

TO DETERMINE THE PREVALENCE OF LOW BONE MINERAL DENSITY (OSTEOPENIA AND OSTEOPOROSIS) IN INDIAN PATIENTS WITH CIRRHOSIS OF LIVER AWAITING LIVER TRANSPLANTATION AS PER CURRENTLY USED HOLOGIC DXA DATABASE

¹Dr. Sharad Deshmukh, ²Dr. Suchita Deshmukh, ³Dr. Sarojni A Parameswaran, ⁴Dr. P Pirmanayagam, ⁵Dr. N Murgan, ⁶Dr. Sangita Patil

¹MD (Medicine), DNB (Gastroenterology), Consultant Gastroenterologist and Hepatologist, Mediliv Hospital, Nashik

²MBBS, DGO, DNB, Consultant Gynaecologist, Mediliv Hospital, Nashik

³MD (Medicine), DM (Gastroenterology), Consultant Gastroenterologist, Apollo Hospital, Chennai

⁴MD (Medicine), DMC (Gastroenterology), Consultant Gastroenterologist, Apollo Hospital, Chennai

⁵MBBS, FRCP, Fellowship in Hepatology, Consultant Hepatologist, Apollo Hospital, Chennai

⁶MBBS, MD (Pharmacology), Medical Reviewer, TCS

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Corresponding author: Dr. Sharad Deshmukh

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Abstract

Background: Abnormalities in the bone metabolism observed in chronic liver disease are referred to as hepatic osteodystrophy. Osteoporosis and osteopenia are each part of this condition. Both conditions have a significant impact on morbidity, causing fractures that may result in chronic pain, long-lasting immobility, and deformity. Prevalence of fracture in patients with liver transplantation ranges from 15% - 65%. A high rate of fracturing is seen within the initial 1–2 years after transplantation.

Aim: To determine the prevalence of low bone mineral density (osteopenia and osteoporosis) in Indian patients with cirrhosis of liver awaiting liver transplantation as per currently used Hologic DXA database

Methods: This was a prospective observational study done at the department of gastroenterology and hepatology, Apollo Hospitals, Chennai from April 2011 to March 2013. All patients who fulfilled the inclusion criteria underwent detailed history taking, physical examination and relevant laboratory investigations. One hundred patients were selected for the scope of the study.

Results: Sixty-eight per cent of patients were in the age group of 45 to 65 years. The mean age \pm SD of the study subjects was 51.2 ± 9.7 years. The mean age for male patients was 50.5 ± 10.1 years, and for females was 54 ± 7.3 years. Cirrhosis was due to alcohol in 36% of the patients, viral hepatitis in 28% (HBV in 10% and HCV in 18%) patients. 42% were in Child's class B, and the remaining 58% were in Child's class C. MELD score was less than 20 in 62% patients. One third was diabetic; one third gave the history of backache. History of smoking was present in one fifth (20%) patients, and a history of fracture (most of them were traumatic) was present in 13% of patients. By using Hologic DXA database at the lumbar spine, osteopenia and osteoporosis were diagnosed in 44% and 38 % patients respectively.

At the femoral neck, osteopenia and osteoporosis were diagnosed in 45% and 9% of patients. By using ICMR database at the lumbar spine, osteopenia and osteoporosis were diagnosed in 38% and 17% patients respectively. Similarly, at the femoral neck, osteopenia and osteoporosis were diagnosed in 34% and 5%. By using the Hologic DXA database, osteopenia and osteoporosis were diagnosed in 42% and 40 % patients. By using ICMR database, osteopenia and osteoporosis were diagnosed in 43% and 19% patients respectively.

Conclusion: In light of the above results, the present study revealed a high prevalence of low bone mineral density (osteopenia and osteoporosis) in Indian patients with cirrhosis of liver awaiting liver transplantation. The lumbar spine was the most frequently and severely affected site in hepatic osteodystrophy.

Keywords: Osteopenia, Osteoporosis, Low Bone Mineral Density, Liver Cirrhosis

Introduction:

Abnormalities in the bone metabolism observed in chronic liver disease are referred to as hepatic osteodystrophy. Osteoporosis and osteopenia are each part of this conditionⁱ. Both conditions have a significant impact on morbidity, causing fractures that may result in chronic pain, long-lasting immobility, and deformityⁱⁱ. Following liver transplantation (OLT), the fracture risk is further increased

due to the use of immunosuppressive therapy, including steroids and prolonged immobility, particularly when complications arise after surgeryⁱⁱⁱ.

Prevalence of fracture in patients with liver transplantation ranges from 15% - 65%. A high rate of fracturing is seen within the initial 1–2 years after transplantation. Pre-transplant fragility fracture and low bone mineral density (BMD) are strong predictors for fracture after transplantation^{iv}.

Dual-energy X-ray absorptiometry (DXA) is the gold standard commonly used to measure bone mass because it is accurate and can measure multiple skeletal sites^v; most commonly applied to the lumbar spine and femoral neck. With orthotopic liver transplantation steadily taking centre stage in the treatment of end-stage liver disease and offering long-term survival^{vi}, the bone disease has snowballed into one of the major determinants of survival and quality of life in this group of patients^{vii}.

As the numbers of cirrhotic patients awaiting liver transplantation are increasing in India and the time they wait for transplant increases, physicians need to maintain a high index of suspicion regarding the possibility of osteopenia/osteoporosis in these patients regardless of the cause of their underlying liver disease^{viii}. Recent studies from India showed a high prevalence of hepatic osteodystrophy among cirrhosis patients. Also currently available DXA scan machines (GE lunar and Hologic) in India use the database (reference standards) for young normal Caucasian regardless of the race of the subject. Recently Indian Council of Medical Research (ICMR) has published cut-off values for diagnosis of osteoporosis and osteopenia in Indian males and females^{ix}.

Aim

To determine the prevalence of low bone mineral density (osteopenia and osteoporosis) in Indian patients with cirrhosis of liver awaiting liver transplantation as per currently used Hologic DXA database

Material and methods

This was a prospective observational study done at the department of gastroenterology and hepatology, Apollo Hospitals, Chennai from April 2011 to March 2013. All patients who fulfilled the inclusion criteria underwent detailed history taking, physical examination and relevant laboratory investigations. One hundred patients were selected for the scope of the study.

Inclusion criteria

Patients with Child-Turcotte-Pugh (CTP) class B or C cirrhosis, undergoing evaluation for liver transplantation as outpatient or inpatient were included in the study. All patients were adults and were predominantly from urban areas.

Exclusion Criteria

1. Chronic kidney disease
2. Primary hyperparathyroidism
3. Cushing's syndrome
4. Thyroid dysfunction (hyperthyroidism or hypothyroidism).
5. Patient on systemic corticosteroid therapy (>5mg/day) for more than three months

6. Patients on long term (>3 months) supplements of calcium or vitamin D
7. Patients on bisphosphonates, calcitonine, hormone replacement therapy, antiepileptic, anticoagulants.
8. Rheumatoid arthritis
9. Patient with foreign nationality
10. Patients admitted to the intensive care unit.

Results

The age of the patient ranged from 28 years to 68 years. Sixty-eight per cent of patients were in the age group of 45 to 65 years. The mean age \pm SD of the study subjects was 51.2 ± 9.7 years. The mean age for male patients was 50.5 ± 10.1 years, and for females was 54 ± 7.3 years.

Table 1: Age distribution of the patients

AGE GROUP (Years)	NO. OF PATIENTS (%) n=100
25 -35	6
36 -45	21
46 -55	32
56 -65	36
>65	5

Among the 100 patients, 79 were males, and 21 were females. Among the 21 females, 3 were premenopausal, and 18 were postmenopausal (Table 2).

Table 2: Sex Distribution

Sex distribution	Number of patients
Male	79
Female	21

Cirrhosis was due to alcohol in 36% of the patients, viral hepatitis in 28% (HBV in 10% and HCV in 18%) patients. Cholestatic disease accounted for 4% of patients (3 with primary biliary cirrhosis and 1 with primary Sclerosing cholangitis). Remaining 32% had cryptogenic cirrhosis (Table 3).

Table 3: Etiology of Liver Disease

Etiology of Liver disease	Number of patients
Alcohol	36
Hepatitis C	18
Hepatitis B	10
Cryptogenic	32
Cholestatic disease	04

Out of 100 patients, 42% were in Child's class B, and the remaining 58% were in Child's class, C. MELD score was less than 20 in 62% patients (Table 4).

Table 4: Severity of liver cirrhosis by Child-Turcotte-Pugh (CTP) class

CTP Class	Number of patients
CTP CLASS- B	42
CTP CLASS -C	58

Risk factors for low BMD were analysed and summarised in table 5. Among the 100 patients, one third was diabetic; one third gave the history of backache. History of smoking was present in one fifth (20%) patients, and a history of fracture (most of them were traumatic) was present in 13% of patients (Table 5).

Table 5: Risk factors of low BMD

Risk Factors	Number of patients
Diabetes	32
H/O Alcohol	36
H/O Smoking	20
H/O Fracture	13

Lumbar spine and femoral neck BMD data were analysed using the Hologic DXA database and by ICMR database. By using Hologic DXA database at the lumbar spine, osteopenia and osteoporosis were diagnosed in 44% and 38 % patients respectively. At the femoral neck, osteopenia and osteoporosis were diagnosed in 45% and 9% of patients (Table 6).

By using ICMR database at the lumbar spine, osteopenia and osteoporosis were diagnosed in 38% and 17% patients respectively. Similarly, at the femoral neck, osteopenia and osteoporosis were diagnosed in 34% and 5%. A greater proportion of patients were diagnosed as having osteopenia and osteoporosis with Hologic DXA database over ICMR Database (Table 6).

Table 6: Prevalence of osteopenia and osteoporosis at the lumbar spine and femoral neck

BMD Category	Lumbar spine (%) (n=100)		Femoral neck (%) (n=100)	
	Hologic DXA database	ICMR database	Hologic DXA database	ICMR database
Normal	18	45	46	61
Osteopenia	44	38	45	34
Osteoporosis	38	17	09	05

The final category of BMD was classified based on the lowest T score among lumbar spine and femoral neck. By using the Hologic DXA database, osteopenia and osteoporosis were diagnosed in 42% and 40 % patients. By using ICMR database, osteopenia and osteoporosis were diagnosed in 43% and 19% patients respectively. By ICMR database greater number (38%) of patients were classified under normal BMD category compared to (18%) by Hologic DXA database (Table 7).

Table 7: Prevalence of Osteopenia and Osteoporosis in final BMD category

	FINAL BMD CATEGORY	
	Hologic DXA Database (%)	ICMR Database (%)
NORMAL BMD	18	38
OSTEOPENIA	42	43
OSTEOPOROSIS	40	19

Hologic DXA database classified 82% patients as having low BMD, while ICMR database classified 62 % patients as having low BMD. A greater proportion of patients were diagnosed as having low BMD with Hologic DXA database over ICMR database (82% and 62%, $p < 0.05$).

Cross-tabulation of BMD category assignment at lumbar spine is shown in table 8, by using the Hologic DXA database and ICMR database. Switching from Hologic DXA database to ICMR database led to the reclassification of 48 patients at the lumbar spine. Among the 44 osteopenia patients as per the Hologic DXA database, 27 (61.3%) were reclassified as normal by ICMR database. Among 38 osteoporosis patients as per Hologic DXA database, 21 (55.2%) were reclassified as osteopenia by ICMR database.

Table 8: Comparison of prevalence of osteopenia and osteoporosis at lumbar spine by using Hologic DXA database and ICMR database

	BMD Category At Lumbar Spine	ICMR Database		
		NORMAL (n=45)	OSTEOPENIA (n=38)	OSTEOPOROSIS (n=17)
Hologic DXA Database	NORMAL (n=18)	18	0	0
	OSTEOPENIA (n=44)	27	17	0
	OSTEOPOROSIS (n=38)	0	21	17

BMD assessment at lumbar spine identified more patients with low BMD by both Hologic DXA database and ICMR database ($p < 0.05$).

Table 9: Bone mineral density at the lumbar spine and femoral neck

Site	Hologic DXA database (%)			ICMR database (%)		
	Normal BMD	Low BMD	P-value	Normal BMD	Low BMD	P-value
Lumbar spine (n=100)	18	82	<0.001	45	55	<0.05
Femoral Neck (n=100)	46	54		61	39	

Similarly, low BMD by ICMR database in male were present in 47 (59.5%) [osteopenia in 34 (43%), osteoporosis in 13 (16.5%)] and in female patients, 15 (71.4%) [osteopenia in 9 (42.9%) and osteoporosis in 6 (28.6%)]. There was no statistically significant difference observed in the prevalence of low BMD in male and female patients ($P > 0.05$) by either database (Table 10).

Table 10: Prevalence of osteopenia and osteoporosis in male and female in the final BMD category

FINAL BMD CATEGORY	Hologic DXA database			ICMR Database		
	Male (%) (n=79)	Female (%) (n=21)	P value	Male (%) (n=79)	Female (%) (n=21)	P value
Normal	16(20.3)	2(9.5)	NS	32(40.5)	6(28.6)	NS
Osteopenia	36(45.5)	6(28.6)		34(43.0)	9(42.9)	
Osteoporosis	27(34.2)	13(61.9)		13(16.5)	6(28.6)	

Discussion

In the present study, 100 patients with Child's class B or C awaiting liver transplantation were studied; 79 were males, and 21 were females. The mean age \pm SD was 51.2 ± 9.7

years. The median CTP score was 10 (IQR 8 – 11); the median MELD score was 17 (IQR 14 -22.7). In a study by **Bansal et al., (2013)**^x involving 96 cirrhotic patients, 88% were male with mean age 50.6 (27 - 82) years, mean CTP score was 10 ± 2.5, MELD score of 18 ± 9.5. Similarly in a study by **Wibaux et al., (2011)**^{xi} from France, out of 99 patients awaiting liver transplantation, 79 were males, and 20 were females, mean age was 55 yrs ± 8yrs. The mean MELD score was 15.74 ± 7.92. In the present study, liver disease was Child's class B in 42% and class C in 58%.

The present study shows a high prevalence of low bone mineral density (both osteopenia and osteoporosis) in patients with cirrhosis of liver awaiting liver transplantation by currently used Caucasian reference standards by the Hologic DXA scan. The overall prevalence of low BMD was 82% (osteoporosis, 40% and osteopenia, 42%) which was consistent with a previously reported study from India by **Chaudhary et al., (2011)**^{xii}. The authors measured BMD using DXA at the femoral neck, lumbar spine and left forearm in 115 Child's class B or C cirrhotic patients. Osteopenia and osteoporosis were defined by WHO criteria similar to the present study.

In the present study, the overall prevalence of low BMD by using Hologic DXA database was 82% (osteopenia 42%; osteoporosis 40%) which is higher compared to 62% (osteopenia 43%; osteoporosis 19%) when ICMR reference standards were used. Switching from Hologic DXA database to ICMR database led to the reclassification of 20% of patients from low BMD group to normal BMD group. There are no studies at present in cirrhotic patients using ICMR BMD database (reference standards). Similar observation was made by **Paul et al., (2012)**^{xiii} and **Melamed et al., (2010)**^{xiv} who studied the impact of Caucasian versus Indian BMD reference standards on the diagnosis of osteoporosis in non-cirrhotic patients.

Conclusion

In light of the above results, the present study revealed a high prevalence of low bone mineral density (osteopenia and osteoporosis) in Indian patients with cirrhosis of liver awaiting liver transplantation. The lumbar spine was the most frequently and severely affected site in hepatic osteodystrophy.

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