

## Vitamin D And Disease Severity In Bronchiectasis



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### ABSTRACT

**Background:** Bronchiectasis is an airway disease of chronic nature, which is associated with irreversible bronchial dilatation and frequent infections. Recent findings indicate that vitamin D because of its immunomodulatory and anti-inflammatory effects could affect the severity of diseases and respiratory outcomes.

**Material and Methods:** The cross-sectional study was a descriptive study done over a period of six months in the department of chest medicine, JPMC, Karachi, upon receiving the ethical approval. Non-probability consecutive sampling was used to enroll 89 adults with HRCT confirmed bronchiectasis. Patients who had traction bronchiectasis, active mycobacterial disease, malignancy, HIV, with the known disease related to vitamin D deficiency were not included. Bronchitis severity index (BSI) severity was determined with demographic, clinical, spirometric (FEV1, FVC), and data regarding the HRCT. The statistical conclusions were made using SPSS 25 with the chi-square and independent-samples t-tests, where  $p \leq 0.05$  is significant.

**Results:** Proper vitamin D deficiency was very high in 89 patients with bronchiectasis (62.9) and 12.4% had normal levels. There was a strong correlation between the deficiency of vitamin D and increased BSI ( $p = 0.01$ ). Patients suffering deficient levels of vitamin D had lower FEV1 than those with normal or adequate levels ( $p = 0.03$ ).

**Conclusion:** Vitamin D deficiency is common in bronchiectasis and is significantly associated with greater disease severity and reduced lung function.

**Keywords:** Bronchiectasis; Pulmonary Function Tests; Severity of Illness Index; Vitamin D.

### INTRODUCTION

Bronchiectasis is a long term progressive respiratory disease that is characterized by permanent enlargement of bronchi, frequent infections, and inflammation in the airways. The past few years have seen an interest in vitamin D as a means of controlling the severity of diseases based on its immunomodulatory, anti-inflammatory, and antimicrobial effects. Initial studies on this subject proved that deficiency of vitamin D had a close correlation with chronic bacterial colonization, recurrent exacerbation, and radiological severity of bronchiectasis patients.<sup>1</sup> These findings were confirmed in later studies which revealed that reduced serum vitamin D levels were associated with high disease burden, dysfunctional lung capacity and elevated symptom scores.<sup>2</sup>

Vitamin D status has also been associated with radiological progression. In a study of adults with non-cystic fibrosis bronchiectasis, the impairment of vitamin D was linked with more radiological changes, which confirmed the hypothesis that insufficient vitamin D can play a role in the development of the structural disease. In addition to

observational relationships, interventional evidence has come into existence.<sup>3</sup> An initial clinical trial investigating the use of vitamin D3 supplementation in the management of bronchiectasis adults showed an improvement in the quality-of-life scores and a tendency on the decrease of the exacerbations which means possible therapeutic effect of vitamin D replacement.<sup>4</sup>

The same has been observed in the pediatric population. The absence of vitamin D in both cystic fibrosis (CF) and non-CF bronchiectasis was linked with worse clinical outcomes and more bacterial colonization, supporting the cross-age applicability of vitamin D in the pathophysiology of airway diseases.<sup>5</sup> This has been further elaborated in the more recent mechanistic and clinical observations; in addition to a high risk of *Pseudomonas aeruginosa* colonization, a pathogen in severe disease and rapid progression, vitamin D deficiency has been associated with an increase in the risk of colonization by other pathogens. This implies that insufficient vitamin D could slow down antimicrobial peptide pathways in favor of persistent airway infection.<sup>6</sup>

The combination of the emerging literature supports the correlation between vitamin D deficiency and the severity of bronchiectasis. In a systematic review, published in 2025, the authors found that vitamin D deficiency was always associated with more severe symptoms, worse lung functioning, and increased frequency of exacerbations in different population groups.<sup>7</sup> More general approaches to nutrition highlight the possible benefit of immunonutrition—such as vitamin D—in regulating chronic airway illness suggesting that micronutrient optimization may enhance the host defences and decrease the inflammatory load.<sup>8</sup>

These findings can also be supported by emerging regional data. The investigation of vitamin D levels as they are related to the severity of the bronchiectasis showed that there is a definite inverse correlation between serum vitamin D and rated clinical severity, which once again confirmed that deficiency can be a modifiable risk factor.<sup>9</sup> Even though a large part of the research is devoted to bronchiectasis in particular, the respiratory literature is significant in the broad sense of the term. Randomized controlled trials have also been meta-analyzed to demonstrate that vitamin D supplementation decreases the occurrence of acute respiratory tract infection, which could be due to the increase of innate immunity.<sup>10</sup> The protective effects were established in a later meta-analysis of an individual-patient-data, especially in patients with baseline vitamin D deficiency.<sup>11</sup>

It has been long established that there is a correlation between pulmonary functioning and serum vitamin D levels. Previous population-based studies had shown that improved parameters of lung functions, such as FEV1 and FVC, were correlated with an increase in serum 25-hydroxyvitamin D, indicating a physiological basis on which vitamin D could have an effect on chronic lung disease outcomes.<sup>12</sup> Collectively, these results demonstrate a strong correlation between vitamin D levels and the severity of bronchiectasis, which contributes to the arguments in favor of further research on the topic of vitamin D status as a biomarker and therapeutic response.

#### MATERIAL AND METHODS

The study was a descriptive cross-sectional study conducted in the ward 12, Department of Chest Medicine, Jinnah Postgraduate Medical Centre (JPMC), Karachi, within a period of six months after obtaining the ethical approval of the Research Evaluation Unit (REU) of the College of Physicians and Surgeons Pakistan (CPSP) and IRB was obtained from the Institutional Review Board of JPMC (Approval No.F.2-81/2025-GENL/270/JPMC). Practices were all in line with institutional ethics and the Helsinki declaration. All participants provided written informed consent before enrolment.

The openEpi software was used to calculate a total sample size of 89 patients based on a proposed prevalence of 64% vitamin D deficiency in patients with bronchiectasis reported in previous literature with a 95% CI and a 10% margin of error. Non-probability consecutive sampling was used in the selection of patients. The patients aged 18 years and above with known bronchiectasis confirmed by the use of high-resolution computed tomography (HRCT) were used. The patients who were excluded included those having traction bronchiectasis as a result of pulmonary fibrosis, active mycobacterial infection, malignant neoplasia, known diseases related to low vitamin D levels, HIV infection, or those who did not want to take part.

Both outpatient and inpatient settings were used to collect data. Demographic information such as age, gender, height and weight were noted and BMI was computed accordingly. Clinical data on comorbid conditions including asthma, COPD, smoking status and alcohol consumption with such symptoms like cough, sputum, dyspnea, wheezing, hemoptysis, chest pain and clubbing was recorded. The diagnosis of bronchiectasis was made by HRCT scans and the severity of the disease was measured on the basis of Bronchiectasis Severity Index (BSI). Tests of the pulmonary functions were conducted, FEV1 and FVC were measured. The 25-hydroxyvitamin D 25-hydroxyvitamin D concentration relied on venous blood. All data were entered on structured proforma. The SPSS version 25 was used to conduct statistical analysis. The quantitative variables included age, body mass index, body specific index score, the lung functional parameters, and serum vitamin D concentration in terms of mean  $\pm$  standard deviation, whereas the qualitative variables included gender, age group, comorbid conditions, symptoms, BSI classification, and vitamin D status in terms of frequencies and percentages. Controlling factors that could be used to control effects modifiers such as age group, gender, asthma, COPD, smoking, alcohol use, and BSI severity took place via stratification. An evaluation of associations was done by chi-square or independent-samples t-test as needed, and a p-value  $\leq 0.05$  was taken to be statistically significant.

#### RESULTS

A total of 89 patients with confirmed bronchiectasis were included in the analysis. The mean age of participants was  $46.8 \pm 13.7$  years, and females comprised a slightly higher proportion of the study population. The baseline demographic and clinical characteristics are summarized in **Table 1**.

Vitamin D deficiency was highly prevalent, with the majority of participants falling in the deficient category. Details of vitamin D distribution across the study population are presented in **Table 2**.

A statistically significant association was observed between vitamin D status and BSI severity ( $p = 0.01$ ), with deficiency being more common among patients in the higher severity classes. Similarly, patients with vitamin D deficiency demonstrated lower mean

FEV1 values compared with those having normal/sufficient levels ( $p = 0.03$ ). Comparative analyses of vitamin D status with clinical variables are provided in **Table 3**.

**Table 1: Demographic and Clinical Characteristics of Patients (n = 89)**

| Variable                             | Mean $\pm$ SD / N (%)                |
|--------------------------------------|--------------------------------------|
| Age (years)                          | 46.8 $\pm$ 13.7                      |
| Gender (Male/Female)                 | 41 (46.1%) / 48 (53.9%)              |
| BMI (kg/m <sup>2</sup> )             | 25.9 $\pm$ 4.8                       |
| Asthma                               | 18 (20.2%)                           |
| COPD                                 | 11 (12.4%)                           |
| Smoking (Current/Ex/Non-Smoker)      | 19 (21.3%) / 14 (15.7%) / 56 (62.9%) |
| Alcohol Use (Current/Ex/Non-Drinker) | 4 (4.5%) / 6 (6.7%) / 79 (88.8%)     |
| Symptoms – Persistent cough          | 72 (80.8%)                           |
| Symptoms – Sputum production         | 69 (77.5%)                           |
| Symptoms – Dyspnea                   | 63 (70.7%)                           |
| Symptoms – Wheezing                  | 31 (34.8%)                           |
| Symptoms – Hemoptysis                | 12 (13.4%)                           |
| Symptoms – Chest pain                | 17 (19.1%)                           |
| Clubbing                             | 9 (10.1%)                            |
| BSI: Mild / Moderate / Severe        | 32 (36%) / 37 (41.5%) / 20 (22.5%)   |
| FEV1 (%)                             | 63.4 $\pm$ 14.9                      |
| FVC (%)                              | 71.8 $\pm$ 12.7                      |

**Table 2: Distribution of Serum 25-Hydroxyvitamin D Levels (n = 89)**

| Vitamin D Category       | N (%)      | Mean Vitamin D Level (ng/ml) |
|--------------------------|------------|------------------------------|
| Normal (>30 ng/ml)       | 11 (12.4%) | 34.6 $\pm$ 3.8               |
| Sufficient (20–30 ng/ml) | 22 (24.7%) | 24.1 $\pm$ 2.7               |
| Deficient (<20 ng/ml)    | 56 (62.9%) | 13.2 $\pm$ 4.1               |

**Table 3: Association of Vitamin D Status with Clinical and Functional Outcomes**

| Variable      | Normal/Sufficient (n = 33) | Deficient (n = 56) | p-value      |
|---------------|----------------------------|--------------------|--------------|
| Mean FEV1 (%) | 69.2 $\pm$ 12.3            | 59.8 $\pm$ 14.8    | <b>0.03*</b> |
| Mean FVC (%)  | 74.9 $\pm$ 11.1            | 69.8 $\pm$ 12.9    | 0.08         |
| BSI: Mild     | 18 (54.5%)                 | 14 (25.0%)         | —            |
| BSI: Moderate | 11 (33.3%)                 | 26 (46.4%)         | —            |
| BSI: Severe   | 4 (12.1%)                  | 16 (28.6%)         | <b>0.01*</b> |

\*Significant at  $p \leq 0.05$

## DISCUSSION

Vitamin D deficiency was very common among bronchiectasis patients in this study and strongly correlated with both the increased severity of the disease and the worsened lung functioning index. Such results are in line with available literature that points out the immunomodulative and respiratory utility of sufficient amounts of vitamin D. The biological plausibility of our findings has already been supported by previous population-based analyses showing that increased serum vitamin D level is associated with better lung functioning markers.<sup>13</sup>

Vitamin D also contributes to the regulation of innate immune responses in the respiratory system, and low levels have been associated with increased vulnerability to respiratory infections.<sup>14</sup> This connection is especially topical regarding bronchiectasis, where serial infections are involved in the progressive airways damage. Overviews of chronic respiratory disease development have placed continual stress on the significance of vitamin D deficiency correction to minimize the frequency of exacerbations and maintain airway stability.<sup>15</sup> The meta-analytic evidence also confirms a positive effect of vitamin D in asthma and shows that the symptoms and the lung functions are improved in

the populations with better vitamin D levels, which partly explains the observation in our study that patients with lower vitamin D levels developed worse bronchiectasis and worse Spiro metric outcomes. These therapeutic and protective possibilities have been confirmed by wider studies of the role of vitamin D in inflammatory lung disease.<sup>16, 17.</sup>

The prescriptive systemic and airway inflammatory burden provided by vitamin D deficiency has also been reported in previous work in the bronchiectasis-related cohorts to argue that low vitamin D would be a suitable marker of disease pathology as well.<sup>18</sup> The same reviews have given a refreshing reiteration to the fact that adequate vitamin D levels could reduce the severity of respiratory disease.<sup>19</sup>

Similar patterns have been observed in observational studies in chronic airway diseases, with poorer clinical outcomes in hospitalized patients with low vitamin D levels, with a longer recovery and high symptom burden.<sup>20</sup> This pattern is in line with our observation that patients with low vitamin D levels were more likely to be classified under moderate and severe BSI. This trend is also supported by the research conducted in pediatric bronchiectasis, in which vitamin D supplementation has become correlated with better clinical outcomes.<sup>21</sup>

Further signs based on pediatric cohort studies have revealed that low vitamin D levels are associated with increased exacerbation and reduced overall respiratory outcomes, which supports the notion that vitamin D deficiency and the chronicity of airway diseases are closely linked.<sup>22</sup> Evidence based on inflammatory lung disease studies has demonstrated several times that low vitamin D levels are associated with higher exacerbation rates and worse overall respiratory outcomes, indicating that vitamin D deficiency and the chronicity of airway diseases are connected.<sup>23</sup>

The finding that vitamin D levels are a predictor of the disease severity of bronchiectasis is further reinforced by recent regional data, which found that patients with lower levels of vitamin D in their serums showed a larger area of structural lung damage on HRCT, which further supports the clinical association that was identified in our study.<sup>24</sup> Radiologic evidence in bronchiectasis non-cystic fibrosis populations has also reinforced this observation, showing that patients with lower serum levels of vitamin D levels indicated greater structural lung damage on HRCT.<sup>25</sup>

Collectively, the results of this study indicate the need to understand the role of vitamin D in patients with bronchiectasis and emphasize the promise of vitamin D in determining the severity of the disease, lung performance, and clinical outcome. Though a

cross-sectional design does not allow to infer causality, the fact that our results were consistent with the findings of the world population makes it likely that vitamin D deficiency is a potential therapeutic goal as well as a modifiable biomarker.

## CONCLUSION

Vitamin D deficiency in bronchiectasis patients was very common among the adults and was closely linked with increased disease severity and decreased lung functioning. Regular testing of vitamin D status could contribute to the detection of patients with a predisposition towards more serious disease and future interventional planning.

## Strengths and Limitations:

The use of the HRCT-confirmed bronchiectasis, standardized spirometry, and both inpatient and outpatient groups contributes to the increased accuracy of diagnoses and representativeness of this study. Nevertheless, it is cross-sectional, which constrains its ability to interpret causally and its use of a single center makes it potentially inappropriate to generalize. The seasonal change, exposure of sun, dietary intake and the history of vitamin D supplementation have not been measured and the presence of unmeasured inflammatory markers might have been a confounding factor to the results.

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