



## Research article

## A study of Spirometric parameters in non asthmatic allergic rhinitis

Devika Thayyeshuth, Rajesh Venkataram<sup>\*</sup>, Vadisha Srinivas Bhat, Rajeshwary Aroor

K S Hegde Medical Academy, Mangalore, India



## ARTICLE INFO

## Keywords:

Absolute eosinophil count  
 Bronchial hyperresponsiveness  
 Forced vital capacity  
 Serum total immunoglobulin E

## ABSTRACT

**Introduction:** Allergic rhinitis (AR) is a common IgE-mediated inflammatory condition characterised by sneezing, nasal congestion, itching and rhinorrhoea. Nasal allergy is a strong risk factor for the onset of asthma in adults. Bronchial hyper-responsiveness (BHR) is a distinct feature of pathophysiology in asthma. Spirometric parameters like Forced Expiratory Volume in first second [FEV1] and Forced Expiratory Flow [FEF<sub>25-75%</sub>] are known to be impaired in patients with allergic rhinitis. We studied these parameters in subjects of AR who have never experienced any chest symptoms. It is well known that, subjects with allergic rhinitis are at greater risk of developing overt bronchial asthma in future.

**Methods:** All patients presented with symptoms of allergic rhinitis without history of bronchial asthma were included. Patients those who were clinically diagnosed with allergic rhinitis were evaluated with absolute eosinophilic count, serum IgE and Spirometric assessment. In spirometry, post bronchodilator FEV1 reversibility and post bronchodilator FEF<sub>25-75%</sub> values were used to assess lower airway abnormalities.

**Results:** Among 61 subjects, 32 were males and 29 were females. The maximum numbers [28] of patients were in 21–35 age group. Absolute eosinophil count was elevated in 38% of patients. 33% of patients showed elevated IgE values above 1000. 43% of patients showed FEV1 reversibility which is a sign of Bronchial hyperreactivity. 5% of patients showed impaired post bronchodilator FEF<sub>25-75%</sub> which indicates presence of small airway disease. There was significant correlation between FEV1 reversibility and elevated IgE.

**Conclusion:** Impaired spirometric parameters indicate coexistence of bronchial impairment and hence predisposition to progression from allergic rhinitis alone to overt asthma in future. Thus careful evaluation of lower airway has to be done to rule out coexisting subclinical asthma.

## 1. Introduction

Allergic rhinitis (AR) is a common IgE-mediated inflammatory condition characterized by sneezing, nasal congestion, itching, and rhinorrhoea. It is considered as a common risk factor for both onset and worsening of bronchial asthma [1]. Bronchial asthma is characterized by reversible airflow obstruction, and small airways (<2mm diameter) are involved in the pathogenesis of asthma [2]. Bronchial hyper-responsiveness (BHR) is a distinct feature in the pathophysiology of asthma and is observed in patients with allergic rhinitis who are exposed to perennial allergens [3, 4].

Spirometric parameters like Forced Expiratory Volume at Timed interval of 1 s [FEV1] and Forced Mid Expiratory flow [FEF<sub>25-75%</sub>] are known to be impaired in patients with nasal allergy or allergic rhinitis. The FEF<sub>25-75%</sub> is a marker of early bronchial impairment in nasal allergy and indicates small airway disease.

There is evidence that, AR treatment, particularly with immunotherapy against pollens in sensitized patients, has a substantial preventive effect

against development of bronchial asthma in future [5, 6, 7]. This study was undertaken with the objective of identifying individuals suffering from AR who haven't yet developed bronchial asthma clinically, but, are at substantial future risk because of nasal atopy. Spirometry- a simple and widely available tool was used to detect the presence of airway reactivity. Though, methacholine challenge test happens to be the gold standard test for detecting BHR, its availability is limited to research laboratories because of its complexity. Further, we looked for correlations between spirometric abnormalities and serum total IgE and absolute eosinophil count from peripheral blood as, these are also simple and widely available tools and known to be the markers associated with allergic disorders.

## 2. Methodology

This was a prospective study conducted on 61 consecutive consenting adult subjects aged more than 18 years, suffering from nasal allergy, attending the department of Otorhinolaryngology, at a tertiary care

<sup>\*</sup> Corresponding author.

E-mail address: [rajdocmmc@gmail.com](mailto:rajdocmmc@gmail.com) (R. Venkataram).

hospital in southern India between August 2017 and September 2018. In all cases, the clinical diagnosis of allergic rhinitis was made by thorough history and clinical examination and favourable response to empirical therapy for allergic rhinitis. Subjects with history of bronchial asthma, history of smoking, urticaria were excluded from the study. All subjects underwent blood investigations- Absolute Eosinophil Count (AEC) and Serum total Immunoglobulin E (IgE). Serum IgE was considered to be significantly elevated when the value was more than 1000 IU/ml [8]. Absolute eosinophil count was considered significantly raised when the value was more than 500/mm<sup>3</sup>, because, value of 400–440/mm<sup>3</sup> is the laboratory reference range in this region. Ethical clearance from institutional Ethical Committee was obtained.

All cases were subjected to spirometry with bronchodilator reversibility testing using Levosulbutamol 50 µg two puffs delivered by MDI (Metered Dose Inhaler) through a spacer. FEV<sub>1</sub> reversibility was considered significant when there was an improvement of post-bronchodilator FEV<sub>1</sub> by 200ml and 12% as per GINA (Global Initiative for asthma) guidelines [8]. Impairment of post-bronchodilator FEF<sub>25–75%</sub> was assessed by comparing the measured value with predicted normal value calculated by the spirometry software. A value of less than 65% of the predicted normal value was considered to be impaired.

### 3. Results

Demographic characteristics, Serum IgE & AEC values and spirometric findings have been tabulated in Table 1. Notably, 46% of the participants belonged to the age group of 21–35 years. IgE values were significantly raised (above 1000IU/ml) in 33% of the subjects while, AEC values were above 500/mm<sup>3</sup> in 38% of the individuals. Spirometry showed significant post bronchodilator reversibility of FEV<sub>1</sub> in 43% of the subjects and only 5% of the subjects had impaired post bronchodilator FEF<sub>25–75%</sub>.

All the study variables were assessed for correlation between them. However, statistically significant correlation was observed only between IgE and FEV<sub>1</sub> reversibility (p = 0.02) (Table 2).

### 4. Discussion

Allergic rhinitis (AR) is the most common allergic disorder and is characterized by an IgE-mediated inflammation induced by allergen exposure. Infiltrating cells, including T cells, eosinophils, mast cells and basophils release several mediators that cause the symptoms and cytokines that promote and amplify the inflammatory cascade. Allergic

**Table 1.** Demographic characteristics, blood investigation and spirometric findings of the study participants (n = 61).

| Characteristics                                    | Range     | Frequency (n = 61) | Percentage (%) |
|--|-----------|--------------------|----------------|
| Age  | ≤20       | 14                 | 23             |
|  | 21–35     | 28                 | 46             |
|  | 36–50     | 12                 | 19.6           |
|  | 51–65     | 07                 | 11.4           |
| Gender   | Male      | 32                 | 52.4           |
|  | Female    | 29                 | 47.5           |
| Absolute Eosinophil Count (cells/mm <sup>3</sup> ) | 1–500     | 38                 | 62.29          |
|  | 501–1000  | 21                 | 34.42          |
|  | 1001–2000 | 02                 | 3.27           |
| Ig E (IU/ml)                                       | 1–1000    | 41                 | 67.21          |
|  | 1001–2500 | 16                 | 26.22          |
|  | 2501–5000 | 04                 | 06.55          |
| FEV <sub>1</sub> Reversibility                     | Present   | 26                 | 42.6           |
|  | Absent    | 35                 | 57.3           |
| FEF <sub>25–75%</sub> Impairment                   | Present   | 3                  | 5              |
|  | Absent    | 58                 | 95             |

**Table 2.** Correlation between Ig E and Fev1 reversibility.

|                               | N  | Correlation value [p] | P Value |
|-------------------------------|----|-----------------------|---------|
| Ig E with Fev 1 reversibility | 61 | 0.290                 | 0.02    |

rhinitis is denoted by the maintenance of the integrity of the respiratory epithelium and lack of basement membrane thickening whereas, in asthma, there is epithelial fragility and subepithelial collagen deposition. Allergic rhinitis and bronchial asthma can be considered as single syndrome, popularly known as “One airway One disease” [9]. The FEV<sub>1</sub> reversibility to inhaled bronchodilators is a marker of bronchial involvement in patients with allergic rhinitis even in the absence of overt chest symptoms. It is also reported that the duration of allergic rhinitis is related to deterioration of nasal airflow limitation which indicates that there is a close relation between nasal and bronchial airflow [10].

In this study, the incidence of nasal allergy was maximum in the age group 21–35 years comprising 46% of total subjects. In a study conducted by Ciprandi et al, the majority of subjects of allergic rhinitis belonged to the age group of 20–30 years [11]. Lim M.Y reported that the highest number of subjects were between 20–40 years [12]. Our study is in agreement with above studies. In our study, the incidence was higher in males with a male to female ratio of 1.13:1 which is close to the study done by Wallace et al who reported 66.3% male and 33.7% female incidence with female to male ratio of 1.96:1 [13].

In this study, almost 38% of subjects were found to have raised AEC values. Poorey et al. reported in their study that 45% had AEC between 501–800/mm<sup>3</sup> [14]. Eosinophils play an important role in allergic airway diseases. Type 1 hypersensitivity reaction initiated by immunological mechanisms, mediated by IgE antibodies and eosinophils, occurs in allergic asthma. Kamfar et al, have found that total peripheral eosinophil count shows a very significant positive correlation with increased asthma severity [15]. However, we could not find any statistically significant correlation between AEC values and any of the other variables.

In the present study, serum IgE values were found to be more than 1000 IU/ml in 33% of subjects. Allergic sensitization mediated by IgE is the basis of allergic diseases like allergic rhinitis and bronchial asthma, and elevated total IgE is included as criteria for the diagnosis of certain allergic diseases. Tegnoor et al have reported that the IgE levels were elevated in more than 90% of subjects of allergic rhinitis with sneezing as the predominant symptom [16].

In the present study two spirometric parameters (FEV<sub>1</sub> reversibility & post bronchodilator FEF<sub>25–75%</sub>) were assessed and 43% of subjects showed significant FEV<sub>1</sub> reversibility which is a sign of Bronchial hyperreactivity irrespective of presence or absence of chest symptoms. 5% of subjects showed impaired post bronchodilator FEF<sub>25–75%</sub> which indicates the presence of small airway disease.

Poorey et al. in their study observed that all three parameters (FVC, FEV<sub>1</sub>, and FEF<sub>25–75%</sub>) were impaired in 6% of subjects and two parameters (FEV<sub>1</sub> and FEF<sub>25–75%</sub>) were impaired in 9% of subjects and only parameter FEF<sub>25–75%</sub> was found impaired in 64% of subjects. They concluded that FEF<sub>25–75%</sub> is a marker of small airway impairment in asthmatics with normal FVC values [14]. Ciprandi et al. in their study of bronchial hyperactivity and spirometric impairment in subjects with perennial allergic rhinitis observed 5 subjects with reduced FEV<sub>1</sub> and 48 with reduced FEF<sub>25–75%</sub> [17]. In another study, Ciprandi et al described the role of FEF<sub>25–75%</sub> as an early marker of bronchial impairment in patients with seasonal allergic rhinitis and concluded that impaired FEF<sub>25–75%</sub> suggests a relevant predictive factor for severe bronchial hyper-responsiveness [18]. In contrast, our study participants were more likely to have FEV<sub>1</sub> impairment rather than impaired post bronchodilator FEF<sub>25–75%</sub>. This may imply that the smaller airways are yet to be involved in our subjects. This finding assumes significance given the fact that, in subjects with clinical asthma, involvement of small airways is related with increased disease severity, poor asthma control and more risk of exacerbations. It is also widely agreed that such subjects need specialised

inhaler devices which can deliver the drug to small airways which are beyond the reach of conventional devices [19].

However, the significant finding of this study remains that, there is statistically significant positive correlation between serum IgE values and FEV1 reversibility in spirometry, which gives further impetus to the theory of “one airway one disease”. This observation strengthens our hypothesis that, clinicians treating patients of AR can use these parameters as markers of hidden bronchial involvement to select the sub population of patients which needs to be carefully observed and regularly followed. As stated earlier, there is evidence that, AR treatment, particularly with immunotherapy against pollens in sensitized patients, has a substantial preventive effect against development of bronchial asthma in future [5, 6, 7]. Moreover, where adherence to medications is an issue, these markers can be utilised to make patients realise the future risk of developing overt asthma and reinforce adherence.

## 5. Conclusion

Our study highlights the presence of subclinical bronchial involvement in patients with allergic rhinitis who have not yet experienced any chest symptoms. Hence careful evaluation of lower airway with spirometry has to be done to identify the subjects who are at risk for developing future bronchial asthma. Additionally, Serum IgE can be utilized as serological marker to strengthen this exercise. This would enable the clinician to identify the susceptible population and treat allergic rhinitis aggressively in them. Also, these findings can be utilized to focus on preventive measures in susceptible population like avoidance of allergen so as to prevent progression to overt bronchial asthma. However, we underline the need for longitudinal studies to track the susceptible population so identified, to see whether clinical asthma actually develops in them.

## Declarations

### Author contribution statement

Devika Thayyehuth: Performed procedure the experiments; Wrote the paper.

Rajesh Venkataram: Analyzed and interpreted the data; Wrote the paper.

Vadisha Srinivas Bhat: Conceived and designed the experiments; Analyzed and interpreted the data.

Rajeshwary Aroor: Analyzed and interpreted the data.

### Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

### Data availability statement

Data will be made available on request.

## Declaration of interests statement

The authors declare no conflict of interest.

## Additional information

No additional information is available for this paper.

## References

- [1] P.P. Plaschke, C. Janson, E. Norman, E. Bjornsson, S. Ellbjär, B. Jarvholm, Onset and remission of allergic rhinitis and asthma and the relationship with atopic sensitization and smoking, *Am. J. Respir. Crit. Care Med.* 162 (2000) 920–924.
- [2] Q. Hamid, Y. Song, T.C. Kotsimbos, E. Minshall, T.R. Bai, R.G. Hegele, J.C. Hogg, Inflammation of small airways in asthma, *J. Allergy Clin. Immunol.* 100 (1) (1997) 44–51.
- [3] J. Corren, The connection between allergic rhinitis and bronchial asthma, *Curr. Opin. Pulm. Med.* 13 (1) (2007) 13–18.
- [4] G. Ciprandi, I. Cirillo, M.A. Tosca, A. Vizzaccaro, Bronchial hyperreactivity and spirometric impairment in patients with perennial allergic rhinitis, *Int. Allergy Immunol.* 133 (2004) 14–18.
- [5] C. Moller, S. Dreborg, H.A. Ferdousi, S. Halken, A. Host, L. Jacobsen, et al., Pollen immunotherapy reduces the development of asthma in children with seasonal rhinoconjunctivitis (the PAT-study), *J. Allergy Clin. Immunol.* 109 (2) (2002) 251–256.
- [6] B. Niggemann, L. Jacobsen, S. Dreborg, H.A. Ferdousi, S. Halken, A. Host, et al., Fiveyear follow-up on the PAT study: specific immunotherapy and long-term prevention of asthma in children, *Allergy* 61 (7) (2006) 855–859.
- [7] E. Novembre, E. Galli, F. Landi, C. Caffarelli, M. Pifferi, E. De Marco, et al., Coseasonal sublingual immunotherapy reduces the development of asthma in children with allergic rhinoconjunctivitis, *J. Allergy Clin. Immunol.* 114 (4) (2004) 851–857.
- [8] Global Initiative for Asthma, Global strategy for the diagnosis and prevention. Global Initiative for Asthma, 2018 (updated 2018).
- [9] S. Guerra, D.L. Sherrill, F.D. Martinez, R.A. Barbee, Rhinitis as an independent risk factor for adult-onset asthma, *J. Allergy Clin. Immunol.* 109 (3) (2002) 419–425.
- [10] G. Ciprandi, I. Cirillo, The lower airway pathology of rhinitis. Update review, *J. Allergy Clin. Immunol.* 118 (2006) 1105–1109.
- [11] G. Ciprandi, I. Cirillo, C. Klersy, G.L. Marseglia, A. Vizzaccaro, E. Pallestrini, M. Tosca, Role of FEF25–75 as an early marker of bronchial impairment in patients with seasonal allergic rhinitis, *Am. J. Rhinol.* 20 (6) (2006) 641–647.
- [12] MY L, JLL. Allergic rhinitis; evidence-based practice. *Singap. Med. J.* 51(7):542–550.
- [13] D.V. Wallace, M. Dykewicz, D. Bernstein, J. Blessing Moore, I Cox, Dportnoy Khan, The diagnosis and management of rhinitis: an updated practice parameter, *J. Allergy Clin. Immunol.* 122 (2) (2008) S1–S84.
- [14] V.K. Poorey, S. Soni, P. Thakur, A. Gupta, Effect of nasal allergy over spirometric parameters: a prospective study, *Indian J. Otolaryngol. Head Neck Surg.* 68 (1) (2015) 6–10.
- [15] H.Z. Kamfar, E.E. Koshak, W.A. Milaat, Is there a role for automated eosinophil count in asthma severity assessment, *J. Asthma* 36 (2) (1999) 153–158.
- [16] S.M. Tegnoor, O.B. Jabri, M. Vijay Kumar, V. Kurlle, Assessment of serum IgE levels in patients of allergic rhinitis, *Al Ameen J. Med. Sci.* 10 (2) (2017) 136–140.
- [17] G. Ciprandi, I. Cirillo, M.A. Tosca, A. Vizzaccaro, Bronchial hyperreactivity and spirometric impairment in patients with perennial allergic rhinitis, *Int. Arch. Allergy Immunol.* 133 (2004) 14–18.
- [18] G. Ciprandi, I. Cirillo, C. Klersy, G.L. Marseglia, A. Vizzaccaro, E. Pallestrini, et al., Role of FEF25–75 as an early marker of bronchial impairment in patients with seasonal allergic rhinitis, *Am. J. Rhinol.* 20 (6) (2006) 641–647.
- [19] T.F. Carr, R. Altisheh, M. Zitt, Small airways disease and severe asthma, *World Allergy Organ. J.* 10 (1) (2017) 20.