# ESTIMATION OF VITAMIN D LEVELS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

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**ABSTRACT**

**BACKGROUND**

Vitamin D deficiency and osteoporosis is a common extra pulmonary manifestation in COPD patients. Evidence suggests that the prevalence of osteoporosis in patients with COPD is high and potentially important with disease progression.
AIM- The aim of this study was to estimate the serum Vitamin D levels in a well-defined cohort of patients with COPD and to correlate stages of COPD with Vitamin D level**.**

**MATERIAL AND METHODS**

It is a case control study, done over a period of 1 year in a tertiary care centre in North India. The study group was consisting of 60 male & female COPD patients diagnosed by spirometry and severity was determined according to GOLD classification criteria as well as age and sex matched 60 healthy controls.

**RESULTS**

Vitamin D level was found to be lower in cases as compared to controls and deficiency was more severe in higher stages of COPD ($p<0.001$).

**CONCLUSION**

Vitamin D deficiency correlated well with severity of COPD. Therefore, an early intervention with vitamin D supplementation might play a significant role in decreasing the comorbidity of COPD.

**KEYWORDS**

Vitamin D, Chronic Obstructive Pulmonary Disease (COPD).

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## BACKGROUND

Chronic obstructive pulmonary disease (COPD) is a common preventable and treatable disease and is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the lung to noxious particles or gases.[1] Patients with moderate to severe COPD often have multi-organ disease like skeletal muscle wasting, lung cancer, pulmonary hypertension, ischemic heart disease, endothelial dysfunction, congestive cardiac failure, metabolic syndrome, obstructive sleep apnea, depression, vitamin D deficiency and osteoporosis.[2] Vitamin D is required to maintain normal blood levels of calcium and phosphate, which in turn is needed for the normal mineralization of bone, muscle contraction, nerve conduction and general cellular function in all cells of the body.[3-4] Several factors that could account for Vitamin D deficiency in COPD patients: Poor diet, reduced capacity of aging skin for Vitamin D synthesis, reduced outdoor activity and therefore sun exposure, an increased catabolism by glucocorticoids, impaired activation because of renal dysfunction, and a lower storage capacity in muscles or fat due to wasting.[5] Evidence suggests that the prevalence of osteoporosis in patients with COPD is high and potentially important with disease progression. This study was planned to evaluate the serum Vitamin D levels in a well-defined cohort of COPD patients. We have also correlated vitamin D levels with the stages of COPD.

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**MATERIAL AND METHODS**

A Case Control Study was done over a period of 1 year at a tertiary care centre in North India. Study population was consisting of COPD patients and normal age sex matched healthy volunteers.

**Inclusion Criteria**

All patients (Men and Women) aged more than 40 years and <70 years, diagnosed as COPD by spirometry and age matched normal volunteers who gave consent for study.

**Exclusion Criteria**

Patients who were seriously ill, having co-morbid conditions (Endocrine disorders, Chronic renal disease, Chronic liver disease, Hypertension, Diabetes mellitus, Connective tissue disorders, neoplastic disease, Malabsorption disorders and other chronic disease), history of chronic intake of any drug that is known to cause osteoporosis (oral corticosteroid, cyclosporine, cytotoxic drugs. anticonvulsants, alcohols, bisphosphonates, aromatase inhibitors, excessive thyroxine etc. in previous months before inclusion), pregnant females and patient immobilized for more than 6 months or bedridden excluded from the study.

A total of 60 cases who were diagnosed as COPD by spirometry fulfilling the inclusion criteria and 60 normal healthy subjects were enrolled in this study. A detailed clinical history and physical examination was carried out for every subject. In the clinical history duration of COPD with history of complication and treatment were elicited. History of presence of risk factor like smoking, hypertension, dyslipidaemia, diabetes mellitus and presence of comorbid conditions like chronic liver disease, chronic kidney disease, drug history any other chronic disease was inquired. Thereafter detailed physical examination was carried out The following investigations were carried out. Complete haemogram, blood urea, serum creatinine, blood sugar, serum electrolytes, chest x-ray (PA View) ECG, ABG, T3, T4, TSH, Pulmonary function test and serum 25(OH) vitamin D.

**Statistical Tools Employed**

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Analysis of Variance: Analysis of Variance (ANOVA) Version 15.0 statistical Analysis Software Chi square test: Student't' test: Level of significance: "p" is level of significance, p>0.05-not significant. p<0.05- significant, p <0.01- highly significant and p <0.001- very highly significant

**RESULTS**

A total of 60 COPD cases and 60 (healthy) age matched controls who either attending OPD or admitted in the Department of Medicine and fulfilling the inclusion criteria were included in the study. Demographic profile of study population are depicted in Table 1.

| | **Cases (n=60)** | **Controls (n=60)** | **Statistical Significance** | |
|---|---|---|---|---|
| | **No. (%)** | **No. (%)** | **$\chi^2$** | **'p'** |
| **Age** | | | | |
| 40- 45 yrs. | 4 (6.67) | 2 (3.33) | 12.938 | 0.024 |
| 46-50 | 8 (13.33) | 4 (6.67) | | |
| 51-55 | 5 (8.33) | 18 (30.00) | | |
| 56-60 | 16 (26.67) | 16 (26.67) | | |
| 61-65 | 14 (23.33) | 15 (25.00) | | |
| 66-70 | 13 (21.67) | 5 (8.33) | | |
| | 59.22±7.88 (40-70) | 57.47±5.65 (43-68) | t=1.399; p=0.165 | |
| **Gender** | | | | |
| Female | 19 (31.67) | 27 (45.00) | 2.256 | 0.133 |
| Male | 41 (68.33) | 33 (55.00) | | |

***Table 1. Comparison of Demographic Variables in Study Population***

Above data shows that there was no statistically significant difference in age and gender of cases and controls (p>0.05). This indicates that cases and controls were age and gender matched.

Severity of chronic obstructive pulmonary disease (COPD) was assessed based on GOLD classifications. Out of 60 patients of COPD, Stage of COPD in 3 (5.0%) was mild, 14 (23.33%) moderate, 26 (43.33%) severe and 17 (28.33%) very severe. Gender-wise no statistically significant differences in COPD stage was found (p=0.462). Proportion of non-smokers was higher in controls (58.33%) as compared to cases (31.67). Difference in current smoking status of cases and controls was found to be statistically significant (p<0.001). Lower number of pack years (<10 years) were found in higher proportion of controls while higher number of pack years (10-20 pack years and >20 pack years) were found in higher proportion of cases, this difference was found to be statistically significant (p<0.001). Use of inhalation steroids was found in 60.0% of cases and in none of the controls. This difference was found to be statistically significant (p<0.001).

| | **Cases (n=60)** | **Controls (n=60)** | **Statistical Significance** | |
|---|---|---|---|---|
| | **Mean±SD** | **Mean±SD** | **'t'** | **'p'** |
| Vit. D (ng/mL) | 14.29 ± 6.22 | 27.73 ± 5.37 | 12.678 | <0.001 |

***Table 2. Comparison of Vitamin D Levels in Study Population***

Mean Vitamin D levels of cases (14.29±6.22 units) was found to be lower than that of Controls (27.73±5.37 units) and this difference was found to be statistically significant (p<0.001) (Table 2).

| Vitamin D levels (ng/mL) | Cases (n=60) | Controls (n=60) | Statistical Significance | |
|---|---|---|---|---|
| | No. (%) | No. (%) | $\chi^2$ | 'p' |
| <20 | 48 (80.00) | 3 (5.00) | 71.574 | <0.001 |
| 20-30 | 12 (20.00) | 41 (68.33) | | |
| >30 | 0 (0.00) | 16 (26.67) | | |

***Table 3. Comparison of Vitamin D in Study Population***

Vitamin D levels <20 were found in higher proportion of Cases (80.0%) as compared to controls (5.00%). Vitamin D levels of 68.33% Controls and only 20.0% of cases were found between 20-30 units. Vitamin D level >30 units was found in 26.67% of controls and in none of the cases. Difference in vitamin D levels in Cases and Controls was found to be statistically significant (p<0.001) (Table 3).

| COPD Stage | No. of Patients | Mean±S.D. | Min. | Max. |
|---|---|---|---|---|
| Mild | 3 | 21.73±2.72 | 19.20 | 24.60 |
| Moderate | 14 | 18.47±4.23 | 11.40 | 25.60 |
| Severe | 26 | 14.21±6.08 | 4.00 | 27.80 |
| Very Severe | 17 | 9.65±4.57 | 3.10 | 18.60 |
| | F = 9.634; p<0.001 | | | |

***Table 4: COPD Stage of Cases and Vitamin D levels***

A subsequently decrease in Vitamin D with increase in COPD stage was observed and this difference was found to be statistically significant (p<0.001) (Table 4).

| COPD Stage | Vit D <20 | Vit D 20-30 | Vit D >30 | Statistical Significance | |
|---|---|---|---|---|---|
| | No. (%) | No. (%) | No. (%) | $\chi^2$ | 'p' |
| Mild | 1 (2.08) | 2 (16.67) | - | 13.251 | 0.004 |
| Moderate | 8 (16.67) | 6 (50.00) | - | | |
| Severe | 22 (45.83) | 4 (33.33) | - | | |
| Very Severe | 17 (35.42) | 0 (0.00) | - | | |

***Table 5. COPD and Vitamin D (ng/ml)***

A statistically significant difference in vitamin D levels of different grades of COPD was observed (p=0.004) (Table 5).

**DISCUSSION**

In our study, out of 60 cases 19 (31.67%) were females and 41 (68.33%) were males, whereas in controls 27 (45.00%) were females and 33 (55%) were males but this difference was not found to be statistically significant (p=0.133). The reason for this difference is that in India COPD is more prevalent among males, due to higher prevalence of smoking among males as compared to females, similar study conducted on Indian population by Jindal SK, et al. concluded that the overall prevalence figures of COPD was 5% in men and 3.2% in women (aged 35 years and above).[6] In another study by Verboom et al. there were more male patients of COPD (67% verses 33%).[7]

The age of cases ranged between 40 and 70 years, with a mean of 59.22±7.88 years, while age of controls ranged between 40-70 years with a mean of 57.47±5.65 years. The mean age of cases was higher than mean age of controls, however this was not found to be statistically significant (p=0.165). Many previous studies shows range of mean age between 60 to 70 years. Similar study conducted on Indian population by Bhattacharyya et al. Concluded that mean age of COPD patients was 65.32±9.58 yrs, which is comparable to our study.[8]

The cases were divided into four groups depending on severity according to GOLD severity criteria.[9] Major proportion of our subjects were having severe 43.33% (n=26/60) and very severe COPD 28.33% (n=17/60) respectively while 5% (n=3/60) had mild, 23.33% (n=14/60) had moderate COPD. The reason for this could be because most subjects were taken from indoor patient.

The prevalence of different COPD grades was compared between males and females which revealed majority of both gender group had severe COPD (M=46.34% and F=36.84%). However, no significant differences in COPD stages was found.

As smoking is a major risk factor for COPD so we tried to study smoking history among cases and as expected proportion of smokers was higher among cases (68.33%) than controls (41.67%) and this difference was found to be statistically significant (p<0.001).

We also compared the current smoking status in study population and we found that proportion of current-smokers was higher in cases (45%) as compared to controls (41.67%). Proportion of ex-smokers was 23.33% in cases Proportion of ex-smokers was 23.33% in cases but there were no ex-smokers in controls. Proportion of non-smokers were (58.33%) in controls as compared to Cases (31.67). Difference in current smoking status of cases and controls was found to be statistically significant (p<0.001).

We further correlated the Consumption of Smoking in Study Population and we found that higher number of pack years (10-20 pack years and >20 pack years) were found in higher proportion of the Cases, while Lower number of pack years (<10 years) were found in higher proportion of controls this difference was found to be statistically significant (p<0.001).

We had already excluded all patients who had taken systemic corticosteroids as these drugs are known to alter bone metabolism so most of cases were on other drugs like inhalational steroids, anticholinergics, theophylline and some patients were also on oxygen therapy depending on COPD severity. Since inhalational steroids can alter bone metabolism so we tried to study impact of inhalational steroids in our cases and as expected we found that inhalation steroids were used in 60.0% of cases and in none of the controls group. This difference was found to be

statistically significant (p<0.001), out of this 40% cases (n=24/60) who were not taking inhalational steroids is because they did not give proper history or did not recall the drugs.

We compared the Vitamin D levels in study population and found that mean Vitamin D levels of cases (14.29±6.22 ng/ml) was lower than that of Controls (27.73±5.37 ng/ml) and this difference was statistically significant (p<0.001), which was similar to observation by Persson LJP et al (2012) in which they have studied subjects aged 40–76 years from Western Norway, including 433 COPD patients (GOLD stage II-IV) and 325 controls and they concluded that COPD status was associated with lower levels of 25 (OH) D (p=0.001) i.e. COPD patients had an increased risk for having vitamin D deficiency. [10]

Numerically Vitamin D deficiency (<20 ng/ml) was present in higher proportion of cases (80.0%) as compared to very few among controls (5.00%). Vitamin D insufficiency (20-30 ngm/ml) was found in 68.33% of controls and only 20.0% of cases. Vitamin D sufficiency/normal levels (>30 ng/ml) was found in 26.67% of controls and in none of the cases. Difference in vitamin D levels between cases and controls was found to be statistically significant (p<0.001) and which was similar to observations by Janssens W et al. in which they stratified all 414 participants into the three subgroups—that is, participants deficient for vitamin D (<20 ng/ml), participants with 25-OHD levels between 20 and 30 ng/ml and participants with 25-OHD levels >30 ng/ml revealed that only 31% of the healthy smokers exhibited vitamin D deficiency, whereas 39, 47 and 60%, respectively, of the patients with GOLD stage 1, 2 and 3, and as many as 77% of GOLD stage 4 patients were deficient for vitamin D.[11]

The difference between cases and controls could be because of, In India major source of vitamin D is sun exposure as food fortification with vitamin D is not prevalent. Majority of COPD patient belong to old age group and had severe disease COPD these patients could be sedentary leads to low sunlight exposure. Another theory is that aging leads to wasting of subcutaneous tissue and fat which leads to lower storage capacity of fat and muscles for vitamin D and inadequate vitamin D production which can aggravate vitamin D deficiency. But this could not be the reason of vitamin D deficiency in our study as cases and controls were age matched.

In our study we also compared COPD stages of the Cases and their Vitamin D levels and there was progressive decrease in Vitamin D levels with increase in severity of COPD and this difference was found to be statistically significant (p<0.001) which was similar to observation by Persson LJP et al. who concluded that higher GOLD stage was associated both with lower mean levels of 25 (OH)D i.e. COPD patients had an increased risk for having vitamin D deficiency and the relationship between lung function and systemic levels of vitamin D was almost linear even after adjustment for a large number of known and potential confounders.[12]

So, it appears from our study that vitamin D deficiency was associated with severity of COPD. Therefore, an early intervention with vitamin D supplementation might play a significant role in decreasing the comorbidity of COPD.

All said and done, it needs to be mentioned that further studies are required in this regard to establish our objectives on a firm basis as our study had limitations of its own. Most notably, this study was not a multicentric study and number of cases studied was somewhat smaller.

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