

A retrospective correlative profiling of lung functions, microbiological, radiological, periodontal, hematological parameters in noncystic fibrosis bronchiectasis patients of North India

ABSTRACT

Introduction: Noncystic fibrosis bronchiectasis (NCFB) is a neglected debilitating condition with scarce epidemiological literature explaining its geographical heterogeneity, especially in lower and middle-income countries. This study aimed to assess and correlate the functional profile of NCFB patients and evaluate the correlation of body mass index (BMI) with several disease variables.

Methods: This mixed-method retrospective research study was conducted on 124 radiologically confirmed NCFB patients in terms of various qualitative and quantitative variables.

Results: Restrictive ventilatory defect was the most common type with the preponderance of male former smokers. Mean platelet lymphocyte ratio (PLR; 104.08 ± 73.59) revealed certain degree of systemic inflammatory burden with a slightly higher mean peripheral leukocyte count (10665.19 ± 4268.81 cell/mm³) and eosinophilia of >2%. Almost all patients had periodontal disease with a higher prevalence of chronic periodontitis (54.83%). Moderately severe and predominantly cystic radiological type was encountered with 61.2% patients positive for *Pseudomonas aeruginosa*. Bronchiectasis aetiology comorbidity index (BACI) i.e., 2.34 ± 2.37 represented an intermediate mortality risk in our patients. On basis of BMI, majority were young underweights with poor pulmonary functions while PLR skewed toward overweight patients (nonsignificant $P > 0.05$). Forced expiratory volume/forced vital capacity displayed a negative weak moderately significant correlation with BACI ($r = 0.24$; $P = 0.008$). Peripheral lymphocyte count demonstrated a weak negative but significant correlation with modified Reiff score ($r = 0.20$; $P = 0.023$) while serum neutrophil count had a weak negative moderately significant correlation with hemoglobin ($r = 0.20$; $P = 0.023$).

Conclusions: NCFB bears great heterogeneity with distinct geographical phenotypes and should be correlated thoroughly in terms of peripheral leukocytes count, pulmonary functions, radiology, BMI, and coexisting comorbidities for adequate management.

Keywords: Body mass index, bronchiectasis, chronic periodontitis, modified Reiff score, platelet lymphocyte ratio

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INTRODUCTION


Bronchiectasis is a chronic infectious immune-inflammatory disease marked by irreversible dilatation of bronchi. It is a common chronic pulmonary disease with geographic variability in prevalence, incidence, etiology,

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microbiology, and clinical phenotypes. The major compelling epidemiological literature is limited exclusively to European countries (USA and Australia)^[1,2] with the paucity of information from low- and middle-income countries.^[3,4] A recent Indian bronchiectasis registry (2015–2017) comparing data from those of Europe and the USA showed marked differences with indigenous population showing more severe forms with substantial radiological involvement, higher rate of cystic dilatation and exacerbations, and consequently increased probability of hospital admissions.^[5]

According to the Global tuberculosis report, 2020 (World Health Organization),^[6] for the period of 2016 to 2020 the revision had included three high burden country list i.e for TB, MDR-TB and HIV-associated TB. Interestingly, India is among the 14 countries that are in all three lists accounting for 63% of the estimated global number of incident TB cases in year 2019. Bronchiectasis is seen as frequent sequelae of pulmonary TB with majority of successfully treated individuals developing radiological bronchiectasis later in life. Nevertheless, other etiologies are postinfective (postpneumonia, whooping cough, etc.), mucociliary disorder, immune disorder (allergic bronchopulmonary aspergillosis, hypogammaglobulinemia), chronic obstructive pulmonary disease (COPD), Alpha 1-antitrypsin deficiency, etc. However, TB is regarded as a major cause of bronchiectasis in Asian countries^[6] including the Indian subcontinent.^[7] Hence, etiological variations are noticed with geographical diversities.

The key microbes found in bronchiectasis are primarily *Pseudomonas aeruginosa*, and members of other genera such as *Streptococcus*, *Staphylococcus*, *Hemophilus*, *Prevotella*, and *Veillonella*. Frequent infections result in poorer pulmonary functions, increased exacerbations, and disease severity. In the recent past, researchers have found an association between periodontitis and chronic respiratory diseases (COPD, asthma, pneumonia) but as far as bronchiectasis is concerned, the truth is still to be unraveled. Interestingly, a study has shown the same clonal types of *P. aeruginosa* in saliva secretion, sputum, and subgingival dental plaque of cystic fibrosis patients highlighting that periodontal tissues might act as a reservoir of lung infection.^[8]

Impairment of pulmonary function is heterogeneous and related to numerous factors like lobes number involved, extent of bronchial dilatation, age, sputum volume, peripheral leukocyte count, and co-existing asthma.^[9] High-resolution pulmonary imaging can detect initial pulmonary damage despite normal lung function (such as forced expiratory volume [FEV₁]). Usually, an obstructive lung function

defect is noticed but restrictive, mixed types, sole air trapping, and normal spirometry are also not uncommon in bronchiectasis.^[10-12] Acute exacerbations are crucial events and frequently associated with the decline in FEV₁ values.^[13] Concurrent existence of comorbidities like COPD and asthma in bronchiectasis patients has been related to enhanced exacerbations and worsened life quality, thereby complicating the management of the disease.^[14]

Malnutrition and weight loss have been seen in some noncystic fibrosis bronchiectasis (NCFB) patients.^[15] Although, low body mass index (BMI) had been clearly associated with high death rates in COPD patients, literature is in paucity regarding such an association in bronchiectasis.^[16,17] Moreover, data associating BMI with the severity of the disease is lacking in the Indian population with only few studies conducted in other Asian countries. For quantitative assessment of comorbidities, bronchiectasis aetiology comorbidity index (BACI) has been recently suggested. It has a prognostic value by speculating the risk of mortality in future, exacerbations, hospitalization, and life quality.^[18] Since compelling literature had shown that 30%–40% of bronchiectasis patients die due to some nonrespiratory diseases this tool can definitely help in better treatment planning and patient care.

Recent evidence has suggested that peripheral high but normal leukocyte count (especially neutrophils and eosinophils) can be a predictor of the presence of subclinical disease and increased systemic disease-associated mortality.^[19] Platelet lymphocyte ratio (PLR), a novel inflammatory marker has been extensively studied in cardiovascular and oncological diseases but with limited value in COPD patients and rather unexplored in bronchiectasis.

Taking into consideration the aforementioned scarce data on highly heterogeneous and somewhat neglected diseases, we retrospectively assessed the medical records of bronchiectasis patients in our tertiary care center to assess lung functions, radiological severity, hematology, dyspnea, periodontal status, microbiology, and comorbidity burden followed by inter-variable correlations. In addition, the association between BMI and variables of disease severity was also evaluated.

METHODS

The ethical clearance (Ref. no: 89th ECM II A/P2 dated 6/04/2018) for the study protocol was obtained by the Institutional Ethical Committee, King George's Medical University, Lucknow, UP, India.

Study design

For the present descriptive exploratory study, we utilized retrospective data obtained from medical records of physician and radiologically confirmed adult bronchiectasis cases (≥ 18 years) between October 2018 and January 2020. It was conducted at the Department of Respiratory Medicine, King George's Medical University, Lucknow, Uttar Pradesh, India. From 346 medical records only 124 patients had complete data in terms of high-resolution computed tomography (HRCT) images of the thorax, sputum/broncho-alveolar lavage bacteriological culture (minimum two reports at least 3 months apart), pulmonary function test, complete blood count, periodontal status, BACI reports and hence included. The exclusion criteria were as follows: (1) patients who were on anti-tubercular treatment (because of its impact on bacterial culture); (2) bronchiectasis due to cystic fibrosis as etiology; (3) mentally disabled; (4) malignancy involving lungs; (5) edentulous patients.

Disease definitions

Bronchiectasis

Individuals with a syndrome consisting of the clinical presence of sputum production, cough, or recurring pulmonary infections as confirmed by a pulmonologist and dilated bronchi as seen on HRCT thorax.

Chronic periodontitis

An individual was said to have periodontitis if clinical attachment loss interdentally (CAL) ≥ 2 mm on nonadjacent teeth, or buccal or oral CAL ≥ 3 mm with periodontal probing depth >3 mm is detectable at ≥ 2 teeth.^[20] The University of California 15 color-coded calibrated periodontal probe (USA) was utilized for these measurements.

Chronic gingivitis

A gingivitis case is one with intact periodontium and bleeding on probing score $\geq 10\%$ while those with lesser than 10% were considered to have healthy gingiva.^[21]

Basic data collection

The demographic data (age, sex, smoking history, BMI), hematological findings (total leukocyte count, neutrophil %, eosinophil % and lymphocyte %, hemoglobin [g/dl], platelet count [cu.mm]), dyspnea/Modified Medical Research Council (mMRC) scale, radiological findings, and BACI were retrieved from medical records.

BMI was assessed by dividing weight (kilograms) by square of height (meters). Accordingly, these were grouped into four (WHO expert consultation for the

Asian population): Underweight (BMI < 18.5 kg/m²), normal weight ($18.5 \leq$ BMI < 25.0 kg/m²), overweight ($25.0 \leq$ BMI < 30.0 kg/m²), and obese (BMI ≥ 30.0 kg/m²).^[22]

Disease severity variables

Radiological classification of bronchiectasis based on chest computed tomography (high-resolution computed tomography score)

Chest CT films were reviewed by one experienced radiologist/pulmonologist that was blinded to the patient's clinical data and bacteriological results. Gudbjerg's criteria were used for diagnosing bronchiectasis based on the presence of enhanced pulmonary markings, honeycomb pattern, obliteration of lung volume (atelectasis), and other pleural changes. The predominant variety, i.e., cylindrical, cystic, and varicose was noted as per Reid's classification of bronchiectasis.^[23] Assessment of radiological severity was done by modified Reiff score^[24] that incorporates number of lobes involvement (considering lingual as separate lobe) and dilatation degree (tubular/cylindrical = 1, varicose = 2, and cystic/saccular = 3). This score had a range between 1 (minimum) to 18 (maximum). HRCT score is divided into tertiles, i.e., mild bronchiectasis 0–6, moderate 7–12, and severe bronchiectasis 13–18.^[10]

Spirometry

Patients performed spirometry (S/N 2014090079/Pulmonary Function Equipment; Cosmed, Italy) for forced vital capacity (FVC) and FEV₁ as per guidelines of the American Thoracic Society.^[25] Accordingly, patients were grouped into three types with FEV₁/FVC $< 70\%$ predicted as obstructive pattern, FEV₁ and FVC values $< 80\%$ predicted and FEV₁/FVC ratio ($> 70\%$) as restrictive type, while mixed diseased patients having FEV₁ and FVC values $< 80\%$ predicted with FEV₁/FVC $< 70\%$.^[26]

Modified Medical Research Council dyspnoea scale

It is a self-assessing method for measuring the amount of disability that dyspnea can exert on daily activities on a scale ranging from 0 to 4^[27] [Table 1].

Table 1: The modified Medical Research Council Scale

Grade	Description of breathlessness
0	I only get breathless with strenuous exercise
1	I get short of breath when hurrying on level ground or walking up a slight hill
2	On level ground, I walk slower than people of the same age because of breathlessness, or I have to stop for breath when walking at my own pace on the level
3	I stop for breath after walking about 100 yards or after a few minutes on level ground
4	I am too breathless to leave the house or I am breathless when dressing

Bronchiectasis aetiology comorbidity index (BACI)

Comorbidities clubbed under this index has been assigned certain points based on their contribution to subsequent risk which in decreasing trend are metastatic malignancy = 12, haematological malignancy = 6, COPD and cognitive impairment = 5, inflammatory bowel disease and chronic liver disease = 4, diabetes, iron deficiency anaemia, asthma, peripheral vascular disease and pulmonary hypertension = 3, and ischaemic heart disease = 2. The concurrence of these diseases amplifies risk of death, exacerbations and worsens quality of life.^[18] The BACI calculator is available online at <http://www.ronchiectasisseverity.com>.

Platelet lymphocyte ratio

PLR ratio was analysed as ratio of absolute platelets count to absolute lymphocytes count with help of hemogram.

Chronic colonization by *Pseudomonas aeruginosa*

During outpatient visits and hospital admissions of bronchiectasis patients, sputum or broncho-alveolar lavage was routinely acquired and processed. Samples with more than 25 polymorphonuclear leucocytes and <10 squamous cells per low-power field were regarded as acceptable for identification through Gram stain. Chronic *P. aeruginosa* colonization was considered in case of minimum of two positive cultures, 3 months apart over a period of 1 year.

Statistical analysis

Statistical analysis utilized SPSS software (PSAW, windows version 21, IBM Corporation, America, United States). The descriptive continuous variables have been summarized as mean \pm standard deviation. The prevalence rate was depicted as % of total cases. The null hypothesis that the values or levels of parameters are almost the same, were tested by one-way ANOVA for univariate and two-way ANOVA for bivariate analysis. On the evidence of significant *F*-value, the mean values were compared for multiple comparisons by the Newman-Keuls test. A $P < 0.05$, $P < 0.01$ and $P < 0.001$ have been designated as significant, moderately, and highly significant. The prevalence depicted by discrete variables was compared by the test of proportions. The product-moment correlation coefficient r was calculated by formula ($r = \text{covariance}(x, y) / \sqrt{\text{variance}(x) * \text{variance}(y)}$). The Pearson's correlation coefficient is based on Student's *t*-distribution with *n*-2 degrees of freedom. Therefore, correlation coefficient r was tested by *t*-test for its null hypothesis, i.e., $r = 0$.

RESULTS

General characteristics

The summarized general features of 124 bronchiectasis patients as depicted in Table 2 showed sufferers with

mean age belonging to the fourth decade of life with male preponderance. Smoking status was skewed toward former smokers. The average BMI was marginally coinciding with the lower limit of normal values ($18.40 \pm 3.73 \text{ kg/m}^2$) with a high prevalence of underweight patients. The restrictive ventilatory defect was the most common pattern seen followed by mixed and obstructive ventilatory dysfunctions. The mean mMRC dyspnea score of 2.07 ± 1.04 pointed toward moderate severity of breathlessness.

Mean hemoglobin was normal and mean total leucocyte count (TLC) approaching the upper normal limit of range with almost normal differential leukocyte count except eosinophils which were somewhat elevated i.e., $3.58\% \pm 4.063\%$ suggesting future exacerbations and severe forms of disease with poor outcomes. Mean PLR in the study population revealed some degree of systemic inflammation. The prevalence of periodontal diseases was 100% with greater individuals affected by chronic periodontitis in comparison to chronic gingivitis.

Modified Reiff score indicated moderate severity of bronchiectasis. Associated comorbidities found were posttubercular sequelae (25.80%), diabetes (11.29%), cardiovascular disorders (5.6%), liver disease (6.4%), renal disease (0.8%), asthma/COPD (9.6%), fungal infections (12.9%), bone disorders (1.6%), and thoracic sitis inversus totalis (0.8%). The mortality risk in terms of BACI denoted intermediate risk with higher exacerbations and poor quality of life.

76 patients had sputum/BAL culture as positive (61.2%) with the most commonly isolated pathogen as *Pseudomonas aeruginosa* accounting for 29.03% followed by 32.3% of varied microorganisms like *Kleibseilla pneumonia*, *Acinetobacter baumannii*, *Escherichia coli*, *Staphylococcus aureus*, *Stenotrophomonas maltophilia* and *Neisseria flava*.

Comparisons among various radiological types

Patients majorly had restrictive ventilatory defect in 81 (65.3%) followed by mixed in 37 (29.8%) and obstructive in 4 (3.2%) patients [Table 3]. FEV1 value was lowest in cystic type while FVC and FEV1/FVC % was lowest in varicose type of bronchiectasis with maximum number of pulmonary lobes involvement (3.80 ± 2.20) amongst the three patterns. Chronic colonization of *P. aeruginosa* was detected more frequently in varicose group followed by cystic.

Comparisons among three body mass index groups

Table 4 showed underweights to be youngest with the highest mean dyspnea score, lowest mean lung

Table 2: Patient's characteristics

Variables	Summary, n (%)	95% CI
Number of patients	124	-
Age (years)	44.25±13.97	41.76-46.74
Sex		
Male	69 (55.64)	-
Female	55 (44.35)	
Smoking status		
Never	17 (13.7)	-
Former	107 (86.2)	
BMI (kg/m ²)	124	18.40±3.73
Normal weight	47 (37.9)	15.66±1.64
Under weight	69 (55.64)	21.00±1.50
Overweight	8 (6.4)	26.80±1.95
Spirometry status		
FVC%	52.11±16.19	49.24-54.99
FEV1%	45.59±18.62	42.28-48.90
FEV1/FVC	80.35±20.34	76.73-83.96
Ventilatory defects		
Restrictive	81 (65.3)	-
Mixed	37 (29.8)	
Obstructive	4 (3.2)	
Normal	2 (1.6)	
mMRC Scale score (range: 0-4)	2.07±1.04	1.89-2.26
Hemogram		
Hb (g/dl)	12.64±2.06	12.27-13.01
TLC (cells per mm ³)	10665.19±4268.81	9906.40-11424.01
Neutrophil (%)	71.29±10.91	69.35-73.23
Lymphocyte (%)	25.07±9.52	23.38-26.77
Eosinophil (%)	3.58±4.063	2.86-4.30
Platelet count (lacs cells/mm ³)	2.22±0.927	2.05-2.38
PLR	104.08±73.59	91.00-117.16
Periodontal diseases		
Chronic periodontitis	68 (54.83)	-
Chronic gingivitis	56 (45.16)	
Modified Reiff score (range: 1-18)	7.52±5.74	6.50-8.54
Etiology as per HRCT findings		
ABPA	16 (12.9)	-
Postinfective	108 (87.09)	
BACI score	2.34±2.37	1.92-2.76
Sputum/BAL culture positive	76 (61.2)	-

Quantitative variables are represented as the mean±SD and range, and qualitative variables as the absolute value and percentage. SD: Standard deviation, BMI: Body mass index, mMRC: Modified Medical Research Council, Hb: Hemoglobin, CI: Confidence interval, FVC: Forced vital capacity, FEV1: Forced expiratory volume, TLC: Total leukocyte count, HRCT: High-resolution computed tomography, BACI: Bronchiectasis aetiology comorbidity index, BAL: Bronchoalveolar lavage, ABPA: Allergic bronchopulmonary aspergillosis, PLR: Platelet lymphocyte ratio

functions values, highest mean modified Reiff score along with the mean degree of dilatation in comparison to other groups. Furthermore, 19.3% (24) individuals had chronic colonization of *P. aeruginosa* who were either of under-weight or over-weight categories. Mean PLR was skewed toward overweight individuals. Mean BACI displayed a rising trend from normal weight followed by overweight and underweight category but all were susceptible to intermediate risk for mortality, future exacerbations. All intergroup comparisons were although

nonsignificant ($P > 0.05$) yet it suggested interesting intervariable links with BMI.

Correlative profiling

Figure 1 demonstrates mean age having a weak positive correlation with BACI yet with high statistical significance ($r = 0.25$; $P = 0.005$). Pulmonary functions parameters like FEV1 and FVC showed statistically high significance with strong correlative values ($r = -0.76$; $P < 0.001$). Also, FVC and FEV1 displayed a weak negative correlation with

Table 3: Disease severity variables according to predominant radiological phenotypes

Variables	Cylindrical (n=30)	Varicose (n=10)	Cystic (n=84)	P		
				Cylindrical versus varicose	Cylindrical versus cystic	Varicose versus cystic
FVC (% predicted)	53.1±17.8	51.7±15.4	51.8±15.9	0.957	0.792	0.985
FEV1 (% predicted)	47.7±19.0	48.2±22.3	44.5±18.2	0.932	0.585	0.803
FEV1/FVC	87.4±17.4	67.8±18.9	79.3±20.8	0.004	0.189	0.063
Normal	-	-	2	1	0.1404	0.145
Obstructive	1 (0.8)	-	3 (2.4)	0.118	0.772	0.072
Restrictive	25 (20.2)	4 (3.2)	52 (41.9)	0.000	0.000	0.000
Mixed	4 (3.2)	6 (4.8)	27 (21.8)	0.000	0.000	0.000
Number of lobes involved (lingual as separate lobe)	2.77±1.763	3.80±2.20	3.10±1.89	0.182	0.561	0.237
Chronic colonization	5 (16.7)	5 (50)	26 (31)	0.000	0.00029	0.00652

Levels of significance $P < 0.05$ (significant), $P < 0.01$ (moderately significant), $P < 0.001$ (highly significant). Quantitative variables are represented as the mean±SD and qualitative variables as the absolute value and percentage. FVC: Forced vital capacity, FEV1: Forced expiratory volume, SD: Standard deviation

Table 4: Comparison of demographic data and functional variables among the three body mass index groups

Variables	BMI groups		
	Underweight (n=69)	Normal weight (n=47)	Overweight (n=8)
Age (years)	42.3±14	46.9±13.8	45.4±16.4
Female/male (n)	39/30	26/21	4/4
Former/never smoker (n)	12/57	5/42	0/8
mMRC dyspnea score	2.1±1.1	2.0±1.0	1.9±1.0
FVC,% predicted (%)	50.0±15.6	54.2±17.0	57.9±15
FEV1,% predicted (%)	42.9±18.6	49.3±19.3	46.6±11.1
FEV1/FVC	78.9±19.2	82.1±23.0	82.8±13.6
Radiological score (modified Reiff score) (n)	8.3±6.2	6.5±4.9	6.3±5.8
Degree of dilatation	2.55±0.80	2.23±1.11	2.0±1.07
Chronic colonization by <i>Pseudomonas aeruginosa</i> (n)	23	12	1
PLR	100.57±51.77	107.4±101.1	114.78±40.63
BACI score	2.61±2.45	1.96±2.29	2.25±2.12

Quantitative variables represented as the mean±SD and qualitative variables as the absolute value and percentage. SD: Standard deviation, BMI: Body mass index, mMRC: Modified Medical Research Council, FVC: Forced vital capacity, FEV1: Forced expiratory volume, BACI: Bronchiectasis aetiology comorbidity index, PLR: Platelet lymphocyte ratio

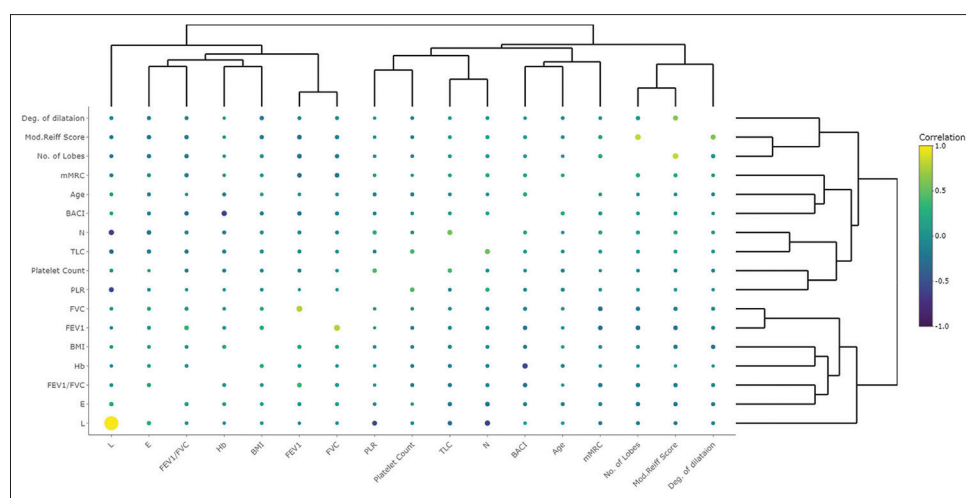


Figure 1: Correlation heat map for functional characterization of bronchiectasis patients

mMRC score yet moderately high significance ($r = -0.26$; $P = 0.004$ and $r = -0.28$; $P = 0.002$). FEV1 and FEV1/FVC

were negatively correlated to BACI (weak strength) but with mild and moderate significance respectively. BMI values were

negatively correlated with weak strength to the degree of dilatation ($P = 0.024$). Modified Reiff score was negatively and weakly correlated with only FEV1 ($P = 0.005$) and with poor correlation to FVC and FEV1/FVC. Although TLC showed throughout poor correlations with all disease severity variables yet lymphocyte count demonstrated negative yet weak but significant ($P = 0.023$) correlation with modified Reiff score. Platelet count showed a weak correlation yet highly significant P value with TLC ($P < 0.001$). Hemoglobin values showed a negative weak yet moderately significant correlation with neutrophils count ($P = 0.009$). The systemic serum marker PLR values showed poor relative values throughout all disease variables.

DISCUSSION

Paucity of comprehensive data on bronchiectasis continues to exist in Asian subcontinent precisely India and China with only few sporadic studies. Geographical variability do exist and it has led to significant ambiguity in understanding the epidemiology, aetiologies, pathogenesis, airway microbiome, genetic susceptibility, and phenotypic characteristics of bronchiectasis patients.

Functional characterization of 124 noncystic bronchiectases suggested that majority of patients were male former smokers (mean age approximately 44 years) with a prior history of TB. Prevalence of tuberculous infection in India in a recent systematic review and meta-analysis has shown male preponderance^[28] that corroborates with findings of the present study. However, contradictory to our finding a multidimensional analysis of seven cohorts from European countries showed female predominance pointing toward geographical heterogeneity.^[29] Smoking has shown to produce around three folds higher chance for developing TB^[30] which is in total agreement with our study.

Studies have shown that in post TB sequelae bronchiectasis, restrictive ventilatory defect is commonly encountered as reported by Panda *et al.*^[31] which was also apparent in our study due to the higher proportion of postinfectious (TB) patients. During the course of TB disease and treatment, lungs undergo permanent deformities primarily due to defective tissue repair explaining the restrictive pattern.^[32] However, since confirmatory tests based on a lower limit of normal, total lung capacity and diffusing capacity of lungs were not mentioned in all medical records hence the reason for noninclusion in this study. Therefore, the categorization presented is an initial quick glimpse of abnormal spirometry for easy association with other variables in the broader sense. Participants in our study complained of breathlessness as

a common symptom with 26.61% having grade 1, 29.03% with grade 2, 32.2% with grade 3, and 6.45% with grade 4. A recent multicentric study by Dhar *et al.* have shown a higher prevalence of Indian patients belonging to grade 2 and 1 as per the mMRC scale.^[5] However, in our study also, although maximum sufferers were dyspnoeic yet with higher severity. A decline in pulmonary functions (FVC% and FEV1%) with increasing mMRC score, i.e., a weak negative but moderately high significance was noticed in our participants. Therefore, dyspnea is an important clinical symptom and should be taken care of by clinicians during initial patient assessment since this score can roughly suggest lung function impairment ruling out the other factors like cardiovascular, neurological, etc.

Recently, evidence have suggested systemic inflammatory reaction in chronic inflammatory pulmonary diseases such as Asthma and COPD but little is cognized for bronchiectasis. Interestingly, few studies on clinically stable bronchiectasis have found leucocyte counts comparable to healthy controls (\sim under 8000 cells/mm³)^[33,34] with findings suggestive of its relation to microbial colonization. In a recent Turkish study on COPD, WBC count of \sim 9200 cells/mm³ was seen in stable patients while those with acute exacerbations had \sim 13500 cells/mm³.^[35] In the current study, 52 patients had WBC count somewhat higher (\sim 11100–25200 cells/mm³), 76 had positive sputum culture (\sim 29% having *P. aeruginosa*) and 68 had compromised oral hygiene with chronic periodontitis thereby suggesting possible airway colonization causing systemic immune dysregulation. Same clonal types of *P. aeruginosa* were found in saliva, sputum, and subgingival plaque samples of cystic fibrosis patients emphasizing the importance of periodontal pathogens as a source of pulmonary infection.^[8]

Although, peripheral eosinophilia is frequently found in asthma and COPD^[36] but its clinical importance in bronchiectasis is undetermined. Bronchiectasis primarily is a neutrophilic disease yet our bronchiectasis participants demonstrated a higher blood eosinophil count ($>2\%$) convincing towards an allergic phenotype besides neutrophilic predominance. The systemic inflammatory burden was assessed through biomarker PLR but in our studied population it had shown very weak correlation throughout all functional variables implicating towards disease complexity.

High resolution CT of thorax is regarded as gold standard diagnostic tool for assessing the extent and radiological type of bronchiectasis.^[37] Patients in our study were of moderate severity based on modified Reiff score which was negatively correlated to FEV1%. Interestingly, this

score had also shown a weak correlation with peripheral lymphocyte count implicating hemato-radiological link. The predominance of cystic type was seen in our patients while spirometric indices (FEV1 predicted %, FVC predicted %, and FEV1/FVC) showed insignificant differences among all three types. Extensive lobar involvement was seen in varicose type followed by cystic and cylindrical which paralleled with their FVC % and FEV1/FVC values. It was seen that patients with cystic type had mainly (41.9%) restrictive ventilatory defect followed by mixed type (21.8%). As compared to other types, cystic bronchiectasis patients had a higher percentage (31%) of positive culture in their sputum/BAL samples next only to the varicose group (50%). Compelling evidence suggests cystic type to enhance and acts as risk factor for airway colonization by bacteria which is similar to our findings.^[38] Hence, radiological classification could be useful in predicting disease severity.

Malnutrition and weight loss have been rather frequent findings in chronic inflammatory respiratory diseases. A few studies pertaining to various geographical regions have although the documented varying prevalence of underweights in bronchiectasis as reported by Qi *et al.*^[39] and in COPD populations by Sun *et al.*^[40] Additionally, these studies have also concluded that such nutritionally depleted patients have increased mortality risk, acute exacerbations, poor pulmonary function indices, extensive radiological involvement, chronic colonization of *P. aeruginosa*, and systemic inflammatory amplification. In the present study similar findings were found for underweights when compared with normal and overweight patients in terms of highest dyspnea scale and modified Reiff score, whereas lowest pulmonary function indices values yet comparisons were insignificant ($P > 0.05$).

Only a handful of studies exist suggesting a prevalence of comorbidities in bronchiectasis patients^[41] which can affect various disease-related outcomes, quality of life^[42], and prognosis.^[18] Yet, none to our knowledge has compared BACI among underweight, normal, and overweight bronchiectasis patients. Our results were although statistically insignificant and all patients had fallen in “intermediate risk” category yet there was a decreasing trend of score from overweight through normal weight toward underweight patients. It implicates that bronchiectasis patients with higher BMI carries a higher prevalence of obesity-dependent comorbidities (like cardiovascular, diabetes, cancer, and mortality risk) as well as independent ones (like iron deficiency anemia, chronic liver disease, etc.). Importantly, BMI had shown a negative correlation with the degree of dilatation (radiological variable) although with weak strength. It conceptualizes that low body mass/malnutrition is somehow associated

with extensive radiological involvement in bronchiectasis sufferers. Therefore, BMI assessment should be done in routine practice to segregate such patients followed by cautious monitoring for early identification of comorbidities and consequently determination of BACI score for predicting future exacerbations and death risk.

In addition, the correlation heat map indicated a weak positive yet highly significant association between age and BACI. Aging can be a causative factor for various chronic diseases, either they become more prevalent or apparent in the geriatric population. More importantly, lungs also suffer age-associated functional decrements that get exposed by the presence of concurrent respiratory disease. The spirometric indices FVC% and FEV1% demonstrated a strong correlation with high significance highlighting the variable interdependency. Interestingly, the BACI score had shown a negative correlative impact (moderate significance) on only one pulmonary index, i.e., FEV1/FVC. Therefore, it gives an idea that bronchiectasis-associated comorbidities included in the BACI score have a direct impact on this variable resulting in poor lung function.

Being a retrospective study, as in our case, the data was entirely dependent on the reliability of medical records. The correlations among most of the variables taken in this study were weak yet they give an important preliminary view about systemic derangement observed in NCFB. The reasons could be small sample size, inability to perform spirometry on same visit, prior medications (antibiotics, systemic corticosteroids etc) being a tertiary care center. Also, it could be because a major number of our patients were recalled ones for the purpose of re-evaluation/counselling and educating airway clearance techniques for pulmonary rehabilitation so there could be a possible disparity between their clinical symptoms, blood, spirometric and HRCT reports. More longitudinal studies with large sample size should be conducted to validate the results.

CONCLUSIONS

Our findings suggest that cystic bronchiectasis with restrictive ventilatory defect was prevalent in North Indian population. These individuals were likely associated with positive sputum/BAL culture with *P. aeruginosa* being the predominant microorganism isolated. Radiological severity (number of lobes affected) was highest in varicose and cystic types of disease. The comorbidity index (BACI) was weakly correlated with spirometric parameter FEV1/FVC. Hemoglobin value showed a negative weak association with blood neutrophil count. It is anticipated that somehow nutrition depletion was related to radiological type (degree of dilatation) because

of a negative weak correlation between the two. It thereby affirms that bronchiectasis bears tremendous geographical heterogeneity and many aspects of its pathophysiology need to be unraveled at the genetic and molecular level for a better understanding of this disease. This will ultimately help in suitable treatment planning and multi-comorbidity management of these patients to reduce morbidity and mortality rates in our region.

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Conflicts of interest

There are no conflicts of interest.

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