



ASSOCIATION BETWEEN SERUM 25-HYDROXYVITAMIN D LEVELS AND FREQUENCY OF EXACERBATIONS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

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Abstract

Objective: To determine the association between serum 25-hydroxyvitamin D levels and frequency of acute exacerbations in patients with chronic obstructive pulmonary disease (COPD).

Methods: This analytical cross-sectional study was conducted from November 2024 to May 2025 in Doctor Hospital and Farooq Hospital Lahore. A total of 150 COPD patients aged ≥ 40 years were enrolled using consecutive sampling. Serum 25(OH) D levels were measured using chemiluminescent immunoassay.

Results: Vitamin D deficiency was observed in approximately 60% of patients. Frequent exacerbations were significantly associated with lower serum vitamin D levels ($p < .001$).

Conclusion: Vitamin D deficiency is highly prevalent among COPD patients and is significantly associated with increased exacerbation frequency.

Keywords: Candida albicans, Commercial cleaners, Miswak, Acrylic resin

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a progressive inflammatory respiratory disease characterized by airflow limitation, lung damage, and inflammation. COPD is a major global health problem, especially in developing countries, causing significant morbidity and mortality. COPD is mainly linked to cigarette smoking, environmental exposures, and occupational exposures. Acute exacerbations of COPD, characterized by increased dyspnea, cough, and sputum production, have a significant impact on disease progression, mortality, and hospitalization (Lokesh et al., 2021).

Recent studies have pointed towards inflammation and immune system disturbances in exacerbations of COPD. Vitamin D, though traditionally known to affect bone metabolism, is now recognized to have immunomodulatory effects. Vitamin D is known to boost innate immune response by cathelicidin, a potent antimicrobial peptide, while modulating adaptive immune

response by inhibiting pro-inflammatory cytokines (Chen et al., 2023). Vitamin D deficiency is common among COPD patients, especially due to reduced exposure to sunlight, cigarette smoking, age, and reduced levels of physical activity. Studies have shown that vitamin D deficiency is associated with disease severity, exacerbation, and increased risk of hospitalization. Severe vitamin D deficiency is associated with exacerbation risk, while mild deficiency is not (Li et al., 2025; Rocha et al., 2025). However, vitamin D supplementation trials have shown inconsistent results, suggesting that vitamin D supplementation benefits COPD patients only if they have severe deficiency (Rafiq et al., 2022). Vitamin D deficiency is highly prevalent in Pakistan, especially in South Asian populations, due to lifestyle factors, dietary habits, etc. Therefore, considering the increasing prevalence of COPD, this study aims to determine the association between serum vitamin D levels and exacerbation frequency in COPD patients.

Methodology

This analytical study was conducted at the Department of Pulmonology, Doctor Hospital, and Farooq Hospital, Lahore, Pakistan, from November 2024 to May 2025. A total of 150 COPD patients aged ≥ 40 years were recruited for the study using consecutive non-probability sampling. The sample size was calculated with an expected 60% prevalence of vitamin D deficiency, a confidence level of 95%, and a margin of error of 8%.

The inclusion criteria for the study were patients with COPD as confirmed by spirometry with an FEV1/FVC of less than 0.70, stable clinical status, and providing informed consent. The exclusion criteria for the study were patients with a history of vitamin D supplementation, chronic systemic disease, malignancy, autoimmune disease, acute infection, or corticosteroid use for any other disease. The study also recruited patients with a history of exacerbation of COPD. Data were also collected on the demographics of patients, smoking status, BMI, disease duration, and exacerbation history over the last 12 months. Serum 25(OH) D level was measured by chemiluminescent immunoassay and classified as deficient (<20 ng/mL), insufficient (20-29 ng/mL), and sufficient (≥ 30 ng/mL). Frequent exacerbators were patients with ≥ 2 exacerbations/year or ≥ 1 hospitalization/year. The study was analyzed using SPSS software version 26. Continuous variables were expressed as mean $\pm$ SD, and categorical variables were expressed as frequency and percentage. The independent t-test and chi-square test were conducted, and multiple logistic regressions were also carried out. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 150 patients suffering from chronic obstructive pulmonary disease were included in the study. The mean age of patients was found to be 61.3 years, with a range of 8.8 years. Most of the patients included in the study were males, accounting for 70% (n = 105) of the total study group. Three-fourths of patients included in the study had a positive history of smoking. The mean body mass index of patients included in the study was found to be 24.6 kg/m², with a range of 3.8 kg/m². Levels of serum 25-hydroxyvitamin D were found to be low, indicating that vitamin D deficiency is highly prevalent among patients suffering from COPD. Out of 150 patients, 95 patients (63%) were found to have vitamin D deficiency, while 30 patients (20%) were found to have vitamin D insufficiency, and 25 patients (17%) were found to have adequate levels of vitamin D. With regard to exacerbation, 86 patients (57%) were found to have frequent exacerbations, while 64 patients (43%) were found to have infrequent exacerbations.

Levels of vitamin D were found to be low in patients suffering from frequent exacerbations compared to those suffering from infrequent exacerbations.

Table1: Comparison of Serum Vitamin D Levels

Variable	Frequent Exacerbators(n=86)	Infrequent Exacerbators(n=64)	p-value
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Serum25 (OH) D level (ng/mL)	17.4 ± 5.3	26.7 ± 7.0	<0.001
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The difference in mean serum vitamin D levels between the two groups was statistically significant, indicating that lower vitamin D concentrations were associated with higher exacerbation frequency. Table2: Distribution of Vitamin D Status

Vitamin D Status	Frequent Exacerbators (%)	Infrequent Exacerbators (%)	Total
Deficient (<20 ng/mL)	70 (81.4%)	25 (39.1%)	95
Insufficient(20–29ng/mL)	10 (11.6%)	20 (31.3%)	30
Sufficient (≥30 ng/mL)	6 (7.0%)	19 (29.6%)	25
Total	86 (100%)	64 (100%)	150

Chi-square analysis demonstrated a significant association between vitamin D status and exacerbation frequency ($p < 0.001$), suggesting that vitamin D deficiency was more common among frequent exacerbators.

Table3: Multivariate Logistic Regression Analysis

Variable	Adjusted Odds Ratio	95% Confidence Interval	p-value
Vitamin D deficiency	2.89	1.61 – 5.19	<0.001
Smokinghistory	1.74	1.02 – 3.15	0.041
GOLDstageIII–IV	2.95	1.56 – 5.62	<0.001

Multivariate logistic regression analysis revealed that vitamin D deficiency wasan independent predictor of frequent COPD exacerbations after adjustment for smoking status, body mass index, and disease severity.

Discussion

This study established a significant association between low serum vitamin D levels and high frequencies of COPD exacerbations. Vitamin D deficiency was highly prevalent, showing a significant association with high frequencies of exacerbations, similar to recent literature (Li et al., 2025; Mullin & Milne, 2023).The immunomodulatory effects of vitamin D could explain these results, as vitamin D is known to increase production of antimicrobial peptides, which reduce inflammation, thereby protecting against respiratory infections (Chen et al., 2023). Severe vitamin D deficiency is associated with a high risk of hospitalization, indicating its potential importance (Rocha et al., 2025).

Similar to previous studies, vitamin D supplementation had variable effects, showing benefits only in patients with severe deficiency (Rafiq et al., 2022). The high prevalence of vitamin D deficiency could have resulted from limited exposure tosunlight, smoking, and lifestyle factors common in South Asian populations (Lokesh et al., 2021).

Smoking is a significant risk factor for exacerbations, which could result from inflammation promoted by smoking, affecting airway defense mechanisms. Smoking, combined with vitamin D deficiency, could have negative effects on exacerbations.

However, despite these results, vitamin D deficiency is not causally related to exacerbations, and further studies are needed to establish causality, showing associations rather than causality.

Longitudinal studies would help determine vitamin D supplementation benefits (Martineau et al., 2021).

Conclusion

Vitamin D deficiency is highly prevalent in COPD patients, showing a significant association with high frequencies of exacerbations. Low serum levels of 25-hydroxyvitamin D independently predict high frequencies of exacerbations. Screening vitamin D deficiency could help manage exacerbations, especially in high-risk patients.

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