Original Article

Association between serum albumin and disease severity of non-cystic fibrosis bronchiectasis

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ABSTRACT

Background

Bronchiectasis is a chronic debilitating but neglected pulmonary disease. It is associated with substantial health related burden and health care costs. However, the biochemical parameters related to disease severity have not been sufficiently assessed.

Objective: Aim of the present study to find out any association between serum albumin and disease severity of non-cystic fibrosis bronchiectasis.

Methods

This was a cross-sectional observational study of 33 subjects with non-cystic fibrosis bronchiectasis at department of Respiratory Medicine, National Institute of Diseases of the Chest and Hospital (NIDCH) from December 2019 to March 2021. After taking informed written consent BSI score be calculated and blood was taken for to measure serum albumin. Data was collected through questionnaire. After completion of the data collection, analysis was done with the help of Statistical Package for Social Science (SPSS) version 22.

Results

Mean age of the study subjects was 43.36 ± 15.65 years with a range of 21 -76 years and more likely to be men (60.6%). History of previous pulmonary tuberculosis found in 48.5% subjects as associated conditions and pseudomonas aeruginosa (21.2%) was the most common organisms in sputum culture. 87.9% of the study subjects had history of exacerbation within last 12 months and 60.6% were hospitalized within last 2 years. More than half (54.6%) of the study subjects had severe, 33.3% had moderate and 12.1% had mild bronchiectasis with the mean BSI score of 9.00 ± 3.05. Mean serum albumin was 3.22 ± 0.84 g/dl. Albumin had a significant negative correlation with BSI score (r = -0.457 and p = 0.008).

Conclusion

The serum albumin had moderate correlation with disease severity of non-cystic fibrosis bronchiectasis.

Keywords:

Non-cystic fibrosis bronchiectasis; Serum albumin; Bronchiectasis severity index.

INTRODUCTION

Bronchiectasis is a chronic respiratory disease that involves a vicious cycle of constant bacterial colonization, chronic airway inflammation, airway damage and remodeling with heterogeneous clinical course and significant co-morbidity. Bronchiectasis is a frequent and neglected chronic lung disease but now becoming a growing global health problem. With the wide use of high-resolution computed tomography (HRCT), it was reported that the incidence, prevalence and mortality of non-cystic fibrosis bronchiectasis was raising in the United Kingdom, even throughout worldwide.[1] In Europe and the United State, the reported that the prevalence of the disease has increased more than 40% in the past 10 years.[2] Asia has the highest prevalence of this disease especially secondary to tuberculosis.[3] But there is no definite data regarding prevalence of bronchiectasis in our country. Bronchiectasis is connected with substantial health related burden, such as a substantially low quality of life[4], increased health

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care costs[5], increased frequency of hospitalization and mortality; however, it has been neglected and regarded as an 'orphan disease' by pulmonologists.[6] Cystic fibrosis (CF) is the most prevalent inheritable cause of bronchiectasis in western populations, and several studies have focused on cystic fibrosis. Studies regarding non-CF bronchiectasis are very few and unsatisfactory. The pathophysiology, treatment, and prognosis of non-CF bronchiectasis may be distinct from those of cystic fibrosis.[7] So data regarding the management of non-CF bronchiectasis are lacking, and current guidelines are based on cystic fibrosis studies and expert opinion.[8] Characterizing patients by combining clinical, radiological, inflammatory, and microbiological data allows identification of those individuals who have a more rapid disease progression or exacerbate frequently.[9] So, a predictive tool for assessment of the disease severity in routine practice is needed which would help in focusing on therapies most likely to benefit the patients and improve their quality of life.[10]

Systematic evaluation of disease severity is fundamental realize the natural course and will be helpful to predict the prognosis of patients with non-CF bronchiectasis. The bronchiectasis severity index (BSI)[11] and FACED[12] have been developed to assess the severity of non-CF bronchiectasis. However, this scoring system is cumbersome to calculate in real clinical practice.

Impaired nutritional status as well as chronic inflammatory response causes low albumin in subjects with non-CF bronchiectasis. In addition, there is also increased energy expenditure due to an increased work of breathing. Several studies showed low albumin is associated with increased morbidity and mortality of different chronic respiratory diseases.

Serum albumin measurement is widely available, cheap and simple to measures. Therefore, this study aimed to find the association of serum albumin with disease severity and the correlation with the BSI score. Ultimately, which help in identification of different risk group patients and may guide to clinical decision making regarding further management.

METHODS

This was a cross-sectional observational study conducted in the Department of Respiratory Medicine of National Institute of Diseases of the Chest and Hospital (NIDCH), Mohakhali, Dhaka, from December 2019 to March 2021. Total 33 of NCFB patients were enrolled as per inclusion and exclusion criteria-

The criteria for recruiting the study subjects included: Patients with non-cystic fibrosis bronchiectasis and age ≥ 18 years. The exclusion criteria were: Patients with acute exacerbation of non-cystic fibrosis bronchiectasis, active tuberculosis, heart failure, chronic liver disease, chronic kidney disease, human immunodeficiency virus (HIV) infection. However, patients incapable of performing spirometry were excluded from this study.

Serum albumin was measured and BSI score was calculated to all enrolled patients. Data were collected with a structured questionnaire. The patients were categorized into three groups on the basis of BSI score. Mean serum albumin for each group were calculated. The one-way ANOVA was used to determine whether there were any statistically significant differences in the means of serum albumin among the three groups of severity of the disease. Pearson's correlation was done to find out the correlation between serum albumin and severity of NCFB.

Operational definitions:

Bronchiectasis-

Patient with clinical symptoms include chronic cough, productive sputum, exertional dyspnoea, recurrent lower respiratory tract infection[8] with HRCT findings include a larger size of the bronchial internal diameter than the accompanying pulmonary artery and lack of tapering of the bronchi in the peripheral lungs.[13] Here bronchiectasis synonymous with the term of 'non-CF bronchiectasis'

BSI (Bronchiectasis Severity Index)-

The BSI uses a combination of clinical, radiological and microbiological features as an assessment of severity tool.[11] It uses the following criteria-

Age (years): <50 (0 points), 50-69 (2 points), 70-79 (4 points), > 80 (6 points),

BMI (Kg/m2): <18.5 (2 points), 18.5-25 (0 points), 26-30 (0 points), >30 (0 points)

FEV1 % predicted: > 80 (0 points), 50-80 (1 point), 30-49 (2 points), <30 (3 points)

Hospitalizations within last 2 years: No (0 points), Yes (5 points),

Numbers of Exacerbations in previous 12 months: 0 (0 points), 1-2 (0 points), ≥3 (2 points),

MRC dyspnoea score: 1-3 (0 points), 4 (2 points), 5 (3 points),

Colonization with pseudomonas aeruginosa: No (0 points), Yes (3 points),

Colonization with other organisms: No (0 points), Yes (1 point),

Radiological severity: <3 lobes affected (0 points), ≥3 lobes or cystic in any lobe (1 point).

Mild bronchiectasis (score 0-4), Moderate bronchiectasis (score 5-8) and Severe bronchiectasis (score ≥9)

Serum albumin-

Albumin is plasma protein with a concentration ranging from 35 to 50 g/L (3.5-5.0 g/dl).[14]

RESULTS

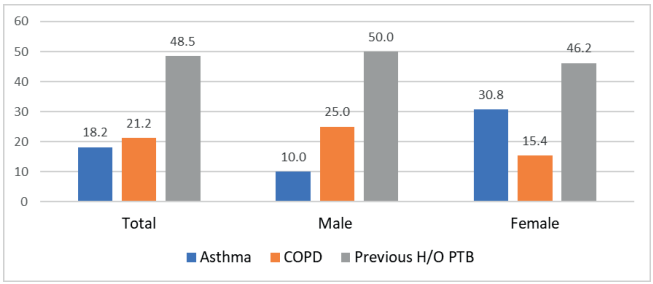
It was revealed from our study that the mean age of the patients was 43.36 ± 15.65 years within the range of 21 -76 years. Males (60.6%) were predominant than females (39.4%). Maximum study subjects were from rural area (69.7%) (Table I).

Table I: Demographic profile of the study subjects (n=33)

	f	%
Age (years)*		
<50	24	72.7
50 – 69	5	15.2
70 – 79	4	12.1
≥80	0	0
Mean ± SD	43.36 ± 15.65	
Min – max	21 - 76	
Gender		
Male	20	60.6
Female	13	39.4
Geographical location		
Rural	23	69.7
Urban	10	30.3

Note. *Age grouping was done according to BSI

Our study showed almost half of the study subjects (16, 48.5%) had previous H/O PTB. COPD was found in 7 (21.2%) cases and Asthma in 6 (18.2%) cases. Among the male (10, 50%) had previous H/O PTB, (5, 25%) had COPD, (2, 10%) had Asthma but in female it was (6, 46.2%), (2, 15.4%) and (4, 30.8%) respectively



(Figure 1).

Figure 1: Distribution of the study subjects according to associated conditions (n=33)

We found that 12.1% subjects were in Grade I, 54.5% in Grade II and 21.2% in Grade III according to MRC dyspnoea scores. 87.9% of the study subjects had history of exacerbation in last 12 months among them 69.7% cases had 1-2 number of exacerbation and only 18.2% had ≥3 number of exacerbations. Mean number of exacerbations was 1.75 ± 1.09. 60.6% study subjects were hospitalized within last 2 years. Regarding BMI 27.3% were underweight, 69.7% were normal weight, 3.0% was overweight and mean was 20.58 ± 3.64 kg/m^2. The mean FEV1 % predicted of the study subjects was 42.9 ± 22.8. We also found that 72.7% study subjects had ≥3 affected lobes in HRCT of chest. 51.5% of the study subjects had positive sputum colonization with microorganisms. Most common organism was Pseudomonas aeruginosa (21.2%) (Table II).

Table II: Characteristics of the study subjects according to severity (BSI) parameters

Characteristics	F	%
MRC dyspnoea scores		
Grade I	4	12.1
Grade II	18	54.5
Grade III	7	21.2
History of exacerbation in last 12 months	29	
Number of exacerbations		
1-2	23	
≥3	6	
Mean ± SD	1.75 ± 1.09	
Hospitalization within last 2 years		
Yes	20	60.6
No	13	39.4
BMI (kg/m^2)		
<18.5	9	27.3
18.5 - 24.9	23	69.7
25.0 – 30.0	0	0
>30.0	1	3.0
BMI (kg/m^2)	20.58 ± 3.64	15.10 - 30.84
FEV_1		
>80	2	6.1
50 – 80	12	36.4
30 – 49	5	15.2
<30	14	42.4
Mean ± SD	42.9 ± 22.8	
Affected lobes in HRCT (number)		
<3	9	27.3
≥3	24	72.7
Sputum colonization		
Positive	17	51.5
Pseudomonas aeruginosa	7	21.2
Klebsiella	6	18.2
Haemophilus influenzae	2	6.1
Moraxella species	2	6.1
Escherichia Coli	2	6.1

In our study 54.6% study subjects had severe, 33.3% had moderate and 12.1% had mild bronchiectasis (Figure 2)

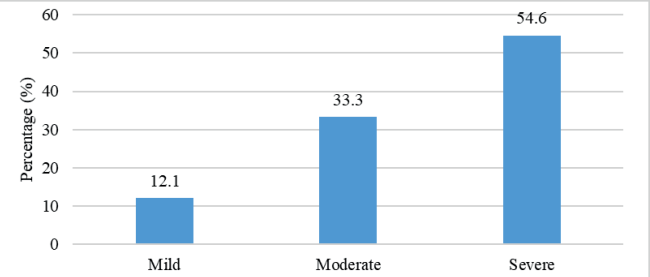


Figure 2: Distribution of the study subjects (n=33) according to severity (BSI score) of non-cystic fibrosis bronchiectasis

The mean value of serum albumin was 3.22 ± 0.84 g/dl (Table III).

Table III: Mean serum albumin of the study subjects (n=33)

	Mean ± SD	Min – max
Serum albumin (g/dl)	3.22 ± 0.84	1.51 - 5.30

We observed that among the respondents the lowest mean albumin was found within those having severe bronchiectasis (2.94±0.72), followed by moderate bronchiectasis (3.18±0.50), mild bronchiectasis (4.62±0.83) and to see whether this difference is statistically significant or not we did one-way ANOVA test. The test showed this difference was significant at p<0.05 among these three groups: F (2,30) = 10.24, p = <0.001 (Table IV).

Table IV: Association of serum albumin in different severity of non-cystic fibrosis bronchiectasis (n=33)

Severity of NCFB	Serum albumin (Mean ± SD)	p-value	F	df
Mild (0-4)	4.62 ± 0.83	<0.001*	10.24	2,30
Moderate (5-8)	3.18 ± 0.50			
Severe (≥9)	2.94 ± 0.72			

*Statistically significant, F= between group ANOVA test value.

Pearson's correlation coefficient test was used to analyze the association between serum albumin and disease severity (BSI score) of NCFB. Preliminary analysis was performed to ensure no violation of the assumptions of normality, linearity and homoscedasticity. There was a negative correlation between serum albumin and BSI score, (r = -0.457, p = 0.008) and this association was statistically significant (Figure 3)

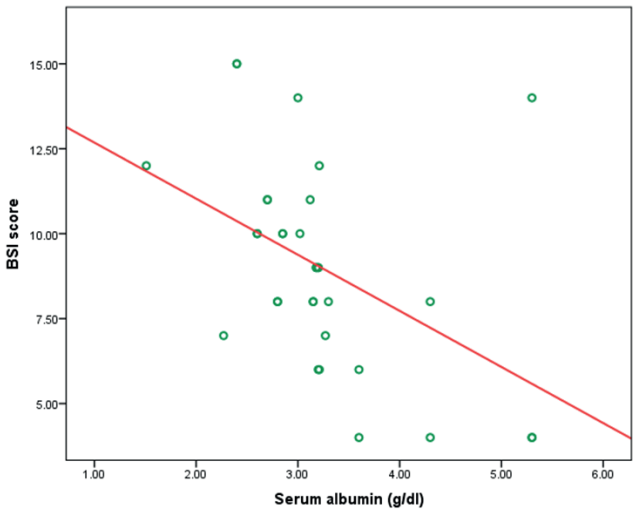


Figure 3: Correlation of serum albumin with BSI score of the study subjects (n=33)

DISCUSSION

The mean age of the study subjects was 43.36 ± 15.65 years within the range of 21 -76 years and males (20, 60.6%) were predominant than females (13, 39.4%). Male to female ratio was 1.54:1. Similar result was found by Dhar et al.[3], where younger patients (median age 56 years) and more men (1249 [56.9%] of 2195) were predominant. This is also in concurrence with the observation of males (45 [59.2%] of 76) predominant with mean age of 56.82 ± 13.53 years made by Kallarakal et al.[16]. On the other hand, Lee et al.[17] found that older patients with mean age of 62.5 ± 10.1 years and female predominant (58 [54.2%] of 107). However, in United Kingdom, bronchiectasis is surprisingly common particularly in older age groups with female predominant (10995 [58.5%] of 18793) was found by Quint et al.[1]. This could be explained by with declining rates of pulmonary tuberculosis in developing countries, and there is increasing the association of non-tuberculous mycobacterial (NTM) infections with bronchiectasis. A Retrospective study have suggested that the incidence of NTM disease in the non-CF bronchiectasis population may be as high as 30% .[18] Again, a prospective study of pulmonary NTM, found that 95% of subjects were females.[19]

Almost half of study subjects (16, 48.5%) had a history of pulmonary tuberculosis, followed by (7, 21.2%) had COPD, and (6, 18.2%) had Asthma as associated conditions. Dhar et al.[3] also observed more subjects (916 [41.7%] of 2195) had a history of previous tuberculosis and 5.3% had COPD, 2.5% had Asthma. Due to high prevalence of tuberculosis in the Indian subcontinent this finding could be explained by as pulmonary tuberculosis was the most common underlying cause of bronchiectasis.[20]

The mean exacerbation in the last 12 months was 1.75 ± 1.09 and 20 (60.6%) respondents had history of hospitalization within last 2 years. Lee et al.[17] found that mean exacerbations in last 12 months were 1.46 ±1.48 and history of respiratory hospitalization was 71 (66.4%).

We observed that majority had normal weight (23, 69.7%) followed by underweight (9, 27.3%), and overweight (1, 3%) with mean BMI of 20.58 ± 3.64 kg/m^2. However, the median BMI was 21.5 kg/m^2 within the range of 18.5 – 24.5 kg/m^2 in the study of Dhar et al.[3] and 21.52 ± 3.63 kg/m^2 found in Li et al.[21]. More than half (19, 57.6%) of the subjects had clubbing. Similar findings (75 [75%] of 100) also found by Bhatta et al.[22]. In this study, mean FEV1 of the study subjects was 42.9 ± 22.8. Median FEV1 was 61.4 in the study of Dhar et al.[3] and Mean FEV1 was 57.6 ± 8.7 in the study of Minov et al.[23]. Number of affected lobes in HRCT of chest was ≥3 among 72.7% of the study subjects in this study. Number of affected lobes was 3.24 ±1.52 in the study of Lee et al.[17].

The current study found that Pseudomonas aeruginosa 21.2% as most frequent organism in sputum culture followed by Klebsiella 18.2%, Haemophilus influenzae 6.1%, Moraxella 6.1% and Escherichia coli 6.1%. Regarding colonization of Pseudomonas (22.4%) similar finding observed by Lee et al.[17]. In India the most common organism in sputum culture was Pseudomonas aeruginosa (301 [13.7%] of 2195) founded by Dhar et al.[3]. According to King et al.[24], the frequency of Pseudomonas isolation in NCFB was 18% but colonization of Haemophilus influenza was 42%. However, colonization with Haemophilus was more found in Europe and the USA [25] but was uncommon in our study and Dhar et al.[3] in India. These observations which reflect the differences in patient characteristics or environmental conditions that help for the growth of certain organisms, including community antibiotic use, but the possibility of technical factors in microbiological sampling and laboratory procedures might affect the results should also be considered. H influenzae in particular can be challenging to isolate and might lose viability after delays in processing. There are many previous studies suggest difficulties in isolating H influenzae in low-income and middle-income countries.[26]

According to BSI score, we found that mild bronchiectasis was 12.1%, moderate was 33.3%, severe was 54.6%, and mean BSI score was 9.00 ± 3.05. Similar result also observed by Lee et al.[17] in where 13.1% with low, 28.8% with moderate, 58.4% with severe and mean BSI score was 9.43 ± 3.81. On contrary, Kallarakal et al.[16] found more subjects (61 [80.3%] of 76) with high BSI score, and mean BSI score was 11.63 ± 3.34. The Indian bronchiectasis registry also showed that 33·2% with mild bronchiectasis, 30·7% with moderate bronchiectasis, and (793 [36·1%] of 2195) with severe bronchiectasis.[3] So, according to our study more patients have severe bronchiectasis as evaluated by BSI scores which was supported by others studies done in India. It could be due to younger age of patients, more extensive radiological disease with cystic dilatation, higher rate of hospitalization for severe exacerbations as well as tuberculosis is the most frequent and common underlying cause of bronchiectasis.

The mean value of serum albumin was 3.22 ± 0.84 g/dl. On the other hand, Kallarakal et al.[16] observed mean value of the serum albumin was 3.86 g/dl. However, Lee et al.[17] found mean value of albumin was 4.11 ± 0.52 g/dl. In this study, serum albumin had a significant negative correlation with BSI score (r = -0.457 and p = 0.008). Similarly, Kallarakal et al.[16], also observed a strong negative correlation of BSI score with serum albumin levels (r =-0.242) which was statistically significant with a p value 0.035. Again, another study by Li et al.[21] also found that serum albumin level was most strongly associated with the BSI. Thus, the serum albumin level exhibited statistically significant negative correlation with disease severity (BSI score) of NCFB.

Bronchiectasis had lower serum albumin as evidence

of inflammation observed by Ip et al.[27]. In addition, malnutrition is highly prevalent in patients with bronchiectasis was also observed by Boussoffara et al.[28]. However, in present study we could not assessed albumin as a marker of inflammation or nutritional depletion rather than as a marker of disease severity which correlate with the BSI score.

So, in present study, we found that, the increment of disease severity (mean BSI score 9.00 ± 3.05) of NCFB was occurred according to reducing level of serum albumin (mean albumin 3.22 ± 0.84 g/dl) and had a statistically moderate significant negative correlation between serum albumin and disease severity (BSI score) of NCFB.

CONCLUSION

This study found that the serum albumin showed moderate association with disease severity of NCFB patients. The simplicity and availability of serum albumin measurement in the context of Bangladesh favor the potential advantage of serum albumin for the assessment of severity of NCFB patients. Thus, the study concludes with that the serum albumin is an effective and most suitable tool to estimate the disease severity of NCFB patients.

Limitations

This was a single-center, cross sectional study with a relatively small number of patients.

Recommendation

Serum albumin can be used as a simple and relevant marker of disease severity in subjects with non-CF bronchiectasis. In further, a more comprehensive study on a large scale should be conducted to confirm the results of our study.

Conflicts of interest: Nothing to declare.

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AUTHORS'S CONTRIBUTION

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