Nutritional Status in Cirrhotic Patients
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ABSTRACT

Background: Malnutrition is prevalent in all forms of liver disease: from 20\% in compensated liver disease to more than 80\% in those patients with decompensated liver disease. Protein-calorie malnutrition (PCM) can be identified in all clinical stages but is easier observed in advanced stages of liver disease. The presence of malnutrition is associated with increased number of complications and increased short and long term mortality.

Aim: to evaluate the nutritional status using of combination of BMI (Body Mass Index), TST (triceps skinfold thickness) and MAMC (mid-arm muscle circumference). Subjective Global Assessment (SGA) of nutritional status was determined for every patient. The features of subjective global assessment are history, physical evaluation and SGA rating. Based on this evaluation, patients were classified into three groups: well, moderately malnourished and severely malnourished.

Material and methods: Our study was designed as a descriptive prospective analysis of patients with cirrhosis, admitted in Elias Emergency Hospital, Gastroenterology Department, during a year, January 2010-January 2011. The diagnosis of cirrhosis was based on the medical history, physical examination, biochemical findings and imagistic methods (ultrasound and / or computed tomography). A series of 176 hospitalized patients with cirrhosis, 114 (65\%) male and 62 (35\%) female, median age 52 (range 18-68 years). Etiology of liver disease was alcoholic in 98 (56\%), hepatitis B virus in 14 (8\%), HCV in 43 (24\%), HBV and HDV in 10 (7\%), 11 patients have other etiology. The evaluation of nutritional status was made by different methods. A detailed history was recorded with appetite, caloric intake, change in body weight. Subjective Global Assessment (SGA) of nutritional status was determined for every patient.

Conclusions: Malnutrition was correlated with clinical severity of liver disease. The mild-moderate malnourished patients are 88\% Child B, over 58\% with viral etiology, 22\% from these patients are alcoholic and 11\% have Child C score (p<0.01). In severely malnourished group, 43\% have alcoholic disease and 31\% are Child C classification(p<0.01). Triceps skinfold thickness (mm) and mid-arm circumference(cm) decrease significantly according to the Child score, a positive correlation was found between these two parameters and the severity of cirrhosis.
**INTRODUCTION**

Malnutrition is prevalent in all forms of liver disease: from 20% in compensated liver disease to more than 80% in those patients with decompensated liver disease (1). Patients with alcoholic cirrhosis have a greater incidence of malnutrition than those with nonalcoholic liver disease. Protein-calorie malnutrition (PCM) can be identified in all clinical stages but is easier observed in advanced stages of liver disease (2). Many patients have subtle changes such as fat-soluble vitamin deficiency, altered cell-mediated immune function, anemia from iron, folate or pyridoxine deficiency and minimal loss of muscle mass. Patients with end-stage liver disease have muscle wasting, decreased fat stores and cachexia.

There are a number of factors that contribute to malnutrition in patient with liver disease (Table 1) (3). Malabsorption also may be caused by several conditions: pancreatic insufficiency, cholestasis, portosystemic shunt, bile deficiency through inadequate absorption of long-chain fatty acids, metabolic alterations (high protein catabolism, reduced glucose homeostasis due to alterations of gluconeogenesis, low glycogen stores, proinflammatory cytokines such as TNFalpha, interleukines) (4).

Nutritional status is considered to be a predictor of morbidity and mortality in patients with advanced hepatic disease (5). Malnutrition also has important implications in liver transplantation and it has been demonstrated that patients with a worse nutritional status before the transplant have increased postoperative complications and higher mortality rates (4,5).

Numerous descriptive studies have shown higher rates of complications and mortality in cirrhotic patients with protein malnutrition as well as reduced survival when such patients undergo liver transplantation (6).

General nutrition guidelines for patients with cirrhosis as they are specified by the European Society for Clinical Nutrition and Metabolism (ESPEN) are listed in Table 2 (7).

Multiple recent studies have shown the importance of maintaining the positive nitrogen balance via increased protein and caloric intake in cirrhotic patients (8). Negative nitrogen balance due to protein restriction leads to protein-calorie malnutrition (PCM) (9). Anorexia, early satiety, ascites, altered mental status and frequent hospitalization lead to decreased protein intake and contribute to PCM. Dietary restrictions, frequent paracentesis, diuresis and lactulose therapy are iatrogenic causes worsening the situation. Advanced liver disease associated with cholestasis, bacterial overgrowth and malabsorption causes severe deficiencies of fat-soluble vitamins and other nutrients (10,11).

PCM is considered a negative prognostic factor associated with life-threatening complications such as refractory ascites, spontaneous bacterial peritonitis, hepato-renal syndrome and variceal hemorrhage (10,11).

PCM should be considered as a prognostic variable in treatment for ascites, spontaneous peritonitis and valiceal bleeding. It well correlates with short and long term mortality, severity of liver disease appreciated by Child-Pugh classification (CP) and Model for End Stage Liver Disease (MELD), liver graft and patient survival after liver-transplantation (10-12).

<table>
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<tr>
<th>Decreased Intake</th>
<th>Decreased Absorption</th>
<th>Metabolic alterations (see text and Table 2)</th>
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**TABLE 1. Etiology of Malnutrition in Cirrhosis.**

Provide 30-35 kcal/kg dry body weight
Provide 50-60% of calories as carbohydrate
Provide 20-30% of calories as protein (1-1.5 g/kg body weight)
Provide 10-20% of calories as fat
Avoid unnecessary dietary restrictions
Prescribe a low-sodium diet (<2 g/day) only if ascites or edema is present
Provide 4-6 small meals, one of which is a late-evening carbohydrate-rich snack
Screen for deficiencies of serum zinc, calcium and vitamins A, D, E and K and supplement as needed
In hepatic encephalopathy (HE), maximize HE treatment; if patient is protein intolerant, consider increasing vegetable protein, dairy protein and branched chain amino acids
Prohibit alcohol

**TABLE 2. General Nutrition Guidelines for Patients With Cirrhosis.**
MATERIALS AND METHODS

Our study was designed as a descriptive prospective analysis of patients with cirrhosis, admitted in Elias Emergency Hospital, Gastroenterology Department, during a year, January 2010-January 2011.

Inclusion criteria were: age between 18 and 80 years, documented liver cirrhosis in a stable hemodynamic condition, compliance to dietary recommendations and medical treatment.

Exclusion criteria were: hepatic coma, active gastrointestinal bleeding, ongoing alcoholism, sepsis, liver failure, hepatocellular carcinoma (using alpha fetoprotein AFP and/or abdominal ultrasound).

The protocol conformed to the Declaration of Helsinki and Guidelines for Good Clinical Practice in Clinical Trials and was approved by the Elias Emergency Hospital Committee.

All patients signed an informed consent. Those who were in a poor condition did not agree to the study, that’s why many patients had Child A score and statistical analysis are not relevant for statistical significance.

The diagnosis of cirrhosis was based on the medical history, physical examination, biochemical findings and imagistic methods (ultrasound and/or computed tomography).

A series of 176 hospitalized patients with cirrhosis, 114 (65%) male and 62 (35%) female, median age 52 (range 18-68 years). 81% from the patients were from urban area and 19% from countryside.

The etiology of liver disease was alcoholic in 98 (56%), hepatitis B virus in 14 (8%), HCV in 43 (24%), HBV and HDV in 10 (7%), 4 patients have primary biliary cirrhosis and autoimmune and the rest 7 have other etiology, included Wilson’s disease, non-alcoholic and cryptogenic cirrhosis.

Clinical variables recorded were degree of encephalopathy (none, grade 1-2, grade 3-4), degree of ascites (absent, slight or moderate) based on the clinical or ultrasound data.

The laboratory data collected included cell blood count (CBC), bilirubin, albumin, prothrombin time (PT), serum ammonium, International Normalized Ratio (INR), serum urea, serum creatinine, which were used to calculate CP and MELD scores; all markers were measured by standard laboratory methods.

The ultrasound evaluation included the measurement of hepatic dimensions, evaluation of portal hypertension and the splenomegaly, the presence of ascites and excluded hepatocellular cancer, if not an alpha fetoprotein was requested.

The evaluation of nutritional status was made by different methods. A detailed history was recorded with appetite, caloric intake, change in body weight.

Subjective Global Assessment (SGA) of nutritional status was determined for every patient. It is sometimes more useful than objective measurers for identifying individuals at nutritional risk because in patients with cirrhosis weight and biochemical values vary with the severity of liver disease independently from nutritional status.

The features of subjective global assessment are history, physical evaluation and SGA rating. The history includes weight change, dietary intake, gastrointestinal symptoms, functional capacity of work and other disease, the last one not applicable in our study, means there were no other significant comorbidities. Physical examination includes loss of subcutaneous fat (triceps, chest), muscle vesting (deltoids), ankle edema, sacral edema, ascites.

Based on this evaluation, patients were classified into three groups: well, moderately malnourished and severely malnourished.

The nutritional status was evaluated also using of combination of BMI (Body Mass Index), TST (triceps skinfold thickness) and MAMC (mid-arm muscle circumference).

RESULTS

A series of 176 hospitalized patients with cirrhosis, 114 (65%) male and 62 (35%) female, median age 52 (range 18-68 years). 81% from the patients were from urban area and 19% from countryside.

The etiology of liver disease was alcoholic in 98 patients (56%), hepatitis B virus in 14 (8%), HCV in 43 patients (24%), HBV and HDV in 10 (7%), 4 patients have primary biliary cirrhosis and autoimmune hepatitis and the rest of 7 patients have other etiology, included Wilson’s disease, non-alcoholic and cryptogenic cirrhosis (Figure 1).

112 patients (64%) are classified as Child A, 56 patients (32%) have Child B cirrhosis and the rest, 8 patients (4%) are Child C (Figure 2).

Ascites was absent in 104 patients (59%), slight in 52 patients (30%) and moderate-to-se-
vere in 20 pts. (11%). Encephalopathy is absent in 132 patients (75%), grade 1-2 in 40 (23%) and grade 3-4 in 4 patients (2%).

Abdominal ultrasound revealed non-atrophic cirrhosis in 108 patients (61%) and in approximately 68 (39%) reduced dimensions of the right hepatic lobe.

Subjective global assessment has permitted classification of the patients into three groups: well-nourished 134 (76%), mild/moderately malnourished 26 (15%) and severely malnourished 16 (9%).

Nutritional parameters measured at initial assessment are mentioned in Table 3.

The well-nourished patients were 134 patients, all Child A and 22 patients were Child B. They have no encephalopathy (88%), or grade 1-2 (8%) or slight ascites (4%), and in 2 cases both elevated serum ammonia and slight ascites.

The etiology of liver disease in those patients is alcoholic in 85 (64%), 9 were HBV infected (7%), 34 have HVC (25%), and 2 (1.33%) HBV and HDV coinfection, 2 with primary biliary cirrhosis (PBC) (1.33%) and 2 with cryptogenic cirrhosis (1.33%).

The mild/moderately malnourished patients were 26; the etiology was alcohol for 6 patients (22%), HBV in case of 3 patients (11%), HCV for 25%, HBV and HDV coinfection in 6 patients (22%), PBC 2 (6%) and other 4 (14%).

Patients with mild/moderate malnutrition were most likely to have grades 1-2 of encephalopathy and ascites slight and moderate.

16 patients were severely malnourished, 7 with alcohol etiology (43%), viral etiology in case of 8 patients (50%) and 1 patient (7%) with other etiology, including cryptogenic. From these 8 patients, 2 have HBV, 2 have HCV and the rest 4 have both HBV and HDV. All these patients have encephalopathy 1-2 or 3-4, ascites moderate or severe.

From all these patients included in the study, the characteristics of nutritional status (SGA) according to Child Pugh classification are included in Table 4.
That means that 76% of patients are well-nourished, 15% are mild/moderately malnourished and 9% are severely malnourished. 88% from mild/moderately malnourished patients are Child B (23) and 12% are Child C. In those patients with severely malnourished cirrhosis 31% have Child C score and only 67% are Child B.

Triceps skin fold thickness (mm) and mid-arm circumference (cm) decrease significantly according to the Child score, a positive correlation was found between these two parameters and the severity of cirrhosis.

Patients with alcoholic cirrhosis have ascites (p<0.05) and hepatic encephalopathy (p<0.001) more frequently and less triceps skin fold thickness than those with non-alcoholic cirrhosis.

Malnutrition was correlated with clinical severity of liver disease.

**DISCUSSIONS**

Subjective Global Assessment (SGA) classified the patients into three groups: well-nourished 134 (76%), mild/moderately malnourished 26 (15%) and severely malnourished 16 (9%).

In our study, 64% from the patients have Child A score, 76% are well-nourished, means that only 24% are mild-moderate malnourished; 59% have no ascites and 75% have no encephalopathy.

15% of all patients have mild-moderately malnourished, many of them (22%) with alcoholic disease. All viral etiology included HBV, HCV and HBV+HDV and is situated at high percentage: 58%. Almost all patients (88%) from these have Child B score. Patients with mild/moderate malnourishment were most likely to have grades 1-2 of encephalopathy and ascites slight and moderate.

The prevalence of alcoholic disease among severely malnourished patients is 43%. 31% have Child C score and only 67% are Child B.

16 patients are severely malnourished 7 of them with alcohol etiology (43%). All these patients have encephalopathy 1-2 or 3-4, ascites moderate or severe (p<0.01).

Triceps skin fold thickness (mm) and mid-arm circumference (cm) decrease significantly according to the Child score, a positive correlation was found between these two parameters and the severity of cirrhosis.

The patients selection for the study that included many patients with Child A score makes the statistical analysis not relevant (p<0.05).

The prevalence of malnutrition in patients with liver disease varies from 10% to 100%, depending largely on the population studied and the methods of nutritional assessment performed (2). Protein-calorie malnutrition can be observed in all clinical stages but is more frequently seen in advanced stages of liver disease. Protein-calorie malnutrition increases patient morbidity and mortality risk (13).

Alcoholic liver disease is most frequently associated with protein-calorie malnutrition. Reported prevalence are between 20% for patients with compensated liver cirrhosis to 100% in hospitalized patients with acute alcoholic hepatitis superimposed on cirrhosis (14).

Assessment for nutritional status is an important component of good medical care. Assessing patient nutritional status is difficult.

Subjective Global Assessment (SGA) is a proven nutritional assessment tool highly predictive of nutrition-associated complications.

In Alberino’s study, malnutrition was shown to be an independent predictor of survival in which the inclusion of mid-arm muscle circumference (MAMC) and triceps skin fold thickness (TST) improved the prognostic accuracy of the Child Pugh score (6).

Nutritional status could be a useful addition to the Child Pugh classification when assessing the prognosis of cirrhotic patients (15).

Abbott et al. investigated the relationship between the Child Pugh classification and nutritional indicators and found that advanced liver disease (CP score) was associated with diminished muscle status and increased malnutrition (16).

The identification of an optimal method of nutritional assessment in patients with cirrhosis is difficult because many of the traditionally measured parameters, such as weight, BMI and biochemical values, vary with the severity of liver disease independently of nutritional status (17).

Subjective Global Assessment (SGA) uses clinical criteria to determine nutritional status and it is more useful than objective measures alone for identifying individuals at nutritional risk because of the ability to encompass the multitude of factors influencing the nutritional status (18).

Subjective Global Assessment (SGA) correlated with the severity of liver disease, and
achieved statistical significance in the multivariable analysis only in the severely malnourished group.

CONCLUSIONS

Our study showed that 76% of all patients are well-nourished. All Child Pugh A patients are well nourished. The prevalence of alcoholic etiology is in this group about 64% (p<0.05).

The mild-moderate malnourished patients are 88% Child B, over 58% with viral etiology. 22% from these patients are alcoholic and 11% have Child C score (p<0.01).

In severely malnourished group, 43% have alcoholic disease and 31% are Child C classification (p<0.01).

Because of the great number of Child A patients included, the statistical significance is present only in moderate and severely malnourished group.

Triceps skin fold thickness (mm) and mid-arm circumference (cm) decrease significantly according to the Child score, a positive correlation was found between these two parameters and the severity of cirrhosis.

Patients with alcoholic cirrhosis have ascites (p<0.05) and hepatic encephalopathy (p<0.001) more frequently and less triceps skin fold thickness than those with non-alcoholic cirrhosis.

Malnutrition was correlated with clinical severity of liver disease.

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