

# Incidence of Osteoporosis in Chronic Obstructive Pulmonary Disease Patients in a Tertiary Care Hospital: A Prospective Clinical Study

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## Abstract

**Background:** The purpose of the present study is to know the incidence of osteoporosis in chronic obstructive pulmonary disease (COPD) patients in relation to its severity and early diagnosis of osteoporosis in COPD patients and its treatment can change quality of life of the patients.

**Methods:** A prospective clinical study consisted of 100 COPD patients above 40 years were undertaken to study the incidence of osteoporosis. Of which, 74 males and 26 females were included in this study. Known COPD patients were assessed by GOLD criteria of severity.

**Results:** The study group consisted of 100 patients, of which 74 are males and 26 are females. Incidence of osteopenia and osteoporosis among males are 16.21% and 60.81% respectively. Incidence of osteopenia and osteoporosis among females are 19.23% and 50.00% respectively ( $P > 0.05$ ). Among men incidence of osteoporosis increases with an increase of grading. It increased from 9.09% for Grade 2 to 81.81% to Grade 4 ( $P < 0.01$ ). Among women incidence of osteoporosis increases with increase of grading. It increased from 20.00% for Grade 2 to 70.00% to Grade 4 ( $P > 0.05$ ). Incidence of osteoporosis is high among patients on oral steroids 82.97%. Incidence among oral inhaled corticosteroid patients is 51.51% and on no steroids is 10% ( $P > 0.05$ ).

**Conclusions:** In the present study, incidence of severity of osteoporosis increases with increased grading of COPD with high use of oral steroids. Early diagnosis of osteoporosis in COPD patients with early treatment can change the quality of life.

**Key words:** Chronic obstructive pulmonary disease, Quality of life, Steroid therapy

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a complex disease; the initial symptoms are cough with mucus production and dyspnea.<sup>1</sup> As the disease progression other symptoms may also develop. Osteoporosis might also develop possibly due to a certain number of factors related to the disease. Etiology of osteoporosis in COPD is probably complex, and various factors may contribute

to its pathogenesis. The pathophysiological mechanisms in COPD are mainly due to oxidative stress, which acts as an important amplifying mechanism in copd. Biomarkers of oxidative stress (e.g. hydrogen peroxide, 8-isprostane) are increased in the exhaled breath condensate, sputum and systemic circulation of COPD patients.<sup>2,3</sup> Osteoporosis is a systemic skeletal disease characterized by a decreased bone mineral density (BMD) and/or deterioration of the microarchitecture, resulting in increased bone fragility and hence an increased susceptibility to fractures. The preclinical state of osteoporosis is called osteopenia. World Health Organization (WHO) definition for osteoporosis is based on the measurement of BMD.<sup>4</sup> Dual energy X-ray absorptiometry (DEXA) is currently the “gold standard” and the most frequently used method of BMD measurement. BMD is expressed in standard deviation (SD) of means, the T and Z-scores. The T-score is a SD compared with a

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young adult sex matched control population. The Z-score is a SD compared with an age- and sex-matched control population. T-scores of  $< -2.5$  are defined as osteoporosis.<sup>5</sup>

The prevalence of osteoporosis has been found to be high in inflammatory bowel disease, sarcoidosis and COPD. The common link in these diseases might be systemic inflammation. Indeed, chronic inflammatory diseases lead to the production of cytokines that stimulate bone turnover. This increased bone turnover may increase bone fragility and hence may be associated with an increased fracture risk. Indeed, Bon *et al.* found a significant correlation between C-telopeptides of Type I collagen (a marker of bone resorption) and interleukine-4 (IL-4) and tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) in COPD patients.<sup>6</sup> In addition, they found a significant correlation between N-terminal procollagen propeptide (a marker of bone formation) and both IL-4 and TNF- $\alpha$ . Another link could be physical inactivity due to the underlying disease, which in turn gives rise to a lower BMD. Another explanation could be that osteoporosis has the same risk factors as some chronic diseases e.g. smoking. The pathogenesis of osteoporosis in chronic diseases is complicated and not fully understood.<sup>7</sup>

About 35% of the COPD patients had markedly low 25-hydroxyvitamin D levels (i.e., 10 ng/mL). Vitamin D deficiency may also contribute to the decreased BMD associated with COPD due to less sun exposure and poor nutrition as a result of decreased functional status. Corticosteroid use decreases luteinizing hormone and follicle stimulating hormone secretion from the pituitary gland. There is a direct effect of glucocorticoids, which decreases estrogen and testosterone production.<sup>8</sup>

## METHODS

A prospective clinical study consisted of 100 COPD patients, who were admitted in Government General Hospital, Kakinada during November 2012-September 2014 were undertaken to conduct this study to look incidence of osteoporosis in COPD patients. 74 males and 26 females were studied. Ethics the protocol was approved by the local committee and written informed consent was obtained from each patient.

### Inclusion Criteria

1. Age  $>40$  years
2. Known COPD patients as assessed by GOLD criteria of severity.

### Exclusion Criteria

1. Patients not willing for follow-up
2. Patients in respiratory or cardiac distress.

Consent was taken. All patients were clinically examined, and investigated by complete blood picture, chest X-ray, and Spirometry. All patients were sent for DEXA scan and serum vitamin D3 estimation.

Data are presented as mean  $\pm$  SD. Differences in categorical variables were analyzed using the Chi-square test.  $P < 0.05$  was considered as statistically significant.

## RESULTS

The study group consisted of 100 patients, of which 74 are males and 26 are females. Among males 14.86% of them are in 40-50 age group, 21.62% of them are in 50-60 age group, 31.08% of them are in 60-70 age group and 32.43% of them are above 70 years age group.

Among females 23.07% of them are in 40-50 age group, 19.23% of them are in 50-60 age group 34.61% of them are in 60-70 age group and 23.07% of them are above 70 years age group (Table 1).

Among males, 9.45% were in Grade 1, 14.86% were in Grade 2, 31.08% were in Grade 3, 44.59% were in Grade 4. Among females 7.69% were in Grade 1, 19.23% were in Grade 2, 30.76% were in Grade 3, 34.61% were in Grade 4 (Table 2).

**Table 1: Age distribution**

Age in years	Males	%	Females	%
40-50	11	14.86	6	23.07
50-60	16	21.62	5	19.23
60-70	23	31.08	9	34.61
Above 70	24	32.43	6	23.07

**Table 2: Distribution with grading**

COPD grading	Males	%	Females	%
Grade 1	7	9.45	2	7.69
Grade 2	11	14.86	5	19.23
Grade 3	23	31.08	8	30.76
Grade 4	33	44.59	9	34.61

COPD: Chronic obstructive pulmonary disease

**Table 3: Incidence of osteoporosis with sex**

Sex	Normal BMD	%	Osteopenia	%	Osteoporosis	%
Males	17	22.97	12	16.21	45	60.81
Females	8	30.76	5	19.23	13	50.00

BMD: Bone mineral density

Incidence of osteopenia and osteoporosis among males are 16.21% and 60.81% respectively. Incidence of osteopenia and osteoporosis among females are 19.23% and 50.00% respectively ( $P > 0.05$ ) (Table 3).

Among men incidence of osteoporosis increases with increase of grading. It increased from 9.09% for Grade 2 to 81.81% to Grade 4 ( $P < 0.01$ ) (Table 4).

Among women incidence of osteoporosis increases with increase of grading. It increased from 20.00% for Grade 2 to 70.00% to Grade 4 ( $P > 0.05$ ) (Table 5).

Osteoporosis incidence increases among men as age advances ( $P < 0.01$ ). Osteoporosis incidence increases among women as the age advances ( $P < 0.05$ ).

Incidence of osteoporosis among premenopausal women is 16.67% and among postmenopausal women is 55% ( $P > 0.05$ ).

Incidence of osteoporosis is high among people with low body mass index (BMI). Its incidence is 75.80% among low BMI people and 36.36% among people with high BMI ( $P < 0.01$ ).

Incidence of osteoporosis is high among patients on oral steroids 82.97%. Incidence among oral inhaled corticosteroid patients is 51.51% and on no steroids is 10% ( $P > 0.05$ ) (Table 6).

## DISCUSSION

In the present study incidence of osteoporosis in low BMI patients is (75.80%) and overweight patients is (36.36%). This association was statistically significant ( $P < 0.05$ ). In the present study, majority of patients who had osteoporosis had Grade 4 COPD (81.81%) and Grade 3 COPD (73.91%). Incidence of osteoporosis increased with grading of copd from 14% (Grade 1) to 80% (Grade 4) among males. Among females also COPD incidence increased from Grade 1 to Grade 4. Present study is on par with Jørgensen and Schwarz study.<sup>9</sup> In the present study, incidence of osteopenia and osteoporosis among males are 12% and 60.81%, respectively. This is on par with the above mentioned studies.

An Indian study which recently was conducted on 37 patients showed, prevalence of osteoporosis of 21.6% and osteopenia 27%. However, this study had used calcaneal ultrasonography for the diagnosis of osteoporosis, which is not considered as standard test.

We have used DEXA scan for the diagnosis of osteoporosis, which is considered a gold standard test and the patients were classified according to the WHO criteria.<sup>9-11</sup>

The incidence of osteoporosis and osteopenia in patients with Grade 4 and Grade 3 severity of COPD is 81.81% and 73.91% respectively as per our study. Hence, we propose that a prophylactic treatment with calcium (1000 mg/day) and vitamin D (800 IU/day) as a standard supplementation,

**Table 4: Incidence of osteoporosis among men based on COPD severity**

Grade	Males	%	Normal BMD	%	Osteopenia	%	Osteoporosis	%
1	7	9.45	6	85.71	1	14.28	0	0
2	11	14.86	8	72.72	2	18.18	1	9.09
3	23	31.08	3	13.04	3	13.04	17	73.91
4	33	44.59	0	0	6	18.18	27	81.81

BMD: Bone mineral density, COPD: Chronic obstructive pulmonary disease

**Table 5: Incidence of osteoporosis among women based on COPD severity**

Grade	Females	%	Normal BMD	%	Osteopenia	%	Osteoporosis	%
1	3	7.69	3	100	0	0	0	0
2	5	19.23	3	60	1	20	1	20
3	8	30.76	1	12.50	2	25	5	62.5
4	10	34.61	1	10	2	20	7	70

BMD: Bone mineral density, COPD: Chronic obstructive pulmonary disease

**Table 6: Incidence of osteoporosis in relation with steroid usage**

Steroid usage	Number of persons	%	Normal BMD	%	Osteopenia	%	Osteoporosis	%
No	20	20	16	80	2	10	2	10
ICS	33	33	9	27.27	7	21.21	17	51.51
Oral	47	47	0	0	8	17.02	39	82.97

BMD: Bone mineral density, ICS: Inhaled corticosteroid

considering that calcium and vitamin D have been shown to reduce fracture risk in men and women (target serum level of 25-OHD  $\geq 30$  ng/mL. An oral bisphosphonate, as alendronate and risedronate, currently considered that first-line treatment for osteoporosis in men should be recommended, with patient education regarding potential side effects. Intravenous bisphosphonates, as zoledronic acid (5 mg once yearly), offer an alternative option for men who cannot tolerate oral bisphosphonates or who find the dosing regimen more convenient.<sup>12-14</sup> Anabolic drugs like the human parathyroid hormone (PTH) analogue teriparatide (PTH 1-34) stimulate bone formation through effects on osteoblasts and osteocytes and may therefore more directly target the main pathophysiological mechanism in osteoclastic giant cells (OGCS)-induced osteoporosis. Teriparatide has been found to be superior to alendronate in OGCS induced osteoporosis, both regarding change in BMD and morphometric vertebral fractures, but there is no evidence for hip fracture reduction. This agent is suitable for men with severe osteoporosis (established osteoporosis; T-scores  $\leq -2.5$  SD in combination with at least one fragility fracture) who continue to fracture after 1 year of bisphosphonate therapy, or multiple risk factors for fracture, or failed previous treatment (those who cannot tolerate or do not have an adequate response to bisphosphonates). Treatment should be reserved for these high-risk patients because of the need for daily injection and high cost.<sup>15-18</sup>

## CONCLUSION

In this study, the incidence of osteoporosis is high in COPD patients with increasing severity and age with corticosteroids usage prophylactic use of calcium and vitamin D3 changes the lifestyle of patients.

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