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Frequency of Osteoporosis in Patients Presenting with Chronic Liver Disease at Tertiary Care Hospital Karachi

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ABSTRACT

Osteoporosis is a disease of low bone mass and micro-architectural deterioration of bone tissue, resulting in bone fragility and an increased risk of fractures. Because osteoporosis suddenly manifests with fractures at multiple skeletal sites, most often at the spine, hip, or wrist, it is termed "silent disease". This becomes even important in CLD patients. **Objective:** To determine the frequency of osteoporosis in patients presenting with chronic liver disease (CLD) at Al Tibri Medical College and Hospital, Karachi. **Methods:** A Total of 120 CLD patients of either gender were included. Data like age, gender, residence, and duration of CLD were recorded and followed by a study of bone mineral density (BMD) in the distal forearm of the non-dominant hand using dual-energy X-ray absorptiometry (DEXA). If BMD <–2.5 SD, then osteoporosis was positive. SPSS version 23.0 was used for analysis. Descriptive statistics were calculated. Effect modification was controlled through Chi-square. p-value<0.05 was considered significant. **Results:** The mean age was 39.49 ± 8.12 years. Mean CLD duration was 5.93 ± 2.29 years. Male were 68.3%. A total of 31.7% of patients with CLD had a BMD score <–2.5 SD and were observed as osteoporosis. The frequency of osteoporosis decreased with increasing age, but not statistically significant. Numerically, male was more affected than female, however, with an insignificant association. The duration of CLD was an effect modifier insignificantly. **Conclusion:** Almost every third patient of CLD has osteoporosis. The current study recommends screening of all such patients.

INTRODUCTION

The process involving both destruction and/or regeneration of hepatic parenchyma that often leads to cirrhosis or fibrosis is known as CLD (Chronic Liver Disease) [1]. Compensated CLD often goes undetected for prolonged periods; thus, the incumbent complications, like skeletal problems, are also often detected [2]. Reduced bone mineral density, as an extrahepatic complication, reported in CLD cases, is well established [3]. In cases with advanced CLD, the bony destruction is called HO (hepatic osteodystrophy), which involves osteoporosis and osteomalacia [4]. Among the two features, in osteoporosis, reduced levels and quality of bone mass are observed, which raises the risk for fragile bones leading to fractures [5]. Low mass of bone is associated with osteoporosis in addition to malformed micro-architecture and weakened structure of bone. Since the liver's involvement in various metabolic pathways is central, any disease of the liver leads to secondary osteoporosis. Nearly 30% of cases having CLD are reported to experience osteoporosis [6]. Nonetheless, the exact cause of loss of

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bone in CLD is multifactorial and not yet fully understood [7]. The link between CLD and osteoporosis is thought to be due to resorption of bone and reduction in the formation of bone [8]. The decreased mass of bone, coupled with loss of strength, causes a fragile fracture resulting in substantial effects on quality of life and morbidity [9]. Osteoporosis is diagnosed by assessing the bone mineral density via T-score below -2.5 [10]. In cases with more than one fracture and those meeting densitometry criteria are termed as established or severe osteoporosis [11]. CLD's prevalence varies in-between 12% and 70% [12]. The causative agent behind CLD leading to osteoporosis is estimated to be viral hepatitis B in 10 % of cases, hepatitis C in 50 % of cases, alcoholic liver steatosis in about 30% of cases, while self-immune disease in around 12 to 55% of cases [13]. In cases with chronic cholestasis, around 37% of females were reported to have a T-score below -2.5 for osteoporosis, coupled with an incidence of fractures around 20.8 % in a research [14]. Osteoporosis is more common in female (30 to 50%) than in male (15 to 30%). The main reason behind this inclination is post-menopause and age >70 years, CLD and chronic therapy with glucocorticoids are known to be the most common causes of osteoporosis [15]. Post-liver transplant, osteoporosis is regarded to be the only remaining complication, persisting for years [16]. Since CLD and osteoporosis are linked together, osteoporosis is often overlooked in cases without cirrhosis [17]. In osteoporosis, the bones become porous, resulting in an increased risk of fractures. These fractures were associated with bone loss due to low osteocalcin levels in patients with chronic liver diseases [18]. Bone loss in liver disease causes vitamin D deficiency. Because osteoporosis suddenly manifests with fractures at multiple skeletal sites, most often at the spine, hip, or wrist, it is termed "silent disease" [19]. This becomes even important in CLD patients, most of whom are nutritionally deficient on hand and have decreased mobility on the other hand [20]. CLD is a quite common chronic disorder in which people have to live with it till it takes their lives. But living a good quality of life is their basic right. This right is deteriorated due to complications like osteoporosis. It is mandatory to identify these complications at the earliest and properly manage them using specific therapies. Limited availability of literature in the local context in Pakistan provided a strong rationale for this study.

This study aims to assess the magnitude of the burden of hepatic osteodystrophic changes in CLD.

METHODS

An observational cross-sectional analytical study was carried out on the outpatients in the Department of Medicine, Al Tibri Medical College and Hospital, Karachi, from June to December 2024. Ethical Approval Letter was taken with reference No: IERC/ATMC/14(01-2024)/49. The sample size was calculated with the help of the WHO sample size calculator. Keeping the following parameters, the sample size came out to be 120: Expected Proportion (p): 32% (based on prior studies of osteoporosis in CLD patients), Confidence Level: 95% (Z=1.96), Margin of Error (d): ±8.5% and Calculated Sample Size: 116 → rounded to 120. A total of 120 patients of both genders aged 25 to 50 years diagnosed with Chronic liver disease were included. The reason behind including patients between 25 to 50 years of age was to reduce confounding variables, as post-menopausal bone loss in females and age-related hypogonadism in males are independent risk factors for osteoporosis. Moreover, the period of ages included represents young to middle-aged patients, where peak bone mass is observed. Therefore, any reduction in BMD in this age range might reflect a pathological process. Patients with malabsorption syndrome, on vitamin D supplements, less sun exposure due to chronic use of veils by housewives, postmenopausal women, patients with child pugh score <5/15, chronic myeloid leukemia or multiple myeloma and liver transplantation, history of metabolic bone disorder prior diagnosis of CLD, hyperparathyroidism, hypoparathyroidism, chronic renal failure and patient taking steroids therapy >3 months for other chronic diseases, anorexia nervosa were excluded. Informed consent was obtained from all patients. For the selection of the sample, non-probability consecutive sampling was used. Patients were considered to have CLD if they had widespread fibrosis and regenerating nodules on liver biopsy, and based on laboratory, clinical and radiological testing. For Osteoporosis, all patients were assessed with dual-energy X-ray absorptiometry (DEXA scan of the distal forearm of the non-dominant hand) for bone mineral density. Osteoporosis was defined based on Bone Mineral Density (BMD) measurements obtained through a dual-energy X-ray absorptiometry (DEXA) scan. According to the World Health Organization (WHO), a person is considered to have normal BMD if the T-score is greater than or equal to -1.0. A T-score between -1.0 and -2.5 is classified as osteopenia, indicating low bone mass. Osteoporosis is diagnosed when the T-score is equal to or less than -2.5. If the T-score be re is -2.5 or lower and the individual has experienced one or more fragility fractures, the condition is classified as severe or established osteoporosis. Data collection was started with permission from the Ethical Committee of Dow University of Health Sciences and the Civil Hospital Karachi. Data were taken on a pre-determined and approved proforma. This included demographic variables like name, age, gender, residence (rural or urban), and duration of CLD. It was followed by a study of bone mineral density (BMD) in the distal forearm of the non-dominant hand using dual-energy X-ray

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absorptiometry (DEXA). The presence of osteoporosis was recorded. The current study used SPSS version 23.0 for data analysis. Descriptive statistics were computed. Mean ± SD was calculated for quantitative variables like age, duration of CLD and bone mineral density (BMD). Frequency and percentage were calculated for qualitative variables, i.e. gender, residence (rural or urban), and osteoporosis (outcome variable). Stratification of age, gender, and duration of CLD was done to evaluate the effect of these modifiers on the outcome variable. It was followed by the application of the chi-Square test to see the association of outcomes with effect modifiers. A p-value ≤0.05 was taken as significant. Selection criteria were strictly followed to control for the confounders.

RESULTS

Average age of patients was 39.49 ± 8.12 years, with range of 25-50 years. Mean duration of CLD was 5.93 ± 2.29 years. Age and duration of disease were stratified in groups. The overall descriptive statistics of age and duration and also according to stratified groups are presented table 1.

Table 1: Descriptive Statistics of Age and Duration of Disease (n=120)

Variables		Mean ± SD	Median	Minimum	Maximum	Range
Age	Overall	39.49 ± 8.12	42.0	25.0	50.0	25.0
	25-35 Years	29.62 ± 2.70	30.0	25.0	34.0	9.0
	36-45 Years	41.92 ± 2.50	42.0	37.0	45.0	8.0
	46-50 Years	48.00 ± 1.41	48.0	46.0	50.0	4.0
Duration of Disease	Overall	5.93 ± 2.29	6.0	3.0	11.0	8.0
	≤ 4 Years	3.29 ± 0.46	3.0	3.0	4.0	1.0
	5-8 Years	6.22 ± 0.85	6.0	5.0	8.0	3.0
	9-12 Years	9.71 ± 0.71	10.0	9.0	11.0	2.0

It was observed that 68.3% of patients were male, and female were 31.7%. The results showed that 35.8% of patients were between 25-35 years, 31.7% of patients were of age 36-45 years, while patients of age 46-50 years were 32.5%. The stratified groups of chronic liver disease showed that less than one third of patients (i.e.30.8%) had CLD since last 4 years, half of all patients (51.7%) had been diagnosed their CLD between 5-8 years while 17.5% were such patients whose CLD history was between 9-12 years. The results are also presented in table 2.

Table 2: Frequency Distribution of Gender, Age Groups, and Duration of Disease Groups (n=120)

Variables		Frequency (%)
Gender	Male	82 (68.3 %)
	Female	38 (31.7 %)
Age Group	25-35 Years	43 (35.8 %)
	36-45 Years	38 (31.7 %)
	46-50 Years	39 (32.5 %)
Duration of Disease	≤ 4 Years	37 (30.8 %)
	5-8 Years	62 (51.7 %)
	9-12 Years	21 (17.5 %)

As far as living area is concerned, it was found that more than three fourths (i.e. 78%) patients were belonged to urban areas while only 22% of patients were belonged to rural areas, as in figure 1.

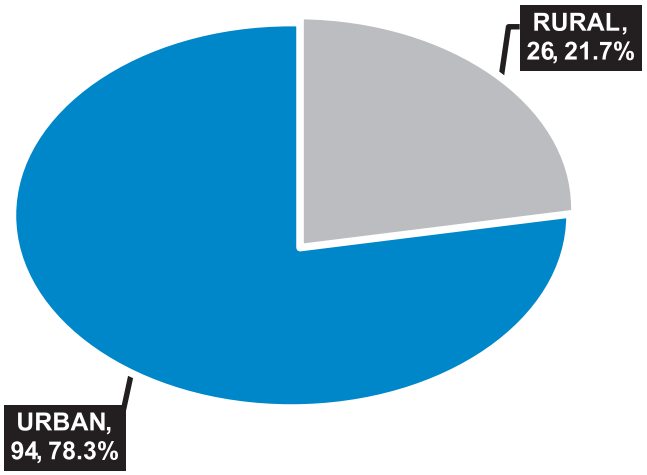

Figure 1: Percentage of Patients Belonged to the Living Area

The study observed that on DEXA scanning method of diagnosis, 31.7% patients had Bone Mineral Density (BMD) Score <–2.5 SD. Remaining 68.3% patients did not have had BMD Score <–2.5 SD, as presented in figure 2.

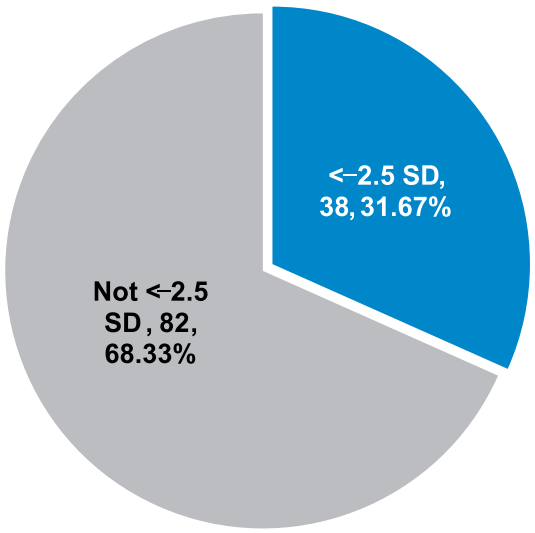

Figure 2: Percentage of Patients According to BMD Score

Thus, as per operational definition criteria used in this study, 31.7% of patients with Chronic Liver Disease had osteoporosis, as presented in figure 3.

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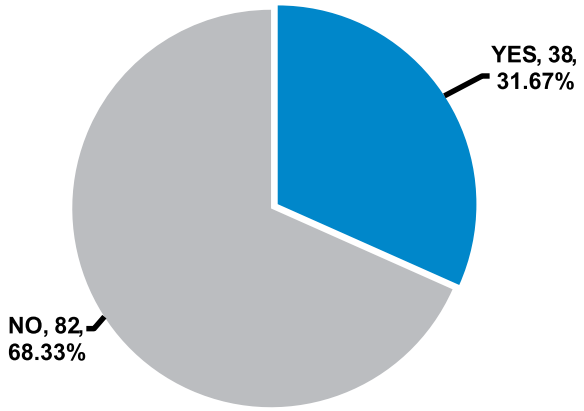

Figure 3: Percentage of Osteoporosis

Stratified analysis of gender showed that it was not significantly associated with gender (p-value=0.391); however, male group of CLD patients was more affected by osteoporosis (34.1%) than the female group (26.3%). The other stratified variable was age, and it showed that the frequency of osteoporosis slightly increased and then decreased with increasing age of CLD patients, but the result of osteoporosis was statistically insignificant (p-value=0.190). The duration of CLD was also a non-significant effect modifier, and it was noted that with increasing disease duration from up to 4 years to 9-12 years, there was more than a two-fold increase in the frequency of osteoporosis (21.6% in the former compared to 47.6% in latter category (p-value=0.122). And lastly, the residence was also insignificantly associated with CLD (p-value=0.911). The results are also presented in table 3.

Table 3: Association of Osteoporosis with Age, Gender, and Duration of Disease (n=120)

Variables		Osteoporosis		Total	p-Value	Confidence Intervals
		Yes (n=38)	No (n=82)			
Gender	Male	28 (34.1%)	54 (65.9%)	82	0.391	23.8% – 44.4%
	Female	10 (26.3%)	28 (73.7%)	38		11.8% – 41.8%
Age Group	25-35 Years	16 (37.2%)	27 (62.8%)	43	0.190	22.6% – 51.8%
	36-45 Years	14 (36.8%)	24 (63.2%)	38		21.4% – 52.2%
	46-50 Years	8 (20.5%)	31 (79.5%)	39		7.8% – 33.2%
Duration of Disease	≤4 Years	8 (21.6%)	29 (78.4%)	37	0.122	8.4% – 34.8%
	5-8 Years	20 (32.3%)	42 (67.7%)	62		20.7% – 44.0%
	9-12 Years	10 (47.6%)	11 (52.4%)	21		25.7% – 69.5%
Residence	Rural	8 (30.8%)	18 (69.2%)	26	0.911	13.1% – 48.5%
	Urban	30 (31.9%)	64 (68.1%)	94		22.4% – 41.4%

DISCUSSION

Chronic liver disease which itself is a syndrome like condition, had many direct and indirect implications and complications. One of such complications is abnormal bone metabolism caused by chronic liver disease. Due to disruption of bone metabolism, the CLD leads to very significant & detrimental effect on bone calcium deposition and remodeling. This eventually appears as brittleness of bone- the osteoporosis [21]. It was observed in the current study that the mean age of patients was 39.49 ± 8.12 years, with a range of 25-50 years. Compared to our findings, one international study reported a much higher mean age, i.e. 52.55 ± 12.34 years, of CLD patients who had osteoporosis [22]. This difference was due to the selection criteria which these studies used regarding the age of enrolled patients. This difference may also be based on the fact that in our country, chronic hepatic infections are more common even at younger ages due to contamination of syringes, blades at barber shops, vertical transmission and above all, contaminated blood transfusions [23]. The current study also noted that males were in the majority, which was more than two-thirds of all participants and also three-fourths of the total sample belonged to urban areas. This was because the study was conducted in an urban setting. But it is a fact that Hepatitis C and CLD are equally prevalent in rural areas of Pakistan, or even more than in the urban population in some areas. Then, it can be expected that these areas may be equally affected by osteoporosis [24, 25]. The main outcome variable of the study, i.e. the osteoporosis, was found to be much common. Almost one third of CLD patients, 31.7%, were diagnosed to have osteoporosis. This rate is quite high and is in line with the results of other studies. The pool of evidence suggests that the frequency of osteoporosis among CLD patients ranges from 11% to 40% [25]. Our results thus highlight the importance of the subject by replicating the available research data. The wide range of frequency of osteoporosis is thought to be due to the regional differences. The study evaluated osteoporosis in CLD patients. The DEXA scanning of the distal forearm of the non-dominant hand was done to evaluate the bone mineral density of enrolled patients. There were two categories: one having BMD below –2.5 SD, while the others did not have BMD below –2.5 SD as per operational definitions.

CONCLUSIONS

Osteoporosis is highly common among patients with chronic liver disease, as reported in this study. Many of the patients affected by this were young to middle-aged. Apart from those who are diagnosed with osteoporosis, many are at risk of developing it if not treated prophylactically. Therefore, the current study recommends screening of all such patients. Their Bone mineral density should be evaluated thoroughly, and to treated for those found to have overt osteoporosis in addition to those who have osteopenia.

Authors Contribution

Conceptualization: HZ
Methodology: HZ, BN, HA
Formal analysis: HK
Writing review and editing: WM, AM, AK

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All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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