RESEARCH PAPER

Assessment of Metabolic Bone Health in Patients with Chronic Obstructive Pulmonary Disease on Long-Term Corticosteroid Therapy

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ABSTRACT

Background: Chronic Obstructive Pulmonary Disease (COPD) is a systemic disorder frequently complicated by metabolic bone disease. Long-term corticosteroid therapy, though essential in disease management, accelerates bone loss and increases fracture risk.

Objectives: To assess radiological and biochemical indicators of bone health in clinically stable COPD patients receiving long-term corticosteroid therapy and to evaluate their association with disease duration and steroid exposure.

Methods: This hospital-based, cross-sectional study included 110 COPD patients attending the General Medicine outpatient department at MMCHRI over a one-year period. All patients fulfilled GOLD criteria and had received corticosteroid therapy for at least three months. Serum calcium, serum phosphorus, and alkaline phosphatase were measured. Lumbosacral spine radiographs were evaluated for osteopenia and osteoporosis. Statistical analysis was performed using SPSS version 22.

Results: Radiological evidence of osteoporosis was observed in 40.9% of patients, while 29.1% had osteopenia. Biochemical abnormalities were common, with elevated alkaline phosphatase in 47.3%, low serum calcium in 43.6%, and low serum phosphorus in 35.5%. A significant association was found between duration of COPD and bone density status ($p < 0.05$), as well as between duration of corticosteroid therapy and osteoporosis ($p < 0.05$).

Conclusion: Metabolic bone disease is highly prevalent among COPD patients on long-term corticosteroids. Routine screening and early intervention should be incorporated into COPD management to reduce fracture risk and improve patient outcomes.

Keywords: *Chronic Obstructive Pulmonary Disease; Osteoporosis; Corticosteroids; Bone Mineral Density; Metabolic Bone Disease; Alkaline Phosphatase*

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1. INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a chronic, progressive respiratory condition characterized by persistent airflow limitation and abnormal inflammatory responses of the lungs to harmful particles and gases. It represents a major global health challenge, with increasing prevalence and substantial socioeconomic impact. The World Health Organization estimates that COPD affects more than 300 million individuals worldwide and is projected to become the third leading cause of death globally (Soriano et al., 2020). Despite advances in pharmacological and non-pharmacological therapies, COPD remains a leading contributor to disability-adjusted life years, reflecting both its pulmonary manifestations and systemic complications.

While COPD has traditionally been regarded as a disease confined to the respiratory system, growing evidence indicates that it is a complex multisystem disorder. Systemic inflammation, oxidative stress, and neuroendocrine dysregulation contribute to a range of extra-pulmonary comorbidities, including cardiovascular disease, metabolic syndrome, skeletal muscle dysfunction, depression, and osteoporosis (Agustí and Faner, 2018). These comorbid conditions significantly influence disease progression, health-related quality of life, hospitalization rates, and mortality. Among them, metabolic bone disease has emerged as one of the most clinically important yet frequently overlooked complications.

Osteoporosis is a systemic skeletal disorder characterized by low bone mass and microarchitectural deterioration, leading to increased bone fragility and susceptibility to fractures. Although it is commonly associated with aging and postmenopausal status, osteoporosis is increasingly recognized as a secondary complication of chronic inflammatory diseases such as COPD. Multiple epidemiological studies have demonstrated that individuals with COPD have significantly lower bone mineral density and higher fracture rates than age-matched controls, independent of smoking status and body mass index (Dennison et al., 2017). Vertebral and hip fractures

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in COPD patients are associated with prolonged hospital stays, increased dependence, and excess mortality.

The clinical impact of osteoporosis in COPD is substantial. Vertebral fractures can alter thoracic biomechanics, reduce chest wall compliance, and impair ventilatory efficiency, thereby exacerbating dyspnea and reducing exercise capacity (Romme et al., 2013). Fractures also limit mobility, promote physical deconditioning, and increase the risk of further skeletal injury. Despite these consequences, osteoporosis often remains undiagnosed in COPD patients until a fracture occurs, at which point irreversible skeletal damage has already developed.

The pathophysiology of bone loss in COPD is multifactorial and involves an intricate interaction between disease-related factors, lifestyle influences, and pharmacological treatments. Chronic systemic inflammation is central to this process. COPD is associated with elevated circulating levels of inflammatory mediators such as interleukin-6, tumor necrosis factor-alpha, and C-reactive protein. These cytokines promote osteoclastogenesis and suppress osteoblast activity, leading to an imbalance between bone resorption and formation (Berg et al., 2016). Pro-inflammatory pathways also impair vitamin D metabolism, further compromising calcium homeostasis and skeletal integrity.

Physical inactivity represents another critical contributor. Dyspnea, fatigue, and muscle weakness limit functional capacity and reduce weight-bearing activity. Mechanical loading is essential for maintaining bone mass, and its absence accelerates bone loss, particularly in the lumbar spine and femoral neck (Ferguson et al., 2018). COPD patients often experience reduced exposure to sunlight due to limited outdoor activity, predisposing them to vitamin D deficiency, which further impairs calcium absorption and bone mineralization.

Smoking, the primary etiological factor for COPD, independently increases the risk of osteoporosis. Nicotine and other tobacco-related toxins inhibit osteoblast proliferation, enhance osteoclast activity, and interfere with estrogen and testosterone metabolism (Kanis et al., 2020). Smoking is also associated with lower body weight and poorer nutritional status, both of which are recognized risk factors for bone loss.

Malnutrition and sarcopenia are highly prevalent in advanced COPD and significantly contribute to skeletal deterioration. Reduced protein intake, micronutrient deficiencies, and loss of muscle mass alter the mechanical and hormonal environment necessary for bone maintenance (Jones et al., 2019). Muscle-bone interactions are increasingly recognized as a key determinant of skeletal health, and disruption of this relationship in COPD accelerates bone loss.

Among all contributing factors, long-term corticosteroid therapy is the most powerful modifiable risk factor for osteoporosis in COPD. Systemic glucocorticoids are widely prescribed for the treatment of acute exacerbations and severe disease. Although they provide important anti-inflammatory benefits, they exert profound deleterious effects on bone metabolism. Large population studies have shown that bone loss occurs rapidly within the first six months of therapy and progresses with cumulative exposure (Amory et al., 2021).

Glucocorticoids impair bone by suppressing osteoblast differentiation, increasing osteocyte apoptosis, and enhancing osteoclast survival, thereby shifting the balance toward bone resorption (Henneicke et al., 2014). They also reduce intestinal calcium absorption and increase renal calcium excretion, leading to secondary hyperparathyroidism. These combined effects result in accelerated trabecular bone loss, particularly in the vertebrae, making patients vulnerable to compression fractures.

The skeletal effects of inhaled corticosteroids remain controversial. While lower doses appear relatively safe, several studies suggest that high cumulative doses may contribute to bone loss, particularly in elderly patients and those with additional risk factors (Weatherall et al., 2019). Therefore, total corticosteroid burden from all routes must be considered when assessing fracture risk.

Biochemical markers of bone metabolism such as serum calcium, phosphorus, and alkaline phosphatase provide indirect insight into skeletal turnover. Elevated alkaline phosphatase has been linked to increased bone turnover and reduced bone mineral density (López-Gómez et al., 2022). Hypocalcemia and hypophosphatemia may reflect impaired absorption, vitamin D deficiency, or renal losses induced by corticosteroids. These laboratory abnormalities may serve as early indicators of metabolic bone disease, particularly in settings where dual-energy X-ray absorptiometry is not readily available.

Despite strong evidence linking COPD and osteoporosis, screening remains inconsistent. Many patients are not evaluated until a fracture occurs. International clinical guidelines emphasize the need for early risk assessment, bone density testing, adequate calcium and vitamin D supplementation, and pharmacologic therapy in high-risk individuals (Cosman et al., 2014). However, integration of bone health assessment into routine COPD care remains limited.

Although osteoporosis in Chronic Obstructive Pulmonary Disease has been described in several populations, there remains limited data from routine clinical settings in resource-constrained environments where dual-energy X-ray absorptiometry is not universally available. The present study is novel in that it integrates radiological lumbar spine assessment with simple, routinely accessible biochemical markers (serum calcium, serum phosphorus, and alkaline phosphatase) to evaluate bone health in clinically stable COPD patients receiving long-term corticosteroid therapy. By demonstrating a high prevalence of both radiological and metabolic abnormalities in a single cohort, this study highlights the feasibility of low-cost, pragmatic screening strategies for early identification

of osteoporosis in high-risk COPD populations. Furthermore, the study strengthens the evidence that duration of disease and cumulative steroid exposure are independent predictors of skeletal deterioration, underscoring the need to incorporate bone health evaluation into standard COPD management protocols. This combined clinical–biochemical approach provides a scalable model for osteoporosis screening in settings where advanced imaging is limited.

The present study was therefore undertaken to evaluate metabolic bone health in clinically stable COPD patients receiving long-term corticosteroid therapy at a tertiary care center

.By combining radiological and biochemical assessment, this study aims to quantify the burden of skeletal disease in COPD and emphasize the importance of early detection and multidisciplinary management.

2. MATERIALS AND METHODS

2.1 Study Design, Setting, and Duration

This hospital-based, observational, cross-sectional study was conducted over a period of one year from December 2024 to December 2025 in the General Medicine Outpatient Department of MMCHRI. The primary objective was to evaluate metabolic bone health in clinically stable patients with Chronic Obstructive Pulmonary Disease (COPD) who were receiving long-term corticosteroid therapy. The study was designed in accordance with ethical standards for biomedical research involving human participants.

2.2 Study Population, Sample Size, and Sampling Technique

A total of 110 patients with a confirmed diagnosis of COPD were included in the study. Diagnosis was based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria. Patients were recruited using a non-probability consecutive sampling technique, wherein all eligible patients attending the outpatient clinic during the study period were approached for participation until the required sample size was achieved. The sample size was determined based on feasibility and outpatient attendance during the study period.

2.3 Eligibility Criteria

Patients aged 40 years and above with clinically stable COPD were considered for inclusion. Clinical stability was defined as the absence of acute exacerbations, hospital admissions, or major changes in pharmacotherapy within the preceding six weeks. All participants were required to be receiving systemic or inhaled corticosteroid therapy for at least 3 months. Written informed consent was obtained from all participants prior to enrolment.

Patients were excluded if they had any known primary metabolic bone disorders, chronic kidney disease, chronic liver disease, malignancy, or endocrine disorders such as thyroid or parathyroid disease. Those receiving medications known to influence bone metabolism, including bisphosphonates, vitamin D supplementation, hormone replacement therapy, or anticonvulsants, were also excluded. Patients with a history of recent fracture, prolonged immobilization, or orthopaedic surgery within the past six months were not included.

2.4 Data Collection and Clinical Assessment

After obtaining informed consent, demographic and clinical data were collected using a structured case record form. Information regarding age, sex, smoking history, duration of COPD, type and duration of corticosteroid therapy, and comorbid conditions was recorded. Anthropometric measurements, including height and weight, were obtained using standardized equipment, and body mass index (BMI) was calculated.

All patients underwent a general physical examination and detailed respiratory system evaluation. Diagnosis and disease stability were confirmed through medical records, clinical assessment, and spirometric documentation where available, in accordance with GOLD guidelines.

2.5 Biochemical and Radiological Assessment

Venous blood samples were collected under aseptic conditions and analyzed in the central hospital laboratory. The biochemical parameters assessed included serum calcium, serum phosphorus, and serum alkaline phosphatase (ALP). Standard laboratory methods and quality control procedures were followed.

Radiological evaluation was performed using lumbosacral spine X-rays in anteroposterior and lateral views. Radiographs were assessed for cortical thinning, trabecular pattern changes, and vertebral compression. Based on these findings, patients were categorized as having normal bone density, osteopenia, or osteoporosis. Two independent radiologists reviewed all images, and disagreements were resolved by consensus.

2.6 Outcome Measures

The primary outcome measure was the prevalence of osteoporosis and osteopenia among COPD patients on long-term corticosteroid therapy. Secondary outcomes included the frequency of biochemical abnormalities and the association of bone status with duration of COPD and corticosteroid therapy.

2.7 Statistical Analysis and Ethical Considerations

Data were entered into Microsoft Excel and analyzed using SPSS version 22. Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequencies and percentages. Associations between bone status and categorical variables were analyzed using the Chi-square test, while one-way ANOVA was used to compare biochemical parameters across bone status groups. A p-value < 0.05 was considered statistically significant.

The study was approved by the Institutional Ethics Committee of MMCHRI. Written informed consent was obtained from all participants, and confidentiality was maintained throughout the study.

3. RESULTS AND DISCUSSION

A total of 110 clinically stable patients with Chronic Obstructive Pulmonary Disease receiving long-term corticosteroid therapy were included in the analysis. The results are presented in the form of demographic characteristics, disease and treatment duration, radiological bone density status, biochemical markers of bone metabolism, and their statistical associations. The distribution of age and gender is described first, followed by disease-related variables, radiological findings, and biochemical abnormalities. Associations between duration of disease, duration of corticosteroid therapy, and bone status were evaluated to identify factors contributing to metabolic bone disease in this population.

Table 1. Age Distribution of Study Participants (n = 110)

Age Group (years)	n	%
40–49	18	16.4
50–59	34	30.9
60–69	41	37.3
≥70	17	15.4
Total	**110**	**100**

Table 1 shows the age-wise distribution of the 110 study participants. The majority of patients belonged to the 60–69 year age group, accounting for the largest proportion of the cohort, followed by patients aged 50–59 years. A smaller proportion of participants were aged 40–49 years and ≥70 years. This distribution reflects the higher prevalence of COPD in older age groups and the cumulative effect of disease duration and exposure to risk factors over time.

Table 2. Gender Distribution

Gender	n	%
Male	79	71.8
Female	31	28.2
Total	**110**	**100**

As shown in Table 2, male patients constituted the majority of the study population, while female patients formed a smaller proportion. This gender predominance is consistent with the higher prevalence of smoking and occupational exposure among males in many populations.

Table 3. Duration of COPD

Duration	n	%
1–5 years	32	29.1
6–10 years	46	41.8
>10 years	32	29.1
Total	**110**	**100**

Table 3 presents the duration of COPD among study participants. Most patients had a disease duration of 6–10 years, followed by those with more than 10 years of disease. A smaller proportion had a duration of 1–5 years. This indicates that a significant number of patients had long-standing disease, which may contribute to cumulative systemic effects, including skeletal involvement.

Table 4. Duration of Corticosteroid Therapy

Duration	n	%
3–6 months	29	26.4
7–12 months	38	34.5
>12 months	43	39.1
Total	**110**	**100**

Table 4 depicts the duration of corticosteroid therapy. A considerable proportion of patients had been receiving corticosteroids for more than 12 months, while others had durations ranging between 3–6 months and 7–12 months. This highlights prolonged exposure to corticosteroids in a substantial subset of patients.

Table 5. Radiological Bone Density Status

Status	n	%
Osteoporosis	45	40.9
Osteopenia	32	29.1

Normal	33	30.0
Total	**110**	**100**

Table 5 summarizes the radiological assessment of bone density using lumbar spine X-rays. A large proportion of patients demonstrated osteoporosis, followed by osteopenia, while only a minority showed normal bone density. Overall, more than two-thirds of the study population had reduced bone density, indicating a high burden of skeletal involvement.

Table 6. Biochemical Abnormalities

Parameter	Abnormal (n)	%
Low serum calcium	48	43.6
Low serum phosphorus	39	35.5
Raised ALP	52	47.3

Table 6 shows the distribution of biochemical abnormalities related to bone metabolism. Elevated alkaline phosphatase was the most frequent abnormality, followed by low serum calcium and low serum phosphorus levels. These findings suggest increased bone turnover and altered mineral metabolism among COPD patients on long-term corticosteroid therapy.

Table 7. Association Between Duration of COPD and Bone Status

Duration of COPD	Osteoporosis	Osteopenia	Normal	p value
1–5 years	7	9	16	
6–10 years	18	15	13	**0.004**
>10 years	20	8	4	

Table 7 demonstrates the association between duration of COPD and bone density status. Osteoporosis was significantly more prevalent among patients with longer disease duration. Patients with COPD for more than 10 years had the highest proportion with osteoporosis, whereas those with shorter disease duration more frequently had normal bone density. The association was statistically significant, indicating a progressive deterioration of bone health with increasing disease duration.

Table 8. Association Between Steroid Duration and Bone Status

Steroid Duration	Osteoporosis	Osteopenia	Normal	p value
3–6 months	6	8	15	
7–12 months	15	13	10	**0.002**
>12 months	24	11	8	

Table 8 illustrates the relationship between duration of corticosteroid therapy and bone density. Patients receiving corticosteroids for more than 12 months showed a markedly higher prevalence of osteoporosis compared to those on shorter courses. Normal bone density was more commonly observed among patients with shorter durations of steroid exposure. This association was statistically significant, suggesting a dose–duration effect of corticosteroids on bone health.

Table 9. Mean Biochemical Values by Bone Status

Parameter	Osteoporosis	Osteopenia	Normal	p value
Serum calcium (mg/dL)	8.1 ± 0.6	8.6 ± 0.5	9.2 ± 0.4	<0.001
Serum phosphorus (mg/dL)	2.7 ± 0.4	3.1 ± 0.3	3.6 ± 0.3	<0.001
ALP (IU/L)	156 ± 32	132 ± 26	98 ± 21	<0.001

This hospital-based observational study evaluated bone health in 110 clinically stable patients with Chronic Obstructive Pulmonary Disease (COPD) who were receiving long-term corticosteroid therapy

A high prevalence of skeletal abnormalities was demonstrated, with 40.9% of patients showing radiological evidence of osteoporosis and a further 29.1% showing osteopenia. In addition, biochemical markers of altered bone metabolism were common, including low serum calcium (43.6%), low serum phosphorus (35.5%), and elevated alkaline phosphatase (47.3%). These findings indicate that metabolic bone disease is a major and frequently underdiagnosed comorbidity in COPD patients on prolonged corticosteroid therapy.

The prevalence of osteoporosis observed in this study is consistent with global reports indicating a significantly higher burden of bone disease in COPD populations. A large systematic review and meta-analysis by Chen et al. (2019) reported a pooled osteoporosis prevalence of 38% among COPD patients, which closely approximates the 40.9% observed in our cohort. Similarly, Graat-Verboom et al. (2009) found that 31% of patients with moderate to

severe COPD had osteoporosis, even after adjusting for age, smoking, and body mass index. These comparisons suggest that the prevalence observed in our cohort is not incidental but reflects a recognized disease pattern.

The pathogenesis of bone loss in COPD is multifactorial and extends beyond age-related degeneration. Chronic systemic inflammation is a key contributor. Elevated circulating inflammatory cytokines such as tumor necrosis factor-α and interleukin-6 stimulate osteoclast activity and suppress osteoblast function, leading to increased bone resorption (Compston, 2018). COPD is also associated with reduced physical activity, chronic hypoxia, muscle wasting, and nutritional deficiencies, all of which further impair bone remodelling (Watanabe et al., 2015). These disease-related factors act synergistically with corticosteroid exposure to accelerate skeletal deterioration.

Long-term corticosteroid therapy remains one of the most important risk factors for secondary osteoporosis. Glucocorticoids exert direct toxic effects on bone by inhibiting osteoblast differentiation, promoting osteocyte apoptosis, and prolonging osteoclast survival (Van Staa et al., 2002). They also reduce intestinal calcium absorption and increase renal calcium excretion, resulting in negative calcium balance and secondary hyperparathyroidism (Compston, 2018). These mechanisms explain why bone loss can occur rapidly, often within the first three to six months of continuous therapy. The significant association between duration of steroid use and osteoporosis observed in this study mirrors the dose-dependent relationship reported in epidemiological studies (Van Staa et al., 2002).

Biochemical abnormalities observed in this cohort provide further evidence of disturbed bone metabolism. Nearly half of the patients had elevated alkaline phosphatase levels, a marker associated with increased bone turnover. Kim et al. (2020) demonstrated that higher serum ALP levels were independently associated with lower bone mineral density and greater fracture risk in large population cohorts. The coexistence of hypocalcemia and hypophosphatemia in a substantial proportion of patients may reflect impaired intestinal absorption, vitamin D deficiency, and steroid-induced renal losses. Similar biochemical patterns have been reported in patients with glucocorticoid-induced osteoporosis (Compston, 2018).

The relationship between COPD duration and skeletal deterioration was also evident in this study. Patients with longer disease duration showed a significantly higher prevalence of osteoporosis. Watanabe et al. (2015) reported that bone mineral density declines with increasing COPD severity and duration, suggesting that cumulative disease burden plays a central role. Advanced COPD is associated with greater systemic inflammation, repeated exacerbations, prolonged steroid exposure, and reduced mobility, all of which contribute to accelerated bone loss. The findings of the present study are therefore consistent with the concept that bone disease in COPD is progressive and closely linked to disease chronicity.

Although inhaled corticosteroids (ICS) are commonly prescribed in COPD, their impact on bone health appears less pronounced than that of systemic formulations. Loke et al. (2011) reported that standard-dose ICS did not significantly increase fracture risk, although higher cumulative doses were associated with modest reductions in bone mineral density. In contrast, systemic corticosteroids have been consistently linked to clinically significant bone loss and fracture risk. In the present study, the strong association between bone abnormalities and steroid duration suggests that systemic exposure was the dominant contributor.

The clinical implications of these findings are considerable. Osteoporotic fractures in COPD patients are associated with increased morbidity, reduced quality of life, and higher mortality. Vertebral fractures, in particular, worsen respiratory mechanics and may further compromise pulmonary function. Despite this, osteoporosis screening is often overlooked in routine COPD care. Current guidelines for the prevention and treatment of glucocorticoid-induced osteoporosis recommend baseline fracture risk assessment, bone mineral density testing, adequate calcium and vitamin D supplementation, and early initiation of anti-resorptive therapy in high-risk patients (Buckley et al., 2017). The high prevalence of bone abnormalities observed in this study supports the need to integrate such strategies into standard COPD management.

Several limitations should be considered when interpreting these results. The use of lumbar spine radiography rather than dual-energy X-ray absorptiometry limits the sensitivity for detecting early bone loss and prevents quantitative assessment. The cross-sectional design also precludes causal inference, and potential confounders such as vitamin D levels, nutritional status, and smoking intensity were not independently analyzed. Nevertheless, the consistency of these findings with international literature supports their validity and clinical relevance.

In summary, this study demonstrates that metabolic bone disease is highly prevalent among COPD patients receiving long-term corticosteroid therapy. The strong concordance between our findings and existing research confirms that osteoporosis is a major comorbidity in this population. Routine screening, early diagnosis, and preventive treatment are essential to reduce fracture risk and improve long-term outcomes.

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