

## CORRELATION BETWEEN BRONCHIECTASIS SEVERITY INDEX AND C- REACTIVE PROTEIN IN PATIENTS OF BRONCHIECTASIS

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### ABSTRACT

**Background:** Bronchiectasis is a chronic airway disease in which the inflammatory cascade based predominantly on airway infections, airway inflammation, and structural damage plays a role in progression and pathogenesis of disease. Conventionally, the severity of disease based on FEV1 and Bronchiectasis Severity Index (BSI) was recently designed as two multidimensional severity grading scales to assess the prognosis of bronchiectasis. **Objective:** Present study was aim to analyze correlation between bronchiectasis severity index and C-reactive protein in patients of bronchiectasis. **Methodology:** Total 77 patients of bronchiectasis were included in the study and severity of disease was analyze using the BSI score. The severity of bronchiectasis was correlated with the CRP. **Results:** Mean age of the study patient was 50.38±19.06 years with high proportion of female patients. BSI score indicate mild bronchiectasis in 14 (18.18%) patients, moderate bronchiectasis in 45 (58.44%) patients and severe bronchiectasis in 18 (23.38%) patients. Total 54.55% of the study patients were with positive CRP and the rest 45.45% were with negative CRP. A significant association between the BSI score and CRP was observed in present study. **Conclusion:** In patients with bronchiectasis, CRP can be a useful biomarker. Our study shows positive results about the correlation between CRP and bronchiectasis severity index in a patients of bronchiectasis. **Keywords:** bronchiectasis, CRP, BSI, lungs, inflammation.

### INTRODUCTION

Bronchiectasis is defined as (bronchus, airway, ectasia, dilatation) is morphological term used to describe abnormal irreversible dilated and often thick-walled bronchi that affects medium sized bronchi often extends to more distal bronchioles. Bronchiectasis is a chronic airway disease associated with symptoms such as cough, sputum production, and haemoptysis and it may develop as a result of various etiologies (1). A vicious cycle, based predominantly on airway infections, airway inflammation, and structural damage, plays a role in progression and pathogenesis of bronchiectasis (2). It is disappointing that there are a limited number of effective treatment strategies and evidence-based management recommendations for

assessment and follow-up of bronchiectasis. The severity of bronchiectasis should be determined to obtain better treatment outcomes. Assessment of bronchiectasis may be a challenge since there is actually no simple measurement method that has been sufficiently validated. Conventionally, previous reports measured the severity of disease based on FEV1 (forced expiratory volume in 1 s), while Reiff and Bhalla scores in HRCT were also used in some studies to measure disease severity (3-5).

The severity of bronchiectasis should be determined to obtain better treatment outcomes. Previous reports measured the severity of disease based on FEV1 (forced expiratory volume). However FEV1 was not effective in terms of clinical decision making and HRCT (High resolution computed tomography) scores had poor correlation with lung functions. Therefore, it became an obligation to create a new scoring system to assess the severity of bronchiectasis. Bronchiectasis Severity Index (BSI) was recently designed as two multidimensional severity grading scales to assess the prognosis of bronchiectasis. Faced score is an 8-item grading system that predicts mortality in patients who had been monitored for 5 years (6). BSI is a seven-item scale that describes future risk of death, hospitalization, and exacerbations. Elevation of systemic inflammatory markers such as C-reactive protein (CRP) and total white blood cell count is known to be associated with the extent of the disease and poor lung functions (7).

In this study, attempt has been made to study correlation between the Bronchiectasis severity index and systemic inflammatory marker- (CRP – C reactive protein) in patients of Bronchiectasis and thereby to assess the prognosis so that further actions can be taken to improve it and also the quality of life in these patients.

## METHODOLOGY

**Study design:** This was a Cross-sectional study and no follow ups were studied. The study was carried out in Out Patient Department and Wards of Pulmonary medicine and General Medicine department in a tertiary care centre in Maharashtra. 77 Suspected patients coming with the complaints suggestive of bronchiectasis were included in the study. Patients with diagnosed case of Bronchiectasis using HRCT were included in the study. Patients with active hemoptysis, patients in respiratory failure, and patients with terminal illness were excluded from the study.

**Investigations:** All patients were subjected to undergo spirometry, and peripheral venous blood samples were obtained from all patients on the day of spirometry. CRP levels were analyzed. For the measurement of serum CRP levels, 3cc of venous blood samples was collected in biochemistry test tubes. Blood samples were transferred to the analyzing laboratory at most 2 hours after sampling, and the analyses were performed on the same day. CRP levels were quantitatively analyzed by the nephelometric method using the BN 200 device. The reference range in healthy humans for the preferred method of analyses will be 0.00–5.00mg/L.

**Bronchiectasis severity:** BSI Scoring system was used to analyze severity of bronchiectasis. Total score varies between 0 and 26 points. In BSI, scores of 0–4 points indicate mild, 5–8 indicate moderate, and 9 or above indicate severe bronchiectasis.

**Statistical analysis:** Mean and standard deviation was calculated for quantitative variable; and fraction of total and percentages was used for qualitative variables. Chi-square test was used to compare two groups by taking the p value <0.05 as statically significant.

## RESULTS

Mean age of the study patient was  $50.38 \pm 19.06$  years. Female proportion in the study was 55.84% while the rest 44.16% were males. Most of the study patients have BMI  $\geq 18.5$  with proportion of 85.71 and remaining 14.29 patients were with BMI <18.5. 20.78% of the study

patients were hospitalised for the similar complaints in the preceding 2 years while the rest 79.22% were not hospitalised for such complaints. Exacerbation in the last 1 year was seen in 11.69% of the study patients (Table 1).

**Table 1: Sociodemographic and clinical determinants of recruited patients.**

Variable	Subdomain	Mean or N	SD or Percentage
Mean age		50.38	19.06
Gender	Male	34	44.16
	Female	43	55.84
BMI	≥18.5	66	85.71
	<18.5	11	14.29
Hospital admission	Yes	16	20.78
	No	61	79.22
Exacerbation	Yes	9	11.69
	No	68	88.31

Most of the study patients 71.43% were having FEV1 50-80%. 11.69% patients were having FEV1 >80% and 16.88% with FEV1 within 30-49%. No patient in the study was having FEV1 <30% (Table 2).

**Table 2: FEV1 of study patients.**

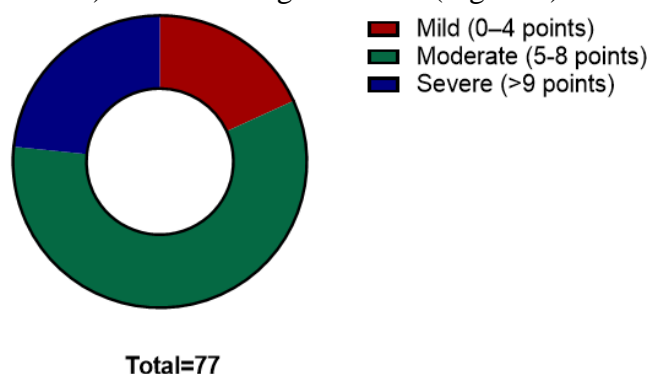
FEV1%	No of study patients	Percentage
>80%	9	11.69
50-80%	55	71.43
30-49%	13	16.88
<30%	0	0.00
Total	77	100.00

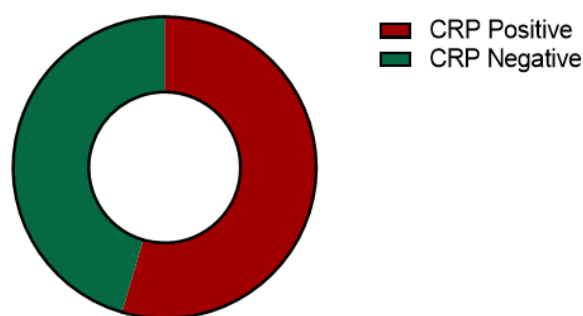
As per MMRC scale, most of the study patients (97.4%) had grading of 0-2 and only 2 (2.6%) had grade 3 MMRC (Table 3).

**Table 3: Medical Research Council Dyspnoea Scale (MMRC) in the study patients.**

Dyspnoea Scale	No of study patients	Percentage
0-2	75	97.40
3	2	2.60
4	0	0.00
Total	77	100.00

BSI score indicate mild bronchiectasis in 14 (18.18%) patients, moderate bronchiectasis in 45 (58.44%) patients and severe bronchiectasis in 18 (23.38%) patients (Figure 1). Total 42 (54.55%) of the study patients were with positive CRP and the rest 35 (45.45%) were with negative CRP (Figure 2).



**Figure 1: BSI score of enrolled patients.**

Total=77

**Figure 2: CRP in study patients.**

Table 3 shows that there was continuous increase with increase in BSI score and the association of BSI score with the CRP was statistically significant with p value of 0.04 when chi-square test was applied.

**Table 4: BSI severity v/s CRP in the study patients.**

Bronchiectasis severity	CRP Positive	CRP Negative	P Value
Mild (0–4 points)	4(28.57%)	10(71.43%)	0.040*
Moderate (5-8 points)	25(55.56%)	20(44.44%)	
Severe (>9 points)	13(72.22%)	5(27.78%)	
Total	42(54.55%)	35(45.45%)	

## DISCUSSION

Bronchiectasis has a wide range of causes. However, because it is marked by a permanent risk of aggravation, bronchiectasis has become one of the most common chronic respiratory disorders; also, as life expectancy has increased, quality of life has become increasingly important. To better understand and manage bronchiectasis, bronchiectasis severity rating systems such as the BSI and FACED scores were developed. In terms of predicting clinically relevant factors such as future exacerbations, hospital admissions, quality of life, and mortality, the BSI score outperforms the FACED score (8).

The FACED score was also compared to the BSI in different populations. The BSI was introduced by Chalmers et al (6). HRCT, FEV1, MRC dyspnoea score, bacterial colonisation (*P. aeruginosa* or other pathogenic bacteria), past hospital admission, and exacerbations were all included in this score. The BSI was proven to be a sensitive technique for predicting future hospitalisation and death risks (6). McDonnell et al. looked examined FACED and BSI ratings in a large group of 1612 patients from seven different European cohorts. For mortality, both scores demonstrated a high discriminating predictive value. The BSI, on the other hand, outperformed the FACED score in predicting a variety of clinically important outcomes, such as respiratory symptoms, Acute exacerbation, hospital admissions, quality of life, exercise capacity, and lung function decrease (9). In additional studies, the two scores were compared and shown to have equal predictive potential for 5-year mortality with excellent specificity, with only a small fraction of patients having conflicting BSI and FACED scores. Both ratings were able to predict 5-year mortality, however FACED score outperformed the others. Another research that included Aboriginal Australians yielded contradictory results. The latter were much younger than the other groups and died at a significantly younger age. A better prognosis was not associated with a milder illness as measured by FACED scores. As a result, extending prognostic ratings from specific cohorts to other populations should be approached with care (10).

It is generally known that a significant proportion of bronchiectasis patients have systemic inflammation, as indicated by peripheral concentrations of substances like neutrophilic elastase. The most frequently held belief is that these people have a more severe form of the disease, as the onset of systemic inflammation has been linked to a higher degree of local inflammation and a number of variables linked to a bad prognosis (11). However, whereas systemic inflammation has been well researched as a predictive factor for exacerbations in other airway disorders, such as COPD and cystic fibrosis, there is relatively little information on bronchiectasis, particularly when it comes to CRP. In reality, just one small retrospective research including 69 patients indicated that a CRP concentration of  $>4.26\text{mg/L}$  was substantially related with a larger percentage of patients who had at least two hospitalizations in the previous year. However, only idiopathic bronchiectasis was included, and the limited sample size makes it hard to draw any meaningful conclusions (12).

The severity of bronchiectasis was determined in this study using the recently created BSI grading methods, while systemic inflammation was determined using CRP levels. In individuals with stable bronchiectasis, correlations between BSI scores and indicators of systemic inflammation were shown to have a strong relationship with CRP levels. These findings are consistent with those of previous research by Coban et al. (13). In 117 individuals with stable bronchiectasis, they discovered a strong positive connection between FACED and BSI scores and CRP levels. Among patients with diverse chronic respiratory disorders, Cano et al. found that individuals with bronchiectasis had the highest CRP level and the lowest BMI, albumin, and prealbumin levels (14). This could indicate that bronchiectasis is a chronic inflammatory and malnutrition-related respiratory disease. CRP has previously been found to be a valuable measure of inflammation and a predictive factor for clinical outcomes in bronchiectasis patients. The BSI and FACED rating systems are also highly linked with CRP levels (8).

After adjusting the results for variables with proven predictive value or associated with exacerbations in bronchiectasis, the findings of Posadas et al. point in the same direction as studies on COPD and cystic fibrosis, showing that a higher peripheral concentration of CRP was associated with a higher risk of future exacerbations. When compared to the control group, a CRP value between 0.4 and  $2.7\text{mg/L}$ , or greater than  $2.7\text{mg/L}$ , increased the probability of a severe exacerbation by 2.9 and 4.2 times, respectively. When this high risk of severe exacerbations is paired with additional clinically important high-risk characteristics, such as the presence of a chronic bronchial infection caused by *Pseudomonas aeruginosa* or past severe exacerbations, the resulting information may be clinically useful (11). Patients with a CRP  $>2.7\text{mg/L}$  and a CBI by PA in a clinically stable phase who had at least one hospitalisation in the preceding year, for example, had a 51 times higher chance of having another hospitalisation than those who did not have any of these three criteria. Furthermore,

CRP values' prognostic capacity for future severe exacerbations was independent of the severity of BE as assessed by traditional scores, implying that this easily accessible and interpretable biomarker could provide prognostic data to supplement the information already provided by these scores, particularly the BSI and E-FACED (11). The CRP levels, on the other hand, did not have any predictive value for mild-moderate exacerbations. This conclusion might indicate that CRP is just a marker for severe exacerbations, but it could also indicate that some mild-moderate exacerbations were missed or unreported in the registry, making the study less reliable in this regard (11).

Jarrar et al. investigated the relationship between systemic inflammation and severity ratings in bronchiectasis. WBC count, ESR, and CRP were measured in clinically stable bronchiectasis patients, and FACED score and BSI were also examined in their retrospective research of patients followed up for bronchiectasis. The mean BSI and FACED scores were respectively

$8.6 \pm 4.2$  and  $4.5 \pm 2.8$ . CRP levels were higher than 20mg/l in 52% of individuals. Similar to the findings of this study, the severity of bronchiectasis as measured by the BSI and FACED increased considerably as CRP levels rise.

C-reactive protein is mostly generated in the liver, with IL-1, IL-6, and TNF-alpha acting as regulators. CRP immunological tests have grown more sensitive, allowing for the detection and comparison of low CRP levels in blood. CRP levels are linked to the development and progression of coronary heart disease and osteoarthritis, according to these sensitive tests. Furthermore, significant links have been found between CRP and diabetes, as well as airway diseases like chronic obstructive pulmonary disease and asthma (12). In this study, illness severity was linked to CRP in individuals with stable bronchiectasis, indicating that CRP might be a useful biomarker for low-grade systemic inflammation in these patients.

This study has some limitations. Since the study was performed as a single-center, study results can only be generalized to a limited extent. We use only one scoring system i.e., BSI score, it is recommended that both FACED and BSI score should be implemented in further studies. The study was conducted in a small population as the sample size is 77 of the study, so results may not be significant. As the institution in which study have been conducted is tertiary care centre so most of the patients are referred from periphery & patients mostly received in critical condition so no definite investigations were carried out. The infective aetiology was significant of bronchiectasis in our patients so the results less signify the other non-infective aetiologies.

## CONCLUSION

In patients with bronchiectasis, CRP can be a useful biomarker that directly reflects the level of systemic inflammation. As CRP is readily available and easy to measure, its evaluation in conjunction with other clinically relevant variables can enable clinicians to make an early identification of patients with a greater probability of severe exacerbations in the future and to implement any necessary preventive and therapeutic measures.

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