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INCIDENCE OF OSTEOPOROSIS IN PATIENTS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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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 Pakistan.*

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

Materials & Methods: *This was a cross sectional observational study. COPD patients were recruited from the Medicine department of Allied Hospital Faisalabad for one-year duration from June 2019 to June 2020. 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 and 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 Pakistani 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 and there is a chronic inflammatory response in the airways and the lungs[1-2]. COPD is currently the fourth leading cause of death in the world. But it is projected to be 3rd leading cause of death by 2020[3-4]. Morbidity and mortality in case of COPD is increasing day by day all over the world as well as in Pakistan. Current estimates suggest that 80 million people worldwide suffer from moderate to severe disease.[5-6] 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. The prevalence of COPD is directly related to tobacco smoking, biomass, cooking habits and socio-economic status. As Pakistan is a developing country and smoking is much prevalent here, more over smoke pollution and cooking habits in Pakistan rural areas play an important role in developing COPD[8]. The prevalence of COPD in Pakistan is 13.5 % by GOLD criteria it is more prevalent in rural than urban area and male are more affected than female. But recently prevalence is increasing in female due to increased life expectancy. COPD is not confined to only lungs it has many systemic effects with widespread co-morbidities like weight loss, depression, cardiac disease, and osteoporosis. Osteoporosis is characterized by reduced bone mass and micro-architectural deterioration of bone tissue with a consequent increase in bone fragility. 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 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. If osteoporosis affects thoracic spine eventually vertebral compression collapse which can causes kyphosis as result develop breathing difficulty and decreased lung volume. Hip fractures cause significant morbidity such as pain, decreased mobility 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. However, there are currently no studies regarding the prevalence of osteoporosis in patients with COPD in Pakistan. The purpose of this study is to determine the prevalence of osteoporosis in COPD patients.

MATERIALS AND METHODS:

This cross-sectional observational study was conducted at the Medicine department of Allied Hospital Faisalabad for one-year duration from June 2019 to June 2020. COPD patients recruited or admitted for an acute exacerbation. The inclusion criteria were previously diagnosed or newly diagnosed COPD. Patients were excluded if they had asthma, any disease affecting bone and calcium homeostasis, or were receiving medications related to bone metabolism (eg, hormone replacement therapy, bisphosphonates, calcium or vitamin D supplements, and a recent oral corticosteroid), use of inhaled corticosteroids, alcohol consumption, history of menopause in women, co-morbidities, duration of treatment, long-term home oxygen therapy, body mass index, treatment history, admission to hospital. Blood was collected for complete blood count, kidney function test, CRP, phosphate, albumin, parathyroid hormone levels. A chest x-ray was performed to rule out concomitant lung cancer and an x-ray of the lumbosacral spine to assess osteopenia or vertebral collapse. Echography was performed to rule out chronic heart failure. Spirometry was performed according to the recommendations of the American Thoracic Society. The current study involved a total of 30 COPD patients with BMD measurements. We classified the severity of COPD according to the GOLD guidelines. Bone mineral density (BMD; g / cm2) was performed using a dual energy x-ray absorptiometry scan (DXA scan) in the second to fourth lumbar (L2-4) and femoral neck. Measurement of BMD by DXA scanning is the gold standard and highly accurate technique for the diagnosis of osteoporosis in accordance with the recommendations of the World Health Organization (WHO). The BMD measurements in the DXA scan were expressed as T-score compared to a young normal control population of the same age, sex and race. T-scores above -1.0 were normal, from -1.0 to -2.5 for osteopenia, and below -2.5 for osteoporosis. The lowest T-score at the L2-4 level or at the femoral neck determined the diagnosis of osteoporosis. No data or information has been collected without the consent of the participants. Participants were encouraged to participate voluntarily in the study. Consent was obtained after presenting all respondents with a short study in Bengali. Confidentiality was ensured and anonymity was maintained; special care should be taken to ensure that no participant can be identified in any report or publication within this study. All statistical analyzes were performed using the SPSS version 25 software package.

RESULTS:

Thirty patients had a mean age of 63.47 ± 8.45 years, age in the normal group 58.23 ± 7.77 and age in the osteoporotic group 67.47 ± 6.672. The male to female ratio was 28: 2 (Table I). Overall, 2 people had not smoked before (6.7%), but 17 (56.7%) and 11 (36.7%) were current and former smokers, respectively. BMI in the whole group was n = 30, mean ± SD 23.09 ± 4.82, while in the group with osteoporosis it was 20.83 ± 2.29 (Tab. I). There were 0 (0%), 6 (20%), 18 (60%), and 6 (20%) patients with COPD grades I, II, III, and IV GOLD, respectively. The mean FEV1 was 44.45 ± 14.64 (Table II). A total of ten patients were currently using inhaled corticosteroids (33.3%), while twelve (40%) had never used inhaled steroids (Table I). The BMD findings were (a) normal in 6 patients (20%) (mean T-score for the normal lumbar spine -1.23 ± 0.65 and hip -1.35 ± 0.56). In turn, osteoporosis in 17 patients (56.7%) (the mean T-score of the lumbar spine and hip joint was -2.40 ± 1.40 and -3.3 ± 0.47, respectively (Table III). Overall frequency of osteoporosis in patients with COPD, it was 56.7%.

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%)

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%)

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-established hypothesis about the pathophysiology of the development of osteoporosis in COPD. Most of the literature suggests that it is multifactorial, including progressive reduction in physical activity, low BMI, drug treatment, systemic inflammation, and hypogonadism. We assessed the frequency of osteoporosis in COPD patients and found 56.7%[9-11]. The result of our study was higher than in the previous three studies involving patients with COPD. In the first study by Graat-Verboom L et al. the incidence of osteoporosis was 21% and osteopenia was 41% in COPD patients, and the mean FEV1 was 42.1% predicted. The second, Ferguson TG and colleagues from the TORCH study found that the incidence of osteoporosis and osteopenia in moderate and severe COPD patients was 23% and 42%, respectively[12]. A recent study by Jorgensen NR et al found that the incidence of osteoporosis and osteopenia in severe COPD patients was 44.8% and 23.3%, respectively. In a recent systematic review, the overall mean incidence of osteoporosis in COPD patients was 35% and the osteoporosis correlates were mainly measuring of body composition, disease severity and corticosteroid use. Women are more likely to develop osteoporosis[12-13]. Since the three studies above included people of both sexes, the overall incidence of osteoporosis and osteopenia was so high. In Pakistan, COPD is not very common in women, so the overall rate of osteoporosis should not be as high in the studies, but interestingly, the incidence of osteoporosis is higher than in the previous study. This could be due to older age or the severity of COPD affecting outcomes[14]. We found significant positive correlations between osteoporosis and BMI (p-value 0.004) and CRP (p-value 0.043). Low BMI is a risk factor for osteoporosis. We found that height was not positively correlated (p-value 971) with osteoporosis, but that overall BMI was positively correlated with osteoporosis (p-value .004). Several studies support the relationship between bone mineral density and BMI. Osteoporosis is less common in obese people. In another cross-sectional study, overweight and obesity showed a significant protective effect in osteoporosis. Osteoporosis is a recognized side effect of long-term systemic corticosteroid treatment, but there is little or no inhalation corticosteroid. In the TORCH study, they did not find any significant differences between the two groups that used the inhaled steroid for 3 years and placebo, respectively. In the EUROSCOPE study, they found no significant change in BMD at L2-4 and femoral neck in 912 patients with mild COPD who received 800 mcg / day of budesonide or placebo for 3 years. Therefore, long-term treatment with corticosteroids may have little or no effect on BMD in COPD patients. On the contrary, a meta-analysis of randomized controlled trials (16 studies) and observational studies (7 studies) showed that ICS use was associated with a modest but statistically significant risk factor for fractures in patients with COPD at the dose of ICS (over 700 micrograms / day) increase the risk of non-vertebral fractures[15]. Hence, the actual incidence of osteoporosis in the entire COPD population cannot be estimated from our observations. As the majority of our volunteers are male n = 28, we could not gather any information on the BMD of women with COPD in our community. With a small number of subjects, it is not possible to make any comparison between the healthy group and the group with osteoporosis.

CONCLUSIONS:

Osteoporosis is underdiagnosed in COPD patients, although the incidence of osteoporosis was very high in COPD patients in Pakistan. We found a significant correlation between bone mineral density and BMI, physical activity. We found no relationship between

bone mineral density and the steroid inhaler. Therefore, BMD screening should be considered in COPD patients with a low BMI.

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