

Study for Assessing Prevalence and Phenotypes of Local Allergic Rhinitis

Maged M. Refaat , Nermine Abd Elnour,

Rasha Y. Shaheen, Sonya A. El-Gaaly

Allergy and Immunology Department of Internal Medicine,
Faculty of Ain Shams University,Egypt.

ABSTRACT

Background: Rhinitis is a global health problem that affects 20-40% of the population in developed countries and whose incidence is rising. Rising is characterized by one or more of the following symptoms: nasal congestion, rhinorrhea, sneezing and itching. It can be induced by different mechanisms and involves several etiological agents. Noninfectious rhinitis has traditionally been classified as allergic rhinitis (AR) and nonallergic rhinitis (NAR).

Objective: To evaluate the prevalence and phenotypes of local allergic rhinitis in patients with clinical manifestations of AR without evidence of systemic IgE sensitization.

Methods: This cross sectional, case-control, and nonrandomized study was conducted on 120 patients with clinical manifestations suggestive of allergic rhinitis (selected from the allergy outpatient clinic at Ain Shams university hospitals and 20 healthy controls.

Results: Local allergic rhinitis was diagnosed in 80% of females and 20% of males. While the patients with systemic allergic rhinitis reached 37.5% for males, and 62.5% were females. Regarding the persistence of symptoms in local allergic rhinitis it reached 88% in comparison to 67.5% in systemic allergic rhinitis. The symptoms were intermittent in 12 % of cases with local allergic rhinitis in comparison to 32.5% in systemic allergic rhinitis. The severe symptoms outweighed the mild symptoms by nearly 50%. The skin prick test reached 80% positive in cases of LAR. Those with normal levels of total IgE level, the nasal provocation test was positive in 12.5% of cases and 7.5% negative.

Conclusion: Local allergic rhinitis is a prevalent entity in patient evaluated with rhinitis.

INTRODUCTION

Rhinitis has been classified as allergic or nonallergic based on clinical history skin prick test (SPT), and serum specific IgE to aeroallergens. ⁽¹⁾ Persistent rhinitis is a highly prevalent disease of the nasal mucosa, which affects up to 20% of general

population. ⁽²⁾ It can be induced by several mechanisms and etiological agents can be involved. ⁽³⁾

Local allergic rhinitis is characterized by local production of s IgE, and nasal cellular Th2 immune response during natural

exposure to the allergen ⁽⁴⁾ and ⁽⁵⁾. Also, according to positive response to nasal allergen provocation test, local increase in serum levels of IgE, tryptase, and eosinophil cationic protein were observed. ⁽⁶⁾

Local allergic rhinitis is a new phenotype of rhinitis in the absence of systemic atopy. ⁽⁶⁾ Idiopathic rhinitis is difficult to define and may be induced by different mechanisms.

These patients are considered nonallergic because they have no evidence of atopy. ⁽⁸⁾ Evidence of local IgE synthesis exists in the nasal mucosa in rhinitis patients ⁽⁹⁾ and the concept that some immune response might be a form of localized allergy in the absence of atopy has been proposed ⁽⁷⁾. The aim of this work is to investigate the prevalence and phenotypes of local allergic rhinitis in patients with clinical manifestations of allergic rhinitis without evidence of systemic IgE sensitization. To test this process, Egyptian middle aged male and female patients with clinical manifestations suggestive of allergic rhinitis are subjected to full detailed history, skin prick test, serum IgE levels, nasal specific IgE with same aeroallergen in skin prick test and nasal provocation tests by common aeroallergens. In our study the LAR and allergic rhinitis patients shared almost a similar demographic profile.

PATIENTS AND METHODS

This study included a total of 120 adult subjects with rhinitis, of both sexes. The mean age for patients with systemic allergic rhinitis was 32 years range of (25-40.5) and for patients with local allergic rhinitis the mean age was 33 years with age range of (25-42). As for Non allergic rhinitis (NAR) the mean age was 28 with age range (24-35.5).

1. The exclusion criteria included the following: individuals that are pregnant, lactating, having immunological diseases, smokers, vasomotor rhinitis, and patients on non steroidal anti-inflammatory drugs.
2. The subjects were subjected to full detailed allergic history taking and clinical examination with special emphasis on rhinitis symptoms. Age of onset of symptoms of rhinitis, suspected precipitating factors, frequency and severity of symptoms.
3. Allergic rhinitis was diagnosed and classified as intermittent, persistent, mild, moderated and severe according to the criteria set out by allergic rhinitis and its impact on asthma guidelines in 2001.
4. **Skin prick test**, using allergens extracts prepared at the allergy department at Ain shams University Hospitals. The skin prick test was performed with a wide panel of most prevalent aeroallergens in our area, which are house dust, hay dust,

mixed mites, mixed moulds, mixed pollens and cat epithelium). In addition to the allergens tested, there should be a positive and negative control. The positive control, usually histamine solution, should become itchy within a few minutes, then red and swollen with a wheal in center. The negative control, usually a saline solution should show no response. ⁽¹⁰⁾.

5. **Serum total IgE** level using a sandwich enzyme linked immunosorbent assay (ELISA) kit (BioCheck, Inc., FosterCity, USA).
6. **Nasal allergen provocation test (NAPT)**: If negative skin prick test and within normal serum total IgE were obtained, NAPT was done by the same common aeroallergen used in skin prick test (11).
7. **Nasal specific IgE**: nasal secretions were taken from the patient, and evaluated by using an enzyme-linked immunosorbent assay (ELISA). (12)

STATISTICAL ANALYSIS

All data were analyzed using software (version 11, SSPS Inc., Chicago, Illinois). Quantitative variables were presented as mean +/- standard deviation, while median and interquartile range (IQR) for continuous variables. Qualitative variables were presented as frequency and percentage for the discrete ones. Student paired t-test was

used for parametric data. The Pearson chi square test, or Fisher's exact test when appropriate, was used to compare between-group differences as regards nominal variables. For comparison of ordinal variables, the chi square test for linear-by-linear association was used. P value < 0.05 was considered statistically significant.

RESULTS

Table 1 shows that the duration of the symptoms ranged from 0.4 to 30 years with mean 6.5+/- SD 5.9.

Table 2 shows that among the 24 patients with negative skin prick test and normal total IgE, 15 patients (12.5%) gave a positive nasal provocation test (NAPT) and 9 patients (7.5%) gave negative NAPT. Among those 24 patients 10 showed high nasal specific IgE, while 14 showed negative nasal-specific IgE.

Table 3 shows that 96 patients (80%) gave positive skin Prick test and total serum IgE, while 24 patients (20%) gave negative skin prick test and within normal serum total IgE.

Table 4 shows that among the patients in this study 96 patients (80%) gave a positive S.P.T and high serum total IgE which represent the patients with systemic allergic rhinitis (SAR). Fifteen patients with LAR (12.5%) gave a negative S.P.T, with normal

total serum IgE and positive nasal allergen provocation test. Nine patients with NAR (7.5%) gave a negative S.P.T, serum total IgE, nasal allergen provocation test and nasal-specific IgE.

Table 5 shows a comparison between the three types of rhinitis in terms of the age, gender, duration of the symptoms, persistency, severity of symptoms and serum total IgE.

Figure 1 shows that in systemic allergic rhinitis 16.9% were presented with mild severity, 38.7 % came with moderate and 44.4% came with severe symptoms. While those with local allergic rhinitis 8% were mild, 32% came with moderate and 60% came with severe symptoms. But in the non allergic rhinitis group 46.6% were mild, 53.4% came with moderate symptoms.

DISCUSSION

Rhinitis is one of the commonest chronic inflammatory diseases that affect 20-40% of the population (13). It can be induced by different mechanisms and involves several etiological agents (14). From an etiological point of view, non infectious rhinitis has been traditionally classified as allergic and nonallergic (15).

In recent years, several studies have shown that many patients previously diagnosed with NAR or idiopathic rhinitis

proved to be local allergic rhinitis (LAR) (14).

This study included 120 adults with rhinitis. Their age had a mean +/- SD (33.6+/- 12.2). The duration of symptoms range from .4 to 30 years with a mean (6.5+/- 5.9). The majority of our patients had moderate to severe rhinitis 82%, and female gender represented 65.3% in the whole study population while the male gender 34.9%. Eighty percent of the rhinitis patients enrolled in this study showed positive skin prick test and high serum total IgE, and they were considered as allergic rhinitis patients with systemic atopy. For the remaining 20% with negative skin prick test and within normal serum total IgE, Nasal Allergen Provocation test (NAPT) with most common aeroallergens was performed, and positive tests were obtained in 12.5 % of them. Also nasal lavage fluid was taken to evaluate nasal specific IgE of patients who have negative skin prick test and normal serum total IgE .

These patients previously given a diagnosis of non allergic rhinitis or idiopathic rhinitis which are now being classified as having LAR according to the nasal allergen provocation test. The NAPT is needed to identify the culprit of allergens, and in a certain proportion of cases local IgE is detected and is required (16).

In our study the LAR and AR patients shared almost a similar demographic profile. Allergic rhinitis patients mean age was 32 years, age range of 25-40.5. Patients with local allergic rhinitis mean age was 33 years with age range of 25-42.

The majority of these patients were females in both groups: 62.5% in AR 80% in LAR. As for NAR the mean age was 28 with age range of 24-35.3 with no sex predilection. This female gender predominance observed in our studied group is consistent with other studies for rhinitis patients. Different from the study of Zhu et al who investigated the differences in age, sex, seasonal distribution, and related environmental factors between patients with non allergic rhinitis and allergic rhinitis. They found NAR patients were more likely to be males before 30 years old, while after 30 years found to be female predominant. This variation in sex predilection detected in different studies could be explained by different sample size (17).

Rondon et al, 2012 (18) observed significantly higher associations in young people (<30 years old) and women in LAR compared with AR and NAR. On the contrary some epidemiological studies performed showed differentiation between LAR and NAR in higher presence of NAR in women, at younger age, and high specific

her association with asthmatic symptoms. (19), (15) and (20).

We detected significant differences in persistence and severity of symptoms between AR, LAR, and NAR groups. **Rondon et al, 2012** found no significant differences in persistence or seasonality of symptoms between LAR and NAR groups, although LAR patients reported severe symptoms more frequently than NAR.

Our findings were consistent to some degree with Rondon et al, 2007 who recruited a total of 110 subjects, divided into 3 groups: persistent NAR, persistent AR and Control group. Nasal total specific IgE were measured and the response to nasal allergen provocation test was assessed. They report significantly higher nasal total and nasal specific IgE to *Dermatophagoides pteronyssinus* (sIgE-DP) levels in allergic rhinitis compared with NAR patients, and detected 6 patients (12%) in the persistent NAR group, with selective sIgE-DP.

Rondon et al, 2008 (21) evaluated 32 patients with seasonal idiopathic rhinitis (IR) and 35 with persistent allergic rhinitis to pollen (**PAR-P**) and compared these with persons with PAR to house dust mite and healthy controls. They measured total and specific IgE to grass and olive pollen in the serum and nasal lavage by using NAPT. Although the nasal level of total IgE were

higher in the **PAR-P** compared to IR and control groups, significant differences were only found between PAR-P and controls (P=0.04). The nasal sIgE showed higher values to grass pollens in the PAR-P group than the IR and control groups (P=0.04 and P=0.007, respectively).

Wedback et al 2005 (22) evaluated the disease entity seasonal nonallergic rhinitis (SNAR), by examining and comparing three groups of patients with the diagnosis of SNAR (17patients), Seasonal allergic rhinitis (SAR) (20 patients) and persistent non allergic rhinitis (PNAR) (13 patients). The groups were compared regarding symptoms and drug consumption during the birch and grass pollen seasons. Skin prick tests was performed with several pollen allergens, and nasal provocation test with extracts of birch or timothy pollen. Skin prick test with 12 different pollen allergens was negative in the SNAR group. Nasal provocation test with birch pollen was positive in three patients of the SNAR group. Furthermore, seven patients reported a late nasal reaction **(23)**.

Although true prevalence data about LAR are not available, results generated in various European centers suggest that among patients with negative skin prick test responses and undetectable sIgE antibodies in serum, LAR might be present in 47 % to 62.5% of patients with perennial **(24)** and seasonal symptoms**(20), (21)** . Many of

these patients were given a diagnosis of IR or nonallergic rhinitis with eosinophilic syndrome previously. These data indicate that LAR might be a common, although underestimated disease. A recent study by Rondon et al, 2012 assessed LAR prevalence among 428 rhinitis patients, they found LAR 25.7%, AR 63.1%, and NAR 11.2 % . We reported almost similar results 12.5 % represent LAR, 80% allergic rhinitis, and 7.5% with non-allergic rhinitis. This mild difference in prevalence rates could be due to different sample sizes. Further studies should be done to detect more differences, by using nearly equal sample sizes.

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Table 1. Duration of symptoms

| Variable | Minimum | Maximum | Mean | SD | Median | IQR |
|-----------------------------------|----------------|----------------|-------------|------------|---------------|----------------|
| Duration of symptoms (yrs) | 0.4 | 30 | 6.5 | 5.9 | 5.0 | 3.0-8.0 |

Table 2. Results of Nasal Provocation test and Nasal Specific IgE level in patients with normal total IgE level and negative skin prick test

| Variable | | Number | Percent |
|------------------------|-------------|---------------|----------------|
| Nasal provocation test | Positive | 15 | 12.5% |
| | Negative | 9 | 7.5% |
| Nasal specific IgE | >0.350 kU/l | 10 | 8% |
| | <0.350KU/l | 14 | 12% |

Table 3. Results of Skin prick test and serum total IgE level in the whole study Population.

| Variable | | Number | Percent |
|------------------------|----------|---------------|----------------|
| Skin prick test | Positive | 96 | 80% |
| | Negative | 24 | 20% |
| Total IgE | >100IU/l | 96 | 80% |
| | <100IU/l | 24 | 20% |

Table 4. Comparison of three types of Rhinitis in relation to positivity/ negativity to other variables

| Ultimate Diagnosis | Number | Percent |
|----------------------------------|---------------|----------------|
| Systemic Allergic Rhinitis (SAR) | 96 | 80% |
| Local Allergic Rhinitis(LAR) | 15 | 12.5% |
| Non- Allergic Rhinitis | 9 | 7.5% |

Table 5. Comparison between three types of rhinitis and other variables

| Variable | Systemic allergic Rhinitis | Local allergic rhinitis | Non allergic rhinitis | P value |
|-----------------------------------|-----------------------------------|--------------------------------|------------------------------|--------------------|
| Total IgE IU/ml | 193 (121-282) | 66 (44.8-83) | 81 (48.9-88) | P=<0.001 |
| Presistent rhinitis | 67.5% | 88% | 20% | P=0.005 |
| Intermittent Rhinitis | 32.5% | 12% | 80% | |
| Severity of symptoms | | | | P=0.006 |
| Mild | 16.9% | 8% | 46.6% | |
| Moderate | 38.7% | 32% | 53.4% | |
| Severe | 44.4% | 60% | 0 | |
| Age | 32 (25-40.5) | 33(25.5-42) | 28(24-35.3) | P=0.49 |
| Gender | | | | P=0.360 |
| Male | 37.5% | 20% | 46.6% | |
| Female | 62.5% | 80% | 53.4% | |
| Durations of symptom (yrs) | 5 (2.5-8) | 5(3.3-7.5) | 6(3-9.3) | P=0.513 |

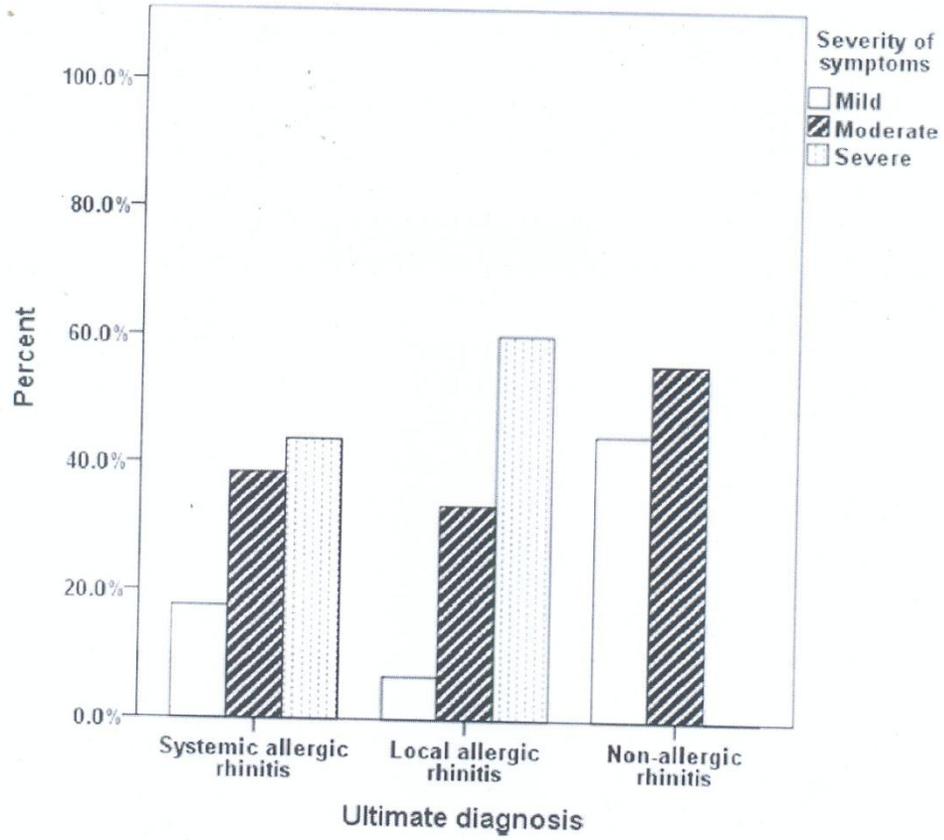


Figure 1 Comparison of the severity of symptoms in the three forms of rhinitis.

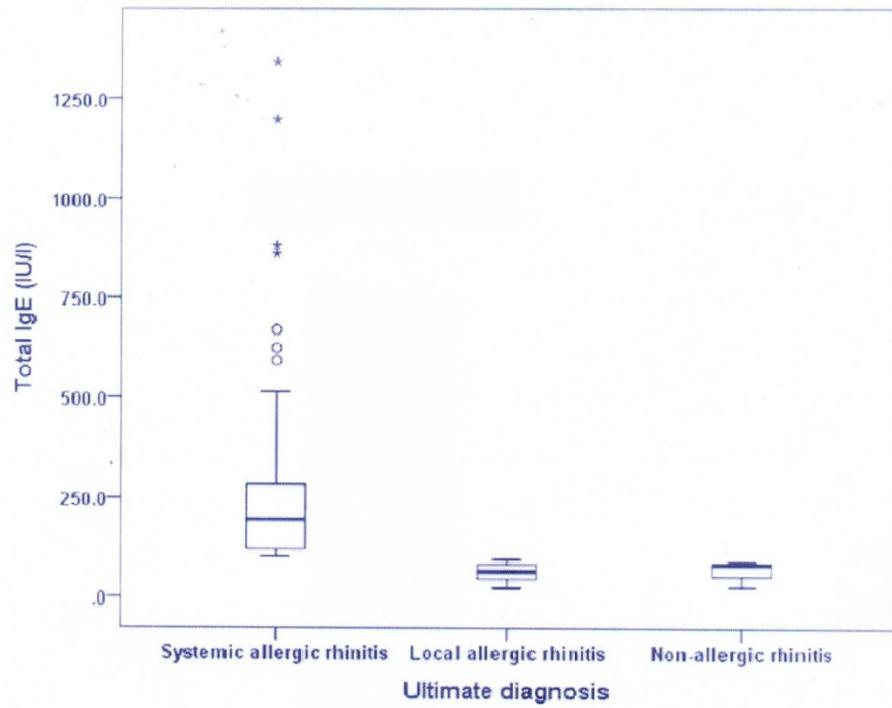


Figure 2 Boxplot showing total IgE level in the three forms of rhinitis.