Nutritional And Clinical Profile Of Patients In Different Stages Of Alcoholic And Virus Related Liver Disease: An Indian Perspective

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Introduction

The liver plays a crucial role in nutritional homeostasis and its dysfunction leads to malnutrition and related diseases. Liver is responsible for several vital functions like detoxification, protein synthesis, and production of hormones necessary for digestion. It also regulates concentration of glucose and amino acids in body. It is a major site of thrombopoietin synthesis and also produces albumin, the major osmolar component of serum which regulate the colloidal oncotic pressure of blood.

Liver cirrhosis is the terminal stage in the natural history of chronic liver diseases. It have a etiologies like hepatitis B virus (HBV) and hepatitis C virus (HCV) infection, alcoholic liver disease, Wilsons disease, haemochromotosis, nonalcoholic steatohepatitis (NASH), cholestatic disorders, autoimmune liver disease, toxic substances, drugs, infections, congenital diseases etc. Among these etiologies, alcoholism in the western countries and HBV infection in India are the most common causes of cirrhosis [1-3]. HBV infection is one of the major causes of liver cirrhosis and affects an estimated 400 million people worldwide. It has been estimated that one million die annually from HBV-related liver diseases [4,5].

Nutritional deficiency is common in patients with end stage liver disease (cirrhosis) and is often associated with a poor prognosis [6,7]. Malnutrition occurs in all forms of cirrhosis [8] as shown by studies of nutritional status in different etiology and of varying degrees of liver insufficiency [9,10]. The prevalence of malnutrition in cirrhosis ranges from 65 to 100% depending upon the methods used for nutritional assessment and the severity of liver disease [11-13]. Whereas the prevalence range in alcoholic patients from 34%-82% and in non alcoholic patients from 27%-87% (14). Previous studies in Western patients have documented malnutrition rates from 20% in compensated liver disease and up to 60% in decompensated liver disease [15].

Chronic liver disease (CLD) causes nutritional deficiencies leading to malnutrition which may influence short as well as long-term outcome. The mechanisms of protein calorie malnutrition (PCM) in cirrhosis are complex and multi-factorial [9,10] such as reduced oral intake, anorexia, restrictive diets, altered taste sensations (related to vitamin A or zinc deficiency), nausea, early satiety. Above all symptoms present with marked ascites, portal-hypertension associated malabsorption, insulin resistance, reduced glycogen storage capacity and increased gluconeogenesis. There is a direct association between PCM and poor nutritional status results in an unfavorable clinical outcome.

Aim of our study was to determine the prevalence of malnutrition in patients with alcoholic and virus related cirrhosis and to assess the nutritional and functional status (To assess presence and severity of disease)of patients in various grades of CLD.

Methods

Selection of the subject:

This was a prospective study carried out at the outpatient unit, Department of Gastroenterology, Sir Sundarlal Hospital, Banaras Hindu University, Varanasi, India. The study was performed on patients with compensated and decompensated liver disease. This study was approved by the ethical committee of Institute of Medical Sciences, Banaras Hindu University Varanasi. Patients with chronic liver disease who were having varices and portal hypertensive gastropathy (PHG) during endoscopy were enrolled in our study after taking informed written consent. The inclusion criteria were oriented to select the CLD patients with alcoholic and virus related, age groups between 10 to 55 years. Patients with hepatocellular carcinoma were excluded from the study. All patients were given an information sheet detailing the objectives and nature of the study. Informed consent was obtained from patients prior to participation.

Cirrhosis definition criteria

The study was performed on 259 patients with alcoholic and virus related liver disease. Liver cirrhosis was diagnosed on the basis of clinical features, routine laboratory tests such as liver function tests (LFT), renal function tests (RFT), prothrombin time,
radiological imaging and patient’s history. Stages of liver disease was assessed using the child-Turcotte pugh score (CTP), which assigns an arbitrary score to bilirubin, albumin and prothrombin time, presence of ascites and hepatic encephalopathy. This classification is considered the most reliable composite score reflecting the severity of liver disease [16,17].

Nutritional Assessment

Nutritional assessment was performed by using anthropometric measurement; visceral proteins, subjective global assessment and twenty four hour dietary recall method.

Anthropometry

Anthropometric measurements were performed on all patients. Body weight was measured with light clothes by a portable digital weight scale (Gold Tech) and height was measured with a portable stadiometer (measuring rod). The body mass index (BMI) was calculated using the formula proposed by Quetlet[18] BMI = weight/height². Mid arm circumference (MAC) was measured with a nonelastic tape measure and triceps skin fold thickness (TSF) was measured with a Harpenden skin fold caliper (Baty Ltd, British Indicators) [17]. The measurement was taken on the back of the arm and mid way between the tip of the acromion and olecranon process, with the patient standing in a relaxed position. TSF and MAC were measured as indexes of body fat and muscle protein compartment, respectively.

Visceral proteins

Serum albumin concentration was the most frequently used laboratory measure of nutritional assessment. It has been used to assess changes in nutritional status and risk of malnutrition. Reduction in serum albumin in the absence of other causes has been shown to represent liver damage [19, 1].

Subjective global assessment:

The Subjective Global Assessment (SGA) was carried out using the protocol developed by Detsky et al. [20]. It relies on the patient’s history including weight loss, dietary intake, gastrointestinal symptoms, functional capacity and physical signs of malnutrition. Patients were classified as well nourished SGA grade A, moderately or suspected of being malnourished SGA grade B and severely malnourished SGA grade C [21].

Dietary assessment

Dietary assessment was done based on the 24-hour dietary recall method following the standard protocol. Standard sized measured utensils were used. Values of various nutrients were calculated (Nutritive value of Indian foods) [22].

Statistical Analysis

A descriptive analysis was performed through mean values and standard deviation for continuous variables of symmetric distribution or median value and interquartile (IQR) amplitude for continous variables of asymmetric distribution. Differences between variables in both groups were compared using the students t-test for continuous variables and the chi square test for categorized factor. Comparison of measured values among CTP grade A,B and C were performed using one way ANOVA. Data analysis was performed using SPSS (Statistical Packages for the Social Sciences version 16.0 Chicago, Illinois, USA) software and p value

Results

A total of 259 patients with liver disease (alcoholic and virus related) were included in this study. The basic demography and nutritional characteristics of patients are highlighted in Table 1. The mean age of the patients was 41.79 ± 10.5 years. Majority of the patients in our study were male (male; 90.7 female; 9.3 %). 65.3% of the subject had viral (HBV and HCV) cirrhosis and 34.7% had alcoholic cirrhosis. Among the study subject 47(18.1%) cases had child-Pugh A, 144(55.6%) child-Pugh B and 68 (26.3%) had Child ‘C’ cirrhosis. Mean calorie and protein intake of all patients was low i.e.1348 ± 355.5 kcal/day and 34.8± 8.2 gm/day respectively. According to SGA all patients had some level of malnutrition i.e. 31 (12.0%) patients had SGA Grade A, 161 (62.2%) patients had SGA Grade B nutritional status and 67 (25.9%) were SGA Grade C.

<table>
<thead>
<tr>
<th>Table 1. Patient profile</th>
<th>Parameters</th>
<th>Patients with cirrhosis n=259</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>41.79±10.5</td>
<td>23/ (90.7%) 14/ (55.6%) 2/ (8.1%)</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td></td>
<td>23/ (90.7%) 14/ (55.6%) 2/ (8.1%)</td>
</tr>
<tr>
<td>Body mass index (BMI)</td>
<td></td>
<td>23/ (90.7%) 14/ (55.6%) 2/ (8.1%)</td>
</tr>
<tr>
<td>Mid arm circumference (MAC) (cm)</td>
<td></td>
<td>23/ (90.7%) 14/ (55.6%) 2/ (8.1%)</td>
</tr>
<tr>
<td>Triceps skin fold thickness (TSF) (cm)</td>
<td></td>
<td>23/ (90.7%) 14/ (55.6%) 2/ (8.1%)</td>
</tr>
<tr>
<td>Serum albumin (g/L)</td>
<td></td>
<td>23/ (90.7%) 14/ (55.6%) 2/ (8.1%)</td>
</tr>
<tr>
<td>Alcohol intake (g/day)</td>
<td></td>
<td>23/ (90.7%) 14/ (55.6%) 2/ (8.1%)</td>
</tr>
<tr>
<td>Sodium intake (g/day)</td>
<td></td>
<td>23/ (90.7%) 14/ (55.6%) 2/ (8.1%)</td>
</tr>
<tr>
<td>Calcium intake (mg/day)</td>
<td></td>
<td>23/ (90.7%) 14/ (55.6%) 2/ (8.1%)</td>
</tr>
<tr>
<td>Protein intake (g/day)</td>
<td></td>
<td>23/ (90.7%) 14/ (55.6%) 2/ (8.1%)</td>
</tr>
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</table>

Data are presented as mean ± standard deviation
The clinical and biochemical characteristics of the cirrhotic patients included in the study are described in Table-2. Patients suffered from alcoholic liver cirrhosis (ALC) were 34.7% and virus related liver cirrhosis (VLC) was 65.3%. The average ages were 43(35-50) and 45(35-50) years old for the VLC and ALC groups respectively. Patients with alcoholic cirrhosis have ascites (P=0.022) was more frequent than those with virus related cirrhosis. The severity of liver was higher in alcoholic patients i.e. CTP grade C.

The anthropometric and nutritional evaluation (Table-3) shown that the TSF and MAC were significantly lower in patients with alcoholic cirrhosis (10.12±1.97 mm and 22.6±3.2cm) than the virus related liver diseases (10.92±1.51mm and 23.4±2.7cm). Visceral protein and total protein levels were lower in alcoholic cirrhosis. Calorie and protein intake was also significantly less in alcoholic patients.

The enrolled patients were assigned to three groups according to severity of liver disease as assessed by child-pugh classification. "Nutritional profile of patients at different levels of clinical severity are shown in Table 4." Differences of nutritional status in Child-Pugh A, B and C liver disease was assessed with the anthropometric measurements, biochemical measurements, SGA and 24-hour dietary recall method. Mean values of anthropometric measurements such as MAC and TSF demonstrated significant differences between cirrhotic patients in Child-pugh grade A, B and C. The BMI was increased in CTP grade C patients due to ascites and edema but difference was not statically significant. However, visceral protein and total protein levels were significantly lower in patients with Child-Pugh C compared to those with Child- Pugh A and B. Caloric and protein intake was further observed to be significantly low in patients with Child-Pugh C patients. The incidence of malnutrition among the study groups as evaluated by SGA. Grade C cirrhotics was severely malnourished than grade B cirrhotics whereas grade A cirrhotics was mildly malnourished.

The clinical and relevant biochemical indices of the three groups are shown in Table 5. The total serum bilirubin and INR levels were significantly higher in grade C patients as compared to grade A and B. Hematological study revealed that hemoglobin (P=.003) and white blood cells (WBC) (P=0.043) were significant.
Data are presented as mean ± standard deviation, one way ANOVA (No.%). AST= Aspartate aminotransferase, ALT= Alanine aminotransferase. Range of ALT, AST is shown in Inter Quartile Range (IQR i.e. 25th, 75th).

The mean value of visceral protein and serum protein in the CTP groups are shown in Fig. 1. Decreasing levels of visceral protein and serum protein shown that the deterioration of nutritional status in patients with advanced liver disease.

Figure.1. comparison of protein-synthesis indices according to stages of cirrhosis (child a, child b and child c). Stages are significantly different from each other at *p=0.000 and from child c at **p=0.000.

Discussion

The relationship between malnutrition and clinical severity of the disease is one of the most important prognostic factors in liver disease [6]. The calorie and protein intake of our study groups was poor according to the recommended level. There are various reasons for this like less food intake due to anorexia, decreased quality and palatability of foods, salt-free diets, decreased nutrient absorption as well as storage and increased energy requirement [24]. Malnutrition frequently occurs in patients with CLD and can influence short and long-term survival of these patients.

In the present study, mean calorie (1348.7±355.5) and protein (34.8±8.2) intake did not satisfy the nutritional requirements of these patients, whereas in malnourished cirrhotic patients most guidelines suggest an intake of 35–40 kcal/kg/day with a protein intake of at least 1.2–1.5 gm/kg/day.

Excessive and chronic alcohol intake is associated with negative dietary habits such as the irregularity of meals and unbalanced nutrient intake. The ALC group showed a lower energy intake (excluding alcohol-derived energy).

A deteriorated nutritional status in advanced liver disease has been associated with a more restrictive diet due to major complications of cirrhosis, such as ascites and encephalopathy that can also be associated with anorexia and weight loss.

Body weight and BMI were overestimated in cirrhotic patients due to ascites and peripheral edema [25]. The disadvantage of using BMI to study nutritional status in CLD patients was underestimation of the prevalence and degree of malnutrition. Although anthropometric tools such as the MAC and TSF are known to be better predictors of malnutrition in adult patients with cirrhosis [26]. Several studies have reported that the TSF thickness was lower in patients with non-alcoholic liver disease than patients with alcoholic liver disease [27,28] and MAC was also found to be lower in patients with alcoholic cirrhosis than in those with non-alcoholic cirrhosis [28]. This frequent reduction in muscle mass in patients with cirrhosis of alcoholic etiology is probably related to a direct effect of alcohol on skeletal muscle mass metabolism [12]. In contrast, Thuluvath and Triger reported [29] TSF thickness showed no significant differences between patients with alcoholic and viral related disease. In this study, the TSF thickness and MAC values were higher in the VLC group than ALC group this difference was found to be statistically significant.

We demonstrated in this study that CTP grade C patients with cirrhosis had significantly lower anthropometric measurements compared to CTP grade A & B cases, CTP score able to differentiate nutritional status in liver disease patients. Nutrient intake was lower in all the three groups as compared to the recommended dietary allowances (RDA). Furthermore, the serum protein and visceral protein levels were significantly differ between child-pugh B and C liver disease. We observed a higher percent of CP grade B and C patients with visceral protein level was less than 3.5 g/dl as compared to group A. However visceral protein and protein reflects the function of the liver, can be affected by the stages of liver disease [27,30]. Decreasing levels of visceral protein...
protein in grade C patients indicate the low synthesis capacity of the liver with the increasing disease severity.

In terms of clinical severity, we were able to demonstrate a higher proportion of subjects in SGA grade C in child-pugh C cirrhosis. The SGA, compared to standard anthropometry, is much more applicable in clinical practice and has previously demonstrated to be highly predictive of malnutrition in advanced cirrhosis [31].

Conclusions

In present study we showed that malnutrition was common finding among patients with liver disease, and there was also some association between nutritional status and cirrhotic stages. Reductions in nutritional status are due to poor dietary intake and metabolic abnormalities in liver disease. Clinically, alcoholic cirrhosis presented with ascites, hepatic encephalopathy and protein energy malnutrition which were more frequent than in the virus related cirrhosis. In addition the comparison of Child-Pugh score, Triceps skin fold thickness and mid arm circumference were statically significant.

Abbreviations

ALD: Alcoholic liver disease
ALKP: Alkaline phosphates
ALT: Alanine amino transferase
AST: Aspartate aminotransferase
BMI: Body mass index
CBC: Cell blood count
CLD: Chronic liver disease
CTP: Child- Turcotte Pugh
HB: Hemoglobin
HCV: Hepatitis C virus
HE: Hepatic encephalopathy
INR: International normalized ratio
IU: International units
LFT: Liver function test
MAC: Mid-arm circumference
PCM: Protein calorie malnutrition
PT: Prothrombin time
RFT: Renal function test
SGA: Subjective global assessment
SD: Standard deviation
SPSS: Statistical Package for the Social Sciences
TSF: Triceps skin-fold thickness

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