Archives of Current Medical Research
Arch Curr Med Res 2026; 7(1): 120-126

Received: 08 July 2025
Revised: 25 July 2025
Accepted: 15 August 2025
DOI: 10.47482/acmr.1737180

ORIGINAL ARTICLE

Clinical Features of Patients with Chronic Rhinitis Symptoms in the Absence of Atopy

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Abstract

Background: Chronic rhinitis occurs in the presence of symptoms of nasal congestion, rhinorrhea, sneezing or nasal/eye itching. It is important to make a differential diagnosis, because the treatments for the possible diagnoses differ considerably. The aim of our study was to determine the clinical characteristics of patients presenting with chronic rhinitis symptoms and without atopy.

Methods: In this prospective, descriptive and cross-sectional study, demographic and clinical characteristics of patients were analysed. Visual Analogue Scale was used to determine the severity of rhinitis symptoms. These patients were examined for nasal endoscopic examination.

Results: The median age of the 22 patients included in our study was 44.5 years (range: 18-61). The presence of nasal serous discharge on nasal endoscopy examination was significantly higher in the suspected LAR group than in the NAR group. (p=0.04) The presence of female gender, presence of concomitant allergic disease, presence of allergic disease in the family, presence of triggers, rhinorrhea and nasal itching scores according to the visual analogue scale were higher in the suspected LAR group than in the NAR group, but no statistically significant difference was found.

Conclusion: Local allergic rhinitis should be suspected, in cases where serous discharge is observed during nasal endoscopy, symptoms are exacerbated by known triggers, or there is a personal or family history of allergic disease.

Keywords: Rhinitis, local allergic rhinitis, allergy, atopy.

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INTRODUCTION

Chronic rhinitis occurs in the presence of symptoms of nasal congestion, rhinorrhoea, sneezing or nasal/eye itching. The diagnosis of chronic rhinitis requires the presence of 2 or more nasal symptoms for more than 1 hour per day for at least 12 weeks per year (1,2). Chronic rhinitis is classified according to the underlying mechanisms as allergic rhinitis (AR), nonallergic rhinitis (NAR), infectious rhinitis and mixed rhinitis and should be differentiated from other nasal anatomical problems with overlapping rhinitis symptoms (2). It is important to make a differential diagnosis in patients with overlapping symptoms, because the treatments of possible diagnoses differ considerably from each other.

Allergic rhinitis is a symptomatic nasal inflammation caused by inhalation of an allergen in susceptible individuals. The diagnosis is based on the induction of symptoms after contact with the sensitized allergen and the detection of allergen-specific Immunglobulin E (IgE) in skin prick test or blood. Local Allergic Rhinitis (LAR) is characterized by the occurrence of allergic rhinitis symptoms in the absence of systemic atopy (3). LAR has 3 clinical signs for diagnosis: (1) clinical presentation after allergen exposure, (2) negative skin prick test (SPT) results and negative serum specific IgE (sIgE), (3) positive response to aeroallergens by nasal allergen provocation test (NAPT) (3,4). In addition, detection of specific IgE in nasal lavage fluid after natural exposure or NAPT and positivity in basophil activation test also support the diagnosis of LAR (5-7). However, NAPT is considered the gold standard test in the diagnosis of LAR due to the difficulty in nasal sIgE detection.

In one study, LAR was seen in 25.7%, AR in 63.1% and NAR in 11.2% of patients with chronic rhinitis. SPT, serum sIgE tests and NAPTs were used in the differential diagnosis of the patients. Watery rhinorrhea, nasal itching and sneezing are most common in patients with LAR, while nasal congestion and mucoid rhinorrhea are more common in patients with NAR. In addition, patients with LAR have moderate/severe, persistent and perennial symptoms and are accompanied by comorbidities such as conjunctivitis and asthma (8). According to the results of this study, we see that different clinical conditions occur between LAR and NAR. Correct diagnosis of patients is important because rhinitis has been implicated in loss of work and school days, decreased cognitive function, inattention and decreased work productivity/absenteeism (9,10). It has been found that employees with allergic rhinitis are absent from work due to rhinitis symptoms and that productivity decreases on days when allergic symptoms are severe (9).

Although NAPT is the gold standard for the diagnosis of local allergic rhinitis, it remains inaccessible in many centers. Furthermore, there are patients who have been diagnosed with allergic rhinitis by otolaryngologists based on the findings of nasal endoscopic examination, even though atopy has not been detected in allergy practice. The aim of our study was to determine the clinical characteristics of patients presenting with chronic rhinitis symptoms in the absence of NAPT and without atopy. We believe that the findings of our study will contribute to the management of patients in the clinical practice of specialists in Immunology and Allergic Diseases and Otolaryngology.

MATERIALS AND METHODS

Study Design

Our prospective, descriptive and cross-sectional study was conducted between December 2022 and May 2023 in the Immunology and Allergic Diseases Clinic and Otolaryngology Clinic of a tertiary care hospital. The study population consisted of patients aged 18 years and over who presented to the Immunology and Allergic Diseases outpatient clinic with chronic rhinitis symptoms (having any two of the symptoms of runny nose, nasal congestion, nasal discharge, nasal itching, decreased sense of smell, sneezing for at least 12 weeks), who were not atopy detected and who were examined in the Otolaryngology clinic for diagnosis.

All patients participating in the study were informed about the study and an Informed Consent Form was obtained from the patients. The study was conducted in accordance with Good Clinical Practice and the articles stated in the Declaration of Helsinki. The study was approved by the Clinical Research Ethics Committee of Ankara Atatürk Sanatoryum Training and Research Hospital (Number: 2012-KAEK-15/2585, Acceptance Date: 26.10.2022).

Detection of Atopy

Skin prick test and/or serum sIgE values, which measure the IgE-mediated hypersensitivity response to inhaled allergens, were used to detect atopy in patients. SPT was performed in accordance with relevant guidelines (11,12). Pollen, house dust mites, animals and moulds allergens were used, taking into account the common panel recommended for clinical use and research across Europe. Before the skin prick test, all systemic and topical medications that may affect the test result were discontinued before the recommended time. After dropping standardized allergen extracts on the volar surface of the forearm and clean skin surface, the skin was punctured with the help of a metal lancet and the wheal formed after 15 minutes was evaluated. Negative control (NaCl 0.9%) and positive control (histamine hydrochloride solution) were used and The positive control should optimally show a wheal diameter 3 mm. Wheal diameters 3 mm are considered positive in SPTs for each allergen (11,12). Specific serum IgE level ≥ 0.35 kUA/L was considered positive.

Demographic and Clinical Characteristics of Patients

Age, gender, concomitant allergic and systemic diseases, medications used, time of onset of rhinitis symptoms, course of symptoms throughout the year (all year/seasonal), presence of allergic diseases in the family, and the relationship of complaints with triggers (perfume, hairspray, food odor, cleaning products, smoking, cold air, etc.) were recorded.

Determination of Symptom Severity

The Visual Analog Scale (VAS) scores were used to assess the severity of symptoms including rhinorrhea, nasal congestion, postnasal drip, and loss of smell. During the outpatient clinic visit, patients self-rated the severity of each symptom on a scale of 0 (minimum) to 10 (maximum). These scores were then recorded on the Case Record Form.

Classification of Patients

All participants underwent nasal endoscopic examination performed by an otolaryngology specialist. Patients presenting with findings suggestive of allergic rhinitis—specifically, pale nasal mucosa and serous discharge—were classified as having "Suspected Local Allergic Rhinitis", while those without such findings were categorized as having "Nonallergic Rhinitis" (NAR).

Statistical Evaluation

Statistical evaluations were made using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY, USA). program. Frequency analysis, Chi-Square test, Fisher's Exact test, Mann Whitney-U test were used as statistical analysis. Variables were expressed with median minimum-maximum values. $p < 0.05$ was considered statistically significant.

RESULTS

The median age of the 22 patients included in our study was 44.5 years (range: 18-61) and 16 of them (72.7%) were female. None of these patients had positive results of SPT and/or sIgE levels indicating atopy. Patients had chronic rhinitis symptoms for a median of 48 months (range: 3-240 months). Postnasal drip was the most bothersome symptom in 40.9% (n=9) of the patients, followed by bilateral rhinorrhea in 27.3% (n=6). While 81.8% of the patients had no comorbid allergic disease, 3 patients (13.6%) had asthma and 1 patient (4.5%) had drug allergy (Table-1).

Endoscopic nasal examination of 14 patients (63.6%) was compatible with allergic rhinitis and "suspected Local Allergic Rhinitis" was considered in these patients. In the remaining 8 patients, "Non-Alergic Rhinitis" was considered. The presence of nasal serous discharge was significantly higher in patients whose nasal endoscopic examination was compatible with allergic rhinitis (p=0.04). The presence of female gender, presence of comorbid allergic disease and presence of allergic disease in the family were found to be higher in patients with allergic rhinitis, but no statistically significant difference was found (Table-1).

According to the VAS, there was no statistically significant difference between the symptoms in both groups. However, rhinorrhea and nasal itching scores were higher in the suspected LAR group than in the NAR. (Table-2) VAS Scores for the symptoms of the patients are shown in Table-2. (Table-2)

Table 1. Demographic and Clinical Characteristics of the Patients

	n	Nasal Endoscopy Compatible with Allergic Rhinitis (suspected Local Allergic Rhinitis) (n=14)	Nasal Endoscopy Incompatible with Allergic Rhinitis (Non-Allergic Rhinitis) (n=8)	Test p
Age (year), median (min-max)	22	45,0(18-59)	36,0(18-61)	2 (2.3%)
Time to symptom onset (months), median (range)	22	48,0(7-180)	42,0(3-240)	0,863
Gender, n				
Female	16	10 (%62,5)	6 (%37,5)	
Male	6	4(%66,7)	2 (%33,3)	0,856
Duration of symptoms				
All year	13	8(61,5)	5(38,5)	
Seasonal	9	6(66,7)	3(33,3)	0,806
Smoking History				
Never Smoked	12	7(58,3)	5(41,7)	
Exand active smoker	10	7(70.0)	3(30.0)	0,454
Symptom Trigger Presence				
Yes	16	11(68,8)	5(31,3)	
No	6	3(50,0)	3(50,0)	0,413
Concomitant Allergic Disease				
No	18	10(55,6)	8(44,4)	
Yes	4	4(100)	0(0)	0,095
Presence of Allergic Disease in the Family				
Yes	9	7(77,8)	2(22,2)	
No	13	7(53,8)	6(46,2)	0,251
Serous Discharge in Nasal Cavity				
Yes	17	**8(88,9)**	**1(11,1)**	
No	5	**6(46,2)**	**7(53,8)**	**0,04**
Rhinorrhea				
Yes	19	11(64,7)	6(35,3)	
No	3	3(60,0)	2(40,0)	0,848
Nasal Congestion				
Yes	16	12(63,2)	7(36,8)	
No	6	2(66,7)	1(33,3)	0,907
Nose Itching				
Yes	18	11(68,8)	5(31,3)	
No	4	3(50,0)	3(50,0)	0,416
Postnasal Drip				
Yes	18	13(72,2)	5(27,8)	
No	4	1(25,0)	3(75,0)	0,076
Sneeze				
Yes	18	12(66,7)	6(33,3)	
No	4	2(50)	2(50,0)	0,531
Eye Symptoms				
Yes	4	3(75,0)	1(25,0)	
No	18	11(61,1)	7(38,9)	0,601

Table 2. Visual Analog Scale Scores				
Visual Analog Scale Scores	**n**	**Nasal Endoscopy Compatible with Allergic Rhinitis (suspected Local Allergic Rhinitis) (n=14)**	**Nasal Endoscopy Incompatible with Allergic Rhinitis (Non-Allergic Rhinitis) (n=8)**	**Test p**
Rhinorrhea	17	8(4-10)	4,5(3-9)	0,067
Nasal Congestion	20	7,5(4-10)	7,5(4-10)	0,937
Sneezing	20	8(4-10)	8(1-10)	0,872
Postnasal Drip	19	6(1-10)	8(5-10)	0,680
Nose Itching	15	8(4-10)	6(4-10)	0,422
Eye Symptoms	13	6(2-8)	7(7-9)	0,342
Loss of Smell	6	5(3-7)	5,5(5-6)	0,814

DISCUSSION

Collaboration with otolaryngologists is common in allergy practice. One of the most frequent patient groups requiring interdisciplinary management includes individuals presenting with chronic rhinitis symptoms but without evidence of atopy. In such cases, the diagnosis and treatment of LAR gain clinical importance. However, due to limited access to NAPT, diagnosing LAR remains a significant challenge. In our study, we evaluated the clinical characteristics of patients whom otolaryngologists suspected to have allergic rhinitis based on nasal endoscopic findings.

According to nasal endoscopic examination findings, we detected suspected LAR in 63.6% of the patients included in our study in whom atopy was not detected. Similar to our study, in a study conducted with idiopathic rhinitis patients, LAR was detected in 62% of the patients after NAPT (13). In another study, 54% of patients with perennial NAR were positive in NAPT test with D. pterynosinus allergen (5). Different studies may show different results in the frequency of LAR. The frequency of referral of patients with severe and uncontrolled rhinitis to allergy outpatient clinics varies between countries, which may explain this difference. Moreover, the level of aeroallergens, exposure to them, temperature, humidity and air pollution may also cause variations in the frequency of LAR.

In our study, the presence of serous discharge on nasal endoscopic examination was statistically significantly higher in the suspected LAR group compared to the NAR group. According to VAS scores, the rhinorrhea score was higher in the suspected LAR group than in the NAR group, but the difference was not significant. In addition, seasonal character of symptoms, exacerbation of symptoms with triggers, presence of concomitant allergic disease, family history of allergic disease were higher in the suspected LAR group, but the difference was not statistically significant. In a previous study, the presence of asthma, atopic dermatitis, conjunctivitis and family history of atopy were associated with higher rates in the LAR group compared to the NAR group. In the same study, it was reported that LAR is a common phenotype in young people, has clinical features similar to AR, has onset in childhood and symptoms increase with triggers (8). The data from this study are consistent with the findings of nasal endoscopic examination and the clinical characteristics of patients suspected of having LAR, which may suggest that nasal endoscopic findings should be evaluated more carefully in the absence of NAPT for the detection of LAR.

In our study, the presence of rhinorrhea, nasal itching, nasal postnasal drip, sneezing and ocular symptoms were found to be higher in the suspected LAR group, although not statistically significant. When VAS scores were evaluated, rhinorrhea and itchy nose scores were higher in the suspected LAR group, but the difference was not statistically significant. In a comprehensive study, the presence of nasal itching and nasal itching VAS scores were found to be higher in the LAR group than in the NAR group, and watery rhinorrhea and nasal itching were reported as the most common symptoms of LAR (8). In the mechanism of LAR, local sIgE production has been demonstrated after natural exposure and after NAPTs (5,6). In addition, proinflammatory cytokines such as tryptase and eosinophilic cationic protein have been shown to increase in nasal secretions with immediate activation of mast cells and eosinophils after NAPT with grass pollen and Dermatophagoides pteronyssinus (14,15). A strong correlation has been found between nasal itching and sneezing and tryptase levels in nasal secretions (14). Considering the presence of mast cells, eosinophils and proinflammatory cytokines involved in the pathogenesis of LAR, the present findings support the symptoms of nasal itching, rhinorrhea and sneezing in suspected LAR patients, as we found in our study.

In allergy practice, otolaryngologic examination is routinely recommended for patients presenting to the outpatient clinic with rhinitis symptoms to evaluate other possible etiologies. LAR detection is important in these patients. Because in a large prospective cohort study conducted between 2005 and 2016, it was shown that rhinitis symptoms progressively worsened in untreated LAR patients, LAR was a risk factor for asthma development and quality of life deteriorated in patients with LAR (16). At the end of 10 years, there was no further development of systemic atopy in the LAR group compared with healthy controls, suggesting that LAR is a different phenotype from AR and that LAR is not a precursor of AR (16). Therefore, it is extremely important to control symptoms, monitor the onset of potential comorbidities, and identify and treat LAR individuals soon after onset due to the increased burden of disease. However, the diagnosis of LAR may be delayed due to overlapping symptoms and patients may be followed up with a diagnosis of NAR (17,18). This can lead to patients receiving the wrong treatment and increased healthcare costs. LAR patients are treated with allergen avoidance measures, antihistamines and nasal corticosteroids. Treatment of LAR and AR is parallel to each other. Recent studies have also demonstrated the efficacy and safety of allergen-specific immunoterpine with grass pollen and D. pteronyssinus in patients with LAR (19,20).

This study has several limitations. The small sample size, single-center design, and the predominance of female participants constitute key limitations. Additionally, the reliance on nasal endoscopic examination findings rather than NAPT the gold standard for diagnosing LAR represents another constraint, as it precludes definitive diagnosis.

In conclusion, the NAPT is accepted as the gold standard test for the diagnosis of LAR, but in the absence of NAPT, which is costly and difficult to access, LAR should be suspected in the presence of serous discharge on nasal endoscopic examination, in the presence of increased symptoms with triggers, in the presence of a history of allergic disease in the patient or in the family, and LAR should be considered and treated in parallel with AR and further investigations should be planned if possible.

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Abbreviations List

AR: Allergic rhinitis
IgE: Immunglobulin E
LAR: Local Allergic Rhinitis
NAPT: Nasal allergen provocation test
NAR: Non-Alergic Rhinitis
sIgE: serum specific IgE
SPT: Skin prick test
VAS: Visual Analog Scale.

Ethics Approval and Consent to Participate

The study was approved by the Clinical Research Ethics Committee of Ankara Atatürk Sanatoryum Training and Research Hospital (Number: 2012-KAEK-15/2585, Acceptance Date: 26.10.2022).

Consent for Publication

Informed consent was obtained from all individual adult participants included in this study.

Availability of Data and Materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Author Contributions

Concept – G.T.V.S., K.A., A.K.T., Y.A. Design – G.T.V.S., K.A., A.K.T., Y.A. Supervision – G.T.V.S., K.A., A.K.T., Y.A. Materials – G.T.V.S., K.A., A.K.T., Y.A. Data collection &/or processing – G.T.V.S., K.A., A.K.T., Y.A. Analysis and/or interpretation – G.T.V.S., Y.A. Literature search – G.T.V.S. Writing – G.T.V.S., K.A., A.K.T., Y.A. Critical review – G.T.V.S., K.A., A.K.T., Y.A.

Acknowledgements

Work was presented at 23rd International Eastern Mediterranean Family Medicine Congress,2024 Adana.