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Long-term natural course of patients with seasonal allergic rhinitis

Długotrwały naturalny przebieg u pacjentów z sezonowym alergicznym nieżytem nosa

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ABSTRACT

Introduction: Seasonal allergic rhinitis (SAR) is typically characterized by rhinorrhea, nasal congestion, sneezing, and itching of the nose, eyes, ears, and pharynx.

Aim: To evaluate the natural course of the disease in patients diagnosed with SAR.

Material and methods: The study included 191 patients diagnosed with SAR before January 2009 and who were followed up in our clinic. A survey was applied to these 191 between June 2019 and June 2020. Patients were asked to compare their initial symptoms and symptoms in the last year.

Results: The median age of the 191 patients in this study was 35 (range: 22–70 years) and median SAR duration was 15 (range: 10–40 years). The most common disease accompanying SAR was asthma (n = 93, 48.7%). The most common sensitizing allergen was *Phleum pratense* (n = 180, 94.2%) and the most common symptoms were nasal discharge (n = 178, 93.2%), nasal itching (n = 176, 92.1%), sneezing (n = 182, 95.3%), ocular itching (n = 136, 71.2%) and ocular discharge (n = 129, 67.5%). Over the past year, nasal symptoms increased in 49 (25.7%) patients, decreased in 78 (40.8%) and did not change in 64 (33.5%). Ocular symptoms increased in 26 (18.7%) patients, decreased in 65 (46.7%) and did not change in 48 (34.5%). Nasal symptoms decreased in patients who applied pollen avoidance strategies (p = 0.008).

Conclusions: The natural course of SAR in long-term follow-up is variable. The implementation of effective pollen avoidance measures can reduce the disease severity in patients with SAR in the long term.

KEY WORDS

seasonal allergic rhinitis, rhinitis, hay fever, pollen allergy, long-term care.

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INTRODUCTION

Allergic rhinitis (AR) is a very common chronic disease worldwide, which is characterized by nasal congestion, nasal discharge, itchy nose and eyes, sneezing and postnasal drip [1]. These symptoms are caused by IgE-mediated allergic inflammation of the nasal mucosa. The allergens responsible may be seasonal or perennial. Seasonal allergens are pollens, while perennial allergens are house dust mites, molds, pet dander, and cockroaches. Diagnosis of AR is based on clinical symptoms and demonstration of allergen sensitivity. The skin prick test (SPT) or serum specific IgE is used to demonstrate allergen sensitivity to environmental allergens [2].

Seasonal allergic rhinitis (SAR), or hay fever, is typically characterized by rhinorrhea, nasal congestion, sneezing, and itching of the nose, eyes, ears, and pharynx. Symptoms in SAR are periodic and occur during the pollination period of the sensitizing plants [3]. Spring and summer are the seasons when many patients with SAR suffer from grass pollen in Turkey [4]. Some patients experience milder symptoms whereas others may have severe symptoms. Although it is generally expected that the severity of symptoms in SAR patients will decrease over the years as the patient ages, seasonal symptoms may become perennial or the severity of symptoms may increase in later years.

AIM

The aim of the present study was to evaluate the natural course of the disease in patients diagnosed with SAR.

MATERIAL AND METHODS

STUDY DESIGN, SETTING AND DATA COLLECTION

This study included 191 patients diagnosed with SAR before January 2009 and followed up in our clinic after that time. In a one-year period between June 2019 and June 2020, a survey was applied to these 191 patients by phone or when they came to the clinic for a routine follow-up examination. Verbal informed consent was obtained from the patients who participated in the study by phone, and written informed consent was obtained from those who participated face-to-face. In the survey, the patients were asked about the duration, severity and seasonality of symptoms, medications, nasal surgery, pet ownership, migration to other geographic areas and the implementation of pollen avoidance measures. The form included questions comparing the nasal and ocular symptoms of the patients in the last year and previous years (Table 1). The diagnosis of SAR was based on the presence of typical symptoms for at least two pollen periods and the demonstration of at least one pollen sensitivity with SPT. The demographic data of the patients, comorbidities, medications, allergen sensitivities, initial symptoms, and the geographical regions where they lived were obtained from the medical records.

Atopy was assessed with SPT to 15 common aeroallergens in Turkey (ALK, Denmark) (*Dermatophagoides pteronyssinus*, *Phleum pratense*, *Olea europea*, *Artemisia vulgaris*, *Parietaria officinalis*, *Corylus avellana*, *Betula verrucosa*, cat, dog, horse, *Alternaria alternata*, *Cladosporium herbarum*, *Aspergillus fumigatus*, cockroach, *Acarus siro*). SPT was performed with a 1 mm lancet on the volar side of the forearm. Histamine (10 mg/ml) and saline were administered as positive and negative controls, respectively. The results were evaluated after 20 min. An induration diameter of ≥ 3 mm was considered positive. SPT was not performed in pregnant women, patients who had taken antihistamines in the last seven days, or patients with dermographism.

ETHICS STATEMENT

The study protocol was approved by the Ethics Committee (no: 2019/13-21). The study was conducted in accordance with the principles of the Declaration of Helsinki. All participants were informed about the nature of the study and written informed consent was obtained.

STATISTICAL ANALYSIS

The data were analyzed using IBM SPSS Statistics v. 20 software. The distribution of numerical data was evaluated with the Kolmogorov-Smirnov test. If numerical data were normally distributed, results were stated as mean ± standard deviation values, and if not normally distributed, as median (minimum-maximum) values. Categorical data were stated as number and percentage. Student's *t* test and the Mann-Whitney *U* test were used to compare the mean values of two independent groups. The χ^2 test and Fisher's exact test were used to compare the proportions of two independent groups. A value of $p < 0.05$ was accepted as statistically significant.

RESULTS

Evaluation was made of 191 patients, comprising 78 (40.8%) males and 113 (59.2%) females with a median age of 35 years (range: 22–70 years). The median SAR duration was 15 years (range: 10–40 years). Nasal surgery had been applied to 25 (13.1%) patients, and 49 (25.7%) patients had moved to another geographical area after the onset of SAR

TABLE 1. Core questions asked in the survey

1. In the last year, except for upper respiratory tract infection, have there been any changes in your nasal symptoms related to hay fever such as nasal itching, nasal discharge, sneezing, and nasal congestion compared to previous years? Increased [ ] Decreased [ ] Did not change [ ]
2. In the last year, have there been any changes in your ocular symptoms related to hay fever such as ocular itching and ocular discharge compared to previous years? Increased [ ] Decreased [ ] Did not change [ ]
3. In the last year, except for upper respiratory tract infection, have your nasal symptoms related to hay fever such as nasal itching, nasal discharge, sneezing, and nasal congestion become persistent throughout the year? Yes [ ] No [ ]
4. In the last year, have your ocular symptoms related to hay fever such as ocular itching and ocular discharge become persistent throughout the year? Yes [ ] No [ ]
5. Have you had nasal surgery? Yes [ ] No [ ] Type of surgery if you have had nasal surgery: ESS (endoscopic sinus surgery) [ ] Nasal septum surgery [ ] Turbinate surgery [ ] Other [ ]
6. After being diagnosed with hay fever, have you moved to another geographical area or abroad? Yes [ ] No [ ] Please indicate the cities and geographical regions where you lived:…….
7. Do you smoke? Current smoker [ ] Ex-smoker [ ] Non-smoker [ ] Duration of smoking: …….
8. Have any other allergic diseases been diagnosed by an allergist, pulmonologist, or dermatology specialist? Asthma [ ] Urticaria [ ] Drug allergy [ ] Food allergy [ ] Bee allergy [ ] Metal allergy [ ] Atopic dermatitis [ ] No other allergic disease [ ]
9. Do you have a pet? Yes [ ] No [ ] If yes, type of pet: Cat [ ] Dog [ ] Other [ ]
10. Do you take any medication for hay fever? Yes [ ] No [ ] Type of medication if you are taking: Oral antihistamine [ ] Nasal steroid [ ] Leukotriene receptor antagonist [ ] Oral steroid [ ] Decongestant [ ] Ocular antihistamine [ ]
11. If you are taking medication due to hay fever, define the frequency of intake. Regularly throughout the year [ ] Seasonal only [ ] Only when I have complaints [ ] I do not take medication [ ]
12. In the last year, except upper respiratory tract infection, in which months did you have nasal and ocular symptoms related to hay fever? ……
13. Have you had immunotherapy for hay fever? Yes [ ] No [ ]
14. Do you perform any pollen avoidance measures? Yes [ ] No [ ] If yes, which pollen avoidance measures do you perform? [ ] Avoiding woodland and grassy environments during the pollen season [ ] Following the weather reports during the pollen season [ ] Keeping doors and windows closed during the pollen season [ ] Using a pollen filter [ ] Wearing masks and glasses outdoors during the pollen season

symptoms. The most common atopic disease accompanying SAR was asthma (n = 93, 48.7%). Of the total patients, 37 (19.4%) reported a pet at home, 28 (14.7%) were taking medications regularly and 83 (43.5%) seasonally for SAR, 5 (2.6%) patients had a history of allergen-specific immunotherapy for SAR, and 29 (15.2%) had implemented pollen avoidance measures. The nasal symptoms of 32 (16.8%) patients and the ocular symptoms of 15 (10.7%) patients had become persistent. The demographic data and general characteristics of the patients are shown in Table 2.

The most common sensitizing allergen was *Phleum pratense* (n = 180, 94.2%). The most common symptoms were nasal discharge (n = 178, 93.2%), nasal itching (n = 176, 92.1%), sneezing (n = 182, 95.3%), ocular itching (n = 136, 71.2%) and ocular discharge (n = 129, 67.5%). Sensitizing allergens and the symptoms of the

TABLE 2. Demographic data and general characteristics of the patients

Parameter	Results
Age [years] median (min.–max.)	35 (22–70)
Gender (male) *n* (%)	78 (40.8)
BMI [kg/m^2] mean ± SD	25.56 ±4.03
Eosinophils [cells/µl] median (min.–max.)	200 (0–700)
SAR duration [years] median (min.–max.)	15 (10–40)
Cigarettes [pack-years] mean ± SD	9.96 ±7.20
Comorbid disease	***n*** **(%)**
Hypertension	8 (4.2)
Thyroid disease	6 (3.1)
Malignancy	4 (2.1)
Coronary artery disease	3 (1.6)
Liver disease	3 (1.6)
Diabetes mellitus	2 (1)
Chronic kidney disease	1 (0.5)
Comorbid allergic disease	***n*** **(%)**
Asthma	93 (48.7)
Chronic urticaria	40 (20.9)
Drug allergy	20 (10.9)
Food allergy	17 (8.9)
Metal allergy	12 (6.3)
Atopic dermatitis	7 (3.7)
Frequency of drug intake	***n*** **(%)**
Regular intake	28 (14.7)
Seasonal intake	83 (43.5)
In case of need	32 (16.8)
Not taking medication	48 (25.1)
Medications	***n*** **(%)**
Antihistamine	131 (68.6)
Intranasal steroid	133 (69.6)
Leukotriene receptor antagonist	94 (49.7)
Topical antihistamine for eyes	17 (8.9)
Oral steroid	3 (1.6)

Parameter	Results
Smoking	***n*** **(%)**
Current smoker	33 (17.3)
Ex-smoker	19 (9.9)
Non-smoker	139 (72.8)
Regions where the patients lived	***n*** **(%)**
Central Anatolia Region	183 (95.8)
Black Sea Region	25 (13.1)
East Anatolia Region	12 (6.3)
Marmara Region	11 (5.8)
Aegean Region	9 (4.7)
Mediterranean Region	6 (3.1)
Southeastern Anatolia Region	3 (1.6)
Abroad	5 (2.6)
Moving to another geographical area	**49 (25.7)**
Familial atopy (+)	**99 (51.8)**
Nasal surgery	**25 (13.1)**
Nasal septum surgery	11 (5.8)
Endoscopic sinus surgery	8 (4.2)
Nasal turbinate surgery	6 (3.1)
Nasal polyp	**8 (4.2)**
Persistent nasal symptoms	**32 (16.8)**
Persistent ocular symptoms	**15 (10.7)**
Immunotherapy	**5 (2.6)**
Pets ownership	**37 (19.4)**
Cat	20 (10.5)
Dog	4 (2.1)
Other	13 (6.8)
Applying a pollen avoidance method	**29 (15.2)**
Use of masks and glasses	25 (13.1)
Staying away from woodlands and lawns	23 (12)
Keeping doors and windows closed	13 (6.8)
Tracking air pollen reports	6 (3.1)

patients at the time of diagnosis are shown in Figures 1 A and B. The most common symptoms of the patients at the time of diagnosis and in the last year were observed in March, April, May and June. The symptoms of the patients by months at the time of diagnosis and in the last year are shown in Figures 2 A and B.

The nasal and ocular symptoms of the patients in the last year were compared with the previous years. There was an increase in nasal symptoms in 49 (25.7%) patients, a decrease in 78 (40.8%) and no change in 64 (33.5%). There was an increase in ocular symptoms in 26 (18.7%) patients, a decrease in 65 (46.7%) and no change in 48 (34.5%). In 39 (72.7%) patients there was at least one ocular symptom accompanying nasal symptoms. Comparison of nasal and ocular symptoms in the last year with previous years is shown in Figure 3.

Comparisons were made between the patients whose nasal symptoms increased and decreased. In patients

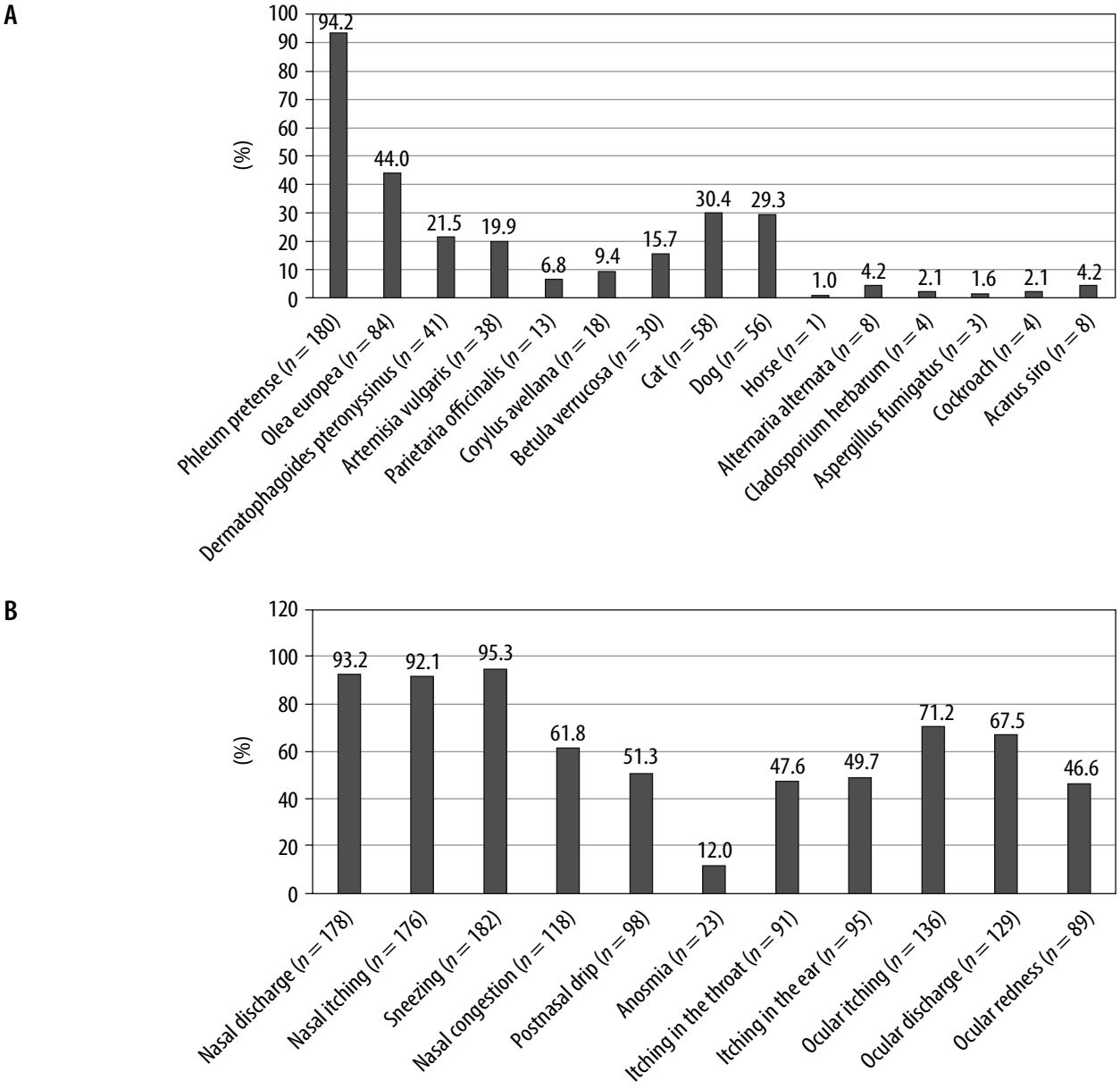

FIGURE 1. **A** – Sensitizing allergens (skin prick test). **B** – Symptoms of patients at the time of diagnosis

whose nasal symptoms increased, medication use was higher ($p = 0.003$). The implementation of pollen avoidance measures was significantly higher in patients whose nasal symptoms decreased ($p = 0.008$). Medication use was higher in patients whose ocular symptoms increased ($p = 0.018$) (Table 3).

DISCUSSION

In this study, the long-term natural course of the disease was evaluated in patients with a diagnosis of SAR, and it was observed that the natural course of the disease was variable in long-term follow-up. A decrease in nasal and ocular symptoms was determined in 40.8% and 46.7% of patients, respectively. Variable results have been reported in previous studies investigating the natural course of AR. In a study by Kong *et al.* [5], 1211 children with AR were followed up for 5 years, after which the prevalence of positive nasal symptoms was 29.4%. Thus, it was concluded that the natural course of AR in children is variable. Danielsson and Jessen [6] applied a questionnaire to 82 AR patients who were not administered immunotherapy. At the end of 12 years of follow-up, symptoms had decreased in 39% of patients, not changed in 39% and increased in 21%. In a study by Linna *et al.* [7], the prognosis of AR was investigated in 154 children. It was reported that symptoms completely resolved in only 15 (10%) patients, conjunctival symptoms decreased in almost all patients

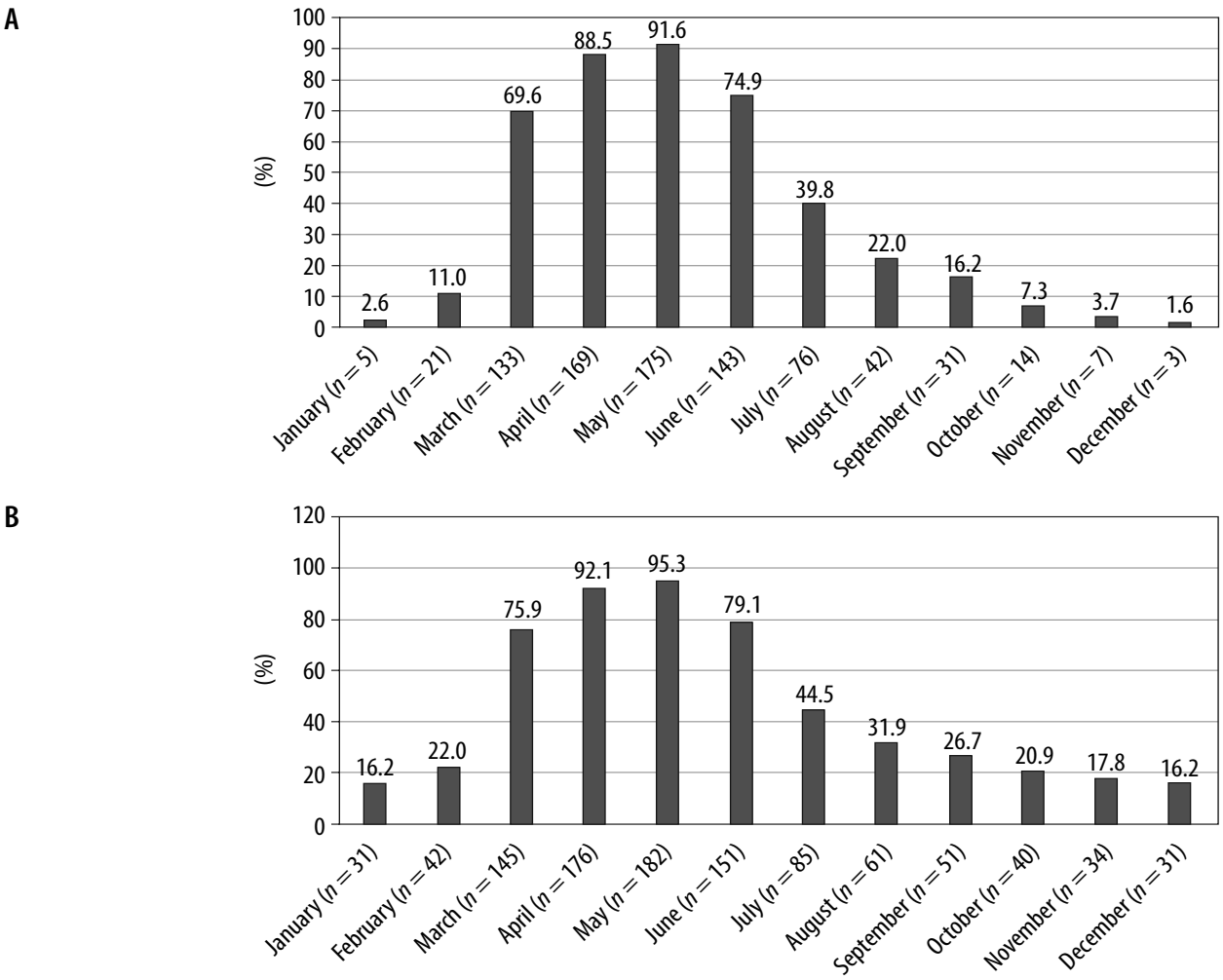

FIGURE 2. **A** – Distribution of symptoms of patients at the time of diagnosis by months. **B** – Distribution of symptoms of patients by months in the last year

with or without medication, and perennial AR developed in 25 (23%) of 110 children with SAR during follow-up. In the current study, the nasal symptoms of 32 (16.8%) patients and ocular symptoms of 15 (10.7%) patients became persistent in long-term follow-up.

Various factors such as the duration of exposure to the allergen, geographic regions, climate changes, medications, and pollen avoidance measures can affect the natural course of SAR. In the current study, it was found that compared to the patients with increased symptoms, patients with fewer symptoms more commonly applied pollen avoidance strategies (p = 0.008). However, it was interesting that there were very few patients using these strategies (n = 29, 15.2%). Allergen avoidance measures and environmental precautions are a part of the AR treatment strategy, together with pharmacological therapy and allergen-specific immunotherapy. It is aimed at minimizing allergen exposure during the pollen season by pollen allergic patients taking avoidance measures [8]. There are various avoidance measures such as staying away from wooded and grassy environments during the pollen seasons, following the weather forecasts, keeping doors and windows of the house closed, using pollen filters, and using masks and eyeglasses. However, there are only a few clinical studies that have evaluated the clinical effectiveness of pollen avoidance measures. In one prospective study from our clinic, 70 patients with grass pollen sensitization were followed up for three successive grass pollen seasons. One group of patients received standard medical treatment, and the other group of patients wore wraparound style glasses in addition to standard medical treatment. The authors found a decrease in nasal and ocular symptoms and a significant improvement in the quality of life in the group that used protection with glasses [9]. There are articles in the literature showing that the use of nasal filters during the pollen period reduces nasal symptoms in patients with SAR [10, 11]. The use of face masks during the COVID-19 pandemic has been shown to decrease AR symptoms [12].

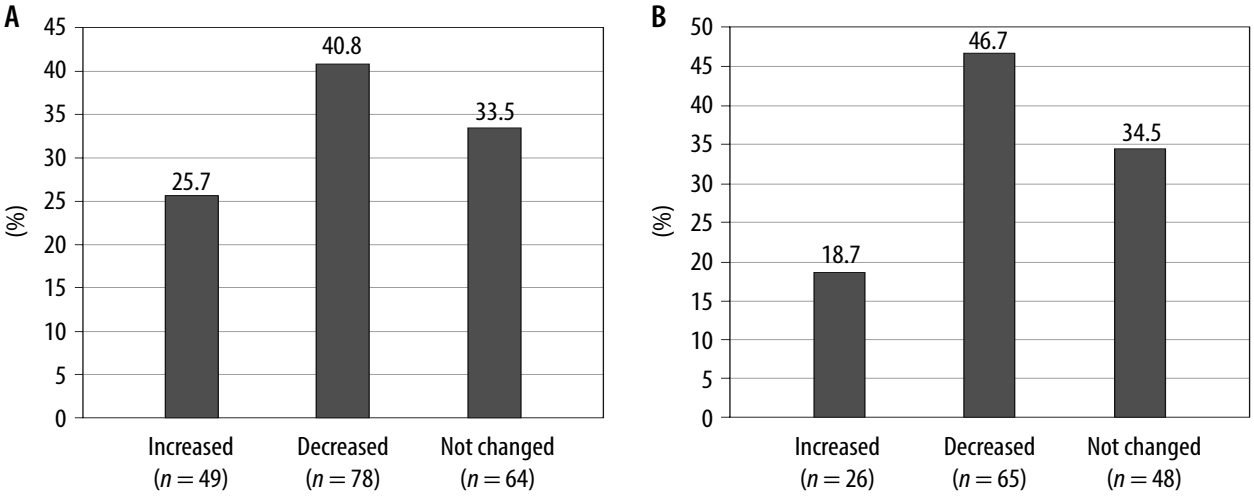

FIGURE 3. Comparison of nasal (**A**) and ocular (**B**) symptoms in the last year with previous years

TABLE 3. Comparison of patients with increasing and decreasing symptoms

Parameter	Increasing nasal symptoms ($n = 49$)	Decreasing nasal symptoms ($n = 78$)	*P*-value
Age [years] median (min.–max.)	28.50 (19–56)	28 (18–59)	0.516¶
Gender (male) *n* (%)	22 (44.8)	33 (42.3)	0.774*
BMI [kg/m^2] mean ± SD	24.64 ±3.31	24.58 ±3.91	0.935§
Eosinophils [cells/µl] median (min.–max.)	150 (0–500)	250 (0–900)	0.330¶
SAR duration [years] median (min.–max.)	14.50 (10–20)	14.50 (10–27)	**0.013¶**
Nasal surgery (yes) *n* (%)	5 (10.2)	11 (14.1)	0.519*
Moved to another geographical area (yes) *n* (%)	11 (22.4)	21 (26.9)	0.572*
Smoking (yes) *n* (%)	19 (38.7)	21 (26.9)	0.162*
Pet ownership (yes) *n* (%)	11 (22.4)	14 (17.9)	0.535*
Regular or seasonal drug intake for SAR (yes) *n* (%)	45 (91.8)	54 (69.2)	**0.003***
Immunotherapy (yes) *n* (%)	2 (4)	2 (2.5)	0.634*
Applying a pollen avoidance measure (yes) *n* (%)	3 (6.1)	19 (24.3)	**0.008***
Parameter	**Increasing ocular symptoms ($n = 26$)**	**Decreasing ocular symptoms ($n = 65$)**	***P*-value**
Age [years] median (min.–max.)	28.50 (19–56)	28 (18–59)	0.493¶
Gender (male) *n* (%)	10 (38.4)	30 (46.1)	0.504*
BMI [kg/m^2] mean ± SD	24.35 ±3.70	24 ±3.86	0.691§
Eosinophils [cells/µl] median (min.–max.)	100 (0–500)	200 (0–900)	0.418¶
SAR duration [years] median (min.–max.)	14.50 (10–20)	14.50 (10–27)	0.064¶
Nasal surgery (yes) *n* (%)	1 (3.8)	8 (12.3)	0.437#
Moved to another geographical area (yes) *n* (%)	7 (26.9)	14 (21.5)	0.582*
Smoking (yes) *n* (%)	10 (38.4)	16 (24.6)	0.187*
Pet ownership (yes) *n* (%)	5 (19.2)	13 (20)	0.934*
Regular or seasonal drug intake for SAR (yes) *n* (%)	25 (96.1)	48 (73.8)	**0.018#**
Immunotherapy (yes) *n* (%)	2 (7.6)	1 (1.5)	0.195#
Applying a pollen avoidance measure (yes) *n* (%)	2 (7.6)	16 (24.6)	0.067*

*χ^2 test, #Fisher's exact test, §Student's *t* test, ¶Mann-Whitney U test.

Today, the most effective treatment method that changes the natural course of AR is immunotherapy. It has been proven that immunotherapy prevents progression to asthma and new allergen sensitization in AR [13]. In a Cochrane systematic meta-analysis comparing the use of subcutaneous immunotherapy with placebo in patients with SAR, it was observed that seasonal symptoms and drug intake were lower in the immunotherapy group [14]. In a meta-analysis comparing subcutaneous immunotherapy with pharmacotherapy, subcutaneous immunotherapy was seen to be at least as potent as pharmacotherapy in controlling the symptoms of SAR [15]. In the current study, there was no significant difference between the groups with increasing and decreasing nasal and ocular symptoms in respect of immunotherapy, but the number of patients who received immunotherapy for SAR was very low (n = 5). Another important finding of the current study was that the use of medication was higher in the group with increased nasal or ocular symptoms. This may be related to the intake of more medication to achieve symptom control in patients with increased symptoms.

Pollens are classified in three groups as tree, grass, and weed pollens. The environmental distribution of pollens varies during spring and summer according to climate and geographical regions. Tree pollen in early spring, grass pollen in late spring-early summer and weed pollen from mid-summer to autumn cause allergic symptoms in Turkey [16]. In atmospheric pollen studies, Cupressaceae/Taxaceae, Pinus and Gramineae pollens have been identified as the most common pollen types in Turkey [17]. In the current study, many of the patients were sensitized to Gramineae (Phleum pratense, n = 180, 94.2%) pollens and symptoms were most common in March, April, May and June. Many of the patients lived in the Central Anatolia Region (n = 183, 95.8%). Grass pollen is the most common type of herbaceous pollen in Turkey, in almost all geographical areas and in all seasons [18].

SAR affects the quality of life of the patient, and there may also be negative effects on school performance, work productivity, and cognitive function. It imposes a serious economic burden on society, including healthcare expenses [3]. Comorbid diseases such as allergic conjunctivitis, asthma, sinusitis, otitis, and sleep disorders can be frequently observed in patients with AR [18]. Approximately 60% of patients with AR have concomitant allergic conjunctivitis. Ocular symptoms are more common, especially in patients with pollen allergy [19]. In patients with rhinitis, the prevalence of asthma varies between 10% and 40%. AR complicates asthma control and increases the frequency of asthma attacks and asthma-related hospitalizations [18]. In the current study, 139 (72.7%) patients had at least one conjunctivitis symptom and 93 (48.7%) patients had asthma accompanying SAR.

This study had some limitations, primarily that the change in symptoms over the years was evaluated based on the patient statements alone, which may not always provide objective measurements. Second, no standard method was used to measure the amount of pollen in the air. The distribution of allergy-causing pollens in the air, especially wind-pollinated allergens, is usually dependent on climate parameters. The climates of countries may vary from year to year, and this can affect the amount of pollen in the air and change the symptom perception of the patients. Despite these limitations, this study is unique in respect of evaluating the long-term prognosis of pollen-allergic adults in Turkey.

CONCLUSIONS

The natural course of SAR in long-term follow-up is variable. The implementation of effective pollen avoidance measures can reduce the disease severity in patients with SAR in long-term follow-up.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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