ORIGINAL RESEARCH ARTICLE

A Case Control Study of Vitamin D Levels in Chronic Obstructive Pulmonary Disease Patients and Healthy Volunteers in South Gujarat, India

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DOI: 10.55489/njmr.12042022931

ABSTRACT

Introduction: The Global Initiative for Chronic Obstructive Lung Disease (GOLD) programme states that COPD is a common, treatable, and preventable disease that is characterized by a persistent airflow restriction that usually progresses and is connected to an exaggerated chronic inflammatory response in the airways and the lung to harmful particles or gases. The combined severity of a patient's co-morbid illnesses and exacerbations increases. The purpose of the study was to assess the vitamin D status of COPD patients and healthy participants.

Methodology: This case-control study was conducted among 75 cases and 75 control at the Surat Municipal Institute of Medical Education and Research General Medicine department.

Result: The mean vitamin D of subjects in cases was 32.21 ± 12.68 and it was 52.05 ± 1.99 in controls. The difference in vitamin D between the two groups was statistically significant (P Value<0.001).

Conclusion: COPD patients had lower amounts of vitamin D. As COPD severity increases, vitamin D levels decrease. Along with a rise in COPD exacerbations, vitamin D levels are also decreasing.

Key words - Vitamin D, COPD, PFT, BMI, Chemiluminescence Immunoassay (CLIA) technique.

INTRODUCTION

The leading cause of illness and mortality worldwide is chronic obstructive pulmonary disease (COPD). Nearly 65 million people worldwide suffer from moderate to severe COPD, and by 2020, it will account for the third leading cause of mortality, according to a World Health Organization assessment. [1] According to a more recent prediction, COPD will rank as the fourth most common cause of death in 2030. [2] In India, the prevalence of COPD is 2.7% for women and 5% for males. [3] Four times as many individuals in India lose their lives to COPD as do so in Europe and the United States, or around 500,000 people.

According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) programme, COPD is a common, preventable, and treatable disease that is characterised by a persistent airflow restriction that is typically progressive and linked to an exacerbated chronic inflammatory response in the airways and the lung to harmful particles or gases. Co-morbid conditions and exacerbations add to a patient's total severity. [4]

Smoking is the primary cause of COPD, although other risk factors include exposure to environmental tobacco smoke, occupational dust and smoke exposure, indoor and outdoor air pollution, untreated asthma, untreated TB, malnutrition, and other environmental variables. Any patient over the age of 40 who exhibits chest symptoms as dyspnea, wheezing, coughing, expectoration, and chest discomfort combined with heavy exposure to risk factors is thought to have COPD. Very infrequently, younger people develop COPD, like congenital emphysema or 1 antitrypsin deficiency syndrome.

Pneumonia function declines in association with vitamin D insufficiency. Multiple populations and a number of skeletal and non-skeletal disorders, such as autoimmune diseases, diabetes, and lung diseases, are prone to vitamin D insufficiency. Patients who suffer from lung conditions including asthma and chronic obstructive pulmonary disease (COPD) are more likely to be vitamin D deficient. The primary pulmonary symptoms of COPD are coughing, expectoration, shortness of breath, and wheezing. Although extrapulmonary symptoms including clubbing, dyslipidaemia, hypertension, muscular weakness, and osteoporosis are also often reported.

One of the significant clinical manifestations of COPD patients that negatively impacts their quality of life is osteoporosis. In addition to wheezing or shortness, COPD sufferers sometimes limit themselves to their homes owing to excruciating bone pain, muscular atrophy, and widespread weakness. Due to inadequate vitamin D consumption, restrictions on physical activity, and extended corticosteroid usage, the skeletal condition develops.

Numerous recent research has shown that vitamin D is crucial in the development of many illnesses, including diabetes mellitus, systemic hypertension, cancer, COPD, and

cancer. [5],[6],[7] Among those with COPD Patients with severe and extremely severe COPD and those who experience frequent exacerbations do commonly suffer from vitamin D inadequacy.

Recent research has shown vitamin D to be protective against the chance of developing diabetes, malignant neoplasms, cardiovascular illnesses, and osteoporosis, among other bone ailments. The human genome has more than 2000 genes that react to vitamin D.[8]

Numerous studies have shown that vitamin D insufficiency is frequent in COPD patients, with prevalence rates ranging from 31-77%. Many studies have examined the relationship between hypovitaminosis D and the prevalence, severity, and exacerbations of COPD, but the findings have varied. Considering this, this investigation was initiated.

METHODOLOGY

All kinds were employed in the inquiry, and a case control study was conducted from November 2021 to November 2022. Patients with chronic obstructive pulmonary disease and healthy volunteers were recruited for the research if they were between the ages of 30 and 75. Surat Municipal Institute of Medical Education and Research General Medicine department provided 75 cases and 75 controls as the study's total sample sizes. The controls were people who regularly underwent health examinations and had no known serious medical conditions that may have affected the study's results. The institutional ethics committee has given its approval to this investigation. each patient provided a written consent and provided samples of vitamin D3, plasma glucose, and renal function (Cases & Controls). For the purposes of the ensuing investigations, blood samples from the case and control groups were collected. The Maglumi 1000 kit was used to test vitamin D3 using the Chemiluminescence Immunoassay (CLIA) technique.

Inclusion criteria: Patients aged 30-75 years and known case of COPD were included as cases while healthy volunteer without COPD were included as control.

Exclusion criteria: Any patients less than 30 years of age, taking vitamin D supplementation, suffering from diseases which affects Vitamin D and calcium metabolism, 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, on treatment with drugs like phenytoin, phenobarbital, carbamazepine, isoniazid, rifampin, tenofovir and efavirenz. Patients not willing to take part in the study.

Patients who have given their agreement to participate in the study and meet the inclusion & exclusion criteria will have a thorough physical examination, history taking, plasma glucose, blood urea, serum creatinine, serum electrolytes, and determination of the serum Vitamin D level. Chemiluminescence immunoassay is used to detect vitamin D levels in the body (CLIA). To analyse the study, appropriate statistical techniques will be employed. In accordance with the Proforma in the annex, history was elicited. A known COPD patient's personal history, job history, and treatment history were all given consideration. The initial step of the screening procedure for people to be included in the research was their historical background. According to the proforma, a general examination including anthropometric measures and a systematic examination was conducted. To get body mass index (BMI), divide weight (Kg) by height squared (m2). The WHO categorised them as follows: Vitamin D 25-OH estimation (CLIA)employing an SNIBE completely automatic analyser to measure 25-OH vitamin D in human blood in a quantitative manner (Maglumi1000). Assessment of glucose method GOD- POD (Glucose oxidase /peroxidase) Method (Trinder 1969) Estimation of blood urea: Method: Quantitative estimation of Blood Urea in Biosystems BA 200 Clinical chemistry analyser by Urease / GLDH (Glutamate dehydrogenase) method Urea in the sample consumes, by means of the coupled reactions described below, NADH that can be measured by spectrophotometry. Estimation of serum creatinine: Method: Quantitative estimation of Serum Creatinine in Biosystems BA 200 Clinical chemistry analyser by Jaffe's method. Estimation of Hemoglobin and Total Leucocyte Count: Pulmonary Function Test: by Spirometry.

RESULTS

Table 1 show that in gender group in the cases, there were 28 (37.33%) female participants and 47 (62.66%) male participants. 34 (45.33%) and 41 (54.66%) of the individuals in the controls, respectively, were female and male. Statistics could not support the gender proportional difference between research groups.

Age - The mean age of subjects in cases was56.9 ± 7.90 years and in nailing group, it was 53.84 ± 9.62years. The difference in the age between the two groups was statistically not significant

Smoker - 46 (61.33%) of the individuals in the cases smoked. 38 (50.66%) of the individuals in the controls were smokers. The proportion of smokers varied between research groups; however, this variation was insignificant.

BMI 16 (21.33%) cases had a BMI of less than 18.5, 43 (57.33%) people had a BMI of between 18.60 and 24.9, and 16 (21.33%) participants had a BMI of more than 25. 60 (80%) of the individuals in the controls had a BMI of 25 or above, whereas 15 (20%) of the participants had a BMI of 18.60 to 24.5.

Vit D level in the cases, 39 (52% of the subjects) had vitamin D levels more than 30, 5 (10%) had levels between 20 and 29.99, and 23 (30.66%) had levels between 10 and 19.99. 9 (12%) people in the controls had vitamin D levels between 10 and 19.99, 13 (17.33%) had levels between 20 and 29.99, and 53 (70.66%) had levels more than 30. The fraction of vitamin D levels that varied between study groups was statistically different (P value 0.001).

The mean vitamin D of subjects in cases was 32.21 ± 12.68 and it was 52.05 ± 1.99 in controls. The difference in the vitamin D between the two groups was statistically significant (P Value<0.001). Among COPD cases with BMI values <18.5, 18.6-24.9, 25-29.9, 30-34.9, ≥ 35 the mean Vitamin D are 26.81±13.84, 32.47±13.03, 39.51±6.75, 33.45±10.84 respectively. The vitamin D levels among COPD cases are significantly less than with Controls.

Table 2 show that comparison of COPD grading, exacerbations, and type of patients with vitamin D level among cases.

Table 1 Comparison of Demographic variables among cases and control

Variables	Case (n = 75)	Control (n =75)	P value
Gender			
Male	47 (62.66%)	41(54.66%)	0.319
Female	28 (37.33%)	34(45.33%)	
Age	56.9 ± 7.90	53.84 ± 9.62	0.034
Smoker			
Yes	46 (61.33%)	38 (50.66%)	0.188
No	29 (38.66%)	37 (49.33%)	
BMI			
up to 18.5	16 (21.33%)	0 (0%)	<0.0001
18.6 to 24.9	43 (57.33%)	15 (20%)	
25 and above	16 (21.33%)	60 (80%)	
Vitamin D level			
10 to 19.99	23 (30.66%)	9 (12%)	0.0161
20 to 29.99	13 (17.33%)	13 (17.33%)	
>30	39 (52%)	53 (70.66%)	
Vitamin D	32.21 ± 12.68	52.05 ± 1.99	<0.001
BMI	**Vitamin D (mean±SD)**	**Vitamin D (mean±SD)**	
<18.5	26.81±13.84	-	-
18.6-24.9	32.47±13.03	52.74±23.36	<0.001
25-29.9	39.51±6.75	47.56±16.35	<0.001
30-34.9	33.45±10.84	56.7±17.23	<0.001
≥35	-	45.25±4.96	-

Table 2 Comparison of clinical variables with Vitamin D level among cases.

Clinical Variables	Cases	Vitamin D (Mean± SD)	P value
Grading of COPD			
I	11(14.67%)	44.87±8.03	<0.001
II	27(36%)	34.64±9.45	
III	24(32%)	32.73±13.03	
IV	13(17.33%)	14.87±1.65	
Exacerbations			
1-2/years	15(20%)	39.36 ± 6.41	<0.001
3-5/ years	37(49.33%)	36.40± 12.24	
>5/ years	23(30.67%)	21.05± 7.89	
Type of patients			
Stable COPD	51(68%)	37.78 ±9.74	<0.001
acute exacerbation	24(32%)	16.35 ± 2.10	

As compared with COPD grading 27(36%) cases were belong from grade 2 with mean and SD 34.64±9.45 with p value <0.0001 which was statically significant.

As per comparison between Exacerbations and vitamin D level among cases 37(49.33%) cases belong from 3 to 5 years group, with mean and SD was 36.40± 12.24 with p value with p value <0.0001 which was statically significant.

As per comparison between Type of patients and vitamin D level among cases 24(32%) cases had acute exacerbation with mean and SD was 16.35 ± 2.10 with p value with p value <0.0001 which was statically significant.

DISCUSSION

In our study population the mean age of COPD cases and controls are 56.9 ± 7.90 and 53.84 ± 9.62. Zhang et al [9] in their study stated the mean age of COPD cases and controls as 63.5±6.9 and 58.6±9.8 respectively. In another study by Persson LJP et al [12] stated the mean age of COPD cases is 64.8±8.5. In a study Dhadke et al [10] mentioned the mean age as 62. In comparison with the age differences of the above three studies, the age group in our study population is less. The reason for this could be due to the exclusion criteria in COPD cases. The other reason might be the difference in spirometric analysis in COPD patients.

in our study gender group in the cases, there were 28 (37.33%) female participants and 47 (62.66%) male participants. 34 (45.33%) and 41 (54.66%) of the individuals in the controls, respectively, were female and male. Statistics could not support the gender proportional difference between research groups. According to a study by Janssens W et al [11], 17.94% of women with COPD and 82.06% of men had vitamin D insufficiency. According to related research by Persson LJP et al [12], 60% of COPD patients were male and 40% were female. The fact that there was a high percentage of males with COPD (82.06%) in the research by Janssens W et al.[11] may have been because COPD patients were only chosen if they had smoked for at least 15 pack years. Male COPD patients have a significant rate of Vitamin D insufficiency when compared to the other two trials.

In our study 46 (61.33%) of the individuals in the cases smoked. 38 (50.66%) of the individuals in the controls were smokers. The proportion of smokers varied between research groups; however, this variation was statistically insignificant. Previous research by Janssens W et al.[11] and Thakuria R et al.[13] has demonstrated a robust link between smokers' vitamin D deficiency and COPD exacerbation.

BMI in our study 16 (21.33%) cases had a BMI of less than 18.5, 43 (57.33%) people had a BMI of between 18.60 and 24.9, and 16 (21.33%) participants had a BMI of more than 25. 60 (80%) of the individuals in the controls had a BMI of 25 or above, whereas 15 (20%) of the participants had a BMI of 18.60 to 24.5. Studies conducted in western nations, such as Monadi M et al [14], have revealed elevated BMI in COPD patients, which conflicts with the research. Food culture is the cause of this conflict. The BMI must have been normal or low in the current research where individuals consume less fat and protein, but the BMI is high in western studies because of the custom of consuming more fat and protein.

In our study the mean Vitamin D level among COPD is 32.21 ± 12.68 and control is 52.05 ± 1.99 respectively. The study's findings are consistent with other previous studies that have demonstrated low vitamin D levels in COPD patients, including Monadi M et al. [14], Persson LJP et al. [12], and Janssens W et al. [11]. The vitamin D levels of the controls in every study were normal. Different geographic distributions & levels of sun exposure among people may contribute to vitamin D insufficiency.

In our study Vit D level in the cases, 39 (52% of the subjects) had vitamin D levels more than 30, 5 (10%) had levels between 20 and 29.99, and 23 (30.66%) had levels between 10 and 19.99. 9 (12%) people in the controls had vitamin D levels between 10 and 19.99, 13 (17.33%) had levels between 20 and 29.99, and 53 (70.66%) had levels more than

30. The fraction of vitamin D levels that varied between study groups was statistically different (P value 0.001). Persson LJP et al study.'s [12] revealed that among patients, 33% had vitamin D levels of 10–19.99 ng/dL, 67% had levels of 20–29.99 ng/dL, while in controls, 34% had levels of 10–19.99 ng/dL and 66% had levels of 20–29.99 ng/dL. indicating that people with COPD had lower vitamin D levels.

In our study comparison of COPD grading, exacerbations and type of patients with vitamin D level among cases. As compared with COPD grading 27(36%) cases were belong from grade 2 with mean and SD 34.64±9.45 with p value <0.0001 which was statically significant. Persson LJP et al study's [12] similarly shown a decline in vitamin D levels in COPD patients with Grade III and Grade IV severity.

In our study as per comparison between Exacerbations and vitamin D level among cases 37(49.33%) cases belong from 3 to 5 years group, with mean and SD was 36.40± 12.24 with p value with p value <0.0001 which was statically significant. Another study[12] conducted by Persson LJP et al. discovered that patients with exacerbations of less than two episodes per year had vitamin D levels of 25.49.9 and those with exacerbations of two episodes or more had levels of 23.710.5. The levels of vitamin D were noticeably lower in COPD patients who experienced exacerbations twice a year or more.

LIMITATION OF STUDY

The limitation of our study was small sample size.

RECOMMENDATION

To determine the therapeutic & treatment outcomes for individuals with COPD receiving Vitamin D as an adjuvant medication, more research with sizable study groups is required.

CONCLUSION

Our study concludes that when compared to healthy volunteers, COPD patients had lower amounts of vitamin D. as COPD severity increases, vitamin D levels decrease. Along with a rise in COPD exacerbations, vitamin D levels are also decreasing.

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