ORIGINAL ARTICLE

Prevalence of Osteosarcopenia and Frailty in Patients with Chronic Liver Disease

Shamim Nazir[1], Zaigham Abbas[2], Shaima Amjad[3], Abeer Altaf[4], Muhammad Ali Qadeer[5], Sania Maqbool[6], Mehreen Siyal[7], Manesh Kumar[8]

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Abstract

Introduction: Chronic liver disease (CLD) can have a significant impact on the nutritional status of patients. Malnutrition is an under-recognized condition in patients with cirrhosis. Malnutrition increases the incidence and severity of decompensation, increases the risk of infections, and increases mortality. The present study aimed to assess osteosarcopenia and frailty in patients with CLD.

Materials and methods: This prospective cross-sectional study included 151 cases of CLD, aged between 18 and 85 years. Anthropometric measurements were performed. Sarcopenia was assessed by handgrip strength using a hand-held dynamometer. Bone mineral density was measured with the help of an office-based DEXA scan (Osteosys). Liver frailty was assessed through performance-based tests.

Results: Out of 151 patients, 98 were male (69.5%); mean age was 51.8 ± 13.2. The presarcopenia was seen in 91 (60%) patients, and sarcopenia in 45(30%). Osteopenia was present in 75 (50%) and osteoporosis in 24 (16%). The patients with osteopenia and osteoporosis had a high liver frailty index (LFI) (p-value < 0.001). A significant correlation between body mass index, waist circumference, LFI, calcium level, bilirubin and Child Pugh scores was seen with T and Z scores. Factors associated with low bone mineral density included increasing age and LFI, low calcium and higher PTH.

Conclusion: There is a high prevalence of pre-sarcopenia, sarcopenia, osteopenia, osteoporosis and high frailty in our patients with CLD. Early detection and timely intervention in these conditions are important to reduce the associated consequences. All patients with CLD should be assessed for osteosarcopenia and frailty, both at baseline and longitudinally.

Keywords: Chronic liver disease, DEXA scan, Dynamometer, Frailty, Osteoporosis, Osteopenia, Sarcopenia.

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Introduction

Chronic liver disease (CLD) encompasses a diverse array of liver pathologies characterized by persistent inflammation, fibrosis, and impaired hepatic function.[1] Among the myriad of complications associated with CLD, musculoskeletal abnormalities, notably osteosarcopenia, have emerged as significant determinants of patient morbidity and mortality.[2] Osteosarcopenia, characterized by the concurrent presence of sarcopenia (loss of muscle mass and function) and osteopenia/osteoporosis (reduced bone mineral density), presents formidable challenges in the management of CLD patients.[3]

The pathogenesis of osteosarcopenia in CLD is multifactorial, influenced by a constellation of factors including metabolic dysregulation, systemic inflammation, and hormonal imbalances.[4] Hepatic dysfunction disrupts crucial metabolic pathways involved in muscle and bone homeostasis, precipitating accelerated muscle wasting and bone demineralization.[5] Complications such as ascites, hepatic encephalopathy, and malnutrition further exacerbate musculoskeletal derangements, culminating in a state of frailty characterized by diminished physiological reserves and heightened susceptibility to adverse outcomes.[6]

Despite the growing recognition of osteosarcopenia in CLD, the dearth of comprehensive assessment tools to evaluate both musculoskeletal health and liver frailty impedes effective clinical management. The liver frailty index (LFI), an amalgamation of laboratory parameters and physical performance assessments, has emerged as a promising modality for quantifying frailty in CLD patients.[7] However, the relationship between osteosarcopenia and the LFI remains inadequately elucidated. Therefore, this study endeavors to explore the prevalence of osteosarcopenia and its correlation with the LFI in CLD patients. By unraveling the intricate interplay between musculoskeletal abnormalities and liver frailty, this research seeks to illuminate the complex CLD-associated complications and facilitate the development of targeted interventions to ameliorate patient adverse outcomes.[8]

[1–8]Department of Gastroenterology and Hepatology, Dr. Ziauddin Hospital Clifton Campus, Karachi, Pakistan

Corresponding Author: Shamim Nazir, Department of Gastroenterology and Hepatology, Dr. Ziauddin Hospital Clifton Campus, Karachi, Pakistan, Phone: +03353850665, e-mail: shamimnazir16@gmail.com

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Materials and Methods

A total of 151 patients have been enrolled from November 2022 to December 2023 at the outpatient Department of Gastroenterology

and Hepatology, Dr. Ziauddin Hospital, Karachi. In this prospective study, the age range was between 18 and 85 years.[9] Patients who had pre-existing bone disease history of pathological fractures, any underlying malignancy other than hepatocellular carcinoma history of skeletal muscle disorders, or were on hormone replacement therapy (HRT) were excluded.[10,11]

The sample size was determined based on an expected prevalence of osteosarcopenia of 30%, with a 95% confidence interval and a 5% margin of error, resulting in a required sample size of 139 patients. To account for potential dropouts and incomplete data, we enrolled 151 patients. Anthropometric measurements, including height, weight, and waist circumference, were recorded for each patient. Sarcopenia was assessed by hand-grip strength using a hand-held Dynamometer. It is a small, portable device. The patient squeezed the device with all his strength three times with a dominant hand, and the average score was used for analysis. A decrease in average score in kg or pounds in accordance with age was considered sarcopenia.[9–11]

Bone mineral density was measured with the help of an office-based DEXA scan (Osteosys).[12,13] It used T and Z scores. A score of ≥1.0 for normality, between −2.5 and −1.0 for osteopenia, and ≤ −2.5 for osteoporosis.[12,14] The LFI was evaluated through a series of performance-based tests, including dominant hand-grip strength, the time taken to perform five chair stands, and the balance duration held in three different body positions: Side, semi-tandem, and tandem. These assessments were conducted using the University of California, San Francisco Functional Assessment in Liver Transplantation calculator described in Table 1.[7,15] Initial blood tests were administered to assess a range of parameters including hemoglobin (Hb) levels in gm/dL, platelet count, total bilirubin concentration in mg/dL, alanine transaminase (ALT) levels in U/L, albumin concentration in gm/dL, creatinine levels in mg/dL, sodium concentration in M. Eq/L, international normalization ratio (INR), phosphorus levels in mg/dL, calcium levels in mg/dL, 25-OH vitamin D levels in ng/mL, and parathyroid hormone levels. These tests were conducted for the majority of the patients mentioned in Tables 2 and 3.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as numbers and percentages in parentheses. Spearman's rank correlation coefficient (rs) and Pearson correlation coefficient (PCC) were employed to assess the associations between various variables.[16,17] Statistical analyses were performed using SPSS (version 26, IBM, Armonk, NY, USA), with statistical significance set at a p-value < 0.05.

Results

The clinical characteristics of the 151 patients diagnosed with CLD in this study are summarized in Table 1. The majority of the participants were male, comprising 106 (70%), a mean age of 51.8 ± 13.2 years. The mean waist circumference measured 100.33 ± 12.81 cm. Regarding Eastern Cooperative Oncology Group (ECOG) performance status, most patients were classified as ECOG 1 103 (68%), followed by ECOG 2 31 (20%), ECOG 0 15 (10%), and ECOG 3 2 (1%). The primary etiology of CLD was predominantly hepatitis C-virus (HCV) in 62 cases (41%), followed by hepatitis B-virus (HBV) in 36 (24%), non-alcoholic fatty liver disease (NAFLD) in 28 (18%), alcoholic liver disease (ALD) in 10 (7%), autoimmune hepatitis (AIH) in 9 (6%), primary biliary cholangitis (PBC) in 4 (3%), and overlap syndrome in 2 cases (1%). The distribution of the Child-Pugh score was as follows: Grade A in 52 patients (34%), grade B in 53 (35%), and grade C in 46 patients (30%).

Table 1: Characteristics of patients with chronic liver disease

Characteristic	*Value*
Gender (*n*, %)	Male: 106 (70%)
	Female: 45 (30%)
Age (years, mean ± SD)	51.8 ± 13.17
Waist circumference (cm, mean ± SD)	100.33 ± 12.81
ECOG performance status (*n*, %)	
0	15 (10%)
1	103 (68%)
2	31 (20%)
3	2 (1%)
Etiology of CLD (*n*, %)	
HCV	62 (41%)
HBV	36 (24%)
NAFLD	28 (18%)
ALD	10 (7%)
AIH	9 (6%)
PBC	4 (3%)
Overlap syndrome	2 (1%)
Child-Pugh score (*n*, %)	
A	52 (34%)
B	53 (35%)
C	46 (30%)
Bone mineral density (*n*, %)	
Normality	52 (34%)
Osteopenia	75 (50%)
Osteoporosis	24 (16%)
Sarcopenia (*n*, %)	
Presarcopenic	91 (60%)
Sarcopenia	45 (30%)
Robust	15 (10%)

Values are shown as median (interquartile range) or number (percentage). ALD, alcoholic liver disease; AIH, autoimmune hepatitis; BMI, body mass index; ECOG, Eastern cooperative oncology group; HBV, hepatitis B-virus; HCV, hepatitis C virus; NAFLD, nonalcoholic fatty liver disease; PBC, primary biliary cholangitis

Bone mineral density measurements revealed osteopenia in 75 patients (50%), normal bone density in 52 (34%), and osteoporosis in 24 patients (16%). Regarding sarcopenia assessment, 91 patients (60%) were presarcopenic, 45 (30%) had sarcopenia, and 15 patients (10%) were categorized as robust. There was a significant correlation between body mass index, waist circumference, LFI, calcium level, bilirubin, Child Pugh scores with T and Z scores. Factors associated with low bone mineral density, including age, LFI, low calcium, and higher PTH are highlighted in Tables 2 and 3.

Discussion

Osteosarcopenia, characterized by the concurrent presence of osteopenia/osteoporosis, and sarcopenia, poses a significant clinical challenge in the management of patients with liver cirrhosis. This delves into the findings of a study involving 151 CLD patients, predominantly male, examining the prevalence of osteosarcopenia and its association with the LFI.[18,19]

Table 2: Correlation of different variables with BMD

Variable	*Z-score (p-value)*	*T-score (p-value)*
Age (years)	0.225	<0.005*
BMI (kg/m^2)	0.017*	0.107
Waist circumference	0.008	0.040
LFI score	0.039	<0.005
Platelets (150–440 × 10^9/L)	0.597	0.344
Creatinine (mg/dL)	0.207	0.577
Calcium (mg/dL)	0.007	0.039
Phosphorus (mg/d)	0.425	0.397
25-OH Vitamin D (ng/mL)	0.294	0.677
Parathyroid hormone (PTH) (pg/mL)	0.707	0.754
Total bilirubin (mg/dL)	0.012	0.014
Albumin (gm/dL)	0.149	0.058
Prothrombin time INR	0.804	0.700
Child-Pugh score	0.022	0.007
Liver frailty index	0.039	<0.005

*Statistically significant *p*-values

Table 3: Factors associated with low BMD in CLD patients

Variable	*Normal BMD (Mean ± SD)*	*Low BMD (Mean ± SD)*	*p-value*
Age (years)	46.98 ± 10.80	55.87 ± 13.31	<0.005
BMI (kg/m^2)	27.35 ± 5.05	25.76 ± 5.50	0.085
Liver frailty index	3.93 ± 0.61	4.34 ± 0.61	<0.005
Hemoglobin (Hb) (gm/dL)	12.03 ± 2.18	11.47 ± 2.38	0.154
Platelets (150–440 × 10^9/L)	123.01 ± 64.33	113.28 ± 64.28	0.384
Creatinine (mg/dL)	0.90 ± 0.36	1.02 ± 1.06	0.316
Calcium (mg/dL)	9.20 ± 0.83	8.74 ± 0.81	0.032
PTH (pg/mL)	30.02 ± 14.46	43.59 ± 31.21	0.008
Total bilirubin (mg/dL)	1.60 ± 1.51	2.14 ± 3.04	0.155
ALT (U/L)	49.80 ± 37.98	38.96 ± 30.30	0.079
Albumin (gm/dL)	3.51 ± 0.74	3.28 ± 0.71	0.073

The investigation revealed a significant prevalence of musculoskeletal abnormalities within the CLD population. Presarcopenia, serving as an early indicator of muscle wasting, was identified in nearly two-thirds of the patients, while overt sarcopenia afflicted close to one-third of the cohort. These statistics underscore the criticality of assessing muscle mass and function in individuals with CLD, as abnormalities in muscle are intricately associated with heightened morbidity and mortality rates.[20,21] Similarly, the prevalence of osteopenia and osteoporosis was noteworthy, impacting approximately half of the patients, respectively. These findings underscore the vulnerability of CLD patients to declines in bone mineral density, predisposing them to fractures and other skeletal complications that further exacerbate their overall health status described in Table 3.[22]

A notable aspect of the investigation was the examination of the relationship between osteosarcopenia and the LFI. The LFI, a comprehensive tool integrating laboratory parameters and physical performance tests, serves as a valuable metric for assessing frailty in individuals with cirrhosis. The study uncovered a significant correlation between osteosarcopenia and elevated LFI scores, suggesting a synergistic connection between musculoskeletal abnormalities and liver frailty.[11–15] This association underscores the intricate interplay between liver dysfunction and systemic manifestations such as sarcopenia and osteopenia/osteoporosis. Liver cirrhosis disrupts metabolic processes, precipitating muscle wasting and alterations in bone metabolism, thereby contributing to the emergence of osteosarcopenia. Conversely, the presence of osteosarcopenia may exacerbate liver frailty, perpetuating a cycle of deteriorating overall health and functionality.[20,21]

The outcomes of this investigation hold significant clinical implications for the care of patients with CLD. Firstly, the elevated prevalence of osteosarcopenia underscores the imperative for regular screening and evaluation of musculoskeletal health in this demographic. Early identification and management of sarcopenia and osteopenia/osteoporosis can help mitigate the risk of adverse consequences such as falls, fractures, and functional decline.[3–23] Moreover, the observed association between osteosarcopenia and liver frailty highlights the necessity for comprehensive frailty assessment in cirrhosis management. Interventions aimed at enhancing muscle mass and bone density may not only attenuate the progression of osteosarcopenia, but also potentially ameliorate liver frailty and improve the overall prognosis.[7–11] Limitations of the study include its cross-sectional nature, which precludes causal inferences, and the single-center design, which may limit generalizability.

Conclusion

In conclusion, osteosarcopenia represents a significant clinical entity in cirrhosis patients, with a high prevalence and detrimental implications for health and outcomes. The association with the LFI underscores the complex interplay between musculoskeletal abnormalities and liver dysfunction, highlighting the importance of comprehensive assessment for osteosarcopenia and frailty both at baseline and longitudinally and management strategies in this population. Future research should focus on elucidating the underlying mechanisms driving osteosarcopenia in CLD and exploring targeted interventions to improve patient outcomes.

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