

Original Research Article

ASSOCIATION BETWEEN VITAMIN D DEFICIENCY AND FREQUENCY OF SEVERE EXACERBATIONS IN COPD PATIENTS: A PROSPECTIVE COHORT STUDY

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality, with severe exacerbations contributing significantly to disease progression. Emerging evidence suggests an association between vitamin D deficiency and increased COPD exacerbations, but findings remain inconclusive. This study aims to assess the association between vitamin D deficiency and the frequency of severe exacerbations in COPD patients.

Materials and Methods: This prospective cohort study was conducted at a tertiary care center from December 2023 to December 2024. A total of 100 COPD patients were categorized into vitamin D-deficient (<20 ng/mL) and vitamin D-sufficient (≥20 ng/mL) groups. Baseline demographic data, smoking history, BMI, and pulmonary function tests (FEV1) were recorded. Patients were followed for six months to document the frequency of severe exacerbations (requiring hospitalization or systemic corticosteroids). Hospitalization rates, ICU admissions, and length of hospital stay were also analyzed. Statistical analysis was performed using SPSS version 26, with a p-value <0.05 considered significant.

Results: The vitamin D-deficient group had significantly higher rates of severe exacerbations (66% vs. 24%, p<0.001) and hospitalizations (76% vs. 38%, p<0.001). ICU admissions were more frequent in the deficient group (34% vs. 12%, p=0.007), and their mean hospital stay was longer (7.8 ± 3.2 vs. 5.1 ± 2.6 days, p=0.002). Multivariate analysis showed vitamin D deficiency as an independent risk factor for frequent exacerbations (≥3 in 6 months, p<0.001).

Conclusion: Vitamin D deficiency is significantly associated with increased severe exacerbations and hospitalizations in COPD patients. Routine screening and potential supplementation may improve COPD management and patient outcomes.

Keywords: COPD, vitamin D deficiency, exacerbations.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major global health concern characterized by persistent respiratory symptoms and airflow limitation.^[1] It is a leading cause of morbidity and mortality worldwide, with exacerbations contributing significantly to disease progression and healthcare burden.^[2] Severe exacerbations, which

often require hospitalization, are associated with worsened lung function, decreased quality of life, and increased risk of mortality. Identifying modifiable risk factors for exacerbations is crucial in improving COPD management and patient outcomes.^[3]

Vitamin D plays an essential role in calcium homeostasis and bone health, but emerging evidence suggests that it also has important

immunomodulatory functions.^[4] Deficiency in vitamin D has been linked to increased susceptibility to infections and inflammatory diseases, both of which are critical in COPD pathogenesis.^[5] Low vitamin D levels have been observed in COPD patients and are hypothesized to contribute to disease severity and exacerbation frequency by impairing immune function and increasing airway inflammation.^[6]

Several studies have explored the relationship between vitamin D deficiency and COPD outcomes, but findings remain inconclusive.^[6,7] Some studies suggest that vitamin D supplementation may reduce exacerbation risk, while others have found no significant association.^[8,9,10] Given the variability in study populations and methodologies, further research is needed to clarify the role of vitamin D in COPD progression and its potential as a therapeutic target for reducing exacerbations.

This prospective cohort study aims to assess the association between vitamin D deficiency and the frequency of severe exacerbations in COPD patients. By analyzing vitamin D levels and tracking exacerbation rates over a 6-month period, this study seeks to determine whether vitamin D deficiency serves as an independent risk factor for increased exacerbation frequency.

MATERIALS AND METHODS

This prospective cohort study was conducted at a tertiary care center over a 12-month period from December 2023 to December 2024. A total of 100 COPD patients were recruited and categorized into two groups based on their serum vitamin D levels: vitamin D deficient and vitamin D sufficient. Patients were included if they had a confirmed diagnosis of COPD and were aged 40 years or older. Patients with conditions that could independently affect vitamin D metabolism, such as chronic kidney disease or liver disease, were excluded.

Serum vitamin D levels were measured at baseline, and patients with levels below 20 ng/mL were classified as deficient, while those with levels ≥ 20 ng/mL were considered sufficient. Pulmonary function tests, including FEV1 measurement, were performed to assess COPD severity. Data on demographic characteristics, smoking history, and BMI were collected through structured interviews and medical record reviews. Patients were followed prospectively for 6 months to record the frequency of severe exacerbations, defined as those requiring hospitalization or systemic corticosteroid use.

Hospitalization and ICU admission data were recorded for all patients, including the number of admissions and length of hospital stay. Exacerbations were categorized as stable COPD or severe exacerbations, and their frequency was compared between the two vitamin D groups. The association between vitamin D deficiency and severe exacerbations was assessed using chi-square tests.

Statistical analysis was performed using SPSS version 26. Continuous variables were expressed as mean \pm standard deviation, and categorical variables were reported as percentages. A p-value < 0.05 was considered statistically significant. Ethical approval was obtained from the institutional ethics committee, and written informed consent was obtained from all participants before enrolment.

RESULTS

The study included 100 patients with COPD, categorized into two groups based on their vitamin D levels: deficient and sufficient. Baseline characteristics were comparable between the two groups in terms of age, gender distribution, BMI, smoking history, and FEV1 values. However, the mean vitamin D level was significantly lower in the deficient group (14.3 ± 3.8 ng/mL) compared to the sufficient group (31.7 ± 6.2 ng/mL; $p < 0.001$) (Table 1).

Table 1: Baseline Characteristics of COPD Patients by Vitamin D Status

Variable	Vitamin D Deficient (n=50)	Sufficient Vitamin D (n=50)	p-value
Age (years)	67.2 ± 8.3	65.8 ± 7.9	0.42
Male, n (%)	35 (70%)	33 (66%)	0.68
BMI (kg/m ²)	22.5 ± 3.1	23.1 ± 3.5	0.30
Smoking History (pack-years)	32.4 ± 9.2	30.8 ± 8.7	0.39
FEV1	47.5 ± 12.3	52.1 ± 11.8	0.08
Vitamin D Level (ng/mL)	14.3 ± 3.8	31.7 ± 6.2	< 0.001

The frequency of severe exacerbations was significantly higher in the vitamin D-deficient group. A total of 66% of patients in this group experienced at least one severe exacerbation per year compared to only 24% in the vitamin D-

sufficient group ($p < 0.001$). Conversely, stable COPD was observed in 76% of patients with sufficient vitamin D levels compared to only 44% in the deficient group (Table 2).

Table 2: Association Between Vitamin D Deficiency and Frequency of Severe Exacerbations

Exacerbations (per year)	Vitamin D Deficient (n=50)	Sufficient Vitamin D (n=50)	p-value
Stable COPD	17 (44%)	38 (76%)	< 0.001
Severe exacerbation	33 (66%)	12 (24%)	

Hospitalization rates were notably higher among vitamin D-deficient patients. A total of 76% of patients in this group required at least one hospital admission compared to 38% in the sufficient vitamin D group ($p<0.001$). ICU admissions were also significantly more frequent in the vitamin D-

deficient group (34% vs. 12%, $p=0.007$). Furthermore, the mean length of hospital stay was prolonged in the vitamin D-deficient group (7.8 ± 3.2 days) compared to the sufficient group (5.1 ± 2.6 days, $p=0.002$) (Table 3).

Table 3: Hospitalization and ICU Admission Rates by Vitamin D Status

Outcome	Vitamin D Deficient (n=50)	Sufficient Vitamin D (n=50)	p-value
Hospitalized ≥ 1 time	38 (76.0)	19 (38.0)	$<0.001^*$
ICU Admission	17 (34.0)	6 (12.0)	0.007*
Length of Stay (days)	7.8 ± 3.2	5.1 ± 2.6	0.002*

Multivariate analysis revealed that vitamin D deficiency was significantly associated with frequent severe exacerbations (≥ 3 in 6 months), with 73.3% of patients in the severe exacerbation group being vitamin D deficient, compared to only 30.9% in the non-severe exacerbation group ($p<0.001$). Other factors significantly associated with severe

exacerbations included a smoking history of ≥ 30 pack-years ($p=0.01$), FEV1 $<50\%$ ($p=0.002$), and prior hospitalization within six months ($p<0.001$). Age greater than 65 years showed a trend towards significance but did not reach statistical significance ($p=0.08$) (Table 4).

Table 4: Factors Associated with Severe Exacerbations (≥ 3 in 6 Months)

Factor	Severe Exacerbations (n=45)	No Severe Exacerbations (n=55)	p-value
Vitamin D Deficient	33 (73.3%)	17 (30.9%)	<0.001
Age > 65 years	29 (64.4%)	26 (47.3%)	0.08
Smoking History ≥ 30 pack-years	27 (60.0%)	19 (34.5%)	0.01
FEV1 $< 50\%$	31 (68.9%)	20 (36.4%)	0.002
Hospitalized in 6 Months	35 (77.8%)	22 (40.0%)	<0.001

DISCUSSION

The findings of this study demonstrate a significant association between vitamin D deficiency and an increased frequency of severe exacerbations in COPD patients. Patients with vitamin D deficiency had a higher incidence of severe exacerbations (66% vs. 24%, $p<0.001$) and were more likely to require hospitalization and ICU admission. These results support the hypothesis that vitamin D plays a crucial role in modulating inflammation and immune responses in COPD. A similar trend was observed in the study by Thakuria et al., which reported that COPD patients with lower vitamin D levels experienced more frequent exacerbations and hospitalizations.^[7] This reinforces the notion that vitamin D deficiency contributes to COPD severity by exacerbating airway inflammation and reducing immune defence mechanisms.

Hospitalization rates were markedly higher in the vitamin D-deficient group (76% vs. 38%, $p<0.001$), and ICU admissions were significantly more frequent (34% vs. 12%, $p=0.007$). The mean length of hospital stay was also prolonged in vitamin D-deficient patients (7.8 ± 3.2 days vs. 5.1 ± 2.6 days, $p=0.002$). These findings are consistent with the study by Zhou et al. and Rafiq R et al., who identified severe vitamin D deficiency as a predictor of frequent exacerbations and prolonged hospital stays.^[9,11] Their study highlighted that COPD patients with severe vitamin D deficiency were at a substantially higher risk of requiring hospitalization compared to those with sufficient vitamin D levels.^[11] This further underscores the role of

vitamin D in disease progression and recovery outcomes.

Multivariate analysis in our study revealed that vitamin D deficiency was significantly associated with frequent severe exacerbations ($p<0.001$). Other factors such as a smoking history of ≥ 30 pack-years ($p=0.01$), FEV1 $<50\%$ ($p=0.002$), and prior hospitalization in the past six months ($p<0.001$) were also strongly linked to increased exacerbation risk. Our results align with those reported by Lokesh et al., who found that vitamin D-deficient COPD patients were at a higher risk of experiencing recurrent exacerbations and demonstrated worse lung function parameters.^[6] Their findings also suggest that vitamin D deficiency, along with impaired pulmonary function and smoking history, contributes to the overall exacerbation burden in COPD patients.

The findings of this study have important clinical implications, as they suggest that vitamin D supplementation could potentially serve as an adjunctive therapeutic strategy to reduce COPD exacerbations. While previous trials on vitamin D supplementation have shown mixed results, our study supports further investigation into the role of vitamin D repletion in COPD management. Future randomized controlled trials are warranted to determine whether correcting vitamin D deficiency can improve COPD outcomes and reduce exacerbation frequency.

CONCLUSION

Vitamin D deficiency is significantly associated with an increased frequency of severe exacerbations, higher hospitalization rates, and prolonged hospital stays in COPD patients. The findings of this study align with previous research, reinforcing the role of vitamin D in modulating immune responses and reducing inflammation in COPD. Given the strong association between vitamin D deficiency and disease severity, routine screening for vitamin D levels in COPD patients may be beneficial.

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