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The Prevalence of Osteoporosis in Chronic Liver Disease Patients Seen in Basrah Gastroenterology and Hepatology Hospital

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ABSTRACT

Background: Osteoporosis (OP) has become an increasingly recognized complication among patients with chronic liver disease (CLD).

Objective: This study aimed to determine the prevalence of osteoporosis among patients with CLD and to identify the risk factors associated with osteoporosis in these patients.

Materials and Methods: One hundred patients who visited Basrah Gastroenterology and Hepatology Hospital between February 2020 and December 2021 with assessed osteoporosis. Using dual energy X-ray absorptiometry (DEXA), bone density was evaluated. The severity of liver disease, smoking, alcohol use, demographic, biochemical characteristics were all taken while assessing the risk factors for osteoporosis.

Results: Of the 100 patients (male/female: 44%/56%, mean age (46 ± 11.5), 50% had CLD diagnoses, 50% did not. Of the 50 patients with CLD,20 patients had OP(40%),while four patients (8%) of the 50 patients without CLD had OP. Twenty-four (24%) of the total patients who undertook the DEXA study showed OP, while seventy-six (76%) did not. Twenty of the twenty-four individuals with OP had CLD (84%) while just four (16%) did not. Child-Pugh A made up 26% of CLD patients, Child-Pugh B 30%, while Child-Pugh C 44%. In this study, osteoporosis and osteopenia were present at rates of 24% and 31% respectively. OP and CLD appeared to be related in a very substantial way (p 0.001). CLD was identified as an independent predictor of OP by multivariate logistic regression analysis (OR (95% CI):9.09(2.18-37.93), p=0.0

Conclusion: It was determined that OP and CLD are significantly correlated. People with CLD were more likely to develop OP. As a result, routine follow-up of these individuals may require biochemical and bone mineral density (BMD) monitoring.

Keywords: Osteoporosis, Chronic liver disease, CLD, DEXA scan

INTRODUCTION

A common metabolic bone illness called osteoporosis (OP) causes the bone tissue to deteriorate structurally, increasing the risk of fracture. It is anticipated that as lifespans expand, this significant public health issue will worsen for the elderly [1]. Osteoporosis in chronic liver illness has a complicated and poorly understood etiology, although the primary causes are increased bone resorption and decreased bone production [2, 3].

There are many mechanisms that contribute to unstable bone remodeling, some of which are still unclear. However, a number of chemicals, such as parathyroid hormone (PTH), vitamin D, and calcitonin, affect how quickly normal bone remodeling occurs. PTH levels that are higher encourage bone remodeling by raising resorption. The active metabolite of vitamin D, 1,25(OH)2D3, is a powerful bone resorption agent and is also necessary for the mineralization of new bone. Growth hormone (GH), thyroid hormone, and sex steroids are other key hormones in bone metabolism. Additionally, some systemic and local variables as interleukin-1 and -6, transforming growth factor (TGF-), and insulin-like growth factors (IGF) might influence osteoblast and/or osteoclast function [4].

The metabolism of bones may be impacted by toxic chemicals, such as aluminium and copper, which build up in liver failure. Increased iron burden in hemochromatosis may reduce osteoblastic activity [5, 6]. It has also been demonstrated that bilirubin inhibits osteoblast growth [7]. Calcium (Ca) malabsorption and low levels of serum vitamin D3 metabolites were discovered in CLD [8–11]. Patients with CLD have been described as having hyperparathyroidism [12].

Osteoporosis and fractures in CLD have also been linked to chronic corticosteroid therapy [13]. Although they have not been identified as independent risk factors for osteoporosis, typical CLD patient characteristics including alcohol use, low body weight, and inactivity can be presumed to be significant [14].

Aim of the study: To determine the prevalence of osteoporosis among patients with chronic liver disease and to identify the risk factors associated with osteoporosis in these patients.

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PATIENTS AND METHODS

This cross-sectional observational study included 100 patients seen at Basrah Gastroenterology and Hepatology Hospital between February 2020 and December 2021. All of the participants received dual energy X-ray absorptiometry to measure their bone mineral density. We also gathered information on smoking status, alcohol consumption, underlying liver and renal disease severity, demographic and biochemical variables, and other aspects. Subjects were divided into groups based on whether they had osteoporosis or not, and they were compared to other individuals without CLD who had measured DEXA scans for other reasons. Using the Child-Pugh score, the prognosis of the underlying chronic liver disease was evaluated.

Measurements:

These included the International Normalized Ratio (INR), albumin, total serum bilirubin, creatinine, calcium, phosphorus, alkaline phosphatase, parathyroid hormone, and 25-hydroxy vitamin D. Demographic details, Child-Pugh classification, smoking history, and laboratory results were also noted. Dual energy X-ray absorptiometry (DEXA) was used to quantify bone densitometry, which was then classified into three categories: normal BMD (T-score -1.0 SD), osteopenia (-2.5 SD T-score -1.0 SD), and osteoporosis (T-score -2.5 SD). According to the US Institute of Medicine (IOM) [15], a level of 12 ng/ml was considered to be deficient in vitamin D.

Ethical approval of institution: In accordance to Helsinki ethical principles, this study was approved by the Ethics Board of the college of Medicine, University of Basrah, Institutional Review Board. The ethics approval and written agreement to participate in the study has been signed by all patients.

Statistical analysis

IBM SPSS statistics version 25 was used to conduct all of the analyses. Percentages and mean/SD were used to express values. For group comparison, continuous variables were compared using the student's t test or the Mann-Whitney test, while qualitative variables were compared using the X^2 test or the Fischer's exact test. To evaluate the independent relationships with osteoporosis, multivariate binary logistic regression analyses were conducted. P-values ≤ 0.05 were regarded as statistically significant for all statistical analyses.

RESULTS

Baseline characteristics: The study included a total of 100 osteoporosis patients (M/F, 44%/56%) with a mean age of 46 ± 11.5 years (range, 12-76). In comparison to 50 patients without CLD, only 4 patients (8%), out of the 50 patients with CLD, had OP (Table 1).

Table (1): Baseline characteristics of all patients

Variables		**%**
Age (mean ± SD)		(46 ±11.5)
Gender	Male	44%
	Female	56%
Alcohol	Alcoholic	6%
	Non-alcoholic	94%
Smoking	Smoker	16%
	Non-smoker	84%
Vitamin D levels	Sufficiency	67%
	Insufficiency	20%
	Deficiency	13%
T-score	**Normal**	**45%**
	Osteopenia	31%
	Osteoporosis	24%

Out of the 100 participants who underwent the DEXA research, 24 (or 24%) had OP and 76 (or 76%) did not. Twenty of the 24 individuals with OP had CLD (84%) while just four (16%) did not (Table 2).

Table (2): The comparison group of osteoporosis and non-osteoporosis patients

Variables	**Osteoporosis group (24)**	**Non-osteoporosis group (76)**	**P-value**
Age (years)	47.67 ± 9.604	45.47 ± 12.07	0.4
Gender (Male/Female)	66.7%/33.3%	36.8%/63.2%	0.01
Alcoholic	33.3%	66.7%	0.6
Smoker	18.8%	81.3%	0.7
CLD	40%	60%	<0.001
T-score	-3.45±0.63	-0.47±1.06	<0.001
Vitamin D level (ng/ml)	25.74±3.19	29.43±1.35	0.3
Vitamin D deficiency	38.5%	61.5%	0.2
Calcium (mg/dl)	8.49±1.57	8.37±2.00	0.7
Phosphorus (mg/dl)	3.11±0.59	3.40±0.93	0.1
ALP (IU)	160.98±13.66	75.34±8.42	<0.001
PTH (pg/ml)	76.73±17.77	47.32±2.71	0.04

Twenty patients (16%) and six (6%) had substance abuse issues. The Child Pugh (Child) scale was used to assess the severity of the illness, it showed that 50% of the patients had CLD and 50% did not. Of the patients who had CLD, 26% had Child-Pugh A, 30% had Child-Pugh B, and 44% had Child-Pugh C (Table 3).

Table (3): T-Score variation according to Child-Pugh Score

		CLD			Total
		A	B	C	
T-SCORE	Normal	10(20 %)	6(12 %)	6(12 %)	22(44 %)
	Osteopenia	1(2%)	5(10 %)	2(4%)	8(16 %)
	Osteoporosis	2(4%)	4(8%)	14(28 %)	20(40 %)
Total		13(26 %)	15(30 %)	22(44 %)	50 (100 %)

Prevalence of bone disease and fragility fractures:

In total, 24% of people had osteoporosis. While 45% of patients were normal, 31% of them developed osteopenia. 13% of the participants in our study had vitamin D insufficiency. Males were more likely than females to have osteoporosis (66.7% versus 33.3%, respectively, p=0.01). Patients with osteoporosis experienced chronic liver illness substantially less frequently (40% vs. 60%, p0.001) than patients without the condition. Patients with osteoporosis had significantly greater parathormone and alkaline phosphatase levels than patients without the condition (p=0.04 and p0.001 respectively). In both groups, the blood chemical profile and mean age were comparable (Table 2).

Risk factors for osteoporosis:

In binary logistic regression analysis, we took into account factors including age, gender, alcohol, smoking, and CLD. The results showed that CLD was an independent predictor and increased the risk of osteoporosis (OR (95% CI): 9.09 (2.18-37.93), p=0.002). A higher risk of osteoporosis was also linked to male sex, advanced age, alcohol use, and vitamin D deficiency (OR (95% CI): 2.03 (0.63-6.48), 1.00 (0.96-1.05), 6.01 (0.29-122.46), and 4.20 (0.82-21.47, respectively) (Table 4).

Table 4. Multivariate analysis risk factors for osteoporosis

Variables	Multivariate analysis Odds (95% CI)	P-value
Age	1.00 (0.96-1.05)	0.6
Male	2.03 (0.63-6.48)	0.2
Alcohol	6.01 (0.29-122.46)	0.2
Smoking	0.11 (0.01-1.38)	0.08
CLD	9.09 (2.18-37.93)	0.002
Vitamin D deficiency	4.20 (0.82-21.47)	0.08

DISCUSSION

The study found that there is extremely strong proof that osteoporosis and chronic liver disease are related (p 0.001). Additionally, multivariate regression analysis showed that osteoporosis is independently predicted by chronic liver illness. Furthermore, osteoporosis risk was increased by advanced age, male sex, alcohol, CLD, and vitamin D deficiency. According to a recent study by **Sokhi *et al.*** [16], the prevalence of osteoporosis and osteopenia was 11.5% and 34.6% respectively, while the prevalence of osteoporosis and osteopenia in our study was 24% and 31%, respectively. According to another study, 48.1% of people had osteopenia and 36.6% had osteoporosis [17].

Osteoporosis and osteopenia were more common than expected, with prevalence rates of 31% and 36%, respectively, according to a retrospective study by **Atay *et al.*** [18]. While a sizable cross-sectional investigation found that the prevalence of osteoporosis was greater than in our sample (72% vs. 72%), this difference may be explained by the fact that 78% of the patients in that study had decompensated cirrhosis and 59% had alcoholic cirrhosis [19].

Males were more likely to develop osteoporosis than females (66.7%/33.3%, p = 0.01), which may be related to the low mean ages of males and females in our sample (47.18 ± 12.36, 45.07 ± 10.83). There was also a significant connection between osteoporosis and gender. Additionally, osteoporosis in males is a heterogeneous clinical condition, where the majority of men lose bone mass as they age. Some men might acquire osteoporosis at a young age, frequently for unknown causes (idiopathic osteoporosis) [20]. Contrary to our findings, a number of researches found that women were more likely than men to develop osteoporosis [18, 21].

Recent NHANES data revealed a substantial rise in osteoporosis prevalence in both genders, however at varying ages and intensities. At the age of 70, the prevalence of osteoporosis in women climbed quickly, while in males, the prevalence by 80 years old, and the prevalence of osteoporosis are doubled [22]. Additionally, our study found substantial evidence (p 0.001) linking osteoporosis and serum alkaline phosphatase (ALP). Alkaline phosphatase levels that are raised could point to increased bone cell activity and probable bone loss. Alkaline phosphatase activity, which may be connected to bone resorption, was also slightly elevated in women with more severe osteoporosis, according to **Hulth *et al.*** [23]. Other research, however, found no connection between osteoporosis and alkaline phosphatase [24–26].

PTH levels that are high cause the bones to release more calcium, which over time can result in weakened bones and a loss of bone density. Our study's finding that PTH and osteoporosis are significantly correlated (p =

0.04) is in line with several studies on the influence of parathyroid hormones on osteoporosis [27–29].

Atay *et al.* [18] (p=0.1) did not discover such a connection.

Low vitamin D levels have been observed in people with osteoporosis. Vitamin D is essential for the metabolism of bone minerals. Other research, however, has not identified a connection between vitamin D and BMD, and vitamin D supplementation have no impact on BMD [30-32]. Similarly, our research found no connection between osteoporosis and vitamin D levels (P=0.3). The current investigation also found compelling evidence (P 0.001) linking chronic liver dysfunction to osteoporosis. Numerous studies have shown links between osteoporosis, or low bone mass, and liver illness. Low bone mass has been noted in a variety of liver illnesses, and osteoporosis prevalence has been reported to range from 11 to 58% in patients with chronic liver disease and liver transplant recipients [4, 33].

Patients with CLD are more likely to develop osteoporosis than those without CLD (OR (95% CI): 9.09 (2.18-37.93), p=0.002). CLD were also discovered to be an independent predictor of osteoporosis. In addition to female sex, lower weight, and height. **Wariaghli *et al.* [21]** found that cholestasis is a risk factor for osteoporosis in CLD. As a result, osteoporosis is essentially a complication of CLD.

CONCLUSION

Osteoporosis is a common side effect of chronic liver disease, particularly in its last stages. According to the study's findings, osteoporosis and CLD are significantly correlated. Patients with CLD are also more likely to develop OP. As a result, routine follow-up of these individuals may require biochemical and BMD monitoring. It is necessary to conduct further in-depth research on the potential causes of osteoporosis and low bone density.

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List of abbreviations:

CLD	**Chronic liver disease**
OP	Osteoporosis
GI &Hep hospital	Gastroenterology and hepatology hospital
ALP	Alkaline phosphatase
PTH	Parathyroid hormone
DEXA scan	Dual energy X-ray absorptiometry
GH	Growth hormone
BMD	Bone mineral density

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