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; Ascents; 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 muscle 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...
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 hypermetabolism. 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. PUFA deficiency has been found in plasma lipids, erythrocytes, platelets, and adipocytes [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 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 indicate bowel bacterial overgrowth in populations with cirrhosis has been described. The prevalence of small bowel bacterial overgrowth in those patients with alcoholic liver disease. Finally, patients with cirrhosis are deficient in vitamin D [59-61]. Undiagnosed pancreatic insufficiency is common. Vitamin A deficiency, and 20–50% of adults with primary biliary cirrhosis and chronic cholestasis have vitamin A deficiency, and 20–50% of adults with primary biliary cirrhosis have vitamin A deficiency. Over one-third of adult patients with chronic cholestasis have been reported with decreased 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, hypermetabolism 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, impaired 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 hypertension 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 renal 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 reported hypermetabolism in patients with cirrhosis [39]. The mean deviation between measured and predicted energy expenditure was 11%, which was less than 200 calories per day.

**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.

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### Table 1: Factors that contribute to malnutrition in patients with liver cirrhosis [68].

| Decreased intake | Decreased absorption | Lactrogenic factors |
|------------------|---------------------|-------------------|
| Anorexia         | Inadequate bile flow| Overzealous dietary restriction |
| Early satiety    | Bacterial overgrowth| Frequent paracentesis |
| Asceltes         | Pancreatic insufficiency | Diuresis (micro nutrient losses) |
| Altered mental status/encephalopathy | | Lactase deficiency |
| Frequent hospitalization | | Lactulose therapy |

### Table 2: Factors that contribute to muscle wasting in cirrhosis (Table 2) for a list of some of the factors which affect the fuel metabolism in cirrhotic patients.

| Decreased 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 [68].

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