

## Frequency Assessment of Osteoporosis in Patients of Liver Cirrhosis

NAJAM-US-SEHAR SAEED, MUHAMMAD ASIF GUL, ADNAN SALIM, ALTAF ALAM, ANWAAR AHMAD KHAN, KASHIF MALIK

### ABSTRACT

**Background:** Osteoporosis is a chronic disease significantly associated with morbidity and increased risk of fracture. On base of bone mineral density measurements (BMD), the prevalence of osteoporosis among patients with liver cirrhosis has been reported as 38% establishing its common trend in patients of liver cirrhosis. The severity of Osteoporosis increases with severity of liver disease. Child's class C cirrhosis has more severe osteoporosis than Child's class A. Liver cirrhosis has multifactorial etiology and most common causes in our country are hepatitis C and hepatitis B. Etiology of liver cirrhosis varies widely among different geographical areas of the world.

**Aim:** To determine the frequency of osteoporosis in patients of liver cirrhosis.

**Methods:** This Cross-sectional survey was conducted at Department of Gastroenterology – Hepatology, Shaikh Zayed Hospital Lahore for Six months. A total of 70 patients of liver cirrhosis were selected using non-probability purposive technique. All patients fulfilling the inclusion criteria were enrolled and informed consent was taken. BMD of lumbar spine (L1, 2, 3) and proximal femur (neck and trochanter) was calculated by DEXA scan (Discovery W S/N 82330). Data were entered and analyzed for appropriate descriptive and stratification using SPSS version 15.

**Results:** A total of 70 patients of liver cirrhosis were included in the study among whom 62 (88.6%) were male patients and 8 (11.4%) were female patients. Mean age of patients was 45.14 years (SD  $\pm 11.04$ ) with age range of 20-60 years. Out of 70 patients, 22 (31.4%) patients had osteoporosis and 24 (34.3%) had osteopenia. Out of 22 patients of osteoporosis, 4 (18.1%) patients had Child class A, 5 (22.7%) had Child class B and 13 (59%) belonged to C ( $P=0.4$ ).

**Conclusion:** Osteoporosis is a common complication of liver cirrhosis and it does not correlate with severity of disease. So it is important to diagnose it early and treat.

**Keywords:** Osteoporosis, Bone mineral density, fracture, liver cirrhosis and Child Pugh class.

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### INTRODUCTION

One of the most threatening skeletal diseases characterized by low bone mass and microarchitectural deterioration is osteoporosis. This condition causes increase in fragility of bone that consequently makes patients susceptible to fractures<sup>1</sup>. Osteoporosis is divided into primary (senile and postmenopausal) and secondary types. About 30–50% of women and 15–30% of men suffer from osteoporosis-related fractures in their lifetime<sup>1,2</sup>. The most typical fractures include the hip, vertebral body and distal forearm. Osteoporosis afflicts 75 million persons in the United States, Europe and Japan and causes 1.5 million fractures annually in the United States at a direct health cost of at least \$13 billion. Though exact prevalence of osteoporosis in Pakistan is not yet known but it is documented to be considerably high<sup>3</sup>.

Various causes in association with liver cirrhosis may aggravate the osteoporosis; especially viral

hepatitis and alcohol etc. are thought to be common causes of secondary osteoporosis. On base of bone mineral density measurements (BMD), the prevalence of osteoporosis among patients with liver cirrhosis has been reported as 38% establishing its common trend in patients of liver cirrhosis<sup>2,4</sup>. The severity of osteoporosis increases with severity of liver disease; Child's class C cirrhosis has more severe osteoporosis than Child's class A. Moreover it worsens initially with liver transplant but gradually improves afterwards<sup>5</sup>.

Liver disease variant of osteoporosis leads to higher fracture threshold with prevalence of atraumatic spinal and peripheral fractures ranging from 8-32% (highest frequency among patients with cirrhosis)<sup>5,6</sup>. Some fractures have also been repeatedly documented in 24–65% of patients in the early (3 to 6 months) postoperative period after liver transplant particularly in the vertebrae, ribs, and long bones. The trabecular bone turnover is mostly seen in osteoporosis patients with hepatic disease along with reduced osteoblast function and low serum osteocalcin levels. Studies have shown varying

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Lahore General Hospital Lahore

Correspondence: Dr. Muhammad Asif Gul, Email: asifgul1@hotmail.com, Cell: 03219466846

pathogenesis mechanism of osteoporosis in CLD that has created controversy not only about indefinite pathogenesis but also for risk factors of osteoporosis in CLD. However the suspected risk factors for metabolic bone disease in CLD include the presence of liver cirrhosis, hypogonadism, steroid therapy and calcium malabsorption<sup>7</sup>.

Though osteoporosis is a histologic diagnosis but still noninvasive imaging studies such as bone mineral density measurements and radiography are preferred mode of diagnosis. This is because noninvasive imaging studies provide an exact assessment of bone mass and fracture risk. The World Health Organization standard definition for osteoporosis as bone mineral density 2.5 standard deviations below the young normal mean (T score) is used to diagnose severity of osteoporosis. Hence, any person who meets the World Health Organization definition and has radiographic evidence of one or more fractures is labeled as having Severe or "established" osteoporosis. The most frequently used method for measuring bone mass is dual energy x-ray absorptiometry because of its precision and use for measuring multiple skeletal sites<sup>8</sup>. Early diagnosis and treatment can reduce the incidence of fractures in this chronic disease.

## MATERIALS AND METHODS

This Cross-sectional survey was conducted at Department of Gastroenterology-Hepatology at Shaikh Zayed Hospital Lahore for six months. Non-probability purposive sampling technique was used to collect desired information from 70 patients with liver cirrhosis. Patients of Liver cirrhosis as per operational definition 20-60 years of age and both genders and of any Child's class were included in this study. Those with BMI <19kg/m<sup>2</sup>, Glucocorticoid use >5mg/day for 3 months, having previous history of fracture or in family, Postmenopausal females, using of other drugs like calcium, vitamin D, calcitonin, bisphosphonates 5 or 6 months before study on previous medical record and among whom cholestatic Liver disease was diagnosed on raised direct bilirubin >1mg/dl, raised alkaline phosphatase >169 IU/ml and ultrasound evidence of obstruction in biliary tree were excluded from this study. Also any patients having any chronic illness like Chronic renal failure, Rheumatoid arthritis, Multiple myeloma and Thyrotoxicosis were not included. An informed consent was taken from these patients. BMD of lumbar spine (L1, 2, 3) and proximal femur (neck and trochanter) was calculated by DEXA scan (Discovery W S/N 82330). BMD was expressed as g/cm<sup>2</sup> as well as T-score, compared to reference data given in software. Low BMD was considered to be T-score of

-2.5 or less obtained at any site and was labeled as osteoporosis. Bone mineral density, demographic, laboratory and other relevant disease data was recorded on Proforma annexed. All the collected information was entered and analyzed using SPSS version 15. The quantitative variables like age were expressed as mean±standard deviation. The qualitative variables like gender, and presence or absence of osteoporosis were presented by calculating frequency and percentages. Data was stratified for Child-Turcotte-Pugh class A, B and C. P value of <0.05 was considered significant.

## RESULTS

A total of 70 patients of liver cirrhosis were included in the study among these, 62 (88.6%) were male and 8 (11.4%) were female patients (Table 1). Overall mean age was 45.14 years (SD±11.04) with age range of 20-60 years. A total of 49(70%) patients (47 males and 2 females) were observed of having Child class C cirrhosis while 9(12.9% - 8 males, 1 female) and 12(17.1% - 7 males and 5 females) patients belonged to Child B and A, respectively. Out of 70 patients, 22(31.4%) patients had osteoporosis and 24 (34.3%) had osteopenia while 24(34.3%) had normal BMD. Out of 22 patients of osteoporosis, 4 (18.1%) patients had Child class A, 5(22.7%) had Child class B and 13(59%) belonged to C (P= 0.4).

Fig 1: Number of patients with osteoporosis

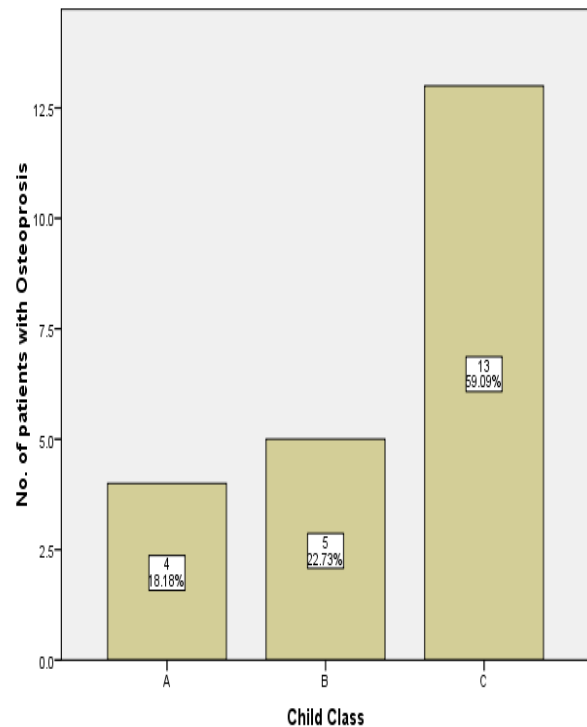


Table 1: Distribution of patients by age

	n	%age
<b>Age (Years)</b>		
20-30	11	15.7
31-40	13	18.57
41-50	29	41.4
51-60	17	24.2
<b>Gender</b>		
Male	62	88.6
Female	8	11.4
<b>Osteoporosis and Osteopenia</b>		
Yes	22	31.4
No	24	34.3
Osteopenia	24	34.3
<b>Child class</b>		
A	12	17.1
B	9	12.9
C	49	70

## DISCUSSION

It is an established fact now that osteoporosis and fractures are more frequent in patients with chronic liver disease as compared to the normal population. Clinically, the concern about hepatic osteodystrophy has amplified with the improvement in survival of patients with chronic liver disease and the development of liver transplantation that has reached at better level. Despite the fact that the issue of osteoporosis has been well addressed recently in Pakistan, its discussion with special reference to liver diseases could not be elaborated well until now. However, some studies have shown the prevalence of osteoporosis and osteopenia in patients with cirrhosis to be considerably high<sup>9,10</sup>. These studies have reported osteoporosis in 20–50% of patients with cirrhosis due to hepatitis B and C, being most common cause of liver cirrhosis in our country<sup>11</sup>, but the miserable fact is that the importance of this potentially controllable complication is still not well recognized in our country. Regrettably, bone disease often remains undiagnosed and raises its head years after potential interventions could have been started. Main risk factors associated with liver disease associated osteoporosis are hypogonadism, low BMI, corticosteroid use, alcohol use, cholestasis, and Vitamin deficiency etc<sup>1,2</sup>.

Our study aimed to evaluate, thus, the frequency of osteoporosis in liver cirrhosis patients. Majority of patients 62(88.6%) included in our study were males clearly indicating the high incidence of liver cirrhosis and subsequently high risk of osteoporosis in males. Out of 70 patients, 22(31.4%) patients had osteoporosis and 24(34.3%) had osteopenia while 24 (34.3%) had normal BMD. Out of 22 patients of osteoporosis, 4(18.1%) patients had Child class A, 5(22.7%) had Child class B and 13(59%) belonged to C (P= 0.4). These results were compatible to many other researches that established a relationship

between severity and duration of liver disease and osteoporosis<sup>2, 5</sup>. Some of these have found a positive correlation between them too. However there was found a wide variation in the frequency of osteoporosis in these studies that can be somewhat justified by the fact that some of these used different imaging modalities and different sites (femoral heads or vertebrae etc) for measurement of BMD<sup>13</sup>. It is notice worthy that despite of considerable frequency of osteoporosis with liver cirrhosis we could not find any statistical correlation between severity of liver disease and osteoporosis. However, the high positive frequency suggests other researchers to choose this area to be focus of future research for exploring other dimensions<sup>13,14</sup>.

## CONCLUSIONS

It is concluded from our study that cirrhosis may be a direct risk factor for the development of bone loss and a high frequency of BMD disorders in cirrhotic patients is seen.

## REFERENCES

1. Nakchbandi I, Merwe S. Current understanding of osteoporosis associated with liver disease. *Nat Rev Gastroenterol Hepatol* 2009; 6:660-70.
2. Cijesvchi C, Mihai C, Zbranca E, GoganNiceanu P. Osteoporosis in Liver Cirrhosis. *Rom J Gastroenterol* 2005; 14:337.
3. Fatima M et al. Determining the risk factors and prevalence of osteoporosis using quantitative ultrasonography in Pakistani adult women. *Singapore Med J* 2009; 50: 20-8.
4. George J, Ganesh H, Acharya S et al. Bone mineral density and disorders of mineral metabolism in chronic liver disease. *World J Gastroenterol* 2009; 15:3516-22.
5. Salama Z, Lotfy A, Azizy H. Evaluation of hepatic osteodystrophy in patients with Liver cirrhosis and correlation with severity of liver disease. *Arab J Gastroenterol* 2007; 8: 10-14.
6. Diamond T et al. Osteoporosis and skeletal fractures in chronic liver disease. *Gut* 1990; 31: 82-7.
7. Collier J. Bone Disorders in Chronic Liver Disease. *Hepatology* 2007; 46: 1271-78.
8. Rouillard S, Lane N. Hepatic Osteodystrophy. *Hepatology* 2001; 33, 301-7.
9. Ahmad K. Pakistan: a cirrhotic state? *The Lancet* 2004; 364, 1843-4.
10. Ali SA, Donahue RMJ, Qureshi H, Vermund SH. Hepatitis B and hepatitis C in Pakistan: prevalence and risk factors. *Int J Infect Dis* 2009; 13(9): 9-19.
11. Nadeem MA, Waseem T, Sheikh AM, Grumman N, Irfan K., Hepatitis C virus: an alarmingly increasing cause of liver cirrhosis in Pakistan. *Pak J Gastroenterol* 2004; 23: 45-6.
12. Hashim R, Hussain AB, Rehman K. Seroprevalence of Hepatitis-C virus antibodies among healthy young men in Pakistan. *Pak J Med Res* 2005; 44: 140- 2.
13. Ijaz A, Shafiq F, Toosi NA, Malik MN, Qadeer R. Hepatitis B and Hepatitis C in blood donors: Analysis of 2-years data. *Ann K E Med Coll* 2007; 13: 59- 61.
14. Bukhtiar N, Hussain T, Iqbal M, Malik AM, Quraishi AH, Hussain A. Hepatitis B and C single and co-infection in chronic liver disease and their effect on the disease pattern. *J Pak Med Assoc* 2003; 53: 136-40.

