Protein Calorie Malnutrition in Liver Cirrhosis

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Abstract

Malnutrition is prevalent in all forms of liver diseases. Protein calorie malnutrition (PCM) is associated with an increased risk of morbidity and mortality in patients with cirrhosis and occurs in 50%-90% of these patients. Although the pathogenesis of PCM is multifactorial, alterations in protein metabolism plays an important role. This article is based on a selective literature review of protein calorie malnutrition in liver cirrhosis. Malnutrition is prevalent in liver cirrhosis due to the presence of ascites, nausea, vomiting, insufficient food intake, malabsorption and metabolic disorders, poor dietary intake, malabsorption, increased intestinal protein losses, low protein synthesis, and hyper metabolism.

Keywords: Malnutrition; Liver cirrhosis; Ascites; Nausea; Encephalopathy; Jaundice

Introduction

The word cirrhosis comes from the Greek word kirrhos, which means orange yellow. Laennec gave cirrhosis its name kirrhos in 1819 in a brief Footnote to his treatise De l’auscultation mediate [1]. The definition of cirrhosis remains morphological, described by a working party for the World Health organization in 1978 as: “a diffuse process characterized by fibrosis and the conversion of normal liver architectures into structurally abnormal nodules”. Protein caloric malnutrition is a syndrome considered as progressive loss of both lean body mass (protein) and adipose tissue (calorie). Significant changes in the metabolism of protein, carbohydrates and lipids appear simultaneously the consumption of muscular and lipid compartments to satisfy a higher energetic demand [2]. This clinical condition is common in patients with chronic hepatopathy and affects 20% of the patients with compensated cirrhosis and more than 60% of these patients with severe hepatic dysfunction [3,4]. Malnutrition is commonly seen in both alcoholic and nonalcoholic liver disease [5-7] and has been shown to adversely affect outcome (Figure 1).

PCM is associated with a number of complications including development of variceal bleeding and ascites, increased surgical morbidity and mortality, reduced survival, and (in some studies) worsening hepatic function [8-14]. Patients with cirrhosis (particularly those with advanced disease) may also have micronutrient deficiencies. Recognition of macro- and micronutrient deficiencies is important since supplemental nutrition has been associated with a reduction in the risk of infection and in-hospital mortality and improved liver function parameters [15-18].

Prevalence of Protein–Calorie Malnutrition in Cirrhosis

Cirrhosis represents the end stage of most chronic liver diseases. The association of PCM with cirrhosis of any etiology is well-known. A high prevalence of PCM exists in end-stage liver disease. Prevalence ranges from 34% to 82% in patients with alcoholic cirrhosis, based on anthropometric parameters. In patients with nonalcoholic cirrhosis, the prevalence of PCM ranges from 27% to 87% [19]. The largest published nutritional survey showed a 30% prevalence of PCM in male patients and 40% prevalence in female patients with cirrhosis [5]. In one study, 81% of cirrhotic patients had decreased levels of visceral proteins, 59% had abnormal results on immunologic tests and 35% had abnormal results on anthropometric tests [6]. Protein calorie Malnutrition is prevalent in all forms of liver diseases; from 20% in compensated liver cirrhosis to more than 80% in those patients with decompensate disease [8,16,20-23]. Patients with alcoholic liver disease are reported to have a greater incidence of malnutrition than those with nonalcoholic disease [24]. Protein calorie malnutrition has been reported in 100% of those who receive liver transplant and malnutrition is an independent risk factor for morbidity and mortality in these patients. Frequently, patients with end stage hepatic failure will present with muscle wasting, decreased fat stores and overt cachexia. However, many more patients will have subtle changes such as fat-soluble vitamin deficiencies, anemia from iron, folate, and pyridoxine deficiency, altered cell-mediated immune function, and slow loss of mass. [20,24-26]. In a study on 300 patients, Carvalho [27] showed that more than 55% of those with advanced hepatic disease had some degree of malnutrition, which was moderate to severe in 40%. In the same study, 95% of Child-Pugh class C patients were malnourished, as also were 74% of class B and 46% of class A patients [4]. Previous studies in Western patients have documented malnutrition rates from 20% in compensated liver cirrhosis up to 60% in decompensated liver cirrhosis [28]. The estimated prevalence of hyper metabolism varies considerably, with the largest study of 473 cirrhotic patients reporting 34% [29]. A smaller study of 50 cirrhotic patients found only 2 hyper metabolic patients [30].

Assessment of Protein–Calorie Malnutrition in Cirrhosis

The traditional nutritional assessment techniques used for most patients and healthy control subjects do not translate well to cirrhotic patients. The diagnosis of depletion of the visceral protein...
compartment in cirrhotic patients is particularly troublesome because most nutritional markers are proteins produced in the liver. Levels of albumin, prealbumin, and retinol-binding protein, as well as immunologic parameters such as total lymphocyte count and delayed hypersensitivity reactions, is all abnormal in patients with cirrhosis. Estimation of fat and muscle protein compartments by anthropometry of the upper extremities has been used by most investigators to determine the prevalence of PCM. New assessment techniques such as bioelectrical impedance have proven unreliable in cirrhotics with ascites or edema [9]. Perhaps the most accurate technique of nutritional assessment in patients with cirrhosis is the measurement of body cell mass. Body cell mass has been shown to decrease even in early stages of cirrhosis [31]. Objective parameters that may be helpful when monitored serially include anthropometric measurements and dietary intake evaluation [32,33]. The best way to perform a nutrition assessment may be to combine these parameters with the subjective global assessment [SGA].

Outcomes of Protein–Calorie Malnutrition in Cirrhosis

Poor nutritional status is associated with a bad prognosis for survival. This prognosis is shown in patients awaiting liver transplantation, decompensated patients with ascites, and cirrhotic patients undergoing abdominal surgery. [34]. Whether PCM is an independent predictor of survival or simply a reflection of the severity of liver insufficiency [15,35]. For many years malnutrition has been suggested as an important factor in the onset of alcoholic liver disease [20,36,37]. The common malnutritional state of the alcoholics, the association between the severity of the alcoholic liver disease and the degree of malnutrition and the experimental production of steatosis and liver cirrhosis upon methionine- and choline-depleted diets strongly support such correlation [37,38]. Malnutrition is worse in alcoholics from lower social classes, as a direct consequence of the poor nutritional condition [39]. It is well established that alcoholism is the main cause of malnutrition, even with an adequate alimentary supply, due to deficient food intake, anorexia, nausea and vomiting, poor gastrointestinal absorption, inadequate caloric and protein ingestion, alterations in the carbohydrate, protein and fat metabolism and rise in the energetic expenditure resulting from the occurrence of sepsis or ethanol in these patients [22,40]. Malnutrition is yet associated with worse clinical outcomes in cirrhotic patients – leading to complications such as ascites, encephalopathy, heporenal syndrome and diabetes [41], besides the association of worse malnutritional status with higher frequency of death [8,42]. In our view and in the view of others, the cirrhotic patients who are more severely affected by malnutrition are more likely to present complications, such as infectious processes, presumably due to immunological deficiencies in the humoral and cellular responses. Since these alterations lead to an increase in the catabolism, which in turn aggravates malnutrition, a vicious circle is established [42–47]. Causes for malnutrition in liver cirrhosis are known to include a reduction in oral intake (for various causes), increased protein Catabolism and insufficient synthesis, and malabsorption/maldigestion associated with portal hypertension. [8,28,48]. 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 [49].

Mechanism of Malnutrition in Cirrhosis

A variety of mechanisms are considered to contribute to malnutrition in cirrhosis, poor dietary intake, malabsorption, increased intestinal protein losses, low protein synthesis, and hyper metabolism. Many of these are not fully understood. In advanced liver disease, patients often have poor dietary intake. Recommended diets may be unpalatable because of the sodium restriction needed for control of ascites and peripheral edema. A distortion or decrease in taste sensation (dysgeusia) associated with zinc or magnesium deficiency is well described and may contribute [3]. Nausea and early satiety are well recognized, secondary to gastro paresis, tense ascites, small bowel dysmotility, and bacterial overgrowth [30,50]. Malnutrition is further worsened as patients are often starved, for instance, for endoscopy. In addition, as glucose storage is reduced in alcohol-induced cirrhosis [51] gluconeogenesis is active and can cause muscle mass breakdown to provide amino acids for glucose formation [52]. Patients need frequent meals to protect muscle mass, which are not always provided. The metabolic disturbances consequent to liver disease, such as increased energy expenditure [53,54] insulin resistance [55] and low respiratory quotient [indicating reduced glucose and increased lipid oxygenation], [44] may contribute to malnutrition even in the early stages. Hyper metabolic patients tend to weigh less, are more frequently malnourished, and have a higher mortality than normal metabolic patients. The cause of hyper metabolism is unclear, with one group finding no association with sex, etiology, severity of disease, protein depletion, and presence of ascites or tumor. Polyunsaturated fatty acid (PUFA) deficiency is common in cirrhosis, especially in alcoholic cirrhosis, because PUFA synthesis from essential fatty acid precursors occurs in the liver [56].

Etiology of Malnutrition in Liver Cirrhosis

Diagrammatically the etiology of malnutrition in liver cirrhosis is depicted in Figure 2.

There are number of factors which contribute to malnutrition in patients with liver cirrhosis (Table 1).

Some of these factors are related to the disease process itself, such as ascites, causing fullness and early satiety. Other factors are related to frequent hospitalizations, overzealous diet therapy, and “hospital food.” In addition, there are some metabolic factors such as increased metabolic rate, fat malabsorption, and impaired glycogen stores that hasten the development and expression of malnutrition in liver cirrhosis.

Decreased intake

Inadequate food intake is one of the primary causes of malnutrition and occurs in up to two-thirds of patients with chronic liver disease.
documented between 35 and 60 percent of patients [62], which may
bowel bacterial overgrowth in populations with cirrhosis has been
incidence of small bowel bacterial overgrowth. The prevalence of small
patients with cirrhosis have also been reported to have an increased
exocrine insufficiency may be another contributing factor to altered
cirrhosis are deficient in vitamin D [59-61]. Undiagnosed pancreatic
have vitamin A deficiency, and 20–50% of adults with primary biliary
formation. Over one-third of adult patients with chronic cholestasis
fat-soluble vitamins (A, D, E, and K) are also dependent on micelle
essential for digestion of fat by pancreatic and luminal enzymes. The
hepatic bile synthesis may impair micelle formation, which is

calories per day.

Anorexia may result from increased circulating levels of tumor necrosis
factor and leptin [57]. Patients with chronic liver disease also have
delayed gastric emptying compared to controls. [58]. In those patients
with ascites, early satiety and fullness are common complaints.

Altered absorption

Reduced bile secretion due to cholestasis, or compromised
hepatic bile synthesis may impair micelle formation, which is
essential for digestion of fat by pancreatic and luminal enzymes. The
fat-soluble vitamins (A, D, E, and K) are also dependent on micelle
formation. Over one-third of adult patients with chronic cholestasis
have vitamin A deficiency, and 20–50% of adults with primary biliary
cirrhosis are deficient in vitamin D [59-61]. Undiagnosed pancreatic
exocrine insufficiency may be another contributing factor to altered
absorption in those patients with alcoholic liver disease. Finally,
patients with cirrhosis have also been reported to have an increased
incidence of small bowel bacterial overgrowth. The prevalence of small
bowel bacterial overgrowth in populations with cirrhosis has been
documented between 35 and 60 percent of patients [62], which may
further alter nutrient absorption.

Energy expenditure

The resting energy expenditure of patients with chronic liver
disease is variable. Those patients with acute hepatitis or advanced
stages of liver failure have an increased metabolic rate. However, hyper
metabolism is not a constant feature of cirrhosis. Approximately 18%
of cirrhotics have been reported with hypermetabolism, and 30%
with hypo metabolism [39]. The mean deviation between measured
and predicted energy expenditure was 11%, which was less than 200
calories per day.

Altered fuel metabolism

Patients with hepatic failure have “accelerated starvation,” with
an early recruitment of alternative fuel sources. Cirrhotic patients
demonstrate significantly increased fat oxidation and gluconeogenesis
with protein catabolism after an overnight fast. It would take a healthy
adult approximately 72 hours of starvation to reach the same level of
fat oxidation and protein catabolism as occurs in an overnight fast in a
cirrhotic patient [63,64]. It is believed that the diminished hepatic
and muscle glycogen stores that occur with cirrhosis are a factor in
this accelerated rate of starvation. Patients without adequate glycogen
stores utilize increased fat and muscle protein for fuel even during
short-term fasting. This contributes to the loss of subcutaneous fat and
muscle wasting that is the hallmark of malnutrition. Insulin resistance
and decreased levels of insulin like growthfactor-1 are also believed to
contribute to muscle wasting in cirrhosis (Table 2) for a list of some of
the factors which affect the fuel metabolism in cirrhotic patients.

Pathogenesis of malnutrition

The pathogenesis of malnutrition in cirrhosis is multifactorial
[22]. Protein, carbohydrate, and lipid metabolism are all affected by
liver disease. Contributing factors include inadequate dietary intake,
damaged digestion and absorption, and altered metabolism.

Anorexia, nausea, encephalopathy, gastritis, ascites, and a sodium
restricted diet and concurrent alcohol consumption can all contribute
to a reduction in dietary intake.

Malabsorption and malnutrition of nutrients can result from bile
salt deficiency, bacterial overgrowth, altered intestinal motility, portal
hypertensive changes to the intestine, mucosal injury, and increased
intestinal permeability [65-69].

Cirrhosis represents an accelerated state of starvation and as such,
fuels other than glucose (protein, lipids) are used [21].

There is an overall loss of protein from reduced synthesis of urea
and hepatic proteins, reduced intestinal protein absorption, and
increased urinary nitrogen excretion. Liver disease is associated with a
lowered ratio of branched-chain to aromatic amino acids.

Abnormal carbohydrate metabolism is associated with insulin
resistance, impaired gluconeogenesis and reduced glycogen stores. As a
result, lipids are preferentially oxidized for energy and the respiratory
quotient (RQ) is less than in patients without chronic liver disease
[21,44]. The RQ is defined as the ratio of the volume of CO₂ production
to the volume of O₂ consumption.

Studies on the effect of chronic liver disease on the resting energy
expenditure have mixed results [50,63,70,71]. One study suggested
that energy expenditure in patients with cirrhosis was similar to
controls after adjusting for body surface area [18]. In contrast, a cross-
sectional study of 473 patients with cirrhosis found that 34 percent
had hypermetabolism as measured by indirect calorimetry [72]. The
increase in resting energy expenditure correlated with lean body mass
but not with the severity or type of liver disease and was, in part,
attributed to an increase in beta-adrenergic activity. Other studies have

- Increased or decreased metabolic rate
- Glucose intolerance/insulin resistance
- Rapid postprandial gluconeogenesis
- Reduced glycogen stores
- Elevated leptin
- Elevated TNF-a
- Decreased insulin-like growth factor-1

Table 2: Metabolic Alterations in Cirrhosis [88].
demonstrated that hypermetabolism persists at least one year after liver transplant and correlates with a reduction in survival [73].

Conclusion
Malnutrition is very common in liver disease and gets worse with the severity of the underlying liver problems. Poor nutritional status is associated with a worse prognosis with respect to mortality, encephalopathy, variceal bleeding and infection. Protein calorie malnutrition occurs in as many as 90% of patients with cirrhosis and leads to a negative prognosis for the patient by increasing the risk of other disease complications. The development of PCM is multifactorial which has strong influence on liver cirrhosis and it is important for healthcare providers to first identify patients at risk of PCM. Second, healthcare providers should provide them with the best and most appropriate nutrition intervention beneficial to patients according to their needs, clinical status, and disease stage.

Author’s Contribution
The author of the paper is doing research work on “Nutritional Assessment & Dietary Habits of Liver Cirrhosis Patients in Kashmir” and the subject review paper is part of a research work. Acquisition, analysis and interpretation of data and subsequent drafting of the Review Paper has been carried out.

The Co-Author had sufficient participation in the work and the Review Paper has been framed under her supervision.

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