

Differences and Similarities between Allergic and Nonallergic Rhinitis in a Large Sample of Adult Patients with Rhinitis Symptoms

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Key Words

Allergic rhinitis • Non allergic rhinitis • Skin prick test • Peak nasal inspiratory flow • Blood eosinophil • Nasal eosinophil • Visual analog scale • Receiver operating characteristic

Abstract

Background: Allergic rhinitis (AR) and nonallergic rhinitis (NAR) may present with different clinical and laboratory characteristics. **Methods:** A total of 1,511 consecutive patients, aged 18–81 years, diagnosed with rhinitis, 56% females and 44% males, underwent complete allergic evaluation including skin prick test, blood eosinophil counts, nasal eosinophil counts, peak nasal inspiratory flow (PNIF) measurement and evaluation of nasal symptoms using a visual analog scale (VAS). **Results:** A total of 1,107 patients (73%) had AR, whereas 404 (27%) had NAR. Patients with NAR were older and predominantly female. A higher nasal eosinophils count was associated with AR and a lack of clinical response to antihistamines. AR patients had more sneezing and nasal pruritus, whereas NAR was characterized mainly by nasal ob-

struction and rhinorrhea. AR patients had more severe symptoms and recurrent conjunctivitis, whereas NAR patients had slightly more frequent episodes of recurring headaches as well as olfactory dysfunction. PNIF, blood eosinophil counts and VAS of nasal symptoms were higher in patients with AR. In a final logistic regression model, 10 variables were statistically different between AR and NAR: age [OR 0.97 (95% CI 0.96–0.98)], sneezing [OR 4.09 (95% CI 2.78–6.00)], nasal pruritus [OR 3.84 (95% CI 2.60–5.67)], mild symptoms [OR 0.21 (95% CI 0.09–0.49)], intermittent/severe nasal symptoms [OR 3.66 (95% CI 2.06–6.50)], VAS [OR 1.06 (95% CI 1.04–1.08)], clinical response to antihistamines [OR 22.59 (95% CI 13.79–37.00)], conjunctivitis [OR 4.49 (95% CI 2.86–7.05)], PNIF [OR 1.01 (95% CI 1.00–1.01)] and nasal eosinophil counts [OR 1.14 (95% CI 1.10–1.18)]. Receiver operating characteristic analysis showed high predictive accuracy for a model including these variables independently of the diagnosis of AR/NAR (cutoff <0.74). **Conclusions:** We showed that the several clinical and laboratory parameters reported above may help to reinforce or exclude the diagnosis of AR obtained with skin prick test.

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Introduction

Rhinitis is an inflammation of nasal mucosa resulting in nasal secretions that are nonpurulent and watery. In noninfectious rhinitis the eosinophils are the predominant inflammatory cell type found [1]. Noninfectious rhinitis includes both allergic rhinitis (AR) and nonallergic rhinitis (NAR). AR is further divided into two groups: seasonal and perennial. An alternative classification system based on the severity of the nasal symptoms and frequency has been proposed by the Allergic Rhinitis and Its Impact on Asthma (ARIA) trial [2, 3].

NAR is a less well-defined condition oftentimes being a diagnosis of exclusion, considered when a patient is found to have negative skin tests or serum specific IgE, in the absence of any sign of infection [4]. Despite having different characteristics, such as skin test reactivity, AR and NAR may share several common features. Few previous studies have addressed the similarities and differences between AR and NAR in a clinical setting [5, 6].

We report the demographic and clinical similarities and differences between AR and NAR. The primary objective of this study was to find clinical and objective parameters that, in addition to the result of the skin prick test (SPT), were predictive of allergic rhinitis. The second was to identify patient characteristics in accordance with the ARIA classification system.

Methods

All patients over the age of 18 years with a diagnosis of rhinitis were consecutively seen and evaluated in the outpatient allergy office of the Dipartimento di Medicina Clinica e delle Patologie Emergenti of the University of Palermo, Italy. This evaluation consisted of the following: skin test (SPT), blood eosinophil count (b-eos) and a nasal lavage with eosinophil count (n-eos). Assessment symptoms were: sneezing, rhinorrhea, nasal pruritus and nasal obstruction. These were graded with the following scale: 0 = absent, 1 = mild (symptoms were present but not troublesome), 2 = moderate (symptoms were present but did not interfere with normal activity) and 3 = severe (symptoms were troublesome and interfered with normal activity) [7]. The severity of all nasal symptoms was evaluated by patients using a visual analog scale (VAS) [8] and was classified, in accordance with ARIA guideline, as severe if there was one or more of the following items: sleep disturbance; impairment of daily activities, leisure or sport; impairment of school or work; or troublesome symptoms. Rhinitis in the absence of all these qualifiers was classified as mild. The nasal symptoms were also classified as intermittent or persistent with intermittent symptoms defined as the presence of symptoms <4 days a week or <4 weeks

per year and persistent symptoms defined as symptoms more frequent than this [3]. Other symptoms reported by patients that correlated with rhinitis were headache, olfactory dysfunction and dysphonia. Headache and dysphonia were dichotomized and reported as present or absent. Olfactory dysfunction was graded as 0 = normal function, 1 = hyposmia and 2 = anosmia.

The study was approved by the Institutional Review Board of the Dipartimento di Medicina Clinica e delle Patologie Emergenti of the University of Palermo, Italy, and it was conducted according to the Declaration of Helsinki. Authorization of the study was not required according to our institutional policy and the ethical committee of our institution, as procedures done were part of routine diagnostic testing. However, written informed consent for the study was obtained from each patient in compliance with our institutional policy.

Skin Prick Test

Patients underwent SPT on the volar aspect of the forearm, using a standard panel of aeroallergens present in our geographic area (Alk Abellò, Milan, Italy). The panel consisted of the following extracts: grass (*Phleum pratense*, *Dactyla glomerata*, *Festuca elatior*, *Lolium perenne* and *Poa pratensis*); weeds [mugwort (*Artemisia vulgaris*)], pellitory of the wall or sticky weed (*Parietaria judaica* and *Salsola kali*); trees [birch (*Olea europea* and *Cupressus*)]; house dust mite (*Dermatophagoides pteronyssinus* and *D. farinae*); moulds (*Alternaria alternata*, *Cladosporium erbarium* and *Aspergillus fumigatus*); animal dander (cat and dog); negative control (glycerinated saline) and positive control (histamine, 10 mg/ml).

Positive responses were defined as any wheal with a diameter 3 mm greater than the negative control, 15 min after application. The diameter was assessed by measuring the minimal + maximal diameter/2. The wheal diameters were reported for each patient [9, 10].

Eosinophil Counts in Nasal Fluid

Nasal lavage was performed using a disposable metered-dose nasal inhaler (Markos, Monza, Italy) filled with sterile normal saline solution at room temperature. The device consists of a plastic cup with two compartments. The central compartment was filled with sterile saline solution, while the external compartment collected the liquid after washing. Total input of saline solution was approximately 8 ml (4 ml in each nostril for 5 min). To collect the nasal washings, the subjects were instructed to actively breathe during a Valsalva maneuver in order to harvest nasal fluid in the cup. The samples obtained were stored on ice and centrifuged at 400 g for 10 min at 4°C. The individual variation in the recovered versus introduced volume was $86 \pm 8\%$. Nasal eosinophil counts were performed on the nasal lavage. One cytopsin slide for each sample (1×10^{-4} cells in 170 µl per slide) was centrifuged at 10 g for 10 min in a Shandon cytocentrifuge (Shandon Southern Ltd., Runcorn, UK). The slides were immediately fixed in 95% ethyl alcohol, dipped in Wright-Giemsa stain, and examined under oil immersion by light microscopy at a magnification of $\times 400$. Eosinophils were expressed as a percentage of 300 cells counted [7, 11, 12].

All specimens were examined by the same blinded microscopist (V.D.), who did not know the clinical histories, the results of the SPT, the severity of the rhinitis symptoms or the subjects' clinical responses to antihistamines.

Peripheral Blood Eosinophil Counts

Absolute peripheral blood eosinophil counts were determined with a Technicon-H1 blood cell counter (Bayer, Leverkusen, Germany), with the normal range being 0.10–0.40 cells/10³ ml [11].

Visual Analog Scale

To evaluate nasal symptoms we used a VAS. The patients assessed their total nasal symptom scores (sneezing, rhinorrhea, nasal obstruction and nasal itching). Subjects were instructed that 0 indicated 'nasal symptoms not at all bothersome' and that 100 indicated 'nasal symptoms extremely bothersome'. The distance between 0 and the mark the subjects made on the scale was measured with a Digimatic caliper (Mitutoyo, Kawasaki, Japan) [8].

Measurements of Peak Nasal Inspiratory Flow

An In-checkTM peak nasal inspiratory flow meter (Clement Clarke International Ltd., Harlow, UK) was used to measure peak nasal inspiratory flow (PNIF). After blowing their nose, patients forcefully inspired with mouth closed. All measurements were made while sitting and with a good seal around soft facemask. The PNIF was reported as a mean of three consecutive recordings and expressed as liter per minute.

Statistical Analysis

Noncontinuous data are reported as percentages. Continuous variables normally distributed are reported as means $\pm$ standard deviation. Data that are not normally distributed are reported as medians (with interquartile ranges in parentheses) or with the entire distribution for variables with limited number of categories. Comparisons between groups were done by χ^2 test, Student's t test or the Mann-Whitney U test for nominal, continuous normally distributed and continuous nonnormally distributed variables, respectively. Moreover, a multivariate analysis by backward stepwise logistic regression was carried out to determine variables significantly associated with AR. All variables that did differ between subjects with AR ($p < 0.10$, with χ^2 , Student's t test or Mann-Whitney analysis) were initially entered in the model, and the least significant variable was removed one at a time. Goodness of fit of the logistic models was assessed using the Hosmer and Lemeshow test. Several multiple logistic regression models were tested in order to determine the most significant and simplest model with the best available fit for the data available. Based on the regression coefficients obtained for each significant factor chosen by logistic regression, a predictive probability equation was used to generate predicted probability of AR for each individual. Therefore, the probability of having allergic rhinitis (p) was calculated using the following equation:

$$p = e^y / (1 + e^y),$$

where $y = \text{constant} + x_1 \times \text{variable 1} + x_2 \times \text{variable 2} + x_3 \times \text{variable 3} \dots$

Subsequently, we assessed the performance of the algorithm by calculating its sensitivity, specificity, positive likelihood ratio, negative likelihood ratio and area under curve.

All analyses were repeated with sneezing, rhinorrhea, nasal pruritus and nasal obstruction as categorical variables. Analyses were done using the statistical package MedCalc[®] (version 2.7.2) and R statistical software package (version 2.10.0). Probability values less than 0.05 were considered significant.

Table 1. Results of SPT in patients with nasal symptoms

Allergens	Patients mono-sensitized	Patients polysensitized		Total
		to other pollens	to other indoor allergens	
<i>Pollens</i>				
Grass	26	142	255	423
<i>Weeds</i>				
Mugwort	10	83	121	214
Pellitory	152	190	329	671
<i>Trees</i>				
<i>Olea europea</i>	15	153	225	393
<i>Cupressus</i>	15	56	150	221
<i>Indoor allergens</i>				
House dust mite ¹	128	457	25	610
Cat dander	5	85	20	110
Dog dander	2	65	9	76

¹ *D. pteronyssinus* and *D. farinae*. All patients with SPT positive to *D. pteronyssinus* had SPT positive to *D. farinae*. We considered these positivities as one positivity.

Results

Our study population consisted of 1,511 patients: 847 (56%) women and 664 (44%) men, with a mean age of 35.0 years. 1,107 patients, 73% of the whole study population, had a diagnosis of AR by clinical history, physical examination and positive SPT for one or more allergens, reflecting that these patients were referred for allergic evaluation by specialists (table 1). The mean number of allergens to which subjects with AR were sensitized was 2.48. A total of 353 patients (31.8%) were monosensitized. The clinical characteristics of the study population divided into AR and NAR subgroups are summarized in table 2.

Demographic Data

The mean age of patients with AR was significantly lower than that of patients with NAR (33.3 vs. 39.8 years, $p < 0.0001$). The frequency of NAR in women was twice than that of men (67.0 vs. 33.0%, $p < 0.0001$). The duration of nasal symptoms was similar in the two groups (7.0 vs. 7.4 years, $p = 0.3$). The prevalence of other respiratory complications in the upper respiratory tract (i.e., sinusitis, nasal polyposis, laryngitis and otitis) was not significantly different between AR and NAR patients (30.9 vs. 26.1%, $p = 0.07$).

Table 2. Characteristics of the patients (n = 1,511) with AR and NAR

Variable	AR (n = 1,107)	NAR (n = 404)	p
Demographics			
Mean age, years	33.3 ± 11.7	39.8 ± 15.0	<0.0001
Males/female	531/576	133/271	<0.0001
Years of rhinitis	7.0 (6.8)	7.4 (7.0)	0.3
Familiarity	377 (34.0)	106 (26.2)	0.004
Seasonal/perennial nasal symptoms	214/893	70/334	0.4
Smoking			
Active smoker	226 (20.4)	81 (20.0)	0.9
Ex-smoker	103 (9.3)	36 (8.9)	0.8
Passive smoker	255 (23.0)	103 (25.4)	0.3
Nasal symptoms in the last 8 weeks			
Sneezing	997 (90.0)	153 (37.8)	<0.0001
Sneezing ^a	3 (2–3)	0 (0–1)	<0.0001
Rhinorrhea	1,028 (92.8)	377 (93.3)	0.8
Rhinorrhea ^a	2 (1–3)	2 (1–2)	0.0009
Nasal pruritus	974 (87.9)	186 (46)	<0.0001
Nasal pruritus ^a	2 (1–3)	0 (0–1)	<0.0001
Nasal obstruction	1,001 (90.4)	392 (97.0)	<0.0001
Nasal obstruction ^a	2 (1–3)	2 (2–3)	0.001
Total symptoms score ^a	8 (6–10)	5 (4–6)	<0.0001
Nasal symptoms according to the ARIA classification			
Intermittent/persistent	676/431	226/178	0.08
Mild/severe	415/692	272/132	<0.0001
Mild/intermittent	298 (26.9)	198 (49.0)	<0.0001
Severe/intermittent	378 (34.1)	28 (6.9)	<0.0001
Mild/persistent	117 (10.1)	74 (18.3)	<0.0001
Severe/persistent	314 (28.3)	104 (25.7)	0.3
VAS ^a	75 (39–85)	41 (27–73.5)	<0.0001
Medication taken in the last 8 weeks			
Effective response to antihistamines	560 (50.5)	44 (10.8)	<0.0001
Concurrent disorders			
Conjunctivitis	409 (36.9)	54 (13.3)	<0.0001
Complications of upper airway			
Presence of complications	289 (26.1)	125 (30.9)	0.07
Sinusitis	264 (23.8)	123 (30.4)	0.01
Nasal polyposis	152 (13.7)	55 (13.6)	0.9
Laryngitis	187 (16.8)	55 (13.6)	0.1
Otitis media with effusion	52 (4.6)	29 (7.1)	0.07
Other Symptoms			
Recurrent headache	272 (24.5)	124 (30.6)	0.01
Smell	264 (23.8)	120 (29.7)	0.02
Smell ^a	1 (1–1)	0 (0–1)	0.04
Dysphonia	264 (23.8)	101 (25.0)	0.6
Objective tests			
PFIN ^a	110 (80–130)	90 (60–120)	<0.0001
Blood eosinophil counts ^a , cells × 10 ⁻³ μl	0.34 (0.26–0.40)	0.33 (0.20–0.40)	0.06
Nasal eosinophil counts ^a	6 (4–9)	2 (1–5)	<0.0001

Figures in parentheses are percentages unless indicated otherwise.

^a Medians with 25th–75th percentiles in parentheses.

Cigarette Smoke Exposure

There was no difference in cigarette exposure found between AR and NAR patients. Specific results are as follows: active smoker (20.4 vs. 20.0%, $p = 0.9$), ex-smoker (9.3 vs. 8.9%, $p = 0.8$) and passive smoker (23.0 vs. 25.4%, $p = 0.3$).

Conjunctivitis

AR was characterized by more frequent episodes of conjunctivitis (36.9 vs. 13.3%, $p < 0.0001$).

Nasal Symptoms

When considering specific symptoms of rhinitis, both sneezing (90.0 vs. 37.8%, $p < 0.0001$) and nasal itching (87.9 vs. 46.0%, $p < 0.0001$) were more frequent in patients with AR, whereas the percentage of patients with rhinorrhea (92.8 vs. 93.3%) was similar in the two groups. On the other hand, the percentage of patients with nasal obstruction was greater among patients with NAR (97.0 vs. 90.0%, $p < 0.0001$).

Nasal Symptoms According to the ARIA Classification

Using the ARIA criteria for classification of rhinitis we found a total of 44% of the subjects with NAR had had persistent symptoms within the last 8 weeks as compared to 38.9% of the subjects with AR ($p = 0.08$), however, a greater proportion of AR patients had severe symptoms (62.5 vs. 32.6%, $p < 0.0001$). The percentage of patients with nasal symptoms indicated as mild intermittent or mild persistent was higher in the patients with NAR (49.0 vs. 26.9%, $p < 0.0001$, and 18.1 vs. 10.1%, $p < 0.0001$, respectively), whereas the percentage of patients with severe intermittent nasal symptoms was higher in patients with AR (34.1 vs. 6.9%, $p < 0.0001$). We found no difference in the percentage of AR and NAR patients who reported severe persistent symptoms (28.3 vs. 25.7%, $p = 0.3$).

Medication Use in the Previous 8 Weeks

All patients had taken oral antihistamines (i.e., cetirizine, loratadine, desloratadine, levocetirizine, terfenadine, rupatadine, mizolastine and ebastine) in the previous 8 weeks. A higher percentage of patients with AR reported an effective response to antihistamines as compared to NAR patients (50.5 vs. 10.8%, $p < 0.0001$). However, the lack of clinical response to antihistamines seemed to correlate with greater numbers of eosinophils both in AR and NAR patients.

Complications of Upper Airway

Upper airway complications diagnosed on physical exam were found in 414 patients (27.3%). Particularly, nasal polyps were noted in 207 patients (13.7%), sinusitis in 387 patients (25.6%), laryngitis in 242 patients (25.6%) and otitis in 81 patients (5.4%). Of these patients, 127 had only one complication (100 sinusitis only, 27 laryngitis only), 124 patients presented with two complications (56 sinusitis + nasal polyposis, 49 sinusitis + laryngitis, 12 sinusitis + otitis and 7 laryngitis + otitis), 131 patients presented with three complications (108 sinusitis + nasal polyposis + laryngitis, 19 sinusitis + laryngitis + otitis and 4 sinusitis + nasal polyposis + otitis) and 39 patients presented with all four complications. Of the 414 patients presenting with one or more complications only 27 (6.5%) did not present with sinusitis and only 2 of these 27 patients were SPT negative. Sinusitis was the only upper airway complication found more frequently in patients with NAR compared to patients with AR (30.4 vs. 23.8%, $p = 0.01$).

Other Symptoms

Recurring headaches and olfactory dysfunction were more common in NAR than AR patients (30.6 vs. 24.5%, $p = 0.01$, and 29.7 vs. 23.8%, $p = 0.02$, respectively). However, there was no difference in the frequency of recurrent dysphonia (23.8 vs. 25.0%, $p = 0.6$).

Objective Tests

We evaluated PNIF, b-eos, n-eos, as well as nasal symptoms measured by VAS. PNIF and n-eos were found to be higher in AR patients compared to NAR patients, and these results were highly statistically significant (all $p < 0.0001$), while no difference was found between AR and NAR regarding the blood eosinophil counts ($p = 0.06$).

Logistic Regression

All variables found to be significantly different between AR and NAR were subsequently analyzed with backward stepwise logistic regression. All variables that differed between these 2 groups ($p < 0.05$ with χ^2 or Mann-Whitney analysis) were initially entered in the model, and the least significant variable was removed one at a time. Goodness of fit of the logistic models was assessed using the Hosmer and Lemeshow test. Table 3 shows the results of logistic regression retaining only the significant covariates in this model. The presence of conjunctivitis, a clinical response to antihistamines, high n-eos, the presence of sneezing, the presence of nasal pruritus

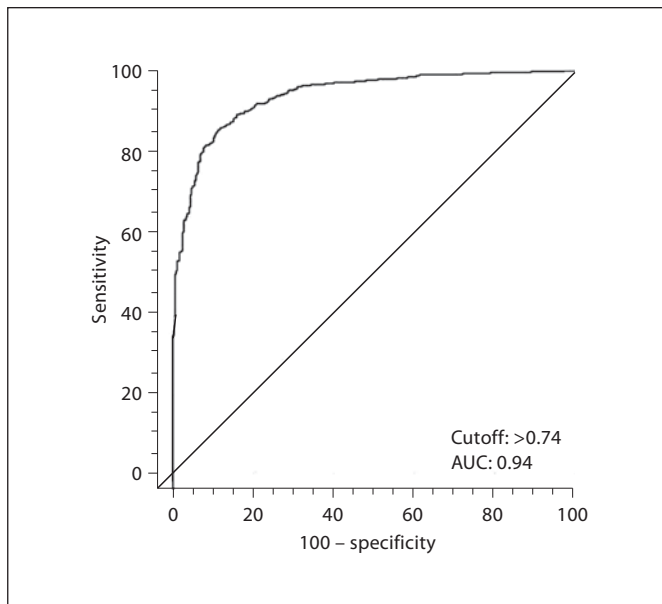


Fig. 1. Receiver operating characteristic curve of the predictive model obtained by applying backward stepwise logistic regression.

Table 3. Factors that significantly distinguish subjects with AR from subjects with NAR by backward stepwise logistic regression

Variable	OR	95% CI	p
Age	0.97	0.96–0.98	<0.0001
Presence of sneezing	4.09	2.78–6.00	<0.0001
Presence of nasal pruritus	3.84	2.60–5.67	<0.0001
Nasal symptoms			
Mild	0.21	0.09–0.49	0.0003
Intermittent/severe	3.66	2.06–6.50	<0.0001
VAS	1.05	1.03–1.07	<0.0001
Conjunctivitis	4.49	2.86–7.05	<0.0001
Effective response to antihistamines	22.59	13.79–37.00	<0.0001
PNIF	1.01	1.00–1.01	<0.0001
Nasal eosinophil counts	1.14	1.10–1.18	<0.0001

ritus, intermittent/severe nasal symptoms and a high VAS score were associated with AR. However, older age, mild nasal symptoms and a lower value of PFIN were associated with NAR.

Subsequently, we performed receiver operating characteristic analysis for all variables that were found to be independently associated with the diagnosis of AR and

NAR in order to identify the optimal cutoff point useful in predicting AR. For the optimal cutoff point useful in predicting AR, based on the above-mentioned logistic regression model, the following equation was generated and used in order to calculate predicted probability (p_i) of having AR:

$$\ln [p_i/(1 - p_i)] = -5.8262 - 0.02808 \times (\text{age in years}) + 1.4088 \times (\text{presence of sneezing}) + 1.3465 \times (\text{presence of nasal pruritus}) - 1.5220 \times (\text{mild nasal symptoms}) + 1.2997 \times (\text{intermittent/severe nasal symptoms}) + 0.05312 \times (\text{VAS score}) + 3.1178 \times (\text{effective response to antihistamines}) + 1.5040 \times (\text{presence of conjunctivitis}) + 0.01371 \times (\text{PNIF}) + 0.1367 \times (\text{n-eos}).$$

This algorithm resulted in a high predictive accuracy, considering as the best cutoff >0.74 : sensitivity 86.2 (95% CI 84.0–88.2), specificity 88.1 (95% CI 84.6–91.1), positive likelihood ratio 7.2 (95% CI 6.9–7.6), negative likelihood ratio 0.16 (95% CI 0.1–0.2) and area under curve 0.94 (95% CI 0.93–0.95) (fig. 1).

Discussion

In the present study, we found that the proportion of patients with AR in an adult population with symptoms of rhinitis is about 70%. This data is in line with the European Community Respiratory Health Survey [13] and with the National Rhinitis Classification Task Force (USA) [14].

The patients with AR have more sneezing and nasal pruritus, whereas the patients with NAR were characterized mainly by nasal obstruction and rhinorrhea. This is similar to results found in other studies [6, 15, 16].

Eighty percent of men with rhinitis symptoms have AR [17]. In general, patients with AR have more severe but equally persistent nasal symptoms when compared to patients with NAR. These data contradict the findings of Mølgaard et al. [6]. In a large sample of adolescents and adults with AR and NAR, they found that NAR patients suffer from more persistent symptoms and that severe symptoms were equally frequent in both AR and NAR patients. However, Bachert et al. [5] found in a questionnaire-based survey in Belgium that AR patients had both more persistent and more severe symptoms than NAR patients.

According to our results, comorbidities also differed in the two groups. Patients with NAR suffered more from sinusitis, whereas patients with AR suffer more frequently from conjunctivitis. The presence of nasal polyposis, laryngitis and otitis was similar in the two groups but re-

curing headaches and olfactory dysfunction were increased in NAR patients, whereas the presence of recurrent headache and olfactory dysfunction in patients with NAR could be partially explained by their having more sinusitis. Recurring headaches are subjective and therefore quite loosely defined. However, our data demonstrate that the frequency of recurring headaches in patients without sinusitis was very low and that the patients with recurring headaches had more severe nasal obstruction as measured by PNIF. These data are consistent with the finding of other authors [18].

It is important to underscore the correlation of nasal eosinophilia with all associated complications (sinusitis, nasal polyposis, laryngitis and otitis) in both AR and NAR patients alike. This data indirectly confirms the importance of nasal cytology for the correct clinical classification of rhinitis and in the pathogenesis of complicated forms of rhinitis.

There are at least two limitations to our study. First, since this study was done with rhinitis patients it may not be possible to generalize the data to the population as a whole. However, our focus was the population seen daily by allergists and otolaryngologists in clinical practice. The results are therefore consistent with the high prevalence of AR and NAR in the general population. Second, we classified the rhinitis only by the presence or absence of a positive SPT. However, in practice, the diagnosis of AR is based only on SPT [3, 19].

However, the study has some important aspects to consider in diagnosing rhinitis. It is important to objectively evaluate possible causes of subjective signs and symptoms such as the nasal obstruction. Not only is it important to inspect the nasal cavity for the presence of nasal polyps, turbinate sizes and condition of the nasal mucosa, but it is also important to objectively measure nasal obstruction using PNIF as a parameter. PNIF can be measured with an inexpensive device. However, based on our data we think nasal cytology is the most important objective measurement. In our opinion a correct diagnosis of rhinitis cannot be made without nasal cytology. Our conclusion is based on the fact that only 50% of AR patients, generally those with few eosinophils found in their nasal secretions, controlled their nasal symptoms only with the antihistamines and that all patients with complications of the upper airway, whether allergic and non-allergic, had higher nasal eosinophil counts in their secretion. Getting this objective data may help in better management of rhinitis in all patients.

This study shows that rhinitis is not a trivial disease. Patients with both AR and NAR presented with coexist-

ing sinusitis, nasal polyposis, laryngitis and otitis, suggesting that there may be a common pathophysiological pathway causing severe rhinitis resulting in complications, such as rhinitis with nasal eosinophilia, and that this is common in both AR and NAR.

Our results underline several clinical and demographic differences between patients with AR and NAR and emphasize the need of a correct diagnosis and medical treatment. This large cross-sectional study shows that AR is a prevalent condition, which is characterized both by intermittent and severe symptoms, most prominently sneezing and nasal pruritus. The majority of patients with AR are young men, while the patients with NAR are middle-aged women who have a tendency to suffer from recurring headaches and recurrent sinusitis as well.

Receiver operating characteristic curves are used in biomedical research to evaluate the effectiveness of biomarkers for distinguishing individuals with the disease from those without that disease, in our study patients with AR from patients with NAR. Future research needs to include closer investigation of subjects with AR and NAR. In particular, more attention should be paid to accurately distinguish between different subtypes of AR and NAR in relation to treatment and to presence of eosinophils in the nasal mucosa.

Acknowledgements

This study was supported by grants from MIUR (Italian University and Research Ministry) (former 60% funds) to Gabriele Di Lorenzo. Vito Ditta is a PhD student of the Pathobiology PhD course (directed by Professor Calogero Caruso) at Palermo University, and this work is submitted in partial fulfillment of the requirement for the PhD degree. The authors thank Professor Anne Marie Ditto, MD, for helpful comments.

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