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ORIGINAL ARTICLE

Bone Mineral Density among Chronic Obstructive Pulmonary Disease Patients Admitted in a Tertiary Level Hospital

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Abstract:

Background: *Chronic obstructive pulmonary disease (COPD) is a major cause of chronic morbidity and mortality throughout the world. It is a preventable and treatable disease with significant extrapulmonary manifestations that may contribute to the severity in individual patients. Osteoporosis is an important systemic feature of COPD and causes significant morbidity. Osteoporosis gradually worsens as the COPD progresses. This study was undertaken to investigate the relationship between BMD and disease severity of COPD patients.*

Objective: *To evaluate the status of BMD among patients with COPD.*

Methods: This was an observational descriptive cross-sectional study carried out in Departments of Medicine of Sir Salimullah Medical College & Mitford Hospital, from July 2017 to December 2017. According to inclusion and exclusion criteria, a total of 50 COPD patients were selected and their BMD was done.

Results: *Of the 50 patients, on the basis of BMD femoral neck t- score, 100% of very severe & severe COPD patient had osteoporosis, 15% of moderate COPD patients had osteoporosis, while mild COPD patients had no osteoporosis. And also, on the basis of lumber spine t-score, osteoporotic changes were highest among very severe COPD patients (100.0%) which reduced with the reduction of severity of COPD while osteopenia was highest among mild and moderate COPD patients. Mean of BMD femoral neck t-test was lowest among very sever COPD patients (-3.21± 0.16) and highest among mild COPD patients (-1.37± 0.83). ANOVA test revealed that this mean difference was significantly associated (p=<0.001, F= 29.07).*

Mean of BMD lumber neck t-test was lowest among very sever COPD patients (-3.53± 0.69) and highest among mild COPD patients (-1.16± 0.51). ANOVA test revealed that this mean difference was significantly associated (p=0.012, F= 4.04).

Conclusion: *BMD alterations are common in COPD patients. A high proportion of patients with COPD experience a significant bone loss which is associated with increased morbidity and mortality. Such patients should be provided with adequate preventive & curative therapy of osteoporosis for better survival.*

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Introduction:

Chronic obstructive pulmonary disease (COPD) is a disease characterized by nonreversible airflow obstruction. Although the main symptoms originate from the respiratory system, COPD is considered a systemic disease.[1] Chronic obstructive pulmonary disease (COPD) is a major cause of mortality worldwide.[2] In the care of patients with COPD, the primary focus of the physician is respiratory function. However, as COPD progresses and the patient becomes more debilitated, osteoporosis is a common finding.[3] COPD not only involves the lungs but also causes extra-pulmonary abnormalities with systemic features, such as, for example, cachexia, fluid water retention and skeletal muscle wasting. Osteoporosis is also an important systemic feature of COPD.[4]

Osteoporosis is a systemic skeletal disease characterized by a low bone mineral density (BMD) and micro architectural changes in bones, leading to increased bone fragility and, increased fracture risk.[5] Osteoporotic fractures cause many symptoms and complications, including the impairment of ventilation, and create a heavy economic burden.[5] To predict the risk of osteoporotic fractures, measurements of bone mineral density (BMD) have been widely used[6] and it has been reported[7] that BMD is lower in COPD patients than in healthy subjects. Thus, it is important to evaluate BMD in the management of COPD.[4]

A bone mineral density test uses X-rays to measure the amount of minerals - namely calcium - in bones. This test is important for people who are at risk for osteoporosis, especially women and older adults.[8] Decreased Bone Mineral Density (BMD), which occurs with age, is an important health problem among elderly persons, contributing to disability and premature mortality. Decreased BMD has also become an important socio-economic issue. Decreased BMD may result in osteopenia and osteoporosis, of which the latter is more serious. An Osteoporosis Risk Assessment study has confirmed that the risk of fracture increases with decreasing BMD.[9] Previous studies reporting osteoporosis in 24-44% of patients with COPD. The aetiology of this loss is likely to be due to multiple factors including female sex, corticosteroid (CS) therapy, smoking, physical de-conditioning, vitamin D deficiency, hypogonadism and chronic systemic inflammation.[10] Although a low BMD is often asymptomatic, subsequent vertebral fractures may further compromise lung function,[11] while hip fractures decrease mobility and increase the mortality risk.[2] Traditionally, loss of BMD, and osteoporosis in particular, have been considered "late manifestations" related to cumulative oral CS treatment of airways disease.[12] However, significant loss of BMD occurs in mild airways obstruction[9] and vertebral fractures have been reported in a high proportion of CS naive men with COPD. That said, BMD is only one, albeit important, contributory cause of vertebral fractures, and other factors for e.g. heavy lifting, may play important roles.[2]

Those patients requiring oral glucocorticoid therapy have lower T scores and more fractures than those treated with bronchodilators only. Patients receiving oral glucocorticoid therapy (average [±SD] cumulative dose, 19.5 ± 24.8 g) have been found to have a 1.8-fold (95% confidence interval [CI], 1.08 to 3.07) increased incidence of one or more vertebral fractures. However, glucocorticoid use does not fully account for the low BMD in these patients.[3]

Smoking has been shown to be an independent risk factor for osteoporosis in both men and women.[13] Reported that lumbar spine BMD was 12% lower in smokers who have smoked 20 pack-years compared to nonsmokers.[14] Several groups have confirmed the finding of a significantly greater rate of bone loss in smokers. The combination of tobacco and alcohol use markedly increases the risk for osteoporosis. Alcohol use has been shown to be independently related to bone loss in a dose-dependent manner.[3]

The gold standard of measuring bone density is dual energy X-ray absorptiometry (DXA). Currently, the method is the examination of choice for diagnosis and follow-up of patients with osteoporosis, as proposed by the International Society for Clinical Densitometry, because of its worldwide availability, low radiation dose, and results' reproducibility.1 However, the technical drawbacks of this method are well acknowledged[15] as DXA is a two-dimensional method assessing bone mineral density (BMD), superimposed tissue may cause artifacts and inaccurate measurements.[1]

We planned to assess the BMD status among COPD patients in a tertiary level hospital

Materials and Methods:

The research has been undertaken with the objective to estimate status of Bone mineral density among Chronic Obstructive Pulmonary

Disease patients admitted in a tertiary level hospital. For achieving the objectives this study have been conducted systematically methodically.

Inclusion criteria:

1. Patient diagnosed as COPD according to clinical and spirometric findings
2. Age more than 18 years
3. Both sexes
4. Agreed to give informed written consent.

Exclusion criteria:

(1) History of pulmonary tuberculosis;
(2) History of chest surgery
(3) COPD with bronchial carcinoma
(4) Disease or durg that may interfere BMD, such as- diabetes mellitus, chronic kidney disease, systemic lupus erythematosus, rheumatoid arthritis, steroid.
(5) Unwilling to give written consent

Operational definition:

COPD:

COPD was confirmed on spirometric examination, when post bronchodilator FEV1 /FVC< 0.70

Severity of COPD:

COPD is divided into five stages according to the severity by GOLD (Global Initiative For Chronic Obstructive Pulmonary Disease) criteria.

GOLD stages of COPD:

Stage	Severity	FEV1
I	Mild	FEV1 /FVC< 0.70 FEV1 ≥80% predicted
II	Moderate	FEV1 /FVC< 0.70 FEV1 50-79% predicted
III	Severe	FEV1 /FVC< 0.70 FEV1 30-49% predicted
IV	Very Severe	FEV1 /FVC< 0.70 FEV1 <30% predicted or FEV1 <50% predicted if respiratory failure present

BMD:
The BMD will be expressed as an absolute value and as a T score (standard deviations from a young).
Osteoporosis will be defined as a T score less than -2.5
Osteopenia as T score less than -1 but greater than -2.5.

Results and Observation:

This study was intended to investigate the relationship between COPD and osteoporosis. To achieve this goal, 50 COPD patients attended in Sir Salimullah Medical College Mitford Hospital were selected as per inclusion and exclusion criteria. Complete history was taken, physical examination and spirometric examination was done for confirmation & staging of COPD and then BMD was done.

Table-I

Age distribution of COPD patients (n=50)

Age groups (years)	Numbers of patients	Percentage
<40	None	0%
40-49	11	22%
50-59	18	36%
60-69	15	30%
≥70	6	12%
Total=	50	Total=100%

All the patients were above 40 years of age, mean age was 56 years, maximum 66% patients were in 50-69 years of age, 22% patients were below 50 years & only 12% were above 70 years of age.

Table-II

Sex distribution of COPD patients (n=50)

Sex groups	Number of patients	Percentage
Male	47	94%
Female	3	6%
	Total=50	Total=100%

Maximum of the respondents were male (94.0%) and 6.0% of the respondents were female.

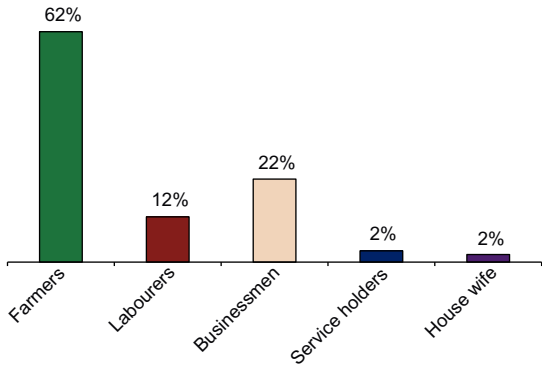

Fig.-1: *Distribution of COPD patients according to occupation (n=50)*

Among COPD patients 62%(31) were farmers, 12%(6) were labourers, 22%(11) were businessman, 2%(1) were service holder and 2%(1) were housewife

More than half of the respondents were illiterate and 32.0% of the respondents completed primary education and only 8.0% of the respondents completed secondary education.

So, COPD found to be more prevalent among less educated persons.

About half of the respondents had income below of 15000 tk per month while 22% of the respondents had income between 15000 - 29999tk and 24% of the respondents had income between 30000 - 49999.

Table-III

Distribution of the respondents by smoking (n=50)

Smoking	Number	Percentage
Present smoker	45	90.0%
Nonsmoker (exposed to biomass fuel)	2	4.0%
Ex-smoker	3	6.0%
Total	50	100.0%

Maximum of the respondents were smoker (90.0%) while only 6.0% of the respondents had past history of smoking and 4.0% had no history of smoking but they were exposed to biomass fuel.

Table-IV

Distribution of COPD patients according to amount of smoking (n=50)

Pack year	Number of patients	Percentage
<10	0	0%
10-20	16	32%
>20	34	68%
	Total =50	Total =100%

68% (34) patients had smoked more than 20 pack year and 32% (16) had smoked 10-20 pack year. Mean amount of smoking was 20 pack year.

Table-V

Common presenting symptoms of COPD patients (n=50)

Symptoms	Number of patients	Percentage
Breathlessness	48	96%
Chronic cough	43	86%
Sputum product	35	70%

96% (48) COPD patients presented with breathlessness, 86% (43) patients presented with breathlessness and 70% (35) patients presented with chronic sputum production.

Table-VI

Common physical signs COPD of patients (n=50)

Signs	Number of patients	Percentage
Barrel shaped chest	17	34%
Edema	10	20%
Cyanosis	05	10%
Wheeze	43	86%
	Total=50	Total=100%

On clinical examination, 34%(17) patients had barrel shaped chest, 20%(10) patients had edema, 10%(05) patients had cyanosis and 86%(43) patients had wheeze.

Table-VII

Distribution of the respondents by severity of COPD (n=50)

Stages of COPD	Number	Percentage
Very Severe FEV1 <30%	6	12%
Severe FEV1 ≥30%,<50%	16	32%
Moderate FEV1 ≥50%, <80%	20	40%
Mild FEV1 ≥80%	8	16%
Total	50	100%

Table-VIII

Relation between severity of COPD and amount of smoking (n=50)

Pack year	Number of patients	Very severe COPD	Severe COPD	Moderate COPD	Mild COPD
<10	0	0	0	0	0
10-20	16(100%)	0	1 (6%)	5 (31%)	10 (63%)
>20	34(100%)	23 (67%)	9 (27%)	2 (6%)	0
	Total =50				

Among our respondents 40.0% of them were in moderate stage, 16.0% of them were in mild stage, 32.0% of them were in severe stage and only 12.0% of them were in very severe stage.

Patients who smoked >20 pack year, 67% of them was suffering from very severe COPD, 27% severe COPD & 6% had moderate COPD. Patients who smoked 10-20 pack year 63% had mild COPD, 31% had moderate COPD & 6% had severe COPD. There was no patient of <10 pack year.

Table-IX

Relationship between severity of COPD & mean amount of smoke pack year (n=50)

Stages of COPD	Number of patients	Mean amount of smoke pack year
Very Severe FEV1 <30%	6	28
SevereFEV1 ≥30%,<50%	16	22
Moderate FEV1 ≥50%, <80%	20	16
Mild FEV1 ≥80%	8	14
Total	50	

Among our respondents mean amount of smoking was highest (28 pack year) in very severe COPD patients and lowest (14 pack year) in mild COPD patients.

Table-X

Distribution of the respondents by BMD Femoral neck t-score (n=50)

BMD Femoral neck t-score	Number	Percentage
Osteoporotic t-score < -2.5	25	50%
Osteopenia -2.5 < t-score < -1	20	40%
Normal t-score > -1	05	10%
Total	50	100%

Among our respondents 42.0% of them had Osteoporotic while 38.0% of them were osteopenia of femoral neck and rest of them (20.0%) was normal.

Table –XI

Distribution of the respondents by BMD Lumber Spine t-score (n=50)

BMD Lumber Spine t-score	Number	Percentage
Osteoporotic t-score < -2.5	26	52%
Osteopenia -2.5 < t-score < -1	17	34%
Normal t-score > -1	07	14%
Total	50	100%

Among our respondents, on the basis of BMD lumber spine t- score, 52%(26) were Osteoporotic, 34%(17) were osteopenic and 14%(7) were normal.

Very severe COPD & severe COPD had osteoporosis 100%. Patient with moderate COPD- 15% had osteoporosis, 17% had osteopenia & 15% had normal BMD. Patient with mild COPD- 75% had osteopenia, 25% had normal BMD. Chi-square test revealed that this difference were statistically significant (p=<0.001).

Table-XII

Relationship between BMD (BMD Femoral neck t-score) and Stages of COPD (n=50)

Stages of COPD	BMD			Mean t-score	P value
	Osteoporotic	Osteopenia	Normal		
Very Severe (6)	6 (100%)	0 (0%)	0 (0%)	-3.21 (±0.16)	<0.001
Severe (16)	16 (100%)	0 (0%)	0 (0%)	-2.90 (±0.32)	
Moderate(20)	3 (15%)	14 (70%)	3 (15%)	-1.80 (±0.66)	
Mild (8)	0 (0%)	6 (75%)	2 (25%)	-1.37 (±0.83)	
TOTAL (50)	25 (52%)	20 (34%)	5 (10%)		
			$\chi^2 = 23.403$		

Table-XIII

Relationship between BMD (BMD Lumber Spine t-score) and Stages of COPD (n=50)

Stages of COPD	BMD			Mean t-score	P value
	Osteoporotic	Osteopenia	Normal		
Very Severe (6)	6 (100%)	0 (0%)	0 (0%)	-3.53 (±0.69)	
0.012					
Severe (16)	12 (75%)	3 (18.8%)	1 (6.3%)	-2.56 (±2.03)	
Moderate (20)	8 (40%)	10 (50%)	2 (10%)	-2.19 (±0.83)	
Mild (8)	0 (0%)	4 (50%)	4 (50%)	-1.16 (±0.51)	
TOTAL (50)	26 (52%)	17 (34%)	7 (14%)		
			$\chi^2 = 23.403$		

Very severe COPD had osteoporosis 100%. Patient with severe COPD- 75% had osteoporosis, 18.8% had osteopenia, 6.3% had normal BMD. Patient with moderate COPD- 40% had osteoporosis, 50% had osteopenia & 10% had normal BMD. Patient with mild COPD- 50% had osteopenia, 50% had normal BMD. Chi-square test revealed that this difference were statistically significant (p=<0.001).

Table-XIV

Statistical relationship between BMD of femoral neck & Lumber spine (t-score) with stages of COPD (n=50)

	Stages of COPD	Mean t-score	SD	F value	P value
BMD Femoral neck t-score	Very severe	-3.21	0.16	29.07	< 0.001
	Severe	-2.90	0.32		
	Moderate	-1.80	0.66		
	Mild	-1.37	0.83		
BMD Lumber Spine t-score	Very severe	-3.53	0.69	4.04	0.012
	Severe	-2.56	2.03		
	Moderate	-2.19	0.83		
	Mild	-1.16	0.51		

Mean of BMD femoral neck t-test was lowest among very sever COPD patients (-3.21± 0.16) and highest among mild COPD patients (-1.37± 0.83). ANOVA test revealed that this mean difference was significantly associated (p=<0.001, F= 29.07).

Mean of BMD lumber neck t-test was lowest among very sever COPD patients (-3.53± 0.69) and highest among mild COPD patients (-1.16± 0.51). ANOVA test revealed that this mean difference was significantly associated (p=0.012, F= 4.04).

Discussion:

Chronic Obstructive Pulmonary Disease (COPD) is a leading cause of morbidity and mortality world-wide and leads to an economic and social burden that is both substantial and increasing. Prevalence and morbidity data greatly underestimate the total burden of COPD because the disease is usually not diagnosed until the patients already have had symptoms for some time and the disease is then often already quite advanced.

Osteoporosis is a systemic skeletal disease characterized by a low bone mineral density (BMD) and micro architectural changes in bones, leading to increased bone fragility and increased fracture risk.[5] Osteoporotic fractures cause many symptoms and complications, including the impairment of ventilation, and create a heavy economic burden.[5] To predict the risk of osteoporotic fractures, measurements of bone mineral density (BMD) have been widely used[6] and it has been reported[7] that BMD is lower in COPD patients than in healthy subjects. Thus, it is important to evaluate BMD in the management of COPD.[4]

A bone mineral density test uses X-rays to measure the amount of minerals — namely

calcium — in bones. This test is important for people who are at risk for osteoporosis, especially women and older adults.[8] Decreased Bone Mineral Density (BMD), which occurs with age, is an important health problem among elderly persons, contributing to disability and premature mortality. Decreased BMD has also become an important socio-economic issue. Decreased BMD may result in osteopenia and osteoporosis, of which the latter is more serious. An Osteoporosis Risk Assessment study has confirmed that the risk of fracture increases with decreasing BMD.[9] In 2015,Liu et al in a study in Turkey found, osteoporosis in 24-44% of patients with COPD.[2]

In our study, there is no patient below 40 years. Mean age was 56 years. Maximum 66% patients were in 50-69 years of age, 22% patients were 40-49 years of age and only 12% were above 70 years old. According to a study conducted in Bangladesh on burden of obstructive lung diseases in Bangladeshi, the main age group involved by COPD is 50-59 years (36%). In NICE study conducted by Fukuchi Y et al[16], in Japan, COPD is significantly more prevalent in older people. 3.5% in 40-49 years old Vs. 24.4% in those >70 years of age and this increasing prevalence with increasing age is consistent with our study upto age of 60 years after which there was a decline in our study.

In our study, we found 94% (47) of the COPD patient were male and only 6% (3) were female, this reflects that more males are habituated to smoking. This finding is consistent with other national studies. Hallin R et al[17] shown their study in South Korea, found 8% COPD patients were female. This is also similar to our study.

According to GOLD (Global Initiative for chronic obstructive lung disease) in its Global strategy for diagnosis, management and prevention-executive summary, updated 2014, the risk of developing COPD is inversely related to socioeconomic status i.e. COPD occurs more in less educated and lower income groups of people. Our study result is consistent with this because our study showed that COPD had occurred more in illiterate (60%), farmers (62%) and low income group population <15000 taka/month (54%).

In our study, 90% COPD patients are present smoker and 6% are ex-smoker, that means 96% COPD cases are due to smoking, 4% COPD patients were exposed to biomass fuel.[18] This result is consistent with other national and international studies. BOLD-BD study showed 88% COPD patients were smoker, 10% COPD patients were ex-smoker and 2% were exposed to biomass fuel.

In our study, 68% COPD patients smoked more than 20 pack year and 32% COPD patients smoke (10-20) pack year. Mean amount of smoking was 20 pack year. In BOLD-BD study, it has been shown that about 80% smokers need to smoke only around 10 pack year to catch the disease and the study has considered this finding as more alarming than the international findings, where 20 pack-year are set as a bench mark in developing COPD.[18] Here, our finding is consistent with international finding.

The mean amount of smoking is respectively 28, 22, 16, 14 pack year among very severe, severe, moderate and mild COPD patients. So it is obvious that severity of COPD depends upon the amount and duration of smoking.

In our study, breathlessness (96%), chronic cough (86%), sputum production (70%) are the most common presenting complaints. GOLD has mentioned any of chronic cough, sputum production and dyspnoea as a key indicator of COPD. In our study, all of these symptoms were present singly or in combination among smokers having COPD.

In our study, we found wheeze (86%), barrel shaped chest (34%) as the commonest signs. Other signs were, edema (20%) and cyanosis (10%). Harikmitra et al[19] showed in their study, in Chennai India, 37% had barrel shaped chest, 26% had edema, 15% had cyanosis and 90% had wheeze. This difference is not very significant.

In our study, according to BMD femoral neck t-score, we found that 50% of COPD patients have osteoporosis, 40% have osteopenia and only 10% have normal bone. According to BMD lumber spine t-score, we found that 52% of COPD patients have osteoporosis, 34% have osteopenia and only 14% have normal bone.

Among our respondents, on the basis of BMD lumber spine t-score, 52% (26) were Osteoporotic, 34% (17) were osteopenic and 14% (7) were normal. The prevalence of low BMD by QCT in patients was high; 37.8% of our patients were osteopenic

and 43.2% were osteoporotic.[1] These results are in accordance with a published meta-analysis, which has shown that, in COPD patients, there is a prevalence of osteoporosis of 35.1% and a prevalence of

osteopenia of 38.4%.[20] The TORCH study[21] demonstrated a higher prevalence of osteoporosis and osteopenia at baseline, in those patients with spirometrically confirmed COPD.

Mean of BMD femoral neck t-test was lowest among very sever COPD patients (-3.21± 0.16) and highest among mild COPD patients (-1.37± 0.83). This mean difference was significantly associated. Other studies, however, support that there is a positive correlation between stage of COPD and osteoporosis which is statistically significant.[22]

In our study, on the basis of BMD lumber spine t-score, very severe COPD had osteoporosis 100%. Patient with severe COPD- 75% had osteoporosis, 18.8% had osteopenia. This difference were statistically significant (p=<0.001).

In another study, majority of patients who had osteoporosis, had very severe COPD (81.81%) and severe COPD (73.91%). Incidence of osteoporosis increased with severity of COPD from 14% (mild) to 80% (very severe) among males. Among females, osteoporosis is also increased with severity of COPD.[23] Study is on par with Jørgensen and Schwarz study.[24] In a study by Stevenson *et al*.[25] it was observed that there was increased incidence of osteopenia and osteoporosis with advancing COPD stage. They observed that 68% had either low bone mass (osteopenia or osteoporosis) or a previously undiagnosed vertebral fracture, with 25% of the included patients having a vertebral fracture. Consistent with the above studies, another study by de Vries *et al*.,[26] observed that the risk of osteoporotic fracture increased in patients with COPD. It was also observed that patients with more severe airway obstruction in COPD had increased risks of osteoporosis and bone fractures as compared with patients without a history of obstructive airway disease.

In 2015, Liu et al in a study in Turkey found that, after adjustment age, sex and FEV1 (%) matched COPD patients with and without osteoporosis, determined that BMDs at the lumbar spine, total hip, and femoral neck sites were lower in COPD patients with osteoporosis. These results are consistent with our study.[2]

In summary, we have found that osteoporosis has a close association with COPD. And BMD value decreases as the disease progresses.

Conclusion:

COPD is a systemic disease. Along with respiratory system it involves other systems of the body. Skeletal involvement is a major effect of COPD. This study showed positive relation between severity of COPD and bone loss. The more severe the COPD is the more severe the bone loss. So, early detection of bone loss by BMD and appropriate preventive and therapeutic measures should be taken to reduce the mortality and morbidity of COPD patients.

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