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Association between Bronchiectasis Exacerbations and FEV1 Changes at A Tertiary Care Center

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ABSTRACT

Bronchiectasis, a common respiratory disease, presents a healthcare challenge since its evaluations do not often include health-related quality of life assessments. **Objectives:** To determine whether there is a correlation between the number of exacerbations experienced with non-cystic fibrosis bronchiectasis at baseline and the number of exacerbations experienced throughout follow-up, and identify any time-related changes in FEV1. **Methods:** 115 bronchiectasis patients were included prospectively. Evaluation of the correlation between exacerbations during the 24-month baseline period and 0-to-24-month and 24-to-48-month follow-up periods was done. Outcomes were changes in FEV1 and percentage of predicted FEV1 after 24 months, with stratification based on frequency of initial exacerbations. SPSS version 24.0 was used to analyze data. **Results:** 78 (67.8%) were female. The mean age was 63.7 years. The mean duration of bronchiectasis was 6.5 years. Mean BMI was 23.7 kg/m^2. The most common comorbidities were asthma and COPD. Frequency of exacerbations was 68 (59.1%). A baseline exacerbation was substantially linked to subsequent exacerbation at 0-24 months ($p=0.006$) and 24-48 months ($p<0.002$). Baseline FEV1 was considerably lower in patients with more exacerbations, but the drop was not significant between exacerbations. With more initial exacerbations, patients had substantially poorer FEV1 % predicted at baseline ($p<0.002$), 12 ($p=0.003$), and 24 months ($p<0.002$). **Conclusions:** Patients with flaring up of bronchiectasis were more likely to experience future exacerbations and have a lower FEV1 to begin with. However, the drop in FEV1 may be unrelated to the frequency of exacerbations at baseline.

INTRODUCTION

Bronchiectasis (BE) is a chronic structural respiratory disease that causes bronchial dilatation and, in extreme cases, hospitalization for an exacerbation [1]. Although the exact prevalence of BE is unclear, the average age-adjusted hospitalization rate in the US is 16.5 per 100,000 people and 9.4 per 100,000 in Germany [2]. There were no obvious signs of hospital need; however, the over-60 age group and women had higher hospitalization rates. The causes behind the wide difference in patients' annual average rates of exacerbations remain unknown [3]. Exacerbations can deteriorate lung function, lead to a bad prognosis, increase mortality, and increase expenditures, just like other chronic respiratory illnesses [4]. The average number of exacerbations each year is two or more for patients with advanced disease stages and high scores on the FACED or Bronchiectasis Severity Index (BSI) [5]. Additionally, these patients typically have lengthier hospital stays [6, 7]. Lung imaging shows abnormal thickening and dilating of the bronchial walls in bronchiectasis, a disorder not caused by cystic fibrosis, along with coughing and sputum production [8]. One substantial feature of the natural history of bronchiectasis

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is the worsening of symptoms with time [9, 10]. Bronchiectasis exacerbations are linked to respiratory distress in addition to deteriorating lung function, increased mortality, diminished quality of life, and hospitalization risk. Adults in the US with bronchiectasis have not had their features studied until recently. Growing evidence from the US Bronchiectasis Research Registry (BRR) suggests that the majority (60 %) of bronchiectasis patients were nonsmokers, while 89 % were white, and 79 % were female. Approximately 63% of patients had Non-Tuberculosis Mycobacteria (NTM) sickness or NTM isolated during first evaluation [11]. The median age of the patients was 64 years. Studies that depended on claims data likely exaggerated the clinical burden of bronchiectasis exacerbations since data on the severity of the ailment are difficult to collect [8, 9]. Predicted FEV1% is negatively correlated with the frequency of exacerbations in chronic obstructive pulmonary disease (COPD) patients; however, this is not necessarily the case [12]. The most prominent feature of lung sickness following tuberculosis is bronchiectasis, which can range from moderate traction bronchiectasis to clinically severe bronchial dysfunction. Regarding the association between this kind of bronchiectasis and other NCFBs, there is a lack of data in the medical literature [13]. The conventional medical terminology for these disorders includes chronic obstructive pulmonary disease (COPD), asthma, and bronchiectasis. Having said that, it is an entirely distinct species. Pulmonary function tests are used to objectively evaluate the state of the lungs. Bronchitis is the most common cause of obstructive disability [14]. If lung function declines, the disease will deteriorate, the risk of mortality will rise, and the likelihood of an exacerbation requiring hospitalization will rise. While dealing with bronchiectasis, airway hyper-responsiveness has a negative correlation with quality of life, baseline spirometric values, and exacerbation frequency [15].

Bronchiectasis is characterized by recurrent exacerbations and progressive lung function decline; however, the longitudinal relationship between baseline exacerbation frequency and subsequent changes in FEV1 remains inadequately defined. While frequent exacerbations are recognized as markers of disease severity, limited prospective data from developing countries have evaluated their predictive value for long-term lung function deterioration. Moreover, regional evidence examining the association between exacerbation burden and spirometric trends in non-cystic fibrosis bronchiectasis is scarce. This gap highlights the need for longitudinal assessment to clarify whether baseline exacerbation frequency predicts future exacerbations and FEV1 decline. This study aimed to find out how FEV1 changed over time in relation to the frequency of bronchiectasis exacerbations at baseline and secondly to evaluate the correlation between the two variables throughout the 48-month follow-up period after the 24-month baseline.

METHODS

This prospective study using non-probability consecutive sampling was conducted at the Department of Pulmonology and Critical Care, Central Park Teaching Hospital, Lahore, during January 2023 to December 2024, after approval from the Ethical Committee Ref. No. IRB-0293-344. Following patients' informed permission, trained personnel at each research location used pre-designed standardized data collection forms of the hospital to collect patients' medical records. The sample size for the study was calculated using the Open-Epi online software for sample size calculation. Keeping the prevalence of bronchiectasis at 8 % as reported in research, the sample size came out to be 114 at a 95 % confidence level and 5 % margin of error [16]. The study only included individuals who consented to reveal bronchiectasis exacerbations. The age range was 18 to 75 years. The 24 months preceding the inclusion of patients served as the baseline period for this inquiry. The purpose of the 48-month follow-up was to determine whether or not the overall number of exacerbations was related to the number of bronchiectasis exacerbations that were present at baseline. In order to determine if there was a correlation between the frequency of bronchiectasis exacerbations and changes in FEV1, participants received both baseline and 24-month FEV1 data. Baseline data were evaluated during the 24 months before enrollment, a follow-up window from 0 to 24 months (combining visits 1 and 2), and a follow-up window from 24 to 48 months (combining visits 3 and 4). Our baseline data were collected during 24 months before enrollment, so that's why we used that interval. Patients were classified over time based on the frequency of bronchiectasis exacerbations, which may be either zero or one or more. A sub-analysis was performed at each time point to further classify patients based on whether they experienced 0, 1, or ≥2 exacerbations. For data analysis, SPSS version 24.0 was used. Using descriptive statistics, the study examined the entire research population as well as subgroups broken down by the existence and frequency of exacerbations. To compare values within the strata, continuous variables were subjected to analysis of variance (ANOVA), whereas categorical variables were tested using chi-squared tests. A significance threshold of $\alpha = 0.05$ was established.

RESULTS

The majority of the presented cases, 78 (67.8%), were female. The mean age was 63.7 years. The mean duration of

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bronchiectasis was 6.5 years. The mean BMI of the cases was 23.7 kg/m^2. The most common comorbidities were asthma and COPD. There were 45 (39.1%) smokers among all cases (Table 1).

Table 1: Characteristics of the Cases That Were Included

Variables	n (%)
Sex	
Female	78 (67.8%)
Male	37 (32.2%)
Mean Age	
Years	63.7
BMI	
Mean (kg/m^2)	23.7
Duration of Bronchiectasis	
Mean (Years)	6.5
Comorbidities	
Asthma	53 (46.1%)
COPD	45 (39.1%)
No	17 (14.8 %)
Smoking Habit	
Yes	45 (39.1%)
No	70 (60.9%)

Frequency of exacerbations was 68 (59.1%), with 44 (38.3 %) experiencing 1 exacerbation, while ≥2 in 24 (20.9 %) patients (Figure 1).

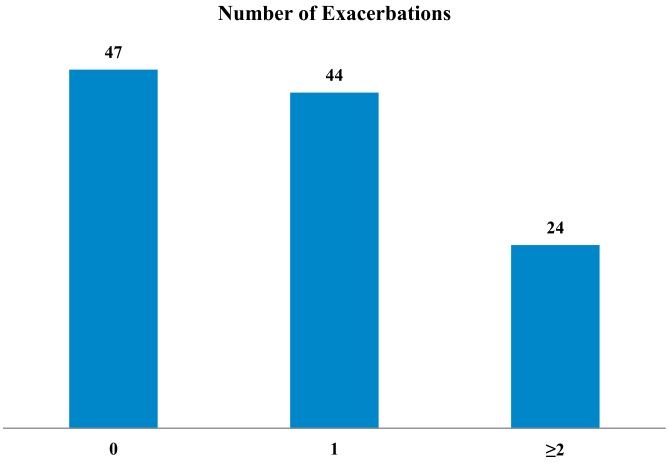

Figure 1: Frequency of Exacerbations in Included Patients (n=115)

At baseline, bronchiectasis exacerbation was substantially linked to a subsequent exacerbation at 0-24 months (p=0.006) and 24-48 months (p<0.002) (Table 2).

Table 2: Relationship Between the Number of Bronchiectasis Exacerbations (0 Or More) At Baseline and at the 0-To-24 and 24-To-48 Month Follow-Ups

Variables	Baseline	0-24 Months	24-48 Months
Bronchiectasis Exacerbation			
0	46.5 %	41.7%	20.6%
≥1	32.5 %	32.7 %	52.5 %
≥2	21 %	25.6 %	26.9 %

The baseline FEV1 was considerably lower in patients with more exacerbations, but the drop was not significant between those with 0, 1, and ≥2 exacerbations. A lower projected FEV1 % was related to more baseline and follow-up exacerbations. There was no difference in the average change from baseline according to the number of bronchiectasis exacerbations present at baseline; however, FEV1 was lower during follow-up visits (Table 3).

Table 3: Overall FEV1 Change from Start, Stratified by Bronchiectasis Exacerbations

FEV1	Exacerbations (0)	Exacerbations (1)	Exacerbations (≥2)
At Start	1.87 (0.51)	1.75 (0.67)	1.67 (0.48)
First Visit (1-12 Months)	-0.037 (0.021)	-0.035 (0.020)	0.004 (0.024)
Second Visit (24 Months)	-0.070 (0.030)	0.068 (0.023)	-0.052 (0.028)

With more initial exacerbations, patients had substantially poorer FEV1 % predicted at baseline (p<0.002), 12 (p=0.003), and 24 months (p<0.002). The predicted FEV1 included a normal FEV1 in 22 (19.13 %) patients, mild obstruction in 38 (33 %), moderate obstruction in 31 (27 %), and severe obstruction in 24 (20.9 %) of patients. An FEV1 of >80 % was considered normal, between 65-79 % as mild obstruction, between 50-64 % as moderate obstruction, and <50 % as severe obstruction (Figure 2).

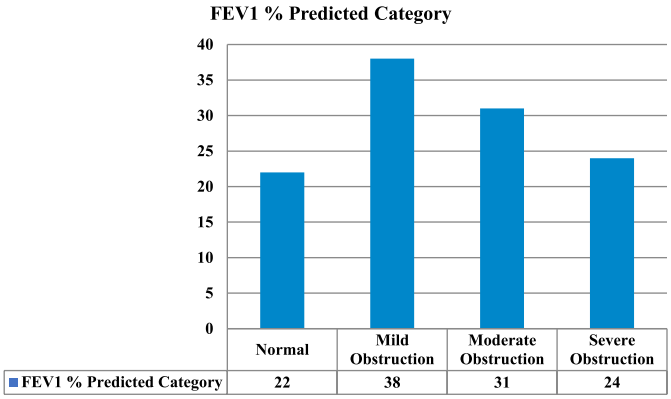

Figure 2: Graphical Representation of Predicted FEV1 at 24 Months (n=115)

DISCUSSION

A lower forced expiratory volume in one second (FEV1) was associated with a higher number of bronchiectasis exacerbations at baseline, and having an elevated risk of future exacerbations was the other finding of this study. Patients with two or more exacerbations at baseline showed a significantly lower mean FEV1 at baseline and throughout time compared to patients without exacerbations at baseline. Exacerbations of bronchiectasis were much more likely to occur throughout the follow-up period if participants had a history of them at baseline, according to this study. There was a statistically significant correlation between the number of

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exacerbations a patient experienced at baseline and the number of exacerbations they experienced over the 0-to-24 months and 24-to-48 months' follow-up periods. Neither the baseline nor the post-intervention numbers of exacerbations were substantially linked to one another. Incorporating the frequency and severity of exacerbations into the E-FACED score enhanced the potential to predict future annual exacerbations, according to research that developed and externally validated the score in 1470 bronchiectasis patients [16]. A study included 2572 bronchiectasis patients from European and Israeli institutions found that a history of frequent exacerbations was the strongest predictor of future exacerbations. The incidence rate ratios rose in tandem with the number of annual exacerbations at baseline, which went from 1 to 2 to 3 or more [17]. There was an increased adjusted likelihood of bronchiectasis exacerbations occurring throughout the follow-up period in this investigation. The risk of future exacerbations was 1.5 times higher for baseline exacerbations and 2.4 times higher for subsequent exacerbations in the two years that followed. Patients who have exacerbations more frequently have a more severe condition, a worse quality of life, and a greater mortality rate [18]. The mortality rate was double for patients with bronchiectasis who experienced three or more exacerbations per year compared to those who did not, according to a prospective cohort analysis of 608 individuals [19, 20]. The current study demonstrated that the mean forced expiratory volume in one second (FEV1) was significantly lower at baseline and throughout time for people with two or more bronchiectasis exacerbations compared to those without such episodes. A robust association between the baseline exacerbation frequency and the FEV1 suggested the existence of a minor pulmonary obstruction. Previous studies have connected patient factors such as systemic inflammation and prolonged *P. aeruginosa* colonization to a worsening of symptoms, as well as decreased forced expiratory volumes in one second (FEV1) [21]. Researchers found that at least one *P. aeruginosa* isolation significantly predicted a quicker FEV1 decline in COPD patients in a post hoc analysis of an 84-month prospective cohort [22]. Reduced FEV1 has also been linked to worsened symptoms in other chronic lung disorders, including cystic fibrosis [23]. Regardless of the number of bronchiectasis exacerbations in the current trial, the rate of fall in FEV1 was not substantially different among the three groups of patients (0, 1, and ≥2 exacerbations during baseline). To have a complete understanding of the correlation between exacerbations and the decrease in FEV1 in bronchiectasis patients, future research should consider the severity of exacerbations.

This study was limited by its single-center design and relatively modest sample size, which may restrict the generalizability of the findings. The observational nature of the study precludes establishing causal relationships between exacerbation frequency and lung function decline. Additionally, factors such as microbiological profile, exacerbation severity, and treatment adherence were not comprehensively analyzed. Future multicenter longitudinal studies with larger cohorts and detailed phenotypic characterization are recommended to better elucidate the impact of exacerbation burden on long-term pulmonary function outcomes.

CONCLUSIONS

The study found that individuals whose bronchiectasis flared up more often were more likely to experience future exacerbations and have a lower FEV1 to begin with. However, the drop in FEV1 may be unrelated to the frequency of exacerbations at baseline.

Authors' Contribution

Conceptualization: MA
Methodology: MA, SF
Formal analysis: AI, AS
Writing and Drafting: MA, UA
Review and Editing: MA, UA, AI, AS, SF

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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