Nutritional management of liver cirrhosis and its complications in hospitalized patients

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Received: 28 September 2020
Accepted: 30 December 2020

ABSTRACT – Background – Cirrhosis is a chronic and progressive liver disease that occurs from prolonged hepatocellular injury. Malnutrition causes complications in cirrhosis patients that worsen the condition to liver failure. Both are closely linked and increase the chances of morbidity and mortality. Regular nutritional screening and monitoring is prime concern for such patients including comprehensive dietary history, laboratory tests, and evaluation of muscle loss and strength capabilities to determine the degree of frailty. For efficient assessment of liver cirrhosis patients Subjective Global Assessment has been used worldwide. The nutritional objectives for such individuals should be to regain liver functions, to prevent complications associated, and to overcome nutritional deficiencies causing malnutrition. Methods – We conducted a literature review using PubMed, Google Scholar and Science Direct for this purpose, a total of 130 articles were reviewed out of which 80 (from the past 5 years) including originally published research, review articles and abstracts were also included. Exclusion criteria of the selected studies was year of publication, irrelevancy and animal studies based on the purpose of current study. The aim of this study was to check nutritional management in patients having complications of liver cirrhosis. Results – According to the guidelines, for the conservation of normal nutritional status of the malnourished patients‘, energy should be provided 35 kcal/kg/day while to prevent hypoalbuminemia and maintain the protein stores in the body, 1.5 g/kg/day protein has been recommended. Carbohydrates and fats for cirrhosis patients are recommended 50% to 60% and 10% to 20% of the total dietary intake respectively. Conclusion – Initial identification and prevention of malnutrition have the probability to lead to better health outcomes, prevention of complications of the disease, and improving quality of life.

Keywords – Cirrhosis; malnutrition; encephalopathy; nutritional support; quality of life.

INTRODUCTION

The liver is one of the major organs of the body that carries more than five hundred functions in the body. Metabolism of all macronutrients carbohydrates, fats and protein takes place in liver accordingly. Liver has been considered very significant in respect to nutrition. Moreover, it plays major roles in enzymatic functions and liver cirrhosis among them chronic hepatitis (B and C), steatohepatitis, alcoholic liver disease, non-alcoholic steatohepatitis (NASH), and non-alcoholic fatty liver disease (NAFLD) are common. Malnutrition is the most prominent issue in hospitalized chronic liver disease patients. Malnutrition occurred by multiple factors such as nausea, vomiting, early satiety, constipation, and liver cirrhosis complications. Malnutrition at the early phase of chronic liver disease may increase the disease burden, early onset of complications, increase the length of hospital stay, morbidity, and mortality.

Nutrition assessment

To combat malnutrition early nutrition screening within 24 to 48 hours of hospital stay should be needed. Malnutrition is closely linked with increases chances of morbidity and mortality in patients that may be explained as loss in mass and strength of skeletal muscles as well as reduced subcutaneous and visceral fat. It may be present in 5% to 99% of the patients and also depends on the tools that are being used for assessment. Complete nutrition

Declared conflict of interest of all authors: none
Disclosure of funding: no funding received
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Limitations

Validity for a length of hospital stay

The results of MUST tool, categorized patients in low risk, moderately malnourished, and severely malnourished. According to the patient’s conditions and ascites or edema, it can be used to identify patients with severe malnutrition.

Other nutrition assessment tools for liver cirrhosis patients include Chair Stand test, it is evaluated by counting the number of times a patient can fully stand up from the chair and sit down within 30 seconds without taking help from hands or any external object. A 6-minute walk test is another test that can be used to assess the functional capacity of hospitalized patients. It is simple, inexpensive, and required no training or special instructions before the test. It may be affected according to the patient’s conditions and skeletal muscular morbidities. Psoas muscle index is an easy method and not affected by the abdominal swelling. It can be used as a predictor of mortality in liver cirrhosis patients. Accuracy of the test may be affected due to excess fluid in the body, BMI, and activity levels. Liver Frailty Index (LFI) is a test for assessment of physical function and related health outcomes in cirrhosis patients. It comprises three tests including handgrip strength, chair stand test, and balance. LFI is non-expensive, safe, and easy to perform in conscious patients, its results may be affected if hepatic encephalopathy exists or due to patient’s efforts. Literature has supported the validity of the frailty index in cirrhosis patients for prediction of mortality.

**Subjective global assessment**

For efficient assessment of liver cirrhosis patients Subjective Global Assessment (SGA) has been using worldwide. In SGA short term and long term data of the patients has been acquired by either questioning or physical assessment. Parameters in SGA are weight change, dietary intake, gastrointestinal symptoms (nausea, vomiting, satiety, constipation, and others), functional capacity and related health outcomes in cirrhosis patients. It comprised three tests including handgrip strength, chair stand test, and balance. LFI is non-expensive, safe, and easy to perform in conscious patients, its results may be affected if hepatic encephalopathy exists or due to patient’s efforts. Literature has supported the validity of the frailty index in cirrhosis patients for prediction of mortality.

**TABLE 1 Anthropometric measurement in liver cirrhosis patients.**

<table>
<thead>
<tr>
<th>Methods</th>
<th>Uses</th>
<th>Limitations</th>
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<tbody>
<tr>
<td>Body mass index (BMI)</td>
<td>Quick, non-invasive method for nutrition assessment of hospitalized patients. For liver cirrhosis patients BMI can be calculated by using dry weight. It can be measured by using the formula BMI = weight in kg/Height in m². BMI classified as: Underweight (BMI &lt; 18 kg/m²), Normal (BMI 18.5-24.9 kg/m²), Overweight (BMI 25-29.9 kg/m²), Obese (BMI ≥ 30 kg/m²)</td>
<td>Reduce reliability for liver cirrhosis patients due to the presence of ascites and edema.</td>
</tr>
<tr>
<td>Mid arm muscle circumference (MAMC)</td>
<td>It is measured by using a measuring tape from the acromion process of the scapula to the olecranon process in cm. It predicts the muscle mass of the body. Its values are also valuable to calculate MAMC of the patients for a clear depiction of muscle mass of the body.</td>
<td>Reliability of this tool is based on the observer experience. Difficult to identify patients with severe malnutrition.</td>
</tr>
<tr>
<td>Triceps skin fold thickness (TSF)</td>
<td>It is the body measurement method used to assess the fat mass. In liver cirrhosis patients for identification of sarcopenia TSF is a better method. TSF values are not affected by fluid retention. It is measured by using the formula MAMC = (MAC-TSF × 0.341)</td>
<td>The reliability of this tool is based on observer experience. Difficult to identify patients with severe malnutrition. Cannot be estimated correctly in people having ascites or edema.</td>
</tr>
<tr>
<td><strong>DEXA</strong></td>
<td>It is a body measurement method that assesses lean soft tissues, bone mineral content, and fat mass.</td>
<td>DEXA miscalculates the prevalence of sarcopenia in patients with fluid overload.</td>
</tr>
<tr>
<td><strong>Bioelectrical Impedance analysis (BIA)</strong></td>
<td>It acts on the conductance of hydrated tissues, measures the total volume of body water and assesses the lean body mass through an equation</td>
<td>It is controversial to use in uncompensated liver cirrhosis. It is an independent factor for mortality but it weekly correlates with muscle mass.</td>
</tr>
<tr>
<td><strong>Hand grip strength</strong></td>
<td>It is used to record the mean value after taking three measurements by the dominant arm gripping the dynamometer and the value is recorded in kilograms</td>
<td></td>
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</table>

There are other assessment tools to identify malnutrition in patients that include the Malnutrition Universal Screening Tool (MUST). In this tool malnutrition among patients can be detected by using weight loss, body mass index, and disease-related dysfunction. The results of MUST tool, categorized patients in low risk of malnutrition, medium and high risk of malnutrition based on the score assembléed subsequently. It can be used to be predictive validity for a length of hospital stay. Mini Nutrition Assess-

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Nutritional management

For hospitalized liver cirrhosis patients, after complete assessment, medical nutrition therapy should be applied. The provision of adequate calories and protein should be ensured to prevent malnutrition. To provide adequate nutrients balanced oral diet is highly recommended. In liver cirrhosis, the patient’s ratio of aromatic amino acid and branched-chain amino acids is disturbed due to hyper metabolism, altered liver function, and decrease dietary intake. Oral supplementation in patients with malnutrition or borderline nutritional status is a better option to avoid further deterioration. General recommendations such as small and frequent meals, snacks enriched in branched-chain amino acids have been supported by many studies for liver cirrhosis patients. Patients that are unable to take essentials through oral diet should be transferred to enteral nutrition. In patients with contraindication of enteral nutrition after assessing their conditions and time of regime practitioner switch it to parenteral nutrition support.

Nutritional support has been prioritized for liver cirrhosis patients to prevent and manage malnutrition as evidenced by literature. The priority of nutrition restoration in cirrhosis patients is the provision of adequate calories and protein. The next priorities for hospitalized patients are the management of meal frequency and quality of protein. For hospitalized patient’s hyperglycaemia has been reported as a common complication in many studies. That is linked with the hyper metabolic state and altered functioning of the liver. For both peripheral parenteral nutrition and total parenteral nutrition, hyperglycaemia should be avoided in the patients by giving glucose 2–3 g/kg/day or less than or equal to 1 g/kg/day. Other than this in patients with ascites and edema fluid overload should be avoided by providing high concentration formulas. According to ESPEN (European Society for Clinical Nutrition and Metabolism) guidelines of nutritional management in liver cirrhosis patients, for the conservation of normal nutritional status of the malnourished patient’s, energy should be provided 35 kcal/kg/day while to prevent hypoalbuminemia and maintain the protein stores in the body, 1.5 g/kg/day protein has been recommended (TABLE 2).

TABLE 2. Nutritional recommendations in liver cirrhosis.

<table>
<thead>
<tr>
<th>Categories (Nutritional status)</th>
<th>Nutritional recommendations</th>
</tr>
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<tbody>
<tr>
<td>Malnourished</td>
<td>Calories 30–40 kcal/kg body weight/day</td>
</tr>
<tr>
<td></td>
<td>Protein 1.2–1.5 g/kg body weight/day</td>
</tr>
<tr>
<td></td>
<td>Lipids 10–20% of daily requirements</td>
</tr>
<tr>
<td>Normally nourished</td>
<td>Calories 35 kcal/kg body weight/day</td>
</tr>
<tr>
<td></td>
<td>Protein 1.5 g/kg body weight/day</td>
</tr>
<tr>
<td></td>
<td>Lipids 10–20% of daily requirements</td>
</tr>
<tr>
<td>Overweight and obese</td>
<td>Calories 20–25 kcal/kg body weight/day</td>
</tr>
<tr>
<td></td>
<td>Protein &gt;1.5 g/kg body weight/day</td>
</tr>
<tr>
<td></td>
<td>Lipids 10–20% of daily requirements</td>
</tr>
</tbody>
</table>

Recent studies have reported that for hospitalized liver cirrhotic patient’s nutrition care process could be better attained by early nutrition screening with the help of a multidisciplinary team, continuous monitoring at certain intervals, and follow up. This kind of approach will help the patients to reduce disease-related malnutrition and complications. Nutrition therapy in cirrhotic patients and chronic alcoholic hepatitis patients has been proved to be beneficial to reduce complications, morbidity, and mortality.

Micronutrient deficiency in liver cirrhosis patients is also stated that is possibly due to inadequate oral intake, restricted diet, altered taste, gastrointestinal problems, and others. A systematic review had reported the effect of severe vitamin D deficiency on mortality rates of hospitalized liver cirrhosis patients. Supplementation within the upper limit ranges can be supplemented to the patients. Moreover, there is a need for conduction of clinical trials to identify the efficiency of vitamin D supplementation on clinical outcomes of the patients. A study was performed to assess trace minerals (copper, selenium, zinc, and magnesium) levels in liver cirrhosis patients and associate them with the severity of the disease. The result showed a significant decrease in the trace minerals except for copper. A significant correlation was found between trace minerals status and severity of disease that was further linked with liver dysfunction.

Biomarkers

Biomarkers that represent serum albumin are very important in assessing the nutritional status of the patient as the synthesis and breakdown of albumin decreases in liver cirrhosis as compared to a person having a normal liver function. Other biomarkers include red blood cell count, liver function tests, cholinesterase, albumin, rapid turnover proteins, vitamins (A, D, E, K, B6, B12, and folate) minerals, adipocytokines and creatinine height index in the urine. Serum albumin concentration can be affected by many factors such as the type and amount of food taken, digestion, and absorption from the intestine. It is the main secretion protein and synthesis occurs in the liver but its concentration decreases in patients with liver cirrhosis as compared to the one having normal liver functions.

To check the short term status of nutrition in liver cirrhosis patients’ rapid turnover proteins that include pre-albumin, retinol-binding protein, and transferrin are also used as biomarkers. Adipocytokines are also important biomarkers for nutritional status. Leptin, adiponectin, and resistin are important peptide hormones. Plasma adiponectin comes in three forms; low molecular weight, medium, and high molecular weight. And in patients with liver cirrhosis, high molecular weight form is increased and is also related to the severity of liver damage in such patients. Vitamins (both fat and water-soluble), as well as trace minerals such as copper, zinc, iron, selenium and manganese, should also need to be considered while having a nutrition assessment of the patient.
Inadequate oral intake in liver cirrhosis patients is the key factor participating in malnutrition. Diseased patients are unable to take adequate calories and protein resulting in deteriorated nutritional status. Various studies stated different methods to increase oral intake of hospitalized liver cirrhosis patients that includes smaller meals with increased frequency, improves sensory characteristics of the meal, mealtime without any interruption, and nutrition education\(^{31,44,45}\). To prevent and reverse the degree of malnutrition in patients, improvement of dietary intake is a crucial factor. A study was conducted to improve the intake of patients enriched with BCAA. For this purpose, late evening snacks enriched with BCAA was introduced to liver cirrhosis patients. Results showed that the Fischer ratio (BCAA: AAA) was significantly increased in patients with late evening snacks as compared to control\(^{46}\). Fischer ratio is defined as the ratio of branched chain amino acids to aromatic amino acids and is important for assessing liver metabolism, hepatic functional reserve and liver dysfunction severity. The study suggested that providing patients with late evening snacks helps in the improvement of total dietary intake as well as the Fischer ratio that prevents patients from further complications\(^{47}\).

A randomized control trial has been conducted in liver cirrhosis patients to investigate the effect of high protein, high fiber diet supplemented with branched-chain amino acids for 6 months. The study showed an increase in muscle mass and a decrease in fat mass in the trail group while the levels of ammonia and glucose in serum did not elevate. Hence, supplementation of BCAA with protein and fiber is worth considering intervention among cirrhotic patients\(^{48}\). Another clinical trial was conducted in post-operative liver cirrhosis patients to assess the efficacy of parenteral fatty acids in the recovery of patients. Results showed that patients receiving 10% of 3 fatty acids for 5 days (post-operation) had reduced morbidity and mortality as compared to other patients as well as there was decrease length of hospital stay and infections among the patients\(^{49}\).

Hospitalized liver cirrhosis patients who are unable to take adequate nutrition related to other complications should be shifted towards enteral nutrition support. Routes can be varying in patients according to the patient’s conditions that would be either nasogastric feeding, nasojugal feeding, or percutaneous endoscopic gastrostomy feeding protocols\(^{50}\). Patients on enteral nutrition should be monitored appropriately to avoid complications.

In critically ill patients, enteral nutrition should be initiated with 10–20 mL per hour with critical monitoring of gastrointestinal symptoms. The energy and protein supply of patients will be planned with a lower level to prevent feeding intolerance\(^{51}\). In liver cirrhosis key objective of nutritional management is the prevention of malnutrition and maintenance of nutritional status in patients. For this purpose, adequate energy and protein intake should be prioritized. Energy expenditure can be calculated by using formulas or directly according to ESPEN (European Society for Clinical Nutrition and Metabolism) guidelines\(^{52}\). Sources of protein should be introduced precisely to the patients according to the condition of patients. Protein sources can vary from animal sources to plant sources by taking BCAA to AAA ratio under consideration to prevent further complications\(^{52}\).

Complications of liver cirrhosis and nutrition management

One of the most common complications reported in decompensated liver cirrhosis patients is ascites. Ascites is well-defined as less than or equal to 200 mL fluid accumulation in the abdominal cavity as a result of any clinical manifestation. Pathophysiology of ascites in liver cirrhosis patients is portal hypertension and hypoalbuminemia for most of the cases. Usually, ascites is further classified into three grades based on the signs and symptoms and volume of fluid accumulated in the peritoneal cavity\(^{53}\). Some of the studies support the nutritional management of ascites as sodium and total fluid intake restriction for the shorter duration of time\(^{44}\), furthermore, providing adequate calories and protein to the patient prevents them, from hypoalbuminemia that will help the patients against ascites\(^{45}\). According to the European association for the study of liver, limited data was available on the sodium levels recommendation in ascites. However, the study supported sodium restriction (1.8–2.0 grams/day) would be helpful in patients with edema and ascites\(^{56,57}\).

Hepatic encephalopathy is another severe liver cirrhosis complication that is defined as brain dysfunction associated with liver insufficiency and portal hypertension leading to end-stage liver disease, morbidity, and mortality in patients\(^{58}\). Hepatic encephalopathy is categorized into four stages that depend upon the signs and symptoms of the patients\(^{59}\). Grade 1 patients are characterized by sleep disorder and altered attention, grade 2 includes patients with complaints of disorientation, personality disorders, and lethargy. Grade 3 is described with confusion, altered speech, and disorientation that is followed by coma categorized as stage 4 of hepatic encephalopathy\(^{60}\). Nutritional management in this stage is very crucial. Although protein restriction is controversial in hepatic encephalopathy. A systemic study reported 16 randomized trials on hepatic encephalopathy patients concluded that the provision of branched-chain amino acid rich sources has beneficial effects on patients. In advanced liver cirrhosis, the patient’s level of branched-chain amino acids (leucine, isoleucine, and valine) in serum decreased resulting in hepatic encephalopathy. Branched-chain amino acids facilitate the synthesis of glutamate by providing nitrogen to alpha-ketoglutarate\(^{61}\). Glutamate is a substrate in brain and muscle cells for ammonia detoxification into glutamine. In advanced liver disease patient ratio of aromatic amino acids (tyrosine, tryptophan, and phenylalanine) and branched-chain amino acids decreases commonly termed as Fischer ratio. A decrease in the Fischer ratio characterizes progression in liver disease resulting in hepatic encephalopathy\(^{62}\). Supplementation of BCAA helps in liver cirrhosis to prevent complications and improve survival rates\(^{63}\). Nutritional recommendations for hepatic encephalopathy are further categorized based on severity. For low-grade hepatic encephalopathy patients (grade 1,2) 25–35 kcal/day calories and 1–1.5 g/kg/day while for severe encephalopathy patients (garde 3,4) 25–35 kcal/day calories and >1 g/kg/day protein is recommended. Protein sources in such types of patients should be shifted towards plant sources with BCAA rich solutions\(^{64,65}\).

A longitudinal study was planned in liver cirrhosis patients to evaluate the effect of branched-chain amino acids in glucose metabolism, skeletal muscle, and survival of patients\(^{66}\). Results revealed that after dietary branched-chain amino acids for 48 weeks there was a significant decrease in intramuscular adipose tissue while skeletal muscle mass increases that improved the survival of liver cirrhosis patients\(^{67}\). Another retrospective cohort study was done recently to evidence the beneficial effects of long term supplementation of BCAA in liver disease. In a group where patients take supplementation for approximately 6 months, there was a significant improvement in the MELD (model for end stage liver disease) score as compared to the control group. A MELD score...
is basically a number that ranges from 6–40 and it tells about the degree of sickness and the need of the transplant, higher score denotes higher need of liver transplant. Moreover, there was a significant difference in serum albumin, bilirubin and CP score between both groups\(^{(66)}\). Systematic reviews supported beneficial effects of BCAA supplementation especially improving muscle strengths, survival rates, edema, and ascites in hepatic encephalopathy patients\(^{(67)}\). Another study was reported to highlight the importance of branched-chain amino acids supplementation in liver cirrhosis patients for improving muscle strength and volume\(^{(68,69)}\).

Another major complication in decompensated liver cirrhosis patients is oesophageal varices. Oesophageal varices is defined as enlarged veins of esophagus resulting due to obstructed blood flow from portal vein. In case of severe complications (as stated above) and inadequate oral intake, first priority of optimizing nutrition is oral supplementation that will progress towards nutritional support based on patient’s condition\(^{(11,33,54)}\).

Portal hypertension is another complication in liver cirrhosis patients further associated with ascites, intrahepatic vascular resistance, hepatic encephalopathy and oesophageal varices. Literature suggested that portal hypertension can be efficiently reduced by various approaches to prevent disease related complications and malnutrition in advanced liver cirrhosis patients\(^{(72)}\).

There are multiple contributing factors for malnutrition in advanced liver disease patients. Most important is an inadequate oral intake that is associated with dysgeusia, anorexia, early satiety, restricted diet, and NPO for a certain duration of time as criteria for testing. Hyper metabolism and malabsorption in liver cirrhosis patients are also a causative factor in malnutrition that is due to ascites, increased protein metabolism, impaired glycogen metabolism, bacterial overgrowth, and impaired bile secretion\(^{(72,74)}\). Cirrhotic patients with the above mentioned complications have an increased probability of malnutrition\(^{(70)}\). Malnourishment in such patients causes deterioration of not only anthropometric measure-

ments but also affects biochemical profile and dietary intake. In liver cirrhosis, malnutrition is linked with decreased liver functioning, handgrip strength, and quality of life\(^{(66-70)}\).

**CONCLUSION**

In summary, malnutrition is exceptionally prevalent among cirrhosis patients. Regardless of cause and severity, it is important to screen all patients to identify the malnutrition in such patients. Although several assessment tools are available for scoring the severity of complications a standardized simple and accurate method for evaluating malnutrition remains a challenge in end-stage liver disease patients. Precise and accurate assessment of nutritional status in cirrhotic patients is the top priority so that proper nutrition intervention can be planned and implemented to prevent complications of the disease. Intake of quality protein and adequate supplementation can overcome deficiencies and complications associated with end-stage liver failure. Guideline for a nutritional recommendations and dietary plan must be referred with ESPEN (European Society for Clinical Nutrition and Metabolism) and EASL (European Association for the Study of the Liver) for chronic liver disease and cirrhosis patients.

**Authors’ contribution**

Javaid N compiled the initial literature review, conceptualize study design and write up the initial draft of the paper. Iqbal AZ complete the literature research as well as review and edit the document at each stage. Hameeda M helped with the write up of initial draft and revision of manuscript.

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