Clinical Prevalence of osteoporosis in Nepalese COPD patients

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ABSTRACT

INTRODUCTION: Osteoporosis is a systemic skeletal disease characterized by low bone mass and micro-architectural weakening of the bone. Osteoporosis is often undiagnosed, overlooked, and undertreated by patients and physicians. Osteoporosis is common in people with COPD. Present study aims to investigate the prevalence of osteoporosis in individuals with COPD.

METHODS: Total of 80 COPD patients admitted in Respiratory ward of Tribhuvan University Teaching Hospital, Kathmandu were included in this study. Demographic information of the patients, their BMI, smoking habit, use of steroid and diabetes as co-morbidity were recorded. They were categorized using Global initiative for chronic Obstructive Lung Disease (GOLD) criteria. All patients underwent for bone mineral densitometry (BMD) using quantitative ultrasound (QUS) from distal radius and anterior tibial crest. Status of the BMD in COPD patients with different severity according to the GOLD criteria, association of osteoporosis with other parameters was analyzed. Prevalence of vertebral fracture among the COPD patients was also noted.

RESULT: The mean age of the patients was 68.58± (9.389) years, and the male to female ratio was M: F = 1: 1.35. Out of 80 patients 68 (85%) were smoker, 24 (30%) were diabetic and 67 (83.8%) were taking glucocorticoids. Overall BMD was low in 82.5% (osteopenia in 56.25% and osteoporosis in 26.25%) of COPD patients. Osteoporosis was observed in 12.5 %, 30.2% 38.4% of patients with GOLD II, III and IV COPD respectively. Mean BMI of patients were 26.014± (3.600), 23.198± (3.020) and 21.428± (3.084) respectively in normal BMD, osteopenia and osteoporosis (P =0.000) groups. Number of smokers was significantly more in low BMD patients (P = 0.000). Diabetes mellitus was a co-morbid condition in 24 patients (30%); but it was not correlated with level of BMD (P = 0.927). Use of oral or inhale glucocorticoids was also not correlated with level of BMD (P=0.591). There were 5(10.8%) patients who had single level vertebral insufficiency fractures.

CONCLUSION: There is higher prevalence of osteoporosis in patients with COPD and it is directly correlated with severity of the COPD, smoking and BMI. Vertebral fracture may be one of the co-morbidity in COPD.

KEYWORDS: Bone mineral density; COPD; GOLD criteria; osteoporosis

INTRODUCTION

Osteoporosis is a systemic skeletal disease characterized by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility.[1] Despite the adverse effects of osteoporosis, it is a condition that is often overlooked and undertreated, in large part because it is so often clinically silent before manifesting in the form of fracture.[2]Gallup survey performed by the National Osteoporosis Foundation revealed that 86% of all women aged 45-75 years had never discussed osteoporosis with their physicians, and more than 80% were unaware that osteoporosis is directly responsible for disabling hip fractures.[3] The prevalence of osteoporosis is estimated to be 2 to 5 times higher in COPD patients as compared to healthy subjects.[4, 5]

Reduction of bone mineral density (BMD) in COPD has been found in about 50% of patients in several studies.[6,7] The degree of the loss of BMD has been found to be proportionate to the severity of the disease.[8] In a cross-sectional study, the prevalence of osteoporosis was 75% in patients with GOLD Stage IV disease and was strongly correlated with reduced FEV1.[8]The prevention of osteoporotic fractures and vertebral fractures particularly is important in COPD patients given the fact that fractures treatment pose an increased operative risk in COPD patients as compared to healthy subjects.[9,10]

Osteoporosis is a preventable disease that can result in devastating physical, psychosocial, and economic consequences. Prevention and recognition of the secondary causes of osteoporosis are first-line measures to lessen the impact of this condition.[11]

Prevalence of chronic obstructive pulmonary disease and osteoporosis individually has been well documented in studies,[9-11] but there are very limited data available for prevalence of osteoporosis in COPD patients available for South Asian countries and Nepal. Findings of this study can help our physicians and patients in optimizing their treatment and thus decreasing the burden of osteoporosis and its devastating consequences.

METHODS

This hospital-based prospective observational study was done in Tribhuvan University Teaching Hospital, a tertiary care referral centre of Nepal. 80 diagnosed case of COPD aged > 50 years were enrolled for the study after ethical clearance from Institutional Review Board. Patients aged < 50 and critically ill patients and with other serious co-morbid conditions were excluded from study. Patient's variable (Age, Sex, Body Mass Index, Pulmonary function test, history of Glucocorticoid use, Smoking, Diabetes Mellitus were recorded as per patient proforma.

The respiratory physicians of the hospital, on the clinical evaluation and investigations, diagnosed COPD. Patients were categorized in I mild, II moderate,III severe and IV very severe (GOLD criteria).[12] Bone mineral density was measured from the anterior tibial crest of leg and distal radius of forearm of the patients with the help of a broadband ultrasound bone densitometer.The system incorporates one ultrasound transducers positioned opposite metaphyseal region of distal radius in upper limb and anterior tibial crest in lower limb.The T-score quantifies the difference between the patient's BMD and the mean value for healthy young adults from the reference group. According to WHO, the normal value for T-score is within 1 SD of the mean value for young adults (–1 to +1). Osteopenia is considered when T-score is between –1 and – 2.5. Osteoporosis is considered to be present when the value for BMD is less than –2.5 SD below the mean for young adults. The lowest T-score at either region determined the diagnosis. Patients who complained of back pain underwent X ray of thoraco-lumbar spine antero-posterior and lateral view to look for vertebral fractures. Vertebral fractures were classified according to their shape: wedge (reduction in anterior height), biconcave (reduction in middle height) or crush (reduction in posterior height).[10]

The selected data were analyzed with the help of SPSS (Statistical package for social science) version 20.0. Percentage, mean, standard deviation were calculated. The appropriate statistical tests were used. Values of P = < 0.05 were considered significant with confidence level of 95% throughout the study

RESULT

The mean age of the patients was 68.58± (9.389) years, ranged from 50 to 90 years of age; 34 male (42.75%) and 46 female (57.5%). The male to female ratio was M: F = 1: 1.35. Out of 80 patients 68 (85%) were smoker, 24 (30%) were diabetic and 67 (83.8%) were taking glucocorticoids. Overall BMD was found to be normal in 14 (17.5%) (mean T score 2.092±1.064435), 45(56.25%) patients were osteopenic (mean T score -2.04889±.438812), and 21 (26.25%) patients (mean T score-3.27143±.86031) had osteoporosis. (Table1)

According to the GOLD criteria, 24 had Grade II (30%), 43 Grade III (53.8%) and 13 (16.2%) had Grade IV COPD. Of 24 grade II COPD patients 11(45.8%) had normal BMD, 10(41.6%) were osteopenic, 3(12.5%) were osteoporotic. Among 43 patients with grade III COPD, 3 (7%) had normal BMD, 27(62.7%) had osteopenia and 13(30.2%) had osteoporosis. Eight (61.5%) patients had osteopenia and 5(38.4%) patients had osteoporosis among 13 cases with very severe COPD. None of them had normal BMD. These differences were statistically highly significant (P = 0.000). As the grade or severity increased number of patients suffering from decreased bone mass density increased. (Table 2)

Table 1: COPD grades with Overall BMD

Variables		COPD grades with Overall BMD			p-values
		Normal (14)	Osteopenia (45)	Osteoporosis (21)	
COPD Grade	II	11	10	3	0.000 (Chi-square Test p-value)
	III	3	27	13	
	IV	0	8	5	

Table 2: COPD grades with Severity

Variables		COPD grades with Overall BMD			Severity		p-values
		Normal (14)	Osteopenia (45)	Osteoporosis (21)	Total (80)	% osteopenia+ osteoporosis	
COPD Grade	II	11	10	3	24	54%	0.000 (p-value)
	III	3	27	13	43	93%	
	IV	0	8	5	13	100%	

Mean BMI of patients were 26.014± (3.600), 23.198± (3.020) and 21.428± (3.084) respectively in normal BMD, osteopenia and osteoporosis (P =0.000) groups.

Seven (50%), 40(88.8%) and 21(100%) patients were smoker among those with normal BMD, osteopenia and osteoporosis respectively, and this was significant (P = 0.000).

Diabetes mellitus was a co-morbid condition in 24 patients (30%); 4 (5%) patients were with normal BMD, 13 (16.25%) had osteopenia and 7 (8.75 %%) had osteoporosis. This was not statistically significant (P = 0.927). Most of the patients were taking oral or inhale glucocorticoids, of them 13(16.25%) had normal BMD, 37(46.25%) were osteopenic and 17(21.25%) had osteoporosis. (P=0.591)

Out of 80 patients, 43(53.75%) complained of back pain and thus underwent X-ray of thoraco-lumbar spine. There were 5(10.8%) patients who had vertebral insufficiency fractures. Among them 2 patient were in osteoporosis group and 2 patient in osteopenia group and 1 patient in normal BMD group. (Table 3) All the patients had single level fractures.

DISCUSSION

COPD, a chronic inflammatory airway disease, is projected to be the third leading cause of death in the world in this decade.[1]This condition is associated with various systemic comorbidities including osteoporosis, but the mechanisms by which osteoporosis develops are debated.[13,14] COPD and osteoporosis are strongly associated because of common risk factors such as age, smoking, and inactivity.[7] The pathogenesis of osteoporosis in COPD is multifactorial, including progressive reduction in physical activity, low BMI, changes in body composition, pharmacologic treatments, and systemic inflammation.[7]

We studied prevalence of osteoporosis in 80 COPD patients admitted in our hospital. In this study there was significantly higher prevalence of lower BMD (56.25% of the COPD patients were osteopenic and 26.25% were osteoporotic only 17.5% were having normal BMD). In a similar study by Bhattacharya.P et al.[5]in India using quantitative ultrasound, 51.35% were osteopenic and 21.62% of the patients had osteoporosis. However, in another study

by Hattiholi et al.[15] in Indian population using DEXA scan more patients were detected to have osteoporosis (66.6%) and osteopenia (19.6%). Gupta RK et al.[16] used DEXA scan to measure bone loss in Saudi Arabian COPD cases and found 65.3% osteoporotic and 28.57% osteopenic patients. This may be attributable to better result of DEXA scan for measurement of BMD. But our findings are similar to the Egyptian study by EL-Gazzaret al.[17] and Thai study by Rittayamai N et al.[18] using DEXA. The National Health and Nutrition Examination Survey (NHANES) done by John Hopkins University demonstrated a 16.9% prevalence of osteoporosis in 995 COPD subjects and an 8.9% prevalence in 14,828 non-COPD subjects aged 45 years or older.[19]

More than 4/5th of our patients had severe COPD (GOLD III and IV), and it was proportionate to the degree of bone mass loss. This finding is in acceptance to a previous study done by RQ Graumam et al[8] reporting that BMD was lower in GOLD III and IV than in GOLD I and II COPD patients. However, the prevalence of osteoporosis was not significantly different after stratification of COPD in Dutch population.[20] Age, body mass index (BMI), and parathyroid hormone (PTH) level were significant independent correlates for osteoporosis.[14]

Age of the patients, their BMI, smoking habit, use of corticosteroids and co morbidity like DM are other factors responsible for osteoporosis and were studied. The mean age of our patients was 68.58± 9.389 years which is comparable to the COPD patients with osteoporosis in Brazil[4] and in India.[5] There was female predominance (M: F = 1:1.35) in this study. Smoking, though the mechanism is poorly understood, has long been recognized as an independent risk factor for osteoporosis and COPD, but the effect appears to be dose-dependent.[21]Positive history of smoking was noted in 68 patients (85%); 89% of patient with osteopenia and 100% with osteoporosis were smoker in our series (P<0.000). In Nepal, prevalence of smoking and tobacco use is 56.5% in men and 19.5% in women, which is higher in comparison to other countries.[22]Furthermore Nepalese female are prone to suffer from respiratory diseases because of use of wood fire for cooking.[22]Positive correlation between low bone mineral density and smoking was found in study done by few studies.[23]Bari et al.[24] studied prevalence of osteoporosis among Bangladeshi male smokers and found that COPD patients were 4.5 times more likely to develop osteoporosis than controls after adjusting age, smoking-pack years and BMI.

BMI value of the patients was directly co related with BMD level. Patients with lower BMI were osteoporotic (normal BMD group - BMI 26.014 ± 3.600 kg/m^2, osteopenia - 23.198 ±3.020kg/m^2 and osteoporosis 21.428-±3.084 kg/m^2). In a meta-analysis with pooled global prevalence from 58 studies, Chen et.al[11] found significant risk factors for osteoporosis in COPD patients were BMI < 18.5 kg/m2 (OR, 4.26) and the presence of sarcopenia (OR, 3.65). Bolton C.E at al.[25] recommended both % IBW (ideal body weight) and BMI as useful anthropometric measurements identifying those with osteoporosis. BMI of our COPD patients with osteoporosis is rather better; however it was proportionately lower in osteoporotic patients than in osteopenic and patients with normal BMD. Decreased physical activity due to frequent exacerbation and chronic lung condition may be responsible for both reduction in BMI and BMD.[12,13]

Oral and inhaled corticosteroids are widely used in COPD patients for the prevention and treatment of exacerbations. Corticosteroids are well known for their ability to induce osteoporosis. Systematic review and meta-analysis of randomized controlled trials and observational studies by Loke Y.K et al.[26] confirmed that the use of inhaled corticosteroids was associated with an increased risk of fracture. In present study, use of steroid was not directly associated with lower BMD. In the TORCH study[27], which included 658 patients done on European population, the use of inhaled corticosteroids had no effect on bone mineral density over a period of 3 years. Study in Indian population[5] found no correlation between glucocorticoid use and osteoporosis and osteopenia. Controversy still exists on the role of corticosteroids in bone

loss. Corticosteroid use may not fully account for the low BMD in COPD patients; the risk of osteoporosis may be more related to the COPD severity.[2]

There were 5(10.8%) patients with vertebral fractures, 4 of them were present in decreased BMD group. Study done in 350 American COPD patients Carter JD et al.[30] found vertebral fractures in 9(2.6%) patients. In a Brazillian study[4] the frequency of vertebral fractures was 18.6% in the COPD group and 9.0% in control group (p = 0.06); and the frequency of reported falls causing fracture was 36.3% in the COPD group and 7.3% in control group (p = 0.001). Thus they concluded that COPD patients present a high frequency of osteoporosis and falls seem to be an important factor for vertebral fracture. Slightly more vertebral fracture was found in male patients with COPD in another study, and the age was said to be the main predictor of vertebral fractures (OR = 1.164 (1.078–9.297).[8] Screening for osteoporosis in patients with COPD and appropriate treatment can prevent osteoporotic fracture, which may lead to improved quality of life as well as better long-term prognosis.[7]

In present study, 24(30%) patients also had diabetes mellitus (DM) as co-morbid condition of COPD. However, it was not correlated with severity of bone loss. The exact mechanism is not known, but systemic inflammation (with elevated markers such as CRP, TNF-a and IL-6) plays an important role in both the progression of COPD and the development of insulin resistance causing increased risk of developing type 2 diabetes.[28]Elevated TNF-α and Interleukin-1 stimulate the differentiation of macrophages into osteoclasts via mesenchymal cells releasing receptor activator of nuclear factor-k B ligand, a member of the TNF-α superfamily.[29] High levels of TNF-α are found in osteoporosis associated with both post-menopausal states and COPD.[29] The above findings may explain the high prevalence of diabetes and decreased bone mass in the present study.

Present study is a non-randomized study with a small sample size; findings may not represent the variation in the general population. Patients with COPD were screened using qualitative ultrasound of distal radius and anterior tibial crest, which is not regarded as the gold standard for the measurement of bone mineral density.

Further randomized multicenter studies are needed to significantly establish the correlation of COPD with osteoporosis in Nepalese population. Quantitative ultrasound may be used as screening for bone mineral density but Dexa scan is necessary to diagnose osteoporosis.

CONCLUSION

Present study identifies a high prevalence of osteopenia and osteoporosis in patients with COPD. There were positive correlations between bone mineral density with tobacco smoking and BMI. It did not find a correlation between bone mineral density with glucocorticoid intake, and diabetes mellitus. Patients with COPD should be screened for osteoporosis and contributing risk factors and should be treated before severe consequences happen.

Conflict of interest: None

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