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ORIGINAL RESEARCH

Evaluation of Vitamin D status of patients hospitalized with acute exacerbation of COPD

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ABSTRACT

Introduction: COPD, which a disease of increasing public health significance in the world, is presently the fourth leading cause of death. In COPD patients, the increased prevalence of osteoporosis and osteopenia may be an indication of a link among deficiency of Vitamin D and COPD. **Aim of the study:** To determine the baseline Vitamin D status of patients hospitalized with acute exacerbation of COPD. **Material and Methods:** The present Prospective observational cohort study was conducted at the Post graduate Department of Medicine among 70 patients for one year. Blood samples were collected at baseline for Vitamin D levels. Three to five ml blood was collected in serum vial and was kept at room temperature for half an hour. After the incubation, serum was separated by centrifuging the tubes at 2000 rpm for 5 minutes to separate serum. Data analysis was done using SPSS 22.00 for windows; SPSS inc, Chicago, USA. **Results:** Out of 70 patients, low and normal vitamin D level was found in 68.57% and 31.43%. When vitamin d level was compared according to BMI, FEVI/FVC ratio, no. of exacerbation/year, no. of hospital stays (in days) and mortality, significant difference was found as $p<0.05$. **Conclusion:** Hypo-Vitaminosis D was significantly associated with AECOPD. Further investigations are required to define the role of genetic susceptibility and base line vitamin D status in the pathogenesis of acute COPD exacerbations.

Keywords: Chronic obstructive pulmonary disease (COPD), Body Mass Index (BMI), FEVI/FVC

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) as "common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases. The chronic airflow limitation that is characteristic of COPD is caused by a mixture of small airways disease (e.g., obstructive bronchiolitis) and parenchymal destruction (emphysema), the relative contributions of which vary from person to person"[1].

COPD, which a disease of increasing public health significance in the world, is presently the fourth leading cause of death[1]. According to the Global Burden of Disease Study, in 2016, a prevalence rate of 251 million cases of COPD worldwide was reported. Worldwide, nearly 3.17 million deaths were caused due to the COPD in 2015 (i.e., 5% of all deaths in 2016)[2].

For many centuries, the significance of Vitamin D in bone health is identified; also, an increasing interest in the extra skeletal roles for Vitamin D comprising lung disorders is observed[3]. Association between Vitamin D insufficiency and enhanced risk as well as severity of respiratory infections is also reported[4]. In COPD patients, the increased prevalence of osteoporosis and osteopenia may be an indication of a link among deficiency of Vitamin D and COPD[3]. Vitamin D can be useful in decreasing exacerbations when taken in appropriate amount and for a prolonged duration[5].

There are conflicting results in the previously conducted studies on Vitamin D and COPD, and there is scarcity of studies conducted in India that evaluated the status of Vitamin D in patients who are hospitalized with acute exacerbation of COPD.

Thus, this study is planned with the aim to determine the baseline Vitamin D status of patients hospitalized with acute exacerbation of COPD.

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MATERIAL & METHODS

The present Prospective observational cohort study was conducted at the Post graduate Department of Medicine.The study included consenting patients of age more than 18 years with AECOPD who presenting to the Department of Medicine, of a tertiary care cum referral centre of North India from 1st November 2020 to October 31st 2021, and required hospitalization.Ethical clearance was obtained from the Institutional Ethical Committee, prior to the start of the study, written informed consent was taken from all study participants&Confidentiality and privacy was ensured at all stages.

Inclusion Criteria for study was Hospitalized COPD patients age > 18 years, both gender&Diagnosed COPD patients with an acute exacerbation attack

Exclusion Criteria was Patients less than 18 years of age, Pregnant female, Diabetic Patients, HIV Positive individuals, Patients not giving any written consent&Patients having known conditions associated with Vitamin D metabolism, absorption or taking Vitamin D containing medications.

Sample Size

The study observed that 76.9% of patients with acute exacerbations of chronic obstructive pulmonary disease were deficient in Vitamin D[6]. Taking this value as reference, the minimum required sample size with 10% margin of error and 5% level of significance is 69 patients. To reduce margin of error, total sample size taken is 70.

Formula used is:-

$$N \geq (p(1-p))/(ME/z_{\alpha})^2$$

Methodology

After recruitment, clinical history and examination was taken in all patients and was recorded on a predefined case record form. History and patterns of smoking, use of any medications, history of exacerbations, comorbidities, and history of previous Vitamin D administration was specifically taken.

Blood samples were collected at baseline for Vitamin D levels. Three to five ml blood was collected in serum vial and was kept at room temperature for half an hour. After the incubation, serum was separated by centrifuging the tubes at 2000 rpm for 5 minutes to separate serum. Vitamin D estimation was performed by chemiluminescence method. The vitamin D values for all the patients were recorded in a predesigned proforma.

During the admission, the AECOPD patients was treated using standard protocols including bronchodilators, oxygen, noninvasive/invasive ventilation, antibiotics, steroids, antivirals (if appropriate), and other supportive measures. Daily monitoring was done and patients were discharged once stabilized.

Statistical analysis: Data so collected was tabulated in an excel sheet, under the guidance of statistician. The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA). Difference between two groups was determined using student t-test as well as chi square test and the level of significance was set at $p < 0.05$.

RESULTS

Out of 70 patients, low and normal vitamin D level was found in 68.57% and 31.43% of the subjects respectively.

Table 1: Age distribution among the study subjects

Vitamin d	Age (in years)		t test	p value
	Mean	SD		
Normal	46.50	7.83	2.41	0.09
Low	52.64	9.24		

Mean age among the study subjects with normal and low vitamin d level was 46.50±7.83 and 52.64±9.24 years respectively. Though vitamin d level decreases with increase in age, but no significant difference was found as p>0.05 (table 1).

Table 2: Mean distribution of different Variable compared with Vitamin D among the study subjects

Vitamin D	Variables		t test	p value
	Mean	SD		
BMI (kg/m2)				
Normal	26.94	4.07	0.71	0.57
Low	26.01	4.78		
FEVI/FVC Ratio				
Normal	56.24	6.13	3.78	0.013*
Low	48.59	7.02		
No. of Exacerbation/year				
Normal	3.93	1.24	6.01	<0.01*
Low	5.62	1.48		
No. of Hospital Stay (In Days)				
Normal	6.68	2.57	4.92	0.031*

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Low	10.79	2.42		

*: statistically significant

Mean BMI among the study subjects with normal and low vitamin d level was 26.94±4.07 and 26.01±4.78 kg/m2 respectively. Though vitamin d level decreases with decrease in BMMI, but no significant difference was found as p>0.05. Mean FEVI/FVC ratio among the study subjects with normal and low vitamin d level was 56.24±6.13 and 48.59±7.02respectively. Hence with decrease in FEVI/FVC ratio, vitamin d level decreases. When vitamin d level was compared according to FEVI/FVC ratio, significant difference was found as p<0.05. Mean no. of exacerbation/year among the study subjects with normal and low vitamin d level was 3.93±1.24 and 5.62±1.48 respectively. Hence with increase in no. of exacerbation/year, vitamin d level decreases. When vitamin d level was compared according to no. of exacerbation/year, significant difference was found as p<0.05. Mean no. of hospital stay (in days) among the study subjects with normal and low vitamin d level was 6.68±2.57 and 10.79±2.42 respectively. Hence with increase in hospital stay (in days), vitamin d level decreases. When vitamin d level was compared according to no hospital stay (in days), significant difference was found as p<0.05. (Table 2)

Table 3: Outcome among the study subjects

Outcome	N	%
Survivor	62	88.57
Mortality	8	11.43
Total	70	100

In our study, mortality was reported in 11.43% of the subjects (Table 3)

Table 4: Outcome among the study subjects according to vitamin d

Outcome	Vitamin d		Chi Square	p value		
	Normal (N=22)		Low (N=48)			
	N	%	N	%		
Survivor	21	95.45	41	85.42	5.58	0.043*
Mortality	1	4.55	7	14.58		

*: statistically significant

Mortality was found in 4.55% and 14.58% of the subjects with normal and low vitamin d level respectively. When vitamin d level was compared according to mortality, significant difference was found as p<0.05. (Table 4)

DISCUSSION

The spotlight has been directed toward the potential role of vitamin D in developing immune response to infections and determining the pathogenesis of COPD extra-pulmonary effects[7]. Specifically, many studies showed that lower 25-hydroxyvitamin D were associated with higher frequencies of respiratory infections and asthma exacerbations[8]. Moreover, publications showed a considerable interest in whether vitamin D deficiency may have an impact on developing frequent exacerbation of COPD[9-10].

Out of 70 patients, low and normal vitamin D level was found in 68.57% and 31.43% of the subjects respectively in our study.Abualnassr KA et al (2019)[11] in their study reported that low vitamin D level was prevalent and represent a health problem among Saudi COPD patients. The mean vitamin D level among all COPD patients was 14.51 ± 4.43 ng/mL with85.7% of COPD patients were vitamin D deficient and 14.3% of them were vitamin D insufficient.

Mean age among the study subjects with normal and low vitamin d level was 46.50±7.83 and 52.64±9.24 years respectively. Though vitamin d level decreases with increase in age, but no significant difference was found as p>0.05 in our study. Similarly, Abualnassr KA et al (2019)[11] in their study found that there was no significant correlation between vitamin D levels and age (p-value0.279).Gupta BK et al (2016)[12] in their study reported that among Indian patients with COPD concluded that COPD is associated with a significantly low level of Vitamin D that was independent of patients' age.

Mean BMI among the study subjects with normal and low vitamin d level was 26.94±4.07 and 26.01±4.78 kg/m2 respectively. Though vitamin d level decreases with decrease in BMI, but no significant difference was found as p>0.05 in our study. Gupta BK et al (2016)[12] in their study reported that among Indian patients with COPD concluded that COPD is associated with a significantly low level of Vitamin D that was independent of patients' BMI.

Mean FEVI/FVC ratio among the study subjects with normal and low vitamin d level was 56.24±6.13 and 48.59±7.02respectively. Hence vitamin d level decreases with decrease in FEVI/FVC ratio. When vitamin d level was compared according to FEVI/FVC ratio, significant difference was found as p<0.05 in our study.Similar findings were reported by Shaheen SO et al (2011)[13].Epidemiological studies in healthy subjects have reported a strong relationship between 25-hydroxyvitamin D serum levels and

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pulmonary function, as assessed by FEV1 and FVC (Janssens W et al, 2010)[9].

Mean no. of exacerbation/year among the study subjects with normal and low vitamin d level was 3.93±1.24 and 5.62±1.48 respectively. Hence with increase in no. of exacerbation/year, vitamin d level decreases. When vitamin d level was compared according to no. of exacerbation/year, significant difference was found as $p<0.05$ in this study.

According to Abualnassr KA et al (2019)[11],Gupta BK et al (2016)[12], Khan DM et al (2017)[5] model showed that low vitamin D level was significantly associated with the mean number of acute exacerbation of COPD in last year in addition to the ABG components PH and PCO2 levels. Interestingly, we found that vitamin D deficient COPD patients develop frequent acute exacerbations compared to vitamin D insufficient COPD patients.

In our study; mean no. of hospital stay (in days) among the study subjects with normal and low vitamin d level was 6.68±2.57 and 10.79±2.42 respectively. Hence with increase in hospital stay (in days), vitamin d level decreases. When vitamin d level was compared according to no hospital stay (in days), significant difference was found as $p<0.05$.Gupta BK et al (2016)[12] in their study too showed that the lower level of Vitamin D was associated with increased frequency of hospitalization. According to Bhat MR et al (2020)[6], decreased Vitamin D levels adversely affect the outcome of A/E of COPD. However, they could not find any statistical significance between Vitamin D levels and number of hospitalizations.

In our study, mortality was reported in 11.43% of the subjects. Mortality was found in 4.55% and 14.58% of the subjects with normal and low vitamin d level respectively. When vitamin d level was compared according to mortality, significant difference was found as $p<0.05$.Similar observation was made by Lee HM et al (2014)[14].Bhat MR et al (2020)[6] in their study revealed that patients with Vitamin D level of <30 have a higher 90-day mortality (29.2%) compared to those with normal Vitamin D levels (6.9%) with a hazard ratio for mortality as 4.789 (95% CI = 1.149–19.961). These findings are similar to our study.

This study opens up newer vistas for possible intervention in AECOPD in our endemically Vitamin D-deficient population.

CONCLUSION

In conclusion, hypo-vitaminosis D was significantly associated with AECOPD. Further investigations are required to define the role of genetic susceptibility and base line vitamin D status in the pathogenesis of acute COPD exacerbations. Hence larger studies are suggested to further study the association and also determine any role of Vitamin D in the treatment of such cases. Nonetheless Vitamin D supplementation in patients with demonstrable deficiency would certainly be of value regardless of its effect on the outcome of COPD whether it helps a favourable outcome needs further study.

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