ORIGINAL ARTICLE

# Osteoporosis among the Chronic Obstructive Pulmonary Disease Patients

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ABSTRACT

**Background:** COPD is a widely prevalent disease with high morbidity and mortality and is associated with various comorbidities, among which is osteoporosis. However, osteoporosis is often undiagnosed in these patients.

**Material and methods:** This study was conducted on 40 patients with COPD and 15 healthy controls (the control group). They were selected from EMCH from Jan 2015 to Dec 2017. All participants were subjected to detailed clinical history taking, a thorough clinical examination, plain chest radiography (posteroanterior and lateral views), blood sampling for complete blood picture, erythrocyte sedimentation rate, and serum calcium and phosphates, ventilatory function tests (spirometry), and measurement of bone density using dual-energy X-ray absorptiometry (DEXA).

**Results:** The results of this study revealed prevalence of osteoporosis was higher in the COPD group compared with the control group ($P \leq 0.00$). Prevalence of osteoporosis increased with increasing severity of COPD ($P \leq 0.00$).

**Conclusion:** Osteopenia and osteoporosis are more prevalent in COPD patients than in healthy controls and the severity of osteoporosis increases with increasing severity of COPD.

**Keywords:** Chronic obstructive pulmonary disease, osteopenia, osteoporosis.

## Introduction

Chronic obstructive pulmonary disease (COPD) is a lifestyle-related chronic inflammatory pulmonary disease and a major cause of morbidity and mortality globally. The projection is that by the year 2020, COPD would become the third leading cause of death globally.[1] The Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2018 update defined COPD as a "common preventable and treatable disease, characterized by persistent airflow limitation that is progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients."[2]

The degree of airflow limitation can be assessed by spirometry and stratified in accordance with the Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD)[3]. Although primarily a pulmonary disease, there are significant extrapulmonary effects in COPD[4-7]. Indeed, the GOLD guidelines incorporated these extrapulmonary effects in their definition of COPD.[3] Examples of extrapulmonary effects are increased arterial stiffness[5], skeletal muscle atrophy[6], systemic hypertension[8] and osteoporosis[9].

The World Health Organization (WHO)[10] defined osteoporosis as "a disease characterized by low bone

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mass and micro-architectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk." 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 microarchitecture analysis, markers of bone turnover, accumulation of microfractures, and mineralization.[11] Various risk factors explaining the prevalence of osteoporosis in COPD patients include aging, smoking, physical inactivity, systemic inflammation, malnutrition, low body-mass index (BMI), hypogonadism, vitamin D deficiency, and the frequent use of corticosteroids.[12]

Management of co morbidities is clinically important as they are associated with hospitalization, mortality and diminished quality of life (QOL) in patients with COPD.[13-15] Osteoporosis is one of the major co morbidities of COPD. Although pathophysiological link between COPD and osteoporosis remains to be established, recent epidemiological studies[16,17,18-20] in Japan have clearly indicated that osteoporosis is very common in COPD patients. On the other hand, a retrospective chart review of 234 newly-diagnosed male osteoporotics in an US bone clinic identified COPD as the leading cause of secondary osteoporosis, more frequent than glucocorticoid use or hypogonadism.[21]

The most common type of osteoporosis-induced fracture is the vertebral compression fractures (VCFs).[22] VCFs are associated with back pain and kyphosis. Kyphosis can cause loss of height, resulting in impaired lung function.[23] Every single VCF decreases the vital capacity by 9%, and the lung function impairment is most notable when kyphotic angle is more than 55°.[24] The impact of reduced lung function would be more pronounced in COPD patients with already poor lung reserve.[25] Patients with rib fractures may develop exacerba-tions of COPD because of chest pain-induced hypoventilation and decreased ability to expectorate.[26] Moreover, osteoporotic fractures in COPD may further decrease the mobility of the patients, thereby, predisposing them to the risk of deep venous thrombosis (DVT) and pulmonary embolism. Therefore, diagnosis and prevention of osteoporosis should be an important goal in the management of patients with COPD.

Therefore, the aim of the current study was to determine the incidence and severity of osteoporosis in COPD patients of different grades.

## Methods

***Study area:*** This prospective observational study was conducted in the inpatient [IPD] and out patient department [OPD of Pulmonology over 4 years at Enam Medical College & Hospital, [EMCH] a tertiary care hospital at Savar in Dhaka over four years period from January 2015 to December 2018.

***Study Design:*** A total of 40 diagnosed cases of COPD were recruited in the study both control and COPD cases were male. Patients and controls were selected by purposive sampling method (Non probability sampling). Data regarding gender, age, life style, socioeconomic status and education were colleted from all participants were collected through structured questionnaire. COPD patients were either previously diagnosed or diagnosed later. subjected to detailed clinical history taking, a thorough clinical examination, plain chest radiography (poster anterior and lateral views), blood sampling for complete blood picture, erythrocyte sedimentation rate, and serum calcium and phosphates, ventilatory function tests (spirometry), and measurement of bone density using dual-energy X-ray absorptiometry (DEXA). Control subjects undergone spirometry and dual-energy X-ray absorptiometry (DEXA) COPD patients were grouped depending on spirometry findings[2], stage 1: FEV1 (forced expiratory volume during first second) $\geq$ 80% of the predicted, stage 2 : FEV1 $<$80% but$>$ 50% of predicted, stage 3 : FEV1 $<$50% but $>$ 30% of predicted and stage 4 : FEV1 $<$ 30% of predicted. Age matched healthy peoples are taken as controls. BMD was measured at the lumbar spine (L2-L4) and femoral necks and left forearm. The T- score, which represents the number of standard deviations of BMD from the reference value for healthy young adults, was the basis for diagnosing osteoporosis. According to the definition of the World Health Organization (WHO) 10 osteoporosis corresponded to a T- score of $\leq -2.5$ and osteopenia to a score of $\leq -1$ and $> -2.5$. Data was then analyzed by SPSS 16. A p- value less than 0.05 is considered significant.

Ethical Information: The informed verbal consents were obtained from the patients and controls who participated in this study.

**Results:**

Total 55 male cases were included in our study where 15 were control subjects and 40 were COPD patients. Age range from 48 to 71 years. Out of 40 COPD patients 10 were very severe COPD, 18 were severe COPD, 12were moderate COPD and no mild cases were found.

Out of 15 control subjects 12(80%) had normal BMD, 03(20%) cases had osteopenia. 09(22.5%) out 40 COPD patients had normal BMD, 14(35%) had osteopenia and 17(42.5%) had osteoporosis ( Table 1).

**Table 1:** BMD findings among control and COPD patients

| Groups | Normal | Osteopenia | Osteoporosis | Total | p value |
|---|---|---|---|---|---|
| Control | 12(80%) | 03(20%) | 00 | 15 | 0.000 |
| Patients | 09(22.5%) | 14(35%) | 17(42.5%) | 40 | |

Out of 12 moderate COPD patients 04(33%) had osteopenia 02(17%)) had osteoporosis and 06(50%) had normal BMD. Among 18 severe COPD patients 03(17%) had normal BMD, 08(44%) had osteopenia and 07(39%) had osteoporosis. 02(20%) out of 10 very severe COPD had osteopenia and 08(80%) had osteoporosis (Table 2).

**Table 2 :** BMD findings in different stages of COPD patients

| Groups | Normal | Osteopenia | Osteoporosis | Total |
|---|---|---|---|---|
| Mild COPD (FEV1 > 80%) | 00 | 00 | 00 | 00 |
| Moderate COPD (FEV1 < 80% but > 50%) | 06(50%) | 04(33%) | 02(17%) | 12 |
| Severe COPD (FEV1 < 50% but > 30%) | 03(17%) | 08(44%) | 07(39%) | 18 |
| Very severe COPD (FEV1 < 30%) | 00 | 02(20%) | 08(80%) | 10 |

There was statistically significant difference in T-score in all sites of BMD measurement. T score at the lumber spine of control was 0.18±0.94 and of COPD was -2.34±1.33 ( p value 0.00), T score at the left femoral neck of control was 0.25±1.06 of COPD patients was -2.10±1.11 ( p value 0.00), T score at the Rt femoral neck of control was 0.40±1.51 and of COPD patients was -2.22±1.59 T score at the left forearm of control was -1.00±0.41 of COPD patients was -3.26±1.76 (p value 0.00) (Table 3).

**Table 3:** T- score among control and COPD patients.

| Groups | T- score (mean±SD) Lumber spine | T- score (mean±SD) Left femoral Neck | T- score (mean±SD) Right femoral neck | T- score ( mean±SD) Left forearm |
|---|---|---|---|---|
| Control (15) | 0.18±0.94 | 0.25±1.06 | 0.40±1.51 | -1.00±0.41 |
| Patients (40) | -2.34±1.33 | -2.10±1.11 | -2.22±1.59 | -3.26±1.76 |
| p value | 0.00 | 0.00 | 0.00 | 0.00 |

**Discussion**

In the present study, there was an increased prevalence of osteopenia and osteoporosis (35% and 43% respectively) in COPD patients in comparison with the control group (20%) and statistically significant. These results matched the findings of Mansour O F *et al.*[27] These results were in agreement with that of the study carried out by Dubois *et al.*[28] in 2004. They found out of 86 patients with COPD 28% of patients had normal BMD, 50% of patients were osteopenic and 22% of patients were osteoporotic. These results were also in agreement with the results of the cross sectional study carried by Jorgensen *et al.* 29 (2007) on 62 COPD patients who found that 78% of patients had low BMD either osteopenic or osteoporotic.

In a similar study by Fouda MA *et al.*[30] in 2017 the prevalence of osteoporosis and osteopenia in were 36.5% and 34.6%, respectively. In COPD patients, the prevalence of osteoporosis was assumed to be two- to five-fold higher than that of age-matched individuals without airflow obstruction.[27] In a recently developed screening tool for men at risk for osteoporosis, the presence of COPD was found to be one of the parameters increasing this risk almost four-fold.[27]

Our study showed, there was a statistically significant difference in mean T score between COPD patients and controls at the lumber spine, right femur neck and left forearm (Mean±SD-2.34±1.33 vs 0.18±0.94, -2.22±1.59 vs 0.40±1.51, -3.26±1.76 vs -1.00±0.41 respectively). These results were in concordance with the results of the study carried by Lung Health Study Research Group (2004) on 412 COPD patients over 3 years,

revealing that BMD was much lower in COPD patients compared with normal individuals of the same sex and age.[31] More recent studies recruiting stable outpatients demonstrated that prevalence of low BMD (T-score $<-2.5$) was approximately 22%-42%.[20,18,32-36]

In the present study, there was a statistically significant difference between COPD patients and controls as regards DEXA scan results ($-2.34\pm1.33$ vs $0.18\pm0.94$ at lumbar spine and $-3.26\pm1.76$ vs $-1.00\pm0.41$ at left fore arm). It was revealed that the relative risk for osteopenia is by 0.33 in patients with moderate COPD and by 0.44 in those with severe COPD and the relative risk of osteoporosis increases by 0.17 in moderate COPD and by 0.39 in severe COPD, compared with normal individuals. These results were in agreement with those of Mansour O F *et al.*[27] These results can be explained as increase in COPD degree is associated with increase of risk factors that lead to occurrence of osteoporosis such as increased inflammatory load of COPD, using more corticosteroid treatment, decrease in pulmonary functions, and decrease in BMI.[37]

Sin *et al.*[38], also revealed that the risk for osteopenia increases by 30% in patients with moderate COPD and by 70% in those with severe COPD and the risk for osteoporosis increases by 2.1- fold in moderate COPD and by 2.8-fold in severe COPD, compared with normal individuals.

Our study showed that among patients with stage II COPD, 04 out of 12 had osteopenia, 02 out of 12 had osteoporosis. In patients with stage III COPD out of 18 patients 08 had osteopenia and 07 had osteoporosis. In 10 stage IV patients 02 had osteopenia and 08 had osteoporosis. So the prevalence of osteopenia and osteoporosis increased with increasing COPD severity. These results matched those of Mansour O F *et al.* [27]. EL Gazzar *et al.*[37], also reported in their study that the prevalence of osteoporosis was higher in COPD, increasing with increasing COPD severity. Warming *et al.*[39] in their study on changes in BMD with age in men and women found that in men there was a small longitudinal bone loss in the hip throughout life and a small bone loss in the distal forearm after the age of 50 years.

So there is increased prevalence of osteopenia and osteoporosis in patients with COPD and its prevalence increases with the advancing stages of COPD. So COPD patients particularly with stage II onwards should undergo BMD measurement by DEXA. Bisphosphonates should be given to these patients to avoid further respiratory compromise caused by VCFs and rib fracture.

## Conclusion

Osteoporosis is characterized by low bone mass and increased susceptibility to fracture. Studies show that osteoporosis may be a part of the extrapulmonary effects of COPD. If it occurs at the important area such as thoracic spine and ribs, the patients might develop breathing difficulty, decreased lung volume or restrictive ventilatory defects which then cause significant morbidity and impair quality of life. However, this condition could be alleviated by early detection and treatment, especially in a high-risk group of patients, to prevent further complications. This will improve the quality of life in COPD patients.

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