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General Medicine

SPUTUM CYTOLOGY IN BRONCHIAL ASTHMA PATIENTS

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ABSTRACT

INTRODUCTION: Airway inflammation plays an important part in the pathogenesis of asthma. However, the pathogenesis and cellular composition of airways inflammatory infiltrate in patients with asthma are different. The cellular composition of inflammatory infiltrate in the airways may be evaluated through a variety of techniques, including bronchial mucosa biopsy, broncho alveolar lavage fluid (BALF), and induced sputum.

AIMS AND OBJECTIVES: To study the sputum cytology profile in bronchial asthma with severity of disease (FEV1).

MATERIALS AND METHODS: This study was carried out in asthma patients admitted in TB and Chest Hospital, Badi, Department of Respiratory Medicine, RNT medical college, Udaipur, Rajasthan, India. Diagnosis and assessment of severity of asthma was done by spirometry as per GOLD (COPD) and GINA (ASTHMA) guidelines 2017.

RESULT: Eosinophilic (40%) phenotype is commonest among asthmatic patients and paucigranulocytic, neutrophilic, mixed were found among 28%, 20%, 12% cases. Paucigranulocytic phenotype had highest (86.14% Predicted) mean fev1 and mixed phenotype had lowest mean fev1. At a threshold of 4% (sensitivity =77.42%, Specificity = 89.47 and Pre + 85.71%, Pre -92.31%, Pre -70.83%),

CONCLUSION: Eosinophilic phenotype is predominant phenotype in most of the asthmatics patients but significant proportion of patients had neutrophilic phenotype. Blood eosinophil counts enabled identification of presence or absence of sputum eosinophilia with reliable accuracy. There is positive correlation between sputum eosinophil and severity of disease (FEV1) in asthma. Specific phenotyping of asthma inflammatory profiles are worthwhile and of clinical importance. Eosinophilic airway inflammation is linked to both exacerbations and decline in lung function. Specific targeting of eosinophilic inflammation may be effective in patients who exhibit an airway eosinophilia.

KEYWORDS : Eosinophilia, Asthma, Phenotype, Fev1

INTRODUCTION

Airway inflammation plays an important part in the pathogenesis of asthma. However, the pathogenesis and cellular composition of airways inflammatory infiltrate in patients with asthma are different.[1]

The cellular composition of inflammatory infiltrate in the airways may be evaluated through a variety of techniques, including bronchial mucosa biopsy, broncho alveolar lavage fluid (BALF), and induced sputum.[2]

Because sputum induction is relatively non-invasive and a easily repeated procedure, cytological evaluation of induced sputum plays an important role in the evaluation and monitoring of the chronic airways inflammation.[2]

AIMS AND OBJECTIVES

1. To study the sputum cytology profile in bronchial asthma.
2. To correlate it with severity of disease (FEV$_1$).

MATERIALS AND METHODS

This study was carried out in asthma patients admitted in TB and Chest Hospital, Badi, Department of Respiratory Medicine, RNT medical college, Udaipur, Rajasthan, India.

After diagnosis and assessment of asthma which includes pre and post bronchodilator assessment, Morning induced sputum was collected and haematoxylin - and eosin - stained specimen underwent cytology.

Sputum was induced after spirometric evaluation (with pre and post bronchodilator assessment) using nebulization with 4.5% saline in participants whose FEV1 was >1 L, using our previously described methods. In those with FEV1,1 L, 0.9% saline was used.[2,3]

Sputum adequacy is determined by less than 10 squamous cell (10x), more than 25 neutrophil per 10x low power field. The sputum differential cell count has been defined in large normal populations (Beldae al 2000).[4] In their study they found following mean for sputum inflammatory cells. Eosinophil: $0.4\ 0\pm0.9\%$; Neutrophil: $37.5\pm20.1\%$; Macrophage: $58.8\pm21.0\%$; Lymphocyte: $1.0\pm1.1\%$; Bronchial epithelial cells: $1.6\pm0.9\%$.

Venous blood samples were sent for differential leukocyte count to be determined by Sysmax CBC analyzer. Diagnosis and assessment of severity of asthma was done by spirometry as per GOLD (COPD) and GINA (ASTHMA) guidelines 2017.[3,5] The Spirometric evaluation of the patients was performed using a Computerized Spirometer Helios 702 as per ATS guidelines. Patients were classified according to severity of disease as under:

Classification of Severity of Airflow Limitation in ASTHMA
- Mild FEV$_1$ ≥ 80% predicted - Moderate 50% > FEV$_1$ < 80% predicted - Severe - FEV$_1$ < 60% Predicted

Shortness of Breath is graded as per Modified Medical Research Council Dyspnea Scale (MMRC Scale).[6]

Modified Medical Research Council Dyspnea Scale (MMRC Scale)
Grade Description
0 - Not troubled with breathlessness except with strenuous exercise
1 - Troubled by shortness of breath when hurrying on the level or walking up a slight hill
2 - Walks slower than people of the same age on the level because of breathlessness or has to stop for breath when walking at own pace on the level

3 - Stops for breath after walking about 100 yards or after a few minutes on the level

4 - Too breathless to leave the house or breathless when dressing or undressing.

EXCLUSION CRITERIA

1. Tuberculosis, bronchiectasis, malignancy or other confounding inflammatory diseases.
2. Clinical or radiological evidence of concurrent respiratory illness,
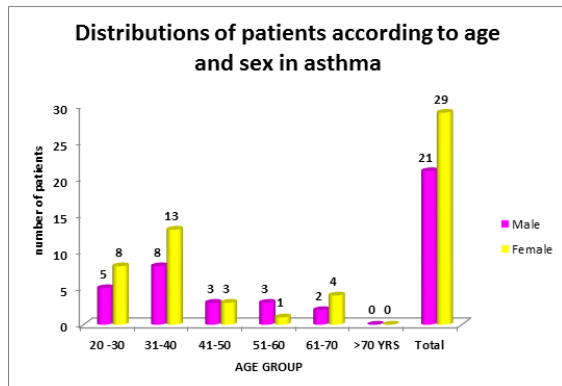3. Use of systemic or inhaled steroid therapy in the preceding one month.

RESULTS

Distributions of patients according to age and sex in asthma

Table no: 1 Distributions of patients according to Severity of asthma

ASTHMA SEVERITY	MALE		FEMALE		TOTAL	
	No	%	No	%	No	%
MILD	6	28	10	34	16	32
MODERATE	15	71	18	62.6	33	66
SEVERE	0	0	1	3.4	1	2
TOTAL	21		29		50	100

p=0.60 (NS)

This table shows that majority of the patients (66%) were having moderate, 32% mild and only 2% had severe asthma severity respectively.

Table no 2. Distributions of patients according to sputum cytological phenotypes

PHENOTYPE	ASTHMA
EOSINOPHILIC	20
NEUTROPHILIC	10
MIXED	6
PAUCIGRANULOCYTIC	14
TOTAL	50

In patients of asthma 40% of subjects were eosinophilic, 28% paucigranulocytic and 12% mixed; there were 20% neutrophilic subjects found.

Table No: 3 Distributions Of Patients In Phenotypes According To Asthma Severity

ASTHMA SEVERITY	EOSINOPHILIC		NEUTROPHILIC		PAUCIGRANULO-CYTIC		MIXED	
	no	%	no	%	No	%	No	%
MILD	4	20	3	30	8	57.14%	1	16.66
MODERATE	15	75	7	70	6	42.85	3	50
SEVERE	1	5	0	0	0	0	2	33.33
TOTAL	20		10		14		6	

Above table shows all phenotype had majority of cases with moderate asthma severity (FEV1) except paucigranulocytic phenotype which had majority of patients (57.14%) with mild asthma severity (FEV1).

TABLE No. 4 Average Sputum Eosinophil with Asthma Severity

Diagnosis		PHENOTYPE			
		Eosinophilic	Diagnosis	Eosinophilic	Diagnosis
FEV1	Mean	80.20	69.00	86.14	73.85
	SD	7.69**	10.64	9.36*	10.93**
TDI	Mean	7.70	7.00	6.43	9.10
	SD	3.37	2.00	2.71	6.47
SI	Mean	50.00	16.67	107.14	36.50
	SD	110.15*	40.82**	125.48*	69.61**
SPUTUM Eosinophil	Mean	1.30	6.17	1.21	15.95
	SD	0.95*	2.32	0.67	10.00**
SPUTUM NEUTROPHIL	Mean	74.20	70.83	56.14	54.30
	SD	7.28	3.76	4.99	5.02

*p<0.05 (s); **p<0.001 (hs)

TABLE No. 5: CORRELATION OF SPUTUM AND BLOOD EOSINOPHIL IN ASTHMA

BLOOD EOSINOPHIL CUTOFF VALUE	SENSITIVITY	SENSITIVITY	Pre+	Pre-	P VALUE
2%	77.42%	89.47%	92.31%	70.83%	p<0.001
3%	72.73%	88.24%	92.31%	62.50%	p<0.001
4%	92.31%	94.59	85.71%	97.22%	p<0.001

DISCUSSION

Fifty patients were admitted to Department of Respiratory Medicine, TB & Chest Hospital (Badi), RNT Medical College, Udaipur (Rajasthan), India to study the sputum cytology profile in bronchial asthma and to correlate it with disease related other factors and spirometry (FEV$_1$).

In the present study eosinophilic (40%) phenotype is commonest among asthmatic patients and paucigranulocytic, neutrophilic, mixed were found among 28%, 20%, 12% cases. Nezar R. Mohamed et al[7] demonstrated in 80 asthma patients 63.8% subjects had eosinophilic inflammation, 10% had neutrophilic, 6.2% had paucigranulocytic, 7.5% had mixed phenotype.

In asthmatics paucigranulocytic phenotype had highest (86.14% Predicted) mean fev1 and mixed phenotype had lowest mean fev1. Schleich et al 2013[8] demonstrated in asthma patients that paucigranulocytic phenotype had highest (90±17% Predicted) fev1 and mixed phenotype had lowest mean fev1 (72% Predicted).

Negative correlation between FEV1 and sputum eosinophils and ECP was found (Balzano et al. 1999)[9] in asthmatics. In addition in work from John V. Fahy et al August 2008 found that the eosinophil percentage (which averaged 6% in this cohort) was independently associated with more severe airflow obstruction.[10]

Whereas in asthmatics patients At a threshold of 4% (sensitivity =77.42%, Specificity = 89.47 and Pre + 85.71%, Pre -92.31%, Pre -70.83%), peripheral blood eosinophil counts enabled identification of the presence or absence of sputum eosinophilia (>3) in 82% of the cases. A threshold of 3% had lesser (78%) classifying ability but lesser specificity (88.24%). In contrast 2% offered a lesser specificity (81.82%) and lesser

sensitivity (61.54%) with 66.00% classifying ability.

Schleich et al. B[8]MC Pulmonary Medicine 2013 concluded that in study done on 508 asthmatics that Predictors of sputum eosinophilia ≥3% were high blood eosinophils. ROC curves showed a cut-off value of 220/mm3 (AUC = 0.79, p < 0.0001) or 3% (AUC = 0.81, p < 0.0001) for blood eosinophils to identify sputum eosinophilia ≥3%.[11]

CONCLUSION

Eosinophilic phenotype is predominant phenotype in most of the asthmatics patients but significant proportion of patients had neutrophilic phenotype. Blood eosinophil counts enabled identification of presence or absence of sputum eosinophilia with reliable accuracy. There is positive correlation between sputum eosinophil and severity of disease (FEV$_1$) in asthma. Specific phenotyping of asthma inflammatory profiles are worthwhile and of clinical importance. Eosinophilic airway inflammation is linked to both exacerbations and decline in lung function. Specific targeting of eosinophilic inflammation may be effective in patients who exhibit an airway eosinophilia.

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