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Correlation of Peripheral Eosinophilia with Severity of Nasobronchial Allergy

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Abstract: ***Introduction: Asthma and allergic rhinitis may present concomitantly and have similar clinical presentations, in accordance with the 'one airway hypothesis'. Pathologically both induce an inflammatory response mediated by eosinophils, mast cells, T cells and cells of monocytic lineage. Aim: This study was undertaken to determine the correlation between peripheral eosinophilia and severity of nasobronchial allergy by symptom score assessment and spirometric evaluation. Methodology: 108 patients diagnosed with nasobronchial allergy were evaluated with questionnaire to assess symptom scores for asthma and nasal& non nasal symptoms of allergic rhinitis and subject to spirometry. Results:Elevated blood eosinophil counts was demonstrated amongst both males and females. A direct correlation was found between the symptom severity score for both allergic rhinitis and asthma symptoms with peripheral eosinophilia. Inverse correlation was found between the total blood eosinophil count and spirometric assessment of lung function by*** FEV_1/FVC, FEV_1 ***and FVC. Conclusion: Peripheral blood eosinophilia is an useful parameter which may be used to assess indirectly the symptom severity and lung function in patients with nasobronchial allergy.***

Keywords: Asthma, Allergic rhinitis, Nasobronchial allergy, Eosinophilia, Spirometry

1. Introduction

Asthma and Allergic rhinitis(AR) may develop concurrently or sequentially and may have similar histories and exacerbations. It may thus be compared to a coin with two different sides and argument is put forward for the unified concept of nasobronchial allergy or allergic rhinobronchitis. The nasal and bronchial mucosa present similarities and one of the most important concepts regarding nose-lung interactions is the functional complementarity[1]. Majority of patients diagnosed with bronchial asthma also report the presence of rhinitis[2] supporting the hypothesis of "one airway one disease".

Asthma and Allergic Rhinitis induce a similar inflammatory reaction in both nasal as well as bronchial mucosa. Endobronchial challenge in rhinitis patients induces a bronchial reaction whereas a bronchial challenge induces nasal inflammation. The commonly recognized mediators include eosinophils, mast cells, T-lymphocytes and cells of the monocytic lineage. The pro-inflammatory mediators elaborated by these cells are also similar in both nasal and bronchial mucosa such as (histamine, CysLT), Th2 cytokines and chemokines. [3],[4],[5].

Evidence against an important role of eosinophils in asthma is provided by studies utilizing anti IL-5 antibody treatment, which has been shown to reduce sputum and blood eosinophil counts by 60%, but still does not improve the symptom severity of asthma.[6][7][8][9][10]

Therefore, in the background of this controversy the current study was undertaken to establish the presence of peripheral eosinophilia in patients with nasobronchial allergy and to demonstrate if the level of peripheral eosinophilia had any impact on the symptom severity and lung functions as assessed by spirometry and peak flow measurement.

2. Aims and Objectives

To determine the correlation between peripheral eosinophilia and severity of nasobronchial allergy as demonstrated subjectively by symptom score assessment and objectively by spirometric parameters.

3. Methodology

This is a prospective randomized, single blinded, comparative, parallel group study; approved by research committee and ethical committee. 108 patients attending outpatient clinic at Chettinad Hospital and Research Institute, Chennai, in the age group of 15-65 years, diagnosed with Asthma as per GINA guidelines and concomitant Allergic Rhinitis (ARIA guidelines) were included. Smokers, Pregnant and/or lactating women, life threatening asthma, chronic persistent severe asthma, significant concurrent diseases; including a recent respiratory tract infection, and significant concomitant chronic respiratory illnesses like Bronchiectasis, Treated Pulmonary Tuberculosis with Obstructive Airway Diseases, recent nasal surgery or anatomic defects of the nose, such as a deviated septum or nasal septal perforation, patients who had received more than

two courses of parenteral corticosteroids within 3 months , any comorbid systemic illness which may affect symptom assessment directly or indirectly were excluded from the study

Patients were administered a self-assessment questionnaire for symptom severity assessment of both Asthma and Allergic Rhinitis on a likert scale with higher score reflecting increasing severity of disease. Spirometry was performed for all subjects and Peak Expiratory Flow was recorded using the Wright's mini peak flow meter. The patients then underwent blood investigations to measure the Total Eosinophil Count (TEC). The data thus collected was recorded, de-identified and then subject to statistical analysis.

4. Statistical Analysis

IBM SPSS statistical software version 21 was used for statistical analysis. [r] Clinical symptom scores and PEFR were taken as primary outcome variables. Descriptive analysis of all the explanatory and outcome parameters was done. All the categorical variables were presented in frequencies and percentages. The numerical variables presented in Means and Standard deviations. Demographic variables like age and gender and clinical variables like symptoms and PFT parameters were correlated, by appropriate cross tabulations. The association between explanatory and outcome parameters was assessed by ODDs ratios. Paired t-test, independent sample t-test and chi square test were used appropriately to assess the statistical significance of these associations and 95% Confidence intervals were also calculated for all the parameters. Graphical representation of the data was also presented in appropriate way.

5. Results

Using a cut off value of 400 cells/ cu mm for defining peripheral eosinophilia, out of the 108 asthmatics recruited into the study 81(75%) were found to have peripheral eosinophilia.

Table1: Descriptive analysis of Total Eosinophil Count (N=108)

TEC	Frequency	Percent
<400	27	25.0
400 or >400	81	75.0
Total	108	100.0

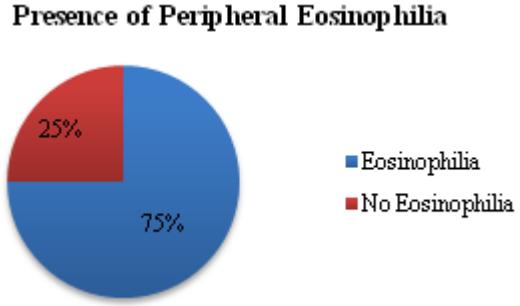

Figure 1: Distribution of Asthmatics with Peripheral Eosinophilia

Gender association of Peripheral Eosinophilia

An equitable distribution of peripheral eosinophilia was noted amongst the male and female asthmatics, with Odds ratio of 0.743 for males versus females (p = 0.504, 95% CI 0.310 – 1.778)

Table 2: Association between Total Eosinophil Count and Gender (N=108)

Sex	TEC		Odds ratio	P value	95% CI	
	<400	400 or>400			Lower	Upper
Male	13(22.4%)	45(77.6%)	0.74	0.50	0.31	1.77
Female	14(28.0%)	36(72.0%)				

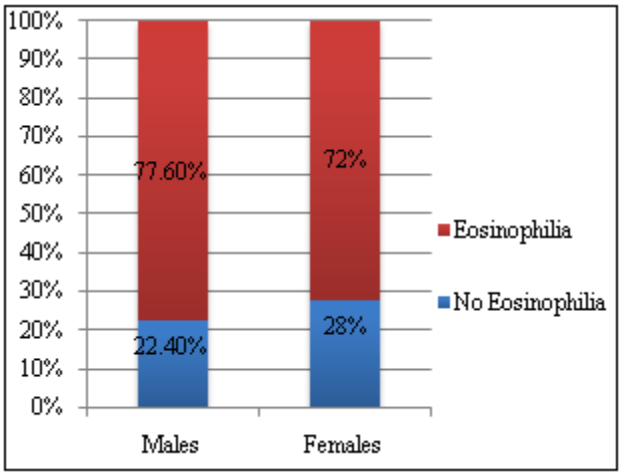

Figure 2: Genderwise distribution of eosinophilia (n = 108, males = 58, females = 50)

Correlation with spirometric parameters – FEV_1 and PEFR

TEC showed a significant negative correlation with the FEV1/FVC ratio (-0.225, p = 0.019). Although FEV_1 and FVC demonstrated a negative correlation but failed to reach statistical significance. (-0.160, p = 0.098 & -0.117, p = 0.226 respectively). No significant correlation could be established between Total Eosinophil Count and Peak Expiratory Flow Rate.

Table 3: Correlation between TEC and spirometric parameters (n=108)

Parameter	Correlation coefficient	P value	95% CI	
			Lower Bound	Upper Bound
FEV_1/FVC	-0.225	0.019	-0.013	-0.001
FEV_1	-0.160	0.098	-0.019	0.002
FVC	-0.117	0.226	-0.015	0.003
PEFR	0.024	0.804	-0.038	0.049

Correlation with symptoms – asthma and allergic rhinitis (nasal and non-nasal)

A direct correlation was observed between the total peripheral eosinophil count and the total symptom severity score for allergic rhinitis, both nasal (0.086, p = 0.379) and non-nasal (0.025, p = 0.794) as well as for asthma symptom score (0.025, p = 0.794).

Table 4: Correlation between TEC and clinical parameters in study group (n=108)

Parameter	Correlation coefficient	P value	95% CI	
			Upper	Lower
TEC and AR Nasal Score	0.080	0.412	-0.001	0.002
TEC and AR Non nasal Score	0.086	0.379	-0.002	0.001
TEC and Asthma Score	0.025	0.794	-0.002	0.002

6. Discussion

A high prevalence of peripheral blood eosinophilia was found in patients of nasobronchial allergy with 75% of the patients demonstrating elevated TEC. This is in concordance with the work of O'Byrne P et al, who have elucidated an increase in eosinophil count in the sputum of asthma patients during the late phase response (7 hours after challenge), and shown it to be further associated with peripheral blood eosinophilia. Wardlaw AJ et al and Christdoulopoulos P et al have attributed this to be due to the influence of IL-5 generated in the inflamed lung tissue and IL-3 and GM-CSF within the asthmatic lungs [11][12][13]. However no gender predisposition could be established for existence of eosinophilia in asthma and allergic rhinitis.

A direct correlation was found between the symptom severity score for both allergic rhinitis and asthma symptoms with peripheral eosinophilia. While an inverse correlation was found between the total blood eosinophil count and spirometric assessment of lung function by FEV_1/FVC, FEV_1 and FVC. Similar findings have been demonstrated by Ulrilk CS, who established a positive correlation between blood eosinophilia and symptom severity and a negative correlation with FEV_1.[14]

Seqwick JB et al have attributed the contribution of eosinophils to nasal and bronchial mucosal inflammation due to increased eosinophil derived neurotoxin content per cell in asthmatics as compared to healthy subjects and patients with allergy but not asthma [15]. Denburg et al have demonstrated an increased bone marrow inflammatory cell production followed by tissue recruitment, in response to an endobronchial allergen provocation, in atopic individuals. Studies that support the critical involvement of the bone marrow in the development of eosinophilic inflammation of the airways points out the systemic nature of these conditions. It is therefore likely that a truly 'systemic' response to the application of inflammatory stimuli to the nasal or bronchial mucosa should be associated with an activation of the mentioned mechanisms.[16],[17],[18],[19],[20],[21]

The limitations of the study which may be responsible for non-attainment of statistical significance in the results are the small sample size and the low racial, cultural, socio-economic and geographic diversity owing to a single center study.

7. Conclusion

From the current study we conclude that total eosinophil count demonstrates a direct correlation with the symptom severity and an inverse correlation with the objective spirometric evaluation (FEV_1/FVC, FEV_1, FVC). However, further large scale multicenter trials need to evaluate this correlation, to permit its use as a cheap, inexpensive and rapid tool for asthma severity evaluation.

Conflict of Interest: None

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