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Prevalence and risk factors of osteoporosis in Chronic Obstructive Pulmonary Disease (COPD) patients from Central India.

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Abstract: The prevalence of osteoporosis in patients with COPD is high and potentially essential. To study prevalence and various risk factors contributing to osteoporosis in COPD patients. The present study is prospective cross sectional study carried out on 80 stable COPD patients attending tertiary care hospital in central India. After taking written consent & detailed clinical history consisting questionnaire about the risk factors, spirometry was done to stage the severity of COPD. DEXA scan of whole body was performed using fan beam X-ray bone densitometer to determine osteoporosis. Chi-square test was used to determine the association between COPD and osteoporosis. Univariate logistic regression was used to analyze the risk factors for developing osteoporosis. In the present study, the overall prevalence of low BMD was found to be 92.5% in COPD patients showing equal prevalence (46.25%) for osteoporosis and osteopenia. The duration & severity of disease along with steroid intake were found to be risk factors of osteoporosis in univariate analysis with risk ratio of 1.32 (95% CI 1.06-1.64), 1.75 (1.11-2.75) and 1.40 (1.00-1.97) respectively (p value <0.05). The prevalence of low BMD was very high in COPD patients at a tertiary care hospital of central India. Duration & severity of disease along with steroid intake were found to be risk factor for osteoporosis in univariate analysis.

Key words: COPD; osteoporosis; DEXA; severity; steroid; BMD.

Introduction

Chronic obstructive pulmonary disease (COPD) is a disease in which there occurs a progressive airflow restriction. It is stimulated by abnormal inflammatory response of the airway and lung parenchyma and result into high morbidity. It is believed to be a systemic ailment with extensive extra-pulmonary symptoms, with low bone mass leading to osteopenia, osteoporosis and fragility fracture.[1] Risk factors for development of COPD are a complex interaction of genetic factors and many different environmental exposures, with cigarette smoking being the most frequent etiological agent. An additional problem arises in managing the patient, when along with pulmonary symptoms co-morbidity is also present. At present the prevalence of COPD lies between 4% and 10% in the adult population. However, World Health Organization has predicted that in the next twenty years COPD-related disabilities and mortality will continue to increase. In 2020, it is expected to be the fifth major public health problem worldwide.[2,3] In India estimated chronic cases of COPD are around 1.49 crore in the age group of 30 and above, which were projected to increase 50% by the year 2016.

Environmental factors and habits like smoking also contribute to the pathogenesis of osteoporosis. Therapy used during the disease i.e corticosteroid treatment (both inhaled and systemic) is also an important risk factors in the development of osteoporosis.[4] The quality of life of COPD patients is usually restricted, which further reduces when fractures occur due to osteoporosis. Therefore, healthcare providers should have knowledge about the risk of development of osteoporosis in COPD patients. An early identification of osteoporosis will help in taking timely preventive and therapeutic measures. It would decrease the consequences associated with osteoporosis in COPD patients.[4]

However data regarding prevalence of low BMD in COPD are lacking from central India. Hence, present study was carried out with the aim to determine the prevalence of osteoporosis in COPD patients, and to analyze the various risk factors contributing to osteoporosis in these COPD patients.

Materials and Methods

The study was conducted in the department of Pulmonary Medicine, Jawaharlal Nehru Main hospital & Research centre Bhilai, Chhattisgarh from May 2013 – May 2014. Jawaharlal Nehru Main hospital & Research centre is one of the oldest tertiary care centres of Chhattisgarh and that serve the population of Bhilai & adjoining area. The patients who were diagnosed COPD on spirometry based on the GOLD guidelines and who were attending chest OPD or admitted in chest ward were randomly selected and included in the study after

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taking a written informed consent.[5] The sample size of 80 diagnosed cases of COPD was calculated taking the overall prevalence of osteoporosis and osteopenia as 65% in COPD patients. The study got approval from the ethical and scientific research committee of Jawaharlal Nehru Main Hospital & Research Centre, Bhilai.

Inclusion criteria

All the stable patients of COPD of both sex, in the age group of 40-80 years and diagnosed as per GOLD criteria and had received treatment with inhaled corticosteroids for not more than 1 year were included in the study.

Exclusion criteria

Patients with age 80 years or more, respiratory failure, Neoplastic disease, any systemic disease which lead to immobilization of patients or affect BMD, Endocrinal disease: hypo or hyperparathyroidism, Diabetes mellitus, thyroid dysfunction, unstable patients with associated hypertension, ischemic heart disease and congestive cardiac failure were excluded from the study.

Procedures and Measurements

Regular investigation along with particular procedures as per hospital requirements were done in all the subjects who were recruited into the study. The clinical profile of each patient was studied by using a questionnaire comprising of age, gender, occupation, present clinical symptoms and exacerbation in past 1 year, duration of illness, associated past and present co-morbid disease, present and previous medications, history of smoking in pack year, diet, physical activity. Complete haemogram, renal function test, liver function test, FBS/PPBS, cardiac enzymes, electrolytes including calcium, ABG, ECG, chest rongentogram were done.

Pulmonary function was assessed via computerized spirometer (Helios RSM 702 spirometer). GOLD guidelines for spirometry was followed.[3] FEV1, FVC, FEV1/FVC ratio, bronchodilator reversibility were determined. Salbutamol nebulisation (2.5mg) were used as bronchodilator. Three measurements were carried out with subjects in sitting pose and the best bronchodilator assessment of FEV1 and FVC was recorded. Difference between highest and lowest value was less than 5%. According to GOLD guideline patients with post bronchodilator FEV1/FVC < 0.7, were diagnosed as COPD and then on basis of FEV1% they were categorized into four stages of severity I: Mild COPD - FEV1/FVC < 0.7; FEV1 ≤ 80% predicted, II: Moderate COPD - 50% ≤ FEV1 < 80% predicted, III: Severe COPD - 30% ≤ FEV1 < 50% predicted, IV: Very Severe COPD - FEV1 < 30% predicted or FEV1 < 50% predicted plus chronic respiratory failure.

Bone mineral density (BMD) was determined by whole body DEXA scan (Dual Energy X-Ray Absorptiometry) using HOLOGIC Discovery Wi QDR(S/N 85753), version 13.2.1 Auto Whole Body (fan beam X-ray bone densitometer). BMD is expressed in terms of standard deviation (SD) as a T score and a Z score. The T score expresses the variation between the BMD of the subject being scanned and the mean BMD of 30 year youth people as standard. The Z score illustrates the variation between the subject's BMD and the mean BMD of age- and gender-matched controls. DEXA results are reported as numeric values for T and Z scores and as a graphic curve normalized for gender and age. [Table I]

Table 1: Classification for Osteoporosis and Osteopenia.

By BOYNOV	By WHO	Result
T-score ≤-2.35 SD	T-score ≤ -2.5 SD	Osteoporosis
-2.35 SD < T-score < -0.9 SD	-2.5 SD < T-score ≤ -1.0 SD	Osteopenia
T-score ≥- 0.9 SD	T-score > -0.1 SD	Normal

Statistical analysis

The statistical analysis has been performed using SPSS software version 20. The statistical analysis of qualitative data (N%) between the groups is done by using Chi-square/Fischer exact test. p-value <0.05 was considered to be statistically significant.

Results

The present study is an institutional based observation study, conducted in a tertiary care hospital involving 80 COPD patients. The prevalence of low BMD by using whole body DEXA scan was found to be 74/80 (92.5%) of which 37 (46.25%) had osteopenia and 37 (46.25%) had osteoporosis. Most of the patients 87.5% (n=70) comprised of elderly population i.e. above 60 years of age. The mean age of study population was 68.89 ± 7.33 years. In males, mean age was 69.4 ± 7.0 years, while in female it was 67.1 ± 8.34 years. There were 18 (22.5%) female and 62 (77.5%) male patients with sex ratio 31:9. Out of 18 female patients, 5 had osteopenia and 13 had osteoporosis while in 62 male patients, 32 had osteopenia, 24 had osteoporosis and 6 had normal BMD.

In the present study, various risk factors like - age, sex, smoking history, duration of disease, steroid intake in past 1 year, severity of disease (GOLD stage), Body mass index (BMI), and Fat free mass index (FFMI) were analyzed. In univariate analysis, duration of illness and severity of disease were found to be risk factors for osteoporosis in COPD patients. However, steroid intake in past 1 year was found to be a risk factor for osteopenia, osteoporosis and low BMD in COPD patients.

In the present study, the duration of illness more than 10 years was found to be 48.6% in osteoporosis group compared to 0% in normal BMD group (p value 0.04). The risk ratio was found to be 1.32 (95% CI 1.06-1.64). The steroid intake was found to be highest 78.4% in osteoporosis group followed by 62.2% in low BMD group and 45.9% in osteopenia group compared to 16.7% in normal BMD group (p value 0.0004, 0.004, 0.04 respectively). The risk ratio (95% CI) was 1.75 (1.11-2.75), 1.21 (1.04-1.42) and 1.3 (1.05-1.61) respectively. The severity of COPD was found to be

risk factor for osteoporosis with GOLD stage >II in 70.3% in osteoporosis group as compared to 16.7% in normal BMD group (p value 0.02). The risk ratio (95% CI) was found to be 1.40 (1.00-1.97) (Table II).

Table 2: Univariate analysis for risk factors of osteopenia, osteoporosis & low BMD in COPD patients

Parameters	Normal BMD N=6	Osteopenia N=37	Osteoporosis N=37	Low BMD N=74	p-value		
	1	2	3	4	1vs2	1vs3	1vs4
Age (years)							
<60	0 (0%)	4 (10.8%)	6 (16.2%)	10 (13.5%)	0.54	0.38	0.44
≥60	6 (100%)	33 (89.2%)	31 (83.8%)	64 (86.5%)			
Sex							
Male	6 (100%)	32 (86.5%)	24 (64.9%)	56 (75.7%)	0.45	0.09	0.20
Female	0 (0%)	5 (13.5%)	13 (35.1%)	18 (24.3%)			
Smoking habit							
Non smokers	1 (16.7%)	16 (43.2%)	15 (40.5%)	31 (41.9%)	0.26	0.31	0.26
Ex-smokers	5 (83.3%)	21 (56.8%)	22 (59.5%)	43 (58.1%)			
Duration of disease (years)							
≤10	6 (100%)	27 (73%)	19 (51.4%)	46 (62.2%)	0.18	0.03* RR= 1.32 95%CI 1.06-1.64	0.07
>10	0 (0%)	10 (27%)	18 (48.6%)	28 (37.8%)			
Steroid intake							
No	6 (100%)	20 (54.1%)	8 (21.6%)	28 (37.8%)	0.04* RR= 1.3 95%CI 1.05-1.61	0.0004* RR= 1.75 95%CI 1.11-2.75	0.004* RR= 1.21 95%CI 1.04-1.42
Yes	0 (0%)	17 (45.9%)	29 (78.4%)	46 (62.2%)			
Gold stage							
≤II	5 (83.3%)	26 (70.3%)	11 (29.7%)	37 (50%)	0.58	0.02* RR= 1.40 95%CI 1.00-1.97	0.14
>II	1 (16.7%)	11 (29.7%)	26 (70.3%)	37 (50%)			
Body mass index							
Normal	5 (83.3%)	23 (62.2%)	17 (45.9%)	40 (54.1%)	0.37	0.12	0.20
Abnormal	1 (16.7%)	14 (37.8%)	20 (54.1%)	34 (45.9%)			
FFMI							
Normal	1 (16.7%)	6 (16.2%)	6 (16.2%)	12 (16.2%)	0.93	0.93	0.92
Low	5 (83.3%)	31 (83.8%)	31 (83.8%)	62 (83.8%)			

*p value significant; RR: Risk Ratio; CI: Confidence Interval

Table 3: Comparison between present and other studies from different parts of the world

Study	Study type	Subjects	Year	Sex (Male: Female)	BMD Measurement	Prevalence of Osteoporosis	Prevalence of Osteopenia	Country
Jorgensen *et al.,* [7]	Cross-sectional	62	2007	16:46	DEXA scan of lumbar spine and femoral neck. X-ray of thoracic and lumbar spine	44.8%	22.4%	Denmark
Graat-Verboom *et al.,* [4]	Cross-sectional	554	2009	62%:38%	Whole-body DEXA scan	21%	41%	The Netherlands
Bhattacharya et al [11]	Cross-sectional	37	2011	35:2	Left heel broadband ultrasound bone densitometer	21.67%	51.35%	West Bengal India
Silva *et al.,* [6]	Cross-sectional	95	2011	62:33	DEXA scans of the hips and lumbar spine	42%	42%	Brazil
Graat-Verboom *et al.,* [8]	Cross-sectional	255	2011	62%:38%	DEXA scan of the hip and of the lumbar spine (L1–L4) and X-ray of thoracic & lumbar spine	51.4%	-	The Netherlands
Rittayamai *et al.,* [12]	Cross-sectional	102	2012	All male	DEXA of lumbar spine and femoral neck.	31.4%	32.4%	Thailand
Hattiholi & Gaude[9]	Cross-sectional	102	2014	64:38	Whole-body DEXA scan	66.7%	19.6%	Karnataka India
Damaraju *et al.,* [10]	Cross-sectional	100	2015	74:26	DEXA scan	60.81% in male & 50% in female	16.21% in male &19.23% in female	Andhra Pradesh India
Lin *et al.,* [18]	Cross-sectional	125	2015	123:2	DEXA of lumbar spine and bilateral femoral neck.	40%	-	Taiwan
Watanabe *et al.,* [19]	Cross-sectional	49	2015	-	DEXA scan	38.8%	-	Japan
Present study	Cross-sectional	**80**	-	**62:18**	**Whole body DEXA scan**	**46.25%**	**46.25%**	**Chhattisgarh India**

Discussion

COPD is defined as a multicomponent disease and so the awareness of a high prevalence of osteoporosis should be raised. As there are very few studies from India and lack of data from Central India regarding prevalence of osteoporosis and osteopenia in COPD patients; an observational study was carried out in tertiary care hospital to study prevalence of osteoporosis and osteopenia in COPD patients.

In the present study prevalence of low BMD was very high (92.5%). The prevalence of osteoporosis was 46.25% with T-scores ≤ -2.35. This finding was found

to be consistent with other studies done on 95, 62 and 255 patients of COPD respectively [Table III].[6-8] However, only the present study had performed whole body DEXA for the analysis of BMD. Three studies have reported the prevalence of osteoporosis from India,[2] from South India had shown higher percentage of osteoporosis than the present study while one study from East India showed lower prevalence of osteoporosis [Table III].[9-11] The low prevalence from West Bengal may be because of less number of patients, dominance of male population and the method used to identify osteoporosis.

In the present study, 46.25% cases of osteopenia were found which showed similarity with other studies reported prevalence 41% to 52%. [6,8,11] However studies reported from Denmark[7], Thailand[12] and South India[9,10] showed lower percentage prevalence of osteopenia. In present study equal occurrence of osteoporosis & osteopenia was observed while South Indian study reported elevated occurrence of osteoporosis as compared to osteopenia and study from East India showed higher prevalence of osteopenia than osteoporosis.

In the present study, various risk factors like - age, sex, smoking history, duration of disease, steroid intake in past 1 year, severity of disease (GOLD stage), BMI, FFMI which affects BMD in COPD patients were studied. In the present study age and sex were not found to be a risk factor for osteoporosis in COPD patient. However, a study reported age to be a significant, independent risk factor for osteoporosis in COPD and not the sex.[4] The present study showed smoking as insignificant risk factor for osteoporosis which was similar to other studies in which smoking was not found to be a risk factor for osteoporosis.[6,7]

In the present study it was found that duration of disease, steroid intake in past 1 year & severity of COPD to be significant risk factors for osteoporosis. The risk factors for osteoporosis in COPD patients have been studied by few investigators. Similar to the present study, study from Karnataka India also showed the severity of COPD to be a risk factor on univariate analysis and also as an independent risk factor in multivariate analysis.[9] Other studies who had meta analysed 13 studies with a total of 775 COPD patients and found that higher GOLD stage and/or a lower FEV1 was correlated with osteoporosis and/or a low BMD.[13-16]

Duration of disease more than 10 years was found to be a significant risk factor for osteoporosis in present study. Among the patients who had received corticosteroids prevalence of osteoporosis increases as cumulative dose of steroid increase. The history of steroid intake in past 1 year was a significant risk factor for osteopenia and osteoporosis as well as for over all low BMD (p value <0.05). In contrast to the present study, few studies found no significant influence of corticosteroids on osteoporosis and osteopenia.[4,6,7] Even though the loss of BMD particularly osteoporosis, have been considered late manifestations related to cumulative oral corticosteroid treatment, but significant loss of BMD was also observed in less severe airways hindrance. The vertebral fractures were reported to be high in male patients with COPD and not taking corticosteroid treatment.[1,17] This supports that factor other than corticosteroid used may contribute to development of low BMD in COPD.

The present study showed abnormal BMI to be an insignificant risk factor for osteoporosis, osteopenia and low BMD (p > 0.05). Variez *et al.,* , (2007) also reported, BMI as not to be a potential risk factor for low BMD in COPD patients.[14] though a study by Graat-Verboom *et al.,* (2009) reported overweight and obesity in COPD patients reduces risk of developing osteoporosis, as compared to average weight upper class people.[4] Overweight and obesity showed a substantial protective effect. FFMI was not a significant risk factor for low BMD (p value > 0.05) in present study. However, one study reported that as the severity of COPD increases there is a decrease in FFMI, and low FFMI results in an increased risk of having low BMD in COPD patients.[1]

Conclusion

The occurrence of osteoporosis and osteopenia was alike in COPD patients. Duration of disease, severity of disease [GOLD stage] and steroid intake were significant risk factor for osteoporosis. Hence high clinical alertness along with early diagnosis and treatment of osteoporosis in COPD patients will help in improving their quality of life.

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