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Osteoporosis in Chronic obstructive Pulmonary Disease (COPD) Patients

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Abstract

Background: *Osteoporosis is one of the most common systemic features of Chronic obstructive pulmonary disease (COPD). But there had been no data regarding osteoporosis in COPD patients in Bangladesh.*

Objectives: *To determine the frequency of osteoporosis in COPD patients.*

Materials & Methods: *This was a cross sectional observational study. COPD patients were recruited from Sarkari kormachari hospital. Patients were excluded if they had asthma, any disease affecting bones and calcium homeostasis or were receiving drugs related to bone metabolism. Demographic data were collected including age, smoking history, inhaled corticosteroid use, body mass index, treatment history hospital admission. Chest x-ray was done to exclude any infection or malignancy. Blood was obtained for complete blood count, renal function test, CRP. Bone mineral density (BMD; g/cm^2) was conducted by using dual energy x-ray absorptiometry scan (DXA scan) at second to fourth lumbar spines (L2-4) and femoral neck.* ***Results:*** *The overall prevalence of osteoporosis according to the lowest T-score at either L2-4 or femoral neck were 56.7%. This is very high than other country. BMI and CRP were significantly associated with osteoporosis.*

Conclusion: *The frequency of osteoporosis in Bangladeshi COPD patients was higher than others. Osteoporosis was associated with low BMI and high level of CRP.*

Key words: *Osteoporosis, COPD, bone mineral density.*

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Introduction:

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease characterized by persistent airflow limitation that is usually progressive[1] and there is a chronic inflammatory response in the airways and the lungs.[2-4] COPD is currently the fourth leading cause of death in the world.[5] But it is projected to be 3rd leading cause of death by 2020. Morbidity and mortality in case of COPD is increasing day by day all over the world as well as in Bangladesh. Current estimates suggest that 80 million people worldwide suffer from moderate to severe disease. Death due to COPD covers 6% of all death globally. The COPD burden is projected to increase in coming decades because of continued exposure to COPD risk factors and aging of population.[6,7]

The prevalence of COPD is directly related to tobacco smoking, biomass, cooking habits and socio economic status. As Bangladesh is a developing country and smoking is much prevalent here, more over smoke pollution and cooking habits in Bangladesh rural areas play an important role in developing COPD.[8] The prevalence of COPD in Bangladesh is 13.5 % by GOLD criteria it is more prevalent in rural than urban area and male are more affected than female.[9] But recently prevalence is increasing in female due to increased life expectancy.[10]

COPD is not confined to only lungs it has many systemic effects with widespread co-morbidities like weight loss, depression, cardiac disease, and osteoporosis.[11-13] Osteoporosis is characterized by reduced bone mass and micro-architectural deterioration of bone tissue with a consequent increase in bone fragility.[14]

The etiology of osteoporosis in COPD is complex till not fully understood, but various risk factors may contribute to its pathogenesis. Osteoporosis is one most common systemic effects of COPD, but the mechanism is unclear and there is no well accepted hypothesis about the pathophysiology

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regarding development of osteoporosis in COPD. Most literatures suggest that it is multifactorial including progressive reduction of physical activities, low BMI, pharmacological treatment, systemic inflammation, and hypogonad.

If osteoporosis affects thoracic spine eventually vertebral compression collapse which can causes kyphosis as result develop breathing difficulty and decreased lung volume.[15] Hip fractures cause significant morbidity such as pain, decreased morbility and eventually mortality.

The reported prevalence of osteoporosis in COPD patients ranges from 23%-50% as diagnosed by BMD, and from 24% to 80% as diagnosed by BMD or vertebral compression fracture.[16-17]

However, there are currently no studies regarding the prevalence of osteoporosis in patients with COPD in Bangladesh. The aim of this study is to find out the frequency of osteoporosis in COPD patients in Sarkari Karmachari Hospital.

Materials & Methods:

This cross sectional observational study was conducted between December 2016 to December 2017. COPD patients recruited from Sarkari Karmachari Hospital from outdoor stable patient or admitted patients due to acute exacerbation. Inclusion criteria were previously diagnosed or newly diagnosed COPD according to GOLD criteria. Patients were excluded if they had asthma, any disease affecting bones and calcium homeostasis or were receiving drugs related to bone metabolism (e.g. hormone replacement therapy, bisphosphonate, calcium or vitamin D supplement and oral corticosteroid recently)

Demographic data were collected including age, smoking history, inhaled corticosteroid use, alcohol consumption, menopausal history in case of female cases, comorbidities, duration of treatment, long term domiciliary oxygen therapy, body mass index, treatment history, hospital admission. Blood was obtained for complete blood count, renal function test, CRP, phosphate, albumin, parathyroid hormone level. Chest x-ray was done to exclude concomitant pulmonary malignancy and X-ray lumbro-sacral spine to assess osteopenia or any vertebral collapse. An echography was done to exclude chronic heart failure. Spirometry was performed according to the recommendation of American Thoracic Society. A total of 30 COPD patients who had undergone measurement of BMD were enrolled in the current study. We classified COPD severity according to GOLD guidelines.[18]

Bone mineral density (BMD; g/cm^2) was conducted by using dual energy x-ray absorptiometry scan (DXA scan) at second to fourth lumbar spine (L2-4) and femoral neck. The BMD measurement by DXA scan is a gold standard and highly accurate technique for diagnosis of osteoporosis according to World Health Organization (WHO) recommendation.[14] The BMD measurement by DXA scan were expressed as T-score compared with a young normal control population of the same age gender and race. T-score values above -1.0 were normal, between -1.0 to -2.5 were osteopenia and below -2.5 were osteoporosis. The lowest T-score at either L2-4 or femoral neck determined the diagnosis of osteoporosis.

No data or any information was collected without permission of the participants. Participants were encouraged to take part in the study voluntarily. Consent was obtained after a brief of the study in Bengali was described to all respondents. Confidentially was assured and anonymity maintained; special caution is taken that no participant can be identified in any report or publication under this study.

All statistical analyses were performed using the SPSS software package version 25.

Results:

Thirty patients with mean age 63.47+_8.45 years, normal group age 58.23±7.77 and osteoporotic group age were 67.47±6.672. Male female ratio was 28:2 (Table I). A total of 2 had no history of smoking (6.7%) but 17(56.7%) and 11(36.7%) were current smoker and ex-smoker respectively. The BMI in total group was n=30, mean ±SD 23.09±4.82 but in osteoporotic group 20.83±2.29 (Table I).

Table I

Clinical and demographic characteristics of COPD patients (n=30).

Characteristics	Number (Percentage)
Age in years, mean±SD	63.47±8.44
Male	28(93.3%)
Female	2(6.7%)
Weight (kg), mean±SD	54.92±9.17
Height (cm), mean±SD	155.10±13.02
BMI, mean±SD	23.09±4.82
Tobacco use	
• Current smoker	17(56.7%)
• Ex-smoker	11(36.7%)
• Never smoker	2(6.7%)
Inhaled corticosteroid use:	
• Regular	10(33.3%)
• Irregular	8(26.7%)
• Never	12(40%)

There were 0(0%), 6(20%), 18(60%) and 6(20%) patients, respectively with GOLD stages I, II, III and IV COPD. The mean FEV_1 was 44.45±14.64 (Table II). Total ten patients were current users of inhaled corticosteroids (33.3%) whereas twelve (40%) never used inhaled steroids (Table I).

Table II
Pulmonary Function and BMD

Characteristics	Number (Percentage)
FEV_1(%predicted), mean±SD	44.45±14.64
GOLD COPD stage	
I: FEV_1 e"80% predicted	0(0%)
II: FEV_1 50-80% predicted	6(20%)
III: FEV_1 30-50% predicted	18(60%)
IV: FEV_1 less than 30% predicted	6(20%)
BMD	
• Normal	6(20%)
• Osteopenia	7(23%)
• Osteoporosis	17(56.7%)

The BMD findings were (a) normal in 6 patients (20%) (the mean T-score being lumbar spine normal group -1.23±.65 and hip joint -1.35±.56). On the other hand osteoporosis in 17 patients (56.7%) (The mean T-score of lumber spine and hip joint were respectively -2.40±1.40 and -3.3±0.47 (Table III). The overall frequency of osteoporosis in COPD patients was 56.7%.

Table III
Demographic and clinical characteristics relative to osteoporosis and normal bone mass.

Characteristics	Normal	Osteoporosis	P value
Age, years, mean ±SD	58.23±7.77	67.47±6.672	.002
Height, cm, mean ±SD	155.00±12.85	154.44±12.75	.971
Weight, kg mean ±SD	60.80±7.39	49.50±6.95	.001
BMI, mean ±SD	25.85±5.87	20.97±2.29	.004
CRP mean ±SD	9.29±3.73	11.50±3.83	.043
T-score of hip mean ±SD	-1.28±.49	-3.25±.51	
T-score of L_{2-4} mean +-SD	-1.33±.56	-2.40±1.36	

Discussion:

Osteoporosis is one of the most common systemic effects of COPD, but the mechanism is unclear and there is no well accepted hypothesis about the pathophysiology regarding development of osteoporosis in COPD. Most literatures suggest that it is multifactorial including progressive reduction of physical activities, low BMI, pharmacological treatment, systemic inflammation, and hypogonadism.[19]

We evaluated the frequency of osteoporosis in COPD patients and found that 56.7%. Result of our study was higher than previous three studies in COPD patients. The first study, Graat-Verboom L et al [24] showed the prevalence of osteoporosis was 21% and osteopenia was 41% in COPD patients and mean FEV_1 was 42.1% predicted. The second, Ferguson TG and colleagues from the TORCH study[20] found the prevalence of osteoporosis and osteopenia in moderate to severe COPD patients were 23% and 42% respectively. The last study, Jorgensen NR, et al 15 reported the prevalence of osteoporosis and osteopenia in severe COPD patients were 44.8% and 23.3% respectively. In recent systematic review [20], the overall mean prevalence of osteoporosis in COPD patients was 35% and the correlates of osteoporosis were mainly measures of body composition, disease severity and use of corticosteroids.

Female are more prevalent to osteoporosis.[22-23] As three above studies included subjects from both genders so that overall prevalence of osteoporosis and osteopenia were so high. In Bangladesh COPD is not much common in female and so overall prevalence of osteoporosis should not be so high in study but interestingly prevalence of osteoporosis is so higher than previous study. This may be due to older age or severity of COPD influence the results.

We found significant positive correlations between osteoporosis and BMI (P value .004) and CRP (P value .043). Low BMI is a risk factor for osteoporosis.[24-25] We found height is not positively correlated (P value .971) with osteoporosis but overall BMI was positively correlated with osteoporosis (P value .004). Several studies support the relationship between bone mineral density and BMI.[26]Osteoporosis is less common in obese people. In another cross-sectional study, overweight and obesity showed a substantial protective effect in osteoporosis.[27]

Osteoporosis has been a recognized side effect of long term systemic corticosteroid therapy but little or no effects from inhaled corticosteroids.[28] In TORCH[20] study, they failed to show any significant differences between two groups who take inhaled steroid for 3 year and placebo respectively. In EUROSCOPE[29] study, they did not find a significant change in BMD at L2-4 and femoral neck in 912 mild COPD patients who received 800 mcg/day of budesonide or placebo for period of 3 years. Thus long term corticosteroid therapy may have little or no effects in BMD in COPD patients. On the contrary, a meta-analysis of randomized controlled trials

(16 trials) and observational studies (7 trials) showed that ICS use was associated with a modest but statistically significant risk factor for developing fracture in COPD patients.[30] Another large case-control study showed the current use of high dose ICS(more than 700 microgram/day) increase the risk of nonvertebral fractures. Therefore the impact of ICS in case of developing osteoporosis in COPD patients should be further evaluated by studies in the future.

All patients were in GOLD II/III/IV stage and we have not noted the BMD of the GOLD I stage COPD patients. Hence, the actual prevalence of osteoporosis in overall COPD population cannot be conferred from our observation.

Since most of our volunteers were male n=28, we could not gather any information about the BMD of female COPD patients in our community. With small number of subjects, it is not possible to make any comparison between normal and osteoporosis groups.

Conclusion:

Osteoporosis is underdiagnosed in COPD patient though the prevalence of osteoporosis was very high in Bangladeshi COPD patients. We found significant correlation between bone mineral density and BMI, physical activity. We did not find any association between bone mineral density and steroid inhaler. So screening of BMD should be considered in COPD patients with low BMI.

Conflict of interest: None.

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