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Bone Mineral Density Assessed By Dual-Energy X-Ray Absorptiometry in Patients with Cirrhosis of Liver

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Abstract
Aims: Aim of the study was to assess bone mineral density by DEXA scan in patients with cirrhosis of liver.Methods and Material: Seventy patients of liver cirrhosis irrespective of their severity in the age group of 18 to 60 years were selected. Standard investigations were done to define cirrhosis, osteopenia and osteoporosis. All data were collected from structured questionnaire. Qualitative data was analyzed by Chi-square test and Quantitative data was analyzed by Student's T-test. P value below 0.05 was considered statistically significant.
Results: Most of the cirrhotic patients were 35-45 years of age. HBV was the predominant etiology. Osteoporosis was found in 45.7% of patients at least at one site. Lumbar spine was more involved than femoral neck. Osteopenia/osteoporosis in lumbar spine and in neck of femur was highly significant with duration of cirrhosis of liver for more than 5 years (P value =0.001). But no significant relation was found with BMI. (P value > 0.7). There was no statistically significant difference in T score in lumbar spine(P value = 0.233) and in neck of femur (P value = 0.513) with Child Pugh stage A,B,C. There was also no statistically significant difference in Z score in lumbar spine (P value =0.271) and neck of femur (P value =0.500) with Child Pugh stage.
Conclusions: Liver cirrhosis is a direct risk factor for the development of the bone loss and there is high prevalence of BMD disorder in cirrhotic patients.

Key words: *Hepatic osteodystrophy, liver cirrhosis, bone mineral density.*

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I. Introduction

Metabolic bone disease occurring in patients with cirrhosis, known as hepatic osteodystrophy, covers both osteomalacia and osteoporosis. Osteoporosis in CLD mainly affects trabecular bone and has been characterized by low bone turnover with reduced osteoblast function and low serum osteocalcin levels.[1]

The reported prevalence of osteoporosis among patients with liver cirrhosis ranges from 20% to 50% depending on patient selection and diagnostic criteria and the prevalence of fracture ranges from 5% to 20%.[2] It was found 26% osteoporosis and 42% osteopenia in cirrhosis patients in pakistan[3] and 68% with low BMD in cirrhotic patients in India.[4]

Bone mineral density (BMD;g/cm2) is measured by non invasive, rapid, accurate and safe method, Dual energy X-ray absorptiometry (DEXA).[5] Since 1994, WHO has recognized a working definition where osteoporosis in caucasian women is defined as a BMD value of 2.5 SDs below the mean for healthy young women. The comparison with the mean BMD for young adults of the same sex is termed the T-score and is expressed as the number of standard deviations from the reference group means value. Thus, according to the WHO definition, a BMD of 2.5 standard deviations or below the young adult mean (T score < -2.5) at any site (spine, hip or mid radius) is considered osteoporosis and a BMD between -2.49 and -1.0 is considered osteopenia. In clinical practice the use of T-scores has also been adopted for men. A Z-score is the number of standard deviations from age-matched and weight adjusted reference population of the same sex.

Osteoporosis can result in bone fractures with a harmful effect on morbidity and quality of life. Therefore, BMD measurement in patients with CLD and early diagnosis of hepatic osteodystrophy is essential to correct reversible risk factors which predispose to bone mass loss. Treatment and prevention strategies include general measures, dietary and lifestyle, calcium and vitamin D3 supplementation and bisphosphonates. However, advanced hepatic osteodystrophy is difficult to treat and special care is required to prevent bone loss in individuals with severe hepatic disease.[1]

This aim of the study was to assess osteopenia and osteoporosis in cirrhosis patient by the reference method (DEXA).

II. Materials and Methods:

We performed an observational cross sectional study which was conducted in the Department of Gastroenterology, BSMMU, DHAKA from March, 2012 to March, 2013. Seventy patients of liver cirrhosis irrespective of their severity in the age group of 18 to 60 years were selected. Patients with HCC, any other malignancy, HIV, deformity or fracture of bone, female with hormonal contraception or with postmenopausal period, CKD, DM, H/O endocrine disease, patients receiving calcium, vitamin D, HRT, corticosteroids, or any drug known to affect bone density were excluded from study. Informed written consent was obtained and their clinical history, examination & initial investigation report was noted in the standard data sheet. The diagnosis of liver cirrhosis was made by combination of clinical features, blood profile and abdominal ultrasound. Stages of liver disease were assessed by using the Child-Pugh Scoring System. Bone mineral density evaluation was done by bone densitometry of the lumbar spine (LS), femoral neck (FN) using DEXA technique by expert radiologist. BMD was expressed as grams per square centimeter. WHO criteria for osteopenia and osteoporosis was used to define low BMD. Exclusion of vertebral deformity was done by X-ray on the Lumbar spine. All data were collected from structured questionnaire and were analyzed by SPSS. Qualitative data was analyzed by Chi-square test and Quantitative data was analyzed by Student's T-test. P value below 0.05 was considered statistically significant. Ethical clearance for the study was taken from the Institutional Review Board of Bangabandhu Sheikh Mujib Medical University.

III. Results

Total 70 patients of 18 – 60 years of age were enrolled in the study. The mean age was (41.73 ± 11.97) years. Maximum patients (35.7%) were in the range of 35-45 years and >45 years of age group. All female patients were <45 years of age.

Among 70 patients, 63 were male and 7 were female. Male and female ratio was 9:1. Among 70 patients, 32.9% were in Child Pugh stage A, 42.9% were in Child Pugh stage B and 24.3% were in Child Pugh stage C. 40 % had osteoporosis in the lumber spine . But osteopenia was more in neck of femur (47.1%).

In the lumbar spine, among stage A cirrhosis, osteopenia and osteoporosis were same 34.8%. Among stage B, osteopenia were 46.7% and osteoporosis were 40%.Among stage C, 41.2% were osteopenia and 47.1% were osteoporosis. In femoral neck, osteopenia was more in all stages. osteopenia were 43.3 % in stage A,50% in stage B and 47.1% in stage C patients. The relation was not statistically significantin lumbar spine and femoral neck.

HBV was predominant aetiology in our study. In the lumbar region, HBV patients had 47.1% , HCV and Wilsons disease had same 50% osteoporosis. Cryptogenic cases were more osteopenic 75%. But in neck of femur, HBV patients had 54.8% and HCV patients had 50% osteopenia. Most of the cryptogenic and Wilsons disease cases had normal BMD. Although relation between bony changes with aetiology of cirrhosis was not statistically significant.

Total BMD was compared in different CP group by ANOVA test. The mean (±SD)BMD in lumbar spine was 0.97 ± 0.14 in child pugh stage A group , 0.92 ± 0.14 in stage B group and 0.92 ± 0.15 in stage C group. In the femoral neck the mean(± SD) BMD was 0.95 ± 0.15 in stage A, 0.89 ± 0.12 in stage B and 0.94 ± 0.11 in stage C. Although it was statistically insignificant.

There was no statistically significant difference in T score in lumbar spine with Child Pugh stage A,B,C (P value = 0.233) and T score in neck of femur with Child Pugh stage A,B,C (P value = 0.513). There was also no statistically significant difference in Z score in lumbar spine with Child Pugh stage (P value =0.271) and Z score in neck of femur with Child Pugh stage (P value =0.500).

Osteopenia/osteoporosis in lumbar spine and in neck of femur was highly significant with duration of cirrhosis of liver (P value =0.001). But no significant relation was found with BMI. (P value > 0.7).

There was no correlation between CP score and BMD in lumbar spine (P value = 0.160). CP score and BMD in neck of femur (P value = 0.655). There was also no significant relation in CP score with T score in lumbar spine (P value = 0.058) and CP score with T score in neck of femur (P value = 0.975) and CP score with Z score in neck of femur (P value = 0.975) but there was significant negative correlation between CP score and Z score of lumbar spine (P value =0.048).

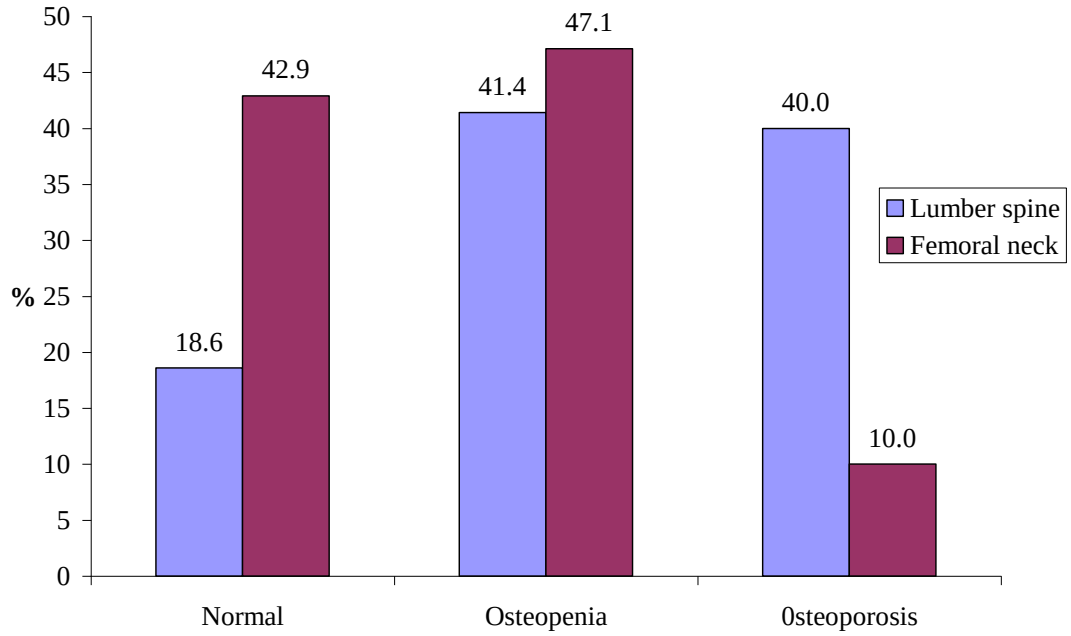

Figure- 1: Bar diagram of bone mineral density disorders

Cirrhotic patient	Normal		Osteopenia		0steoporosis		P value	
	Femoral neck	Lumber spine	Femoral Neck	Lumber spine	Femoral Neck	Lumber spine	Femoral Neck	Lumber spine
Stage A	47.8	30.4	43.5	34.8	8.7	34.8	0.870	0.490
Stage B	36.7	13.3	50.0	46.7	13.3	40.0		
Stage C	47.1	11.8	47.1	41.2	5.9	47.1		
Total	**42.9**	**18.6**	**47.1**	**41.4**	**10.0**	**40.0**		

.**Table- 1 :** Distribution of bone mineral density disorders of cirrhotic patients

Aetiology	Normal		Osteopenia		0steoporosis		p value*	
	Lumber spine	Femoral neck	Lumber spine	Femoral neck	Lumber spine	Femoral neck	Lumber spine	Femoral neck
HBV	26.2	40.5	33.3	54.8	40.5	4.8	0.176	0.054
HCV	0	33.3	50.0	50.0	50.0	16.7		
Wilson's Disease	12.5	62.5	37.5	37.5	50.0	0		
Cryptogenic	12.5	50.0	75.0	12.5	12.5	37.5		
	18.6	**42.9**	**41.4**	**47.1**	**40.0**	**10.0**		

Table- 2 : Distribution of bone mineral density disorders by aetiology

		Stage			p value*
		Stage A	Stage B	Stage C	
BMD	Lumber spine	0.97 ± 0.14	0.92 ± 0.14	0.92 ± 0.15	0.455
	Femoral neck	0.95 ± 0.15	0.89 ± 0.12	0.94 ± 0.11	0.231
T SCORE	Lumber spine	-1.91 ± 1.14 (41.35)	-2.36 ± 1.14 (33.27)	-2.40 ± 1.11 (31.53)	0.233
	Femoral neck	-1.18 ± 1.18 (36.83)	-1.43 ± 0.92 (32.42)	-1.11 ± 0.77 (39.15)	0.513
Z SCORE	Lumber spine	-1.02 ± 1.25 (40.33)	-1.38 ± 1.09 (34.98)	-1.60 ± 1.16 (29.88)	0.271
	Femoral neck	-0.33 ± 1.13 (37.26)	-0.45 ± 0.91 (32.27)	-0.27 ± 0.77 (38.82)	0.500

Table- 3: Mean ± SD of BMD, T score and Z score of cirrhotic patients

	Normal		Osteopenia		Osteoporosis		p value*	
	Lumber spine	Neck of femur	Lumbe r spine	Neck Of femur	Lumber spine	Neck of femur	Lumber spine	Neck of femur
Duration of cirrhosis	1.42 ± 0.64	2.02 ± 1.21	3.52 ± 1.86	4.58 ± 1.24	4.98 ± 1.62	6.93 ± 1.48	0.001	0.001
BMI	20.03 ± 3.02	20.36 ± 3.31	20.91 ± 4.05	20.72 ± 3.10	20.58 ± 2.63	21.21 ± 4.72	0.736	0.807

Table- 4: Distribution of bone mineral density disorders by duration of cirrhosis and BMI

CP score Vs	Correlation coefficient r value	p value
BMD		
• Lumber spine	-0.170	0.160
• Femoral neck	-0.054	0.655
T score		
• Lumber spine	-0.228	0.058
• Femoral neck	-0.004	0.975
Z score		
• Lumber spine	-0.237	0.048*
• Femoral neck	-0.004	0.975

Table- 5: Correlation of BMD, T score and Z score with CP score

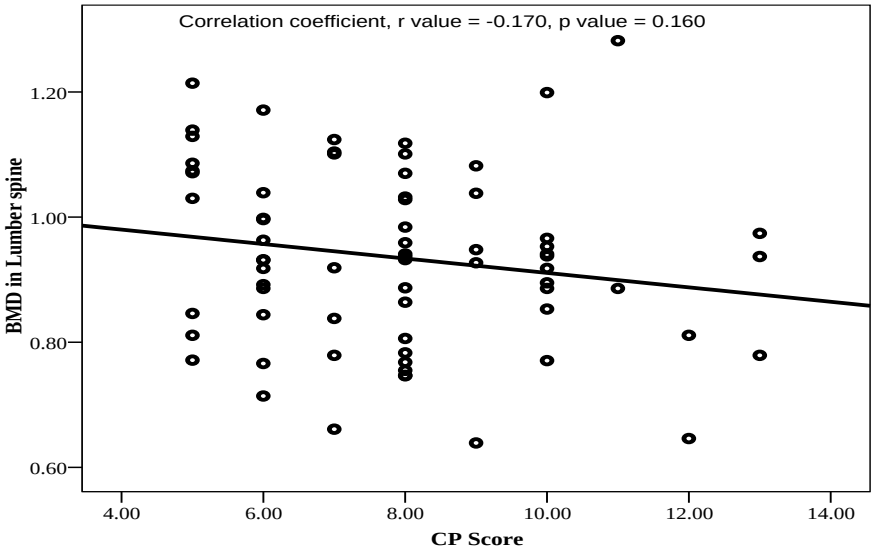

Figure- 2: Correlation of BMD in lumber spine with CP score

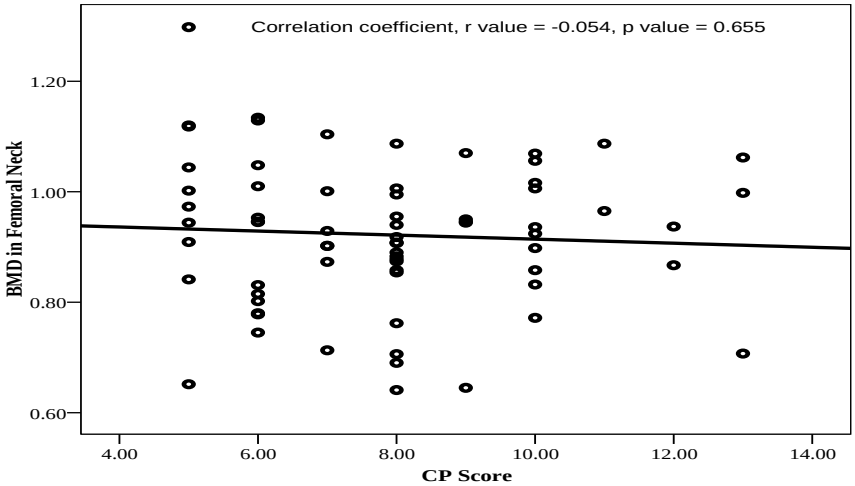

Figure- 3: Correlation of BMD in femoral neck with CP score

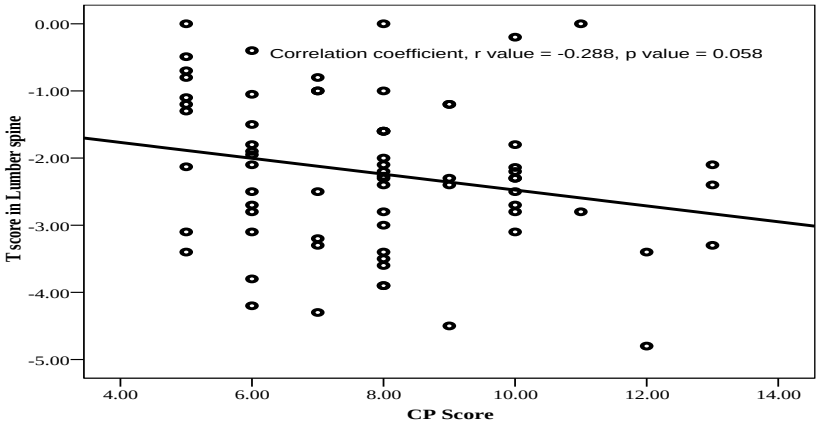

Figure- 4: Correlation of T score lumber spine with CP score

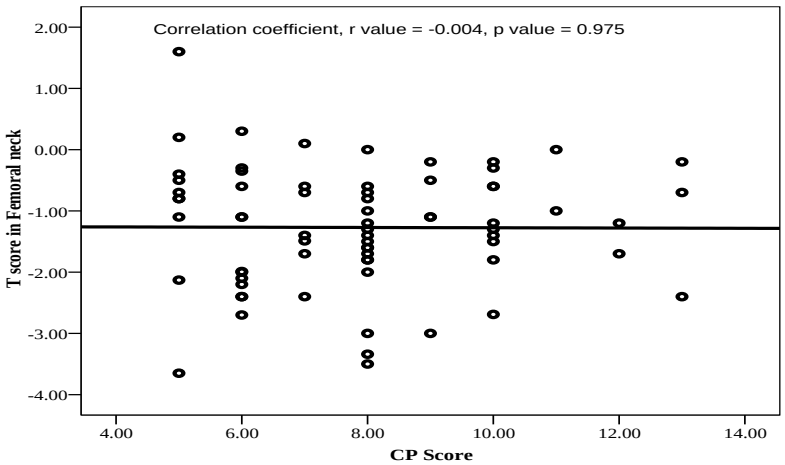

Figure- 5: Correlation of T score femoral neck with CP score

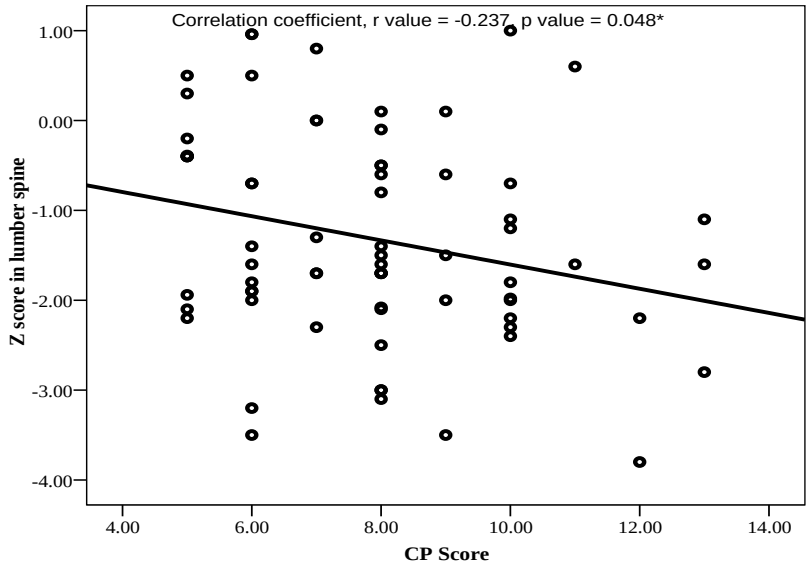

Figure- 6: Correlation of Z score in lumber spine with CP score

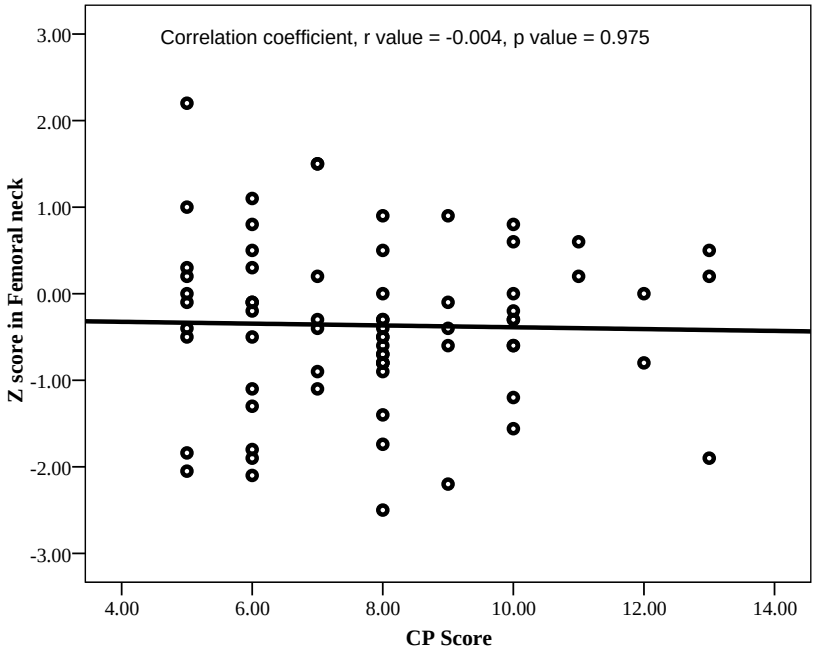

Figure- 7: Correlation of Z score in femoral neck with CP score

IV. Discussion

Osteopenia is a moderate reduction in bone mass, while osteoporosis is defined as a decrease in bone density with alterations of bone micro-architectures and a consequent increased risk of fractures. In its early asymptomatic stage, osteopenia and osteoporosis can only be detected by measuring BMD. Early detection of reduced BMD is an important means of prevention, and DEXA is the most helpful modality and remains the gold standard for measurement of bone density. It is simple to perform, non invasive and widely available test. It requires the least exposure to radiation (10 to 30 mSv). Fracture risk increases 1.5- to 3-fold or more for each standard deviation (SD) decrease in BMD from that of young adult (T score). Osteopenia is considered to be present when BMD is between -1 and -2.5 SD; osteoporosis is defined by the World Health organization (WHO) as BMD more than -2.5 SD below that of a young adult.[6]

This study was carried out to assess BMD by DEXA scan in patients with cirrhosis of liver and also to see the relation of severity of hepatic cirrhosis with osteopenia and osteoporosis. We investigated seventy cirrhotic patients irrespective of aetiology. BMD were done to evaluate the bony changes.

Osteoporosis and fractures are more common in patients with cirrhosis as compared to the normal population. The reported prevalence of osteoporosis among patients with liver cirrhosis ranges from 20% to 50% depending on patient selection and diagnostic criteria and the prevalence of fracture ranges from 5% to 20%.[7] In the present study, osteoporosis was found in 45.7% of patients at least at one site. In the lumbar spine, 41.4% had osteopenia and 40% had osteoporosis. In the neck of the femur, 47.1% had osteopenia and 10 % had osteoporosis. The prevalence of osteoporosis was 30%-48% in patients with CLD of different etiologies.[8]Our figure was higher than the study conducted by Cristina Cijevschi et al., where they found 38% of cirrhotic patients have low BMD.[9]

Age is recognized as an independent risk factor for low BMD, In our study the age ranges of patients were 18 years to 60 years. Post menopausal females were excluded from the study because of increased chance of having low BMD. The mean age of study patients was 41.73 ±11.97 years. The highest incidence of cirrhotic patients were found at 35-45 years age group and >45 years age group. BMD tends to decrease with age in patients with cirrhosis at a rate similar to the healthy controls.[10]. In our study we did not find any correlation between age and bony changes which supported previous study in 2007. [11]

In this study male were 90% and female were 10% . There was male predominance in the study population. No significant difference was observed in bony changes between male and female which had the similarities with other studies.[12] This can be explained by the fact that all females in our study was in the reproductive age.

In this study, among 70 patients 23 were in child's group A, 30 were in child's B and 17 were in child's C. Osteoporosis were more in the lumbar spine and osteopenia were more in neck of femur. In the lumbar spine, 34.8% of child's A,40% of child's B and 47.1% of child's C had osteoporosis But in the femoral neck 43.3% of child's A,50% of child's B and 47.1% of child's C had osteopenia, In the lumbar spine bony

changes were increased from child's A to child's C which was matched with the results of the previous research. [13,14]

In our study, aetiology of cirrhosis of liver was HBV, HCV, Wilson's disease and cryptogenic. 42 patients were HBV which is the highest population of the study. 12 were HCV, 8 were Wilson's disease and 8 were cryptogenic. 50 % of HCV patients and 50 % of Wilson's disease had osteoporosis in lumbar spine. Osteoporosis was more prevalent in HCV and Wilson's disease than HBV in the lumbar spine but osteoporosis was more in the neck of the femur (37.5%) with cryptogenic aetiology. In different study, osteoporosis was not significantly influenced by the aetiology of cirrhosis. [3] In our study, it was also not statistically significant (p value = 0.176 for lumbar spine, p= 0.054 for femoral neck). We think variation in size of population may be one of the cause.

To evaluate which type of bone got more affected, BMD was measured by DEXA at lumbar spines (i.e.: trabecular bone) and femoral neck (i.e.: cortical bone). Our results demonstrated that there was decrease in BMD at both sites in cirrhotic patients. The trabecular bone was more affected than cortical although it was not statistically significant. This is probably because the rate of turnover in the cortical bone is much lower than in trabecular bone. This was in agreement with previous study by Duarte et al. (2001) who found that mean T–score was more negative in areas where trabecular bone predominates, such as lumbar spine.[15] Another study reported that BMD at both lumbar spines and femoral neck were significantly lower in cirrhotic patients than reference population.[13,] Also our results demonstrated increase in BMD loss at lumbar spines and femoral neck in Child A, Child B and Child C with no significant difference between them. Though some authors found that lumbar mean BMD values worsened progressively from Child A to Child C patients.[14]

Bone mass loss in liver cirrhosis is probably multi-factorial. Our results showed that, osteopenia and osteoporosis were significantly higher in those with long duration (more than 5 years) of liver disease (p value =0.001) which is an identified risk factors for low BMD. Similar observations were found by previous researcher where they reported a positive correlation between the duration of the disease and severity ofthe osteopenia.[9, 16] No significant relation was found between osteopenia / osteoporosis and body mass index (p value= 0.736) which also supported other studies. [11,17]

In our study we could demonstrate the increase in prevalence and severity of decreased bone mineral density with the liver dysfunction. We found significant negative correlation between CP score with Z score in lumbar spine (p value= 0.048) but no relation between CP score with BMD and T- score. There was no significant difference in BMD between Child's A , B and C. Our finding was similar to the study conducted fracisco j et. al 1998, where they found no significant differences among CP scores.[13] In a study conducted by Chen CC et al. 1996 found no differences in BMD of lumber spine in different child Pugh group.[18]

In our study, we have tried to assess bony changes measured by BMD in cirrhotic patients irrespective of aetiology and severity. Liver cirrhosis is a direct and independent risk factor for the development of osteopenia and osteoporosis. There were more BMD disorders in cirrhotic patients and also more involvement of lumbar spine than femoral neck. However, no correlation was found between degree of hepatic dysfunction measured by Child Pugh score and severity of bone changes. No correlation was found between aetiology of cirrhosis with bone changes. We also found, bony changes occur significantly with long duration of liver disease >5 years of age but we did not find any relation with BMI.

V. Conclusion

The findings obtained from this study suggested that bone changes occurred in cirrhosis as evident by low BMD. But that was not correlated with the severity of liver cirrhosis.

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