

# Prevalence & Correlates of Osteoporosis in Chronic Obstructive Pulmonary Disease Patients in Kashmir Valley

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## ABSTRACT

**Background:** Chronic Obstructive Pulmonary Disease is defined as a disease state characterized by airflow obstruction that is not fully reversible and for which there is no other explanation for the obstruction. Osteoporosis is a major co morbid condition with advanced COPD. COPD patients have higher risk of osteoporosis as compared to healthy subjects. **Methods:** In the present study, the prevalence of osteoporosis was 66.7% and another 19.6% had osteopenia. As the severity of COPD increased, the risk of osteoporosis increased. **Results:** GOLD stage III and stage IV patient had significantly lower BMD as compared to stage I and stage II of COPD disease. Stage IV COPD disease, use of oral or parenteral glucocorticoids, and repeated number of exacerbations were found to be independent risk factors for osteoporosis in COPD patients. **Conclusion:** Thus, high clinical suspicion and early diagnosis and treatment is required in the evaluation of osteoporosis in COPD patients so that the quality of life can be improved in these patients.

**Keywords:** COPD, DEXA scan, osteoporosis, repeated exacerbations.

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common respiratory condition characterized by airflow limitation.<sup>[1,2]</sup> It affects more than 5 percent of the population and is associated with high morbidity and mortality.<sup>[3,4]</sup> It is the third-ranked cause of death in the United States, killing more than 120,000 individuals each year.<sup>[5]</sup>

The Global Initiative for Chronic Obstructive Lung Disease (GOLD), a project initiated by the National Heart, Lung, and Blood Institute (NHLBI) and the World Health Organization (WHO), defines COPD as follows:<sup>[6]</sup>

COPD is a 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. It is now considered a systemic disease with widespread extra-pulmonary manifestations. The comorbid conditions, in association with pulmonary

manifestations, pose additional problems in the management of the disease.<sup>[7]</sup> It remains a major public health problem and is projected to be rank fifth in 2020 in burden of disease worldwide.<sup>[8]</sup> In India, it is estimated that there are around 1.49 crore chronic cases of COPD in the age group of 30 years and above.<sup>[9]</sup>

However, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines include “significant extra pulmonary effects” in the definition of COPD, indicating that COPD can be considered a multi component disease with marked extra-pulmonary effects.<sup>[8]</sup> The most common comorbidities responsible for the clinical manifestations and natural history of COPD are cachexia, skeletal muscle abnormalities, osteoporosis, metabolic syndrome, coronary artery disease, heart failure, pulmonary infections, cancer, and pulmonary vascular disease.<sup>[10]</sup>

Osteoporosis, with resulting fractures is one such major comorbid condition in patients with advanced COPD. The prevalence of osteoporosis in COPD patients is 36–60% and that of osteopenia is 35–72%.<sup>[11]</sup> COPD patients have a higher risk of osteoporosis as compared to healthy subjects, and the loss of bone occurs over an extended period of years.<sup>[12]</sup> The etiology of osteoporosis in COPD is probably complex and various factors may contribute to its pathogenesis, with chronic inflammatory changes in the lung contributing to the

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majority of the consequences that lead to osteoporosis.<sup>[13]</sup>

Osteoporosis is the most common metabolic bone disorder worldwide and is a significant comorbidity in COPD patients.<sup>[14,15]</sup> The World Health Organization (WHO) defined osteoporosis as “a disease characterized by low bone mass and micro-architectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk.<sup>[16]</sup> The strength of the bone depends on bone mineral density (BMD) and bone quality. The BMD is measured by the dual-energy X-ray absorptiometry (DEXA) scan, whereas the bone quality is measured by the micro architecture analysis, markers of bone turnover, accumulation of micro fractures, and mineralization.<sup>[17]</sup>

In patients with advanced pulmonary diseases (COPD, cystic fibrosis, idiopathic pulmonary fibrosis, and other lung diseases) awaiting lung transplantation, a high prevalence of osteoporosis and osteopenia has been reported.<sup>[18]</sup>

The present study was undertaken to study the prevalence of osteoporosis in COPD among Kashmiri patients, and to analyze the various risk factors contributing to the development of osteoporosis and osteopenia in these patients.

## MATERIALS AND METHODS

All the patients diagnosed as a case of COPD, based on GOLD guidelines were included in this study. The diagnosis of COPD was done based on clinical history and pulmonary function testing and staging was done as per GOLD criteria. Patients with following conditions were excluded:

1. Bronchogenic carcinoma
2. Untreated Thyroid dysfunction
3. Rheumatic diseases
4. Diseases affecting bone or calcium homeostasis
5. Primary or Secondary Hyperparathyroidism
6. Cushing's syndrome
7. Established Osteoporosis
8. Patients taking treatment with bone active agents

A total of 120 patients were enrolled and were given a questionnaire concerning age, gender, previous bone fractures, present and previous medications, cigarette smoking in pack years, daily exercise, daily diet and duration of respiratory disease and number of exacerbations in past three years. The cumulative dose of corticosteroids were calculated by taking into account the total dose of parenteral steroids for the previous three years and equivalent dose of prednisolone was calculated. BMI of all the patients was calculated and was classified as underweight, normal, overweight and obese with a BMI <18.5, 18.5-24.9, 25-29.9, >30 respectively.

The patients were subjected to pulmonary function tests and dual energy X-ray absorptiometry (DEXA) scan to stage the severity of COPD and osteoporosis respectively. Pulmonary function test was done

using spirometry. The following values were obtained from the test: FEV1, FVC, FEV1/FVC, slow vital capacity (SVC), and maximal voluntary ventilation (MVV). FEV1 and FVC and FEV1/FVC ratio were the main parameters to stage the COPD patients according to GOLD guidelines. Post bronchodilator spirometry was performed in all patients to exclude the diagnosis of bronchial asthma.

**Table 1: WHO Classification for Osteoporosis and Osteopenia**

T-Score	What the score means?
<-1 SD	Normal bone density
Between -1 SD and -2.5 SD	Osteopenia (low bone density)
>-2.5 SD	Osteoporosis

The study was a cross-sectional study and was approved by ethical committee of Government Medical College, Srinagar and study subjects had signed informed consent before performing any study related procedure.

**Table 2: Baseline demographic characteristics of the patients**

Parameter	Range/ Values	Number	%age
Age (in years)	40-49	6	5
	50-59	24	20
	60-69	35	42
	70-79	40	33.33
	>80	15	12.5
Gender	Male	76	63.3
	Female	44	36.67
BMI	Underweight	45	37.5
	Normal	48	40
	Overweight	19	15.83
	Obese	8	6.67
Duration of Illness (years)	1-5	35	29.2
	6-10	71	59.2
	11-15	14	11.7
Complications	-	9	7.5
Deaths	-	5	4.2

**Table 3: Bone mineral density and severity of COPD**

COPD Severity	NORM AL (BMD) kg/m <sup>2</sup>	Osteopenia (BMD) kg/m <sup>2</sup>	Osteoporosis (BMD) kg/m <sup>2</sup>	Mean+SD
Stage I	1.239	1.182	0.892	1.11+0.20
Stage II	1.145	1.018	0.814	0.97+0.21
Stage III	1.397	0.96	0.74	0.85+0.22
Stage IV	0	0.98	0.703	0.71+0.14

Bone mineral density (BMD) was determined by using whole body densitometer, DEXA scan. A patient's BMD was given a T-score, which was derived by comparing to an average score for a healthy 30 year old of the same sex and race. The difference between the normal young score and the patients score is called standard deviation (SD). A WHO criterion for definition of osteoporosis was

applied and patients with a T-score of  $>2.5SD$  was diagnosed to have osteoporosis,  $-1SD$  to  $-2.5SD$  was diagnosed to have osteopenia and  $<-1 SD$  as normal.<sup>[5]</sup>

## RESULTS

### Baseline characteristics

A total of 120 patients were included in the study 76 male patients (63.3%) and 44 female patients (36.67%) [Table 2]. 80 patients had osteoporosis (66.7%), 24 patients (19.6%) had osteopenia, while the rest 16 patients (13.7%) had normal bone densitometry. Age of the patients ranged from 42 to 85 years. Mean age of the male patients was  $66.6 \pm 7.74$  years and that of female patients was  $64.4 \pm 11.48$  years. Complications like pneumothorax, congestive cardiac failure, pulmonary thrombo-embolism, respiratory failure requiring intubation, and mechanical ventilation occurred in 8 patients. Four of these patients expired.

### Association of Osteoporosis and COPD

Osteoporosis was mainly found in patients who had stage III and stage IV COPD disease (64.7%), lesser prevalence of osteoporosis was found in patients with Stage I and stage II COPD disease. Thus, osteoporosis risk increased with severity of COPD. The severity of osteoporosis was compared with the number of exacerbations patient suffered in last 3 years. Majority of the patients with  $>3$  exacerbations in the past 3 years had osteoporosis, while all the patients with  $>5$  exacerbations in the past 3 years had osteoporosis. Mean BMD was calculated by DEXA scan. Significant difference ( $P > 0.0001$ ) was shown by BMD among the different stages of COPD [Table 3]. Higher the stage of COPD, greater the reduction in mean BMD. Significant difference in BMD ( $P > 0.0001$ ) was also noticed among normal, osteopenia, and osteoporosis group.

### Risk factors of Osteoporosis

Analysis of various risk factors for osteoporosis in COPD such as body mass index (BMI), smoking and use of corticosteroids in COPD patients was done. Higher prevalence of osteoporosis (29.4%) was found in patients with low BMI as compared to overweight patients. Protective effect against development of osteoporosis (4.9%) was found in obese individuals. But this association was not statistically significant ( $P > 0.073$ ). In this study, all female patients were nonsmokers. The number of patients with osteoporosis in nonsmokers was higher ( $P > 0.1$ ) as female patients already have high risk of osteoporosis. No association was found between smoking and osteoporosis. But comparison was done only among smokers, osteoporosis was prevalent more in patients with  $>10$  pack years smoking history (19.6%) as compared to the patients having pack year history of  $<10$  (10.8%). But this

association was not statistically significant ( $P > 0.3$ ). Steroids are used during exacerbations, and use of steroids may increase with number of exacerbations and hospitalizations. Patients were categorized as those not on any steroids, those who used only inhaled steroids, those who used  $<1,000$  mg of steroids (cumulative dose; equivalent of prednisolone) and those who used  $>1,000$  mg (cumulative dose; equivalent of prednisolone). It was observed that osteoporosis was more prevalent in patients with  $>1,000$  mg (cumulative dose, prednisolone) and the association was statistically significant ( $P > 0.0001$ ). The risk of developing osteoporosis was almost same between COPD patients using inhaled corticosteroids as those not using inhaled corticosteroids (3.9% versus 6.8%, respectively).

### Univariate and Multivariate Analysis of Various Risk Factors for Osteoporosis in COPD

To run binary logistic regression, normal and osteopenia patients were taken as reference population and considered non-disease and osteoporosis group was considered diseased. The risk factors for osteoporosis in COPD were found to be female sex, number of exacerbations, BMI and severity of COPD by performing simple univariate analysis [Table 4].

**Table 4: Univariate analysis of various risk factors for osteoporosis in COPD**

Risk Factors	Univariate Analysis		P value
	Unadjusted odds ratio	95% CI	
Gender (M/F)	4.15	1.52-11.30	0.005
No. of exacerbations			
<3	Reference population		
3-5	35.71	10-125	0.0001
>5	125	13.5-1000	0.0001
BMI			
NORMAL	Reference population		
UNDERWEIGHT	2.93	1.08-7.93	0.034
OVERWEIGHT	1.30	0.39-4.27	0.660
OBESE	1.95	0.34-11.23	0.453
COPD SEVERITY			
STAGE I	Reference population		
STAGE II	2.78	0.47-16.39	0.256
STAGE III	6.25	1.09-35.71	0.039
STAGE IV	41.66	4.9-33.33	0.001
STEROID USE (CUMULATIVE DOSE)			
NO	Reference population		
ICS	5.26	0.99-27.57	0.52
<1000MG	2.14	0.53-8.62	0.283
>1000MG	35.71	7.69-166.66	0.0001

With multivariate logistic regression analysis,  $>3$  exacerbations, GOLD stage IV disease and cumulative use of  $> 1,000$  of prednisone equivalent [Table 5] were found to be the significant risk factors for the development of osteoporosis in COPD.

**Table 5: Multivariate analysis of risk factors for osteoporosis in COPD**

Risk Factors	Univariate Analysis		P value
	Unadjusted odds ratio	95% CI	
Gender (M/F)	1.30	0.22-7.78	0.771
No. of exacerbations			
<3	Reference population		
3-5	30.30	4.74-200	0.0001
>5	83.33	4.62-1000	0.0001
BMI			
NORMAL	Reference population		
UNDERWEIGHT	2.62	0.39-17.54	0.661
OVERWEIGHT	3.03	0.34-27.02	0.416
OBESE	3.54	0.12-111.11	0.649
COPD SEVERITY			
STAGEI	Reference population		
STAGEII	1.43	0.07-31.25	0.552
STAGEIII	2.01	0.1-40	0.350
STAGEIV	13.51	0.48-333.33	0.024
STEROID USE (CUMULATIVE DOSE)			
NO	Reference population		
ICS	10.04	0.63-166.66	0.101
<1000MG	1.97	0.22-17.85	0.545
>1000MG	7.35	0.92-58.52	0.05

## DISCUSSION

The prevalence of Osteoporosis is more among COPD patients as compared to healthy subjects<sup>19</sup>. It thus recognizes the importance to determine the risk factors and establish the strategies to manage osteoporosis in COPD patients so as to prevent the osteoporotic fractures that deteriorate quality of life and prognosis. The present study was done to determine the prevalence of osteoporosis in COPD patients and also to recognize the various risk factors for reduced BMD in COP patients. In the present study, prevalence of osteoporosis observed was 66.7% and that of osteopenia 19.6%. Various studies previously done in different parts of the world showed prevalence of osteoporosis to be 9–69% in COPD patients versus 0–13% in healthy individuals.<sup>[20]</sup> A study by Graat-Verboom et al,<sup>[21]</sup> and TORCH trial,<sup>[22]</sup> were landmark studies done in COPD patients with Osteoporosis. They found prevalence of osteoporosis to be 21% and 65% and that of osteopenia 41% and 65%, respectively. Whole body DEXA scan was used in our study for the diagnosis of osteoporosis, which is considered a gold standard test and classification for osteoporosis was done according to the World Health Organization (WHO) criteria.<sup>[23]</sup> The methodological differences in the assessment of BMD and also the characteristics (age, sex, past use of bone medications, and stable COPD patients) of patient population chosen for the study can be the reason for varied difference in the prevalence of osteoporosis in different studies. Female sex is at increased risk for development of osteoporosis, due to the effect of estrogen, as compared to male sex. In our study, we also found the high prevalence of COPD in female population ( $P > 0.005$ ). But by multivariate analysis, the difference in prevalence of osteoporosis in male

and female patients was statistically insignificant. In a meta-analysis done by Graat-Verboom et al,<sup>[20]</sup> involving 13 studies with a total of 775 COPD patients, it was observed that there were more male patients (67% versus 33%), and the prevalence of osteoporosis varied from 9% to 69%. In addition, the prevalence of osteopenia varied from 27% to 67%. Patients with osteoporosis consisted of a higher proportion of women. However, in our study there was no significant difference observed in the prevalence of osteoporosis among male and female population.

A definite relation was established between COPD severity and osteoporosis risk both in terms of T-score and BMD. In our study, most of patients with osteoporosis had Grade IV COPD (93.7%). Also mean BMD was comparable between Stage II, Stage III, and Stage IV patients (which was statistically significant) ( $P > 0.004$ ).

In a study by Jørgensen et al,<sup>[24]</sup> increased incidence of osteopenia and osteoporosis was found with advancing COPD stage. Only GOLD stage III and IV patients were included, and patients with already known osteoporosis were excluded. Either low bone mass (osteopenia or osteoporosis) or a previously undiagnosed vertebral fracture was found in 68% of patients, with vertebral fracture in 25% of the included patients.

Another study by de Vries et al,<sup>[25]</sup> found that patients with had increased risk of osteoporotic fracture COPD (crude odds ratio (OR) 1.61; 95% confidence interval (CI) 1.52–11.7). Patients with more severe airway obstruction in COPD had increased risks of osteoporosis and bone fractures as compared to patients without the history of obstructive airway disease. Graat-Verboom et al<sup>26</sup> studied the osteoporosis with whole body and local DEXA scan in evaluation of osteoporosis in COPD patients. As severity of COPD increased, the prevalence of osteoporosis also increased as observed in by them.

In contrast to the above mentioned studies, Karadag et al,<sup>[27]</sup> compared BMDs of,<sup>[28]</sup> clinically stable male COPD patients and 20 male volunteers with normal pulmonary function, as a control group. No statistically significant difference in the BMD values was found between COPD and control groups. The TORCH study 22 demonstrated a higher prevalence of osteoporosis and osteopenia at baseline in those patients with spirometrically confirmed COPD, but no association between FEV1 impairment and BMD was found when adjusted by age and gender. In this study, the lack of association between the COP severity and osteoporosis could be due to less number of patients with mild stages of COPD.

A correlation between BMI and development of osteoporosis was also done in the study. We observed that patients with lower BMI had higher prevalence of osteoporosis (37.3%) as compared to overweight patients. But this association was not



statistically significant ( $P > 0.64$ ). A study by Bisboking et al<sup>28</sup> observed the direct correlation between bone mass and BMI. Both men and women with high BMIs have higher BMD. This is attributed partially to the effect of the greater weight-bearing load on the bones. In addition, increased estrogen levels due to the increased aromatization of testosterone to estrogen in adipose tissue in obese individuals with resulting higher estradiol levels may help to explain the higher BMD in obese persons, since estradiol levels in both men and women correlates with BMD. Many patients with end-stage COPD lose weight as the disease progresses due to decreased intake and increased energy requirements.<sup>[29]</sup> Iqbal et al,<sup>[30]</sup> reported that the lowest BMD was seen in a group of patients with BMI below the normal median and reported an independent correlation between BMI and BMD ( $r = 0.34$ ;  $P > 0.05$ ).

Smoking has been shown to be an independent risk factor for osteoporosis in both men and women.<sup>[31]</sup> Slimed et al,<sup>[32]</sup> reported that smokers with more than 20 pack years have lumbar spine BMD 12% lower as compared to nonsmokers. Several studies,<sup>[32-35]</sup> have confirmed the finding of a significantly greater rate of bone loss in smokers. Both vertebral fractures and hip fractures are increased in smokers.<sup>[36]</sup> The underlying mechanism for the lower bone mass and increased fracture risk in smokers is unclear.<sup>[37]</sup> One study showed decreased calcium absorption in the gastrointestinal (GI) tract in smokers compared to nonsmokers.<sup>[33]</sup> In our study, all female patients were nonsmokers. Since female patients are already predisposed to high risk of osteoporosis, it was higher in nonsmokers and also statistically smoking showed no association with COPD ( $P > 0.11$ ). But when comparison was done among smoking group (male population), osteoporosis was more found to be more prevalent in those with  $>10$  pack years. In patients with smoking  $>10$  pack years, the prevalence of osteoporosis was 19.6% and while in those with smoking of  $\leq 10$  pack years it was 10.8%. Other significant contributing factors to the development of osteoporosis among COPD patients is use of parenteral corticosteroids. The above findings can be explained by increased intake of systemic steroids in the patients with higher rate of exacerbations. The dose of steroids during exacerbation of COPD is much higher which may contribute in the long run to the higher incidence of reduced BMD. Prolonged immobilization in the group having higher number of exacerbations can also contribute. The rising prevalence of glucocorticoid induced bone loss is so common that the National Osteoporosis Foundation formulated the guidelines regarding these patients and recommended that all patients receiving chronic GC treatment ( $>1$  month) with 7.5mg/day of prednisone or equivalent should undergo screening for osteoporosis. In our study,<sup>[37]</sup> patients were

prescribed steroids during exacerbations most often. The patients were categorized as those not on any steroids, those who used only inhaled steroids, those who used  $<1,000$  mg of steroids (cumulative dose; equivalent of prednisolone) and those who used  $>1,000$  mg (cumulative dose; equivalent of prednisolone). Higher rates of Osteoporosis were observed in those using  $>1,000$  mg (cumulative dose, prednisolone) and the association was statistically significant ( $P > 0.0001$ ). COPD patients on high-dose glucocorticoid therapy exhibit a rapid loss of BMD within the first 6 months.<sup>[38]</sup> Normal bone metabolism is a result of the equilibrium between bone formation by osteoblasts and bone resorption by osteoclasts. The glucocorticoids induce bone loss by decreased bone formation and increased bone resorption.<sup>[39]</sup>

We also observed in our study that osteoporosis risk in COPD patients using inhaled corticosteroids was almost same as those not using inhaled corticosteroids (3.9 versus 6.8% respectively). Similar results were observed in a study by deVries et al.<sup>[25]</sup> They studied patients with more severe COPD and found them to be having higher risks of fracture, and the risks were comparable between users and nonusers of inhaled corticosteroids. The adjusted OR for osteoporotic fracture was 1.47 (95% CI: 1.25–1.74) in nonusers and 1.48 (95% CI: 1.29–1.71) in users of inhaled corticosteroids with more severe COPD. TORCH study<sup>22</sup> investigated the long-term effects of therapy with inhaled corticosteroids fluticasone propionate (FP) alone, salmeterol (SAL) alone, and a SAL/FP combination (SFC) on BMD and bone fractures in patients with moderate-to-severe COPD. No significant differences were observed between treatment arms (adjusted mean percent change from baseline at hip was 3.1% for placebo, 1.7% for SAL, 2.9% for FP and 3.2% for SFC therapy respectively; while, the corresponding changes for the lumbar spine were 0, 1.5, 0.3, and 0.3% for placebo, respectively, SAL, FP, and SFC therapy). The incidence of fractures was low and was similar for all treatments (5.1–% to 6.3%). Thus even in the TORCH study<sup>22</sup> no significant effect on BMD was detected for inhaled steroids therapy compared with placebo. Thus, it was concluded that inhaled corticosteroid (ICS) use does not cause thinning of the bone.

The administration of systemic corticosteroids (SCSs) at high doses, and if administered over a prolonged period, is thought to cause osteopenia and osteoporosis. Whether blood levels produced by ICS therapy can adversely affect BMD is not certain, but even a small effect over an extended period of time may produce serious side effects.<sup>[40]</sup> Finally, in COPD the lungs are a source of pro-inflammatory molecules and a contributor to systemic inflammation. If ICS therapy can reduce the lung source of these molecules, it may actually be beneficial to the bones.<sup>[41,42]</sup>

**Summary**

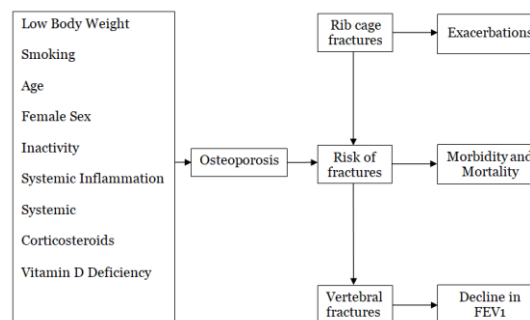
Chronic obstructive pulmonary disease (COPD) is complex disease characterized by progressive airflow limitation caused by the abnormal inflammatory reaction of the airway and lung parenchyma. With disease progression multiple organ systems get involved. Osteoporosis might develop due to a number of factors related to the disease. The prevalence of osteoporosis in COPD patients in Indian population is unknown.

We wanted to investigate the prevalence of osteoporosis in COPD and to define various risk factors associated with reduced bone mineral density (BMD) in COPD.

The study was done in the Department of Medicine of a tertiary care hospital. All the diagnosed cases of COPD according to the Global Initiative for Obstructive Lung Disease (GOLD) guidelines were included in this study. The present study was a prospective study in for a period of one and a half years. A brief history regarding duration of illness, number of exacerbations in the past 3 years, smoking in pack years, and history of steroid use (both systemic and inhaled steroids) after which cumulative dose of steroids was calculated was taken. Spirometry was done in all these patients to stage the severity of COPD according to GOLD criteria. Whole body DEXA scan was done to determine osteoporosis. A World Health Organization (WHO) criterion for definition of osteoporosis was applied and patients with T-score of  $> -2.5$  standard deviation (SD) were diagnosed to have osteoporosis,  $-1$  SD to  $-2.5$  SD were diagnosed to have osteopenia and  $< -1$  SD as normal. Statistical analysis for association of COPD with osteoporosis was done using chi-square test. Risk factors for osteoporosis were identified by univariate and multivariate logistic regression analysis.

A total of 120 COPD patients were included in the study. Among these, 80 patients (66.7%) had osteoporosis and 24 patients (19.6%) had osteopenia. Majority (64.7%) of the patients who had osteoporosis had stage III and stage IV COPD disease. It was observed that the risk of osteoporosis also increased as the severity grade of COPD increased. The bone mineral density (BMD) showed a significant difference among different stages of COPD. As the severity of the stage of COPD increased, BMD decreased. It was also observed that patients with lower body mass index (BMI) had higher prevalence of osteoporosis (37.3%) as compared to overweight patients. On univariate analysis, it was observed that risk factors for osteoporosis were female sex, higher number of exacerbations, BMI, and severity of COPD. After using multivariate logistic regression analysis, stage IV COPD (odds ratio (OR): 34.48, 95% confidence interval (CI): 1.59–1,000,  $P < 0.02$ ), number of acute exacerbations  $>3$  (OR: 30.3, 95% CI: 4.74–200,  $P < 0.01$ ), and steroid cumulative dose  $>1,000$  mg (OR:

7.35, 95% CI: 0.92–58.5,  $P < 0.04$ ) were observed to be significant risk factors for osteoporosis in COPD patients.



Chronic obstructive pulmonary disease (COPD) related factors for osteoporosis and its functional consequences

**CONCLUSION**

In conclusion, it is now established that risk factors for osteoporosis in COPD patients are multiple. The clinical significance of these individual risk factors varies in different studies. It is evident from our study that the patients who have moderate-to-severe COPD have advanced nature of the disease which predisposes them to osteoporosis, by virtue of being elderly or chronically disabled, and having chronic systemic inflammation. COPD is now increasingly being recognized as an inflammatory condition of the lung; and over the past decade, it has been recognized for its systemic inflammation and having extra pulmonary manifestations. Patients with COPD are often treated with oral or parenteral glucocorticoids, during exacerbations. Such oral or parenteral glucocorticoid therapy along with various other risk factors clearly increases the risk for the development of osteoporosis.

Hence in an ideal set up, all patients with COPD should be screened for osteoporosis using BMD measurements made by DEXA, which is considered the GOLD standard method for the early diagnosis and proper therapy of this condition can be advised at the earliest. This will help in improving the quality of life in these patients and thus improving the morbidity of this condition.

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