

# **Anthropometric, biochemical and clinical assessment of malnutrition in Malaysian patients with advanced cirrhosis**

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## Abstract

### Background

There is limited data on the nutritional status and appropriateness of nutritional markers in Asian patients with advanced liver cirrhosis. This study aimed to determine the level of malnutrition and identify appropriate nutritional assessment tools in Malaysian patients with pre-dominant non-alcohol related liver disease.

### Methodology

A cross-sectional study of adult patients with decompensated cirrhosis was conducted. Nutritional status with anthropometry, serum visceral proteins and subjective global assessment (SGA) was assessed and compared with clinical severity and cirrhosis aetiology.

### Results

Thirty six patients (mean age  $59.8 \pm 12.8$  years; 66.7% males; 41.6% viral hepatitis) with decompensated cirrhosis were recruited. 16 (44.4%) and 20 (55.6%) of patients had Child-Pugh grade B and C disease respectively. Anthropometry with mid-arm circumference (MAC) and mid-arm muscle circumference (MAMC) revealed severe malnutrition in 52.8% (19 patients with  $MAC < 5^{\text{th}}$  percentile) to 58.3% (21 patients with  $MAMC < 5^{\text{th}}$  percentile). When assessed against clinical severity, serum albumin ( $17.9 \pm 4.4$  vs  $24.1 \pm 6.0$ ,  $p=0.001$ ), serum transferrin ( $1.3 \pm 0.6$  vs  $2.0 \pm 0.5$ ,  $p<0.0001$ ) and SGA grade C (40% Vs 25%,  $p= 0.5$ ) were lower in Child-Pugh C versus B liver cirrhosis. Alcohol induced liver cirrhosis had lower anthropometric, biochemical and higher proportions of SGA grade C (41.7% vs 29.2%) compared to non-alcohol related cirrhosis, but these were not statistically significant.

**Conclusion**

Severe malnutrition is common in Malaysian patients with advanced cirrhosis. Serum visceral proteins and SGA correlated better with clinical severity compared to anthropometry.

Key words: malnutrition, liver cirrhosis, nutritional assessment, nutritional markers,

Asian

## Introduction

Cirrhosis of the liver is a devastating condition, commonly the result of decades of chronic inflammation from toxin (eg alcohol), viral infection (eg Hepatitis B) or immune mediated disease (eg autoimmune disease). As a result of the complex pathophysiological processes associated with cirrhosis, it results in significant morbidity such as gastrointestinal bleeding from portal hypertension, and eventual mortality in many patients. [1] The prognosis of patients with advanced cirrhosis is grim, with a 5-year survival rate of <10%. Patients with decompensated liver cirrhosis form the majority of cases that are admitted into gastroenterology units world-wide and represent a significant burden on health-care resources. [2]

In addition to the associated morbidity highlighted above, protein-energy malnutrition (PEM) has been often observed in patients with liver cirrhosis [3, 4]. Previous studies in Western patients have documented malnutrition rates from 20% in compensated liver cirrhosis up to 60% in decompensated liver cirrhosis. [5] Causes for malnutrition in liver cirrhosis are known to include reduction in oral intake (for various causes), increased protein catabolism and insufficient synthesis, and malabsorption/ maldigestion associated with portal hypertension. [3, 5, 6] Although a consequence of the disease, malnutrition alone can lead to further morbidity in patients with liver cirrhosis. Increased rates of septic complications, poorer quality of life, and a reduced life span have all been observed in cirrhotics with poorer nutrition status compared to those without. [7, 8]

In Asia, the high prevalence of chronic Hepatitis B infection, has resulted in large numbers of people developing liver cirrhosis with its' associated complications. [9] Most

of the data on malnutrition in patients with cirrhosis have been derived from Western patients in whom chronic alcohol ingestion has been the commonest aetiology. Alcoholic patients are known to develop malnutrition for other reasons apart from liver damage per se.[10] It is uncertain, therefore, if Asian patients with cirrhosis have the same degree of malnutrition and its' resultant morbidity as patients with cirrhosis from other parts of the world.

We aimed to characterize in detail the nutritional status of patients with advanced liver cirrhosis in this multi-racial Asian population, using several methods including anthropometry, biochemical parameters and bio-electrical impedance. Nutritional parameters between patients with varied severity and aetiology of liver disease were analysed as well.

## **Methods**

### **Patients**

Local institutional ethics committee approval was sought before commencement of the study. A cross-sectional study of Asian patients admitted for decompensation of cirrhosis to this tertiary institution, between August 2006 and March 2007, was undertaken. Eligible patients were given an information sheet in both English and Malay language detailing the objectives and nature of the study. Informed consent was obtained in all patients prior to participation.

### **Clinical criteria**

The diagnosis of cirrhosis was based on clinical assessment, radiological features or liver biopsy results. Clinically, patients were suspected to have cirrhosis if they had developed clinical features of portal hypertension, particularly abdominal ascites and/or gastro-esophageal varices, confirmed by upper gastrointestinal endoscopy. Additional laboratory parameters including deranged liver function tests, low platelet count or deranged clotting profile would be used to support the diagnosis of cirrhosis. Radiological criteria (either ultrasound or computerised tomography) of a shrunken liver with or without features of portal hypertension were obtained in all cases. Liver biopsy, where performed, was used as the gold standard to confirm the presence of cirrhosis. Severity of liver disease was calculated according to the Child-Pugh score with grades A (mild) to C (severe) indicating degree of hepatic reserve and function.[11]

## **Nutritional Assessment**

Nutritional assessment was based on the following: anthropometry, biochemical markers, lean body mass and subjective global assessment (SGA). All measurements were taken by the same single investigator, to avoid any inter-observer variation.

### *Anthropometry*

All patients in the study had a baseline body mass index (BMI), i.e. weight (kg)/height (meter)<sup>2</sup> performed. Although a crude measure of nutritional status, BMI was used as a baseline comparison between cirrhotic patients and the local healthy population. [12] Further anthropometric measurements included the following: midarm circumference (MAC), triceps skinfold thickness (TST), midarm muscle circumference (MAMC) and handgrip strength. MAC, an established measure of muscle protein mass, was measured to the nearest centimeter with a measuring tape at the right arm. [13] TST, an established measure of fat stores, was measured to the nearest millimeter at the right arm using Harpenden skinfold caliper (Baty Ltd, British Indicators) in a standard manner. [13] Three measurements were taken for both TST and MAC, with average values calculated and recorded. Mid-arm muscle circumference (MAMC) was calculated from MAC and TST using a standard formula. [13] MAMC has previously been shown to be a sensitive marker for the presence and severity of protein-energy malnutrition. [13]

Handgrip strength, a simple and effective tool to measure nutritional status, was measured with a hydraulic hand dynamometer (JAMAR) in kilogram force (Kg/F). [14] Three measurements were made on each arm and an average taken from all measurements. A combination of handgrip strength < 30 kg/F and MAMC < 23 cm had

previously been shown to have 94% sensitivity and 97% negative predictive value in identifying malnourished patients. [15]

### *Biochemical parameters*

Serum albumin concentration is the most frequently used laboratory measure of nutritional status. Although non-specific, it has been used to assess change in nutritional status and stratifying risk of malnutrition. [16]. A reduction in serum albumin in the absence of other causes has been shown to represent liver damage and hence forms part of the normal items for a classic liver function test. Serum transferrin has a half-life of 9 days, making it intermediate between prealbumin and albumin in its sensitivity for incipient malnutrition. Serum prealbumin (transthyretin) is a more reliable indicator of nutritional status than albumin because its half-life of 24 to 48 hours makes the plasma concentration more reflective of the current nutritional status. Good correlation between prealbumin and transferrin levels with the Child-Pugh score has been demonstrated before,[17] and a reduced level of serum transferrin is additionally indicative of decreased caloric intake. [16] However, as both albumin and transferrin are negative acute phase proteins it is important to demonstrate that no inverse relationship exists with an inflammatory marker such as C-Reactive Protein (CRP).

### *Subjective global assessment*

Subjective global assessment (SGA) is a simple evaluation tool that allows physicians to incorporate clinical findings and subjective patient history into a nutritional assessment.[18] Based on history taking and physical examination nutritional ratings of patients are obtained as follows: well-nourished-A, moderately malnourished-B and

severely malnourished-C. The SGA has been shown to be valid and a useful clinical nutritional assessment tool for patients of various medical conditions. [19]

#### *Dietary intake and assessment*

Assessment of individual patient's oral intake was determined by the dietary recall method done every three days for two weeks and an average intake was calculated and recorded. The objective was to determine the adequacy of caloric intake per patient with minimum reporting bias. Calculation of calories of food and drinks intake (composition of the diet) was based on local reference data. [20]

#### **Statistical Analysis**

All data was entered into Statistical Packages for the Social Sciences (SPSS) version 13.0 (Chicago, Illinois, USA) software for analysis. Baseline comparisons of nutritional parameters were initially performed between the study population and referenced values for normal healthy adults. Nutritional parameters were subsequently analysed against disease severity, i.e. Child-Pugh grade, and aetiology of liver disease. Continuous variables were expressed as means with standard deviation and analysed with student's t-test or Mann-Whitney where appropriate whilst categorical data were analysed using the  $\chi^2$  test.

## Results

A total of 36 patients with decompensated liver cirrhosis were recruited during the study period. The basic demography and clinical features are highlighted in Table 1. The mean age of the patients was  $59.8 \pm 12.8$  years and the commonest reason for admission was for paracentesis of abdominal ascites. Viral hepatitis was the commonest aetiology of cirrhosis ( $n=15$ , 41.6%) and all patients had advanced liver disease with 16 (44.4%) cases of Child-Pugh B and 20 (55.6%) cases of Child-Pugh C cirrhosis.

### Nutritional assessment

Nutritional parameters in patients with cirrhosis were significantly less than normal referenced values in healthy adults (Table 2). In particular, MAC ( $24.3 \pm 5.3$  cm), TST ( $9.3 \pm 3.4$  mm) and hand grip ( $16.5 \pm 7.6$  kgF) values in patients with cirrhosis were much lower than referenced values. The degree of malnutrition was assessed using MAC and MAMC values. Moderate malnutrition in Malaysian cirrhotics ranged from 72.2% (26 patients had MAMC < 25<sup>th</sup> percentile) to 75% (27 patients had MAC < 25<sup>th</sup> percentile), whilst severe malnutrition was observed in 52.8% (19 patients with MAC < 5<sup>th</sup> percentile) to 58.3% (21 patients with MAMC < 5<sup>th</sup> percentile). The mean BMI of cirrhotic patients however, was  $24.3 \pm 5.3$  kg/m<sup>2</sup>, which was within the normal healthy adult range.

Biochemically, the mean serum albumin ( $20.6 \pm 6.0$  g/l) and the mean serum transferrin ( $1.6 \pm 0.7$  g/l) were lower than normal values. Pearson's test revealed a weak correlation between serum albumin ( $r=0.31$ ) and serum transferrin ( $r=0.29$ ) and CRP levels,

indicating that the levels of visceral protein were not being affected by inflammation. The mean caloric intake of all cirrhotic patients was additionally reduced at 15.2 kcal/kg/day.

### **Clinical severity and nutritional parameters**

Anthropometric measurements, such as MAC, TST and hand grip strength, were not significantly different between patients with Child-Pugh C and B liver cirrhosis (Table 3). However, serum albumin ( $17.9 \pm 4.4$  vs  $24.1 \pm 6.0$  g/L,  $p=0.001$ ) and transferrin ( $1.3 \pm 0.6$  vs  $2.0 \pm 0.5$  g/L,  $p<0.0001$ ) levels were demonstrated to be significantly lower in patients with Child-Pugh C liver cirrhosis compared to those with Child-Pugh B disease. SGA grading additionally demonstrated a higher proportion of Grade C, i.e. more malnutrition, in patients with Child-Pugh C (40%) compared to Child-Pugh B (25%) liver cirrhosis. Caloric intake was further observed to be significantly less in patients with Child-Pugh C disease compared to patients with Child-Pugh B disease ( $13.3 \pm 4.9$  vs  $17.6 \pm 5.7$  Kcal/kg/day,  $p=0.018$ )

### **Aetiology of liver disease and nutritional parameters**

Comparisons were made between patients with and without alcohol-induced cirrhosis. Anthropometric measurements demonstrated a trend towards lower measurements in patients with alcohol-induced cirrhosis, compared to non-alcohol induced liver cirrhosis (Table 4). Lower values for TST ( $8.4 \pm 3.6$  vs  $9.7 \pm 3.2$  mm), MAC ( $24.5 \pm 5.1$  vs  $27.2 \pm 5.5$  cm) and MAMC ( $21.9 \pm 4.1$  vs  $24.2 \pm 4.8$  cm) were recorded in patients with alcohol-induced cirrhosis, although these were not statistically significant. Similarly, biochemical parameters demonstrated lower serum albumin ( $20.3 \pm 7.5$  vs  $20.8 \pm 5.2$  g/L) and serum transferrin ( $1.5 \pm 0.8$  vs.  $1.7 \pm 0.6$  g/L) levels in alcohol-related cirrhotic patients, but

these differences were marginal. There was a higher proportion of patients with SGA grade C in the alcohol group compared with non-alcohol induced liver disease.

## **Discussion**

Basic anthropometric and biochemical measurements, together with clinical assessment (SGA) have demonstrated that malnutrition is common in Asians with predominant non-alcohol related liver cirrhosis. 75% of these patients had evidence of moderate malnutrition with almost 60% having features of severe malnutrition. Additionally, nutritional status appeared to correlate with severity of clinical disease (as assessed by the Child-Pugh score) and some differences were observed between alcohol and non-alcohol related liver disease. The lack of statistical significance pertaining to the latter findings may have been related to the small sample size of this study.

These findings concur with observations from many Western cohorts [5, 7, 21] and some recent studies of Asian cirrhotic patients.[22, 23] In a study of 1402 patients with cirrhosis in Italy, there was a higher incidence of malnutrition in alcoholic cirrhosis patients as compared to other aetiologies of liver cirrhosis. [21] In addition, alcoholic cirrhosis patients had poorer liver function and worse Child-Pugh scores. In another Italian study on 212 patients with cirrhosis, it was found that malnutrition was common in cirrhosis and the degree of malnutrition was worse with advanced liver disease. [7] In a Thai study of 60 patients with cirrhosis, the degree of malnutrition was higher in patients with alcoholic cirrhosis and also in more advanced liver cirrhosis. [22] In a study of 66 South Korean outpatients with cirrhosis, nutritional abnormalities were present, albeit mild. [23]

Various tools have been utilized to assess nutritional status in patients with cirrhosis. In this study, we observed that basic anthropometry confirmed malnutrition in Malaysian patients with cirrhosis but failed to differentiate between more advanced stages of disease. BMI was not a good marker of nutritional status in our group of cirrhotic patients. BMI measurements in both cirrhotic patients and the general population were similar, and there was poor correlation with clinical severity or aetiology. This is mainly due to the fact that ascites and peripheral oedema contribute significantly to body weight in cirrhotic patients, and true lean body mass was not taken into account. [24] Other anthropometric measurements such as TST, MAC and hand grip strength additionally did not prove useful in accurately differentiating between clinical severity of liver cirrhosis and various aetiologies. These findings contrast with some other published reports indicating that TST [23] and MAMC [25] were good markers of malnutrition in patients with advanced cirrhosis and even alcoholic cirrhosis.

Conversely, biochemical visceral proteins, such as serum albumin and transferrin levels, appeared to reliably differentiate between severity of liver disease. Although previous authors have suggested that serum proteins merely reflected liver function impairment rather than nutritional status, [26] several other studies have reported similar findings to ours with respect to the correlation of serum proteins with malnutrition in liver disease [6, 22]. The poor correlation with CRP in this study indicated no relationship with inflammation. Furthermore, reduced levels of serum transferrin is recognized as an indicator of decreased caloric intake [16] which was clearly evident among Malaysian patients with advanced cirrhosis.

This study has further demonstrated that clinical assessment in the form of the SGA appeared to correlate better with clinical severity and in cirrhosis aetiology. Higher rates of SGA grade C were observed in patients with Child-Pugh C (40%) compared to Child-Pugh B (25%) cirrhosis, and in alcohol-induced liver cirrhosis (41.7%) compared to non-alcohol related liver cirrhosis (29.2%). Few studies have explored the utility of the SGA in liver cirrhosis. Alvares-da-Silva and Reverbel da Silveira previously reported that the SGA was less predictive of nutritional status compared to hand grip strength in a study of 50 South American patients with cirrhosis [27]. However, 88% of the patients studied had Child-Pugh A disease, and hence these findings may not be applicable to more advanced liver cirrhosis patients. In support of the findings from this study, Roongpisuthipong et al reported significantly higher proportions of SGA grade C in 66 Thai patients with Child-Pugh C cirrhosis compared to Child-Pugh B or A disease.[22] The SGA has been shown to be simple and yet effective in assessing for malnutrition in various clinical diseases [19] and data from this study further supports its' utility in assessing nutritional status in Asian patients with advanced cirrhosis.

## **Conclusions**

In summary, malnutrition in Malaysian patients with predominant non-alcohol induced liver cirrhosis is common. A high proportion of these patients have severe malnutrition and an inadequate nutritional intake. Anthropometric tools were useful for detecting malnutrition (apart from BMI) but not predictive of clinical severity nor aetiology. Biochemical parameters and clinical assessment with the SGA were able to correlate with clinical severity and differentiate between alcohol and non-alcohol related liver disease,

suggesting that these nutritional tools may be more appropriate in routine clinical assessment of Malaysian patients with advanced liver cirrhosis.

## **Competing interests**

All authors declare that they have no competing interests

## **Author's contributions**

MLST designed the study, performed data collection, data analysis and drafted the manuscript. KLG made critical revision of the manuscript. SHMT provided technical support. SR assisted in data analysis and interpretation. SM assisted in data interpretation and critical revision of the manuscript. All authors reviewed and approved final version of the manuscript.

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**assessing malnutrition and predicting clinical outcome in cirrhotic outpatients.** *Nutrition* 2005, **21**(2):113-117.

## Tables

**Table 1 – Details of patients with cirrhosis in the study**

	<b>Patients with cirrhosis n=36</b>
<b>Age</b>	59.8 ± 12.8 years
<b>Gender (Male: Female)</b>	1.8: 1
<b>Ethnicity</b>	Malay n=11 (30.6%) Chinese n=14 (38.9%) Indian n=11 (30.6%)
<b>Aetiology</b>	Alcohol n=12 (33.3%) Viral hepatitis n=15 (41.6%) Autoimmune n=2 (5.6%) Cryptogenic n= 7 (19.4%)
<b>Child-Pugh grade</b>	Child Pugh B n=16 (44.4%) Child Pugh C n= 20 (55.6%)
<b>Reason for admission</b>	Ascites n=15 (41.7%) Infection n=7 (19.4%) Diarrhoea n=3 (8.3%) Abdominal pain n=2 (5.6%) Upper gastrointestinal bleed n=2 (5.6%) Diabetic ketoacidosis n=2 (5.6%) Others n=5 (13.9%)

**Table 2 – Nutritional parameters in Malaysian patients with cirrhosis**

	<b>Cirrhosis patients n=36</b>	<b>Normal range/expected values</b>
<u>Anthropometry (mean±SD)</u>		
BMI (kg/m <sup>2</sup> )	24.3±5.3	18.5 to 25.0
MAC (cm)	26.3±5.5	28
TST (mm)	9.3±3.4	15
MAMC (cm)	23.4±4.6	27.2
Hand grip (kgF)	16.5±7.6	34.1±7.1
<u>Biochemical</u>		
Albumin (g/l)	20.6±6.0	35-50
Transferrin(g/l)	1.6±0.7	1.8-2.7
<u>SGA** grade</u>	66.7%	
B	33.3%	NOT APPLICABLE
C		
Caloric Intake (Kcal/kg/day)	15.2±5.6 kcal/kg/day	35-40 kcal/kg/day

\*BMI=body mass index; MAC=mid-arm circumference; TST=triceps skinfold thickness; MAMC=mid-arm muscle circumference

\*\* Subjective Global Assessment

**Table 3 – Nutritional parameters and clinical severity of cirrhosis**

	CHILD-PUGH B n=16	CHILD-PUGH C n=20	p value
<u>Anthropometry</u>			
BMI (kg/m <sup>2</sup> )	24.3±4.6	24.4±6.0	0.94
MAC (cm)	26.3±5.2	26.4±5.8	0.96
TST (mm)	9.0±3.1	9.5±3.6	0.67
MAMC (cm)	23.4±4.4	23.4±4.9	0.97
Hand grip (kgF)	16.7±7.6	16.3±7.7	0.86
<u>Biochemical</u>			
Albumin (g/l)	24.1 ± 6.0	17.9 ± 4.4	0.001
Transferrin(g/l)	2.0 ± 0.5	1.3 ± 0.6	<0.0001
<u>SGA** grade</u>			
B	12 (75%)	12 (60%)	0.48
C	4 (25%)	8 (40%)	
Caloric Intake (Kcal/kg/day)	17.6±5.7	13.3±4.9	0.018

\*BMI=body mass index; MAC=mid-arm circumference; TST=triceps skinfold thickness; MAMC=mid-arm muscle circumference

\*\* Subjective Global Assessment

**Table 4 – Nutritional parameters and aetiology of liver disease**

	ALCOHOL n=12	NON-ALCOHOL n=24	p value
<u>Anthropometry</u>			
BMI (kg/m <sup>2</sup> )	22.4±5.4	25.3±5.1	0.13
MAC (cm)	24.5±5.1	27.2±5.5	0.164
TST (mm)	8.4±3.6	9.7±3.2	0.301
MAMC (cm)	21.9±4.1	24.2±4.8	0.16
Hand grip (kgF)	18.9±9.2	15.4±6.6	0.21
<u>Biochemical</u>			
Albumin (g/l)	20.3±7.5	20.8±5.2	0.786
Transferrin(g/l)	1.5±0.8	1.7±0.6	0.395
<u>SGA** grade</u>			
B	7 (58.3%)	17 (70.8%)	0.48
C	5 (41.7%)	7 (29.2%)	

\*BMI=body mass index; MAC=mid-arm circumference; TST=triceps skinfold thickness; MAMC=mid-arm muscle circumference

\*\* Subjective Global Assessment