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ORIGINAL ARTICLE

RELATION BETWEEN SARCOPENIA AND HEPATIC ENCEPHALOPATHY IN LIVER CIRRHOSIS IN A TERTIARY CARE HOSPITAL

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Abstract:

Background: *Liver cirrhosis is a common medical problem associated with high morbidity and mortality. Consequences of cirrhosis leading to encephalopathy are a neuropsychiatric manifestation requiring hospital admission and poor prognosis. Similarly, sarcopenia in cirrhosis, resulting from multifactorial cause confers prognostic significance. The objective of this study is to find the relation between sarcopenia and hepatic encephalopathy.* ***Methods:*** *A retrospective observational study was conducted and data was taken from electronic medical records of patients admitted with hepatic encephalopathy in department of gastroenterology of Tribhuvan university Teaching hospital, Nepal. A total of 96 cirrhotic patients were included during one and half year study duration. Sarcopenia was assessed using assessment tool like hand grip strength, chair stand test and CT measurement of either skeletal muscle area (SMA) or skeletal muscle index (SMI). Hepatic encephalopathy was graded according to West Haven criteria among admitted patients.* ***Results:*** *Among 96 patients with cirrhosis, 85 patients (88.5%) were found to have sarcopenia. Prevalence of sarcopenia was higher among female compared to male (97% vs 84%). Similarly, sarcopenia was found to be higher in patients with HE-2 and HE-3 compared to HE-1 (91% vs 93% vs 79% respectively).* ***Conclusion:*** *Sarcopenia is commonly associated with hepatic encephalopathy.*

Keywords: *Cirrhosis; hepatic encephalopathy; Sarcopenia.*

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Introduction:

Liver cirrhosis is a chronic liver disease characterized by the scarring of liver tissue, leading to impaired liver function over time. This condition develops gradually, often as a result of long-term liver damage from various causes such as chronic alcohol consumption, viral hepatitis (especially hepatitis B and C), fatty liver disease, autoimmune liver diseases, and certain genetic disorders. Liver cirrhosis represents a major global health burden, often complicated by sarcopenia and hepatic encephalopathy, which significantly impact patient morbidity and mortality[1].According to the World Health Organization (WHO) report on the leading causes of mortality in 2020, liver cirrhosis has been ranked among the top 10 diseases in low and lower-middle income countries.[2]

Hepatic encephalopathy stands as a critical complication of chronic liver disease, affecting around 40% of individuals with cirrhosis[3]. This condition arises due to elevated levels of ammonia in the bloodstream, resulting from impaired liver function and porto-systemic shunting[4]. The reported mortality rate among hospitalized patients with hepatic encephalopathy can soar to as high as 15%[5].Sarcopenia" describes the deterioration of muscle quality and quantity, characterized by a progressive and widespread decline

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in muscle mass and strength. This condition is notably common in liver cirrhosis,[6]affecting approximately 50-70% of individuals with this condition.

Liver cirrhosis represents a major global health burden, often complicated by sarcopenia and hepatic encephalopathy, which significantly impact patient morbidity and mortality. This study aims to investigate the relationship between sarcopenia and hepatic encephalopathy (HE) in patients with liver cirrhosis treated at a tertiary care hospital, shedding light on the potential bidirectional pathophysiological mechanisms and clinical implications of these coexisting conditions.

Methods:

Study Design: This study employed a retrospective observational design to investigate the relationship between sarcopenia and hepatic encephalopathy in individuals diagnosed with liver cirrhosis. The study was conducted at a tertiary care hospital specializing in liver diseases, where patients with liver cirrhosis receive comprehensive medical care and management and informed consent was obtained from all participants or their legal guardians. The study was done over a period of one and half year.

Study Population: The research involved 96 adult patients (aged 18 years and older) diagnosed with liver cirrhosis. These individuals underwent evaluations for both sarcopenia and meeting the predefined cut off criteria. Sarcopenia was defined as meeting the criteria in at least two out of three assessment tools, comprising hand grip strength (HGS), the chair stand test, and computed tomography (CT) measurements of either skeletal muscle area (SMA) or skeletal muscle index (SMI). Additionally, assessments for hepatic encephalopathy were conducted, graded according to the West Haven criteria (grades I to III), during their hospitalization at the tertiary care facility.

Data Collection: Data were extracted from electronic medical records, including demographic information (age, gender), clinical characteristics (etiology of cirrhosis, severity of liver disease), laboratory parameters (liver function tests, serum ammonia levels), imaging findings (assessment of muscle mass and hepatic encephalopathy), and clinical outcomes (occurrence and severity of hepatic encephalopathy).

Assessment of Sarcopenia: Sarcopenia was assessed using established diagnostic criteria, which typically include measurements of muscle mass, strength, and function. A Camry hand dynamometer was used to measure hand grip strength (HGS), a validated tool for this purpose. HGS was assessed on the dominant hand with the arm positioned by the side of the body and the elbow flexed at ninety degrees. Three readings were taken, and the highest value was recorded as the patient's HGS. A cutoff of less than 26 kg for males and less than 18 kg for females was used to define sarcopenia . Tools used includes SARC-F questionnaire, Chair Stand Test and 400 Meter Walk Test.For patients who underwent an abdominal CT scan for clinical indications, the skeletal muscle area (SMA) at the third lumbar vertebra was manually calculated. To obtain the skeletal muscle index (SMI), the SMA was divided by the square of the patient's height in meters. The specific cutoff values for SMA and SMI to define sarcopenia in males and females aretaken as per protocol.

Assessment of Hepatic Encephalopathy: Hepatic encephalopathy was assessed based on clinical manifestations, laboratory parameters (including serum ammonia levels), and imaging findings indicative of neurological impairment associated with liver dysfunction.

Statistical Analysis: Statistical analysis was conducted using appropriate methods, including descriptive statistics to summarize patient characteristics and analytical techniques (such as chi-square tests, t-tests, or regression analysis) to explore the relationship between sarcopenia and hepatic encephalopathy while controlling for potential confounders. Statistical analysis was done using Graph Pad Prism software, Version 5.

Informed Consent: Informed consent was obtained from all participants or their legal guardians prior to inclusion in the study, ensuring their voluntary participation and understanding of the research objectives and procedures. The eligible participants were explained, in their native language about the nature of the research.

Results:

The prevalence of sarcopenia in patients with hepatic encephalopathy was 88.5%. Sixty-two were male and 34 were female. Among the 96 patients studied, Out of the 62 male patients, 53(84%) had sarcopenia, while 9 did not. Among the 34 female, 33(97%) are suffering from sarcopenia, only one patient did not had sarcopenia. This shows that Sarcopenia was more prevalent in females. The gender distribution of the study is illustrated in Figure 1.

The age distribution of patients in the study followed a normal distribution pattern. The median age of the patients was 51 years. The ages ranged from 24 to 80 years, encompassing a broad spectrum of adult and elderly patients. The majority of the patients fell within the 50 to 60-year age group, suggesting that liver

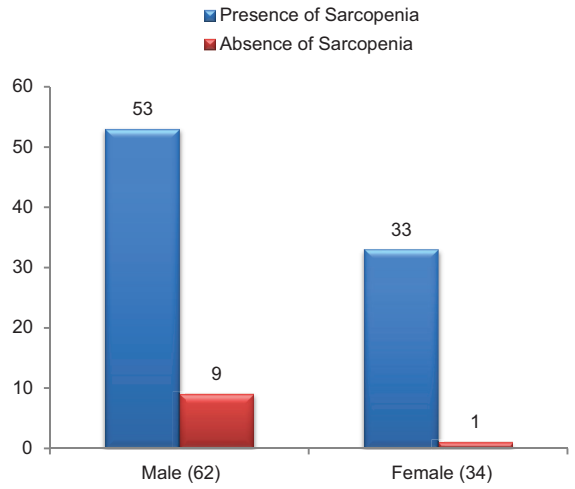

Figure 1: *shows the gender wise distribution of sarcopenia.*

cirrhosis and its complications, such as sarcopenia and hepatic encephalopathy, are more prevalent or more likely to be diagnosed in this age range. The detailed age distribution is illustrated in Figure 2

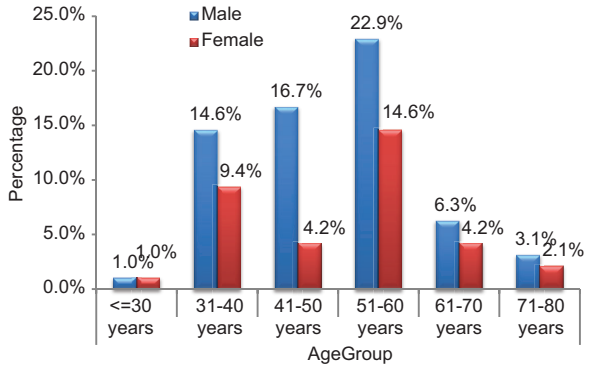

Figure 2: *Shows the Age wise distribution of sarcopenia among male and female patients of HE*

Additionally, sarcopenia prevalence was higher in patients with HE grades 2 and 3 compared to those with HE grade 1. Specifically, 79% of patients with HE grade 1 had sarcopenia, while 91% and 93 % of patients with HE grades 2 and 3 respectively were affected with sarcopenia (Table I).

Table-I

Prevalence of Sarcopenia in patient with HE grades

HE Grade	Presence of Sarcopenia	Absence of Sarcopenia	P value
HE1	15(78.9%)	4(21.1%)	0.001
HE2	56(91.8%)	5(8.2%)	0.0001
HE3	15(93.8%)	1(6.2%)	0.001

Understanding alcohol consumption in sarcopenia patients was crucial as excessive or chronic alcohol use was a significant risk factor for liver disease, including cirrhosis, which in turn can lead to sarcopenia due to its detrimental effects on muscle health. Among the patients studied, alcohol consumption was prevalent, with 86(89.5%) out of 96 patients reporting a history of alcohol use (Figure 3).

The duration of hospital stay was notably longer in patients with sarcopenia, with a mean stay of 10 days compared to an 8-day mean stay for patients without sarcopenia (Figure 4).

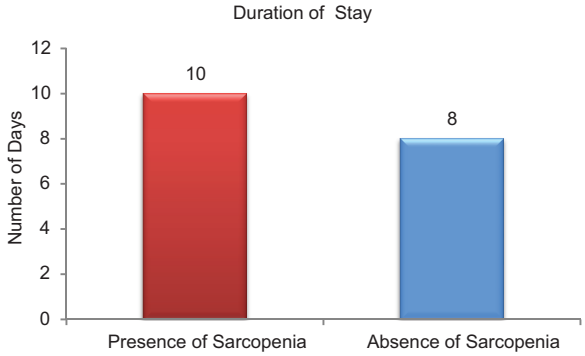

Figure 4: *Presents data illustrating the average duration of hospital stays for patients undergoing treatment of HE with or without sarcopenia.*

Data shows that all 10 fatalities observed in the study occurred in patients diagnosed with sarcopenia. This visual representation provides insights into the frequency and severity of mortality in this specific patient population (Figure 5).

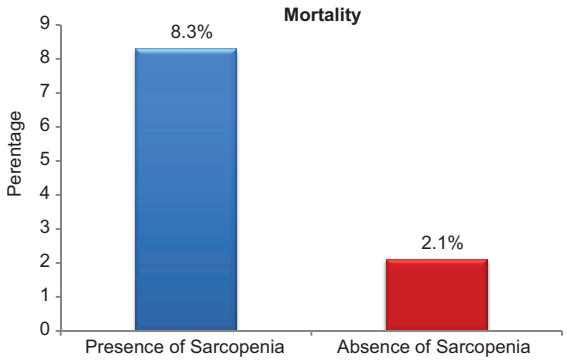

Figure 5: *Presents data depicting the mortality rate among individuals affected by both sarcopenia and hepatic encephalopathy (HE).*

The identification of trends and patterns in test results among sarcopenic patients, aiding in the selection of appropriate interventions and monitoring strategies.

This significant difference underscores the more pronounced physical debilitation observed among female patients with liver cirrhosis. The disparity in completion rates between male and female patients was statistically significant, with a p-value of 0.02 (Figure 6).

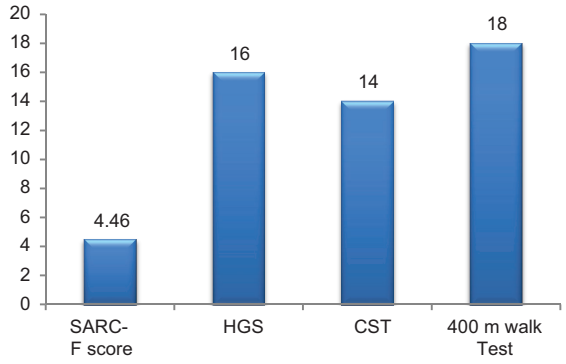

Figure 6: *Provides a representation of the average number of patients passing various tests conducted during the evaluation of sarcopenia.*

The mean Skeletal Muscle Area (SMA) for male patients was 120 cm^2, whereas for female patients, it measured 66 cm^2. This substantial difference in SMA highlights a significant gender-based disparity in muscle mass. Additionally, the mean Skeletal Muscle Index (SMI) for male patients was 45 cm^2/m^2, whereas for female patients, it was 29 cm^2/m^2 (.Figure 7).

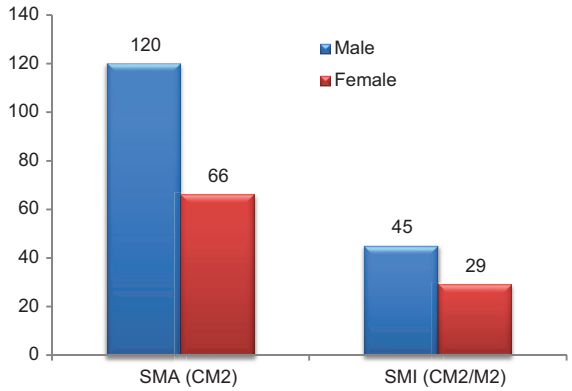

Figure 7: *Presents data illustrating the Mean Skeletal Muscle Area (SMA) and Skeletal Muscle Index (SMI).*

Discussion:

Sarcopenia is a common complication in chronic liver disease. Studies suggest that sarcopenia and hepatic encephalopathy (HE) might be interlinked, potentially representing two manifestations of the same underlying metabolic abnormality. Episodes of HE are more common in patients with muscle depletion due to the role of muscle in ammonia detoxification, compensating for the impaired urea synthesis in the cirrhotic liver. Muscle depletion exacerbates hyperammonemia, promoting HE, while hyperammonemia impairs muscle protein synthesis through myostatin down-regulation, creating a vicious cycle where sarcopenia worsens HE and vice versa.

The mean age of patients in this study was 50 years, which aligns with similar studies[7], which reported a mean age of 49 years. The study cohort consisted of 65% male and 35% female patients, comparable to a previous study in a tertiary hospital in Nepal that found 73% male and 27% female patients.

Alcohol was the predominant cause of liver cirrhosis, accounting for 90% of the cases. Non-alcoholic causes included non-alcoholic steatohepatitis (NASH), chronic hepatitis B, Wilson disease, chronic Budd-Chiari syndrome, and cardiac cirrhosis. This distribution is comparable to the study by[11]. which reported alcohol as the cause in 50.5 % of cases. The mean age of patients in study was 54 years, similar to the mean age of 50 years in this study[8].

This study found a high prevalence of sarcopenia (88.5%) among patients with hepatic encephalopathy, with an even higher prevalence in female patients. A similar study bysome authors[9] reported a prevalence of sarcopenia (diagnosed by EWGSOP criteria) of 82% in male patients, though the prevalence in females was lower than in this study. The patient population in this study was older (mean age 50 years) and had a higher incidence of alcohol consumption (90%), with a mean intake of 86 grams per day among females. Contributing factors to the higher prevalence of sarcopenia included older age, higher alcohol intake, non-functional aldehyde dehydrogenase, delayed presentation (median duration of symptoms: 2 weeks), malnutrition, and low socioeconomic status.

The study showed that patients with sarcopenia had a prolonged hospital stay, averaging two extra days compared to those without sarcopenia. All mortalities occurred in sarcopenic patients. These findings are consistent with the results of the large longitudinal prospective PURE study, which also demonstrated worse outcomes in sarcopenic patients.

Various studies have established the relationship between sarcopenia and hepatic encephalopathy. A 2020 meta-analysis [10]demonstrated an increased prevalence of HE in patients with sarcopenia. A 2022 pilot study [11]also found a correlation between sarcopenia and HE. This study showed a higher prevalence of sarcopenia in patients with HE grades 2

and 3 compared to those with HE grade 1.Specifically our study showed that, 79% of patients with HE grade 1 had sarcopenia, compared to 91% in patients with HE grades 2 and 93% in grade 3. However, Spearman rank correlation analysis did not show a significant correlation between sarcopenia and HE. Minimal HE and grade 4 HE patients were excluded due to the lack of diagnostic tools and the inability to perform clinical tests required to diagnose sarcopenia.

Conclusion:

Sarcopenia and hepatic encephalopathy (HE) are interconnected complications in liver cirrhosis. The longer hospital stays and higher mortality rates among sarcopenic patients underscore the critical need for early identification and intervention to manage sarcopenia in cirrhotic patients. Early detection and targeted treatment of sarcopenia remain crucial in improving the prognosis for patients with liver cirrhosis.

Limitations:

Small sample size and this single hospital based study did not reflect exact scenario of the whole community.

Data Availability:

The datasets analysed during the current study are not publicly available due to the continuation of analyses but are available from the corresponding author on reasonable request.

Conflict of Interest:

The authors stated that there is no conflict of interest in this study

Funding:

This research received no external funding.

Ethical consideration:

The study was conducted after approval from the Institutional Review Board of Tribhuvan university Teaching hospital, Nepal. The confidentiality and anonymity of the study participants were maintained.

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