Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v2023i1.221
*Biol. Clin. Sci. Res. J., Volume, **2023**: 221*
Original Research Article

HIGH INCIDENCE OF OSTEOPOROSIS IN CHRONIC LIVER DISEASE BEFORE LIVER TRANSPLANTATION

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(Received, 20th October 2022, Revised 27st February 2023, Published 6th March 2023)

Abstract: *A prospective study was conducted in Nishtar Medical Hospital from January 2022 to January 2023 to assess the incidence of osteoporosis before liver transplant in patients with chronic liver disease. A total of 70 patients were included in the study. A liver biopsy was used to confirm the hepatological diagnosis. Dual-energy X-ray absorptiometry through a densitometer was used for measuring bone mineral density. Results showed that the prevalence of osteoporosis at the femoral neck and lumbar spine was 37%, and in only 14.3% of cases, bone density at these sites was normal. More patients had osteopenia and osteoporosis at the femoral neck (41.7%) compared to the lumbar spine (24.2%) (P=0.009). Osteoporosis was not associated with the severity of the disease; its prevalence was 39%, 32%, and 36% in those with Child-Pugh A, B, and C, respectively (P=0.78). Lower weight (P=0.0007) and increasing age (P=0.038) were independent risk factors for osteoporosis during chronic liver disease. Results show that osteoporosis is highly prevalent in subjects with chronic liver disease before a liver transplant score.*

Keywords: Osteoporosis, Chronic liver disease, liver transplant, bone mineral density

Introduction

Osteoporosis is common in patients with chronic liver disease, with fractures occurring in 35% of patients after liver transplant(Linares et al., 2019). It occurs due to multiple factors, but prior bone disorder associated with chronic liver disease has a significant role. Bone disease is a common complication of chronic liver disease. Cholestatic liver disease may result in osteomalacia, but osteoporosis is the most common bone disease in these patients (Loosen et al., 2022). A study used dual photon absorptiometry (DPA) for estimating bone mineral density (BMD) in cirrhosis patients, and the results showed decreased bone density at Ward's triangle of the proximal femur and lumber spine (Yang and Kim, 2021).

Similarly, in another study, bone density at the forearm and spine was measured in cirrhosis patients, and results showed that 29% of the study sample had osteoporosis (Danford et al., 2020). Hypogonadism and cirrhosis were independent risk factors for osteoporosis, and their prevalence was not affected by the etiology of liver disease. Recently different studies have reported the association between bone loss and liver transplants. A study reported that 15-57% of patients had osteoporosis at the lumber spine (osteoporosis was defined as bone mineral density < 0.98g/cm^2) (Pravisani et al., 2019). However, another study reported that the BMD of patients with chronic liver disease at the radius, femur and lumbar spine was not significantly different from sex and age-matched controls(Rodríguez-Aguilar et al., 2021). Another study also reported that bone mineral density at the femoral neck and lumbar spine was normal (Zavatta and Clarke, 2021). Local studies are scarce on the assessment of osteoporosis in patients with chronic liver disease. Thus, this study aims to assess the incidence of osteoporosis before liver transplant in patients with chronic liver disease.

Methodology

A prospective study was conducted in Nishtar Medical Hospital from January 2022 to January 2023. The study included patients who had chronic liver disease. Those with osteoporosis due to reasons other than chronic liver disease were excluded. A total of 70 patients were included in the study. The informed consent of the patients was recorded. The ethical board of the hospital approved the study. 49 (70%) participants were listed for a liver transplant. According to the Child-Pugh classification, 3 (4.2%), 20 (28.5%), and 47 (67.1%) patients were classified as Child-Pugh A, B, and respectively. A liver biopsy was used to confirm the hepatological diagnosis. During the study period, 3 patients were taking

vitamin D and calcium. 3 post-menopausal women were on hormone replacement therapy. 10 patients had been taking prednisolone for over 8 years due to autoimmune hepatitis.

Dual-energy X-ray absorptiometry through a densitometer was used for measuring bone mineral density. Precision values at the lumber spine and femoral neck were 1% and 1.5 to 3%, respectively. The result was represented as a Z score (Standard deviation in relation to sex and age-matched control group) and a T score (Standard deviation in relation to maximum bone mass). WHO classification defined osteoporosis (Carey et al., 2022).

Data analysis was done using SPSS version 23.0. Data were expressed as mean and standard deviation. Univariate analysis was done through a t-test or chi-square test. ANOVA was used to measure bone mineral density differences among various disease categories. A multivariate regression model was used to assess independent risk factors for osteoporosis. P value < 0.05 was considered statistically significant.

Results

The mean age of the participants was 51.2 years. There were 36 (51.4%) males and 34 (48.5%) females. There were 9 (26.4%) post-menopausal women. The prevalence of osteoporosis at the femoral neck and lumbar spine was 26 (37%), and in only 10 (14.3%) cases, bone density at these sites was normal. More patients had osteopenia and osteoporosis at the femoral neck (41.7%) compared to the lumbar spine (24.2%) (P=.009). Though the BMD T score at the femoral neck (−1.814 ± .086) was lower than the lumber spine (−1.599 ± 0.101), this difference was statistically insignificant. Osteoporosis at the femoral neck and L1-4 was reported in 23 (23%) male and 27 (38%) female patients. The association between osteoporosis and gender was insignificant, suggesting that both genders are equally affected. Menopausal status had more effect on osteoporosis of FN, with 3 (12%) premenopausal vs. 3(33%) post-menopausal women affected (P =.017). In men, there was no significant association between osteoporosis and age, while in women, females with normal BMD were about 19 years younger than those with osteoporosis **(**P =.002). Moreover, men with osteoporosis were younger than women with osteoporosis (P=.007). Osteoporosis was not associated with the severity of the disease; its prevalence was 39%, 32%, and 36% in those with Child-Pugh A, B, and C, respectively (P=.78). Patients with osteoporosis had significantly lower body weight compared to those with average bone density (P=.003).

BMD with different disease categories was assessed (Table I). Subjects with cystic fibrosis had the lowest BMD; T scores at the hip and spine were −3.22 ± 0.57 and −4.08 ± 0.68, respectively; however, T scores at the femoral neck in these subjects were not significantly different from other disease categories.

According to logistic regression analysis, lower weight (P=.0007) and increasing age (P=.038) were independent risk factors for osteoporosis during chronic liver disease in females (Table II).

Table I: Z and T score for osteoporosis according to disease category.

Diagnosis	T lumber spine (L1-4)	T femoral neck	Z lumber spine (L1-4)	Z femoral neck
Alcoholic	−0.95 ± 1.37	−1.47 ± 1.16	−0.33 ± 1.42	−0.31 ± 1.06
Chronic active hepatitis	−1.51 ± 1.41	−1.71 ± 1.75	−0.76 ± 0.92	−0.71 ± 1.54
Cystic fibrosis	−4.17 ± 1.65	−3.31 ± 1.36	−3.05 ± 0.83	−2.67 ± 0.68
Cryptogenic	−1.23 ± 1.52	−1.44 ± 1.28	−0.67 ± 1.54	−0.23 ± 1.21
Haemochromatosis	−1.85 ± 2.78	−2.61 ± 1.44	−1.36 ± 1.58	−2.02 ± 1.55
Hep B	−1.39 ± 1.72	−1.89 ± 1.13	−0.65 ± 1.87	−0.57 ± 1.23
Hep C	−1.58 ± 1.61	−1.67 ± 1.26	−0.96 ± 1.54	−0.52± 1.27
Primary biliary cirrhosis	−2.18 ± 1.55	−2.27 ± 1.52	−0.78 ± 1.47	−1.02 ± 1.36
Primary sclerosing cholangitis	−2.02 ± 1.28	−1.69 ± 1.13	−1.26 ± 1.23	−0.77 ± 0.96
Sarcoidosis	−0.82 ± 1.85	−1.42 ± 1.32	−0.27± 1.95	−0.05 ± 1.25

Table II Summary of logistic regression analysis

	Male			Female		
	OR	**CI(95%)**	**P**	**OR**	**CI (95%)**	**P**
Age	1	0.96–1.04	.951	1.13	1.05–1.22	.004
Diagnosis	1.07	0.35–3.24	.891	1.55	0.66–3.66	.326
Weight	0.96	0.95–1.01	.057	0.96	0.92–0.98	.01
Menopausal status				0.25	0.04–1.33	.10

[Citation: Chughtai, T., Khan, A., Raza, A. (2023). High incidence of osteoporosis in chronic liver disease before liver transplantation. *Biol. Clin. Sci. Res. J.*, **2023***: 221*. doi: https://doi.org/10.54112/bcsrj.v2023i1.221]

Discussion

In this study, the prevalence of osteoporosis at the femoral neck and lumbar spine was 37%, and in only 14.3% of cases, bone density at these sites was average. There was no association between gender and osteoporosis. Lower body weight and increasing age were independent risk factors in females. In men, there were no independent risk factors for developing osteoporosis. This study's results align with previous studies, which reported that osteoporosis is highly prevalent in patients with chronic liver disease. A study by Loomes et al., 2019 reported the prevalence of osteoporosis at the femoral neck or lumber spine to be 46% (Loomes et al., 2019). In our study, osteopenia or osteoporosis was significantly more significant at the femoral neck than at the lumbar spine. A study by Schmidt et al., 2020 showed that the proximal femur had significant bone loss (Schmidt et al., 2020), though the work of Jadzic et al., 2021 does not confirm lesser bone density at the femur compared to the spine (Jadzic et al., 2021).

On the other hand, a liver transplant results in more sustained bone loss than the femur and spine (Li et al., 2021). In our study, there was no association between gender and osteoporosis, but lower body weight and increasing age were considered independent risk factors in females. A previous study by Cherukuri et al., 2021 reported strong association between low body weight and osteoporosis in the general population (Cherukuri et al., 2021). A study by Barchetta et al.,2022 reported that low urinary creatinine levels indicate low muscle mass and are correlated with low BMD in chronic liver disease (Barchetta et al., 2022).

In this study, no association was found between body weight and the severity of liver disease, which suggests that the severity of the disease does not increase the risk of osteoporosis in patients with a lower weight. A previous study by Jeong, 2019 showed that hypogonadism and cirrhosis are significant risk factors for osteoporosis in both genders in chronic liver disease (Jeong and Kim, 2019). In our study, post-menopausal women were affected more than premenopausal women, though the difference was statistically insignificant. The difference may not be statistically practical because only a small sample was post-menopausal. In our study, the hormonal status of men was not assessed; a tough significant portion was likely hypogonadal. Conventionally, cholestatic bone disease causes more severe bone loss than parenchymal liver disease (Pedersen and Mayo, 2020). This study shows that cholestatic liver disease has been associated with an increased prevalence of osteoporosis and lower T score, but this may be explained older age of the patients. Considering weight, sex, and age, cholestatic liver disease was not found to be an independent risk factor for developing osteoporosis. However, these patients are more vulnerable to bone fractures after liver transplant. Compared to other disease categories. In this study, subjects with cystic fibrosis had the lowest BMD; these findings align with a previous study by Daley et al. (Daley et al., 2019). It can be seen that chronic liver disease increases the risk of osteoporosis, irrespective of etiology. The limitation of this study is that it is a small single-centered study; a more extensive detailed study is recommended for confirming the results of our study.

Conclusion

Osteoporosis is highly prevalent in subjects with chronic liver disease before a liver transplant. These results suggest prophylactic measures should be taken in subjects with chronic liver disease to optimize bone health.

Conflict of interest

The authors declared an absence of conflict of interest.

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