

# Vitamin D Deficiency: A Factor For Exacerbation of COPD: Myth or Fact

Riturag Thakuria<sup>1</sup>, Tanushree Maitra<sup>2</sup>, Jyotismita Deka<sup>3</sup>

## ABSTRACT

**Introduction:** Chronic obstructive pulmonary disease (COPD) and vitamin D deficiency are two very common disease entities in our present health scenario. Although a number of pathophysiological mechanisms have been described linking the presence of hypovitaminosis D with the risk of development and severity of COPD, no conclusive results are available. So, this study was taken up to determine the association of vitamin D deficient status with the prevalence and severity of COPD and also to compare its association between stable COPD and exacerbations.

**Material and methods:** The study was a cross-sectional study conducted in the Dept. of Medicine and Physiology, Silchar Medical College and Hospital, Silchar, Assam with 180 COPD patients of which 41.11% presented with exacerbations.

**Results:** The studied population showed a mean age of 63.29 years (SD 10.73 years) with a male to female ratio of 5.92:1. The presence of hypovitaminosis D was in 48.14% patients with moderate disease, 70.11% patients with severe COPD and 82.05% patients with very severe disease. In patients with exacerbations, 64.86% cases were found to be vitamin D deficient. Although the frequency of vitamin D deficiency significantly correlated with the severity of COPD, no statistical association in prevalence was found between stable COPD and those with exacerbations.

**Conclusion:** The pleiotropic effects of vitamin D have made it a common factor in the development and severity of various respiratory diseases including COPD. Larger studies are required to find the exact degree of co-relation between these two disease entities.

**Keywords:** Chronic Obstructive Pulmonary Disease, Vitamin D deficiency, exacerbation of COPD

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterized by airflow limitation that is not fully reversible and which is associated with significant extra pulmonary effects that may contribute to its severity and prognosis in individual patients.<sup>1</sup> Vitamin D deficiency and insufficiency are common in patients with COPD. The prevalence of hypovitaminosis D varies from 31-77% in patients with COPD among various studies.<sup>2-4</sup> The precise role of vitamin D in the pathogenesis of COPD is unclear however studies have described that vitamin D can alter the activity of various immune cells, regulate airway smooth muscle and inhibit inflammatory responses.<sup>5-7</sup> The dietary intake of vitamin D is also reduced in COPD patients particularly in elderly.<sup>8-9</sup> Patients with certain gene variants of the vitamin D transport protein shows significant correlation between serum levels of vitamin D and severity of COPD. Polymorphisms of the vitamin D binding protein have also been reported to reduce the risk of developing COPD or preventing its exacerbations.<sup>10-11</sup> The association of hypovitaminosis D with the prevalence and

severity of COPD as well as its contribution to exacerbations has been carried out by a number of researches but a huge disparity in the results still exists. So, keeping this in view, the following study was taken up with the following aims and objectives. Firstly to study the vitamin D deficiency and insufficiency prevalence in patients with moderate to severe COPD and secondly, to determine and compare the prevalence of hypovitaminosis D in stable patients and patients with exacerbations of COPD.

## MATERIAL AND METHODS

The study was a single centre, cross-sectional study, conducted in the Department of Medicine and Physiology, Silchar Medical College and Hospital, Silchar, Assam, for a period of 6 months from November 2015 to April 2016. The ethical committee of the institute gave the approval for the study. A total of 180 patients with moderate to severe COPD were included in the study.

The inclusion criteria were patients with moderate to severe COPD who gave written consent for the study. Patients who failed to comply with the study protocol, patients with FEV<sub>1</sub> / FVC > 0.7 after bronchodilator administration and patients with mild COPD were excluded from the study. Also excluded were patients with concomitant history of tuberculosis, cystic fibrosis, lung malignancy, sarcoidosis, ILD and patients on antiepileptic drugs, glucocorticoids, antiretroviral drugs and antiestrogen drugs.

All patients were evaluated with a detailed history and physical examination. Relevant investigations including estimation of vitamin D levels were done in all cases. The diagnosis and staging of COPD was made according to the GOLD criteria by spirometry and bronchodilator testing and patients were classified into moderate, severe and very severe COPD on the basis of their FEV<sub>1</sub>/FVC ratios.

The presence of vitamin D deficiency was defined as 25(OH)D levels < 20.0ng/ml, Vitamin D insufficiency as 25(OH)D levels 20ng/ml- 29ng/ml and Vitamin D sufficiency as 25(OH)D levels >30ng/ml-100ng/ml and toxic >150ng/ml.

The data entry and analysis were done using Microsoft Excel and SPSS software packages. The significance of difference between two proportions was carried out using Fisher's exact t

<sup>1</sup>Assistant Professor, <sup>2</sup>Registrar, Department of Medicine, <sup>3</sup>Associate Professor, Department of Physiology, Silchar Medical College and Hospital, Silchar, Assam, India

**Corresponding author:** Dr. Riturag Thakuria, Assistant Professor, Department of Medicine, Silchar Medical College and Hospital, Ghungoor, Silchar, Assam, India. PIN- 788014

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test. The statistical significance was accepted with a P value of less than 0.05

**RESULTS**

The studied population showed a mean age of 63.28 years (SD 10.725 years) with a male to female ratio of 5.92:1. A history of smoking was present in 81.66% of the patients. The most common presenting symptom was dyspnoea in 73.33% patients followed by fatigue in 65.55% of the patients. Fever was present in 36.11% of the patients.

After spirometric evaluation and bronchodilator testing 30% of the patients were classified into moderate COPD, 48.33% were classified as severe COPD and 21.6% patients were found to have very severe disease. Hypovitaminosis D ie. both deficiency and insufficiency was present in 48.14% patients in moderate disease, 70.11% patients in severe COPD and 82.05% patients with very severe disease (Figure-2). The presence of both vitamin D deficiency and insufficiency showed a positive co-relation with increase in severity of COPD and was significantly high in patients with severe and very severe disease when compared with patients with moderate disease; 48.14% vs 70.11% between moderate and severe COPD, p- 0.012 and 48.14% vs 82.05% between moderate and very severe COPD, p- 0.001. However, there was no statistical significance in the occurrence between the severe and very severe groups (70.1% vs 82.05%, p- 0.19)

Of the 180 patients, 74 of them (41.11%) presented in exacerbation. The frequency of exacerbation increased with the severity of the disease and was present in 11 patients (14.8%) with moderate disease, 32 patients (43.24 %) with severe COPD and 31 patients (41.89%) with very severe disease. Of the total 74 patients with exacerbations, 48 of them had vitamin D deficiency (64.86%). When compared to patients with stable COPD, the presence of vitamin D deficiency in the exacerbation group was not statistically significant (66.98 % in stable COPD vs 64.86% in exacerbation patients, p- 0.87) (Figure-3).

The duration of hospital stay was 6.538 days (SD -1.513 days) in the stable COPD group and 8.405 days (SD- 1.63 days) in patients with exacerbation (p- <0.001). However there was no association between the duration of hospital stay and vitamin D levels.

**DISCUSSION**

The study was conducted in the Department of Medicine and Physiology, Silchar Medical College and Hospital to determine the prevalence of vitamin D deficiency and insufficiency in patients with moderate to severe COPD and to compare the prevalence of hypovitaminosis D in stable patients and in patients with exacerbations of COPD.

The studied population showed a mean age of 63.288 years (SD 10.725 years) with 62.2% cases being above 60 years of age. 85.55 % of the study population were males. A history of smoking was present in 81.66 % of the population, and was also more common in males than their female counterparts. This is in conjunction with various studies conducted by Parasuramalu *et al*, Jindal *et al* and Mahesh *et al* which showed that the prevalence of COPD increases with age and is more common in males. Also the association is more common in people who smoke than in those who are non smokers.<sup>12-14</sup>

Exertional dyspnoea followed by fatigue were the most common

Total number of patients (n)	180
Sex	
Male	154 (85.55%)
Female	26 (14.44%)
Age (years)	63.288±10.725
Smoking History +	147 (81.66%)
Presenting Complaints	
Exertional Dyspnoea	132 (73.33%)
Fatigue	118 (65.55%)
Cough	72 (40%)
Fever	65(36.11%)
Musculoskeletal Pain	54 (30%)
COPD Stage	
Moderate	54 (30%)
Severe	87 (48.33%)
Very Severe	39 (21.66%)
Exacerbation +	74 (41.11%)

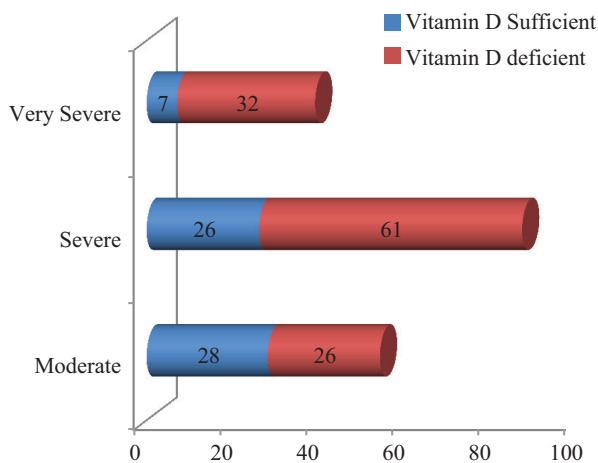


Figure-1: Table comparing Vitamin D levels with the severity of COPD

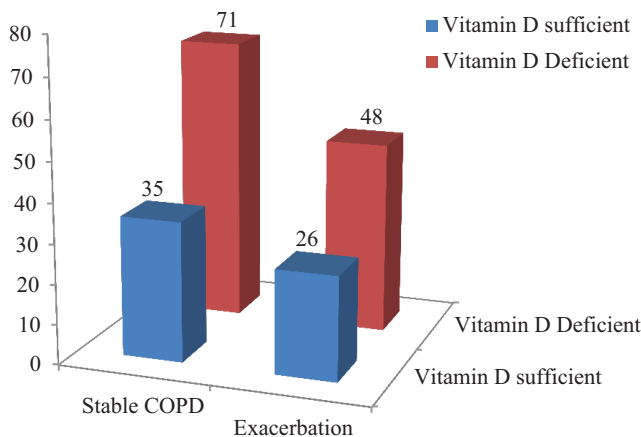


Figure-2: Comparison of Vitamin D levels between stable COPD and patients with Exacerbations

presenting symptoms among the patients, present in 73.33% and 65.55% of the patients respectively. Although in most of the reports on COPD dyspnoea, particularly with physical activity is the most common presenting symptom, fatigue may be explained to a certain extent to the presence of Vitamin D deficiency among the study patients. A study conducted by Hornikx *et al* showed significant improvement in inspiratory

muscle strength and oxygen consumption with supplementation of vitamin D.<sup>15-16</sup>

In our study, the presence of hypovitaminosis D ie. both deficiency and insufficiency was 48.14% in patients in moderate disease, 70.11% patients in severe COPD and 82.05% patients with very severe disease. The FEV1 level in COPD patients had a significant correlation with circulating level of serum 25-OH D unlike healthy smokers which was found in the study by Janssens et al.<sup>17</sup> Although increased intake of vitamin D appears to be associated with better lung function and reduced prevalence of COPD, however no relationship between low basal levels of vitamin D and deterioration of respiratory function was found when a study comparing patients mild to moderate COPD with current smoker was carried out.<sup>18</sup>

Our study revealed, no difference in the presence of vitamin D deficiency in patients with stable disease compared to those with exacerbations (66.98 % in stable COPD vs 64.86% in exacerbation patients, p- 0.87). This finding has similarities to the trial conducted by Lehouck et al on the effectiveness of incidence of exacerbation in COPD patients with high doses of vitamin D supplementation. No significant differences were found in time to first exacerbation or first hospitalization due to COPD, the annual rate of exacerbations or mortality.<sup>19</sup> A number of other studies are going on ((VidiCo, NCT00977873, Lung VITAL substudy) to determine the effectiveness of vitamin D supplementation on the risk and frequency of COPD exacerbations and results should be available soon.

## CONCLUSION

The presence of vitamin D deficiency is common among patients with COPD and the frequency increases with the severity of the disease. Although our study could not conclude showing any correlation between the exacerbations of COPD with the presence of vitamin D deficient status, larger studies with greater number of patients and longer duration of follow up are necessary to determine the exact degree of association between these two common phenomenon.

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