Original Article

Prevalence of osteoporosis and osteopenia in stable patients of chronic obstructive pulmonary disease in Sub-Himalayan region of Himachal Pradesh, India

Nishant Nayyar[1], R. G. Sood[1], Malay Sarkar[2], Ashwani Tomar[1], Vijay Thakur[1], Rohit Bhoil[1]

Departments of [1]Radiodiagnosis and [2]Pulmonary Medicine, IGMC, Shimla, Himachal Pradesh, India

Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a lifestyle-related chronic inflammatory pulmonary disease and a major cause of morbidity and mortality globally. Osteoporosis and osteopenia are common observations in COPD and degree of the loss of bone mineral density (BMD) has been found to be proportionate to the severity of the disease. **Objectives:** Our objective was to study the prevalence of osteoporosis and osteopenia in stable COPD patients in Indian Sub-Himalayan population. **Materials and Methods:** This study was performed on 84 patients of COPD attending as outpatient in the Pulmonary Medicine Department after application of inclusion and exclusion criteria. A control group of 60 healthy controls was selected for comparison with COPD group. Spirometry was done on patients to stage the severity of COPD according to global initiative for chronic obstructive lung disease criteria. Dual-energy X-ray absorptiometry scan of the lumbar spine was done using bone densitometer to determine the severity of reduced BMD. The patients were categorized according to the World Health Organization criterion for definition of reduced BMD. **Results:** In the present study, a total of 45.2% patients had osteoporosis, 41.6% patients had osteopenia while the rest 13% patients had normal bone density in the COPD group. The prevalence of low bone density was about 4 times higher in COPD group as compared to control group. There were 15.48 times higher chances of low BMD in COPD patients as compared to healthy controls. **Conclusions:** Reduced BMD is a common comorbid entity in COPD patients which leads to increase in bone fragility and susceptibility to fracture. It is recommended that all the patients with COPD should be screened for osteoporosis to initiate the treatment for the disorder before they develop fractures.

Keywords: Bone mineral density, chronic obstructive pulmonary disease, dual-energy X-ray absorptiometry, fracture, global initiative for chronic obstructive lung disease criteria, spirometry

Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung in response to noxious particles or gases.[1-5] It is a major public health problem worldwide due to its increased prevalence, morbidity, mortality, and the resulting socioeconomic impact.[2] As compared to developed nations, its incidence is relatively more in developing countries. According to the recent World Health Organization (WHO) statistics, in the year 2012, more than 3 million people died of COPD, accounting for 6% of total deaths that occurred globally.[1,2] More than 90% of these deaths occurred in developing countries in Africa, Asia, including the Indian subcontinent and China.[2] COPD has been projected to become the third leading cause of death by the year 2030.[3] The management of COPD should include assessment of comorbidities as these are associated with increased risk of

Address for correspondence: Dr. Rohit Bhoil, Department of Radiodiagnosis, IGMC, Shimla - 171 001, Himachal Pradesh, India.
E-mail: rohitbhoil@gmail.com

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morbidity and mortality. The conditions commonly associated with COPD are reduced bone mineral density (BMD), cardiovascular disorders (coronary artery disease and chronic heart failure, hypertension), metabolic diseases (diabetes mellitus, metabolic syndrome, and obesity), stroke, lung cancer, cachexia, skeletal muscle weakness, anemia, depression, and cognitive decline.[4,6-9]

Osteoporosis and osteopenia are common observations in the patients of COPD, and the degree of decrease in BMD has been found to be proportionate to the severity of the disease.[5] There is a relative paucity of studies regarding the prevalence of osteoporosis and osteopenia among the COPD patients in India, especially in the tribal areas of the Sub-Himalayan belt.

The present study was undertaken to find out the prevalence of osteoporosis and osteopenia in patients having stable COPD in the Sub-Himalayan region of Himachal Pradesh in India, using dual-energy X-ray absorptiometry (DEXA) scan.

Materials and Methods

The study was conducted at Indira Gandhi Medical College, Shimla, Himachal Pradesh, India, in the Department of Radiodiagnosis between July 2015 and June 2016. Our objective was to study the prevalence of osteoporosis and osteopenia in stable COPD patients in Indian Sub-Himalayan population. Prior approval was obtained from the Institutional Ethics Committee.

Criteria of selection

All stable patients of COPD attending the outpatient Department of Pulmonary Medicine of our institute were included in the study.

A detailed assessment of smoking status, biomass exposure, frequency and nature of exacerbations for the past 2 years, physical activity, and prednisolone-equivalent corticosteroid dose was obtained.

Exclusion criteria

- Diagnosed case of osteoporosis or on anti-osteoporotic drugs
- COPD with exacerbation in previous 6 weeks
- Corticosteroid use for the past 6 months before recruitment
- Malignancy
- History of fracture in past 6 months
- Patients with artificial prostheses
- Patients with interstitial lung disease, bronchial asthma, rheumatic diseases, chronic liver or renal disease, primary or secondary hyperparathyroidism, Cushing's syndrome, and thyroid dysfunction.

Number of patients

A total of 116 patients were enrolled in the study; however, 32 patients were excluded as they were found to be ineligible based on the protocol of the study. This was a case-control study conducted on 84 stable patients with COPD, who fulfilled the inclusion and exclusion criteria. A control group of 60 healthy age- and sex-matched individuals having normal results on spirometry test was selected for comparison.

Methodology

Written informed consent was obtained from all the patients who were included in the study. Diagnosis of COPD was based on relevant clinical history and was confirmed by spirometry. Staging of COPD patients was done according to global initiative for chronic obstructive lung disease (GOLD) guidelines.[1] Spirometry was performed using standard calibrated spirometer (Vitalograph Compact Spirometer) as per the American Thoracic Society/European Respiratory Society standards.[3-5] Postbronchodilator spirometry was done in all the patients.

Measurement of bone mineral density

The patients were subjected to DEXA scan using DEXA HOLOGIC Discovery QDR series 4500A DEXA machine. BMD of the patient was determined using lumbar spine scan [Figure 1] to stage the severity of reduced BMD; whole-body scan was also done to know the body composition parameters. Severity of reduced BMD was graded according to the WHO classification[8] based on T-score as per table given below.

T-score	Diagnosis
≥-1 SD	Normal
−1-−2.499 SD	Osteopenia
≤-2.5	Osteoporosis
≤-2.5 with fracture	Severe or established osteoporosis

SD: Standard deviation

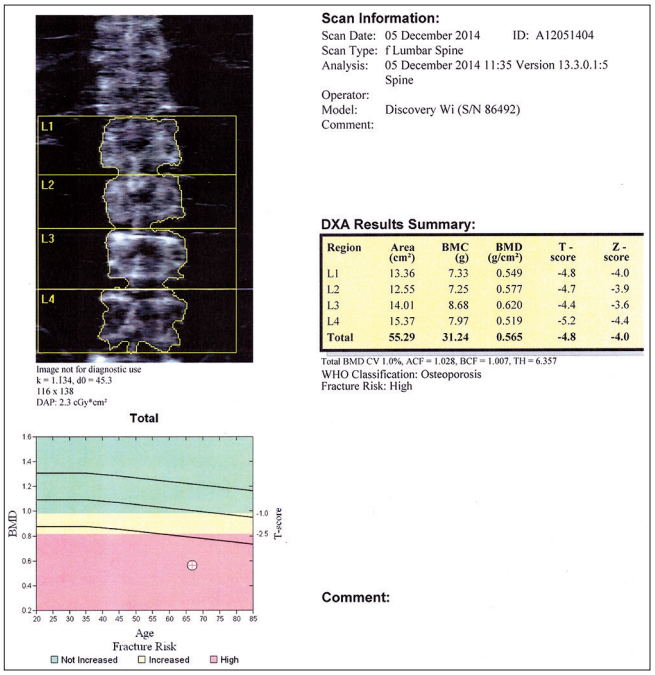

Figure 1: DEXA Scan report of a 66 year old patient showing oesteoporosois and indicating increased risk of fracture

Statistical analysis

The current study was case-control study in which the prevalence of reduced BMD was evaluated in COPD patients. The prevalence of osteopenia and osteoporosis was also sought in control group and compared with COPD group. Independent (unpaired) Student's *t*-test and Chi-square test were used to analyze these parameters. A $P < 0.05$ was considered statistically significant.

Observations

In the present study, a total of 84 eligible patients of stable COPD and 60 healthy controls were enrolled. The age of patients ranged between 40 and 70 years. There were 42 male patients (50%) and 42 (50%) female patients. Mean age of the male patients was 63.33 ± 4.70 years and that of female patients was 59.48 ± 7.75 years. We used the DEXA scan method for diagnosing osteoporosis and osteopenia, which is considered to be the gold standard method.[9]

A control group of 60 healthy age- and sex-matched controls was selected to know the prevalence of reduced BMD and compared with the COPD study group. There were 24 male patients (40%) and 36 (60%) female patients in the control group. Mean age of the male patients was 57.04 ± 7.17 years and that of female patients was 54.36 ± 7.52 years BMI of all the patients was calculated, and they were classified as underweight, normal, overweight, and obese with a BMI<18.5, 18.5–24.9, 25–29.9, ≥30, respectively, [Table 1].

Table 1: Demographic characteristic of the patients and controls

	COPD patients, *n* (%)	Control group, *n* (%)
Age group		
40-49	7 (8.3)	13 (21.66)
50-59	16 (19)	25 (41.66)
60-70	61 (72.6)	22 (36.66)
Total	84 (100)	60 (100)
Sex		
Male	42 (50)	24 (40)
Female	42 (50)	36 (60)
Total	84 (100)	60 (100)
BMI		
Underweight	22 (26.1)	8 (13.33)
Normal	36 (42.8)	24 (40)
Overweight	20 (23.8)	20 (33.33)
Obese	6 (7.1)	8 (13.33)
Total	84 (100)	60 (100)

BMI: Body mass index; COPD: Chronic obstructive pulmonary disease

Table 2: Association between chronic obstructive pulmonary disease and low bone mineral density

Study groups	Outcome		Total
	Low BMD (%)	Normal BMD (%)	
COPD group	73 (86.90)	11 (13.10)	84
Control group	18 (19.78)	42 (79.25)	60
Total	91	53	144

OR: 15.48 (6.68-35.89). *P*<0.001. OR: Odds ratio; COPD: Chronic obstructive pulmonary disease; BMD: Bone mineral density

Results

In the present study, a total of 38 (45.2%) patients had osteoporosis, 35 (41.6%) patients had osteopenia while the rest 11 (13%) patients had normal bone density in the COPD group. Overall prevalence of low bone density among the patients of COPD in this study was found to be 86.90%. In control group, a total of 6 (10%) patients had osteoporosis, 12 (20%) patients had osteopenia, and 42 (70%) patients had normal bone density. BMD results of both COPD and control group were compared to know the strength of association between COPD and low BMD. It was observed that prevalence of low bone density was about 4 times higher in COPD group as compared to control group. Odds ratio (OR) calculation in our study suggested that there were 15.48 times higher chances of low BMD in COPD patients as compared to healthy controls. There was a significant strength of association between low BMD and COPD (OR 15.48, confidence interval 6.68–35.89, $P < 0.001$) [Table 2 and Figure 2].

Association of reduced bone mineral density with severity of chronic obstructive pulmonary disease

A total of 35 patients had osteopenia, 27 (77.2%) of whom had Stage II and Stage III COPD disease. Thirty-one (81.6%) patients with osteoporosis had Stage III and Stage IV COPD disease. Stage I and Stage II COPD disease had low prevalence of osteoporosis. It was observed that, as the grade of COPD increased, the risk of osteoporosis also increased. Application of

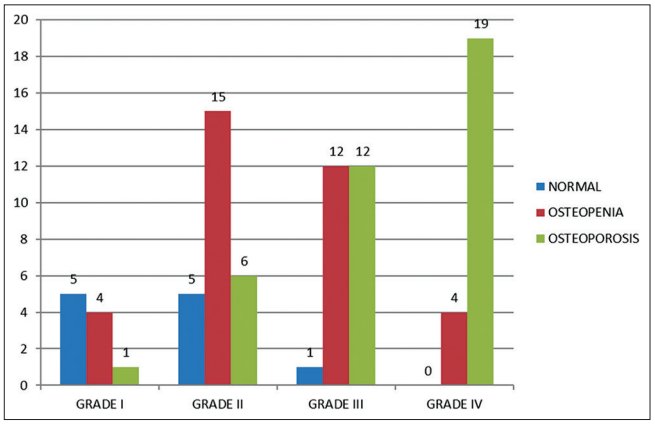

Figure 2: Association of reduced bone mineral density with severity of chronic obstructive pulmonary disease

Chi-square test showed significant association of COPD severity with osteoporosis ($P < 0.001$).

Discussion

The GOLD[1] 2016 update defined chronic COPD as "a common preventable and treatable disease, which is characterized 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 comorbidities contribute to the overall severity

in individual patients." COPD is a major public health problem globally because of its high prevalence, morbidity, mortality, and resulting socioeconomic impact.[2]

COPD is a lifestyle-related chronic inflammatory pulmonary disease with significant extrapulmonary involvement. One of the major systemic manifestations of COPD is reduced BMD,[1-3] which is more prevalent among COPD patients than among healthy controls. Thus, it is important to recognize the strategies to manage these patients to avoid osteoporotic fractures that would deteriorate the quality of life in such patients.

In the present study, out of the total 84 eligible patients, a total of 38 (45.2%) patients had osteoporosis, 35 (41.6%) patients had osteopenia while the rest 11 (13%) patients had normal bone density in the COPD group. In the control group, a total of 6 (10%) patients had osteoporosis, 12 (20%) patients had osteopenia while 42 (70%) patients had normal bone density.

In a study by Jørgensen *et al.*,[10] out of 62 total patients with COPD, 54 underwent DEXA scan of hip and lumbar spine. Both bone mass measurements and the knowledge of previous low-energy fractures of individual patients were included for diagnosis of osteoporosis. Combining this data, it was observed that 26 patients (44.8%) had osteoporosis while 13 patients (22.4%) had osteopenia and 15 patients (25.9%) had normal bone mass. Although our results were inconsistent with the study, the difference may be accounted by the fact that they used low-energy fracture as criteria for diagnosis of osteoporosis.

Graat-Verboom *et al.*[11] in 2009 studied a large cohort of 554 patients with moderate to severe COPD who were subjected for whole-body DEXA scan for the screening of osteoporosis. It was found that 21% of them had osteoporosis and 41% of them had osteopenia. Results of our study are in agreement with this study; however, the drawbacks of this study were that they included only moderate to severe degree of COPD patients and they employed whole-body DEXA scan for BMD measurements which, according to the WHO, are not an optimum site for grading of BMD.[8]

The prevalence of osteoporosis was also higher in a major TORCH trial,[12] which was conducted in an 88 US centers involving 658 patients (a subset of 6,184 international patients in TORCH trial). Baseline and yearly bone density measurements at the hip and spine were performed. At baseline, the overall prevalence of both osteoporosis and osteopenia was high at 65%.

There are very few Indian studies related to the prevalence of osteoporosis in COPD patients. Bhattacharyya *et al.*[7] did a study on 37 COPD patients; BMD was assessed using commercially available ultrasound bone densitometer. Of the 37 COPD patients studied, 19 patients (51.3%) had osteoporosis and another eight patients (21.6%) had osteopenia and ten patients (27%) had normal BMD. Results of this study were consistent with our observations; however, they included only advanced COPD patients and measured BMD at a single heel of patients by ultrasound bone densitometer which is not considered a gold standard for diagnosis.[9]

Another Indian study by Hattiholi and Gaude[6] in 2010 measured the BMD in COPD patients by DEXA scan. They reported osteoporosis in 68 patients (66.6%) and osteopenia in 20 patients (19.6%). The varied difference from our study may be attributed to the age difference and different geographical region of studies.

Graat-Verboom *et al.*[5] in a systematic review of 13 studies involving 775 patients with moderate to severe COPD reported an overall prevalence of osteoporosis of 35.1% (range 9%–69%) and osteopenia of 38.4% (range 27%–67%). Most of the participants in this study were male patients.

In brief, the prevalence of osteoporosis in COPD patients in the present study was consistent with other studies which varied from 9%–69% comapred to 0-13% in healthy population. In addition, the prevalence of osteopenia varied from 27% to 67% and was also in agreement with our study. The prevalence of osteoporosis and osteopenia was higher in COPD patients than in healthy controls. The differences in reduced BMD observed in different studies can be attributed to the difference in patient groups selected for the study, geographical regions, demographic characteristics such as age, sex, BMI, physical activity, and procedural methods used for grading BMD. The prevalence of osteoporosis and osteopenia in various studies is summarized below [Table 3].

Jørgensen *et al.*[10] examined the relationship between the severity of COPD and osteoporosis and it was observed that there was an increased incidence of osteopenia and osteoporosis with advancing stage of COPD. They included only GOLD Stage III and IV patients and excluded those patients with already known osteoporosis. They observed that 68% of cases had either low bone mass or a previously undiagnosed vertebral fracture.

Graat-Verboom *et al.*[13] in 2010 used whole-body and local DEXA scans in evaluation of osteoporosis in COPD patients. They observed that, as severity of COPD increased, the prevalence of osteoporosis also increased. The prevalence of osteoporosis was 6%, 19%, and 16% in Stage I, Stage II, and Stage III, respectively, while it increased to 59% in Stage IV COPD patients. In another study by Vrieze *et al.*,[14] similar findings of higher prevalence of osteoporosis in Stage III and Stage IV COPD disease as compared to Stage I and Stage II COPD were observed.

Findings of our study are in agreement with these studies. In the current study, majority (81.6%) of the patients having osteoporosis had Stage III and Stage IV COPD disease. A total of 35 patients had osteopenia, most (77.2%) of which had Stage II and Stage III COPD disease. Stage I and Stage II COPD disease had less prevalence of osteoporosis while 50% of the patients, who had osteoporosis, had Grade IV COPD. Based on the results of our

Table 3: Prevalence of osteoporosis and osteopenia in chronic obstructive pulmonary disease patients

Study	Patient group	Number of patients	Method of BMD measurements	Prevalence of osteoporosis (%)	Prevalence of osteopenia (%)
Jørgensen *et al.*[10]	Ambulatory COPD outpatients	62	BMD LS and FN (DEXA)	44.8	22.4
Ferguson *et al.*[12]	COPD patients	658	BMD LS and FN (DEXA)	24	41
Graat-Verboom *et al.*[11]	COPD patients	554	Whole-body BMD (DEXA)	21	41
Bhattacharyya *et al.*[7]	COPD patients	37	Left heel BB ultrasound bone densitometer	22	51
Hattiholi and Gaude.[6]	COPD patients	102	DEXA lumbar spine	66.7	19.6
Present study	Stable COPD patients	84	Whole-body BMD, lumber spine (DEXA)	45.2	41.6

BMD: Bone mineral density; DEXA: Dual-energy X-ray absorptiometry; FN: Femoral neck; LS: Lumbar spine; BB: Broad band; COPD: Chronic obstructive pulmonary disease

study, it was demonstrated that the prevalence of osteopenia and osteoporosis increased with severity of COPD. These results can be explained by the fact that an increase in severity of COPD is associated with increase of risk factors that lead to occurrence of osteoporosis such as increased inflammatory load of COPD, an increase in dose of corticosteroids in treatment, and a decrease in pulmonary functions.

Conclusions

COPD is a lifestyle-related chronic inflammatory pulmonary disease associated with significant morbidity and mortality worldwide. Reduced BMD is a common comorbid entity in COPD patients leading to increase in bone fragility and increased susceptibility to fracture. Primary care physicians should be aware that the management of comorbidities such as osteoporosis should be incorporated into the comprehensive management of COPD as this will also have an effect on the outcome in COPD patients. The present study was undertaken to evaluate BMD in rising population of patients with COPD in Sub-Himalayan region of Himachal Pradesh, India, and to improve their quality of life by timely intervention. Based on the findings in our study, we recommend that all patients with COPD should be screened for low BMD with DEXA scan, which is considered gold standard for the diagnosis of osteopenia and osteoporosis.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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