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Original Research Article

To Assess The Prevalence Of Osteoporosis In Cld Patients And Compare It To Controls Who Are Similar In Terms Of Age And Sex.

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INTRODUCTION

Osteoporosis, defined by the World Health Organization as a disorder of bone resulting in decreased bone strength, is an extremely common disorder of aging that currently affects 10–12 million people in the United States alone[1]. Fractures represent the main clinical manifestation of osteoporosis. Half of all women over the age of 50 years will suffer an osteoporotic fracture during their lifetime. Moreover, the increased prevalence of osteoporosis at the hip is expected to lead to a tripling of the number of hip fractures worldwide by 2050[3].The medical and economic burden of fragility fracture is substantial. When the impact of hip fracture on the quality of life is considered in disability-adjusted life years, the global burden of disease has been estimated at 1.75 million years, with approximately one-quarter occurring in China and India, and 50% occurring in Western countries alone[5].

Osteoporosis is defined as a skeletal disorder characterized by compromised bone strength that leads to an increased risk of fracture [6].The amount of bone mineral present or the BMD is the major determinant of the strength of bone in the general population. Although BMD can be measured by a number of different radiographic and ultrasonographic techniques, the most widespread imaging modality in clinical use for measurement of BMD is DXA of the spine and proximal femur. However, the strength of bone is also influenced by the quality of the bone that is present. Bone quality is, in turn, determined by a number of material and structural characteristics of bone, including architecture and microarchitecture, bone remodeling activity or turnover, mineralization, collagen properties, and accumulation of micro damage [7, 8]. Histologically, osteoporosis is characterized by a reduced quantity of normally mineralized bone. In addition, the osteoporotic bone is structurally abnormal. Microstructural studies reveal thinning and increased porosity of the cortices and fewer, disconnected, widely spaced bony trabeculae. The microarchitectural changes usually result from an increase in the rate of bone remodeling and/or an

imbalance between the bone resorbing activity of osteoclasts and the bone forming activity of osteoblasts. The most common scenario leading to osteoporosis is one in which bone resorption is increased and bone formation is also increased, but insufficiently to compensate. However, the histological changes of osteoporosis can also develop as a result of a decrease in bone formation whereas resorption proceeds at a normal pace. Measurement of biochemical markers that reflect osteoclast and osteoblast activities can be used to assess the rate of bone remodeling activity [9].
Remodeling of bone continues throughout life in response to mechanical stimuli and other regulatory factors. The normal sequence of bone remodeling involves 4 steps, the first of which is activation of osteoclast by osteoblast [10]. The next step is bone resorption, which involves replication of osteoclast precursors and their differentiation, migration and fusion into mature osteoclasts. The third phase begins when the osteoclasts have resorbed most of the mineral and matrix. This is the reversal step or coupling, meaning the reversal from bone resorption to formation, the signal for which is not definitely known [11]. The last step is the formation of new bone by osteoblasts filling the resorption cavity. Mineralization then follows within a few days. This sequence of activation, resorption, reversal, formation and mineralization occurs normally on 10 percent of the bone surface and has duration of several months [12]. The remodeling process is regulated by circulating hormones and by local factors. Hormones that influence the rate of normal bone remodeling are most notably parathyroid hormone (PTH), vitamin D and calcitonin. Increased PTH levels stimulate bone remodeling by increasing resorption. There are two types of bone tissue in adult life, trabecular and cortical bone. Bone mass is higher in men than in women throughout adult life, and in women there is an accelerated bone loss the first years after menopause of about 2% per year [15-16].During the course of their lifetime, women lose about 50% and men 30% of their trabecular bone .

There is a disintegration of the bone matrix with normal ratio of mineral to matrix [17]. Primary osteoporosis includes postmenopausal osteoporosis (type l osteoporosis) and senile osteoporosis (type ll osteoporosis) of elderly women and men. Secondary osteoporosis refers to bone loss caused by a specific defined clinical disorder (Table 1). Secondary osteoporosis can be either high or low bone turnover osteoporosis depending on the cause.

Table 1. Causes of secondary osteoporosis in adults

Endocrine/metabolic
Hypogonadism
Hyperadrenocorticism
Thyrotoxicosis
Systemic mastocytosis
Drugs
Glucocorticosteroids
Chronic heparin administration
Anticonvulsants
Nutritional
Malabsorption/malnutrition
Chronic liver disease
Vitamin D deficiency
Anorexia nervosa
Alcoholism
Gastric surgery

Other
Osteogenesis imperfecta
Ehler-Danlos syndrome
Marfan syndrome
Myeloma

Measurements of bone mineral density
Bone mineral density (BMD; g/cm2) is measured by non-invasive methods based on radiology [21]. A specified amount of electromagnetic energy, in the form of a gamma or X-ray beam, is sent through a region of interest and the amount exiting is quantified by a detector. Single photon absorptiometry (SPA), introduced in the 1960s measures BMD reliably only at peripheral sites, having small amounts of surrounding tissue, such as the heel and the wrist. Dual-energy X-ray absorptiometry (DXA) was introduced in the late 80-ies and is now the most widespread technique for evaluating BMD in patients at risk of osteoporosis. With DXA, two distinct energy levels are used to resolve contributions from soft tissue and bone making it possible to measure BMD at central sites such as the spine and the proximal femur. The precision error for DXA is about 1-2% which is important when estimating bone loss in longitudinal studies. If expected bone loss is of the same order, i.e. 1-2% per year, measurements should be performed with not less than 1-2 years interval [22].Since 1994 the World Health Organization (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 [22] (Table 2). No such generally accepted definition of osteoporosis exists for men at the present.

Table 2. World Health Organization (WHO) working definition.

Bone mineral density	Classification
Above –1 SD	Normal
Between –1 SD and –2.5 SD	Low bone mass or osteopenia
Below –2.5 SD	Osteoporosis

1SD = standard deviation

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´s definition, a woman with a T-score below –2.5 has osteoporosis. 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.

Metabolic bone disease in chronic liver disease
Chronic liver disease (CLD) can be classified into diseases with primarily hepato-cellular damage and cholestatic diseases. Examples of hepato-cellular CLD are autoimmune chronic hepatitis, chronic viral hepatitis B and C, and alcoholic liver disease. Autoimmune CAH is a disease of unknown etiology, has a prevalence of about 5- 10/100.000, occurs mainly in young women (sex ratio 8:1) and is treated with long-term corticosteroid therapy. Alcoholic liver disease includes steatosis, which is reversible upon abstinence, alcoholic hepatitis and cirrhosis. Alcohol is the most common cause of liver cirrhosis in the European countries. Cholestatic CLD includes primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC). The prevalence of PBC is about 10-15/100.000 and it mainly affects women (sex ratio 9:1) between the ages of 40 and 59. It is characterized by a progressive destruction of intra-hepatic bile ducts leading to cholestasis. The etiology is unknown but profound immunological disturbances are found and PBC is often associated with other autoimmune disorders. There is no specific treatment for PBC. PSC occurs in about 5-10% of those with inflammatory bowel disease, mainly ulcerative colitis. Males are twice

as commonly affected as females, usually between the ages of 25 and 45. It is characterized by a chronic, fibrosing, inflammatory process that involves all parts of the biliary tree resulting in its obliteration and ultimately in biliary cirrhosis. The etiology is unknown and there is no specific treatment for PSC. The final stage of chronic inflammation in the liver is cirrhosis. Liver cirrhosis gives rise to portal hypertension and complications such as bleeding esophageal varices, ascites and encephalopathy. Hepato-cellular failure results in hyperbilirubinemia, hypoalbuminemia and prolonged prothrombin time. Child´s grade is used to assess hepato-cellular function in cirrhosis based on these factors. The Child-Pugh classification is a modified grading system shown to be reliable in predicting survival of patients presenting with variceal bleedings but is also widely used as a method of assessing liver function [23].

Table 3.

Criteria	1	2	3
Encephalopathy	None	1-2	3-4
Ascites	None	Slight	Moderate
Bilirubin(umol/L)	<35	35-50	>50
Albumin(g/L)	>35	28-35	<28
PTI (%)	>70	40-70	<40

Grade A score 5-7
Grade B score 8-9
Grade C score 10-15

Hepatic osteodystrophy

In 1939 a 69 year old woman with long-standing intrahepatic obstructive jaundice and spinal osteoporosis with vertebral compressions was described [24]. Since then it has been firmly established that chronic cholestasis, and also other forms of CLD, are associated with metabolic bone disease [25]. In the era of liver transplantation, metabolic bone disease complicating CLD has become a major 25

Liver transplantation the combination of high dose corticosteroids and immobilization accelerates bone loss leading to a high post-transplant fracture rate ranging from 17-65% [26]. Decreased BMD pre-transplant, however, is a major risk factor for the development of post-transplant fracture. The term “hepatic osteodystrophy” covers both osteomalacia and osteoporosis . Steathorrhea with malabsorption of fat-soluble vitamins, including vitamin D, accompanies symptomatic cholestatic liver disease. Therefore osteomalacia might be expected to complicate CLD, as in fact was reported in earlier studies . Over the last two decades, better histomorphometric techniques (including double-tetracycline labeling for diagnosing osteomalacia) have made it clear that the main bone abnormality in CLD, cholestatic or hepato-cellular, is osteoporosis and that osteomalacia is very rare [27]. Low levels of serum vitamin D3 metabolites and calcium (Ca) malabsorption are found in CLD [28]. Whether vitamin D deficiency is associated with metabolic bone disease in CLD is uncertain. Hyperparathyroidism, despite vitamin D replacement, has been described in PBC [58].Others have not found evidence of hyperparathyroidism in patients with CLD .Treatment with corticosteroids and hypogonadism in men and women are reported by some as risk factors for osteoporosis in CLD . Others have not found treatment with corticosteroids to be associated with low BMD in CLD . Other general factors in patients with CLD such as alcohol consumption, low body weight and physical inactivity have not been reported as independent risk factors for osteoporosis in CLD but can be assumed to be important (Table 4).

Table 4. Potential pathophysiological factors in osteoporosis in chronic liver disease.

Lack of growth factors produced by the liver
Accumulation of toxins

Cholestasis
Hyperbilirubinemia
Vitamin D deficiency
Vitamin K deficiency
Calcium deficiency
Hypogonadism
Treatment with corticosteroids
Alcohol consumption
Low body weight
Physical inactivity

Insulin-like growth factors and insulin-like growth factor binding proteins

Somatomedins or IGF-l and IGF-ll, are peptide hormones that play a pivotal role in the regulation of proliferation, differentiation and specific functions of many cell types. IGF-l is the main mediator of the effects of GH on growth and development. In contrast to other hormone peptides, the IGFs are not stored in endocrine glands but form a circulating reservoir in the plasma. More than 99% of the IGFs in serum are complexed with the binding proteins IGFBP-1 to -6 and at least 95% are bound to IGFBP-3 [29]. The functions of the IGFBPs are not completely known but apart from regulating the bioavailability of the IGFs they also seem to modulate the action of the IGFs at cellular level . The liver is the major source of IGFBP-1 and -3 and probably also of IGFBP-2.

Insulin-like growth factors in chronic liver disease

In patients with CLD, irrespective of etiology, IGF levels are low and levels of GH high [30]. The reduction is most pronounced in those with advanced liver disease and is also related to the degree of portal hypertension and Porto-systemic shunting .Malnutrition is often seen in cirrhosis and may to some extent contribute to the low IGF concentration in these patients but the liver dysfunction probably is more important. IGF-l has been suggested as an early marker of liver dysfunction in CLD. Furthermore, IGF-l has been shown to be an independent marker of survival in patients with liver cirrhosis [31]. IGF-ll and IGFBP-3 levels are reduced in CLD and positively related to the severity of the liver disease. On the contrary, increased levels of IGFBP-1 are found in liver cirrhosis [32]. The reason for this is not clear but may be due to increased hepatosplanchnic generation and/or lower renal extraction. One suggestion is that the role of IGFBP-1 is to limit the bioavailability of IGF-l and hence it's potential hypoglycemic effects in the state of low substrate availability as seen in liver cirrhosis. As for IGFBP-1, increased levels of IGFBP-2 and a positive correlation with Child-Pugh score has been found in liver cirrhosis

Insulin-like growth factors and bone

There are numerous reports that IGF-l and -ll have prominent anabolic effects on bone in vitro, enhancing protein synthesis and osteoblastic proliferation [33]. The

Clinical studies have found serum leptin levels to be elevated in patients with alcoholic liver cirrhosis and it has been suggested that elevated serum leptin levels may be involved in the malnutrition of liver cirrhosis [34].

BMD should be measured in patients with liver cirrhosis too, both in biliary and in non-biliary one, before hepatic transplant. Indications to BMD measurement are less clear in patients with cholestatic liver disease, not waiting for transplant. For example, the guidelines of the American Gastroenterological Association suggests that BMD should be measured in all patients with primary biliary cirrhosis at diagnosis time, while others recommendations suggests BMD measurement only in cholestatic patients with bilirubin greater than 3 times the upper limit of normal range. Considering, then, that osteoporosis may also be first clinical manifestations of an underlying cholestatic liver disease, it is advisable to screen for anti-mitochondrial antibodies all osteoporotic

patients with low BMD and high cholestasis markers (gamma-glytamyl transpeptidase, γ-GT and alkaline phosphatase).Finally, it seems there are no indication to routine
measurements of serum and urinary markers of bone turnover neither to stratify fractures risk, nor to assess deterioration of bone health during followup. That is why this study was carried out to know the prevalence and related risk factors of osteoporosis besides age in CLD patients. The study can be important tool in assessing the impact of CLD on prevalence of osteoporosis as an independent risk factor when compared to controls.

MATERIAL AND METHODOLOGY

The present work is a hospital based study that was carried out in the Department of Gastroenterology, in a tertiary care Institute in Northe India . 70 known cases [21 males (30%) and 49 females (70%) who attended Gastroenterology OPD or were admitted in the concerned ward were enrolled as cases . Age of subjects ranged from 21 years to 65 years with mean age of 51.09 ± 14.138 years. 70 subjects [30 males (43%) and 40 females (57%) were taken as controls. The mean age here was 45.12 ± 14.469 years.

ETHICAL CONSIDERATIONS

Informed consent was taken from all subjects, and assent from the older subjects themselves, for participating in the study.

STUDY POPULATION

70 subjects with CLD fulfilling the below mentioned inclusion criteria admitted in the Department of Gastroenterology or attending OPD clinic were included in this study as cases and subjects fulfilling the criteria for controls were included in this study.

INCLUSION CRITERIA FOR CASES:

- Patients in the age group of >18 yrs to 65 yrs.
- All patients with CLD (Child Pugh class A, B and C).

EXCLUSION CRITERIA FOR CASES:

1. Age >65
2. Patients on steroids
3. Post liver transplant patients
4. Patients on bisphosphonates, HRT, contraceptives, calcitonin.
5. Early menopause <45 or bilateral ovariectomy.
6. Pregnancy

INCLUSION CRITERIA FOR CONTROLS:

- Subjects in the age group of >18 years to 65 years
- Non diabetic, non alcoholic
- No evidence of secondary or surgical menopause
- No evidence of secondary osteoporosis
- No evidence of steroid intake, gonadotrophin use.

Of 90 subjects initially taken as controls, only 70 fulfilled the criteria for controls and were enrolled for the study after due consent.

METHODOLOGY

After proper consent, subjects with CLD were enquired about the history of related risk factors (smoking, hypertension, diabetes, steroid intake, surgical menopause) and their medical records were checked.

Patients were considered active smokers if they had smoked at all during the last month; ex-smokers if they had ever smoked; and non-smokers if they had never smoked.
They were thoroughly examined and were subjected to baseline investigations including kidney function test, serum calcium levels, serum phosphorus levels, liver function test, complete blood count, lipid profile.
All subjects with CLD were subjected to Dual Energy X-ray Absorptiometry (DEXA) Scan (GE Lunar-1 Co. Prototype).
The same methodology (consent, history, thorough examination) was done for the controls before subjecting them for DEXA scan.
The DXA definition of osteoporosis and the bone mass criteria followed for its diagnosis were adopted from the World Health Organization (WHO) definition of osteoporosis (1994).
The WHO definition of osteoporosis has 2 clear and different components: The first is the BMD changes, which does not yield any information related to micro architectural changes. It is likely, though, that in the near future, new, sophisticated techniques such as quantitative micro-computed tomography (micro CT), high-resolution QCT and finite element analysis, so far not available for clinical practice, may help us to study, in the clinical setting, quality and micro architectural changes. The second component of the WHO definition of osteoporosis is the clinical consequence of having low bone mass and micro architectural deterioration, as represented by the bone fragility fracture, also called an osteoporotic fracture.
The T-score was used for the evaluation of BMD and for the definition of the different stages of BMD according to the WHO definition of osteoporosis. Each T-score difference in BMD represents 1 SD from the peak bone mass.
Osteoporosis was defined as T-Score of equal to or below -2.5 at femoral neck or L1L2 spine or both.

CRITERIA

T-score >	-1 SD (standard deviation)	Normal
T-score >	-1to-2.5SD	Osteopenia
T-score:	< or = 2.5SD	Osteoporosis

T-score<or=-2.5SD

STATISTICAL ANALYSIS

Data obtained were subjected to statistical analysis. The Categorical variables in the study have been shown in terms of frequency and percentages. The Pearson chi square test and Fisher exact test have been used to analyze the data. Continuous variables were analyzed by ANOVA technique. The statistical software SPSS version 20.0 has been used. P values less than 0.05 were considered to be statistically significant. Data obtained from case study were compared with controls.

OBSERVATIONS AND RESULTS

The study was carried out at a tertiary care institute of the valley in the department of Gastroenterology.Of 70 subjects enrolled as cases 49(70%) were females and 21(30%) were males. The age of cases ranged from 21 years to 65 years with a mean age of 51.01±14.138 years. District wise distribution of cases from Kashmir Valley. Maximum (25.7%) cases were from district Anantnag . District wise distribution of cases. Districts of Kashmir Valley: Others (0). Srinagar (1), Ganderbal (2), Budgam (3), Baramulla (4), Kupwara (5), Bandipora (6), Anantnag (7), Pulwama (8), Kulgam (9), Shopian (10), Doda (11).All the patients were known cases of CLD (Diagnosed or first time evaluated) admitted or following Gastroenterology OPD at SKIMS. Of 70 cases, 9(12.85%) were Child Pugh class A, 15(21.40%) were Child Pugh class B, and 46(65.70%) were Child Pugh class C.16(22.5%) subjects were smokers, 16(22.5%) subjects were ex-smokers, and 38(55%) subjects were nonsmokers. Average BMD at femoral neck in cases stood at 0.88±0.085

g/m², while BMD at L1L2 spine measured at 0.96±0.087 g/m².With a mean T Score of- 1.13±1.802 at femoral neck, 32(45.7%) subjects (with T-Score ≤ -2.5) had osteoporosis, 27(38.6%) had osteopenia i.e. T-Score between –1 and -2.5 and 11(15.7%) fulfilled the criteria for normal BMD with T sc0re upto –1. Mean T-Score at L1L2 spine was-1.29±1.492. Out of 70 cases enrolled, 29(41.4%) qualified for osteoporosis with T-Score ≤ -2.5 at L1L2. 28(40.0%) subjects had osteopenia and 13(18.6%) had T-Score within normal range.

Table 1. Comparison of prevalence of osteoporosis between two sites femur and lumbar spine**.**

Cases	Femur neck	L1-L2
Normal	11(15.7%)	13(18.6%)
Osteoporosis	32(45.7%)	29(41.4%)
Osteopenia	27(38.6%)	28(40.0%)

P=0.84, chi 0.33

Table 2: Sex and Osteoporosis (fem. neck)

	Osteoporosis at femur neck		Total
	Male	Female	
osteoporosis	10	22	32
No	11	27	38
Total	21	49	70

Table 3: Osteoporosis and sex distribution among cases based on Femoral Neck.

Sex Cases	Osteoporosis Femur			Total
	Normal	Osteoporosis	Osteopenia	
Male	7(33.3%)	10(47.6%)	4(19.0%)	21
Female	4(8.3%)	22(44.9%)	23(46.9%)	49
Total	11	32	27	70

Table 4: Sex and Osteoporosis at L1L2

	Osteoporosis L1L2		Total
	Male	Female	
Osteoporosis	5	24	29
No	16	25	41
Total	21	49	70

Table 5: Osteoporosis and sex distribution based on L1L2 T-Score

Sex cases	Osteoporosis L1L2			Total
	Normal	Osteoporosis	Osteopenia	
Male	11(52.4%)	5(23.8%)	5(23.8%)	21
Female	2(4.1%)	24(49%)	23(46.9%)	49
Total	13	29	28	70

P=0.0001, chi 22.6

Table 6: Child class and osteoporosis distribution (Fem. Neck)

Osteoporosis Femur neck	Child class			Total	P value
	A	B	C		
Normal	3	5	3	11	0.013
Osteoporosis	2	3	27	32	
Osteopenia	4	7	16	27	
Total	9	15	46	70	

Table 7: Osteoporosis and DM at femur neck

DM Cases	Osteoporosis Femur Cases			Total	P value
	No	Yes	Osteopenia		
No	20	17	11	48	0.56912
Yes	11	5	6	22	
Total	31	22	17	70	

Table 8: BMI and Osteoporosis at femur

BMI Cases	Osteoporosis At Femur			Total	P Value
	No	Yes	Osteopenia		
<18.5	1	16	0	17	0.0001
18.5-25	24	1	14	39	
≥25	6	6	2	14	
Total	31	23	16	70	

Table; 9 Comparison of prevalence of osteoporosis between two sites femur and lumbar spine in controls

controls	Femur	L1-L2
Normal	38(54.3%)	44(62.9%)
Osteoporosis	13(18.6%)	11(15.7%)
Osteopenia	19(27.1%)	15(21.4%)

P=0.58, chi=1.07

Table 10: Comparison of prevalence of Osteoporosis in cases and controls**.**

	Femoral neck (cases)	Femoral neck (controls)
Normal	11(15.7%)	38(54.3%)
Osteoporosis	32(45.7%)	13(18.6%)
Osteopenia	27(38.6%)	19(27.1%)
	L1-L2 spine (cases)	**L1-L2 (controls**
Normal	13(18.6%)	44(62.9%)
Osteoporosis	29(41.4%)	11(15.7%)
Osteopenia	28(40.0%)	15(21.4%)

P=0.0001

Table 11: Comparison of sex distribution of osteoporosis among cases and controls.

	Femur neck cases		Femur neck controls	
	Female	Male	Female	Male
Normal	4(8.3%)	7(33.3%)	14(35%)	24(80%)
Osteoporosis	22(44.9%)	10(47.6%)	11(27.5%)	2(6.6%)
Osteopenia	23(46.9%)	4(19.0%)	15(37.5%)	4(13.3%)
	P=0.012	**Chi=8.91**	**P=0.001**	**Chi=14.0**
	L1-L2 spin cases		**L1-L2 spine controls**	
	Female	**Male**	**Female**	**Male**
Normal	2(4.1%)	11(52.4%)	18(45%)	26(86.6%
Osteoporosis	24(49%)	5(23.8%)	8(20%)	3(10%)
Osteopenia	23(46.9%)	5(23.8%)	14(35%)	1(3.3%)
	P=0.0001	**Chi=22.67**	**P=0.001**	**Chi=13.8**

CLD and its impact on osteoporosis

Table 12: Impact of CLD on prevalence of osteoporosis

Osteoporosis	CLD	Non CLD	Total	P vaue
Yes	32(71.1%)	13(28.9%)	45(100%)	0.001
No	38	57	95	
Total	70	70	140	

Although there have been studies involving thousands of patients with osteoporosis, very few of these have included any patients with CLD.

DISCUSSION

This study was carried out to know the prevalence and related risk factors of osteoporosis besides age in CLD patients.The study can be important tool in assessing the impact of CLD on prevalence of osteoporosis as an independent risk factor when compared to controls. Majority (65.70%) of cases in this study belonged to Child-Pugh class C. The reason for this may be that patients in this part of the world seek medical attention only when the disease becomes advanced. Further osteoporosis was more prevalent in Child-Pugh class C patients in our study (58.7% at femur neck).This is evident in other observational studies which have also found that prevalence of osteoporosis is more in advanced Liver diseases.

The prevalence of osteoporosis in CLD patients was almost twice than that in controls at femur (45.7% vs. 18.6%) as well as at L1-L2 (41.4% vs. 15.7%).This prevalence was statistically significant with a p value of 0.0001. Prevalence of osteopenia was also statistically significant in cases compared to controls at both sites (p=0.001).

Prevalence of osteoporosis and osteopenia differed only slightly when the two sites i.e. femur and L1-L2 were compared for both cases as well as controls (p=0.84, chi 0.33 in cases and p=0.58, chi 1.07 in controls).

Osteoporosis was more common in females at both femur and L1-L2 in cases as well as in controls (p=0.012, chi 8.91 and p=0.0001, chi 22.67 in cases at femur and L1-L2 respectively with p=0.001, chi 14.09 and p=0.001, chi 13.84 in controls at femur and L1-L2 respectively)

In this study BMI had positive correlation with osteoporosis, low BMI subjects were at higher risk for osteoporosis (with sig. P value of 0.0001, chi 33.95).Diabetes Mellitus is an important risk factor for CLD, however it does not increase the risk of osteoporosis (p=0.56912)

Of all osteoporotic subjects, i.e. cases and controls taken together, 71.1% subjects had CLD and only 28.9% subjects who were having osteoporosis were among non-CLD. The statistical significant difference with a p value 0.001, chi 11.82 was found between the two groups. The data showed that CLD is an important and an independent risk factor for osteoporosis. The reverse however is no true; osteoporosis had no impact on CLD.Findings in our study imply that CLD is an independent risk factor for osteoporosis, hence patients who are first time diagnosed CLD should be screened for osteoporosis with central or peripheral DXA, and subsequently managed to prevent complications and morbidity associated with osteoporosis.

This study was carried out to know the prevalence and related risk factors of osteoporosis besides age in CLD. The study can be important tool in assessing the impact of CKD on prevalence of osteoporosis as an independent risk factor when compared to controls. In the general population, epidemiological studies have claimed that BMD measurement may predict up to 70% of the fracture risk, and every standard deviation (SD) decrease in BMD doubles the fracture risk. The T-score is used for the evaluation of BMD and for the definition of the different stages of BMD according to the WHO definition of osteoporosis. Each T-score difference in BMD represents 1 SD from the peak bone mass. Values up to −1 SD BMD below the mean peak bone mass are considered normal;

values between −1 SD BMD and −2.5 SD are indicative of osteopenia and values below −2.5 SD BMD are indicative of osteoporosis. Even though a BMD <−2.5 SD is a good predictive risk factor for osteoporosis, the strongest risk factors predicting osteoporotic fractures are older age and the presence of a previous bone fragility fracture at any site.

The reported prevalence figures for osteoporosis in patients with CLD range from 9 to 53%.**Yadav et al (35)** found that the prevalence varied between 11% to 58% in patients with CLD [112]. **Loria et al(36)** reported the overall prevalence of osteodystrophy as 40% while as **Collier(37)** found it to be in the range of 10-56 %

It was also found that high rate of osteoporosis occurred in patients classified as Child-Pugh B and C compared with the Child-Pugh A group. About 84.3% of patients having osteoporosis at femur belonged to Child-Pugh group C. This is supported by other studies that have found the highest prevalence of metabolic bone disease in patients with advanced liver disease whereas in earlier stages of liver disease no evidence of bone disease has been found.

Low BMI is a known risk factor for osteoporosis and increased rate of bone loss in the normal population as mentioned in The Framingham study conducted Showed that sixteen (94.1%) of patients in our study with a low BMI of <18.5 had osteoporosis while as this number was only 3% in patients with BMI in the range of 18.5 to 25. Reasons for low BMI in patients with CLD are probably multi-factorial including malnutrition resulting from malabsorption and anorexia, decreased physical activity and increased resting metabolic rate associated with progression of the liver disease. Using only BMI as a measure of nutrition, we probably underestimated the frequency of malnutrition. BMI is frequently used when evaluating nutritional status in patients with CLD, but somewhat imprecise. Although there have been studies involving thousands of patients with osteoporosis, very few of these have included any patients with CLD.

Majority (65.70%) of cases in this study belonged to Child-Pugh class C. The reason for this may be that patients in this part of the world seek medical attention only when the disease becomes advanced. Further osteoporosis was more prevalent in Child-Pugh class C patients in our study (58.7% at femur neck).This is evident in other observational studies which have also found that prevalence of osteoporosis is more in advanced Liver diseases.

The prevalence of osteoporosis in CLD patients was almost twice than that in controls at femur (45.7% vs. 18.6%) as well as at L1-L2 (41.4% vs. 15.7%).This prevalence was statistically significant with a p value of 0.0001. Prevalence of osteopenia was also statistically significant in cases compared to controls at both sites (p=0.001).

Prevalence of osteoporosis and osteopenia differed only slightly when the two sites i.e. femur and L1-L2 were compared for both cases as well as controls (p=0.84, chi 0.33 in cases and p=0.58, chi 1.07 in controls).

SUMMARY AND CONCLUSION

Osteoporosis was more common in females at both femur and L1-L2 in cases as well as in controls (p=0.012, chi 8.91 and p=0.0001, chi 22.67 in cases at femur and L1-L2 respectively with p=0.001, chi 14.09 and p=0.001, chi 13.84 in controls at femur and L1-L2 respectively)

In this study BMI had positive correlation with osteoporosis, low BMI subjects were at higher risk for osteoporosis (with sig. P value of 0.0001, chi 33.95).

Diabetes Mellitus is an important risk factor for CLD, however it does not increase the risk of osteoporosis (p=0.56912)

Of all osteoporotic subjects, i.e. cases and controls taken together, 71.1% subjects had CLD and only 28.9% subjects who were having osteoporosis were among non-CLD. The statistical significant difference with a p value 0.001, chi 11.82 was found between the two groups. The data showed that CLD is an important and an independent risk factor for osteoporosis. The reverse however is no true; osteoporosis had no impact on CLD.

Findings in our study imply that CLD is an independent risk factor for osteoporosis, hence patients

who are first time diagnosed CLD should be screened for osteoporosis with central or peripheral DXA, and subsequently managed to prevent complications and morbidity associated with osteoporosis.

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