ORIGINAL ARTICLE

Assessing Prevalence of Osteoporosis and Identifying Risk Factors in Interstitial Lung Disease Patients

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ABSTRACT

Background: Chronic lungdiseases are severe diseases which have a wide prevalence of osteoporosis in them. These chronic lung diseases include cystic fibrosis, bronchial asthma, bronchiectasis, and chronic obstructive pulmonary disease. However, there is only limited data available that define its risk factors and its prevalence in patients that have Interstitial Lung Disease (ILD).

Objective: The purpose of this research is to study patients with ILD and determine the risk factors and prevalence of osteoporosis in ILD patients.

Study Design: A cross-sectional study

Place and Duration: This study was conducted at Gulab Devi Chest Hospital Lahore from December 2021 to December 2022

Methodology: A total of 80 patients participated in this research. This research is a cross-sectional analysis of all of those patients who had ILD. Every patient that was already admitted to the hospital was a part of this study. The clinical data and demographics of each participant were noted down. In order to measure the density of the bone mineral, an absorptiometry scan (x-ray), which was of dual-energy, of the femoral neck of the patient was performed. To identify osteoporosis, T-scores were considered, as we were following the guidelines of the World Health Organization. The risk factors were identified by conducting multivariate as well as univariate logistic regression analysis.

Results: The majority of the sample size were females, representing 67.5 percent of the participants (n=54). The average age was 55.8 years. There were 32 patients in whom osteoporosis was identified. Univariate analysis showed certain factors that were positively related to osteoporosis. These factors include the time period of symptoms, female gender, and a low hemoglobin level. Multivariate analysis showed the hemoglobin level and the time period of symptoms as independent risk factors.

Conclusion: In patients that are diagnosed with Interstitial Lung Disease, osteoporosis is a common problem. The existence of osteoporosis in these patients can be determined by low hemoglobin levels and the longer time period of the symptoms.

Keywords: Interstitial Lung Disease. Osteoporosis, chronic lung disease, adults

INTRODUCTION

Pulmonary fibrosis characterizes interstitial lung disease (ILD) which is a group of more than two hundred diseases [1]. It leads to progressive short of breath and cough. ILD is linked with certain comorbidities like gastroesophageal reflux, depression, pulmonary hypertension, and sleep-disordered breathing [2, 3, 4, 5]. All of these also add to the symptoms which makes the health of the patient severe and worsens their quality of life.

Chronic lung diseases are severe diseases which have a wide prevalence of osteoporosis in them. These chronic lung diseases include cystic fibrosis, bronchial asthma, bronchiectasis and chronic obstructive pulmonary disease(COPD) [6,7]. There are a few factors that increase the risk of osteoporosis in patients with these chronic lung diseases. These risk factors include long-term corticosteroids, old age, nutritional status is being poor, no physical activity, systemic inflammation, and smoking tobacco [8]. All those patients presenting with one or more pre-existing these risk factors are at high risk of developing osteoporosis. According to prior research studies, the rate of prevalence of osteoporosis in people with ILD is said to be 13 to 44 percent [9]. There are certain factors that increase the risk of osteoporosis in people with ILD. Those factors include Hispanic ethnicity, a very low BMI, and old age. Hence, the purpose of this research was to study patients with ILD and determine the risk factors and prevalence of osteoporosis in ILD patients.

METHODOLOGY

This research is a cross-sectional analysis. Overall, 80 hospitalized patients having age more 50 years were included in this research. All participants were diagnosed as case of interstitial lung disease (ILD) on the basis of symptoms duration examination findings, radiological investigations along with spirometry. Written consent from all patients was taken. Those participants who had lower respiratory tract infection, acute exacerbation, concomitant COPD, renal dysfunction, liver dysfunction, malignancies, and heart failure were not a part of this research.

Every participant's detailed history was recorded. The data on the history included the existence of diabetes, duration of symptoms, smoking history, time period of symptoms, exposure to the environment and occupation to inciting agents, and prior Antituberculosis therapies. In order to calculate the time period of the symptoms, the time from the start of symptom related to ILD was recorded. The records of each participant were checked and verified whenever available so that the type and time period of the symptoms are confirmed. In order to record a detailed treatment history of the patient, the medical records of those individuals were checked and the time period and dose of steroids were explained verbally. If a patient had consumed prednisone of more than 10 mg of more than three months, it is said that the use of steroids is significant for that individual [11]. Certain tests, such as liver function, renal function, and complete blood count (CBC) were conducted. Routine spirometry values, distance for a six-minute walk (6-MWD), and arterial oxygen saturation (SaO2) was used to determine the severity of the disease. RMS Helios 401 spirometer was used to perform spirometry. As required by ATS, spirometry was conducted which included the values of FEV1/FVC. The 6-MWT was conducted in which the distance that the individual covered was recorded. The change in saturation of oxygen was also recorded. The BMD was measured by taking a dual-energy x-ray absorptiometry scan of the femoral neck of the individuals. A Hologic DXA system was used to conduct this test. To express the values of BMD, T scores (the SD compared to an adult which is a young, sex-matched control population) and Z scores (the SD compared to age and sex-matched control population) were used. If the T score is less than -2.5, osteoporosis was determined.

The results were expressed in terms of the percentage of patients having ILD and osteoporosis. Certain factors such as BMI, age, time period of symptoms, gender, SaO2, hemoglobin level, FVC, 6-MWD, and diabetes were examined to identify their relationship with osteoporosis. All of these factors were analyzed using logistic regression analysis.

Statistical Analysis: The mean, median, and standard deviation were quantitative variables. On the other hand, the qualitative variables were expressed in terms of percentage or frequency. In order to have a comparison of nominal and continuous variables between the individuals having ILD, the chi-square test, and Mann-Whitney U-test were performed in both conditions, with osteoporosis or without osteoporosis. The association between the existence of osteoporosis, factors related to therapy, the participants, and the disease was analyzed through multivariate logistic regression, following the forward LR method. 95% confidence intervals were measured with the odds ratios through a multivariate model to predict the risk factors linked with osteoporosis. A P-value below 0.05 was considered significant. For the statistical analysis, SPSS software version 23 was used.

RESULTS

A total of 80 individuals were a part of this research. The majority of the sample size was females, representing 67.5 percent of the participants (n=54). The average age was 55.8 years. One-third of the participants were old people, which means there were 27 old people out of 80 participants. A total of 28 participants were obese, representing 35 percent of the sample size. There were 5 people whose body mass index was lower than 18.5 kilogram/m2, representing .25 percent of the participants.

The most common symptom was exertional dyspnea which was found in 91.25 percent of the population, which means there were 73 people who had this symptom. The average time period for the symptoms was 2 years. There were 60 patients (75 percent) who had one or more than one extrapulmonary symptoms. Overall 37.5% of people were using the steroid significantly which makes 30 patients. This steroid was a part of the ILD surgery. There were the majority of females who had developed osteoporosis had the most time period of the symptoms. The most common type of ILD identified in our research was hypersensitivity pneumonitis. The others were connective tissue disease and pulmonary fibrosis. Table number 1 shows the baseline features of the participants who were having ILD. The average t-score of this research was -3.12. Table number 2 shows the t scores and z scores.

Table 1: baseline features of the participants

Parameters	No Osteoporosis (n=48)	Osteoporosis (n=32)
Mean Age (years)	55.8	55.8
Females (54)	31	23
Males (26)	17	09
Time period of symptoms (years)	1.5	3
Previous ATT	8	3
Body mass index (kg/m2)	23.2	23.5
Hemoglobin (g/dl)	12.8	11.8
SaO2	94.0	93.1
FVC (%)	69	71
Smokers	8	5
Steroid use	20	10
6-MWD (meter)	317	284
Diabetes	15	6

Table 2: T scores and Z scores

Parameters	Min	Max	SD
BMD	0.5	1.1	0.8
Z score	-4.8	2.1	-1.2
T score	-5.1	0.6	-2.12

T score <-2.5 is Osteoporosis

Table number 3 shows the relationship between different parameters of osteoporosis in patients having ILD. There were 32 patients in whom osteoporosis was identified, representing 40% of the participants. By using the univariate regression analysis, we found that there is a positive correlation between osteoporosis and low hemoglobin, female gender, and the time period of the symptoms. On the other hand, by using multivariate regression analysis, we analyzed that low hemoglobin level and the time period of the symptoms are the two independent risk factors that determine osteoporosis in patients with ILD.

Table 3: relationship between different parameters of osteoporosis in patients having ILD

Parameters	Univariate	Multivariate
Age (years)	0.9	0.61
Females	2.9	0.02
Time period of symptoms (years)	1.24	1.29
Non-IPF diagnosis	0.9	0.54
Hemoglobin (g/dl)	0.59	0.59
FVC (%)	0.99	0.56
Steroid use	1.36	0.56
6-MWD (meter)	1.01	0.21
Diabetes	0.51	0.22

DISCUSSION

According to our research's findings, there is a greater prevalence of low bone density in people who are diagnosed with ILD, with a 40 percent prevalence of osteoporosis. The results of our research show that the likelihood of a diagnosis of osteoporosis is increased when the hemoglobin levels are low and the time period of the symptoms are greater.

Low bone mass and microstructural deterioration of bone tissue, which increase the risk of fracture and include the strength of the bone, are characteristics of the skeletal disorder called osteoporosis [12]. People with COPD are likely to develop low bone fragility but there is insufficient data to explain the relationship between chronic respiratory diseases with osteoporosis [13]. There was research conducted by Caplan-Shaw and his fellow authors conducted a study on 86 people who had lung transplantation [14]. They found out that osteoporosis had a prevalence of 13 percent in their study. There was another prior research which was conducted on 196 people who were newly diagnosed with interstitial lung disease. That research showed that osteoporosis had a prevalence of 44 percent in those patients [15]. Although the subtypes of ILD and the profile of the participants were different, osteoporosis was found to have a higher prevalence which is similar to our research.

Studies have found that the prevalence of osteoporosis is wide in young and healthy adults. According to some research studies, women having osteoporosis represent 20 percent and men, who are above the age of 50, represent 10 to 15 percent of the population who have osteoporosis. There was research conducted on more than 31 thousand young and healthy adults in which the prevalence of osteoporosis was found to be 18.3 percent [16]. If we compare this rate of prevalence with our research, our study has a higher rate because of the disease in patients. The disease had a causal role in predisposing to osteoporosis. Hence, by analyzing the results, we can say that osteoporosis is likely to increase its prevalence risk in people if the people are diagnosed with any disease or had any therapy in the past.

If the time period of the symptoms are more, the duration of the disease is increased. Our research predicted osteoporosis through the time of the first symptom of ILD in those patients. This may be due to the constant response seen in many different types of ILD. The different types of ILD include hypersensitivity, IPF, and non-IPF interstitial pneumonia. These types of ILD can cause bone resorption by using a few chemical mediators. Then this would result in the development of osteoporosis. As the activity of osteoclasts and osteoblasts increases, the turnover rate of bone increases. This is seen in people who have pulmonary fibrosis and

these patients have a growth factor as a mediator. The increase in this activity leads to the development of osteoporosis [17]. Our research results also show that there is no relation between osteoporosis and with 6-meter walk distance test, arterial oxygen saturation, and lung function test. We conclude that the severity of the disease does not increase the risk of osteoporosis. In fact, it is the chronicity of ILD that increases the risk of osteoporosis. These results are also similar to a number of previous research studies in which none of the studies claimed that the severity of the disease caused osteoporosis to occur.

Due to hormonal changes, osteoporosis is likely to be diagnosed in females more than the males [18]. This statement is also proved by our research which showed 67.5 percent of the participants were female. Overall 23 (28.75%) females out of 80 participants were diagnosed with osteoporosis. Themean age of females was 55.8 years. However, multivariate analysis showed no significant association. The third variable that showed a significant relationship with osteoporosis was low hemoglobin level. In the general population, there is a risk factor, called anemia, which indicates poor nutritional status [19]. Nevertheless, the role of anemia in association with osteoporosis in patients with ILD was not studied in previous research studies. Instead, previous studies show that a low body mass index is said to be an independent risk factor for osteoporosis. If we look at our research, the body mass index values were not significant in the two groups studied. However, the findings suggest that the risk of developing osteoporosis is also increased with a decrease in nutritional intake. Therefore, the treatment of patients having ILD should include nutritional management.

In the general population, it is seen that people with old age have a likelihood of developing osteoporosis [20]. But still, this factor has shown different results in previous studies. Even our own research could not find a significant relationship between osteoporosis and old age. One reason for this could be that the individuals who were involved in this research were mostly middle-aged. Another risk factor of osteoporosis is the use of corticosteroids for a longer period of time. However, our research does not show a significant relationship between osteoporosis and the use of steroids. One reason for this can be that only 30 patients were using steroids in their treatments. Lastly, there was also no significant relationship between the development of osteoporosis and the etiology of ILD. The etiology of ILD includes IPF v/s non-IPF.

CONCLUSION

In patients that are diagnosed with Interstitial Lung Disease, osteoporosis is a common problem. The existence of osteoporosis in these patients can be determined by low hemoglobin levels and the longer time period of the symptoms. There are also a few other general risk factors that help in determining osteoporosis in the patients. The results of our research suggest that there should be future research studies conducted that should include a large sample size and should be for a longer duration which can be used to determine the long-term effects of osteoporosis on patients with ILD and should also use different options to treat this disease.

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REFERENCES

1. King CS, Nathan SD. Pulmonary hypertension due to interstitial lung disease. CurrOpinPulm Med 2019;25:459‑67
2. Chen YW, Ramsook AH, Coxson HO, Bon J, Reid WD. Prevalence and risk factors for osteoporosis in individuals with COPD: A systematic review and meta‑analysis. Chest 2019;156:1092‑110
3. Consensus development conference: Diagnosis, prophylaxis, and treatment of osteoporosis. Am J Med 1993; 94:646‑50.
4. Parra ER, Kairalla RA, Ribeiro de Carvalho CR, Eher E, Capelozzi VL. Inflammatory cell phenotyping of the pulmonary interstitium in idiopathic interstitial pneumonia. Respiration 2007; 74:159‑69.
5. Vasakova M, Selman M, Morell F, Sterclova M, Molina‑Molina M, Raghu G. Hypersensitivity pneumonitis: Current concepts of pathogenesis and potential targets for treatment. Am J RespirCrit Care Med 2019;200:301‑8
6. Pan ML, Chen LR, Tsao HM, Chen KH. Iron deficiency anemia as a risk factor for osteoporosis in Taiwan: A nationwide population‑based study. Nutrients 2017; 9:616.
7. Mitrache C, Passweg JR, Libura J, Petrikkos L, Seiler WO, Gratwohl A, et al. Anemia: An indicator for malnutrition in the elderly. Ann Hematol 2001; 80:295‑8.
8. Lane NE. Epidemiology, etiology, and diagnosis of osteoporosis. Am J ObstetGynecol 2006; 194:S3‑11.
9. Hershcovici T, Jha LK, Johnson T, Gerson L, Stave C, Malo J, et al. Systematic review: The relationship between interstitial lung diseases and gastro‑oesophageal reflux disease. Aliment PharmacolTher 2011;34:1295‑305
10. Clarson LE, Bajpai R, Whittle R, Belcher J, Abdul Sultan A, Kwok CS, et al. Interstitial lung disease is a risk factor for ischaemic heart disease and myocardial infarction. Heart 2020;106:916‑22
11. Tschopp O, Boehler A, Speich R, Weder W, Seifert B, Russi EW, et al. Osteoporosis before lung transplantation: Association with low body mass index, but not with underlying disease. Am J Transplant 2002;2:167‑72
12. Raghu G, Remy‑Jardin M, Myers JL, Richeldi L, Ryerson CJ, Lederer DJ, et al. Diagnosis of idiopathic pulmonary fibrosis. An official ATS/ERS/JRS/ALAT clinical practice guideline. Am J RespirCrit Care Med 2018; 198:e44‑68.
13. Kumar R, Gupta N, Goel N. Spectrum of interstitial lung disease at a tertiary care centre in India. PneumonolAlergol Pol 2014; 82:218‑26.
14. Caplan‑Shaw CE, Arcasoy SM, Shane E, Lederer DJ, Wilt JS, O'Shea MK, et al. Osteoporosis in diffuse parenchymal lung disease. Chest 2006; 129:140‑6.
15. Kanis JA. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: Synopsis of a WHO report. WHO Study Group. OsteoporosInt 1994;4:368‑81
16. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: Guidelines for the six‑minute walk test. Am J RespirCrit Care Med 2002;166:111‑7
17. Okazaki R, Watanabe R, Inoue D. Osteoporosis associated with chronic obstructive pulmonary disease. J Bone Metab 2016;23:111‑20
18. Aggarwal D, Palta A, Jindal R, Kumar A, Sodhi MK, Saini V. Prevalence and predictors of osteoporosis in patients of interstitial lung disease: An observational study from North India. Indian Journal of Respiratory Care¦ Volume. 2022 Oct; 11(4):354.
19. Marot M, Valéry A, Esteve E, Bens G, Müller A, Rist S, Toumi H, Lespessailles E. Prevalence and predictive factors of osteoporosis in systemic sclerosis patients: a case-control study. Oncotarget. 2015 Jun 6; 6(17):14865.
20. Gupta L, Lawrence A, Edavalath S, Misra R. Prevalence and predictors of asymptomatic vertebral fractures in inflammatory myositis. International Journal of Rheumatic Diseases. 2018 Mar; 21(3):725-31.