Original Research Article

ESTMATION OF VITAMIN - D LEVELS IN COPD PATIENTS AND CORRELATION OF VITAMIN-D LEVELS WITH DISEASE SEVERITY IN COPD

Dr Radhika Sharma [1], Dr. Suresh Sagadevan [2], Dr. Sabarish.V.S [3], Dr. Deepthi [4]

1.   *Assistant Professor, Department of Respiratory Medicine, Ayaan Institute of Medical Sciences, Kanakamamidi village, Moinabad Mandal, Rangareddy District, Telngana, India.*
2.   *Assistant Professor, Department of Respiratory Medicine, Chettinad Hospital and Research Institute, Kelambakkam, Tamilnadu, India.*
3 &4. *Assistant Professor, Department of General Medicine, Ayaan Institute of Medical Sciences, Kanakamamidi village, Moinabad Mandal, Rangareddy District, Telngana, India.*

ABSTRACT

Aim & Objective: To analyse the vitamin D levels in COPD patients and to correlate with disease severity

Methodology: A case control study was carried out during the period of January 2018 to June 2019. Chronic obstructive pulmonary disease patients and healthy volunteers with age group of more than 30 to 75 years were selected for the study. The total numbers of samples for the study were 40 cases and 40 control attending the outpatient & inpatient Department of Pulmonary medicine and General medicine, Ayaan Institute of Medical Sciences, Hyderabad, Telangana, India. **Results:** The study concludes that there is an increase in the incidence of COPD among males (64%). The mean age of the COPD cases and Controls are 55.9 ± 6.90 and 52.74 ±8.62. 62.5% of the COPD patients are smokers, while 38% had COPD due to various factors like Biomass fuel exposure, Occupational exposure. Most of the COPD patients were within the normal BMI (75%). 15% of them are underweight and 10% had high BMI. The mean Vitamin D level among COPD patients and Healthy volunteers in the present study are 30.11 ± 11.58 and 50.05 ± 2.99 respectively. Vitamin D deficiency is present in 40% of COPD patients and 12% of controls. Vitamin D levels correlate inversely with the increase in severity of COPD. In the present study the mean Vitamin D levels among COPD patients with less than 2 exacerbations/year and more than ≥2 exacerbations/year are 39.26±6.41 and 31.04±13.11 respectively. **Conclusion:** Vitamin D levels are reduced with increase in the severity of COPD. There is also reduction in vitamin D level with increased exacerbations of COPD.

Keywords: Vitamin D, COPD, Exacerbation, BMI

INTRODUCTION

Chronic obstructive pulmonary disease (COPD)" is one of the most important cause for morbidity and mortality across the globe. According to the World Health Organization report nearly 65 million people are suffering moderate to severe COPD and it will be the third cause of death by 2020. [1] A newer projection estimated COPD will be the fourth leading cause of death in 2030.[2] In India prevalence of COPD is 5% in men & 2.7% in women.[3] About half a million people in India die due to COPD, which is four times the number of COPD deaths in Europe & USA.

COPD is suspected in any patients aged above 40 years with chest symptoms like breathlessness, wheeze, cough, expectoration, chest pain along with strong exposure to risk factors. Very rarely the COPD do occur in younger patients like congenital Emphysema, α1 anti-trypsin deficiency syndrome.

Vitamin D deficiency is associated with pulmonary function deterioration. Vitamin D deficiency is common across various populations as well as among several skeletal and nonskeletal conditions including autoimmune diseases, diabetes, pulmonary diseases. The patients with pulmonary diseases such as asthma and chronic obstructive pulmonary disease (COPD) are at greater risk of vitamin D deficiency.

The clinical manifestations of COPD are predominantly pulmonary symptoms like cough, expectoration, breathlessness and wheeze. Although the extra pulmonary manifestations like osteoporosis, dyslipidemia, hypertension, muscle weakness, psychosis, clubbing also occur commonly.

Recent studies have showed evidence of vitamin D in protection against risk for cardiovascular diseases, malignant neoplasms and diabetes along with osteoporosis and other bone disorders. More than 2000 genes in the human genome respond to vitamin D.

Many studies revealed that Vitamin D deficiency are common in patients with COPD and its prevalence among COPD varies from 31-77%.[4,5,6] The association of hypovitaminosis D with the prevalence, severity of COPD and its exacerbations has been carried out by a number of researches but there is a variations in the results. So, keeping this in view, this study was taken up with the following aims and objectives.

1. To compare vitamin- D levels in COPD patients & healthy volunteers.
2. To analyse the level of vitamin-D levels in stable COPD patients & in COPD patients with exacerbations.
3. To analyse the vitamin-D levels according the severity of COPD in patients.

MATERIALS AND METHODS

A case control study was carried out during the period of January 2018 to June 2019 among patients attending Department of Pulmonary Medicine. Chronic obstructive pulmonary disease patients and healthy volunteers with age group of more than 30 to 75 years were selected for the study. The total numbers of samples (80) for the study were 40 cases and 40 control attending the outpatient & inpatient Department of Pulmonary medicine and General medicine, Shadan Institute of Medical Sciences, Hyderabad. The controls were the persons attending regular health checkup who have no known significant medical illness which can affect the outcome of the study.

This study was approved by the institutional ethical committee. Age and Body mass index was quantified by bioelectrical impedance analysis.

Bioelectrical impedance analysis:

It is a method for measuring body composition based on the rate which an electrical current travels through the body. Body fat causes greater resistance than fat-free mass, which slows at which the current travels.

Vitamin D_3, Plasma glucose, basic haemotological work-up was done along with a written consent was taken from every patient (Cases & Controls). Blood samples from cases as well as control group were obtained to determine the following investigations.

Vitamin D_3 was measured by Chemiluminescence Immunoassay (CLIA)method, using Maglumi 1000 kit.

Biological Reference Interval:

Vitamin D_3: 30-100ng/mL.

ASSESMENT PARAMETER:

INCLUSION CRITERIA

1. Age: (30-75years)
2. Gender (males and females)
3. Personal History: Smoking, Exposure to fuel woods, occupational exposure, chemical exposure.
4. Known case of COPD – Number of Exacerbations, Grades of COPD and treatment.
5. Diagnosed case of COPD by gold Guidelines

EXCLUSION CRITERIA:

1. Patients less than 38 years of age
2. Patients taking vitamin D supplementation
3. Patients suffering from diseases which affects Vitamin D and calcium metabolism like Renal dysfunction, Osteomalacia, Malignancy, Thyroid disorders, Parathyroid dysfunction, , Inflammatory bowel diseases, History of small bowel resection, Cholestatic liver disease, Pancreatitis, Cystic fibrosis, Bronchiectasis, Granulomatous disorder.
4. Patient on treatment with drugs like Phenytoin, Phenobarbital, Carbamazepine, Isoniazid, Rifampin, Tenofovir, Efavirenz
5. Patients not willing to take part in the study

Estimation of hemoglobin and total leucocytecount: [7]

Statistical analysis:

This study done to evaluate serum Vitamin D level, in COPD patients and healthy volunteers and was done in total number of 80 subjects of which 40 were COPD patients and 40 were Healthy volunteers. The data were analyzed by using standard Mean deviation, student's T test, and % graph to compare the levels of various biochemical parameters in age- categorized male and female patients. P-value of <0.05 was considered as statistically significant.

RESULT:

A total of 80 subjects were included in the final analysis.

Table 1: Descriptive analysis of study group in the study population (N=80)

Study group	Frequency	Percentages
Cases	40	50.00%
Controls	40	50.00%

Among the study population, 50% participants were cases and another 50%participants were controls.

Table 2: Comparison of gender between study group (N=80)

Gender	Study group	
	Cases (N=40)	Controls (N=40)
Male	30 (75%)	22 (55%)
Female	10 (25%)	18 (45%)

Among the cases, 30 (75%) participants were male and 10 (25%) participants were female. Among the controls, 22 (55%) participants were male and 18 (45%) participants were female.

Table 4: Comparison of smoker between study group (N=80)

Smoker	Study group	
	Cases (N=40)	Controls (N=40)
Yes	25 (62.5%)	17 (42.5%)
No	15 (37.5%)	23 (57.5%)

Among the cases, 25 (62.5%) participants were smokers. Among the controls, 17 (42.5%) participants were smokers.

Table 5: Comparison of BMI between study group (N=80)

BMI	Study group	
	Cases (N=40)	Controls (N=40)
up to 18.5	6 (15%)	0 (0%)
18.6 to 24.9	30 (75%)	5 (12.5%)
25 and above	4 (10%)	35 (87.5%)

Among the cases, 6 (15%) participants were BMI up to 18.5, 30 (75%) participants were 18.60 to 24.9 and 4 (10%) participants were BMI 25 and above. Among the controls, 5 (12.5%) participants were 18.60 to 24.5 and 35 (87.5%) participants were BMI 25 and above.

Table 6: Descriptive analysis of grading of COPD among the COPD Cases(N=40)

Grading of COPD	Cases	Percentages
I	2	5%
II	16	40%
III	20	50%
IV	2	5%

Table 7: Descriptive analysis of no of exacerbations among the COPD cases alone(N=40)

No of exacerbations	Cases	Percentage
1 to 2 / year	5	12.5%
3 to 5 / year	20	50%
>5 year	15	37.5%

Among the cases, 5(12.5%) participants had 1-2 exacerbations/ year, 20(50%) participants had 3 – 5 exacerbations/ year, 15(37.5%) participants had exacerbations > 5exacerbations / year.

Table 8: Descriptive analysis of Vitamin D level between study group (N=80)

Vitamin D level	Study group	
	Cases (N=40)	Controls (N=40)
10 to 19.99	12 (30%)	1 (2.5%)
20 to 29.99	5 (12.5%)	4 (10%)
>30	23 (57.5%)	35 (87.5%)

Among the cases, 12 (30%) participants were vitamin d level 10 to 19.99, 5 (12.5%) participants were 20 to 29.99 and 23 (57.5%) participants were >30. Among the controls, 1 (2.5%) participants were vitamin d level 10 to 19.99, 4 (10%) participants were 20 to 29.99 and 35 (87.5%) participants were >30.

Table 9: Comparison of grading of COPD with vitamin d levels among theCOPD cases (N=40)

Grading of COPD	Vitamin D level		
	10 to 19.99	20 to 29.99	>30
Grade I & II (N=18)	0 (0%)	2 (11.1%)	16 (88.8%)
III & IV (N=22)	10 (45.45%)	3 (13.63%)	9 (40.9%)

Out of 18 participants with grading of COPD I & II, 2 (11.11%)participants had vitamin d level 20 to 29.99 and 16 (88.8%) participants had >30. Out of 22 participants with grading of COPD III& IV, 10 (45.45%) participants had vitamin d level 10 to 19.99, 3 (13.63%) participants had 20 to 29.99 and 9 (40.90)participants had >30.

Table 11: Comparison of vitamin D between the study groups (N=80)

Parameter	Study group		P value
	Cases (N=40) (Mean± SD)	Controls (N=40) (Mean± SD)	
Vitamin D	30.11 ± 11.58	50.05 ± 2.99	<0.001

The mean vitamin D of subjects in cases was 30.11 ± 11.68 and it was 50.05 ± 2.99 in controls. The difference in the vitamin D between the two groups was statistically significant (P Value<0.001).

Table 15: Mean and standard deviation of vitamin D levels in stable patients and patients with acute exacerbations.

Type of patients	Vitamin D (mean and standard deviation)
Stable COPD patients	35.68 ±8.64
Patients with acute exacerbation	14.25 ± 1.10

DISCUSSION

With reference to age: [6]

In our study population the mean age of COPD cases and controls are 55.8 ± 6.90 and 52.74 ± 8.52. Persson LJP et al [6] in their study stated the mean age of COPD cases and controls as 63.5±6.9 and 58.6±9.8 respectively.

With reference to Gender: [5,6]

In our study the percentage of male participants are 75% and female participants are 25%, which suggest that incidence among males is almost double. Study done by Janssens W et al[5] found that 82.06% of COPD cases were males and 17.94% were females with vitamin D deficiency. Similar study by Persson LJP et al[6] found that 60% of COPD cases were males and 40% of COPD cases were females.

The incidence among Smokers: [5]

In our study the incidence is 62.5% among smokers with COPD. Previous studies done by Janssens W et al[5]] have shown a strong correlation between vitamin D deficiency in smokers which is a strong factor for exacerbation of COPD.

BMI & COPD [8]

In our study 75% of the patients had normal BMI, 15% of patients had low BMI, and 10% high BMI. The studies done in western countries like Monadi M et al[99] have shown increased BMI in COPD patients which is contradictory to the study. This contradiction is due to food style. In the present study where people take less fat and protein diet the BMI must have been normal or low, whereas the BMI is high in western studies due to the habit of taking high fat and protein diet.

Vitamin D levels & COPD: [8,6,5]

In our study the mean Vitamin D level among COPD is 30.11 ± 11.58 and Healthy volunteers is 50.05 ± 2.99 respectively. The result of the study correlates with various other studies like Monadi M et al [8], Persson LJP et al [6], Janssens W et al[5], which have shown a low vitamin D level among COPD patients.

Grading of Vitamin D levels: [6]

In our study 30% of the patients had vitamin D levels between 10-19.99ng/dL, 12.5% had levels 20 to 29.99ng/dL, 57.5% with >30ng/dL. 87.5 % of controls had vitamin D levels > 30 ng/dL. Study done by Persson LJP et al [6] had shown 33 % had vitamin D levels of 10-19.99 ng/dL, 67% had 20 to 29.99ng/dL among cases and in controls 34% had vitamin D level of 10-19.99ng/dL and 66% had 20 to 29.99ng/dL . Suggesting that there is reduced levels of vitamin D among COPD patients.

Comparision of severity of COPD & vitamin D levels: [6]

In our study vitamin D levels have shown marked reduction with severity of COPD. Our studies was correlated with other study done by Persson LJP et al [6] also has shown reduction of vitamin D level in Grade III & Grade IV severity of COPD.

CONCLUSION

The above findings suggest that there is Vitamin D deficiency in all COPD patients. Further studies involving large study groups is needed for adding Vitamin D as an adjuvant therapy in patients with COPD to find out therapeutic & treatment output.

REFERENCES
1. World Health Organization. Chronic obstructive pulmonary disease (COPD). [Online].; 2015 [cited 2015 12 1.
2. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med 2006;3:e442
3. Jindal SK (2006) Emergence of chronic obstructive pulmonary disease as an epidemic in India. Indian J Med Res 124: 619-630.
4. Forli L, Halse J, Haug E, et al. Vitamin D deficiency, bone mineral density and weight in patients with advanced pulmonary disease; J Intern Med. 2004;256(1):56-62.
5. Janssens W, Bouillon R, Claes B, et al. Vitamin D deficiency is highly prevalent in COPD and correlates with variants in the vitamin D-binding gene; Thorax. 2010 Mar;65(3):215-220
6. Persson LJ, Aanerud M, Hiemstra PS, et al. Chronic obstructive pulmonary disease is associated with low levels of vitamin D; PLoS ONE. 2012;7(6):e38934.
7. Robert H. Caraman. LaboratoryTraining Committee, Christian Medical Association of India. Hand book of Medical Laboratory Technology 2nd Editon. Pgno - 95-105.
8. Monadi M, Heidari B et al. Relationship between serum vitamin D and forced expiratory volume in patients with chronic obstructive pulmonary disease (COPD).Caspian J Intern Med 2012; 3(3): 451-455.