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Prevalence of osteoporosis in patients with liver cirrhosis.

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Abstract

Background: In the recent past, numerous researchers have analyzed dissimilar aspects of osteoporosis in liver cirrhosis, we still have deficient indigenous literature. The present study aims to determine the frequency of osteoporosis with liver cirrhosis.

Methodology: A prospective observational study was carried out at the Tertiary referral center of Karachi. Osteoporosis of liver cirrhosis patients was established as specified by WHO using dual-energy X-ray absorptiometry (DXA) on the L1-L4 spine and having spine bone mineral density (BMD) expressed as T score <-2.5. Short history related to the duration of the disease was recorded. The patient's BMD expressed as a T score was measured using DXA on the spine.

Results: Among patients who had presented with a duration of cirrhosis of 5 years or less, 20(6.75%) had osteoporosis, whereas 62(20.9%) had it with a duration > 5 years (p=0.000). As far as outcome of the patients is concerned 52(17.5%) and 30(10.1%) patients had osteoporosis with BMI < 25 kg/m^2 and > 25 kg/m^2 respectively (p=0.590). When layered according to the Childs Class, among patients with Class A, B, and C, 0.33%, 3.37%, and 23.9% of patients had osteoporosis (p=0.050).

Conclusion: In conclusion, the prevalence of osteoporosis in patients with cirrhosis was found to be 27.7%. Furthermore, patients with a longer duration of disease, low BMI, and with child class C are at greater threat of the occurrence of osteoporosis and require early detection and prompt treatment.

Keywords

Liver Cirrhosis, Osteoporosis, Bone Mineral Density, Fracture, Child-Pugh Class.

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Introduction

Worldwide, liver Cirrhosis is triggered by multiple etiologies, which eventually is liable for major mortality and morbidity[1]. In Pakistan, cirrhosis is one of the frequent disease leading to hospitalization (where Hepatitis B and C virus-related disease shares the most imminent cause)[2]. The international osteoporosis foundation has established that greater than 30% of females and more than 20% of males over 50 years developed osteopenia or osteoporosis, making them easily susceptible to fractures[3]. The word osteoporosis is marked by decreased bone mass and micro architectural degradation leading to increased brittleness of bones[4]. Previously the term Hepatic osteodystrophy was used synonymously for bone disease in liver cirrhosis[5], but it mainly signified osteomalacia related to bone demineralization[6], which was infrequent as compared to osteopenia and osteoporosis[7].

Currently, osteoporosis is considered a communal form of bone disorder in patients with cirrhosis of the liver[8]. It pretenses an advanced fracture threshold with an incidence of traumatic vertebral and peripheral fractures ranging from 8-32%[9]. Vertebral osteoarthritis and fractures afflicted bone mineral density causing overvalue of bone minerals leading to a decreased estimation of fracture threat[10]. The most interesting factor is that it can be directly attributed to the severity of cirrhosis. Moreover, it worsens initially with liver transplant and is estimated to affect 38% of patients awaiting liver transplantation[11]. The mechanism of development of hepatic osteodystrophy is indistinct, which has led to several controversies in its pathogenesis and accompanying risk dynamics[12-15]. Several aspects, in particular malnourishment, restricted mobility, and hormonal disruptions, are believed to bear an etiological impact in its evolution[16-17]. Subsequently imparting a decremental effect on bone mineral content destroying the trabecular structure and ultimately bone archietecture[18-20].

As the liver amalgamates numerous particles that can act as growth factors or hormones, it has been hypothesized that liver structural disruption resulting from cirrhosis causes osteoporosis through the compromised assembly of bone-active liver particles[21]. Diverse methods have been devised to score for bone mineral density, out of which dual-energy x-ray absorptiometry (DEXA) scan is the most commonly used and recommended gold standard method for diagnosing and predicting fracture risk occurring[22]. Even though, in the recent past, numerous researchers have analyzed dissimilar aspects of osteoporosis in liver cirrhosis, we still have deficient indigenous literature. Thus our study focus on identifying the frequency of osteoporosis in liver cirrhosis based on which effective strategies for thorough screening and prompt management can be developed.

Methodology

A prospective observational study was carried out from July 2017 to June 2018, two hundred ninety-six liver cirrhosis patients of either gender were enrolled after obtaining informed consent and approval from the Ethical Review Board (Ref No: CPSP/REU/MED-2012-174-7596) at the Internal Medicine Department of Abbassi Shaheed Hospital, Karachi-Pakistan. The sample size was calculated by taking the prevalence of osteoporosis 26%[23], the margin of error=5%, and the confidence level CI=95% with the help of WHO software.

Patients having liver cirrhosis for more than 6 months and presenting with any 3 or more of the following on ultrasound scan of the abdomen was used for specific labeling of disease (reduction of liver size, i.e., longitudinal diameter of the right and the left lobes < 90 mm and 70 mm; nodularity of liver surface; coarsening of liver echo texture; ascites index ≥ 50 and portal hypertension with portal vein size > 13 mm).

Osteoporosis was established as specified by WHO using dual-energy X-ray absorptiometry (DXA) on the L1-L4 spine and having spine BMD expressed as T score ≤ -2.5[25]. Unacceptance and those with longstanding incurable diseases like malnourishment, diabetes mellitus type II, hypothyroidism, chronic renal failure, stroke, chronic obstructive pulmonary disease, congestive

heart failure, and post-menopause were excluded. Short history related to the duration of the disease was recorded. The patient's BMD expressed as a T score was measured using DXA on the spine. The findings of variables mentioned above were entered in a pre-designed Performa.

Data was analyzed on SPSS version 20.0. Mean and standard deviations calculated quantitative variables like age, BMI, and duration of cirrhosis. Qualitative variables like gender, child Pugh class, and osteoporosis (yes/no) were calculated by frequencies and percentages.

Post-stratification Chi-square test was applied, taking a p-value ≤ 0.05 as statistically significant.

Results

Two hundred ninety-six patients meeting the criteria were enrolled in the study. Of these liver cirrhosis patients, 82 (27.7%) had, and 214 (79.3%) did not have osteoporosis. Patients' mean age, BMI, and disease duration were 48.90 ± 5.61 years, 26.34 ± 4.52 kg/m^2, and 4.23 ± 2.60 years, respectively (Table 1).

Table 1: Patient characteristics.

Variables		N=296
Gender	Male	167(56.42)
	Female	129(43.58)
Age Group	30-45 years	181(61.14)
	46-60 years	115(38.86)
Child-Pugh Class	A	09(3.04)
	B	56(18.92)
	C	231(78.04)
Osteoporosis	Yes	82(27.7)
	No	214(79.3)
Age (years); Mean±SD		38.90±5.61
Duration of liver cirrhosis (years); Mean±SD		4.23±2.6
Body mass index (kg/m^2); Mean±SD		26.34±4.52

The outcome measure, osteoporosis, was then stratified according to age, gender, duration of liver cirrhosis, BMI, and Childs Pugh Class. In male patients osteoporosis was found in 11.8% compared to 15.8% in females patients (p=0.000). Only 64(21.6%) patients younger than 45 year had osteoporosis compared to 18(6.08%) in patients above 45 year age group (p=0.000). Among patients who had presented with a duration of cirrhosis of 5 years or less, 20(6.75%) had osteoporosis, whereas 62(20.9%) had it with a duration > 5 years (p=0.000). As far as outcome of the patients is concerned 52(17.5%) and 30(10.1%) patients had osteoporosis with BMI < 25 kg/m^2 and > 25 kg/m^2 respectively (p=0.590). While graded according to the Childs Class, among patients with Class A, B, and C, 0.33%, 3.37%, and 23.9% of patients had osteoporosis (p=0.050) (Table 2).

Table 2: Outcome stratified with patient characteristics.

Variables		Osteoporosis		p-value
		Yes	No	
Age	30-45 years	64(21.6)	117(39.5)	0.0002*
	46-60 years	18(6.08)	97(32.7)	
Gender	Male	35(11.8)	132(44.5)	0.0039*
	Female	47(15.8)	82(27.7)	
Duration of liver cirrhosis	≤ 5 years	20(6.75)	96(32.4)	0.0014*
	> 5 years	62(20.9)	118(39.8)	

Body mass index	≤ 25 kg/m^2	52(17.5)	127(42.9)	0.59
	> 25 kg/m^2	30(10.1)	87(29.3)	
Child-Pugh class	Class A	01(0.33)	08(2.70)	0.056*
	Class B	10(3.37)	46(15.5)	
	Class C	71(23.9)	160(54.0)	

*p<0.05 is considered significant.

Discussion

Liver cirrhosis shares a great burden of illnesses in developing countries like Pakistan. Osteoporosis has emerged as a major and devastating consequence of liver cirrhosis which is surprisingly asymptomatic and results in a dramatic impairment and eventual decline in the quality of life. Interestingly, osteoporotic fractures are fairly common among cirrhotic patients compared to the normal population. Liang et al., in their study, conclude osteoporotic fractures are twice as common in cirrhotic as compared to noncirrhotics[23]. The etiology of osteoporosis is multifactorial and poorly understood. In this study, the prevalence of osteoporosis was found to be 82(27.7%) out of 296 patients with liver cirrhosis. In this perspective, previous studies done locally showed the incidence of 20-50%, and western literature showed the prevalence of 20-30%[26], and 13-55%[27,28], even some studies show the prevalence of up to 75% during illness[29-30]. The wide variability in different studies can probably be explained by different patient selection factors, etiologies, and techniques of bone mass measurement and definition of osteoporosis.

Age and gender have been shown to impact the development of osteoporosis. The findings of our study were consistent with previous studies, which showed a female predominance of 15.8% and were found to be statistically significant[16-17]. This could be attributed to endocrine factors along with cirrhosis. Hormones like estrogen and progesterone are deficient in females, especially in the older age group. One of the strongest postulation of our study is the early commencing of a Bone Dexa Scan for cirrhotic patients for early recognition of this disabling disease.

Osteoporosis was significantly high (p=0.000) in cases that had cirrhosis for more than 5 years, affecting 62(20.9%) cases in contrast to 20 (6.75%) cases with a duration of less than 5 years. In this regard, the results of Javed et al., were compatible with our study. Weight loss is linked with an overall amplified possibility of fractures[24]. Unswervingly, this work infers that lesser BMI was a threat for osteoporosis in liver cirrhotic. Comparison of Child-Pugh classification with osteoporosis showed that most patients belonged to Child class C as paralleled to class A and B. Our outcome is consistent with the studies done by Javed et al. [24] and Salama et al.[21], which have established an association between the graveness of liver disease and osteoporosis. Management of osteoporosis involves early identification of the BMD valuation using a dual-energy X-ray absorptiometry scan and treating it early for risk stratification.

Our study also encountered certain limitations. Firstly, being a sole center working with limited participants, study subjects are perhaps not a true representative of all cirrhotic populations in the community. Secondly, all cirrhotic patients were selected irrespective of etiologies and child class. The isolated effect of different etiologies on bone metabolism and the development of osteoporosis could not be concluded confidently. Furthermore, as we had subjects from all stages of cirrhosis (Child Class A-C), the presence of ascites might have affected patient weight and bone mineral density assessment. We recommend a multicenter study with a large sample size that incorporates all etiologies distinctly and also emphasizes the need for further studies to document the role of different treatment modalities on bone mineral density to minimize the morbidities secondary to osteoporosis.

Conclusion

In conclusion, the prevalence of osteoporosis in patients with cirrhosis was found to be 27.7%.

Furthermore, patients with a longer duration of disease, low BMI, and with Child Class C are at greater threat of the occurrence of osteoporosis and require early detection and prompt treatment.

Conflicts of Interest

The authors have declared that no competing interests exist.

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