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HIGH PREVALENCE AND INDEPENDENT PREDICTORS OF OSTEOPOROSIS IN HOSPITALIZED PATIENTS WITH INTERSTITIAL LUNG DISEASES

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Abstract

Background:
Interstitial lung diseases (ILDs) are a heterogeneous group of chronic pulmonary disorders characterized by varying degrees of inflammation and fibrosis. Patients with ILDs are frequently exposed to multiple risk factors that adversely affect bone health.

Objective:
To identify the prevalence of osteoporosis in hospitalized patients with ILDs as well as to determine the demographic, clinical, biochemical, and predictors of the disease related to low bone mineral density.

Methodology:
The study was a cross-sectional descriptive study, which was completed in a 6-month period in the Department of Pulmonology in a tertiary care hospital. A total of 20-75 years adult inpatients with a confirmed ILD were enrolled using consecutive sampling. The mineral density of bone was measured by using dual-energy X-ray absorptiometry of lumbar spine, neck of the femur, and total hip and categorized as per the world health organization criteria. Multivariate logistic regression analysis was employed in identifying independent predictors of osteoporosis and $p < 0.05$ was regarded as statistically significance.

Results:
The average age was 60.2 ± 10.8 years and 60% of the respondents were males and 40% females. Osteopenia was found in 27% of patients and osteoporosis in 55%. Deficiency in vitamin D was found in 68% and 74% had a history of taking systemic corticosteroids. Independent predictors of osteoporosis were age ≥60 years, use of corticosteroids, vitamin D deficiency, and severe ILD.

Conclusion:
Osteoporosis is highly prevalent among hospitalized ILD patients. Incorporating routine bone health assessment into ILD management may reduce fracture risk and improve clinical outcomes.

INTRODUCTION

Interstitial lung diseases (ILDs) are a heterogeneous group of long-term parenchymal lung diseases, which are different degrees of inflammation and fibrosis, often resulting in a progressive loss of respiratory function, functional impairment and elevated morbidity. In addition to pulmonary involvement, ILDs have been

increasingly noted to be systemic conditions with extensive extra pulmonary expressions with an adverse impact on overall health status. [1] Osteoporosis is one of these, and is a comorbidity with little significance yet with a huge impact among hospitalized patients with advanced or active disease. A number of processes associate ILDs and poor skeleton health. Chronic systemic inflammation, decreased physical activity caused by dyspnea, malnutrition and long term immobilization during hospitalization, respectively, favor bone loss. Moreover, calcium-vitamin D metabolism disturbances are prevalent in patients with chronic LD, and have been linked to worse lung function and worse clinical outcomes in ILD-associated with connective tissue disease-associated ILDs. These effects are exacerbated by aging since it has been shown that there is a strong correlation between pulmonary fibrosis and osteoporosis in the elderly populations. These results point to the fact that the deterioration of bone health in patients with ILD is complex and cannot be limited to changes associated with age. [2]

The pharmacological aspects are very critical as well. Glucocorticoids will continue to play a central role in the treatment of a number of ILDs in spite of the established adverse impacts on skeletal remodeling. Osteoporosis that develops as a result of glucocorticoid use is typified by bone depletion and an augmented risk of fractures, in spite of a low dose or brief therapy termination. [3] Therefore, ILDs patients are especially susceptible to the accumulated steroid exposure along with risk factors associated with the disease itself. On a larger scale, osteoporosis is becoming more recognized across respiratory diseases, a fact that demonstrates the necessity of combined pulmonary-skeletal evaluation. [4]

There is further evidence of disease that proves this association. Idiopathic pulmonary fibrosis has been reported to decrease BMD, regardless of the conventional osteoporosis risk factors, indicating disease-specific mechanisms. [5] Clinical practice guidelines in countries with access to modern medicine acknowledge the importance of early diagnosis and active treatment of osteoporosis to prevent fractures and enhance patient outcomes in the long-term perspective 6, 7. Nonetheless, the majority of recommendations are based on general or rheumatologic populations and might not be sufficient in relation to the specific risk profile of the hospitalized ILD patients. The research on chronic obstructive pulmonary disease also shows that osteoporosis is prevalent, under-diagnosed and under-treated in chronic lung diseases, which again justifies the topicality of this concern in respiratory diseases. [9] ILDs have now been perceived as multisystem diseases that are complex in nature. Proper diagnosis of osteoporosis, which is mainly conducted by Dual-Energy X-Ray Absorptiometry (DEXA) is vital to initiate timely treatment and risk categorization. [10]

Nonetheless, there is limited information on the prevalence and the causes of osteoporosis in in-patients with ILDs specifically, particularly in resource-strained environments. The knowledge about the burden and determinants of osteoporosis in this vulnerable group is thus very important to inform screening measures, better inpatient management, and minimizing preventable complications.

METHODS

The cross-sectional descriptive design to identify the prevalence of osteoporosis and its determinants in in-patients with interstitial lung diseases (ILDs). The study carried out in inpatient wards of the Department of Pulmonology at Jinnah Postgraduate medical Centre (JPMC), Karachi, a tertiary care referral hospital with a good diagnostic service of ILDs, which includes high-resolution computed tomography, pulmonary function test, arterial blood gas test, and well-established dual-energy x-ray absorptiometry (DEXA) unit within the Department of Radiology. The length of the study was 6 months to recruit patients, collect data, perform imaging, and conduct laboratory tests and statistical analysis in ILD admissions.

The study was conducted under the ethical approval of the Institutional Review Board of JPMC after they are approached. All the processes were done based on the Declaration of Helsinki. The participants that meet the requirements were explained the goals of the study, the research

processes, the risks, and advantages of the research. Informed consent was taken prior to enrolling written consent. The confidentiality was ensured via use of unique identification codes, and all the data gathered was kept in databases that had password-protected and accessible only to the research team.

The standard formula of calculating the accuracy of prevalence studies was used to calculate the sample size with an expected prevalence rate of osteoporosis assumed to be 15% expected prevalence of osteoporosis among ILD patients 95% confidence interval and margin of error set to 0.05. The final sample size was 100 participants to allow the researcher to overcome potential non-response, incomplete or unavailability of DEXA scan data, and to obtain sufficient statistical power to ascertain the presence of statistically significant associations.

Consecutive sampling method was used. Sequential screening and enrolment of all adult patients admitted in the pulmonology wards who have a confirmed diagnosis of ILD during the period of study were included till the complete sample size achieved. The inclusion criteria was to include patients aged 20-75 years with a confirmed diagnosis of ILD by clinical assessment and radiological and/or histopathological findings, current hospitalization to receive treatment of ILD, and provide informed consent. All patients with a known metabolic bone disease, bone-affecting malignancy, contraindication to DEXA scanning, or pregnancy were excluded in order to reduce confounding.

The instruments that utilized in data collection included a structured, pretested questionnaire, and clinical examination, review of medical records, laboratory investigations, and DEXA scanning. The demographic data was gathered, anthropometric data was taken, smoking history gathered, clinical ILD profile, duration of the disease, parameters of the lung functions, oxygenation, and corticosteroid use dose and duration were collected. Lifestyle variables leading to physical exercise, calcium and vitamin D in the diet, sunlight exposure, and the history of falls or fractures were also documented. Measured Bone Mineral Density (BMD) obstructed at the lumbar spine, neck of the femur and overall hip under standardized DEXA protocols and findings were coded as per the world health organization T-score. Biochemical tests were involved at the levels of serum calcium, phosphorus, alkaline phosphatase, and 25-hydroxyvitamin D.

The SPSS version 26 was used to analyze data. The continuous variables were summarized using means and standard deviations whereas the categorical variables were presented using frequencies and percentages. Categorical variable associations was done through chi-square tests and the difference in mean bone mineral density between subgroups was done through independent t-tests or analysis. The analysis was done by the multivariate logistic regression to determine the independent predictors of osteoporosis such as corticosteroid exposure, ILD duration, disease severity and vitamin D status. A value that is below 0.05 was taken as significant.

RESULTS

A total of 100 hospitalized patients with confirmed interstitial lung diseases (ILDs) were included in the final analysis. Data were analyzed using SPSS version 26. In accordance with the Pakistan Journal of Medical Research style, results are presented concisely using three comprehensive tables with accompanying descriptive text. **(Table I)**

Table I. Demographic, Anthropometric, and Clinical Characteristics of Study Participants (n = 100)

Variable	Category	N (%)
Age (years)	20–39	10 (10.0)
	40–59	34 (34.0)
	60–75	56 (56.0)
Gender	Male	60 (60.0)

	Female	40 (40.0)
BMI	Underweight	18 (18.0)
	Normal	44 (44.0)
	Overweight/Obese	38 (38.0)
Smoking status	Never	42 (42.0)
	Ever (former/current)	58 (58.0)
ILD subtype	IPF	36 (36.0)
	CTD-associated ILD	28 (28.0)
	Others*	36 (36.0)
ILD duration	<2 years	24 (24.0)
	2–5 years	44 (44.0)
	>5 years	32 (32.0)
Pulmonary function (FVC %)	Mild (>70%)	14 (14.0)
	Moderate (50–70%)	38 (38.0)
	Severe (<50%)	48 (48.0)

*Others include hypersensitivity pneumonitis, sarcoidosis, and occupational ILDs.

The mean age of participants was 60.2 ± 10.8 years, with more than half aged ≥60 years. Males constituted 60% of the cohort. Nearly one-fifth of patients were underweight. Idiopathic pulmonary fibrosis was the most frequent ILD subtype. Almost half of the patients had severe pulmonary function impairment based on forced vital capacity. Hypocalcemia was observed in 26% of patients, while no cases of hypercalcemia were detected.

(Table II)

Overall, 55% of hospitalized ILD patients were diagnosed with osteoporosis, while 82% demonstrated reduced bone mineral density (Osteopenia = 27%

Table II. Bone Mineral Density Status, Biochemical, and Lifestyle Characteristics (n = 100)

Variable	Category	N (%)
BMD status (DEXA)	Normal	18 (18.0)
	Osteopenia	27 (27.0)
	Osteoporosis	55 (55.0)
Site-specific osteoporosis	Lumbar spine	48 (48.0)
	Femoral neck	42 (42.0)
	Total hip	36 (36.0)
Vitamin D status	Deficient (<20 ng/mL)	68 (68.0)
	Insufficient	20 (20.0)
	Sufficient	12 (12.0)
Serum calcium	Low	26 (26.0)
	Normal	74 (74.0)
	High	0 (0)
Physical activity	Sedentary	62 (62.0)
History of falls/fracture	Fragility fracture	22 (22.0)
	Falls without fracture	24 (24.0)

Osteoporosis = 55%). The lumbar spine was the most commonly affected skeletal site. Vitamin D deficiency was highly prevalent, observed in more than two-thirds of participants. Sedentary lifestyle

patterns and a notable history of falls or fragility fractures were frequently reported. **(Table III).**

Table III. Factors Associated with Osteoporosis and Multivariate Logistic Regression Analysis

Variable	Osteoporosis n (%)	Adjusted OR (95% CI)	p-value
Age ≥60 years	38/56 (67.9)	3.4 (1.5–7.6)	0.003
Steroid use >12 months	36/74 (48.6)	4.2 (1.8–9.8)	0.001
Vitamin D deficiency	44/68 (64.7)	3.1 (1.3–7.2)	0.009
Severe ILD (FVC <50%)	34/48 (70.8)	2.7 (1.1–6.3)	0.020

On multivariate logistic regression analysis, age ≥60 years, prolonged systemic corticosteroid use, vitamin D deficiency, and severe ILD were independently associated with osteoporosis. Prolonged corticosteroid exposure emerged as the strongest predictor.

DISCUSSION

The given cross-sectional study illustrates that hospitalized patients with interstitial lung diseases (ILDs) have a high burden of osteoporosis, as more than half of the study group had a diagnosis of osteoporosis and more than four-fifths showed a decrease in bone mineral density. These results support the idea of ILDs being systemic diseases with severe skeletal outcomes, which can be seen especially in patients who need inpatient treatment. The prevalence observed is greater than that available in general populations and fits with the currently emerging data that bones loss is significantly increased in chronic inflammatory lung diseases, where the duration of treatment and hospitalization is required. [11]

The good and independent relationship between the long-term exposure of systemic corticosteroids and osteoporosis is one of the most significant results of the current research. The strongest predictor in the multivariate analysis is long term glucocorticoid therapy, which is congruent with the present day evidence characterizing rapid bone loss, the impaired functioning of osteoblasts and the increase in osteo-fracture risk posed by glucocorticoids. [11, 13] Even though inhaled corticosteroids can be viewed as safer, recent meta-analytic findings point to the possibility of cumulative corticosteroid exposure, despite the use of inhaled routes, contributed to the risk of increased fracture in the population with chronic lung disease.[12] The skeletal effect is consequently likely to be more severe in ILD patients who often take systemic steroids at increased doses and duration.

Another critical risk factor of osteoporosis in this group was the increase in age. The odds of patients aged 60 years and above, developing osteoporosis were significantly greater considering both age-related bone loss and disease-related risk factors. The results are in line with regional ILD-specific studies whereby an increased prevalence of osteoporosis was observed in aged patients. [13-15] Other studies have indicated similar associations in observational studies of ILD patients in South Asia, now highlighting the importance of regular evaluation and rectification of vitamin D status.[15] An aged condition is linked to a decreased capacity of bone remodeling, altered hormones, and more sensitive to the catabolic impact of inflammatory processes and corticosteroids, both of which are pertinent in ILD groups.[16]

In this study, deficiency of vitamin D was very high and was independently related with osteoporosis. Low vitamin D levels are often associated with chronic respiratory disease with low sunlight exposure, poor nutrition and systemic inflammation all being factors that contribute to these levels of vitamin D being low. [17] Vitamin D deficiency also worsens secondary hyperparathyroidism and increases the rate of bone resorption, which contributes to the exacerbation of the effects of glucocorticoids and physical inactivity. [18]

The severity of the disease was also important with higher chances of patients with a severely impaired pulmonary functionality to develop osteoporosis. Acute ILD is in most cases accompanied by chronic hypoxia, loss of mobility, and wasting of

muscles, which causes mechanical unloading of bone and rapid bone loss. This relationship is supported by evidence in other chronic respiratory diseases in which an unfavorable lung functioning is associated with a reduced bone mineral density and heightened risk of fracture. [19]

The clinical applicability of osteoporosis in hospitalized patients with ILD is also further demonstrated by the high prevalence of sedentary lifestyle patterns, as well as a history of falls or fragility fractures among the cohort that were considered. Decreased exercise not only deteriorates pulmonary outcomes but also leads to sarcopenia as well as skeletal vulnerability. [20]

On the whole, the results of this work are in line with the increasing trends in the literature of various countries that osteoporosis is prevalent, multimorbid, and unidentified in chronic respiratory disease patients. The high prevalence level among hospitalized patients with ILD shows that why systematic screening of bone health, reasonable corticosteroids use, vitamin D and calcium status optimization, and timely preventive approaches are necessary. By including the concept of bone health assessment within the standard ILD inpatient services, it can be considered that the risk of fractures, functional outcomes, and the overall burden of the disease can be lowered in this risk group.

Conclusion

The prevalence of osteoporosis in hospitalized patients with interstitial lung diseases is high where over half of the patients have the condition and most of them have a low bone mineral density. Older age, long time systemic use of corticosteroid, deficiency of vitamin D, and gross pulmonary impairment were detected as important independent predictors. These results demonstrate the systematic observation of ILDs and the necessity of routine osteoporosis testing, early risk assessment, and bone health management as an element of routine inpatient treatment to decrease the risk of fractures and promote the desired overall clinical outcome.

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Availability of Data: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical Approval:

Conflict of Interest: None declared.

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