Assessment of Clinical Severity of Bronchial Asthma in Correlation with Sputum Eosinophil Count, Peripheral Blood Eosinophil Count & Serum Total IgE Level in a Tertiary Care Hospital

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Abstract:

Context: Asthma is a chronic respiratory disorder of the airways characterised by bronchial hyper responsiveness, respiratory symptoms, structural remodelling and reversible and variable airflow limitation. Eosinophils and serum IgE both considered a good marker of airway inflammation and correlation of these clinical markers of airway inflammation in asthma is not well established.

Aims: This study aims to correlate between serum IgE, sputum eosinophil count, peripheral blood eosinophil count and severity of bronchial asthma.

Methods: This study includes all adult asthmatic patients who came to pulmonary medicine OPD and selected for the study on the basis of inclusion criteria and GINA guidelines. Blood collected for peripheral eosinophil count & serum IgE levels and sputum for sputum eosinophil count.

Results: Present study showed majority of cases were mild asthma (52%) with sputum eosinophil <3%, whereas the sputum eosinophil counts ≥3% was nil in mild asthma but was 16% each in Moderate and Severe asthma (p value <0.001). Mean value of AEC in mild cases was 402.53, moderate cases was 603.13, severe cases was 295.55(p value 0.089, which means it doesn't have any positive correlation). Mean serum IgE level was 269.80 iu/ml in mild cases, 983.65 iu/ml in moderate cases and 997.91 iu/ml in severe asthmatic patients implying increase in level according to increased severity (p value 0.008).

Conclusion: Assessment of sputum eosinophil count is a cheap and non-invasive measure which directly measures airway inflammation. Present study shows positive correlation between sputum eosinophilia and serum IgE with severity of asthma.

Keywords: Asthma, Sputum Eosinophil Count, Peripheral Blood Eosinophil Count, Serum IgE, Haematoxylin and Eosin stain.

Introduction

Asthma is a chronic respiratory disorder of the airways characterised by bronchial hyper responsiveness, respiratory symptoms, structural remodelling and reversible and variable airflow limitation. [1] With the case burden of approximately 358.2 million worldwide, prevalence of asthma increased by 12.6%.

The Indian study on epidemiology of asthma, respiratory symptoms and chronic bronchitis (INSEARCH) estimate the prevalence rate of asthma is 2.05% between 2007 and 2009 (with an estimated burden of 17.23 million in 2011).[2] (More recently Agrawal et al estimated the prevalence of self-reported asthma at around 2%).

It has been observed in many studies that serum IgE level is elevated in asthmatic and correlates with the severity of asthma. Eosinophil infiltration to the airway is hallmark feature of pathogenesis of asthma which triggers the chronic inflammation and are raised in acute exacerbations.

Hence assessing eosinophil count is considered as a marker of asthmatic airway inflammation. In asthma patients, eosinophils are demonstrated in blood, sputum, bronchial lavage and bronchial biopsy specimens, and increase in number matching with disease severity, airway obstruction and bronchial hyper reactivity.[3]

Aims and Objectives: To study the correlation between sputum eosinophil count, peripheral blood eosinophil count and serum IgE with severity of bronchial asthma.

Materials and Methods: The study was conducted among adult patients having asthma who presented to OPD and IPD of Pulmonary medicine department, SCB medical college, Cuttack during September 2018 to September 2019.

Inclusion criteria

1. All stable cases of bronchial asthma attending Pulmonary Medicine OPD,
2. All cases of bronchial asthma with acute exacerbation who presented to OPD and IPD of Pulmonary medicine.

Exclusion criteria

1. Patients with Asthma - COPD overlap syndrome (ACO),
2. Cases of Pulmonary Eosinophilia due to other causes
3. Patients who didn't give written informed consent.

Based on history and clinical criteria 57 patients of Bronchial Asthma were screened. Patients with family history of asthma, those with childhood episodic attacks and those who had complaints of cough, wheeze, breathlessness and chest tightness, nocturnal awakenings were thoroughly examined and categorized as Intermittent, Mild persistent, Moderate persistent and Severe persistent asthma according to GINA guidelines (2019). 50 patients were selected for the study after written informed consent that fulfilled the inclusion criteria.

Spirometric Method: We used Schillar SP-1 Spirometer. The degree of reversibility was taken as "increase in forced expiratory volume in 1st sec (FEV1) of 12% and 200 ml from the pre bronchodilator value" was considered of asthma as per GINA guidelines 2019.

Method of Sputum Eosinophil Count: The sputum was homogenized by adding phosphate-buffered saline, vortexed for 30s and centrifuged for 10 min. Centrifuge was transferred to the slide after adding 0.1% dithiothreitol Staining was done by H&E stain and analysed using microscope.[4] Sputum eosinophil count $\geq$3% was considered to be abnormal.

Method for Serum IgE Level: Blood samples were measured using Human IgE kit E0188Hu in EVOLIS twin plus analyser. The kit uses monoclonal antibodies specifically directed against IgE. Total IgE levels more than 100 iu/ml were taken as abnormal [5][6].

Method for Absolute Eosinophil Count: EDTA blood was sent to pathology department where it was subjected to automated analyser for absolute eosinophil count and confirmed by peripheral smear.

After collecting the reports of blood, serum, and sputum the findings were matched with spirometric results and interpreted to evaluate the correlations between each finding to derive the final conclusion in each variety of asthma patients.

Results:

Statistical Analysis: Statistical analysis was performed by statistical software package (SPSS FOR WINDOWS VERSION 21; SPSS Inc. Chicago, IL, USA). Data was presented in a descriptive fashion as the mean standard deviation (SD) or the median (range) A total number of 50 patients was enrolled for the study. Demographic, clinical, lab parameter and spirometric data is provided in table no. 1. Mean age of our study is 42.48 years among which 60% is female and 40% is male.

Demographic, Clinical, Lab Parameter and Spirometry Data

<div align="center">Table 1:</div>

Baseline Characteristics	Result
Age	42.48±15.75
Sex: Male Female	 40% 60%
BMI Underweight Normal Overweight Obese	 10% 50% 34% 6%
Family History Present Absent	 56% 44%
History Of Allergy Dust Allergy	 66%

Food Allergy	4%
No Allergy	30%
Comorbidities	
Allergic Rhinitis	34%
DM	4%
Eczema	14%
GERD	16%
Hypertension	14%
Obesity	6%
Hypothyroidism	4%
Symptoms	
Cough	92%
Breathlessness	76%
Chest Tightness	58%
Wheezing	100%
Clinical Signs	
Pulse Rate	79.64±7.85
Respiratory Rate	18.76±2.76
Blood Pressure(SBP/DBP)	114.68±8.37/78.44±7.44
Spo2	96.16±3.01
Chest X-Ray Pa View	
Normal	94%
Hyperinflation	6%
Absolute Eosinophil Count	443.46±295.77
Sputum Eosinophil Count	2.78±5.47
Serum IgE	615.01+98.97
FEV1(% Of Predicted)-Pre BD	62.04±25.06
FEV1(% Of Predicted)-Post BD	72.28±25.40
FEV1/FVC	85.30+8.12
PEFR Pre BD	43.96±21.43
PEFR- Post BD	54.99±24.34
Severity Of Asthma	
Mild	52%
Moderate	30%
Severe	18%

Table 2:

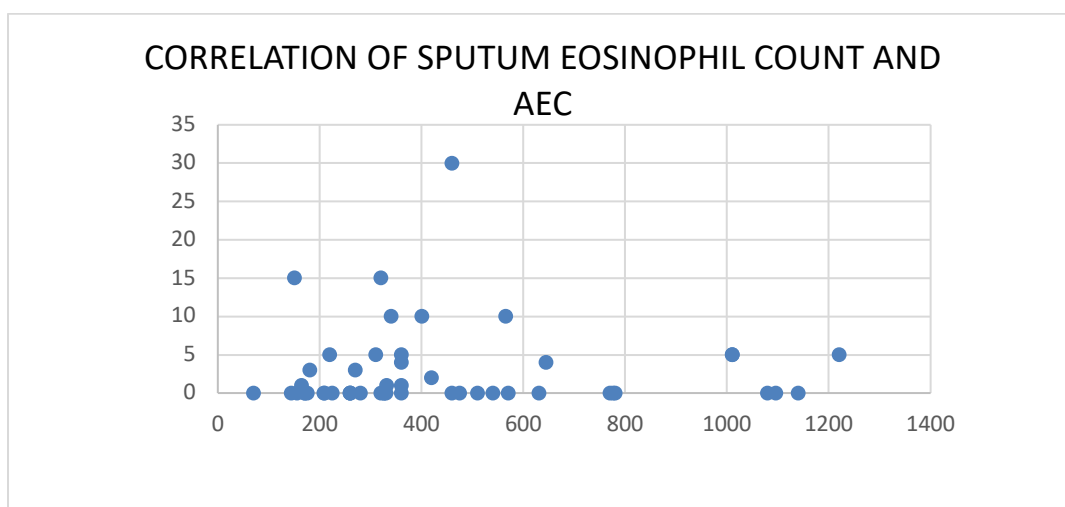| Asthma	Mild	Moderate	Severe
AEC	603.13±351.15	424.04±295.02	298.75±105.61
Sputum Eosinophil	0.15±0.46	3±3.60	10±8.90
S. IgE	269.80±369.90	983.65±737.73	997.91±901.55

Figure 1: Correlation of Sputum Eosinophil Count and AEC

This diagram showed sputum eosinophil count was increasing when absolute eosinophil count was decreasing irrespective of severity.

Discussion:

1. Sputum Eosinophil Count and Severity of Asthma

In our study we observed 32% cases of asthma were associated with sputum eosinophil count ≥3% which was more or less similar to the study by Kumar RM et al(in which26.3% cases had moderate and severe persistent asthma.) and Manise M et al(who reported 41% cases had sputum eosinophil count ≥3%)[7,19].

Ronchi et al found that sputum eosinophils (range 0-61%) were significantly greater in asthmatics than normal subjects and found that the most severe group having highest score.[8] But conflicting results were reported by Gibson et al and Palomino et al [9,10]. Bandyopadhyay A et al and Duncan CJ et al reported that higher sputum eosinophil count was associated with increased severity of asthma [11,12], which was also found in our study with significant correlation (P<0.001).

2. Absolute Eosinophil Count (AEC) and Severity of Asthma

In our study absolute eosinophil count was ranged between 70 to 1220 cells/cmm, Mean AEC in study population was 433.73 which is more or less similar to Koshak et al (Mean AEC 393, range 22-2470), Kamfar HZ, Milaat et al (Mean AEC 581.7, range 10-2100). As with Roshan MK et al and Palomino et al, we found no significant correlation between AEC and asthma severity (P=0.089) [10,13,14]. One of the reasons could be due to elevation of peripheral eosinophil count in other condition such as allergic rhinitis, parasitic infection which may not be related to asthma severity. Eosinophils are present in intravascular space for a brief period only. One of the hypotheses could be influx of peripheral blood eosinophils rapidly into the airways suggests that the relationship between peripheral blood eosinophil count with airway inflammation may be transitory [15,16].

3. Serum IgE and Severity of Asthma

We found 80% of the study population have serum IgE >100 iu/ml alike Kartasamita et al (94%), Manise M et al (70%), Kumar RM et al (96.1%) [17,19,20]. In our study Mean serum IgE level in mild, moderate & severe asthma was 269.80iu/ml, 983.65iu/ml, 997.91iu/ml respectively which was comparable with studies of Janeway et al (304.6, 882.4, 1420.48) Srikantaiah et al (250, 846, 1045.32). Janeway et al and Sandeep T et al demonstrated more or less similar figure in serum

IgE level with increasing order of severity similar to our study(P=0.008) [18].

Manise M et al found significant correlation between sputum eosinophil and raised serum IgE similar to our study (P=0.007). In our study there was significant inverse correlation between serum IgE level and predicted FEV1 (P value=0.009) which correlates with Kumar RM et al (P=0.011).

Conclusion

Sputum eosinophilia is a hallmark of asthma and thought to be a major effector cell responsible for pathogenesis of asthma. From blood stream eosinophils migrate across the endothelium to the airway lumen. Assessment of sputum eosinophil count is simple, inexpensive, non-invasive and direct measurement of airway inflammation that could help to identify eosinophilic or neutrophilic asthma. The present study showed strong correlation of sputum eosinophilia and serum IgE level with asthma severity rather than absolute eosinophil count. So, it is very much helpful in guiding the asthma phenotype and management for initiation of steroids in asthmatic patients in day-to-day practice by the physicians. Further studies may be carried out to establish the above relationships to assess treatment policy in severe asthmatic patients in future.

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