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Occurrence of Osteoporosis in COPD Patients- A Comparative Study with Age & Sex Matched Control

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ABSTRACT
Introduction: *Chronic Obstructive Pulmonary Disease (COPD) has been found to be associated with a variety of systemic manifestations and reduced bone mineral density being one of them. Due to scarcity of available Indian data, there is a need to evaluate the problem of osteoporosis in Indian population.*
Methods: *This prospective observational study was conducted with the objectives of studying the occurrence of osteoporosis in COPD patients as compared to age-sex matched controls and to assess the co-relation of osteoporosis with the severity of COPD.60 COPD (35 males & 25 females) cases, age & sex matched 60 control were classified. GOLD criteria 2013 was used to grade severity. Detailed clinical history & examination, blood investigations, spirometry & DEXA for bone density measurement was done.*
Results: *Among 60COPD patients, 37 had osteoporosis (40.5% females, 59.45% males), 22 had osteopenia. As apposed, only 11.6%&68.3% control group patients had osteoporosis & osteopenia respectively. We found Lumbar spine osteoporosis to be more common. 22.2%moderate, 96% severe & 85.7%very severe COPD patients had osteoporosis, which was statistically significant.*
Conclusion: *COPD patients are at a greater risk for osteoporosis when compared to age-sex matched control group patients. This risk increased with the severity of COPD.*
Keywords: *COPD, Osteoporosis, spirometry, DEXA.*

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD), a common preventable and treatable disease, is characterised by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and co-morbidities contribute to the overall severity in individual patients. [1]

The prevalence of COPD in the adult population ranges between 4% and 10%and World Health Organization projections predict that COPD - related mortality and disability will continue to increase worldwide during the next two decades.[2] COPD has been found to be associated with a variety of systemic manifestations, and amongst these, reduced bone mineral density (BMD) has been recognized as one of the systemic effects of

COPD irrespective of the stage of the disease. As there is a predicted worldwide increase in COPD, with subsequent bone problems such as fractures, identification of such patients with a high risk of osteoporosis is essential.[3] Increased awareness is therefore essential in order to diagnose and treat bone loss to reduce the risk of fractures.

The prevalence of osteoporosis in COPD patients is 36% to 60% and that of osteopenia is 35% to 72%. Moreover, COPD patients have a higher risk of osteoporosis as compared to healthy subjects.[4] According to World Health organization, osteopenia (T-score between −1.0 and −2.5) and osteoporosis (T-score below −2.5) are conditions characterized by a decrease in bone mass and density, leading to fragility of the bone. [5]

One of the most obvious causes of osteoporosis in these patients is treatment with glucocorticoids, various studies done on the role of inhaled corticosteroids (ICS) with osteoporosis in COPD patients concluded that, ICS does not aggravate bone mineral loss in COPD patients.[6,7,8] Even in glucocorticoid naive patients, BMD is found to be lower than in age-matched control subjects, and consequently, fracture risk higher.[6]

Other risk factors for developing osteoporosis in COPD are smoking, aging, female sex, low body mass index, decreased physical activities and systemic inflammation [9]

There are a lot of studies available describing the prevalence of osteoporosis in COPD in the western literature but, there are hardly any studies available that has studied this problem in Indian population. to improve their quality of life by appropriate preventive strategies.

This study was conducted with the aim of assessing osteoporosis in a sample of COPD patients in comparison with the clinical and functional characteristics of osteoporotic, osteopenic, and normal-bone-mass patients which will be helpful to improve their quality of life by appropriate preventive strategies.

MATERIAL & METHODS

The subjects of this case-control study was clinically stable COPD patients (cases). The control group consisted of healthy volunteers with age and sex matched, coming for their routine health check-up in our tertiary care center. The duration of our study was 18 months. This study was conducted with the aim of assessing the occurrence of osteoporosis in COPD patients as compared to age-sex matched controls along with correlating it with the severity of COPD. The degree of airflow limitation was assessed by spirometry and stratified in accordance with the Global Initiative for Chronic Obstructive Pulmonary Disease. We included subjects of both gender and of age group in between 50 to 86 years (60 in each, COPD and the control group) fulfilling inclusion criteria.

1. Diagnosed case of COPD on the basis spirometry criteria (patients with post-bronchodilation FEV1/FVC <0.7) and also those who had a history of exposure to risk factors.
2. Clinically stable for the last 4 weeks (no exacerbations).
3. Healthy controls with osteoporosis based on T-score and without vertebral fractures, as well as healthy controls without osteoporosis based on T-score and without vertebral fractures.

Patients excluded from the study were those with history of respiratory disease other than COPD, chest surgery, Bone disease or Osteomlacia, Chronic Liver Disease, Rheumatoid Arthritis, Heart Failure(ejection fraction <45%), Renal Failure and History of steroid intake among control group. Demographic data of the patients were noted. Number of COPD exacerbations in the last 1 year, history of smoking, presence of comorbidities Documented evidence of control group patients having no respiratory complains or disease was noted.BMD at the lumbar spine (L1-L4), the bilateral femoral neck and whole body was measured by Dual X-Ray Absorptiometry (Lunar prodigy). BMD is reported as an absolute

value (g/cm^2) and a T score, which represents the number of standard deviations from a young, sex- and ethnic group-specific reference mean. Cases and Control Subjects, both were grouped according to the WHO criteria, and diagnosed as osteoporotic, osteopenic, or normal bone mass according to T-score for BMD. The lowest T-score at either region determined the diagnosis. Thus, if the T-score at either region was below −2.5, the individual was diagnosed as having osteoporosis. If the lowest T-score at either region was between −2.5 and −1.0 the subject was diagnosed with osteopenia. If hip, lumbar spine and whole body T-score was above −1.0 the study subject was grouped as having normal bone mass. The incidence of osteoporosis/osteopenia occurring in COPD patients was assessed and compared to the control group (healthy volunteers).Informed written consent from all subjects who participates in the study. Samples were taken by using universal sample technique.

RESULTS

As seen in table 1 and 2 the study population (cases and control group) was age and sex matched

Table 1: Equal distribution of gender between COPD & Control group

Gender	Group		Total
	COPD (%)	Control (%)25	
Female	25 (41.7%)	25 (41.7%)	50 (41.7%)
Male	35 (58.3%)	35 (58.3%)	70 (58.3%)
Total	60 (100%)	60 (100%)	120 (100%)

Table 2: Mean Age group between COPD patients & Control group

Variables	Group	Mean	SD	Median	IQR	t-value	p-value
Age (Yrs)	COPD	66.82	8.06	66.00	11.75	0.011	0.991
	Control	66.82	8.06	67.00	11.75	Difference is not significant	

Table 3: Correlation between Gender & Lumbar (AP spine) Bone Mineral Density (T-score) among COPD patients.

Gender	BMD t- score (lumbar spine)			Total
	Osteoporosis	Osteopenia	Normal	
Female	14 (56%)	11 (44%)	0 (0%)	25 (100%)
Male	20 (57.1%)	14 (40%)	1 (2.9%)	35 (100%)
Total	34 (56.7%)	25 (41.7%)	1 (1.7%)	60 (100%)

Chi-Square Tests	Value	Df	p-value	Association
Pearson Chi-Square	0.774	2	0.679	Not significant

Table 4: Correlation between Gender & Dual Femur (neck) Mineral Density (T-score) among COPD patients.

Gender	BMD t- score (Dual femur- neck)			Total
	Osteoporosis	Osteopenia	Normal	
Female	5 (20.0%)	19 (76.0%)	1(4.0%)	25(100.0%)
Male	15 (42.9%)	14 (40.0%)	6(17.1%)	35 (100.0%)
Total	20 (33.3%)	33(55.0%)	7(11.7%)	60 (100.0%)

Chi-Square Tests	Value	Df	p-value	Association is- Significant
Pearson Chi-Square	7.881	2	0.019	

Table 5: Correlation between Gender & Whole Body Mineral Density (T-score) among COPD patients.

Gender	t- score (Whole body)			Total
	Osteoporosis	Osteopenia	Normal	
Female (%)	2 (8.0%)	19 (76.0%)	4 (16.0%)	25 (100.0%)
Male (%)	8 (22.9%)	18 (51.4%)	9 (25.7%)	35 (100.0%)
Total (%)	10 (16.7%)	37 (61.7%)	13 (21.7%)	60 (100.0%)

Chi-Square Tests	Value	Df	p-value	Association is
	3.994	2	0.136	Not significant

Tables 3-5 show that males were more osteoporotic than females. Overall 23/35 (65.71%) males and 14/25 (56%) females were diagnosed with osteoporosis. The association of Gender with osteoporosis was not statistically significant.

Table 6: Lumbar spine Bone Mineral Density among cases and control.

BMD t- score (lumbar spine)	Group		Total
	COPD	Control	
Osteoporosis	34 (56.7%)	5 (8.3%)	39 (32.5%)
Osteopenia	25 (41.7%)	38 (63.3%)	63 (52.5%)
Normal	1 (1.7%)	17 (28.3%)	18 (15.0%)
Total	60 (100.0%)	60 (100.0%)	120 (100.0%)

Chi-Square Tests	Value	Df	p-value	Association is
	38.469	2	4.43E-09	Significant

Table 7: Dual Femur (neck) Bone Mineral Density among the cases and control.

BMD t- score (Dual femur-neck)	Group		Total
	COPD	Control	
Osteoporosis	20 (33.3%)	2 (3.3%)	22 (18.3%)
Osteopenia	33 (55.0%)	34 (56.7%)	67 (55.8%)
Normal	7 (11.7%)	24 (40.0%)	31 (25.8%)
Total	60 (100.0%)	60 (100.0%)	120 (100.0%)

Chi-Square Tests	Value	df	p-value	Association is
	24.065	2	5.95E-06	Significant

Table 8: Whole Body Bone Mineral Density among cases and control.

T-score (Whole body)	Group		Total
	COPD	Control	
Osteoporosis	10 (16.7%)	0 (0.0%)	10 (8.3%)
Osteopenia	37 (61.7%)	22 (36.7%)	59 (49.2%)
Normal	13 (21.7%)	38 (63.3%)	51 (42.5%)
Total	60 (100.0%)	60 (100.0%)	120 (100.0%)

Chi-Square Tests	Value	Df	p-value	Association is Significant
	26.068	2	2.18E-06	

Tables (6, 7 &8) show that COPD patients are more osteoporotic compared to control group and that, their difference is statistically significant. Among COPD patients osteoporosis is more common in AP spine (56.7%, T-score -2.50) as opposed to dual femur (33.3% ,T-score -2.05) & whole body(16.7%).

Table 9: Distribution of COPD patients in relation to severity of COPD (Gold Staging)

GOLD Staging	No. (%)
Moderate	27(45%)
Severe	24 (40%)
Very severe	9(15%)
Total	60(100%)

Table10: Association between Severity of COPD (Gold staging) and Lumbar spine Bone mineral density.

GOLD Staging	BMD t- score (Lumbar spine)			Total
	Osteoporosis	Osteopenia	Normal	
Moderate	4 (14.8%)	22 (81.5%)	1 (3.7%)	27 (100.0%)
Severe	22 (91.7%)	2 (8.3%)	0 (0.0%)	24 (100.0%)
Very severe	8 (88.9%)	1 (11.1%)	0 (0.0%)	9 (100.0%)
Total	34 (56.7%)	25 (41.7%)	1 (1.7%)	60 (100.0%)

	Value	Df	p-value	Association is-
Chi- Square Test	35.094	4	4.44E-07	Significant
Pearson Chi-Square	0.000	1	1.000	Not significant

Table 11: Association between Severity of COPD (Gold staging) Dual Femur neck Bone mineral density.

GOLD Staging	BMD t- score (Dual femur neck)			Total
	Osteoporosis	Osteopenia	Normal	
Moderate	2 (7.4%)	18 (66.7%)	7 (25.9%)	27 (100.0%)
Severe	13 (54.2%)	11 (45.8%)	0 (0.0%)	24 (100.0%)
Very severe	5 (55.6%)	4 (44.4%)	0 (0.0%)	9 (100.0%)
Total	20 (33.3%)	33 (55.0%)	7 (11.7%)	60 (100.0%)

	Value	df	p-value	Association is-
Pearson Chi-Square	19.676	4	0.00058	Significant
Chi-Square test	0.384	1	0.536	Not significant

Table 12: Association between Severity of COPD (Gold staging) and Whole Body Bone mineral density(T-score).

GOLD Staging	T- score (Whole body)			Total
	Osteoporosis	Osteopenia	Normal	
Moderate	0 (0.0%)	16 (59.3%)	11 (40.7%)	27 (100.0%)
Severe	8 (33.3%)	15 (62.5%)	1 (4.2%)	24 (100.0%)
Very severe	2 (22.2%)	6 (66.7%)	1 (11.1%)	9 (100.0%)
Total	10 (16.7%)	37 (61.7%)	13 (21.7%)	60 (100.0%)

	Value	Df	p-value	Association is-
Chi-Square	17.120	4	0.00183	Significant
Pearson Chi-Square	10.709	2	0.005	Significant

The above tables (10,11,12) show, that percentage of osteoporosis & osteopenia increases as the severity of COPD increases.

This association was statistically significant only for Whole Body bone densitometry (p-value 0.005).

DISCUSSION

The study population, both the cases and control were age and sex matched

Out of 37/60(61.66%) COPD patients, 56% of females and 65.71% of males had osteoporosis. 22/60(36.66%) COPD patients had osteopenia. As apposed, only 11.6% and 68.3% control group patients were diagnosed to have osteoporosis and osteopenia respectively. A similar study done by Sin DD, et al. showed prevalence of osteoporosis to be 9%-69% in COPD patients versus 0%-13% in healthy individuals. [10]

In our study we observed that osteoporosis was more common in males than female patients. Osteoporosis was diagnosed in 57.1% of men using measurements of the Lumbar spine, 42.9% using the dual femur, and 22.9% using the total

body. As opposed to in females it was 56%, 20% and 8% respectively. However, this difference was not statistically significant.

Subjects were grouped according to the WHO criteria, and diagnosed as osteoporotic, osteopenic, or normal bone mass according to T-score for BMD. Thus, in our study 23/35(65.71%) males and 14/25(56%) females were diagnosed to have osteoporosis.

A study done by J.M. Vaquero-Barrios, et al. supports the results of our study. In their study 88.2% of men and 69.2% of women had osteoporosis. [10]

According to WHO, female gender was not a significant risk factor for osteoporosis although in the overall population women are at increased risk of osteoporosis as compared to their male peers. Also a study by Jorgensen NR, et al., said that incidence of osteoporosis is higher in women than in men, and it is to be expected that women with COPD would be even more susceptible to develop osteoporosis than women with normal lung function. [11)

In our study, osteoporosis & osteopenia were more in COPD patients as compared to the control group.

Osteoporosis of Lumbar spine was 56.7% and osteopenia 41.7% among COPD patients, compared to 8.3% and 63.3% respectively in control group.

The median BMD T-score (Lumbar spine) for COPD patients was also lower than control group patients. -2.50 and -1.40 respectively.

Osteoporosis of Dual Femur was 33.3% and osteopenia 55% among COPD patients, compared to 3.3% and 56.7% respectively in control group.

The median BMD T-score (Dual femur) for COPD patients was also lower than control group patients. -2.05 and -1.25 respectively.

Osteoporosis of Whole Body was 16.7% and osteopenia 61.7% among COPD patients, compared to 0% and 36.7% respectively in control group.

The median BMD T-score (Lumbar spine) for COPD patients was also lower than control group patients. -1.50 and -0.20 respectively.

Subjects were grouped according to the WHO criteria, and diagnosed as osteoporotic, osteopenic, or normal bone mass according to T-score for BMD. The lowest T-score at either region (Lumbar spine/dual femur / whole body) determined the diagnosis.

Thus, 65.71% of COPD patients had osteoporosis and 11.6% of controlgroup patients had osteoporosis. Also COPD patients were more prone to lumbar spine osteoporosis than that of dual femur or whole body. In accordance to our results a study done by Jorgensen NR, et al., also showed that in COPD patients lumbar spine was more osteoporotic. [5]

Comparison studies done by Bolton et al, Sabit et al and Dimai et al in an age-matched control group of healthy subjects in COPD, the prevalence of osteoporosis is assumed to be two- to five-fold higher than in age-matched subjects without airflow obstruction. The prevalence of osteoporosis in COPD was increased compared with the healthy subjects (overall mean prevalence of osteoporosis of 31.7% in COPD *versus*5.8% in healthy subjects, $p<0.001$). .In another study done by Jorgensen NR, et al., 44.8% were osteoporotic, and 22.4% were osteopenic and 25.9% had normal bone mass. [5]

Moderate grade COPD patients with a mean postbronchodilator-FEV1

of 0.57 (±0.05) and mean duration from diagnosis of COPD was 6 years (min -1year, max -20years) had T-score of median -1.80(-3.20,0.60) of Lumbar spine,median -1.60 (-3.30,1.50) of dual femur and median -1.10 (-2.30,1.60) of whole Body.

Severe grade COPD patients with a mean postbronchodilator-FEV1 0.43 (±0.04) and mean duration from diagnosis of COPD was 9 years (min -2years, max -30years) had T-score of median -2.75(-4.50,-1.90) of Lumbar spine,

median -2.55 (-4.50,-1.20) of Dual femur and median -2.10 (-4.0, -0.50) of whole body.

Very Severe grade COPD with a mean postbronchodilator-FEV1 0.30 (0.04), and mean duration from diagnosis of COPD was 8 years (min -1years, max -15years) had T-score of median -2.50 (-3.20,-1.90) of Lumbar spine, median -2.0 (-3.40,-1.10) of dual femur and median -1.40(-3.30,0.80) of whole body.

So, Severe and Very severe COPD patients had a lesser median value of T-score compared to moderate COPD patients.

We found statistically significant bivariate co-relation between whole body T-score and severity of COPD. Also there was statistically significant association between the time from diagnosis of COPD and Dual femur (neck) T-score, when compared to COPD patient with normal BMD. In our study osteoporosis was diagnosed in 6/27 (22.2%) moderate COPD patients, 25/26(96%) severe COPD patients and 6/7 (85.7%) very severe COPD patients.

These results were in agreement with Iqbal et al., who found that, in COPD group who had osteoporosis BMD decreases in linear pattern with the decrease of FEV1%. [12] Also, these results were in agreement with the results of the cross sectional study carried by Jorgensen et al. who found that, BMD had direct relation with FEV1% in COPD patients who had osteoporosis. [5]

Also a study by Sin et al., revealed that risk of osteopenia increases by 30% in moderate COPD and by 70% in severe COPD more than normal personnel, and the risk of osteoporosis increases by 2.1 fold in moderate COPD and by 2.8 fold in severe COPD more than normal personnel. [12]

CONCLUSIONS

In conclusion, we found that COPD patients are more osteoporotic when compared to age –sex matched control group patients and also the risk of osteoporosis increases with the severity of COPD. However we suggest that the similar study with larger sample size with periodic following up of the cases is necessary for endorsing our findings. Based upon the findings of the present study we recommend that there should be periodic active screening of the COPD patients for osteoporosis by BMD and these patients should also receive calcium and vitamin D supplements.

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