RESEARCH ARTICLE

Prevalence and risk factors of sarcopenia in patients with cirrhosis: An observational study

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Abstract

Objective: To identify the prevalence and predictors of sarcopenia in cirrhotic patients.

Method: This observational, cross-sectional study was conducted at the National Institute of Liver and Gastrointestinal Diseases, Karachi, from January 30 to July 31, 2021, and comprised cirrhotic patients of either gender between aged 18-60 years. Clinical and laboratory data was recorded for each patient. Body weight was adjusted for ascites. Sarcopenia was determined based on the Asian Working Group for Sarcopenia-2019 guideline via hand grip strength and chair standing. Independent predictors for sarcopenia were identified. Data was analysed using SPSS 26.

Results: Out of 434 cirrhotic patients assessed, 386(89%) were enrolled. Of them, 237(61.4%) were males, 149(38.6%) were females, 327(84.7%) were aged >45 years and 201(52.1%) had moderate professional activity. Sarcopenia was detected in 314(81.3%) patients; 185(59%) males and 129(41%) females. Age, chair exercise and hand grip scores as well as haemoglobin, albumin and potassium levels were significantly associated with sarcopenia ($p<0.05$)

Conclusion: Sarcopenia was found to be very common in patients with cirrhosis. Increasing age, concomitant comorbidities, and presence of liver decompensation increased the risk of sarcopenia.

Keywords: End-stage liver disease, Hand strength, Frailty, Potassium, Serum albumin. (JPMA 73: 2004; 2023)

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Introduction

The burden of cirrhosis has increased extensively over the past few years. Patients with cirrhosis are malnourished as the liver is the main organ involved in metabolic pathways, like glycolysis, gluconeogenesis and fat absorption, etc.[1] Anorexia of chronic disease, encephalopathy, gastrointestinal (GI) bleed, salt-restricted diet, early satiety due to ascites, malabsorption due to bowel oedema, impaired function of the liver, and multiple hospitalizations lead to decreased oral intake, malnourishment and ultimately sarcopenia.[2] Overall, it is estimated that 50-60% of cirrhotic patients are malnourished and has been shown to correlate with morbidity and mortality.[1]

Sarcopenia is a condition characterized by a decline in muscle mass and strength.[3] It reflects a state of protein-energy malnutrition, and is related to poor prognosis, complications and higher mortality, especially in Asians.[4] It can decline the performance status of patients which can ultimately affect treatment modality in patients with hepatocellular carcinoma (HCC) even when they have disease within Milan criteria[5,6] and good Child Pugh class.[7,8] Furthermore, prognostic markers, like Model for end-stage liver disease (MELD)[9,10] with and without sodium and Child Pugh class, do not include malnourishment or sarcopenia, which can underestimate the prognostic risk in patients with cirrhosis.[4] Therefore, early identification of sarcopenia is essential to manage its adverse effects, and to improve patients' quality of life as it is a modifiable risk factor.

Adequate nutrition and physical activity in cirrhosis is very important, though the data available is limited.[11] There is myth in our part of the world regarding diet in patients with liver disease. Patients often stop taking healthy diet, including essential nutrients and animal proteins, when they come to know regarding their disease in the fear of the disease getting worsened. The concept of avoiding red meat, eggs, oily food and green leafy vegetables is deeply entrenched in our population which makes patients restrict their diet even on the advice of family and friends.[12]

The current study was planned to identify the prevalence and predictors of sarcopenia in local cirrhotic patients.

Patients and Methods

This observational, cross-sectional study was conducted from January 30 to July 31, 2021, at the outpatient department (OPD) of the National Institute of Liver and Gastrointestinal Diseases, Dow University Hospital, Ojha Campus, Karachi. After approval from the ethics review board of the Dow University of Health Sciences (DIHS), Karachi, the sample was collected using purposive

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sampling technique. Those included were patients of either gender aged 18-60 years who had been diagnosed with cirrhosis of any aetiology, irrespective of the child class. Cirrhosis was diagnosed based on clinical decompensations (hepatic encephalopathy and ascites), haematological indices (platelet count <100,000 and prothrombin time [PT] >3sec) and confirmed by ultrasound findings (shrunken or altered echotexture of liver and ascites) or fibrosis stage 3 or more (F3-F4) on fibroscan regardless of the duration of illness.

Those excluded were pregnant women, and subjects with obesity, neurological or rheumatic diseases, any deformity in the dominant hand, motor disability or with fractures of upper and lower limbs in the preceding 6 months. Patients with heart failure, chronic kidney disease, potassium levels ≤2.5 mEq/L, corrected calcium (Ca) level ≤7.5 mg/dl, and magnesium level ≤1.5 mg/dl were also excluded. Obese patients were excluded as hand grip strength and walking speed have not been well studied in sarcopenic obesity.[13] End-stage renal disease (ESRD) patients were excluded as the condition can accelerate loss of muscle mass in patients with cirrhosis due to concomitant albuminuria and protein catabolism by various mechanisms.[14]

After taking informed written consent, data was collected from the patients. For patients with ascites, dry weight was calculated by subtracting the percentage of weight depending on the severity of ascites; 5%, 10% and 15% of the weight was reduced for mild, moderate and severe of ascites, respectively. Additional 5% was reduced if there was any evidence of bilateral pedal oedema.[15] Muscle mass was assessed by using hand-held dynamometer with the dominant hand 3 times and the average value was used for further analysis. The patients were asked 5 times to sit on a chair after standing for for which time was recorded at their first encounter in the OPD.[16,17] According to the Asian Working Group for Sarcopenia-2019 (AWGS-2019) criteria, patients were diagnosed to have sarcopenia if their hand grip strength was <28kg for males and <18 kg for females, and 5-time chair stand test ≥12 seconds.[18] Patients fulfilling both hand grip strength and chair stand criteria were labelled as definite, while those with single criterion were labelled as cases of probable sarcopenia.

The sample size was calculated using OpenEPi.com[19] with prevalence 50%, confidence level 95% and bound of error 5%. Data was analysed using SPSS 26. Patients' clinical and laboratory characteristics were recorded. Mean and standard deviations were used for quantitative variables, whereas frequencies and percentages were used for categorical variables. Chi-square test was applied to assess the association between sarcopenia and other demographic variables. Student t-test was also applied for identification of differences in quantitative demographics and clinical characteristics between patients with and without sarcopenia. The normality test confirmed that quantitative data was normally distributed. Logistic regression analysis was performed to identify independent predictors for sarcopenia. P≤0.05 was considered significant.

Results

Of the 434 patients assessed, 386(89%) patients were enrolled, while 48(11%) were excluded based on ESRD dependent on haemodialysis, low potassium levels, low corrected calcium, congestive heart failure, recent injury in the dominant hand, wheelchair-bound and for having a recent lower limb injury.

Of the 386(89%) patients enrolled, 237(61.4%) were males, 149(38.6%) were females, 327(84.7%) were aged >45 years and 201(52.1%) had moderate professional activity. The most common etiology was chronic viral hepatitis

Table-1: Association of demographic and clinical characteristics with sarcopenia.

			Sarcopenia		
		n=386	**Present (n=314)**	**Absent (n=72)**	***p*-value**
		n (%)	n (%)	n (%)	
Gender	Male	237 (61.4)	185 (78.1)	52 (21.9)	0.036*
	Female	149 (38.6)	129(86.6)	20 (13.4)	
Age (years)	<=45	59 (15.3)	38(64.4)	21 (35.6)	<0.0001*
	> 45	327 (84.7)	276 (84.4)	51(15.6)	
Occupation	Low activity	108(28.0)	82(75.9)	26(24.1)	0.173
	Moderate activity	201 (52.1)	170(84.6)	31(15.4)	
	High activity	77 (19.9)	62(80.5)	15(19.5)	
Diabetes	No	288 (74.6)	224(77.8)	64 (22.2)	0.002*
	Yes	98 (25.4)	90(91.8)	8 (8.2)	
Hypertension	No	282(73.1)	222 (78.7)	60 (21.3)	0.029*
	Yes	104(26.9)	92 (88.8)	12 (11.5)	
Aetiology	Viral	330 (85.5)	270(81.8)	60(18.2)	0.564
	Non-viral	56 (14.5)	44(78.6)	12(21.4)	
Smoking	Yes	113 (29.3)	86(76.1)	27(23.9)	0.089*
	No	273 (70.7)	228(83.5)	45(16.5)	
Child class	A	125(32.4)	88 (70.4)	37 (29.6)	< 0.0001*
	B/C	261 (67.6)	226 (86.6)	35 (13.4)	
Hepatoma	Yes	128 (33.2)	103(80.5)	25(19.5)	0.768
	No	257 (66.6)	210(81.7)	47(18.3)	
Statins	No	262(67.9)	204(77.9)	58(22.1)	0.011
	Yes	124 (32.1)	110(88.7)	14(11.3)	
Haemoglobin	>10	286 (74.1)	232 (81.1)	54 (18.9)	0.846
	≤10	100 (25.9)	82 (82)	18 (18)	
Potassium	> 3.50	314 (81.3)	249 (79.3)	65 (20.7)	0.031*
	≤3.50	72 (18.7)	65 (90.3)	7 (9.7)	
Albumin	>2.50	256 (66.3)	202 (78.9)	54 (21.1)	0.084
	≤2.50	130 (33.7)	112 (86.2)	18 (13.8)	

Table-2: Quantitative view of demographic and clinical characteristics of the patients with sarcopenia status.

		Sarcopenia		
		Present	Absent	*p*-value
	Mean±SD	Mean±SD	Mean±SD	
Mean Age (years)	52.13±8.46	52.83±8.28	49.11±8.62	0.001*
Mean BMI (kg/m^2)	23.8±4.11	23.7±4.11	24.00±4.11	0.65
MELD Na	14.49±5.543	14.35±5.43	15.11±5.40	0.285
Chair-exercise (seconds)	17.08±6.54	18.45±6.36	11.32±3.55	<0.0001*
Hand grip (kg)	20.57±8.48	18.44±7.28	29.83±7.02	<0.0001*
Haemoglobin (g/dl)	11.44±1.89	11.32±1.87	11.98±1.89	0.007*
Albumin (g/dl)	2.83±064	2.77±0.612	3.04±0.749	0.002*
CPK (U/L)	70.63±46.64	70.91±50.93	69.41±18.96	0.806
Calcium (mg/dl)	8.91±0625	8.933±0.615	8.82±0.66	0.185
Magnesium (mg/dl)	2.11±0.389	2.10±0.39	2.175±0.374	0.148
Potassium (mEq/L)	3.99±2.13	3.87±0.406	4.53±4.85	0.018*

CPK: Creatine phosphokinase

Table-3: Identification of potential factors of sarcopenia in patients with cirrhosis.

		Univariate Logistic Regression			Multivariable Logistic Regression		
		COR	*p*-value	C.I	AOR	*p*-value	C.I
Gender	Male	Ref	0.038*	1.033--3.182	Ref	0.083	0.932---3.093
	Female	1.813			1.698		
Age(years)	≤45	Ref	<0.0001*	1.623---5.509	Ref	0.018*	1.144---4.182
	> 45	2.9991			2.187		
Diabetes	No	Ref	0.003*	1.481---6.974	Ref	0.044*	1.027---7.835
	Yes	3.214			2.837		
Hypertension	No	Ref	0.032*	1.065---4.032	Ref	0.246	0.709---3.825
	Yes	2.072			1.647		
Child class	A	Ref	<0.0001*	1.608---4.583	Ref	< 0.0001*	1.585---4.806
	B/C	2.175			2.76		
Statins	No	Ref	0.012*	1.192---4.186	Ref	0.693	0.320---2.132
	Yes	2.234			0.826		
Potassium	> 3.50	Ref	0.036*	1.061---5.537	Ref	0.024*	1.138---6.473
	≤3.50	2.424			2.715		

COR: Crude odds ratio, AOR: Adjusted odds ratio, CI: Confidence interval.

330(85.5%), of which hepatitis secondary to hepatitis C virus (HCV) was predominant 213(55.2%). There were 128 (33.2%) patients with hepatoma, while 124(32.1%) were on statins.

Sarcopenia was detected in 314(81.3%) patients; 185(59%) males and 129(41%) females. The cases included definite 226(71.97%) and probable sarcopenia 88(28.03%) Overall, child class B/C was more prominent in 261(67.6%) subjects and this class was also prominent among sarcopenia patients. Of the total, 98(25.4%) patients were diabetic and 104(26.9%) were hypertensive. Sarcopenia was prevalent among diabetes 90(91.8%) and hypertensive patients 92(88.8%)

There were 72(18.7%) patients with potassium level ≤3.50, and, among such patients, sarcopenia was prevalent in 65(90.3%). Among the patients using statins, sarcopenia was found in 110(88.7%) patients. Gender, age, diabetes, hypertension, child class, statins and potassium level showed significant association with sarcopenia (Table 1).

Table 2 shows mean difference for demographic and clinical characteristics of the patients with sarcopenia status. There was significant mean difference for age, chair exercise, hand grip, Hemoglobin, Albumin, and Potassium between with and without sarcopenic patients. (Table 2).

Univariate logistic regression analysis showed that the female gender, patients with age >45 years, diabetes, hypertension, child class B/C, statins and potassium level ≤3.50 mEq/L had greater likelihood of sarcopenia ($p < 0.05$). When multivariable logistic regression analysis was performed it was found that only age, diabetes, child class and Potassium were significant predictors for sarcopenia. (Table 3).

Discussion

Sarcopenia is a major health problem in cirrhosis and carries a negative impact on overall outcomes independent of MELD and child scores. The present study showed high prevalence of sarcopenia in a sample of cirrhotic population, and highlighted increasing age, female gender, advance child class and presence of diabetes and hypertension comorbidities as the risk factors.

Literature has shown sarcopenia in chronic liver disease (CLD) patients ranging 14-78% which was lower than in the current finding.[20] This might be related to the lower socioeconomical status (SES) of the majority of the patients and self-imposed dietary restrictions in the current study.

A study showed that male patients were more likely to be sarcopenic than females.[21] This might be related to hypogonadism/low testosterone which is common in patients with cirrhosis.[22] However, in the current study, female patients were found more prone to sarcopenia. This might be related to low muscle mass in females, which could be compounded by dietary restrictions, causing nutritional deficiencies, and age-related hormonal changes in these patients. Furthermore, women generally display higher rates of frailty components, such as, weakness, low levels of physical activity, and exhaustion.

Old age is an independent risk factor for sarcopenia.[11] Advanced age accelerates the loss of muscle by increased apoptosis via various mechanism, and in cirrhosis along with malnutrition, this process can be hastened 2-3 folds. In a study, sarcopenic patients were older ($p<0.01$).[4] In another study, there was no difference in the mean age of sarcopenic vs non-sarcopenic patients ($p=0.801$).[23] In the

current study, sarcopenic patients were older with 2-fold risk of sarcopenia when aged >45 years.

Diabetes can cause imbalanced protein turnover, while increased insulin resistance leads to mitochondrial dysfunction and ultimately a state of chronic inflammation develops which leads to sarcopenia.[24] The current study found significant association of diabetes with sarcopenia ($p<0.044$). One metaanalysis revealed that sarcopenia was prevalent in 31.1% of type 2 diabetic patients compared to the controls 16.1% ($p<0.001$).[25] Statins have been used for cardiovascular disease and dyslipidaemia patients, and there is an evolving role of statins in the prevention of HCC in patients with CLD.[26] However, as statins have been associated with significant myopathies, it has been observed that they increase the risk of sarcopenia.[27] In the current study, use of statins was significantly associated with sarcopenia on univariate analysis, but lost its significance on multivariate analysis.

In some studies, sarcopenia was correlated with child and MELD-Na scores, but in some studies the degree of liver dysfunction was not correlated with sarcopenia.[28] In the current study, significant association was found with child score, but not with the MELD-Na score. This is particularly important for deceased donor liver transplant waitlist, which is prioritized according to MELD-Na score, where sarcopenic patients' survival on waitlist could be underestimated as frailty and sarcopenia are not reflected in these scores.

Measurement of electrolytes is crucial to exclude other causes of muscle dysfunction. Potassium is a major cation involved in effective muscular contractions and plays a role in bone mineral metabolism.[29] Though, in one study sarcopenia was more prevalent in patients with higher serum potassium levels ($p=0.035$),[30] in the current study low potassium had significant association with sarcopenia. As data is scarce about association between potassium and sarcopenia, this requires further research. Some studies have suggested that calcium, magnesium and selenium supplements improved outcomes in patients with sarcopenia by increasing muscle strength and performance, but no direct association has been shown of potassium and sodium with development or improvement in sarcopenia.[31] This could be due to the reason that all such studies were observational, and more randomised controlled trials (RCTs) are required to clarify the possible advantages of mineral intake for sarcopenia prevention and/or treatment, and to promote healthy ageing.[31]

The current study has limitations of being a single-centre research. It did not measure serum ammonia levels, which has gained clinical interest in recent practice as it can cause mitochondrial dysfunction and increased expression of myostatin which can result in decreased protein synthesis.[32] Serum testosterone and vitamin D levels also remained unaddressed, which could potentially affect sarcopenia and muscle strength. Furthermore, patients were not followed prospectively to see the impact on future decompensations, infections, mortality and hospitalisations.

Despite the limitations, however, the current study, to the best of our knowledge, is the first and the largest study from Pakistan to report high prevalence of sarcopenia in cirrhotic patients, and it identified the associated factors as well. By employing these simple bedside techniques, regular monitoring of sarcopenia can be possible, aiding in its early detection. Patients will also receive immediate guidance for weight-bearing exercises and seek out dietician consultation, and all such steps will improve their quality of life.

Conclusion

Sarcopenia was found to be very common in patients with cirrhosis. It can affect patients' quality of life. Special measures should be taken for patients with risk factors of sarcopenia to improve their quality of life as it is a modifiable risk factor.

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