

Comparison of clinical differences between patients with allergic rhinitis and nonallergic rhinitis

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Abstract

We conducted a retrospective study to investigate the clinical differences between subtypes of rhinitis patients. Our findings were based on a detailed history and nasal examination. The study population was made up of 910 patients who had at least two rhinitis symptoms. These patients were categorized into one of three rhinitis groups: nonallergic rhinitis (NAR), seasonal allergic rhinitis (SAR), and perennial allergic rhinitis (PAR); there were 212 patients (23.3%) in the NAR group, 473 (52.0%) in the SAR group, and 225 (24.7%) in the PAR group. In addition to demographic data, we compiled information on the season when each patient presented, specific symptoms and their triggers, parental history, associated allergic diseases (e.g., skin, lung, and eye allergies), and nasal examination findings. The SAR patients represented the youngest of the three groups. Most SAR patients presented in spring and summer, and this group had the highest incidence of eye itchiness, pharyngeal itchiness, eye redness, and palatal itchiness. In terms of triggering factors, a visit to a green area was significantly more common in the SAR patients, while detergent odor, sudden temperature change, and cold air were significantly more common in the NAR patients. On nasal examination, a pale nasal mucosa was significantly more common in the NAR group. In clinical practice, it is crucial to differentiate between allergic and nonallergic rhinitis. We conclude that relevant information from

the history can predict allergic rhinitis. Future studies of prevalence should take into consideration the important findings of our study, including the significance of age and the seasonality of exacerbation of rhinitis symptoms.

Introduction

Ascertaining the exact prevalence of allergic and nonallergic rhinitis is challenging because it can be difficult to differentiate the two.^{1,2} Questionnaire-based epidemiologic studies may overestimate the prevalence of allergic rhinitis by incorrectly including patients with nonallergic rhinitis.³ One way to improve differentiation is to obtain a detailed history. We conducted a study to investigate the clinical differences between subtypes of rhinitis based on a detailed history, as well as on nasal examination findings.

Patients and methods

Our study population was selected from among 1,349 registered patients who had been referred to the Department of Otorhinolaryngology at the Inonu University Faculty of Medicine in Malatya, Turkey, with at least two of three symptoms of chronic rhinitis: rhinorrhea, nasal congestion/obstruction, and sneezing. Patients who were either undiagnosed or diagnosed with another disease were excluded from the study. For example, we excluded patients with a diagnosis of chronic recurrent sinusitis and/or nasal polyposis, those whose dominant symptom was nasal obstruction, and those with a septal deviation.

A total of 910 patients—364 males and 546 females, aged 6 to 72 years (mean: 30.8)—met our study criteria (table 1). Patients were categorized into three groups on the basis of their type of rhinitis; 212 patients (23.3%) had nonallergic rhinitis (NAR), 473 (52.0%) had seasonal allergic rhinitis (SAR), and 225 (24.7%) had perennial allergic rhinitis (PAR). Patients had been diagnosed by a detailed allergy history (including clinical symptoms,

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season of the year, triggers, and parental history), a nasal examination, and a skin-prick test. Patients with rhinitis symptoms who had had a negative reaction to their skin-prick test were included in the NAR group.

Of the 212 patients with NAR, 6 were diagnosed with hormonal rhinitis, 5 with rhinitis medicamentosa, and 2 with nonallergic rhinitis with eosinophilia syndrome (NARES). None of the NAR patients had a history of occupational rhinitis. The remaining 199 patients all had idiopathic rhinitis.

History. In addition to demographic data, we analyzed the history for information on the season when each patient initially

presented, their specific symptoms and their triggers, their description of any nasal discharge (i.e., viscosity and color), their parental history of allergies, and any associated allergic diseases (e.g., skin, lung, and eye allergies) they might have had.

Nasal examination. Both anterior rhinoscopy and nasal endoscopy were used to perform nasal examinations, and the results were entered into an electronic database. Points of interest were the viscosity and color of the nasal secretions and changes in the nasal mucosa. We did not take into consideration other organic abnormalities that are independent of inflammatory rhinitis.

Allergy testing. Skin-prick tests were performed with multiple-test applicators (Multi-Test II; Lincoln Diagnostics; Decatur, Ill.) and the standardized allergen extract solutions with negative (physiologic saline/0.4% phenol) and positive (histamine 1+999 w/v/0.4% phenol) controls (Allergopharma; Merck KGaA; Darmstadt, Germany). The allergy panel, based on the allergy profile in the south of Turkey, consisted of the following indoor and outdoor allergens:

- grasses: velvet grass, orchard grass, rye grass, timothy grass, bluegrass, and meadow fescue;
- cereals: barley, oat, wheat, and rye;
- weeds: mugwort, stinging nettle, dandelion, and English plantain;
- trees: alder, hazel, poplar, elm, and sallow (all early blossoming), as well as birch, European birch, oak, and plane (all blossoming midyear);

Table 1. Sex and age distribution

	NAR (n = 212)	SAR (n = 473)	PAR (n = 225)
Sex, n (%)			
Male	82 (38.68)	197 (41.65)	85 (37.78)
Female	130 (61.32)	276 (58.35)	140 (62.22)
Age, yr			
Mean (SD)*	34.51 ± 13.21	28.86 ± 12.39	31.40 ± 12.09
Range	7 to 72	6 to 71	8 to 65
Age groups, n (%)			
6 to 20 yr	25 (11.79)†	131 (27.69)†	43 (19.11)
21 to 40 yr	120 (56.60)	254 (53.70)	124 (55.11)
≥41 yr	67 (31.60)†	88 (18.60)†	58 (25.78)

* Based on mean age, the SAR group was significantly younger than both the NAR and PAR groups ($p < 0.01$).

† The differences between the NAR and SAR groups in these two age categories was statistically significant ($p < 0.05$).

• mites: *Dermatofagoides farinea* and *Dermatofagoides pteronyssinus*;

• molds I: *Alternaria alternata*, *Botrytis cinerea*, *Cladosporium herbarum*, *Curvularia lunata*, *Fusarium moniliforme*, and *Helminthosporium halodes*;

• molds II: *Aspergillus fumigatus*, *Mucor mucedo*, *Penicillium notatum* (now called *Penicillium chrysogenum*), *Pullularia pullulans*, *Rhizopus nigricans*, and *Serpula lacrymans*;

• animal epithelia/dander I: golden hamster, dog, rabbit, cat, and guinea pig;

• animal epithelia/dander II: horse, cow, sheep wool, pig, and goat;

• cockroach: *Blattella germanica*.

Statistical analysis. Normal distribution of the three groups and the homogeneity of variances were analyzed by the Kolmogorov-Smirnov test and the Levene test, respectively. One-way ANOVA and further analysis by Scheffé or Dunnett T3 test according to the equality of variances and multiple chi-square tests were used for the comparison of groups. Statistical significance was determined as $p < 0.05$.

Results

Demographics. There were no significant differences among the three groups in terms of sex distribution (table 1).

Based on mean age, the SAR group was significantly younger than both the NAR and PAR groups ($p < 0.01$).

For further analysis of age, patients were classified into three subgroups: 6 to 20 years, 21 to 40 years, and 41 years and older. The youngest subgroup contained a significantly greater proportion of SAR patients than NAR patients ($p < 0.05$), and the oldest subgroup contained a significantly greater proportion of NAR patients than SAR patients ($p < 0.05$). No significant differences were noted in the middle age group. Expressed another way, SAR was more likely to affect younger patients and NAR was more likely to affect older patients. No significant differences were found between the PAR group and either of the other two groups, regardless of age category (table 1).

History. Information gathered from the history included the season of the initial presentation, symptoms, nasal discharge, triggers, parental history, and known concomitant allergies (e.g., allergic eczema, asthma, and allergic conjunctivitis):

- **Seasonality.** Compared with the NAR and PAR groups, a significantly greater proportion of SAR patients presented in the spring ($p < 0.05$) and summer ($p < 0.05$) and a significantly smaller proportion presented in winter ($p < 0.01$) (table 2).

- **Symptoms.** Symptoms of rhinitis are shown in table 2 according to their overall prevalence.

Sneezing was significantly less common in the NAR group than in the other two groups ($p < 0.05$).

Eye itchiness, pharyngeal itchiness, eye redness, and palatal itchiness were all significantly less common in the NAR group and significantly more common in the SAR group ($p < 0.01$ for all).

Postnasal drip ($p < 0.01$), headache ($p < 0.01$), and smell disturbance ($p < 0.05$) were all less common in the SAR group than in the other two groups.

No significant differences were found among the three groups in the prevalence of rhinorrhea, nasal congestion/obstruction, nasal itchiness, and tearing.

- **Triggers.** Triggering factors are shown in table 3 according to their overall prevalence. The leading triggering factors in the NAR group were outdoor dust, detergent odor, other strong odors, and a sudden temperature change. In the SAR group, the two most common triggers by far were a visit to a green area and outdoor dust.

Intergroup comparisons revealed that detergent odor, sudden temperature change, and cold air were significantly associated with NAR ($p < 0.01$), and a green area visit was significantly associated with SAR ($p < 0.01$).

- **Nasal discharge.** Analyses of information obtained from the history about the viscosity and color of the nasal discharge revealed no significant differences among the three groups. In the great majority of patients, the discharge was serous (NAR: 90.56%; SAR: 93.87%; PAR: 89.78%) and colorless (NAR: 95.75%; SAR: 94.93%; PAR: 91.11%).

- **Parental history.** There were no statistically significant differences among groups in parental history. Among all patients whose parental history was known, a positive allergy history was present in 13.23% of mothers and 6.38% of fathers.

- **Concomitant allergies.** No significant differences were found in the presence of concomitant allergies. Among the entire study population a dermatologic allergy was present in 13.30% of patients, allergic ocular disease in 9.12%, and asthma in 7.58%.

Table 2. Season of first visit and presenting symptoms

	NAR (n = 212)	SAR (n = 473)	PAR (n = 225)
Season, n (%)			
Winter	48 (22.64)	41 (8.67)*	49 (21.78)
Spring	59 (27.83)	153 (32.35)†	61 (27.11)
Summer	42 (19.81)	182 (38.48)†	55 (24.44)
Autumn	63 (29.72)	97 (20.51)	60 (26.67)
Symptom, n (%)			
Sneezing	180 (84.91)†	436 (92.18)	204 (90.67)
Rhinorrhea	173 (81.60)	398 (84.14)	191 (84.89)
Nasal C/O	161 (75.94)	328 (69.34)	160 (71.11)
Nasal itchiness	130 (61.32)	321 (67.86)	149 (66.22)
Tearing	115 (54.25)	278 (58.77)	133 (59.11)
Eye itchiness	100 (47.17)*	284 (60.04)*	115 (51.11)
Postnasal drip	115 (54.25)	215 (45.45)*	133 (59.11)
Pharyngeal itchiness	67 (31.60)*	218 (46.09)*	97 (43.11)
Eye redness	69 (32.55)*	215 (45.45)*	88 (39.11)
Headache	91 (42.92)	158 (33.40)*	98 (43.56)
Palatal itchiness	42 (19.81)*	196 (41.44)*	68 (30.22)
Smell disturbance	74 (34.91)	120 (25.37)†	64 (28.44)

* $p < 0.01$.

† $p < 0.05$.

Key: C/O = congestion/obstruction.

Nasal examination. Data on nasal examinations are shown in table 4. A serous discharge was more common than a purulent discharge in all three groups, with no significant differences among the groups. In most cases, examination revealed that the nasal mucosa was pale; a pale mucosa was significantly associated with NAR ($p < 0.01$). According to our overall nasal examination criteria, normal results were found in significantly fewer NAR patients (25.47%) than SAR patients (40.80%) and PAR patients (35.11%) ($p < 0.01$).

Allergy testing. None of the patients with NAR was found to be allergic to any allergen. Monosensitization rates were 42.07% in the SAR group and 43.11% in the PAR group. Polysensitization rates (2 to 7 positive reactions) were significantly more common in the PAR group (47.11%) than in the SAR group (32.35%) ($p < 0.05$).

Discussion

The history, nasal examination, and skin-prick testing for common aeroallergens have been described as the gold standard for the diagnosis of allergic rhinitis.⁴ In our study, all patients were meticulously investigated at their first visit and reassessed during at least two more follow-up visits. We found that our SAR group was more than twice as big as our NAR and PAR groups, which was consistent with the findings of a study by Bauchau and Durham.⁵

Other reports have suggested that NAR is not rare in the general population.³ Patients are diagnosed with NAR on the basis of negative allergen reactions to skin-prick testing and a negative allergy history. Few of them could be further diagnosed into specific subgroups of NAR (e.g., hormonal rhinitis, rhinitis medicamentosa, and NARES); most were classified as having "idiopathic rhinitis." In our study, approximately one-fourth of all patients were in the NAR group, a

Table 3. Triggering factors

Trigger, n (%)	NAR (n = 212)	SAR (n = 473)	PAR (n = 225)
Outdoor dust	56 (26.42)	163 (34.46)	77 (34.22)
Green area visit	16 (7.55)	176 (37.21)*	40 (17.78)
Strong odors (e.g., perfume)	35 (16.51)	53 (11.21)	26 (11.56)
Sun exposure	24 (11.32)	60 (12.68)	29 (12.89)
Detergent odor	39 (18.40)*	48 (10.15)	22 (9.78)
Smoke (burning tobacco, wood)	25 (11.79)	48 (10.15)	31 (13.78)
Sudden temperature change	35 (16.51)*	40 (8.46)	28 (12.44)
Indoor dust	25 (11.79)	43 (9.09)	26 (11.56)
Cold air	23 (10.85)*	22 (4.65)	17 (7.56)
Foods	12 (5.66)	17 (3.59)	13 (5.78)
Occupational agents	6 (2.83)	10 (2.11)	11 (4.89)
Animals	5 (2.36)	10 (2.11)	9 (4.00)

* $p < 0.01$.

proportion that is in accordance with the findings of a study by Mølgaard et al.⁶

An important finding of our study was that the patients in the SAR group were significantly younger overall than the patients in each of the other groups. In subgroup analysis, SAR was more common in patients 20 years of age and younger, and NAR was more common in patients aged 41 years and older. The age group comprising 21 to 40 years could not be characterized in terms of the type of rhinitis, since NAR, SAR, and PAR were equally distributed among this group (approximately 55% each.) Based on these findings, we conclude that

Table 4. Nasal examination findings

Finding, n (%)	NAR (n = 212)	SAR (n = 473)	PAR (n = 225)
Discharge			
Serous discharge	84 (39.62)	202 (42.71)	91 (40.44)
Purulent discharge	6 (2.83)	24 (5.07)	14 (6.22)
Other/none	122 (57.55)	247 (52.22)	120 (53.33)
Mucosa			
Pale nasal mucosa	151 (71.23)*	280 (59.20)	146 (64.89)
Edematous nasal mucosa	20 (9.43)	55 (11.63)	27 (12.0)
Bluish nasal mucosa	12 (5.66)	17 (3.59)	6 (2.67)
Other/normal	29 (13.68)	121 (25.58)	46 (20.44)
Polypoid formation	0	2 (0.43)	3 (1.33)

* $p < 0.01$.

studies of the epidemiology of allergic rhinitis should take age into consideration.

In our study, patients with SAR experienced a pollinosis-related increase in symptoms during the spring and summer. Likewise, a study by Ciprandi et al found that patients with SAR reported more symptoms between March and September.⁷ Thus, any increase in the frequency or severity of seasonal symptoms should also be investigated in epidemiologic studies.

The symptoms of allergic and nonallergic rhinitis can be similar.⁶ In our study, the four most common symptoms independent of the subgroups were sneezing, rhinorrhea, nasal congestion/obstruction, and nasal itchiness. At a minimum, these four symptoms affected roughly two-thirds of all our rhinitis patients. As for rhinorrhea, asking patients about the features of any nasal discharge could provide a valuable clue in differentiating rhinitis from sinusitis. However, in our study it was not at all useful in differentiating among the specific types of rhinitis, since more than 90% of all patients complained of serous and colorless rhinorrhea.

All common symptoms can be used for the diagnosis of allergic rhinitis. The mostly histamine-related symptoms—ocular, pharyngeal, and palatal itchiness and eye redness—were significantly more common in our SAR patients and significantly less common in our NAR patients. Others have reported ocular symptoms in patients allergic to outdoor allergens.⁴

All rhinitis patients may exhibit an exaggerated response to nonspecific stimuli.^{8,9} In our study, physical and chemical triggers of rhinitis symptoms—such as detergent odor, sudden temperature change, and cold air—were found to cause a hyper-reaction of the nasal mucosa, particularly in patients with NAR. However, patients with allergic rhinitis were also reactive to these irritative factors. Therefore, sensitivity to physical and chemical triggers is not helpful in distinguishing between allergic and nonallergic rhinitis.

Sudden changes in temperature were previously found to induce nasal symptoms in patients with allergic rhinitis.¹⁰ Based on our findings, the onset of rhinitis symptoms associated with a visit to a green area or some activities in rural areas could be a valuable positive sign for SAR.

Since allergic rhinitis is an etiologically multifactorial disease with genetic and environmental components,⁴ one could expect that a positive family history would be useful in the differential diagnosis. However, in our study we could not find any significant association between allergic rhinitis and a positive parental history. Patients with NAR whose relatives are allergic are often

referred to an allergy clinic. In a survey study, Bachert et al found that asthma and skin allergy as comorbidities were significantly more prevalent in patients with allergic rhinitis than in patients with nonallergic rhinitis.³ Our study could not confirm this.

The most common findings on nasal examination in our study were serous drainage and a pale nasal mucosa. Pale nasal mucosa was significantly more common in the NAR group. The character of nasal mucosal secretions during the nasal examination was not found to be relevant in differentiating the subgroups. Very few patients presented with a bluish mucosa.

Skin-prick testing is the current reference method in rhinitis diagnosis.¹¹⁻¹⁴ It is highly reproducible by trained investigators.¹⁵⁻¹⁷ Correlating the results of skin-prick testing with the clinical history is essential for the management of allergic rhinitis. Testing should be performed meticulously and in accordance with previously described technical processes.¹⁸ Sufficient wheal-and-flare reactions should be obtained with a positive control solution.¹⁸

Skin-prick testing was performed in our study as described in the Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update⁴ with the relevant allergens of our region, including the major grasses, cereals, pollens, and mites. Some studies have found that most patients were sensitized to many different allergens throughout the entire year.^{19,20} In our study, fewer than half of the SAR and PAR patients were monosensitive, a finding that is consistent with those of previous studies.²¹ Polysensitization was significantly more common in the PAR group; more than half of them were allergic to both indoor and outdoor allergens.

Despite our precise categorizing of patients as having either NAR, SAR, or PAR in actual clinical practice, rhinitis is more complex than that, as patients can have both allergic and nonallergic components (mixed rhinitis). Allergic rhinitis patients may also exhibit nasal hyper-reactivity to the same nonspecific stimulants as do NAR patients. In our study, 4.65 to 12.44% of patients with allergic rhinitis experienced symptoms after exposure to one of four nonallergic triggers: strong odors, detergent odor, sudden temperature change, and cold air (table 3). Settipane reported that 34% of rhinitis patients had mixed rhinitis.²²

In clinical practice, it is not always easy to diagnose and subgroup rhinitis patients at the first visit, and further follow-up is often necessary. Therefore, some of the patients at our ENT clinic were not included in our study because they remained undiagnosed despite

a positive skin-prick test. Quan et al recently discussed the clinical value of subgrouping rhinitis patients.²³

At our clinic, we insist on establishing a correct diagnosis based on a structured history, nasal examination, skin-prick testing, and long-term follow-up, all of which lead to better treatment. It is important to realize that some patients who are diagnosed with SAR at their first visit might actually have mixed rhinitis and need medical help to treat the nonallergic component of the mixed rhinitis, even in the off-season.

The main conclusions we draw from this clinical-experience-based study are that relevant information obtained from the history can be used to predict allergic rhinitis. Our study is one of the rare studies to investigate the differences and similarities between allergic and nonallergic rhinitis. Besides demographic and clinical data, we report nasal examination findings. Future prevalence studies should take into consideration patients' age and the seasonality of exacerbation of rhinitis symptoms, which are important factors in diagnosing allergic rhinitis, particularly for SAR.

In addition to the common rhinitis symptoms, histamine-related symptoms such as itchiness and ocular redness usually indicated allergic rhinitis in our study. The presence of a watery nasal discharge did not differentiate among rhinitis types, nor did common physical and chemical triggers, with the exception of a green area visit and some activities in rural areas.

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