Original Article

Chronic obstructive pulmonary disease and low bone mass: A case-control study

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ABSTRACT

Background and Objective: Low bone mass (osteopenia and osteoporosis) is one of the effects associated with chronic obstructive pulmonary disease (COPD). There is very little data from Saudi Arabia on COPD and low bone mass. This retrospective study was done to assess the prevalence of osteoporosis and osteopenia in COPD patients attending King Fahd Hospital of the University (KFHU), Alkhobar. **Patients and Methods:** After obtaining the ethical approval from the research committee, all patients seen between at the King Fahd Hospital of the University between January 2010 and December 2012 were included. The inclusion criteria included a follow up of a minimum 2 years, and the Medical Records should have the details of forced expiratory volume in one second (FEV_1), blood bone profile and bone biomarkers and dual-energy X-ray absorptiometry (DEXA) scan. Patients were labeled as osteopenia if the T score was -<1 to <-2.5 and osteoporosis of <-2.5 as per the WHO definition of osteopenia and osteoporosis. **Results:** Seventy-three patients were being followed in the clinics and 49 patients satisfied the inclusion criteria. The average age was 60.6 ± 10.47 years; males were 43 and females 6. Three (6.1%) were normal and the remaining 46 (93.9%) were with low bone mass. Thirty-two (65.3%) were osteoporotic and 14 (28.57%) were osteopenic. The average duration of COPD was 4.5 ± 6.2 years. Majority (n = 36, 73.4%) of patients were in the Global Initiative for COPD (GOLD) class II and III. FEV_1 was significantly lower in the patients with low bone mass 1.66 ± 0.60 versus 3.61 ± 0.58 (P < 0.001). **Conclusions:** Our study shows that over 90% of Saudi Arabian patients with COPD suffer from osteopenia and osteoporosis and unfortunately they remain under-diagnosed and undertreated.

KEY WORDS: Chronic obstructive pulmonary disease, osteopenia, osteoporosis, secondary osteoporosis

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a debilitating disease with wide systemic consequences and high morbidity. One of the serious systemic manifestations is reduced bone mass leading to osteopenia, osteoporosis and fragility fractures.[1] The cause of low bone mass in patients with COPD is multifactorial. COPD *per se* causes a decrease in physical activity due to poor respiratory reserves and reduced skeletal muscle mass. Use of corticosteroids can be an additional contributor to osteoporosis.[2,3]

Osteoporosis and osteopenia are reported to be common in patients suffering with COPD[4-7] and the prevalence in the range of 24-44% is reported.[1,2,7,8] Osteoporosis often remains overlooked and undertreated, mainly because it is clinically a silent disease until it manifests in the form of a pathologic fracture. Therefore, the primary focus of physicians in patients with COPD is to improve and maintain lung function without realizing that these patients suffer from low bone mass, which in turn increases the risk of fragility fractures and this could lead to an increase in pain and a worsening of respiratory function. There is paucity of studies on COPD and osteoporosis and unfortunately is available from Saudi Arabia. The present study was performed with an objective to find the bone mass status of Saudi Arabian patients with COPD, who attended King Fahd Hospital of the university in AlKhobar,

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Saudi Arabia and were investigated with a dual-energy X-ray absorptiometry (DEXA) scan to asssess bone mass.

PATIENTS AND METHODS

This is a retrospective analysis of all patients with a diagnosis of COPD attending the outpatient clinics of King Fahd Hospital of the University, AlKhobar, a teaching institution of University of Dammam. The inclusion criteria were a follow-up of a minimum 2 years and the medical records giving the details of forced expiratory volume in 1 sec (FEV_1), blood bone profile, bone biomarkers and DEXA. scan in the medical records. Demographic data of the patients' were collected from the Quadra Med patient care database, which included age, sex, weight and height, duration of the COPD investigations like serum calcium, phosphorous, alkaline phosphatase, parathormone, results of DEXA and medications dispensed to the patients. Spirometry was performed as per the protocols of American Thoracic Society (ATS)[9] using Master Screen PFT System, ERICH JAEGER GmbH Hoechberg, Germany. Patients with history of using systemic steroid, severe medical co-morbidities, including liver cirrhosis, thyroid dysfunction, other endocrinology disorders, malignancies, chronic renal disease (creatinine >2.0 mg/dl), and patients treated with bisphosphonate, levothyroxin, lithium, calcium and vitamin D preparations were excluded. Patients were classified as active or sedentary depending on the number of days they could exercise.[10]

The data were analyzed using Statistical Package for the Social Sciences (SPSS), version 14.0, Chicago, Illinois, USA. Data were expressed as mean ± standard deviation (SD). A $P < 0.05$ was considered as significant.

RESULTS

After obtaining the ethical approval from the research committee, all patients seen at the King Fahd hospital of the university between January 2010 and December 2012 were included. The inclusion criteria were a follow-up of a minimum 2 years and the medical records giving the details of forced expiratory volume in one second (FEV_1), FVC, blood bone profile and bone biomarkers and DEXA scan. Patients were labeled as osteopenia if the T score was -<1 to <-2.5 and osteoporosis of <-2.5 as per the WHO definition of osteopenia and osteoporosis.

Seventy-three patients were being followed in the clinics and 49 patients satisfied the inclusion criteria. The mean age was 60.6 ± 10.47 years; males numbered were 43 and females 6.

The demographic data are given in Table 1, which shows that majority of patients 36 (73.4%) were of GOLD class II or III. The average duration of COPD was 4.5 years. Three (6.1%) were normal and the remaining 46 (93.9%) were with low bone mass. Table 2 gives the details of bone profile and lung functions of all the patients.

Table 1: Demographic data

Age	63.17±12.4 years
Sex	
Males	44
Females	5
Height	166.6±7.5
Weight	64.2±16.2
Duration of COPD	4.5±6.2 years
GOLD class of COPD	
Stage I	9
Stage II	15
Stage III	17
Stage IV	8
Life style	
Active	23
Sedentary	26
Spirometry	
Normal	0
Mild	15
Moderate	21
Severe	10
Unable	3

COPD: Chronic obstructive pulmonary disease

Table 2: Bone profile and lung function of all patients

Parameter	Normal (3)	Osteopenia (14)	Osteoporosis (32)
Age (years)	52.5±6.36	58.7±9.1	59.7±5.9
Duration of disease (years)	6.3±6.3	5.4±3.3	9.4±4.8
FEV_1 (l/sec)	3.19±0.58	2.01±0.74	1.31±0.47
FVC	4.47±0.42	2.66±0.27	2.01±0.87
FEV_1/FVC (ratio)	69	67.45	63.29
Calcium (g/dl)	9.85±0.35	9.07±0.56	8.9.±0.41
Phosphorus (g/dl)	3.71±0.42	3.12±0.5	3.26±0.42
Alkaline phosphatase (IU)	75±11.2	87.23±29.7	97.8±26.3
Parathyroid hormone (pg/ml)	5.9±0.6	10.35±3.92	12.6±6.3

FEV_1: Forced expiratory volume in one second, FVC: Forced vital capacity

Table 3: DEXA results for 49 patients

Parameter	Normal (3)	Osteopenia (14)	Osteoporosis (32)
Age (years)	52.5±6.36	58.7±9.1	59.7±5.9
Duration of disease (years)	6.3±6.3	5.4±3.3	9.4±4.8
Spine BMD (g/cm^2)	0.938±0.03	0.953±0.07	0.713±0.1
Spine T score)	0.55±0.6	−1.46±0.6	−3.4±0.6
Hip BMD (g/cm^2)	0.955±0.2	0.918±0.12	0.775±0.31
Hip T score	0.3±0.14	−1.50±0.35	−2.1±0.9

BMD: Bone mineral density, DEXA: Dual-energy X-ray absorptiometry

The results of the DEXA scan are given in Table 3. Thirty-two (65.3%) were osteoporotic and 14 (28.57%) were osteopenic. FEV1 was significantly lower in the patients with low bone mass (1.66 ± 0.60) versus 3.19 ± 0.58 ($P < 0.001$).

DISCUSSION

Our study shows that 90% of our patients had low bone mass; incidence of osteopenia was 35.5% and osteoporosis 58.04%. Patients who were suffering from that of osteoporosis were older, had longer duration of COPD and

lower FeV_1. Graat-Verboom *et al*. (2009)[11] in a review of 13 studies with a total of 775 COPD patients reported that the prevalence of osteoporosis in COPD patients varies between 9 and 69% and that of osteopenia between 27% and 67%. The prevalence of osteopenia and osteoporosis in our study was comparable to the reported studies.

Researchers have correlated the incidence of osteoporosis to the stage of COPD. Bolton *et al*. (2008)[12] in a study of 58 patients reported a prevalence of osteoporosis in 20% of GOLD stage II patients, whereas Tschopp *et al*. (2002)[13] in a study of 74 patients found 69% of their GOLD Stage II patients had osteoporosis. The incidence of osteoporosis with GOLD class II COPD was reported between 49% and 60%, but the mean age was 72 years.[14-16] In our study, the prevalence of low bone mass in GOLD class II was 38.7% and half of them were with osteoporosis even as our patients were much younger. According to a study by Alsayad *et al*. from south region of Saudi Arabia,[17] it was found that the prevalence of osteopenia and osteoporosis was 26.8% and 21.4% at the lumber spine and 30.4% and 23.2% at total hip, respectively. It was significantly higher in patients already on inhaled or oral corticosteroids. In our study, firstly, the prevalence was much higher, and secondly the study of Alsayed had all male patients and the patients were younger than our group. This could be one of the reasons for a higher prevalence as compared to the previous study.

Low body mass index (BMI) is a well-established risk for osteoporosis in healthy people.[18-21] and studies in COPD patients found that majority of the patients had low BMI and low fat free mass index (FFMI) was significantly related to low BMD and low bone mass.[12,19,22]

It has been suggested that patients with COPD have low BMD due to decrease in the physical activity, decreased bone formation due to low mechanical loading and factors which influence proteolysis.[23-28] Contrary to the reports in the literature, majority of our patients were within the normal weight category with the BMI of 22.76 kg/m^2.

In the systematic review of Graat-Verboom *et al*., it has been clearly mentioned that as compared to the other pulmonary diseases the prevalence of osteoporosis was higher in patients with COPD.[11] The serious complication of osteopenia and osteoporosis is a fragility fracture of proximal femur that has a high morbidity and mortality. The incidence of fractures can be reduced by successful treatment. The mismanagement of patients with secondary osteoporosis is not uncommon,[29-31] and in this study except only 2 patients had received calcium and vitamin D whereas the rest were not on any treatment. Similar to the findings of Oschatz *et al* (2009)[29] with similar numbers, we did not encounter any fragility fractures.

Our study has few limitations, one being the retrospective nature and secondly the smaller number of patients studied, and lastly we had to reduce the follow up to increase the number of patients. The strength of the study is that we were able to detect missed cases of low bone mass among COPD patients which gave a cue to screen all patients with COPD and institute appropriate treatment.

In conclusion, it is reasonable for us to state that in patients with COPD, low bone mass is quite common, particularly from GOLD class II onward. We emphasize that every patient of COPD should be investigated for low bone mass by DEXA scan and be assessed for vitamin D deficiency and treated accordingly.

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