospectively analyzed.

Results: The median age of 874 AR patients was 8.3 (5.1-12.2) years, and 478 (54.7%) were male. AR was most commonly diagnosed in children aged 6 to 12 years (40.8%). 42.2% of AR patients had moderate-to-severe persistent AR. The most common complaints were nasal obstruction (86.3%) and rhinorrhea (84.3%). Nasal obstruction (96.4%) was the most common symptom in moderate-to-severe AR patients, while sneezing (46%), and rhinorrhea (88%) were most common in mild AR patients. The most frequent comorbidities were rhinosinusitis (42.7%), conjunctivitis (39.7%), asthma (36.4%), atopic dermatitis (25.7%), sleep disturbance (24.7%). Overall, patients with persistent, moderate-to-severe AR (87.5%, $p = 0.004$) were more likely to present comorbidities, except for atopic dermatitis (23.6%, $p = 0.210$) and oral allergy syndrome (0.8%, $p = 0.244$). Sensitization to mold (82.1%, $p = 0.001$) and polysensitization (59.3%, $p = 0.001$) were associated with moderate-to-severe persistent AR.

Conclusion: Our study revealed that 42.2% of AR patients presented with the moderate-to-severe persistent disease in the pediatric population in Sivas. Rhinosinusitis and conjunctivitis were the most common comorbidities. The likelihood of comorbidities, particularly respiratory comorbidities, was higher in patients with moderate-to-severe, persistent AR. Mold sensitization and polysensitization were significantly associated with the severity of AR.

Keywords: Allergic rhinitis, comorbidity, rhinosinusitis, mold, children

SIVAS İLİNDE ALERJİK RİNİTLİ ÇOCUK HASTALARIN KLİNİK ÖZELLİKLERİ VE KOMORBİD HASTALIKLARI ÖZET

Giriş: Çalışmamızda Sivas ilinde alerjik rinit (AR) tanısı alan çocuk hastaların klinik özelliklerini ve eşlik eden (komorbid) hastalıklarını değerlendirmeyi amaçladık.

Materyal ve method: Mart 2019 ile Şubat 2020 tarihleri arasında alerjik rinit tanısı alan 874 çocuğun (0-18 yaş) tıbbi kayıtları retrospektif olarak incelendi.

Bulgular: 874 AR hastasının ortanca yaşı 8.3 (5.1-12.2) yıl idi ve 478'i (%54.7) erkekti. AR en sık 6-12 yaş arası çocuklarda (%40.8) teşhis edildi. AR hastalarının %42.2'sinde orta-şiddetli persistan AR vardı. En sık şikayetler burun tıkanıklığı (%86.3) ve burun akıntısı (%84.3) idi. Orta-şiddetli AR hastalarında en sık görülen semptom burun tıkanıklığı (%96.4), hafif AR hastalarında en sık hapşırma (%46) ve burun akıntısı (%88) idi. En sık eşlik eden hastalıklar rinosinüzit (%42.7), konjonktivit (%39.7), astım (%36.4), atopik dermatit (%25.7), uyku bozukluğu (%24.7) idi. Genel olarak, persistan, orta-şiddetli AR'si (%87.5, $p = 0.004$) olan hastalarda, atopik dermatit (%23.6, $p = 0.210$) ve oral alerji sendromu (%0.8, $p = 0.244$) dışında, komorbid hastalık gösterme olasılığı daha yüksekti. Küf duyarlılığı (%82.1, $p = 0.001$) ve polisensitizasyon (%59.3, $p = 0.001$), orta-şiddetli kalıcı AR ile ilişkiliydi.

Sonuç: Çalışmamız, Sivas'taki çocuk popülasyonunda AR hastalarının %42,2'sinin orta-şiddetli persistan hastalıkla başvurduğunu ortaya koydu. Rinosinüzit ve konjonktivit en sık görülen komorbiditelerdi. Komorbidite olasılığı, özellikle respiratuar komorbiditeler, orta-şiddetli, persistan AR'si olan hastalarda daha yüksekti. Küf duyarlılığı ve çoklu duyarlılık, AR'nin şiddeti ile önemli ölçüde ilişkiliydi.

Anahtar Sözcükler: Alerjik rinit, komorbidite, rinosinüzit, küf, çocuklar

INTRODUCTION

Allergic rhinitis (AR) is the most common IgE-mediated chronic inflammatory disease of the upper respiratory airways in children, manifesting as nasal congestion, rhinorrhea, sneezing, and nasal itching¹.

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The global prevalence of self-reported AR in children has been estimated to be between 2% and 25%². According to studies conducted in our country, the prevalence of AR in children ranges from 2.9 to 39.9%³. The eyes, paranasal sinuses, nasopharynx, middle ear, larynx, and lower respiratory tract are all anatomically and functionally connected to the nose. As a result, patients with AR are more likely to have comorbid diseases such as asthma, chronic sinusitis, recurrent otitis media, and allergic conjunctivitis. Furthermore, rhinitis frequently coexists with sleep disturbances and some allergic diseases in children, such as atopic dermatitis and pollen-food syndrome. AR and



comorbidities have a significant negative impact on children's and adolescents' quality of life and health in the physical, social, and psychological domains⁴.

The effects and costs of rhinitis comorbidities should be considered in the management of rhinitis in the pediatric population. However, studies on the comorbidities of rhinitis in children are limited³⁻⁵. Additionally, there is little information available regarding the phenotypes, characteristics, and epidemiology of rhinitis, including AR, in Turkish children. The previous studies were mostly conducted on patients selected from tertiary hospitals and therefore consisted of a higher rate of patients with moderate-to-severe AR. Based on this fact, the results of our study reflect a more population-based study. We aimed to investigate the clinical presentations, phenotypes (according to the ARIA classification), severity, and comorbidities of AR in Turkish children in Sivas. Our findings could aid in the development of a rhinitis prevention and treatment strategy, as well as in improving the quality of life of Turkish children and adolescents suffering from AR. More nationwide and longitudinal studies will be conducted to better understand the relationship between these diseases.

MATERIAL and METHODS

The skin test results of 2422 children (0-17 years old) who visited our allergy outpatient clinic at Sivas Numune Hospital in Sivas between March 2019 and February 2020 with rhinitis complaints were analyzed retrospectively. The skin prick test (SPT) was used to assess aeroallergen sensitivity in patients with house dust mites, mold (fungus), and pollen (tree, cereal grain, weed, and grass). The study included 874 pediatric patients diagnosed with AR who had positive SPT results. Our patients' demographic characteristics (age, gender), outpatient application complaints (nose itching, obstruction, rhinorrhea, sneezing), and allergy skin test results were all recorded retrospectively. Patients were divided into four groups based on their age at diagnosis: (1) 1-year-old and under (infant age), (2) 2-5 years old (preschool age), (3) 6-12 years old (school age), and (4) over 12 years old (adolescent age). The ARIA severity scoring was used to determine the

severity of allergic rhinitis, as well as any associated comorbid diseases (rhinosinusitis, conjunctivitis, otitis media, atopic dermatitis, oral allergy syndrome, and sleep disorder).

Definition and classification of AR:

Rhinitis was diagnosed in patients who presented multiple rhinitis symptoms, such as sneezing, rhinorrhea, nasal obstruction, and itching. If a patient tested positive for sensitization to inhaled allergens, AR was diagnosed by a physician. AR was categorized as intermittent or persistent and of mild, or moderate to severe severity using the ARIA guidelines. Symptoms lasting less than 4 days per week or for fewer than 4 consecutive weeks were classified as intermittent, while symptoms lasting more than 4 days per week and for longer than 4 consecutive weeks were classified as persistent. Depending on sleep disturbance, impairment of daily activities, leisure, sport, school, and/or work, and bothersome symptoms, the severity of AR was categorized as mild, moderate, or severe.

Definition of comorbid diseases:

Conjunctivitis was identified by its signs and symptoms, such as red, itchy, watery eyes, and eye rubbing. Coughing, wheezing, and exercise-induced bronchospasm were the symptoms, and spirometry results were used to diagnose asthma in people older than six years old. A prolonged nasal obstruction, purulent rhinorrhea or postnasal drainage, and complaints like a headache, facial pain, or cough were all considered to be signs of rhinosinusitis. Sleep disturbances comprise a history of disturbed sleep, snoring, apnea, tiredness, and irritability¹. Following an ear examination by a physician, otitis media was diagnosed⁴. The criteria proposed by Hanifin and Rajka were used by physicians to diagnose atopic dermatitis⁶. Cross-reactivity between aeroallergens, such as birch pollen, and fruits and vegetables, such as apples, is known as oral allergy syndrome (OAS, pollen-food syndrome), and it manifests as oral pruritus or swelling⁷.

The 1964 Declaration of Helsinki and the institutional and/or national research committee's ethical standards were followed in all aspects of studies involving human subjects. This research study was approved by the Sivas Cumhuriyet University of Medicine's ethics committee in Türkiye (approval number: 2021-04/03).



Statistical analysis

Statistical analyses were made with the SPSS 22.0 (SPSS, Inc., Chicago, IL, USA) statistical program. A descriptive analysis was applied to the demographic characteristics of the study population. Variables (sex, age, atopic diseases, detected inhalant allergens, etc.) were defined by the mean or median±standard deviation, or percentile results (%). Whichever is appropriate to compare different patient groups, the Kruskal-Wallis or Pearson chi-square statistical analysis test was applied. Results with a statistical p-value below 0.05 were considered significant.

RESULTS

Demographics of children with allergic rhinitis

The median age of 874 allergic patients was 8.3 years, and 478 (54.7%) were males. AR was most commonly diagnosed in children aged 6-12 years (school age) (n: 357, 40.8%), and males were more common in all age groups (Fig. 1).

Clinical characteristics and phenotypes of allergic rhinitis

42.2% of AR patients had moderate-to-severe persistent AR. Nasal congestion (86.3%), discharge (84.3%), itching (52.7%), and sneezing (41.4%) were the most common complaints. Most of the patients (83.2%) had comorbidities associated with AR. Rhinosinusitis (42.7%) and conjunctivitis (39.7%) were the most common comorbidities, followed by asthma (36.4%), atopic dermatitis (25.7%), sleep disturbance (24.7%), otitis media (19.6%), and oral allergy syndrome (1.4%). Pollen (61.2%) was the most common inhalant allergen observed in AR patients' skin tests, followed by house dust mites (54.9%) and mold (7.7%). The specialties that most frequently referred patients to the allergy polyclinic to investigate and test for allergic rhinitis were pediatricians (64%) and ENT physicians (18.1%) (Table 1).

Nasal obstruction was more significantly associated with moderate-to-severe AR (96.4%) than with mild AR (75.6%) ($p < 0.001$). However, rhinorrhea (88%, $p = 0.003$) and sneezing (46%, $p = 0.007$) were more significantly associated with mild AR than moderate-to-severe AR. On the other hand, nasal obstruction and rhinorrhea were also more significantly associated with

persistent AR than with intermittent AR ($p = 0.003$ and $p = 0.028$, respectively). However, nasal itching was more significantly associated with intermittent AR (59%) than with persistent AR (50.4%) ($p = 0.022$) (Table 2).

Respiratory comorbidities such as rhinosinusitis (50.4%), conjunctivitis (50.2%), and asthma (46%) were more common in patients with moderate-to-severe AR when compared to patients with mild AR ($p < 0.001$). However, there was no significant relationship between the severity and duration of AR and any other comorbidities, including atopic dermatitis, otitis media, and oral allergy syndrome (Table 2).

In our study, polysensitization was observed among 428 patients (48.9%) and monosensitization was observed among 446 patients (51.1%). Mold sensitivity ($p = 0.001$) and polysensitization ($p = 0.001$) were related to the severity and persistence of AR. Monosensitization was significantly found in mild (66.4%, $p = 0.001$) and intermittent AR patients (66.1%, $p = 0.001$), whereas polysensitization (at least two allergen sensitizations) was found in moderate-to-severe (64.3%, $p = 0.001$) and persistent AR patients (55.5%, $p = 0.001$) (Table 2).

Comparison of comorbidities according to severity classification using ARIA

We analyzed and compared the clinical characteristics of comorbid diseases according to severity classification using ARIA (mild intermittent/persistent, moderate-to-severe intermittent/persistent) (Fig. 2).

The majority of the comorbidities were significantly found among patients with persistent, moderate-to-severe AR, except for atopic dermatitis (38.7%, $p = 0.210$) and oral allergy syndrome (25%, $p = 0.224$) (Fig. 2). The percentage of comorbidities, including rhinosinusitis (50.7%, $p < 0.001$), asthma (57.9%, $p < 0.001$), conjunctivitis (53.3%, $p < 0.001$), otitis media (50.3%, $p = 0.017$), and sleep disturbance (67.6%, $p < 0.001$), was significantly higher in patients with persistent and moderate-to-severe AR (Fig. 2).

Comparison of comorbidities according to sensitization patterns



We analyzed and compared the clinical characteristics of comorbid diseases of AR based on sensitization patterns (Fig. 3).

We evaluated the connections between inhalant sensitization patterns and comorbid diseases. Pollen sensitization was more prevalent in patients with AR who suffered from comorbid rhinosinusitis (66.8%, $p = 0.004$), conjunctivitis (73.2%, $p < 0.001$), sleep disturbance (74.5%, $p = 0.001$), and oral allergy syndrome (91.7, $p = 0.029$). House dust and mold sensitization were more prevalent in patients with AR who suffered from comorbid eczema (60.9%, $p = 0.037$; 11.1%, $p = 0.024$) or asthma (61.6%, $p = 0.003$; 11%, $p = 0.005$). Besides, patients who suffered from otitis media as comorbidity had a significantly higher incidence of mold

sensitization (24.6%, $p < 0.001$). When a patient with AR presented with any comorbid disease, mold sensitization was more prevalent (8.8%, $p = 0.005$). Polysensitization was found to increase the frequency of rhinosinusitis (56.6%, $p < 0.001$), conjunctivitis (61.4%, $p < 0.001$), sleep problems (69.4%, $p < 0.001$), and oral allergy (83.3%, $p = 0.016$) (Fig. 3). When we compared the percentages of rhinitis symptoms according to sensitization patterns, nasal obstruction was significantly associated with pollen (89.2%, $p = 0.002$) and mold sensitization (98.5%, $p = 0.002$); while rhinorrhea was significantly associated with only pollen sensitization (90.1%, $p < 0.001$) (Fig. 4).

Table 1. Demographic and clinical features of the patients (n: 874)

Demographic and clinical characteristics	Total number: 874
Boys, n (%)	478 (54.7)
Girls, n (%)	396 (45.3)
Age, median (SD) (year)	8.3 (4.2)
Rhinitis symptoms, n (%)	
-Nasal obstruction	754 (86.3)
-Rhinorrhea	737 (84.3)
-Nasal itching	462 (52.7)
-Sneezing	363 (41.4)
ARIA classification, n (%)	
Mild	
-Intermittent	175 (20.0)
-Persistent	254 (29.1)
Moderate-to-severe	
-Intermittent	76 (8.7)
-Persistent	369 (42.2)
Rhinitis comorbidities, n (%)	
-Rhinosinusitis	373 (42.7)
-Conjunctivitis	347 (39.7)
-Asthma	318 (36.4)
-Atopic dermatitis	225 (25.7)
-Sleep disturbance	216 (24.7)
-Otitis media	171 (19.6)
-Oral allergy syndrome	12 (1.4)
Aeroallergen sensitivity distribution, n (%)	
-Pollen	535 (61.2)
-House dust mite	480 (54.9)
-Mold (fungus)	67 (7.7)
Referring physicians, n (%)	
-Pediatricians	559 (64.0)
-Otolaryngologists	158 (18.1)
-Ophthalmologists	84 (9.6)
-Family physicians	34 (3.9)

Table 2. Investigation of the association between nasal symptoms, comorbidities, allergen sensitization, and ARIA classification

Characteristics	Mild, n (%)	Moderate -severe, n(%)	P value	Inter-mittent, n (%)	Persistent, n (%)	P value
Rhinitis symptoms, n (%)						
	332 (75.6)	432 (96.4)	< 0.001	203(80.9)	551 (88.4)	0.003
-Nasal obstruction	375 (88.0)	362 (80.8)	0.003	201 (80.1)	536 (86.0)	0.028
-Rhinorrhea	225 (52.8)	237 (52.9)	0.980	148 (59.0)	314 (50.4)	0.022
-Nasal itching	196 (46.0)	166 (37.1)	0.007	114 (45.4)	248 (39.8)	0.128
-Sneezing						
Comorbidities, n (%)						
-Rhinosinusitis	147 (34.5)	226 (50.4)	< 0.001	96 (38.2)	277 (44.5)	0.093
-Conjunctivitis	122 (28.6)	225 (50.2)	< 0.001	98 (39.0)	249 (40.0)	0.801
-Asthma	112(26.3)	206 (46.0)	< 0.001	75 (29.9)	243 (39.0)	0.011
-Atopic dermatitis	114 (26.8)	111 (24.8)	0.503	63 (25.1)	162 (26.0)	0.782
-Sleep disturbance	44 (10.3)	172 (38.4)	< 0.001	62 (24.7)	154 (24.7)	0.996
-Otitis media	74(17.4)	97(21.7)	0.111	43 (17.1)	128 (20.5)	0.250
-Oral allergy syndrome	7 (1.6)	5 (1.1)	0.503	5 (2.0)	7 (1.1)	0.318
Aeroallergen, n (%)						
-Pollen	248 (58.2)	288 (64.3)	0.066	153 (61.0)	383 (61.5)	0.886
-House dust mite	227 (53.3)	253 (56.5)	0.344	132 (52.6)	348 (55.9)	0.380
-Mold (fungus)	11 (2.6)	56 (12.5)	< 0.001	2 (0.8)	65 (10.4)	< 0.001
Monosensitization, n (%)	283 (66.4)	155 (34.6)	< 0.001	166 (66.1)	272 (43.1)	< 0.001
Polysensitization, n (%)	140 (32.9)	288 (64.3)	< 0.001	82 (32.7)	346 (55.5)	< 0.001

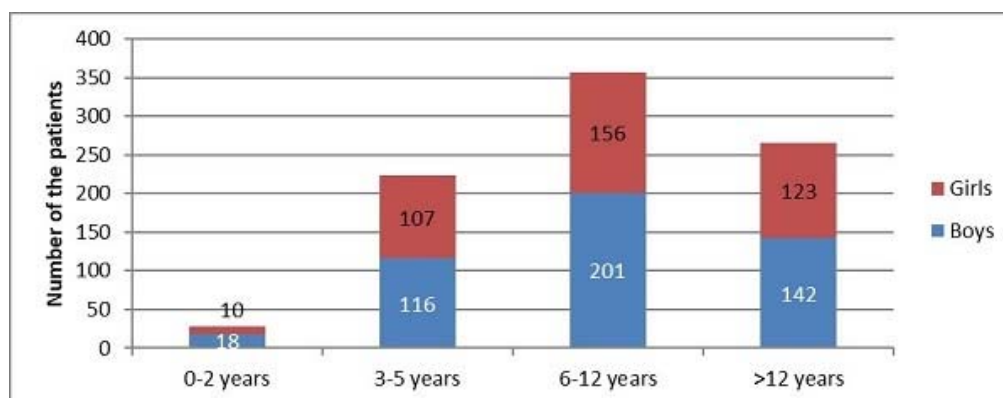


Fig. 1: Distribution of patients by age and gender groups

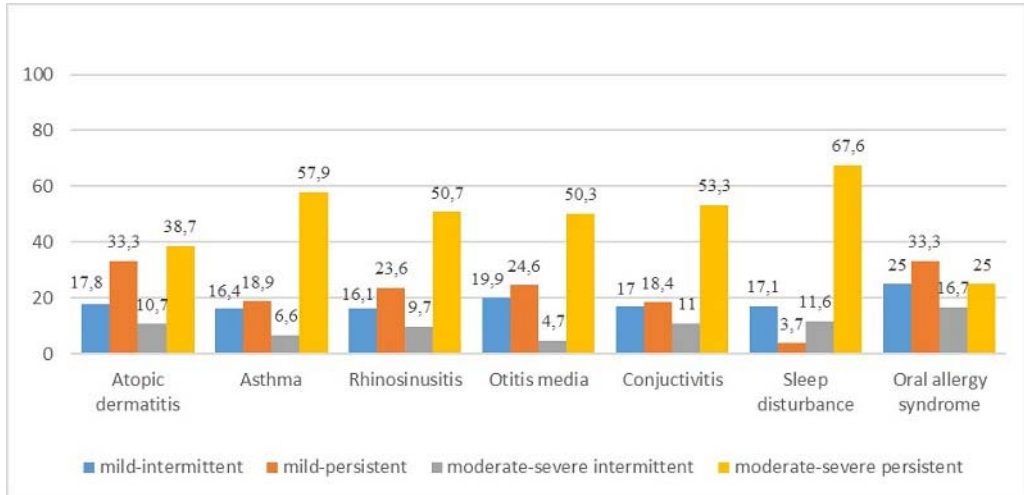


Fig. 2: Percentage of comorbidities of AR according to severity classification using ARIA

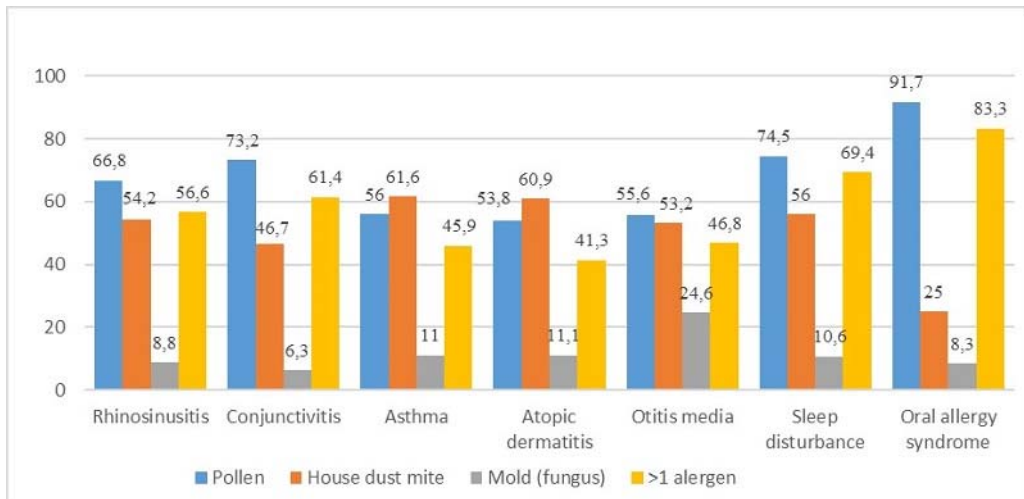


Fig. 3: Percentage of comorbidities of AR according to sensitization patterns

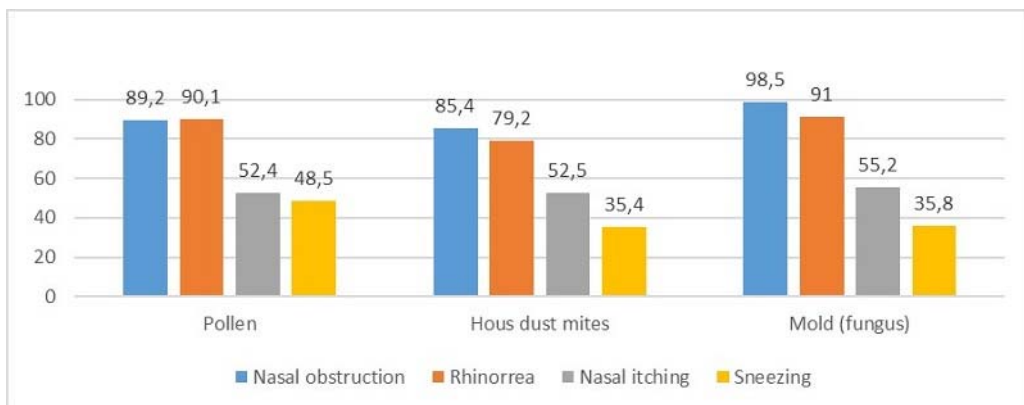


Fig. 4: Percentage of rhinitis symptoms according to sensitization patterns



DISCUSSION

Allergic rhinitis (AR) is considered one of the most common allergic diseases in children, characterized by rhinorrhea, nasal obstruction, itching, and sneezing. In addition to nasal mucosa inflammation, eye, ear, and throat symptoms are often present. The disease's prevalence is increasing globally, and the morbidity and economic consequences are becoming more significant¹. A study conducted in 5 different centers in Türkiye found that the frequency of doctor-diagnosed AR in the previous year ranged from 11.8% to 36.4%⁸. In this study, we evaluated and compared the clinical features in the pediatric population of Sivas, as well as the comorbidities of AR according to severity classification and sensitization patterns. This study involved 874 Turkish children with ages ranging from 0 to 18 and a median age of 8.3 years. In Sivas, as well as other regions of Türkiye and the world, this is the age group where children are most likely to have AR^{1,3,8,9}.

Similar to previous studies, there were significantly more boys (54.7%) than girls in this study^{3,8-10}. This fact is unclear, though it could be explained by the higher prevalence of atopy in male children^{1,9}. In our study, based on the severity classification using ARIA, the percentage of moderate-to-severe AR patients was lower than in the other studies carried out in Türkiye and Spain^{5,9,11}. The higher prevalence of moderate-to-severe patients in these studies, which primarily enrolled patients from tertiary centers, may account for this difference.

The eyes, paranasal sinuses, nasopharynx, middle ear, larynx, and lower respiratory tract are anatomically and functionally connected to the nose. Because of this, patients with AR frequently exhibit symptoms of asthma, chronic sinusitis, recurrent otitis media, adenoid hypertrophy, and allergic conjunctivitis^{12,13}. It is understood that in people with moderate-to-severe AR, mucosal edema interferes with sinus aeration, raising the possibility of bacterial colonization and resulting in the development of chronic rhinosinusitis. Similarly, impaired eustachian function with

mucosal edema may cause chronic inflammatory changes in the mucosa to develop more easily and predispose to serous otitis. In the task force report which was prepared on behalf of the European Academy of Allergy and Clinical Immunology, Cingi et al. mentioned that AR is a systemic disease and accompanies asthma, dermatitis, food allergy, eosinophilic esophagitis, conjunctivitis, chronic middle ear effusion, rhinosinusitis, adenoid hypertrophy, olfactory disorder, obstructive sleep apnea, sleep disorder, and accompanying behavioral and educational disorders in adult patients¹⁴. According to various studies conducted among pediatric patients, the prevalence of rhinosinusitis is 26.1-48.4%, conjunctivitis is 31.6-53.6%, asthma is 10-49.5%, and otitis media with effusion is 11.5-49%^{9,15-17}. In accordance with previous studies, the majority of our patients (83.2%) had AR-related comorbidities such as rhinosinusitis, conjunctivitis, asthma, atopic dermatitis, otitis media, and sleep disturbance^{1,4,5,8,9}. Based on the literature, patients with persistent, moderate-to-severe AR were more likely to develop comorbidities^{1,9}. In accordance with those, the severity of AR had a positive and significant impact on the frequency of the respiratory comorbidities in our study, such as rhinosinusitis (42.7%), conjunctivitis (39.7%), asthma (36.4%), and otitis media (19.6%), confirming the hypothesis that inflammation of contiguous structures of the nose is common^{5,9}.

In a previous study by Koksall et al., 23.7% of the patients in the general population in Kayseri had conjunctivitis, while 39.7% of the pediatric patients in our study had conjunctivitis¹⁸. Notably, a link was found between the severity and duration of AR and conjunctivitis symptoms. Similar to previous studies, ocular symptoms were more prevalent in children with persistent and moderate-to-severe AR than in those with intermediate or mild AR^{9,15}.

In comparison to studies from Türkiye (48.5%-52.8%) and Spain (49.5%), this study found a lower correlation between asthma and rhinitis (36.4%)^{5,9,19}. The higher percentage of patients with moderate-to-severe AR in the other studies and the subsequent selection of patients



with severe clinical findings account for the difference in the prevalence of the two conditions. As in previous studies, the frequency of an asthma diagnosis in patients with AR was correlated with the duration and severity of AR in our study^{5,9,17}. Additionally, numerous studies have revealed that people with persistent AR are more likely to develop asthma²⁰.

Atopic dermatitis was common among AR patients (25.7%), similar to a previous study in Korea (29.7%), but lower than a previous study in Spain (40%) and higher than a previous study in Türkiye (10.4%)^{5,9,17}. Atopic dermatitis has been identified in earlier research, as a risk factor for developing AR and an even more severe form of AR^{9,21}. However, atopic dermatitis prevalence and the prevalence of moderate-to-severe AR showed no significant relationship in this study.

The other more common comorbidity was chronic otitis media with effusion, which confirmed the hypothesis of one airway inflammation. According to previous studies, the presence of otitis media was linked to severe AR^{9,15}. Similar to these studies, our study's patients with persistent and moderate-to-severe AR had a significantly higher percentage of otitis media. However, the relationship between chronic otitis media (COM) and allergic rhinitis (AR) is still unclear. When we analyze the Turkish literature, Gorgulu et al. study claimed that AR contributes to the etiology of COM, but Guler et al. study came to the opposite conclusion and claimed that there is even an inversely proportional relationship between AR and COM^{22,23}. Nasal obstruction was the most prevalent AR symptom in our study (86.73%), and nasal obstruction was significantly associated with both the severity and persistence of AR, which was very similar to the findings of previous studies^{20,24}. These studies also highlighted the significance of nasal obstruction since it significantly affected the quality of life^{20,24}. According to the authors, treating nasal congestion improves sleep quality in patients with AR because it is linked to sleep-disordered breathing and appears to be a major cause of sleep impairment²⁵. Similar to earlier studies, in our study, sleep disturbance was significantly

more common in children with moderate-to-severe AR than in those with mild AR^{9,17,25}.

The information on allergen sensitization was similar to previous studies conducted in Türkiye and Spain, where pollen and house dust mites were the most frequently encountered allergens in the population^{3,8,9,21}. In accordance with the findings of previous studies, oral allergy syndrome was significantly more common in those who had pollen sensitization or polysensitization^{20,26}. According to a previous study from Türkiye, the frequency of oral allergy syndrome has been reported as 5-8% among pollen-induced allergic rhinitis, while this comorbidity occurred in 1.4 of our patients²⁷. When studies conducted in Türkiye are examined, the rate of obtaining a positive reaction against at least one allergen in AR patients varies between 29.3-56.7%^{28,29}. An Italian multicenter study of 1,360 children with AR found that 84.9% were allergic to more than three allergens and that there was a strong correlation between pollen-induced AR duration and severity²⁶. In our study, polysensitization was 48.9% and found to be significantly associated with both the severity and persistence of AR. Furthermore, in our study, polysensitization was found to increase the incidence of rhinosinusitis, conjunctivitis, sleep issues, and oral allergy. Sensitizations to cats, Japanese hop, and Dermatophagoides pteronyssinus (Der p) were linked to moderate-to-severe persistent AR in a recent study from Korea³⁰. In another study, 68.4% of children who were sensitive to house dust mites also had asthma, eczema, or rhinitis. This study also demonstrated a graded effect, with the risk of allergic disease (including asthma, eczema, and rhinitis) in the child rising with the quantity of positive skin prick test reactions³¹. According to a recent study conducted by K. Koodziejczyk and A. Bozek, patients with mold sensitivity have a clinically milder type of AR; however, they have a significantly higher predisposition for nasal obstruction and bronchial asthma in adults³². In a study conducted by Tamay et al, dampness at home was significantly associated with AR³³. Evident indoor dampness or mold is consistently linked to a variety of respiratory or allergic health effects, including the onset or



exacerbation of asthma, allergic rhinitis, eczema, and symptoms of the upper respiratory tract, such as otitis media, according to epidemiologic evidence from primary studies and quantitative meta-analyses. Similar to these evidence from the literature, mold, and pollen sensitization was significantly associated with nasal obstruction in our study, and both sensitizations were significantly associated with moderate-to-severe AR and asthma. Mold sensitization was the most prevalent sensitization which was more likely to develop any AR comorbidity, such as otitis media and eczema. Pollen sensitization was also linked to rhinosinusitis and oral allergy syndrome in our study similar to previous studies^{31,32,34}. Additionally, in our study, AR patients with concurrent eczema or asthma were frequently linked to sensitizations to house dust mites.

CONCLUSION

In conclusion, our study revealed that 42.2% of AR patients presented with the moderate-to-severe persistent disease in the pediatric population in Sivas. Rhinosinusitis and conjunctivitis were the most common comorbidities. The likelihood of comorbidities, particularly respiratory comorbidities, was higher in patients with moderate-to-severe, persistent AR. Mold sensitization and polysensitization were significantly associated with the severity of AR.

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REFERENCES

1. Lack G. Pediatric allergic rhinitis and comorbid disorders. *J Allergy Clin Immunol* 2001; 108:S9-15.
2. Katelaris CH, Lee BW, Potter PC, Maspero JF, Cingi C, Lopatin A, Saffer M, Xu G, Walters RD. Prevalence and diversity of allergic rhinitis in regions of the world beyond Europe and North America. *Clin Exp Allergy* 2012; 42(2):186-207.
3. Tuncer A, Yüksel H (eds). *Alerjik rinit epidemiyolojisi. Alerjik Rinit Tanı ve Tedavi Rehberi*. Ankara: Bilimsel Tıp Yayınevi, 2012:3-5.
4. Mariño-Sánchez F, Valls-Mateus M, de Los Santos G, Plaza AM, Cobeta I, Mullol J. Multimorbidities of Pediatric Allergic Rhinitis. *Curr Allergy Asthma Rep* 2019; 19(2):13.
5. Özlem Sancaklı, Halil Belverenli. Clinical features of patients with allergic rhinitis and evaluation of adenoid hypertrophy as a comorbidity. *J Dr Behcet Uz Child Hosp* 2019; 9(2):125-130.
6. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol* 1980; 60:44-7.
7. Webber CM, England RW. Oral allergy syndrome: a clinical, diagnostic, and therapeutic challenge. *Ann Allergy Asthma Immunol* 2010; 104(2):101-8.
8. Civelek E, Yavuz ST, Boz AB, Orhan F, Yuksel H, Uner A, Cakir B, Sekerel BE. Epidemiology and burden of rhinitis and rhinoconjunctivitis in 9- to 11-year-old children. *Am J Rhinol Allergy* 2010; 24(5):364-70.
9. Ibáñez MD, Valero AL, Montoro J, Jauregui I, Ferrer M, Dávila I, Bartra J, Del Cuvillo A, Mullol J, Sastre J. Analysis of comorbidities and therapeutic approach for allergic rhinitis in a pediatric population in Spain. *Pediatr Allergy Immunol* 2013; 24(7):678-84.
10. Ibáñez MD, Navarro A, Sánchez MC, Rondón C, Montoro J, Matéu V, Lluch-Bernal M, Fernández-Parra B, Dordal MT, Dávila I, Conde J, Antón E, Colás C, Valero A; SEaic Rhinconjunctivitis Committee. Rhinitis and its association with asthma in patients under 14 years of age treated in allergy departments in Spain. *J Investig Allergol Clin Immunol* 2010; 20(5):402-6.
11. Jáuregui I, Dávila I, Sastre J, Bartra J, del Cuvillo A, Ferrer M, Montoro J, Mullol J, Molina X, Valero A. Validation of ARIA (Allergic Rhinitis and its Impact on Asthma) classification in a pediatric population: the PEDRIAL study. *Pediatr Allergy Immunol* 2011; 22(4):388-92.
12. Brozek JL, Bousquet J, Agache I, Agarwal A, Bachert C, Bosnic-Anticevich S, Brignardello-Petersen R, Canonica GW, Casale T, Chavannes NH, Correia de Sousa J, Cruz AA, Cuello-Garcia CA, Demoly P, Dykewicz M, Etxeandia-Ikobaltzeta I, Florez ID, Fokkens W, Fonseca J, Hellings PW, Klimek L, Kowalski S, Kuna P, Laisaar KT, Larenas-Linnemann DE, Lødrup Carlsen KC, Manning PJ, Meltzer E, Mullol J, Muraro A, O'Hehir R, Ohta K, Panzner P, Papadopoulos N, Park HS, Passalacqua G, Pawankar R, Price D, Riva JJ, Roldán Y, Ryan D, Sadeghirad B, Samolinski B, Schmid-Grendelmeier P, Sheikh A, Togias A, Valero A, Valiulis A, Valovirta E, Ventresca M, Wallace D, Wasserman S, Wickman M, Wiercioch W, Yepes-Nuñez JJ, Zhang L, Zhang Y, Zidarn M, Zuberbier T, Schünemann HJ. Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines-2016 revision. *J Allergy Clin Immunol* 2017; 140(4):950-958.
13. Higuchi O, Adachi Y, Itazawa T, Ito Y, Yoshida K, Ohya Y, Odajima H, Akasawa A, Miyawaki T. Relationship between rhinitis and nocturnal cough in school children. *Pediatr Allergy Immunol* 2012; 23(6):562-6.
14. Cingi C, Gevaert P, Mösges R, Rondon C, Hox V, Rudenko M, Muluk NB, Scadding G, Manole F, Hupin C, Fokkens WJ, Akdis C, Bachert C, Demoly P, Mullol J, Muraro A, Papadopoulos N, Pawankar R, Rombaux P, Toskala E, Kalogjera L, Prokopakis E, Hellings PW, Bousquet J. Multimorbidities of allergic rhinitis in adults: European Academy of Allergy and Clinical Immunology Task Force Report. *Clin Transl Allergy* 2017; 7:17.
15. Sih T, Mion O. Allergic rhinitis in the child and associated comorbidities. *Pediatr Allergy Immunol* 2010; 21:e107-13.
16. Eriksson J, Bjerg A, Lötvall J, Wennergren G, Rönmark E, Torén K, Lundbäck B. Rhinitis phenotypes correlate with



- different symptom presentation and risk factor patterns of asthma. *Respir Med* 2011; 105(11):1611-21.
17. Lee KS, Yum HY, Sheen YH, Park YM, Lee YJ, Choi BS, Jee HM, Choi SH, Kim HH, Park Y, Kim HB, Rha YH; Korean Academy of Pediatric Allergy and Respiratory Disease (KAPARD) Work Group on Rhinitis. Comorbidities and Phenotypes of Rhinitis in Korean Children and Adolescents: A Cross-sectional, Multicenter Study. *Allergy Asthma Immunol Res* 2017; 9(1):70-78.
 18. Kerem Kökoğlu, Ömer Kutlu. Evaluation of allergic rhinitis patients and their skin prick test results in Kayseri province. *Praxis of ORL* 2020; 8(3): 137-144.
 19. Mısırlıoğlu ED, Cengizler R. Perennial ve mevsimsel alerjik rinitli çocukların değerlendirilmesi. *Astım Alerji İmmünoloji* 2003; 1:11-16
 20. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, Zuberbier T, Baena-Cagnani CE, Canonica GW, van Weel C, Agache I, Ait-Khaled N, Bachert C, Blaiss MS, Bonini S, Boulet LP, Bousquet PJ, Camargos P, Carlsen KH, Chen Y, Custovic A, Dahl R, Demoly P, Douagui H, Durham SR, van Wijk RG, Kalayci O, Kaliner MA, Kim YY, Kowalski ML, Kuna P, Le LT, Lemiere C, Li J, Lockey RF, Mavale-Manuel S, Meltzer EO, Mohammad Y, Mullol J, Naclerio R, O'Hehir RE, Ohta K, Ouedraogo S, Palkonen S, Papadopoulos N, Passalacqua G, Pawankar R, Popov TA, Rabe KF, Rosado-Pinto J, Scadding GK, Simons FE, Toskala E, Valovirta E, van Cauwenberge P, Wang DY, Wickman M, Yawn BP, Yorgancıoğlu A, Yusuf OM, Zar H, Annesi-Maesano I, Bateman ED, Ben Kheder A, Boakye DA, Bouchard J, Burney P, Busse WW, Chan-Yeung M, Chavannes NH, Chuchalin A, Dolen WK, Emuzyte R, Grouse L, Humbert M, Jackson C, Johnston SL, Keith PK, Kemp JP, Klossek JM, Larenas-Linnemann D, Lipworth B, Malo JL, Marshall GD, Naspitz C, Nekam K, Niggemann B, Nizankowska-Mogilnicka E, Okamoto Y, Orru MP, Potter P, Price D, Stoloff SW, Vandenplas O, Viegi G, Williams D; World Health Organization; GA(2)LEN; AllerGen. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). *Allergy* 2008; 63 Suppl 86:8-160.
 21. Batlles Garrido J, Torres-Borrego J, Bonillo Perales A, Rubí Ruiz T, González Jiménez Y, Momblán De Cabo J, Aguirre Rodríguez J, Jiménez Liria R, Losilla Maldonado A, Daza Torres M. Prevalence and factors linked to atopic eczema in 10- and 11-year-old schoolchildren. Isaac 2 in Almería, Spain. *Allergol Immunopathol* 2010; 38(4):174-80.
 22. Gorgulu O, Ozelci M, Ozdemir S, Yasar M, Olgun MK, Arikan OK. The role of allergy in the pathogenesis of chronic suppurative otitis media. *Journal of International Advanced Otolaryngology* 2012; 8(2):276-281.
 23. Güler Y, Güler R, Şen A, Özdamar K and Üstyol AE. Evaluation of the Relationship Between Chronic Otitis Media and Allergic Rhinitis. *Kafkas Journal of Medical Sciences* 2018; 8:178-182.
 24. Meltzer EO, Blaiss MS, Derebery MJ, Mahr TA, Gordon BR, Sheth KK, Simmons AL, Wingertzahn MA, Boyle JM. Burden of allergic rhinitis: results from the Pediatric Allergies in America survey. *J Allergy Clin Immunol* 2009; 124(3):43-70.
 25. Craig TJ, Sherkat A, Safaee S. Congestion and sleep impairment in allergic rhinitis. *Curr Allergy Asthma Rep* 2010; 10(2):113-21.
 26. Dondi A, Tripodi S, Panetta V, Asero R, Businco AD, Bianchi A, Carlucci A, Ricci G, Bellini F, Maiello N, del Giudice MM, Frediani T, Sodano S, Dello Iacono I, Macri F, Massaccesi V, Caffarelli C, Rinaldi L, Patria MF, Varin E, Peroni D, Chinellato I, Chini L, Moschese V, Lucarelli S, Bernardini R, Pingitore G, Pelosi U, Tosca M, Paravati F, La Grutta S, Meglio P, Calvani M, Plebani M, Matricardi PM; Italian Pediatric Allergy Network (I-PAN). Pollen-induced allergic rhinitis in 1360 Italian children: comorbidities and determinants of severity. *Pediatr Allergy Immunol* 2013; 24(8):742-51.
 27. Guvenir H, Dibek Misirlioglu E, Buyuktiryaki B, Zabun MM, Capanoglu M, Toyran M, Civelek E, Kocabas CN. Frequency and clinical features of pollen-food syndrome in children. *Allergol Immunopathol* 2020; 48(1):78-83.
 28. Keles E, Karlıdağ T, Alpay HC, Akyiğit A, Kaygusuz İ, Yalçın Ş. Alerjik rinitli olgularımızda semptomlar ve cilt testi ile saptanan alerjenlerin dağılımı. *KBB-Forum* 2010; 9:20-4.
 29. Konuk S, Bilgin C, Çoban H, Nalbant A. Assessment of the Results of the Prick Tests Carried Out in Düzce Province. *Aasrc* 2017; 9:232-6.
 30. Jung S, Lee SY, Yoon J, Cho HJ, Kim YH, Suh DI, Yang SI, Kwon JW, Jang GC, Sun YH, Woo SI, Youn YS, Park KS, Lee E, Cho HJ, Kook MH, Yi HR, Chung HL, Kim JH, Kim HY, Jung JA, Woo HO, Lee JK, Chang WS, Do NH, Cho H, Hong SJ. Risk Factors and Comorbidities Associated With the Allergic Rhinitis Phenotype in Children According to the ARIA Classification. *Allergy Asthma Immunol Res* 2020; 12(1):72-85.
 31. Arshad SH, Tariq SM, Matthews S, Hakim E. Sensitization to common allergens and its association with allergic disorders at age 4 years: a whole population birth cohort study. *Pediatrics* 2001; 108(2):E33.
 32. Kolodziejczyk K, Bozek A. Clinical Distinctness of Allergic Rhinitis in Patients with Allergy to Molds. *Biomed Res Int* 2016; 2016:3171594.
 33. Tamay Z, Akcay A, Ones U, Guler N, Kilic G, Zencir M. Prevalence and risk factors for allergic rhinitis in primary school children. *International journal of pediatric otorhinolaryngology* 2007; 71(3):463-471.
 34. Mendell MJ, Mirer AG, Cheung K, Tong M, Douwes J. Respiratory and allergic health effects of dampness, mold, and dampness-related agents: a review of the epidemiologic evidence. *Environ Health Perspect* 2011; 119(6):748-56.