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A Cross-sectional study to assess the prevalence of Sarcopenia among patients with Chronic liver disease in a tertiary care hospital.

[1]Dr. Chandrababu Devarapu, [2]Dr. Amogh Chandrashekar, [3]Dr. Sidhartha Naidu B, [4]Dr. Chandrakanth Koutarapu

[1]Associate Professor, Department of Medical Gastroenterology, Vydehi Institute of Medical Sciences, Bengaluru.

[2]Assistant professor, Department of Medical Gastroenterology, Institute of Gastroenterology and Organ Transplant, Bangalore, Karnataka

[3]Assistant Professor, Department of Medical Gastroenterology, Vydehi Institute of Medical Sciences and Research Centre, Bengaluru, Karnataka.

[4]Consultant Medical Gastroenterologist, Aster RV hospitals, Bengaluru, Karnataka.

Correspondence:
Dr Sidhartha Naidu B.
Assistant Professor, Department of Medical Gastroenterology, Vydehi Institute of Medical Sciences and Research Centre, Bengaluru, Karnataka.

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Abstract

Background: Sarcopenia is the most common feature of chronic liver disease associated with adverse outcomes among cirrhosis patients. Early identification allows early intervention to prevent complications. Hence the current study was conducted.

OBJECTIVES:

1. To assess the prevalence of sarcopenia among patients with chronic liver disease.
2. To determine the association of Sarcopenia with severity of chronic liver disease and other socio-demographic factors. ***METHODS***: This was a cross-sectional study conducted among 65 study subjects aged ≥18 years, with chronic liver disease (CLD) admitted under the Department of Medical Gastroenterology, Vydehi Institute of Medical Sciences and Research Centre , Bengaluru, Karnataka for a period of 9 months. After obtaining consent, data was collected using a semi-structured questionnaire about socio-demographic profile, clinical history and examination. European working group on sarcopenia in older people (EWGSOP) criteria was used for diagnosis of sarcopenia.and Child Turcotte Pugh (CTP) scoring for assessing severity. Independent t-test was used to find the difference in means and Chi-square or Fisher's exact test was used to express the association. A P-value of less than 0.05 was considered statistically significant. ***RESULTS***: The mean age of the study subjects with chronic liver disease was 49.3±11.1 years and majority of the study subjects were in 51 to 60 years age-group and were males (86.2%). 90.8% were probable cases of sarcopenia, 86.2% were confirmed cases and 47.7% were having severe sarcopenia. Higher proportions of probable (35.6%) and severe (38.7%) cases of sarcopenia belonged to class B CTP score and confirmed cases belonged to class A CTP score (35.8%). Most of the probable (95.2%) and severe (52.4%) cases belonged to class B/C CTP scores, but there was no significant association between the type of sarcopenia and age, sex and severity of chronic liver disease. ***CONCLUSION***: The estimated prevalence of probable cases of sarcopenia was 90.8%, confirmed cases was 86.2% and severe sarcopenia was 47.7%. Majority of the probable and severe cases of sarcopenia belonged to class B/C indicating higher severity, hence indicating the greater loss of muscle mass with the deteriorating liver function, but significant association was not established in our study.

Keywords: Sarcopenia, chronic liver disease, severe disease, prevalence.

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INTRODUCTION

Chronic liver disease (CLD) is a continuous process of inflammation of the liver, destruction and regeneration of liver parenchyma leading to fibrosis and cirrhosis, along with progressive deterioration of liver functions for more than six months including the synthesis of clotting factors, other proteins, detoxification of harmful products of metabolism, and excretion of bile [1]. Being one of the leading causes of mortality and morbidity worldwide and also in the Asia Pacific region, it is associated with a significant reduction in health-related quality of life [2].

Liver cirrhosis is often associated with impaired nutritional status resulting in malnutrition in more than 20-50% of the cases [3]. Sarcopenia is the major component of malnutrition and is a frequent complication in cirrhosis that adversely affects clinical outcomes. These include survival, quality of life, development of other complications and post liver transplantation survival [4]. Sarcopenia is a syndrome characterized by progressive and extensive loss of strength and skeletal muscle mass. Hyperammonemia appears to be the main driver of sarcopenia in cirrhosis through several molecular

signalling pathways. The prevalence of sarcopenia varies from 23-60% and is more commonly observed among individuals with Alcoholic Liver Disease (ALD) and males [5,6]. It is an independent mortality factor that implies a worse outcome after liver transplantation (LT) and is also considered big economic problem because patients with sarcopenia who are waiting for LT have higher health care costs compared to patients who don't have sarcopenia. Hence screening the patents for sarcopenia will help in identifying high risk patients and allows early intervention to prevent complications. [7,8].

According to the newer guidelines on the definition and diagnosis of sarcopenia by the European Working Group on Sarcopenia in Older People (EWGSOP), both low muscle mass and low muscle function (strength or performance) should be used to diagnose sarcopenia. Considering muscle strength as the key characteristic of sarcopenia with low muscle strength leading to a diagnosis of probable sarcopenia; subsequent identification of low muscle mass in individuals who have low muscle strength is used to confirm its presence and, when physical performance is also poor, its severity is assessed [9]. The current "gold standard" in evaluating sarcopenia is skeletal muscle mass estimation by means of computed tomography (CT) scans or magnetic resonance imaging (MRI) whereas surrogate markers like Subjective Global Assessment (SGA) score and anthropometric measurements such as mid-arm muscle circumference (MAMC) and hand grip strength (HGS) show correlations with the skeletal muscle index in cirrhotic patients [10]. Child-Turcotte-Pugh (CTP) score is commonly used to assess the severity of hepatic dysfunction in patients with cirrhosis [11].

As there were only a very few studies from Indian literature on the prevalence and consequences of sarcopenia among individuals with cirrhosis of the liver. Hence the present study was conducted to assess the prevalence of sarcopenia among patients with chronic liver disease and to determine the association of Sarcopenia with severity of chronic liver disease and other socio-demographic factors.

MATERIALS AND METHODS

This was a cross-sectional study conducted among patients diagnosed with chronic liver disease for a period of 9 months from January2023 to September 2023 admitted under Department of Medical Gastroenterology, Vydehi Institute of Medical Sciences and Research Centre, Bengaluru, Karnataka.

Considering a prevalence of Sarcopenia in chronic liver disease patients (p) as 20.0% according to a previous study [12], q=100-p i.e., 80.0%, and with an absolute precision of 10% (d), z value being 1.96 at 95% confidence interval, based on the formula, $n = z^2 (pq/d^2)$ the total sample size was estimated to be 61 which was rounded off to 65. A total of 65 study subjects who were aged 18 years and above diagnosed as having chronic liver disease were included in the study by purposive sampling whereas the subjects diagnosed with extra hepatic malignancy, malabsorption syndrome, coexisting tuberculosis, CKD stage 4 and 5, retroviral disease and chronic pancreatitis were excluded from the study. Ethical clearance was obtained from the Institutional Ethics Committee. After obtaining a written informed consent, the data was collected using a semi-structured questionnaire consisting of different sections on socio-demographic profile, clinical history and examination.

The criteria recommended by the European working group on sarcopenia in older people (EWGSOP) [9] was used for diagnosis of sarcopenia which includes the following steps.

1. Clinical suspicion of Sarcopenia was based on the following anthropometric measurements

- BMI (Body mass Index) < 17.5kg/m^2
- TSFT (Triceps skinfold thickness) < 5mm
- MAMC (mid-arm muscle circumference) < 15cms and
- MAA (mid arm muscle area) < 23 cm^2

2. Among the clinically suspected cases of Sarcopenia, muscle strength was elicited using physical performance tests based on Hand grip and chair stand test to objectively assess performance.

- Hand grip test: Includes the assessment using dynamometer. Participants were instructed to grip the dynamometer as strongly as possible using their dominant hand. Three measurements were taken and the average of 3 recordings in the dominant hand was measured in Kg. Impairment in muscle strength was defined as a handgrip strength less than the value recommended for the corresponding age and sex as per the reference values of the dynamometer.
- Chair stand test is the time to complete five chair rises. The participant was encouraged to complete as many full stands as possible within a 30 second time limit and was instructed to be fully seated between each stand. The score was the total number of stands executed correctly within 30 seconds. For those requiring 12 seconds or more to complete the 5 times sit-to-stand test was considered a positive test.

3. If either of the above tests was found positive they were considered as probable case of Sarcopenia and were further tested for muscle quantity using BIA (Bioelctrical Impedance Analysis) / MRI (Magnetic resonance imaging). Bio electrical impedance analysis was used to assess the skeletal muscle mass. MRI cuts at L3 level to analyze total cross-sectional area (cm^2) of abdominal skeletal muscles which was then normalized to height for calculating the skeletal muscle index (cm^2/m^2). Skeletal muscle mass index (SMI) was calculated by dividing the skeletal muscle mass (cm^2)

by the square of the height (m^2). Skeletal muscle index thresholds of 40.31 cm^2/m^2 for males and 30.88 cm^2/m^2 for females was used as cutoff for sarcopenia. Psoas muscle, para spinal and abdominal wall muscles were considered core skeletal muscles that are relatively independent of activity and water retention, but are consistently altered by the metabolic and molecular perturbations of cirrhosis. If found positive in any of the two tests they were considered as Confirmed cases of Sarcopenia.

4. Among the confirmed cases of Sarcopenia Gait speed test were performed to find the severe cases of Sarcopenia and if found positive they were considered as severe cases of Sarcopenia.

- Gait speed test – To test walking speed, a four-metre walking course was used with no obstructions for an additional one-metre at either end. Participants are instructed to: "walk to the other end of the course at usual speed, just as if walking down the street to go to the store". Participants could use assistive devices if needed and each participant was timed for two walks. The faster of the two walks was used for analyses. Gait speed of longer than 5 seconds to walk 4 metres (<0.8 m/s) suggested an increased risk of frailty.

Child Turcotte Pugh score - The severity of chronic liver disease was assessed using Child Turcotte Pugh scoring as follows [13]

Parameter	1 Point	2 Point	3 Point
Total bilirubin (mg/dl)	<2	2-3	>3
Serum albumin (g/L)	>3.5	2.8-3.5	<2.8
INR	<1.7	1.7-2.3	>2.3
Ascites	None	Mild or controlled by diuretics	Moderate to severe (or refractory to diuretics)
Hepatic Encephalopathy	None	Grade 1-2	Grade 3-4

Class A=5-6, Class B=7-9, Class C=10-15

Statistical Analysis:

All the data were entered into Microsoft Excel 2021. The continuous data was expressed in mean and standard deviation and proportions were expressed in percentage. The means were compared between the groups of with or without sarcopenia using independent t-test and the association between the categorical variables and the presence or absence of sarcopenia were elicited using Chi-square test or Fisher's exact test. A P-value of less than 0.05 was considered for statistical significance.

RESULTS

The mean age of the study subjects with chronic liver disease was 49.3±11.1 years and majority of the study subjects were in 51 to 60 years age-group and mostly were males (86.2%). The mean weight, height and body mass index (BMI) were 49.3±11.1 kgs, 1.6±0.2 m and 23.5±4.4 kg/m2 respectively. The respective mean values of triceps skin fold thickness (TSFT), mid arm muscle circumference (MAMC) and mid arm muscle area (MAA) were 1.6±0.5 mm, 25.4±3.7 cms and 20.4±2.8 cm2. [Table – 1]

Among those who were clinically screened based on BMI, TSFT, MAMC and MAA, 90.8% were probable cases of sarcopenia, 86.2% were confirmed cases and 47.7% were having severe sarcopenia. [Table – 2]

Among the study subjects, 38.9% of the probable cases, 42.8% of the confirmed cases and 38.5% of the severe cases of sarcopenia, belonged to 51to 60 years age-group and were males (probable – 86.4%, confirmed – 83.9% and severe - 80.6%). Higher proportions of probable (35.6%) and severe (38.7%) cases of sarcopenia belonged to class B CTP score and confirmed cases belonged to class A CTP score (35.8%). [Table – 3]

Most of the probable (95.2%) and severe (52.4%) cases belonged to class B/C CTP scores, but there was no significant association between the type of sarcopenia and age, sex and severity of chronic liver disease. [Tables 4A, 4B and 4C]

Table 1: Distribution of study subjects based on age, sex and anthropometric measurements (n=65)

Variables	Frequency (n)	Percentage (%) / Value
Age-group in years (Mean $\pm$ SD: 49.3 ± 11.1)		
≤ 40	14	21.5
$41 - 50$	18	27.7
$51 - 60$	25	38.5
> 60	8	12.3
Sex		
Male	56	86.2
Female	9	13.8
Weight in kgs (Mean $\pm$ SD)	—	49.3 ± 11.1

Height in m (Mean $\pm$ SD)	—	1.6 ± 0.2
BMI in kg/m^2 (Mean $\pm$ SD)	—	23.5 ± 4.4
TSFT in mm (Mean $\pm$ SD)	—	1.6 ± 0.5
MAMC in cms (Mean $\pm$ SD)	—	25.4 ± 3.7
MAA in cm^2 (Mean $\pm$ SD)	—	20.4 ± 2.8

BMI - Body Mass Index; TSFT (Triceps Skin Fold Thickness); MAMC - Mid Arm Muscle Circumference; MAA - Mid Arm Muscle Area

Table – 2: Prevalence of Sarcopenia (n=65)

Sarcopenia	Frequency (n)	Percentage (%)
Probable cases	59	90.8
Confirmed Cases	56	86.2
Severe Cases	31	47.7

Table – 3: Distribution of Sarcopenia according to some socio-demographic factors and severity of chronic liver disease (n=65)

Particulars	Probable Cases (n=59)	Confirmed Cases (n=56)	Severe Cases (n=31)
Age-group in years n (%)			
≤40	12 (20.4)	09 (16.1)	04 (12.9)
41 – 50	17 (28.8)	16 (28.6)	10 (32.3)
51 – 60	23 (38.9)	24 (42.8)	14 (45.1)
>60	07 (11.9)	07 (12.5)	03 (09.7)
Sex n (%)			
Male	51 (86.4)	47 (83.9)	25 (80.6)
Female	08 (13.6)	09 (16.1)	06 (19.4)
CTP n (%)			
Class A	19 (32.2)	20 (35.8)	09 (29.0)
Class B	21 (35.6)	18 (32.1)	12 (38.7)
Class C	19 (32.2)	18 (32.1)	10 (32.3)

Table – 4: Association of Probable (A), Confirmed (B) and Severe (C) Sarcopenia with some socio-demographic and severity of chronic liver disease (n=65)

A)

Particulars	Probable Cases		χ^2-value (*P*-value)
	Yes	No	
Age-group in years n (%)			
≤50 (n = 32)	29 (90.6)	03 (9.4)	0.002
>50 (n = 33)	30 (90.9)	03 (9.1)	(0.97)
Sex n (%)			
Male (n = 56)	51 (91.1)	05 (08.9)	0.04
Female (n = 09)	08 (88.9)	01 (11.1)	(0.83)
CTP n (%)			
Class A (n = 23)	19 (82.6)	04 (17.4)	
Class B/C (n = 42)	40 (95.2)	02 (04.8)	(0.17)

B)

Particulars	Confirmed Cases		χ^2-value (*P*-value)
	Yes	No	
Age-group in years n (%)			
≤50 (n = 32)	25 (78.1)	07 (21.9)	3.41
>50 (n = 33)	31 (93.9)	02 (06.1)	(0.06)
Sex n (%)			
Male (n = 56)	47 (83.9)	09 (16.1)	
Female (n = 09)	09 (100.0)	00 (0.0)	(0.34)
CTP n (%)			
Class A (n = 23)	20 (86.9)	03 (13.1)	0.02

Class B/C (n = 42)	36 (85.7)	06 (14.3)	(0.89)

C)

Particulars	**Severe Cases**		**χ^2-value (*P*-value)**
	Yes	**No**	
Age-group in years n (%)			
≤50 (n = 32)	14 (43.7)	18 (56.3)	0.39 (0.53)
>50 (n = 33)	17 (51.5)	16 (48.5)	
Sex n (%)			
Male (n = 56)	25 (44.6)	31 (55.4)	1.51 (0.22)
Female (n = 09)	06 (66.7)	03 (33.3)	
CTP n (%)			
Class A (n = 23)	09 (39.1)	14 (60.9)	1.05 (0.31)
Class B/C (n = 42)	22 (52.4)	20 (47.6)	

DISCUSSION

Sarcopenia in liver cirrhosis is noted to be associated with worsening of the severity of chronic liver disease [14]. Multiple modalities exist to assess each component of sarcopenia, but it lacks a standard assessment tool to define sarcopenia and its diagnosis itself is a challenge [14, 15]. Screening for probable sarcopenia itself can provide a treatment window where an intervention at the earliest would be beneficial leading to the reversal of changes [15]. Hence identifying sarcopenia prevalence especially where the data is lacking in this current study setting acts as a stepping stone to identify its predictive ability and helps us in early intervention furthering its next approach.

Balakrishnan B et al., reported the mean age of the study subjects with chronic liver disease as 58.24±9.9 years and males accounted for 77% and females for rest 23%, however the mean age among our study subjects was 49.3±11.1 years and most of them were males accounting for 86.2%. The difference in the mean and proportion might be due to the difference in the distribution of the study subjects based on the cause of chronic liver disease and also study settings [5]. Most of them were in the age group of 51 to 60 years in our study which was in concordance with the proportion of study subjects in 51 to 60 years according to Evuri P et al., but nearly similar proportions were also existing in the 41 to 50 years [16].

Iacob S et al., recorded a mean BMI of 26.4±4.2 kg/m2 which was slightly lesser among our subjects which was 23.5±4.4 kg/m2 [17].

In the previous literature by Anand A and Saraya A, based on various diagnostic criteria, the prevalence varied from 5.9% and 82.1% [15]. 24.6% had confirmed sarcopenia, 8.8% had severe, 21.1% had probable and 45.6% had no Sarcopenia as per Evuri P et al whereas, 90.8% had probable cases of sarcopenia, 86.2% had confirmed cases and 47.7% were having severe sarcopenia among the current study subjects [16].

There was no significant association between the type of sarcopenia and age, sex and severity of chronic liver disease in this study but the mean age was significantly higher among the confirmed cases of sarcopenia (50.5±10.3 vs 42.0±13.6; t-value [95% CI] - 2.18 [-16.21 to -0.71 and P=0.03]. Evuri P et al., and Xiao LY et al., demonstrated significant association with age distribution but the statistical difference was not significant among men and women [16, 12]. This disparity might be due to different age groups, etiology catering among different study settings. There is also lack of standardized definitions and sex-specific cutoff values of SMI which can lead to masked sex differences [18].

Though majority of probable and severe cases of sarcopenia belonged to class B/C indicating higher severity, which indicates greater loss of muscle mass with the deteriorating liver function, significant association was not established in our study and this finding is in discordance with few literatures in respect to statistical significance [5,16,12,19]. Biological plausibility is etched stating that dysregulated muscle protein turnover leads to progression of sarcopenia among the patients with chronic liver disease [18]. This difference in the findings might be due to confounding factors like nutritional status, BMI, lack of specific definitions, different biochemical factors like total cholesterol, serum albumin, serum alkaline phosphatase and also level of physical activity, which might be existing [14, 12]. These confounders need to be addressed and adjusted, moreover occurrence of sarcopenia can be better elicited in a case control study rather than a descriptive study. However, eliciting the outcome and its association with the occurrence of sarcopenia was beyond the objectives of our study.

CONCLUSION

The estimated prevalence of probable cases of sarcopenia was 90.8%, confirmed cases was 86.2% and severe sarcopenia was 47.7%. Majority of the probable and severe cases of sarcopenia belonged to class B/C compared to class A indicating

higher severity hence indicating the greater loss of muscle mass with the deteriorating liver function, but significant association was not established in our study. There was no significant association between the type of sarcopenia and other socio-demographic factors. Further studies are indicated to establish the association between the sarcopenia and severity of chronic liver disease.

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