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Status of Vitamin D among Patients Admitted with Acute Exacerbation of COPD in Cox's Bazar Medical College Hospital

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Abstract:

Background: *Acute exacerbations of COPD (AECOPD) are common and strongly affect disease severity and relative healthcare costs. Vitamin D deficiency is frequent among COPD patients and its role in disease exacerbations is widely debated.*

Method: *This study was carried out in the medicine department of Cox's Bazar medical college. A total of 50 patients admitted with AECOPD were selected consecutively who had given consent and agreed to carry out 25 (OH) D level assays during the period from January 2021 to December 2021. Inclusion criteria were patients with confirmed cases of COPD. At the enrolment visit, patients were subjected to full clinical history and examination, and pulmonary function testing. Vitamin D [25 hydroxyvitamin D, 25(OH) D] assay was done by Automated Immunoassay Analyzer Model "MINI-VIDAS" using Biomerieux reagent in ELFA (Enzyme linked fluorescence assay) Technology. Vitamin D deficiency was defined as 25(OH) D <=20ng/ml, Vitamin D insufficiency was recognized as 21-29 ng/ml and Vitamin D level >30 ng/ml was recognized as sufficient.*

Results: *Among 50 patients 38 were males and 12 were females. The mean age of patients in this study was 72.2±13.8 years. The mean 25(OH) D level was 22.026±6.0519 ng/ml (95%CI 8.1-40.2). The mean level of vitamin D in males was (22.06±6.08 ng/ml) and in females (21.93±6.24ng/ml) (P= 0.948). Associated comorbidities are present in 54% of patients, among which Hypertension (HTN) contributes in 26%, Diabetes Mellitus (DM) in 18%, coronary artery disease (CAD) in 8%, and cerebrovascular disease (CVD) in 2%. The majority of the participants were former smokers (60%), and the mean pack-year of smoking was 22.09±6.14. In this study, vitamin D levels did not differ among various smoking groups. It was 21.9±8.1 ng/ml in non-smokers, 21.4±5.1 ng/ml in current smokers, and 22.3±6.1 ng/ml in ex-smokers groups (P= 0.904). 56% of the patients belong to low socioeconomic conditions in this study, and 42% were from lower-middle-class families. Most of the patients (86%) were from rural areas, followed by 10% from urban areas and 2% from slum areas. Regarding vocational status, 70% were retired, 10% were housemakers, farmers 6%, and the rest were service holders or business people with mean vitamin D levels of 22.2±5.9 ng/ml, 20.1±8.6 ng/ml, 24.3±2.8 ng/ml and 21.4±6.5 ng/ml respectively. The majority (44%) of patients had mMRC Grade -2 dyspnea, followed by 40% in Grade- 1, 10% in Grade-3, and only 6% of patients had Grade- 4 dyspnea. In the study, only 12% of the patients had sufficient levels of serum vitamin D. The majority had an insufficient level of serum vitamin D (52%) and 36% had a deficient level of serum vitamin D.*

Conclusion: *This study finds a high prevalence of hypovitaminosis D (88%) in AECOPD patients. Vitamin D deficiency and insufficiency are more prevalent in females. In this study, vitamin D levels did not differ between smoking groups.*

Keywords: *AECOPD, 25(OH) D, Vitamin D.*

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Introduction:

Acute exacerbations of COPD (AECOPD) are common and strongly affect disease severity and relative healthcare costs. Vitamin D deficiency is frequent among COPD patients and its role in disease exacerbations is widely debated. By 2030, COPD will be the fourth cause of mortality worldwide.[1] The prevalence of COPD is increasing and this has a substantial

influence on healthcare costs,[2] particularly because of frequent disease exacerbations (AECOPD) and hospital admissions. Vitamin D deficiency and insufficiency are common among COPD patients but its contributory role in disease exacerbations is widely debated. According to the available studies, the prevalence of hypovitaminosis D in COPD patients varies between 31–77%.[3] The concentration of vitamin D in COPD patients is reduced when compared to a control group.[4,5] Available studies suggest that vitamin D may have an impact on quality of life,[8] lung function[6,7] and the natural course of COPD (number of exacerbations) [8,9]. On the other hand in a secondary analysis of a study performed on exacerbation-prone COPD patients,[10] no association between baseline vitamin D levels and subsequent risk of acute exacerbations was found; negative results have also been reported in a primary care setting.[11] A single-center randomized trial on 182 COPD patients[12] demonstrated that vitamin D supplements were able to reduce COPD exacerbations only in the 30 subjects with severe deficiency. However, according to Janssens et al.[4] vitamin D deficiency occurs in over 60% of patients with severe COPD and is quantitatively related to disease severity. Epidemiological studies indicate that decreased vitamin D is associated with an increased frequency of respiratory infections not only in COPD patients but also in healthy people.[4,13] This may be due to the involvement of vitamin D in both innate and adaptive immunity regulation.[14,15] These findings raise the question of the role of vitamin D deficiency and the benefit of its correction in COPD. We aimed to assess the relationship between serum vitamin D levels with acute exacerbation of COPD and also assess the socio-demographic profile of these patients and see any difference between different professionals. In our country, there are few studies where the association between vitamin D levels and acute exacerbation of COPD was assessed. In our country, most people are poor and cannot access health services easily. Assessment of vitamin D level and finding its association with AECOPD may be helpful to make such people aware of vitamin D supplements which are abundant in our geographical condition as its main source is sunlight. This will reduce our health costs and patients' suffering. So, it is very rational to carry out this study in our settings.

Materials and Methods:

This study was carried out in the medicine department of cox's Bazar medical college. A total of 70 patients admitted with AECOPD were selected consecutively who had given consent and agreed to carry out 25 (OH) D level assays during the period from January 2021 to December 2021. The diagnosis of COPD was made according to GOLD (Global Initiative for Chronic Obstructive Lung Disease) criteria [1]. Finally, 50 patients were included because others were unable to carry out vitamin D assay. Inclusion criteria were patients with a history of chronic cough with sputum production for the last 2 years admitted with acute exacerbation of symptoms and post bronchodilator ratio of forced expiratory volume in 1 second (FEV1) to forced vital capacity (FVC) <0.7.

Exclusion criteria were Patients or relatives who did not give informed written consent, did not fulfill clinical or spirometry criteria of acute exacerbation of COPD, and patients who had been treated with vitamin D in either oral or injectable form within the last 3 months. Patients who were previously diagnosed with CKD, CLD, Hyper or Hypo-parathyroidism, Nephrocalcinosis, Paget's disease, malignancy, tuberculosis, sarcoidosis, and malabsorption syndromes were also excluded from the study. The study was approved by the Ethical review board of Cox's Bazar medical college and written informed consent was taken from each patient.

At the enrolment visit, patients were subjected to full clinical history and examination, and pulmonary function testing. Vitamin D [25 hydroxyvitamin D, 25(OH) D] assay was done by Automated Immunoassay Analyzer Model "MINI-VIDAS" using Biomerieux reagent in ELFA (Enzyme linked fluorescence assay) Technology. Vitamin D deficiency was defined as 25(OH) D <=20ng/ml, Vitamin D insufficiency was recognized as 21-29 ng/ml and Vitamin D level >30 ng/ml was recognized as sufficient.[16]

The spirometry was performed using Spiro Analyzer ST-150 of the latest Fukuda Sangyo quality, Japan. Post bronchodilator spirometry was performed 15 min after inhalation of 400mcg Salbutamol according to ERS/ATS recommendations.[17] Pre- and post-values were obtained for FVC, FEV1, and FEV1/ FVC. Symptom scoring of patients was done using modified Medical Research Council (mMRC) questionnaires.

Associated co-morbidities such as DM, CAD, HTN, CVD, etc. were considered to be present if these patients were previously diagnosed and taking medicines.

Statistical analysis: Statistical analyses were carried out with the SPSS for Windows software, version 23.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as mean ± standard deviation and categorical variables—as frequency and percentages. Independent sample t-test or F test (ANOVA) was used to determine whether the differences in the means of serum vitamin D levels among different groups were statistically significant. $P < 0.05$ was considered a statistical significance, and the confidence interval was set at 95%.

Results:

Fifty COPD patients admitted for acute exacerbation of COPD were included from the medicine ward, Cox's Bazar Medical College. Among them 38 (76%) were males, and 12 (24%) were females. There was male predominance (76%). The mean age of patients in this study was 72.2±13.8 years, with the majority in 61-70 years. The mean 25(OH) D level was 22.03±6.05 ng/ml (95% CI 8.1-40.2). The mean vitamin D level was higher in males (22.06±6.08 ng/ml) than the females (21.93±6.24ng/ml), but the difference failed to reach statistical significance (P= 0.948). The majority of the participants were former smokers (60%), and the mean pack-year of smoking was 22.09±6.14. In this study, vitamin D levels did not differ between smoking groups. Among non-smokers, it is 21.9±8.1 ng/ml, it is 21.4±5.1 ng/ml in those who are current smokers, and 22.3±6.1 ng/ml among Ex-smokers (P= 0.904).

56% of the patients belong to low socioeconomic conditions in this study, and 42% were from lower-middle-class families. Poor patients had a comparatively lower vitamin D level than middle-class socioeconomic (21.56±4.61 ng/ml versus 22.62±7.58 ng/ml) without statistical significance (p=0.545, independent sample t-test). Regarding the residential locations, most of the patients (86%) were from rural areas, followed by 10% from urban areas and 2% from slum areas.

The majority (44%) of patients had mMRC Grade -2 dyspnea, followed by 40% in Grade- 1, 10% in Grade-3, and only 6% of patients had Grade- 4 dyspnea (p=0.273) (Table I).

Table 1. *Baseline characteristics of patients along with vitamin D level.*

Variables	Frequency	Percent (%)	Mean±SDof vitamin D (ng/ml)	P-value
Age				
≤ 60 years	12	24	21.30±3.21	0.458*
61-70 years	27	54	21.48±.99	
70 years	11	22	24.16±8.26	
Gender				
Male	38	76	22.0±6.08	0.948†
Female	12	24	21.93±6.24	
Smoking History				
Never smoker	7	14	21.98±8.13	0.904*
Ex-smoker	30	60	22.31±6.08	
Current smoker	13	26	21.39±5.13	
mMRC				
Grade 1	20	40	23.58±6.43	0.273*
Grade 2	22	44	21.59±5.55	
Grade 3	5	10	20.8±8.18	
Grade 4	3	6	16.70±2.06	

*F (ANOVA) test; †Independnet sample t-test.

Table 2. *Mean Vitamin D level among different occupations.*

Type of occupation	Frequency	Percent (%)	MeanSDof vitamin D(ng/ml)	P-value*
Retired	35	70.0	22.22±5.92	0.809
Housemaker	5	10.0	20.12±8.61	
Farmer	3	6.0	24.26±2.75	
Shopkeeper/Business/ Caretaker	7	14.0	21.44±±6.50	

*F (ANOVA) test

Regarding vocational status, 70% were retired, 10% were housemakers, farmers 5%, and reset of the 15% were service holders or business people. The mean level of vitamin D was high among farmers (24.26±2.75ng/ml) compared to other occupational groups (Table 2).

Table 3. *Prevalence of vitamin D deficiency and insufficiency in patients with acute exacerbation of COPD.*

Vitamin D level	Frequency	Percentage
Normal	6	12
Insufficient	26	52
Deficient	18	36

In the study, only 12% of the patients had sufficient levels of serum vitamin D. The majority had an insufficient level of serum vitamin D (52%), and 36% had a deficient level of serum vitamin D (Table 3).

Discussion:

According to the available studies, the prevalence of hypovitaminosis D in COPD patients varies between 31–77%.[3] This study found the highest prevalence (88%) in hypovitaminosis D compared to previous studies (Fig.-1). The prevalence and severity of hypovitaminosis D in our study were significantly higher when compared to unselected Bulgarian population [18]. Prevalence of hypovitaminosis D is high in Bulgaria (75.8%) and it is even higher in COPD patients admitted for exacerbation (83.6%) (20). Vitamin D is low in COPD patients and our study showed it is further reduced in patients admitted for exacerbation. Our result could be explained by differences in lifestyle between the populations (outdoor activities, skin protection, sunlight exposure, etc.). For example, the use of vitamin D fortification in food and drinks is more common in other countries than ours. Furthermore, patients in this study had been hospitalized due to exacerbation which represents the most severe group of COPD patients. So the COPD patients admitted for an exacerbation are a risk group for vitamin D deficiency and insufficiency and prophylaxis should be considered.

In this study most of the affected patients are male, this is because males are more commonly smokers than females in our country. Among those females who were admitted with AECOPD, many of them were not a smoker but were still affected which can be explained by exposure to passive smoking and the use of biomass fuel while cooking. We found most of the patients were from the rural area and either primarily educated or illiterate reflecting poor access of the rural people to health services and lack of knowledge regarding a healthy diet containing vitamin D or proper exposure to sunlight which is the main source of vitamin D in our area

In this study, we found vitamin D deficiency is a little bit more common among females which correlates with a previous study where vitamin D deficiency and insufficiency were significantly more prevalent among females (97.7% vs 77.8%; $p = 0.003$).[13]

In the present study, vitamin D level among farmers was (24.26±2.75) but this is not significant because only three patients belonged to this occupation. So it needs to include a large number of patients from these professionals to show any significant difference.

There is evidence that smoking is a risk factor for vitamin D deficiency[20], but our study did not find significant differences in the prevalence of hypovitaminosis D related to smoking status ($p = 0.904$) which is similar to the previous study.[18]

Our study showed differences in mean vitamin D levels in patients with fewer symptoms (mMRC- 1) compared to patients with more symptoms (mMRC- 4) (mean 23.58 vs 16.7 ng/ml) which is similar to the results from other studies about the positive correlation between low vitamin D concentration and reduced quality of life.[21]

Study limitation

This study observes single-center hospitalized COPD patients. Further studies are needed to determine if these results apply to all COPD patients including those who are not hospitalized. As this is a cross-sectional study, establishing the cause-effect relationships is not possible. Results of vitamin D supplementation data were not gathered.

Conclusions:

This study finds a high frequency of hypovitaminosis D (88%) in AECOPD patients. Vitamin D deficiency and insufficiency are more prevalent in females. In this study, vitamin D levels did not differ between smoking groups. Preventing exacerbations is a major treatment goal of COPD and the benefit of vitamin D supplementation may be an intervention that warrants further assessment. However randomized controlled trials are needed to clarify whether the observed association in the present study is causal and is attributable to vitamin D deficiency.

Competing interests:

The authors declare that they have no competing interests.

Authors' contributions:

The Principle Investigator, Dr. Ummay Fatema Khatun, oversaw all activities related to the conduct of the study and contributed to the study idea, discussion, and writing of the manuscript. Dr. Ayesha Zerin contributed to the data collection. Dr. Abu Mohammad Shamsuddin contributed to the literature review All authors accepted the final version. All authors read and approved the final manuscript.

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