ORIGINAL RESEARCH PAPER

Pulmonary Medicine

SPUTUM NEUTROPHILIA IN ACUTE EXACERBATION OF BRONCHIAL ASTHMA

KEY WORDS: Bronchial Asthma, Neutrophilia , FeNO

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ABSTRACT

Background : Asthma is a common respiratory condition that affects an estimated 358 million people worldwide. Neutrophilic asthma is an asthma inflammatory phenotype associated with exacerbation, airflow limitation, and steroid resistance. **Objective :** The aim of the study was to observe the severity of Bronchial asthma in patients with Sputum Neutrophilia .**Methods:** This is a prospective cross sectional study by Department of Pulmonary Medicine including 50 patients with Acute Exacerbation of Bronchial Asthma as determined by ACQ. **Results:** Patients with sputum neutrophilia were seen to have higher ACQ scores, poor bronchodilator reversibility , low expiratory volumes and poor response to inhaled corticosteroids with a higher risk of exacerbation. The correlation between sputum Neutrophilia and Bronchodilator reversibility using spirometry is statistically significant(p value = 0.0001) with a greater incidence of hospitalization for asthma. **Conclusion:** Neutrophilic asthma is associated with less atopy and these patients have lower levels of exhaled nitric oxide (FeNO), greater incidence of hospitalization for asthma and higher incidence of steroid resistance. Sputum neutrophilia has a positive correlation with smoking and is more often seen in older males.

INTRODUCTION:

- Asthma is a heterogenous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation which may become persistent later. Asthma is a common respiratory condition that affects an estimated 358 million people worldwide.[1]

- The asthma phenotypes include eosinophilic, neutrophilic, mixed granulocytic and pauci-granulocytic asthma.Neutrophilic asthma is an asthma phenotype associated with exacerbation, airflow limitation, and steroid resistance. It is the most common phenotype in adult patients presenting with acute severe asthma.[8]

- Sputum neutrophilia is seen in patients with severe refractory disease (3.6-10%) who are uncontrolled despite high doses of inhaled corticosteroids and long-acting 2-agonists.Neutrophilic airway inflammation plays a role in the progression of persistent airflow limitation in adult asthma and was significantly higher in the elderly age group.[2]

- Neutrophils release oxygen free radicals, cytokines, and enzymes like elastase, which affect bronchial epithelium by degrading elastin and extracellular matrix proteins. Airway inflammation is mainly caused by the Th2 immune response, which is a hallmark of bronchial asthma pathogenesis.[3] Eosinophilic asthma correlates with Th2-associated inflammation whereas neutrophilic asthma strongly correlates with Th17 cells. Neutrophil elastase is involved in the pathogenesis by causing airway mucus gland hyperplasia, smooth muscle cell proliferation and mucus secretion and increases IL-8 production from airway epithelial cells which promotes recruitment of neutrophils in the airways causing further damage.[7]

- Patients with neutrophilic asthma have frequent visits to emergency, hospitalization and intubation and this phenotype of asthma has been associated with sudden-onset fatal asthma in about 23% of the patients. Hence, the main objective of the study is to analyze Sputum Neutrophilia in Acute Exacerbation of Bronchial Asthma.[5]

MATERIAL AND METHODS:

AIM AND OBJECTIVE: The aim of the study was to observe the severity of Bronchial asthma in patients with Sputum Neutrophilia .

STUDY DESIGN: This study is an analytical study with a cross-sectional design.

PLACE OF RESEARCH: Rajarajeswari medical college and hospital, Bangalore.

STUDY PERIOD: September 2021 to December 2021

SAMPLE SIZE: 50

INCLUSION CRITERIA: aged >18 years and willing to be research subjects by signing the consent form after explanation.

EXCLUSION CRITERIA : Subjects having other infections, GERD, Malignancy

METHODOLOGY:

- All study subjects underwent sputum testing to determine the sputum cytology.
- FeNO was measured first followed by spirometry with bronchodilation and sputum induction.
- Spirometry was performed according to the American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines.[6]
- Induced sputum was obtained by having subjects inhale nebulized 3% saline after 400 g salbutamol inhalation. Saliva was spit out and sputum was coughed into a separate sterile cup.

- All study subjects were also subjected to descriptions of clinical and demographic characteristics based on age, gender, symptoms, family history, smoking history, allergic history, nocturnal symptoms, bronchodilator reversibility and obesity.
- Smokers were excluded.
- Neutrophilic asthma was characterized by a neutrophil count in induced sputum above 60% or a neutrophil count of 500×10^4/Ml.
- The correlation analysis between sputum Neutrophilia and bronchodilator reversibility and post FEV1 values was carried out which showed a poor response with a p value of < 0.005 which was statistically significant .

RESULTS :

Study included a total 50 Asthma patients. Mean age of the study population was >40 years of whom 52%(26) were males and 48% (24) were females. 70% of the subjects have significant family history of asthma. 36%(18) have allergic history and 74%(37) had seasonal variation.

TABLE 1 : SYMPTOMS OF THE STUDY SUBJECTS

Symptoms	Number	Percentage
Breathlessness	22	44.0
Cough	10	18.0
Wheeze	18	36.0
Total	50	100.0

TABLE 2 : CHARACTERISTICS OF STUDY PARTICIPANTS

Characteristics	Mean	Standard Deviation
Age	41.08	8.62
Post FEV1	49.92	9.39
FeNo	21.22(19.50)	15.23(11.75,25.25)
Sputum Neutrophilia	71.00	18.73

TABLE 3 : CORRELATION BETWEEN SPUTUM NEUTROPHILIA AND POST FEV1, AGE AND FENO

Variables	r Value	P Value
Sputum Neutrophilia	-0.304	0.032
Post FEV1		
Sputum Neutrophilia	0.532	0.0001
Age		
Sputum Neutrophilia	-0.710	0.0001
FeNO		

TABLE 4 : CORRELATION BETWEEN SPUTUM NEUTROPHILIA AND ALLERGIC HISTORY

Allergic History	r Value	P Value
No	0.595	0.003
Yes	0.269	0.136

TABLE 5 : CORRELATION BETWEEN SPUTUM NEUTROPHILIA AND BRONCHODILATOR REVERSIBILITY

Parameter	Bronchodilator reversibility		P Value
	Yes	No	
Sputum Neutrophilia	59.85±23.81	78.43±8.84	0.003

FIGURE 1 : CORRELATION BETWEEN SPUTUM NEUTROPHILIA AND BRONCHODILATOR REVERSIBILITY

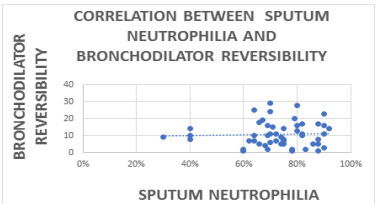
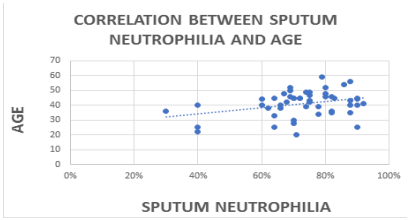


FIGURE 2 : CORRELATION BETWEEN SPUTUM NEUTROPHILIA AND AGE



DISCUSSION :

- Neutrophilic asthma is the most common phenotype in adult patients presenting with acute severe asthma compared with eosinophilic asthma.(4)
- Histopathologically, it is characterized by airway smooth muscle hyperplasia and hypertrophy, increase in ECM proteins and subepithelial basement membrane fibrosis, which contributes to fixed airflow limitation.(8)
- Neutrophilic asthma is worse at night with frequent nocturnal attacks.(2)
- Sputum Neutrophilia is associated with severe persistent asthma, fixed airway obstruction and very low FEV1 and post-bronchodilator FEV1.(6)
- Patients with neutrophilic asthma are less atopic compared to patients with eosinophilic asthma.
- Smoking increases airway hyperresponsiveness by the induction of airway inflammation and changes of the airways due to airway smooth muscle hypertrophy, mucus hypersecretion, and loss of alveolar attachments showing a positive correlation with sputum neutrophilia. (3)
- In this study an inverse relationship between ΔFEV1 and the percentage of neutrophils in sputum of smoking asthmatics is seen. A significant negative correlation between percentage of sputum neutrophils and FeNO level is observed. An increase in sputum neutrophils is seen in elderly asthmatics ($p < 0.0001$).

CONCLUSION :

- Neutrophilic asthma is not responsive to high dose inhaled corticosteroids and monoclonal antibody therapies. Therefore, this study highlights sputum neutrophilia in acute exacerbations of bronchial asthma and response of such patients to inhaled corticosteroids.
- Presence of neutrophils in sputum or BAL fluid lacks precision to serve as an independent biomarker because of the confounders that can influence their presence including GERD, Obesity, smoking and medications.
- Thus there is a need to explore other treatment modalities such as long-acting phosphodiesterase 4 inhibitors, macrolide antibiotics and bronchial thermoplasty.

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