

Relationship between pulmonary function test and sputum inflammatory cells in adult asthmatic patients

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Objectives: To investigate sputum inflammatory cell indices and to correlate them with the pulmonary function test in asthmatic adults to assess the severity of asthma.

Methodology: This cross sectional study was carried out from February 2017 to December 2018 in the Department of Physiology, University of Karachi with the collaboration of Department of Chest Medicine, Jinnah Postgraduate Medical Center, Karachi. A total of 140 asthmatic patients of age between 20-60 years of either gender were selected. Patients were diagnosed to be asthmatics according to Global Initiative for Asthma Guideline (GINA). Patient's biophysical parameters were age, gender and body mass index. Vitalograph compact was used to perform spirometry. Sputum cell profile was performed by Leishman's stain. The study was analyzed

statistically by SPSS version 21 and $p < 0.05$ was used to assess the statistical significance.

Results: All 140 patients were divided into neutrophilic, eosinophilic and mix asthmatic groups according to the presence of dominant inflammatory cells in sputum. Out of 140, 104(74%) patients were mix asthmatics, 11(8%) were eosinophilic and 25(18%) were neutrophilic. Sputum eosinophils and neutrophils were significantly correlated with FEV1/FVC (for eosinophils $r = -0.281$, $p = 0.004$, for neutrophils $r = -0.468$, $p = 0.000$).

Conclusion: It is concluded that more inflammatory cells in sputum may increase the severity of asthma and impair the lung functions. (Rawal Med J 202;45:58-61).

Keywords: Asthma, inflammatory cells, pulmonary function test.

INTRODUCTION

Asthma is the disease of the airways. Symptoms are breathlessness, wheeze and coughing with or without sputum. It is diagnosed by the symptoms, response to therapy and spirometry.¹ Clinically, asthma may show a normal spirometry to severe obstruction when examined in the same person from normal condition and during asthmatic episode.^{2,3} Prevalence of asthma in different countries is about 1-18%.⁴ In Pakistan, prevalence of allergic asthma is very high and the commonest allergen is house dust mite.⁵ The prevalence of occupational asthma is about 5-25%. The common occupation associated with this condition are baking, nursing, painting with spray, food processing, hairdressing etc.⁶ Atopy is the most important risk factor for asthma. A positive family history increases the chances of asthma in childhood.^{7,8}

Asthma causes narrowing of the airway and wheezing. Airways are infiltrated by neutrophils,

eosinophils, T-lymphocytes, cytokines, histamines, chemokines, macrophages, and leukotrienes. In chronic asthmatic condition, the airways smooth muscles increase in size and also there is increased number of mucous glands.^{9,10}

GINA has classified it on the basis of symptoms, FEV₁, and PEF.¹¹ It has also been classified on the basis of clinical features into Intermittent, mild persistent, moderate persistent and severe persistent.¹² In Pakistan, the reports are rare to provide assistance in diagnosing the type of Asthma. This study was aimed to investigate the cellular profile of sputum in asthmatic adults to provide help in diagnosing the type of asthma.

METHODOLOGY

This cross sectional study was conducted in the department of physiology, University of Karachi with the collaboration of Department of Chest Medicine Jinnah Postgraduate Medical Center,

Karachi. Total 140 asthmatic subjects of 20-60 years from either gender were selected in this research. complete history was taken. A medical proforma was filled by each participant. All asthmatics were diagnosed as per guidelines of GINA. Pregnant patients, patients having other pulmonary disorders or any chronic disease were excluded from the study. Approval was taken from Institutional Ethical Review Board (IERB) of JPMC and a Consent form was signed by all patients.

Patients were divided into three groups according to their sputum inflammatory cell profile: 1. Neutrophilic asthmatics; when sputum showed more than 40% of neutrophils and less than 1.4% of eosinophils, 2. Eosinophilic asthmatics; when sputum showed less than 40% of neutrophils and more than 1.4% of eosinophils and 3. Mixed asthmatics; when sputum showed more than 40% of neutrophils and more than 1.4% of eosinophils. Pulmonary function test (spirometry) was performed by vitalograph and best values for FVC and FEV1 were taken.

Subjects were instructed to wash their mouth with water and blow the nose to avoid contamination with saliva and post nasal drip. Then, they were instructed to take deep breath and cough up sputum directly into wide mouth sterile plastic container. Volume of sputum had to be about 2-5ml. Sample examination was performed within two hours of collection. The smear was air dried for 15-30 minutes. Leishman's stain was used and slide was examined under microscope. Normal Sputum cell indices were: Neutrophil 2-40% and Eosinophil 0-1.4%.

Statistical Analysis: Data were analyzed with SPSS version 20. Mean and standard deviation were calculated for all continuous variables. Frequency and percentages were calculated for categorical variables. Correlation values are determined by Pearson correlation. $p < 0.05$ was used to assess the statistical significance.

RESULTS

Mean ages of neutrophilic, eosinophilic and mix asthmatics were 43.89 ± 10.458 , 26 ± 4.243 and 44.89 ± 10.071 years, respectively. This age difference among these groups was statistically

significant ($p=003$). Differences between means of height, weight and BMI among groups were not statistically significant. Table 1 describes the comparison of biophysical parameters among subgroups of patients ($n=140$).

Table 1. Comparison of Biophysical parameters among subgroups of asthma.

Variables	Neutrophilic asthma (N=25)		Eosinophilic asthma (N=11)		Mix asthma (N=104)		P-value
	Mean	±SD	Mean	±SD	Mean	±SD	
Age(years)	43.89	10.458	26.00	4.243	44.89	10.071	0.003*
Height(ft)	5.3111	.41366	5.3300	.38236	5.4286	.35801	0.645
Weight(kg)	60.00	14.816	64.75	4.113	68.00	9.764	0.131
BMI(kg/m ²)	24.8333	4.96462	26.9000	4.46841	27.0081	4.10734	0.398

Table 2. Comparison of pulmonary function test among subgroups of asthma.

Variables	Neutrophilic asthma		Eosinophilic asthma		Mix asthma		P value
	Mean±SD	Mean±SD	Mean±SD	Mean±SD			
FEV1(L)	1.36	0.28	1.40	0.26	1.41	0.28	0.90
FVC(L)	2.24	0.46	2.24	0.36	2.34	0.40	0.76
FEV1/FVC%	61.13	5.64	62.40	2.93	59.66	4.48	.042

Table 3. Comparison of sputum inflammatory cell profile among subgroups of asthma.

Asthma Groups	N=140	Dominant cells	Sputum Cells Mean ± SD
Asthma Type			
Neutrophilic asthmatics (neutrophils>40%)	25(18%)	Neutrophils	N=75.88±8.12
Eosinophilic asthmatics (eosinophils>1.4%)	11(8%)	Eosinophils	E=6.25±2.52
Mix asthmatics (neutrophils>40%) (Eosinophils>1.4%)	104(74%)	Neutrophils Eosinophils	N=77.83±10.64 E=6.18±3.31

Table 4. Correlation of sputum neutrophils and eosinophils with pulmonary function test.

Variables	Neutrophils		Eosinophils	
	Correlation (r)	P value	Correlation (r)	P-value
FEV1(L)	-0.048	0.612	-0.023	0.815
FVC(L)	-0.023	0.818	-0.053	0.599
FEV1/FVC(%)	-0.468	0.000	-0.281	0.004

Table 2 describes the comparison of pulmonary function test among subgroups of asthma. There was no statistically significant difference among these

parameters in these groups. Out of 140 patients, 25 (18%) were neutrophilic asthmatics, having $75.88 \pm 8.12\%$ neutrophils, 11 (8%) were eosinophilic having $6.25 \pm 2.52\%$ eosinophils and 104 (74%) were mixed asthmatics having $77.83 \pm 10.64\%$ and $6.18 \pm 3.31\%$ neutrophils and eosinophils, respectively (Table 3). The ratio between FEV1/FVC was significantly correlated with neutrophils ($r = -0.468$, $p = 0.000$) and eosinophils ($r = -0.281$, $p = 0.004$). However, correlation of neutrophils and eosinophils with FEV1 and FVC are insignificant statistically (Table 4).

DISCUSSION

In this study, sputum cell report revealed that patients had different types of airway inflammation. Out of 140 patients, 18% were diagnosed as neutrophilic asthma, while 8% as eosinophilic and 74% asthmatic patients had mix airway inflammation based on sputum inflammatory cell profile.

We observed that mix type of disease pattern was more prevalent as well as more in severity as compared to neutrophilic and eosinophilic types. Moreover, mixed asthmatics were usually resistant to routine treatment of asthma which may lead to status asthmaticus. This may be due to the fact that mixed asthmatics had more neutrophils (77.83%) in their sputum as compared to neutrophilic disease (75.88%), which may be the cause of resistant and severe disease in this type. A study by Thompson observed that more than 50% of asthmatic patients had non eosinophilic asthma.¹³

Asthma is characterized by airway inflammation with enhanced activity of Th2-cells, which then cause IgE production, resulting in eosinophilic airway inflammation and hyperresponsiveness.^{14,15} A study by Chesné et al showed that on the basis of sputum cell count asthmatic patients can be divided into neutrophilic and eosinophilic.¹⁶ Wood et al classified their patients as non-neutrophilic or neutrophilic asthmatics, making cellular profile of sputum in asthmatic patients of great importance.¹⁷

We compared pulmonary function test among different groups of asthma but we did not find any significant difference among them but when we correlated them with sputum eosinophils and neutrophils and found negative correlation of

eosinophil with FEV1 and FVC. However, this result was not statistically significant ($r = -0.023$ and -0.053 , respectively). A study by Mohamed et al showed weak positive correlation between eosinophils and FEV1 and FVC which was not significant.¹⁸ A study by Kumar et al found significant negative correlation between FEV1 and sputum eosinophils.¹⁹

We also noticed a significant negative correlation of FEV1/FVC with eosinophils ($r = -0.281$, $p = 0.004$), as reported by Hastie et al.²⁰ We did correlation of sputum neutrophil count with pulmonary function test and we found non-significant negative correlation of FEV1 and FVC with neutrophils but significant inverse correlation with FEV1/FVC ($r = -0.468$ $p = 0.000$). A study by Iyer et al demonstrated negative correlation between FVC and sputum neutrophils in asthmatic patients.²¹

This study was based on to determine the severity of asthma directly by taking sample of sputum. In comparison with blood count of inflammatory cells, sputum cells give more accurate diagnosis of different phenotypes of asthma. As this test is usually not performed in patients, they were not willing to give sputum sample due to hesitation. For this reason, our sample was limited to 140 patients.

CONCLUSION

On the basis of sputum cell indices, we can understand the pathophysiology of asthma which may guide us about particular line of treatment in different types of asthma. To determine the type and severity of asthma and its effects on lung function it should be a routine investigation to perform sputum inflammatory cell profile for both diagnostic and prognostic purposes.

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