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Predictors of Health-Related Quality of Life in Sarcopenic Patients: Result from BCAAS Study

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Abstract **Original Research Article**

Background: Liver cirrhosis is a major burden that includes marked metabolic dysfunction and sarcopenia which may influence patients' HRQoL. The main aim of the study was to analyse the mental, physical, and social well-being in sarcopenic population with liver cirrhosis (LC) using Chronic Liver Disease Questionnaire (CLDQ). ***Methods:*** The six domains of CLDQ were applied in a cross-sectional study during the 18 months of research in Rajasthan, India. Severity of the liver disease was determined through CTP and MELD. For the physical evaluation of sarcopenia, participants had undergone TAMA, hand grip strength, and gait speed test. For the statistical analysis, mean, SD, median, interquartile range, and multi logistic regression was used for final analysis. The total sample size was 138 patients. ***Result:*** The mean age of participants was 47.42±13.47 years, alcohol induced cirrhosis was the major factor contributing LC. CLDQ showed association with CTP, Meld Na, Ascites and Sarcopenia. CTP and MELD Na had an inverse effect with all domains of CLDQ and it showed a direct association with TAMA, hand grip strength and gait speed test. ***Conclusion:*** LC sarcopenic patients do worst in the domains of CLDQ that impair the health-related quality of life, as evidenced by CTP and MELD scores.

Keywords: HRQoL, CLDQ, Liver Cirrhosis, Sarcopenia, CTP.

INTRODUCTION

The liver is a vital organ for nutrient metabolism after intestinal absorption. Nutrient metabolism is often impaired in chronic liver dysfunction leading to the heterogeneity of nutritional disorders such as protein-energy malnutrition (PEM), loss of muscle mass & muscle strength (sarcopenia), which accounts as a major marker for morbidity and mortality [1, 2]. A major contributing factor of sarcopenia in chronic liver disease is an imbalance in muscle protein turnover, which can result from decreased muscle protein synthesis and increased muscle protein breakdown. Sarcopenia measuring anthropometric parameters including Hand grip strength (HSG), gait speed, total abdominal mass area (TAMA) are major indicators of overall skeletal muscle mass, muscle strength, total muscle area and these tools are used to diagnose sarcopenia in cirrhotic patients [3].

A number of conditions are thought to contribute to this imbalance, including accelerated hunger, hyperammonemia, amino acid deficiency, chronic inflammation, excessive alcohol consumption, and physical inactivity [4, 5]. Patients with chronic liver dysfunction, histopathological occurrence of regenerative nodules are encapsulated by fibrotic tissues owing to chronic liver injury [6]. That culminates portal hypertension, ascites, hepatic encephalopathy, frailty, and end-stage liver disease, among many others [7]. The patients have sickened with abdominal discomfort, fatigue, various systemic complaints, loss of appetite, anxiety, worry and other emotional problems that have a negative impact on day-to-day health-related quality of life (HRQoL) [8]. Hence, managing individuals with liver cirrhosis is not only to prolong survival with poor quality of life, but also to improve and maintain a relatively good quality of life.

The validated health-related quality of life questionnaire (HRQoL) can be used in this regard to assess overall well-being in a patient with liver cirrhosis. CLDQ is a disease-specific questionnaire that produces both a summary score and domain scores that correlate with liver disease severity [9]. Higher CLDQ scores correspond to better HRQoL [10, 11].

The study aimed to determine the overall impact of patients with LC sarcopenia on the mental, physical, and social well-being of the patients using CLDQ for assessing the HR-QoL.

METHODOLOGY

Ethics: The study was conducted in accordance with the Declaration of Helsinki principles (1975) and the reporting guideline of the World Association for Public Opinion Research. This was approved by the Institutional Ethics Committee NIMS University Rajasthan (Vide approval # NIMSUNI/IEC/217/22). The study was explained in detail to each participant and written informed consent form was obtained [12, 13].

Population selection

The current cross-sectional, in-patient investigation was derived from broader research called the BCAAS study [14]. The study was conducted at National Institute of Medical Sciences and Research, NIMS University Rajasthan, Jaipur, India between April 2019 and October 2020. Patients with a confirmed diagnosis of liver cirrhosis based on clinical and laboratory data were included in this research study. Severity of liver disease was determined through Child-Turcotte-Pugh Score (CTP) and Model for End-stage Liver Disease (MELD).

DATA COLLECTION

After initial screening informed consent was obtained from all patient enrolled in the study. Socio-demographic, clinical data, laboratory data (Total Bilirubin, Creatinine, PT-INR, Sodium levels), self-administered HRQOL questionnaire; Chronic Liver Disease Questionnaire (CLDQ), a specified and validated Liver Disease HRQOL questionnaire were collected at the time of hospitalization. Sarcopenic patients were identified according to the updated European Working Group on Sarcopenia in Older People 2, 2018 (EWGSOP2) guidelines, participants had undergone physical evaluation (quantitative) for sarcopenia using: a) Grip strength [low muscular strength (kg m -2)]: the mean of 3 hits measured with a hand dynamometer with the dominant hand; b) Gait Speed test [low muscle quantity, and low physical performance (m s -1)]: the time patient took to walk 6m; and b) TAMA: total abdominal area of skeletal muscles and fat tissues.

BMI was calculated and classified as per WHO guidelines [15]. Clinical status of patient was stratified using Child-Turcotte-Pugh Score, the decompensate cirrhotic patients were classified as group B (score 7-9) and group C (score10-15) were enrolled in the study.

The Chronic Liver Disease Questionnaire is a unique questionnaire designed to track changes in health status in patients with chronic hepatic disease over time. "Fatigue," "emotional function," "worry," "activity," "abdominal symptoms," and "systemic symptoms" are the domains of 29 items on the questionnaire. A seven-point Likert scale answering style was used for all questions ranging from 1 (all the time) to 7(none of the time). Overall Cronbach's alpha for the CLDQ score was 0.93.

STATISTICAL ANALYSIS

SPSS 23 version (Statistical Package of Social Science, Version 23.0. owned by IBM Corp) was used for the statistical interpretation of data. The descriptive analysis includes mean, SD, median, and IQR, and multivariate logistic regression was used for CLDQ score (grouped in ≤5 and >5) analysis.

RESULT

Demographics

The total n=138 patients were enrolled in the study, majority of the study population were male 85.5% (n-118). The mean age of the cohort was47.42±13.47 (range: 32 - 69). The total mean BMI was 21.44±2.89, Child-Turcotte-Pugh score 10.54±2.25 (48.9% in group B while 51.45% in group C), MELD Na 13.9±4.67, Moderate ascites 36.23% and alcohol-induced cirrhosis was the major etiology (70.28%) followed by viral-induced (17.39%) (Table 1).

Table-1: Demographic characteristics of 138 patients enrolled in the study.

Characteristics	Total (N=138)
Age (in years)	47.42 ± 13.47
Gender	
Male	118 (85.50)
Female	20 (14.49)
Etiology	
Alcohol	97 (70.28)
Viral	24 (17.39)
Autoimmune	5 (3.62)
Cryptogenic	12 (8.69)
Body Mass Index (Kg/m^2)	21.44 ± 2.89
Child-Turcotte-Pugh Score	10.54 ±2.25
Child-Turcotte-Pugh Classification	
- **B**	67 (48.55)
- **C**	71 (51.45)

Characteristics	Total (N=138)
Hepatic Encephalopathy	
None	96 (69.56)
Grade I	25 (25.36)
Grade II	17 (12.32)
MELD-Na	13.9 ± 4.67
Total Bilirubin (mg/dl)	4.60 ± 1.81
Creatinine (mg/dl)	1.04 ± 0.89
INR	13.87 ± 2.48
Sodium (mEq/L)	129.47 ± 6.78
Ascites	
Mild	23 (16.66)
Moderate	50 (36.23)
Refractory	35 (25.36)
Sarcopenic Parameters	
Hand grip strength (kg m^{-2})	23.21 ± 5.71
Gait speed (m s^{-1})	0.85 ± 0.05
TAMA (cm^2 m^{-2})	25.8 ± 5.46
Values are expressed in Mean and standard deviation (Mean ±SD), number and percentage n (%). MELD = Model for End-stage Liver Disease, INR = International Normalized Ratio, TAMA = Total Abdominal Muscle Area *p*-value was statistically significant at 0.05.	

The overall median score of each CLDQ domain in LC sarcopenic patient was found to be less in Emotional [3.28(IQR- 2.55-4.28)], followed by activity [3.33 (IQR- 2.85-4.33)], and Fatigue [(IQR- 3.00-4.19)] (Figure 1).

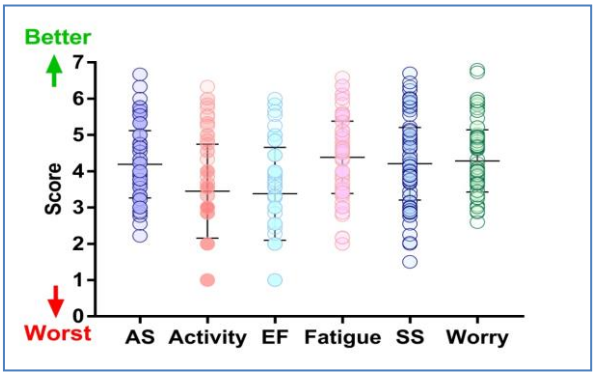

Fig-1: Overall Chronic Liver Dsesse Questionaire (CLDQ) score in domains.

CLINICAL FINDINGS

The association between CLDQ with demographic and laboratory parameters (age, gender, etiology, BMI, CTP Score, hepatic encephalopathy, Meld Na, Ascites and sarcopenic parameters) was calculated by using multivariate logistic regression (Table 2).

Table-2: Association of CLDQ using independent demographic and clinical variables

	Standard coefficient β	95% Confidence Interval		*p*-value
		Lower	Upper	
Constant	132	119.45	168.92	**<0.001**
Age (in years)	0.09	-5.92	10.63	0.247
Gender	1.02	-7.32	19.45	0.118
Etiology				
Alcohol	-0.84	-16.24	19.62	0.053
Body Mass Index (Kg/m^2)	-1.35	-8.63	18.34	0.330
Child Turcotte Pugh Score	**-0.085**	-11.49	16.67	**0.002**
Hepatic Encephalopathy	**-0.51**	-12.78	9.84	**0.010**
MELD-Na	**-0.34**	-14.34	16.97	**0.003**
Ascites	0.366	-5.62	9.45	0.259
Sarcopenic Parameters				
Hand grip strength (kg m^{-2})	**0.34**	-5.78	9.25	**0.031**
Gait speed (m s^{-1})	**0.42**	-2.67	11.52	**0.042**
TAMA (cm^2 m^{-2})	**0.14**	-7.82	12.12	**0.011**

Every one unit increase in CTP score, MELD Na and hepatic encephalopathy had a significant invers effect on the overall CLDQ score *(p=<0.01)*. Likewise, sarcopenic parameters, hang grip strength *(p=0.031)*, gait speed test *(p=0.042)*, and TAMA *(p=0.011)* shows significant effect on CLDQ (Table 2).

DISCUSSION

The present study found that the sarcopenic patients with chronic liver disease (CLD) had poor HRQoL compared with healthy individuals, which had been found to be similar in many other studies [8, 16]. As the scarcity of disease specific questionnaire, we used disease specific HRQoL instrument (CLDQ) or patients with CLD by using a comprehensive methodological framework and existing conventional prognostic markers [9, 17]. Younossi *et al.*, 1999 summarized their paper as that disease-specific questionnaire (CLDQ) better detected HRQoL impairment than generalized questionnaire. Moreover, CLDQ has moderate to high internal consistency, good discrimination among disease severity groups, and ease of administration [18].

In our study, males are more frequently diagnosed with alcoholic liver cirrhosis as compared to females. Guy *et al.*, 2013 described that women are more susceptible to the toxic effects of alcohol in the liver, despite males abusing or relying on alcohol more than women over the age of 26 [19]. Mann *et al.*, 2003 reported that cirrhosis mortality rates in men are about two times higher than in women. These figures reflect the fact that males drink more than females and that the proportion of heavy drinkers and alcoholics among men is substantially higher as heavy drinkers and alcoholics can advance from alcoholic fatty liver to alcoholic hepatitis to cirrhosis, with 10 percent to 15% of alcoholics developing the disease [20].

We also found that a significant proportion of patients belonged to CTP C with a median age of 47 years with high rates of complications as hepatic encephalopathy and ascites that influenced HRQoL in severe liver disease. Jananiet *al.*, 2018 justified our findings [11], and Marchesini*et al.*, 2001 observed ascites to be a predictor of poor HRQoL [21]. MELD and CTP scores were negatively associated with CLDQ that illustrating that more MELD and CTP scores signified impairment in HRQoL. Zuberi *et al.*, 2007 also reported lower CLDQ scores in patients with CTP C [22]. As CLDQ incorporates 29 Likert items categorized into six domains, LC sarcopenic patients were found to be less emotional, followed by activity in our study. The CLDQ domains showed a decreasing gradient with increasing disease severity in cirrhotic patients.

Despite that, by multivariate logistic regression shows CLDQ scores were affected by factors such as Child Turcotte Pugh (CTP) score, hepatic encephalopathy, and MELD-Na. In one study, investigators reported that increasing MELD does not seem to be related to the quality of life, but hepatic encephalopathy and ascites are the contributing factors that influenced CTP score in LC sarcopenic patients [23]. In our study, hepatic encephalopathy is negatively associated with CLDQ score as hepatic encephalopathy worsens activity and emotional function domains. Ridola *et al.*, 2018 support our findings [24].

Our study showed that sarcopenic parameters such as handgrip strength, gait speed, and TAMA were positively associated with CLDQ domains that influence HRQoL. Many studies enlightened our findings and showed that reduced values of sarcopenic parameters were worsened patients' quality of life. Hence, the improved sarcopenic parameters lead to enhance LC patients' HRQoL [25-27]. Limitations of the study: our study was single-centric, it would have been better if the study will be multi-centric. An in-depth study is also required to address the effects of individuals with other co-morbid conditions on HRQoL.

CONCLUSION

In summary, LC sarcopenic patients do worse in CLDQ as compared to healthy individuals. HRQoL is affected by disease severity as evidenced by CTP and MELD scores. The domains of CLDQ, emotional and activity, showed worse in LC sarcopenic patients leading to impairment in HRQoL.

Conflict of interest& funding

The authors do not have any conflict of interest and no funding provided.

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