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Research Article
Impact of Malnutrition on Nutritional and Non Nutritional Factors in End Stage Liver Disease

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Abstract

Background and Objective: Malnutrition has a negative effect on the outcome of liver transplantation surgery. However, there are very few studies focusing on association of nutrition status on nutritional and non-nutritional factors before the surgery which can further guide nutrition therapy and prevent nutrition mediated complications. The objective of study was to analyze the impact of nutrition status on both nutritional and non nutritional factors in patients with End Stage Liver Disease (ESLD). **Materials and Methods:** The study recruited 54 ESLD adult patients. Subjective Global Assessment was used for nutritional assessment. Nutritional factors like anthropometric profile, body composition, dietary intake, dietary advice received and consumption of dietary supplements were assessed. Non-nutritional factors like aetiology, severity of the disease [Child Turcotte Pugh (CTP) grades], degree of ascites, biochemical status, Quality of Life, Performance Status and functional inability were assessed during the course of study. The analysis was performed by SPSS version 17.0, associations between factors were analyzed by chi-square test and kruskal-wallis test with the significance level of <0.05. **Results:** Majority (75.8%) of the patients were moderately malnourished while 9.1% were severely malnourished. Malnutrition in ESLD was significantly ($p<0.05$) associated with non-nutritional factors like aetiology, CTP grade C, tense ascites, lower haemoglobin levels, higher functional inability, fatigue and lower grades of Performance Status. Also, nutritional factors like normal triceps levels, higher fat mass and body fat%, lower muscle mass and Fat Free Mass, higher weight loss and lower calorie intake were significantly ($p<0.05$) associated to malnutrition. **Conclusion:** Nutritional status assessment is a crucial step in treatment of ESLD. The present study showed association of malnutrition with various nutritional and non-nutritional factors which could become major challenges in prognosis and treatment of ESLD patients.

Key words: End stage liver disease, nutrition status, subjective global assessment, nutrition factors, non-nutritional factors

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Patients with End Stage Liver Disease (ESLD) frequently have varied metabolic abnormalities of carbohydrate, protein and lipid metabolism that lead to gradual deterioration of their health and nutritional status. The diagnosis of Protein Energy Malnutrition (PEM) in ESLD is marked by muscle wasting and subcutaneous fat loss. Protein breakdown is prevalent in approximately 20% cirrhotics without any complications[1]. Child and Turcotte[2] classification developed primary prognostic score for liver disease which included nutrition status as a major determining factor for liver disease severity. There are a number of factors that contribute to malnutrition in hepatic failure such as ascites, anorexia, encephalopathy, altered gustatory sensations, frequent hospitalizations, overzealous diet restrictions and unpalatable "Hospital food" which leads to early satiety, nausea and low dietary intake[3].

Previous studies have shown 100% prevalence of malnutrition in ESLD patients. Nutritional status has been reported as one of the variable that is highly correlated with patients' survival. Also, malnutrition is independent of the disease status therefore it is potentially reversible[4-9]. Malnutrition by different assessment tools has been found to be significantly ($p<0.05$) associated to various clinical variables like aetiology, CTP (Child Turcotte and Pugh) Scores, MELD (Model for End Stage Liver Disease) Scores, degree of ascites, blood product usage, blood loss during the surgery, mortality, body composition analysis (fat mass, fat free mass, muscle mass and body fat%), prolonged ventilator support and longer stay in the intensive care unit and hospital[8,10-12]. Nutrition intervention has been reported as a crucial factor for the recovery of malnourished ESLD patients. Since these patients are at higher risk for nutritionally mediated complication, therefore nutrition interventions are considered comparatively cost-effective during the preoperative period of liver transplant. It is therefore important to identify and correct nutritional deficiencies in ESLD patients[13-18]. However, the accurate nutritional status assessment in ESLD patients is difficult, mainly because of overlap with other complications like fluid retention and hypoproteinemia. Liver disease has varied aetiology which affects conventional markers of nutrition like serum proteins levels synthesized by the liver (albumin, transferrin, retinol-binding protein) and immunological dysfunction. Irrespective of these problems in nutrition assessment, malnutrition can be assessed in 20% of patients with compensated liver disease and in >80% with decompensated liver disease[6,19]. It is necessary to obtain complete nutrition evaluation of liver disease patients and to identify the possible areas for nutrition interventions.

European Society for Parenteral and Enteral Nutrition (ESPEN) guidelines on liver disease 2006 recommended simple bedside methods such as Subjective Global Assessment (SGA) and/or anthropometric parameters to diagnose patients with poor nutritional status. Further, Bio Impedance Analysis (BIA) which can be used to quantify malnutrition despite of certain limitations of the technique in patients with ascetic decompensation. An appropriate nutritional evaluation should include combination of various methods like SGA, anthropometry and body composition analysis to assess nutrition status of ESLD patients[20,21].

The SGA is a clinically useful, simple, inexpensive and safe bedside tool and thus remains the gold standard for new bedside assessment tools. It is an integrated tool that utilizes clinical judgment of a practitioner to identify patients at risk of or with malnutrition[22]. It is also able to predict nutrition-associated complications such as infections, use of antibiotics and length of hospital stay. It is the preferred assessment method for ESLD patients[22-25]. SGA has high specificity (96%) and low sensitivity (22%) for diagnosing malnutrition in patients with Chronic Liver Disease (CLD). It has been used as a nutrition assessment tool from about 2 decades now in liver disease patients[22,25].

Considering the high prevalence of malnutrition in ESLD patients and its association with disease severity and outcome, the present study was undertaken to analyze the association of nutrition status with various factors (nutritional and non-nutritional) using SGA as a nutrition assessment tool.

MATERIALS AND METHODS

This exploratory study was performed on adult (age $\geq$18 years) ESLD patients (n = 54) at 3 tertiary level care multispecialty hospitals in Delhi-NCR, India. Those patients who gave informed consent were purposely recruited (54) during the study period of September 2013- March 2014. Ethical Clearance was obtained from the Lady Irwin College Institutional Ethical Committee. The following category of patients were excluded: Patients' aged below 18 years as there is different protocol of paediatric ESLD treatment and patients with acute liver disease who had to undergo emergency transplantation.

Data collection

Subjective global assessment: Nutrition assessment was performed by SGA. The five features of SGA were analyzed (Fig. 1) to provide the complete nutrition profile of patients. The first was weight loss in the past 6 months. Weight loss of about or <5% was considered as normal, between 5 and 10% is considered as potential significant weight loss and greater

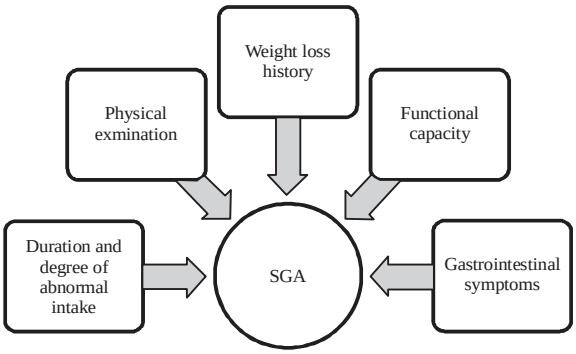

Fig. 1: Components of subjective global assessment
SGA: subjective global assessment

than 10% as highly significant weight loss. The pattern of weight loss was also considered. The second feature was considering dietary intake with respect to patients' usual dietary pattern. Patients were then categorized as normal or abnormal intake. The degree and duration of abnormal intake were also considered (starvation, hypo caloric liquids, full liquid diet and suboptimal solid diet). The third feature is the presence of significant gastrointestinal symptoms like anorexia, nausea, vomiting and diarrhoea. These symptoms should be persisting on a daily basis for more than 2 weeks. Shorter duration of diarrhoea or intermittent vomiting is not considered significant. Vomiting daily or twice daily secondary to obstruction is considered significant. The fourth feature was patient's functional ability from bedridden to full ability to perform daily routine functions. The last feature was about the metabolic stress due to the underlying disease state[23,24].

Assessment of nutritional factors: Certain nutrition factors which are related to the diet, intake and nutrition status were also studied during the course of the study. This included the Simplified Nutrition Assessment Questionnaire (SNAQ) Score which was calculated to analyze the appetite affected weight loss[26]. Nutritional parameters included various anthropometric measurements like present body weight (Kg), Height, Mid Upper Arm Circumference (MUAC)[27], Triceps Skin Fold and Mid Arm Muscle Circumference (MAMC)[28]. Patients' body composition was analyzed by Bio Impedance Analysis (BIA) on available patients to provide data on body weight, Fat Mass, Fat Free Mass (FFM), Body Fat%, Muscle Mass of ESLD patients[29]. Dietary intake assessment was performed by 24 h dietary recall[30]. The patients calorie intake was categorized in three ranges >75, 75-50 and <50%. Information regarding advice given by dietician to increase intake, recommendation of dietary supplement, were also gathered.

Assessment of non-nutritional factors: Information on the following non-nutritional factors was collected: Disease severity by CTP Grades A, B, C[2] and MELD Scores[31] where higher grades depict more severe liver failure; diagnoses of the patients; levels of ascites which was graded as no, mild and tense ascites; information regarding laboratory parameters such as Heamoglobin, WBCs, Platelets, Albumin, Bilirubin (Total), ALT, AST, Alkaline phosphatase, creatinine, sodium, potassium were gathered.

Assessment of quality of life: The Quality of Life (QoL) of the patients was analyzed by calculating the two composite scores: Physical Component Summary (PCS) and Mental Component Summary (MCS) from Short Form-36 (SF-36) Questionnaire[32].

Assessment of performance status: Performance Status (PS) was analyzed using Eastern Cooperative Oncology Group (ECOG) Scores; the patient's functional ability was analyzed by observing the patient's ability to perform normal daily routine activities (none/moderate/severe) and the reasons for inability (fatigue, anxiety, discomfort and drowsiness) were also recorded[33].

Statistical analysis: All statistical analysis were performed using the Statistical Package for Social Science (SPSS) version 17.0 for Windows (SPSS Inc., Chicago, IL, USA)[34]. Categorical variables were presented as frequencies. Associations between categorical variables were evaluated through chi-square tests. Normal variables were presented as mean±SD and were analyzed by Kruskal Wallis test. An acceptable level of statistical significance was $p<0.05$.

RESULTS

Demographic profile of ESLD patients: The data showed that 74.0% of the ESLD patients were men and the mean age of the sample population was 48.8±10.2 years. Majority of the patients were Indians and 40.7% of the patients had blood group B+ (Table 1).

Common symptoms because of the underling liver conditions were pale stools (25.9%), dark urine (57.4%), excessive fatigue (81.4%), jaundice (100%) and tense ascites (58.1%). Low mean albumin levels (2.2 g L^{-1}) and high bilirubin levels (5.6 mg dL^{-1}) were reported. Majority (98%) had no food allergies. According to SNAQ, 68.5% of the patients had low appetite because of which they had risk of $\geq$5% weight loss within 6 months. The mean weight loss was 4.4 kg± 5.3 in the past six months.

Table 1: General and medical history of end stage liver disease patients

Parameter	Category	Result
Age years (Mean±SD)		48.8±10.2
Gender % (N)	Male	74.0 (40)
	Female	25.9 (14)
Nationality % (N)	Indian	61.1 (33)
	Other Asian Countries	38.8(21)
Blood group % (N)	A+	22.2 (12)
	AB	3.7 (2)
	B+	40.7 (22)
	O+	33.3 (18)
Symptoms % (N)	Pale Stools	25.9 (14)
	Dark Urine	57.4 (31)
	Excessive Fatigue	81.4 (44)
	Jaundice	100 (54)
Ascites % (N)	No ascites	32.6 (14)
	Mild ascites	9.3 (4)
	Tense ascites	58.1(25)
Bilirubin (T) (Mean±SD (mg dL^{-1})		5.6±4.3
Albumin (g L^{-1}) (Mean±SD)		2.2±0.8
Food allergy % (N)	No	98.1(53)
	Yes	1.9 (1)
Weight loss Kg (Mean±SD)		4.4±5.3
SNAQ Score % (N)	No risk of weight loss	31.5 (17)
	Risk of ≥5% weight loss within 6 months	68.5 (37)
CTP Grade % (N)	A	1.9 (1)
	B	37.0 (20)
	C	61.1 (33)
MELD Scores % (N)	>24	7.4 (7)
	19-24	51.9 (28)
	<19	40.7 (22)
Etiology % (N)	HCV related CLD	27.8 (15)
	HBV related CLD	18.5 (10)
	HBV related CLD with HCC	1.9 (1)
	Ethanol + HCV related CLD	7.4 (4)
	Ethanol related CLD	22.2 (12)
	HCC	5.6 (3)
	Cryptogenic CLD	11.1 (6)
	Autoimmuno CLD	1.9 (1)
	Obstructive Jaundice	1.9 (1)
	HBV+HCV related CLD	1.9 (1)
Other illness % (N)	Diabetes	20.4 (11)
	Hypertension	13.0 (7)
	Diabetes +hypertension	5.6 (3)
	No	59.3 (32)
	Diabetes+Hypotension	1.9 (1)
CAGE Score	≥2	31.5% (17)
	Nonalcoholic	68.5% (37)

%: Percentage, N: No. of patients, SD: Standard deviation, CLD: Chronic liver disease, HBV: Hepatitis B Virus, HCV: Hepatitis C Virus, SNAQ: Simplified nutrition appetite questionnaire, CTP: Child turcotte and pugh, MELD: Model for end stage liver disease, Kg: Kilogram, HCC: Hepato cellular carcinoma

The CTP Scores depicted 61.1% of the patients in CTP grade C and 51.9% of the patients in the MELD range of 19-24. Diagnostically 27.8 and 22.2% of the patients were suffering from liver disease because of HCV related infections and ethanol related CLD, respectively. 59.3% of the patients were not having any other medical problem whereas 20.4% of the patients were diabetics. According to CAGE questionnaire 31.5% of the patients were alcoholic (Table 1).

The PS assessment of the patients showed that 51.2% were capable for all self-care activities but were unable to carry routine work activities, 27.9% were capable of only limited self-care, confined to bed and 14% were completely disabled. The QoL assessment by SF-36 showed a patient score of <50±10 in the two summary scores, PCS 19.43±9.12 and MCS 21.65±7.77 (Table 2).

Dietary profile: The dietary profile of the patients (Table 3) showed 88.9% of the patients were on dietary restrictions like salt which were recommended as per the symptoms. Fluid was restricted in 79.7% of the patients. Amount of fluid

Table 2: ECOG-PS and Quality of Life assessment of ESLD patients

Parameter	Category	Result	
		No.	%
ECOG-PS	0-Fully active, able to carry on all pre-disease performance without restriction	0	0
	1-Restricted in physically strenuous activity but ambulatory and able to carry out sedentary work	7	3
	2-Ambulatory and capable of all self-care but unable to carry out any work activities	51.2	22
	3-Capable of only limited self-care, confined to bed or chair more than 50% of waking hours	27.9	12
	4-Completely disabled. Cannot carry on any self-care. Totally confined to bed	14.0	6
	5- Dead	0	0
Quality of Life (QoL) (Mean±SD)	Physical component summary scores	19.43±9.12	
	Mental component summary scores	21.65±7.77	

ECOG-PS: Eastern cooperative oncology group- Performance Status, percentage, N: No. of patients, SD: Standard deviation

Table 3: Dietary profile of ESLD patients

Parameter and category	Result	
	No.	%
Special diet		
Yes	88.9	48
No	11.1	6
Type of diet		
Normal	94.4	51
Soft	5.6	3
Food restricted		
Salt	59.3	32
Fried and spicy	1.9	1
Salt and fluid	25.9	14
No restriction	13.0	7
Chewing problem		
No	100	54
Yes	0	0
Fluid restriction		
Yes	79.7	43
No	20.3	11
Fluid permitted		
<1.5 L	59.3	32
<1 L	11.1	6
Gastro Intestinal problem		
Yes	0	0
No	100	54
Dental problem		
Yes	0	0
No	100	54

%: Percentage, N: No. of patients

restriction also varied with 59.3% of the patients' recommended restricting fluid to <1.5 L and 11.1% of the patients had fluid restriction of less than 1 L. Salt was restricted in about 59.3% of the patients and 25.9% of the patients were having both salt and fluid restriction. A small percentage (1.9%) was advised to avoid fried and spicy food. About 94.4% of the patients were recommended a normal diet (in terms of consistency). None of the patients reported any gastrointestinal (GI) symptoms, chewing or dental problems.

Nutrition assessment: The nutrition status of ESLD patients was analyzed by SGA method. All the five features of SGA

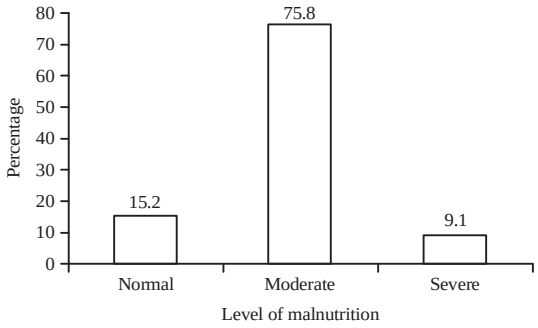

Fig. 2: Nutrition assessment by subjective global assessment (SGA)
SGA: subjective global assessment

(Fig. 1) were analyzed and the patients were graded as normal, moderate malnourished or severe malnourished. Majority of the patient (Fig. 2) were moderately malnourished (75.8%), about 9.1% of the patients were severely malnourished and only about 15.2% of the patients had normal nutritional status.

Association of malnutrition with non-nutritional factors

Nutrition status with prognostic factors: Malnutrition affected various prognostic factors like CTP, MELD Scores, indications of liver disease, degree of ascites and laboratory parameters (Table 4). The CTP Scores showed significantly higher moderately malnourished patients in grade C ($p = 0.010$) than A and B whereas MELD Scores did not present any significant relation with nutrition status. Higher moderate malnutrition among ESLD patients were significantly associated to all the indications of liver disease except HCC, HBV+HCC ($p = 0.002$). The patients with moderate and severe malnutrition had significantly higher ($p = 0.03$) tense ascites than normal patients. Among the laboratory parameters only haemoglobin showed significantly lower ($p = 0.02$) levels in moderately and severely malnourished ESLD patients.

Nutrition status assessment with performance status and QoL: Table 5 shows lower performance status with higher

Table 4: Association of various prognostic factors with nutrition status

	SGA Grade						
	Normal		Moderate malnutrition		Severe malnutrition		
Prognostic factors	No.	%	No.	%	No.	%	p-value
CTP Grade							
A	1	16.7	0	0	0	0	0.010*
B	4	66.7	14	31.1	2	66.7	
C	1	16.7	31	68.9	1	33.3	
Total	6	100	45	100	3	100	
MELD Grade							
1	0	0	3	6.7	1	33.3	0.230
2	4	66.7	24	53.3	0	0	
3	2	33.3	18	40	2	66.7	
Total	6	100	45	100	3	100	
Indications of ESLD							
HCV related CLD	1	16.7	14	31.1	0	0	0.002**
HBV related CLD	0	0	10	22.2	0	0	
HBV With HCC	1	16.7	0	0	0	0	
Ethanol+HCV related CLD	0	0	4	8.9	0	0	
Ethanol related CLD	0	0	9	20	3	100	
HCC	2	33.3	1	2.2	0	0	
Cryptogenic CLD	1	16.7	5	11.1	0	0	
Autoimmuno CLD	1	16.7	0	0	0	0	
Obstructive jaundice	0	0	1	2.2	0	0	
HBV+HCV related CLD	0	0	1	2.2	0	0	
Total	6	100	45	100	3	100	
Ascites							
No	5	83.3	14	31.1	0	0	0.030*
Mild	1	16.7	3	6.7	0	0	
Tense	0	0	28	62.2	3	100	
Total Laboratory parameters (Mean±SD)	6	100	45	100	3	100	
Hemoglobin	11.52±1.33	9.53±2.07	9.40±1.75	0.022*			

%: Percentage, *significant (p<0.05), **Highly significant (p<0.01), N: No. of patients, SD: Standard deviation, CLD: Chronic liver disease, HBV: Hepatitis B virus, HCV: Hepatitis C Virus, CTP: Child turcotte and pugh, MELD: Model for end stage liver disease, HCC Hepato cellular carcinoma

ECOG-PS scores. Malnourished patients had significantly higher ECOG-PS scores than the normal patients (p = 0.049). Moderately malnourished patients were significantly higher in ECOG-PS Grade 2, 3 and 4 than normal patients (p<0.05). The functional inability of the patients showed that malnourished patients showed significantly higher moderate and severe inability to perform daily routine activities than normally nourished patients (p<0.001*). The data on reasons for functional inability showed significantly higher fatigue (p = 0.017*) in malnourished patients than the normal patients. Other reasons of functional inability like anxiety, discomfort and drowsiness did not show any significant relation with nutrition status. The QoL assessment with malnutrition showed lower PCS and MCS scores in malnourished patients than the patients with normal nutrition status but it did not show any significant difference.

Association of malnutrition with nutritional factors

Nutrition status with anthropometric parameters: Various anthropometric parameters were used to measure the physical changes among the patients. MUAC, MAMC, present body weight and BMI did not show any significant relation with nutrition status assessment by SGA among ESLD patients. However, Triceps skin-fold measurement showed significantly (p = <0.001**) normal triceps levels in moderate malnutrition depicting no effect of malnutrition on triceps skin fold thickness (Table 6).

Nutrition status assessment with other nutrition parameters: The nutrition status is a dynamic state and it gets affected by various nutritional factors like appetite, intake and dietary advice. Malnourished patients were having significantly lower calorie intake (75-50%, <50%) than the normal nourished patients (Table 7) (p = 0.013). Also significantly higher body weight loss in the past 1 month was seen in malnourished patients than the normal patients (p = 0.045). No significant association was seen with other nutrition parameters like advice given to increase intake by the dietician, provision of dietary supplement and Appetite (SNAQ Score).

Table 5: Association performance status and quality of life with nutrition status

	SGA Grade						
	Normal		Moderate malnutrition		Severe malnutrition		
Parameters	No.	%	No.	%	No.	%	p-value
ECOG-PS							
1-Restricted in physically strenuous activity but ambulatory and able to carry out sedentary work	1	20.0	2	5.7	0	0	0.049*
2-Ambulatory and capable of all self-care but unable to carry out any work activities	4	80	17	48.6	1	33.3	
3-Capable of only limited self-care, confined to bed or chair more than 50% of waking hours	0	0	12	34.3	0	0	
4-Completely disabled. Cannot carry on any self-care. Totally confined to bed	0	0	4	11.4	2	66.7	
Total	5	100	35	100	3	100	
Functional inability							
None or moderate for few days	3	50.0	1	2.2	0	0.0	<0.001**
Moderate for weeks or months or severe for weeks	3	50.0	28	62.2	1	33.3	
Severe and bedridden for weeks or months	0	0.0	16	35.6	2	66.7	
Total	6	100	45	100	3	100	
Fatigue							
Yes	5	83.3	45	100	3	100	0.017*
No	1	16.7	0	0.0	0	0.0	
Total	6	100	45	100	3	100	
Quality of Life by SF-36							
PCS (Mean±SD)	21.47±8.12		19.68±9.26		11.75±6.91		0.213
MCS (Mean±SD)	26.43±5.67		21.54±7.69		13.69±7.50		0.084

ECOG-PS: Eastern cooperative oncology group, SF-36: Short form-36, N: Number of patients: Percentage: MCS, Mental component summary scores, PCS: Physical component summary scores, *Significant (p<0.05), **Highly significant (p<0.01), SD: Standard deviation

Table 6: Association of anthropometric parameters with nutrition status

	SGA Grade						
	Normal		Moderate malnutrition		Severe malnutrition		
Anthropometric parameters	No.	%	No.	%	No.	%	p-value
MUAC Cut off							
Severe	0	0	5	11.1	0	0	0.536
Moderate	0	0.0	7	15.6	1	33.3	
Normal	6	100	33	73.3	2	66.7	
Total	6	100	45	100	3	100	
MAMC cut off							
Normal	5	83.3	31	68.9	2	66.7	0.934
Moderate	1	16.7	12	26.7	1	33.3	
Severe	0	0.0	2	4.4	0	0	
Total	6	100	45	100	3	100	
Triceps							
Normal	6	100	33	73.3	0	0	<0.001**
Moderate	0	0	11	24.4	0	0	
Severe	0	0	1	2.2	3	100	
Total	6	100	45	100	3	100	
Present weight Kg (Mean±SD)	63.22±8.23		72.87±13.21		70.07±3.02		0.213
BMI N							
Norma	4	66.7	22	48.9	3	100	0.736
Underweight	0	0.0	2	4.4	0	0.0	
Overweight	1	16.7	10	22.2	0	0.0	
Obese	1	16.7	11	24.4	0	0.0	
Total	6	100	45	100	3	100	

MUAC: Mid Upper arm circumference, MAMC: Mid arm muscle circumference, *Significant (p<0.05), **Highly significant (p<0.01), N: No. of patients, Percentage, SD: Standard deviation

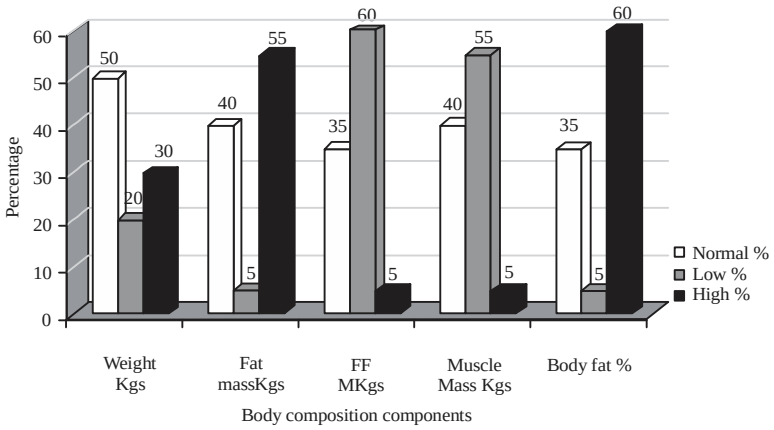

Fig. 3: Body composition analysis by bio impedance analysis
BIA: Bioelectrical impedance analysis, wt.: weight, FFM: Fat free mass, Mus., muscle, percentage, Kgs: Kilograms

Table 7: Association of various nutrition parameters with nutrition status

	SGA Grade						
	Normal		Moderate malnutrition		Severe malnutrition		
Nutrition parameter	No.	%	No.	%	No.	%	p-value
Intake calories %							
>75%	1	16.7	0	0.0	0	0.0	0.013*
75-50%	3	5	9	20	0	0.0	
<50%	2	33.3	36	80	3	100	
Total	6	100	45	100	3	100	
Advise to increase intake given or not							
Yes	4	66.7	34	75.6	3	100	0.539
No	2	33.3	11	24.4	0	0	
Total	6	100	45	100	3	100	
Dietary supplement							
Yes	0	0	14	31.1	2	66.7	0.103
No	6	100	31	68.9	1	33.3	
Total	6	100	45	100	3	100	
Body weight loss before 1 month							
<5%	6	100	29	64.4	0	0	0.045*
5-9%	0	0	6	13.3	1	33.3	
≥10%	0	0	10	22.2	2	66.7	
Total	6	100	45	100	3	100	
SNAQ score							
≤14	2	33.3	33	73.3	2	66.7	0.140
>14	4	66.7	12	26.7	1	33.3	
Total	6	100	45	100	3	100	

MUAC: Mid upper arm circumference, MAMC: Mid arm muscle circumference, *significant (p<0.05), **highly significant (p<0.01), N: No. of patients, percentage, SD: Standard Deviation

Nutrition status assessment with body composition analysis: The body composition of ESLD patients analyzed using Bio Impedance Analysis (Fig. 3), showed low levels of Fat Free Mass (FFM) and Muscle mass in 60 and 55% of the ESLD patients respectively along with higher fat mass (55%) and body fat % (60%). This showed disturbed body composition of the patients in ESLD.

Moderately malnourished patients had significantly higher fat mass and body fat% and significantly lower FFM and Muscle mass (p<0.05) than the normally nourished patients (Table 8).

DISCUSSION

In the present study, nutrition status assessment by SGA showed only 15.2% of the patients as normal whereas 75.8% of the patients were moderately malnourished and 9.1% as severely malnourished (Fig. 2). Considering the high

Table: 8: Association of body composition parameters with nutrition status

	SGA Grade						
	Normal		Moderate malnutrition		Severe malnutrition		
Body composition analysis	No.	%	No.	%	No.	%	p-value
BIA wt. Kg							
High	0	0	6	37.5	0	0	0.415
Low	1	50	3	18.8	0	0	
Normal	1	50	7	43.8	2	100	
Total	2	100	16	100	2	100	
BIA fat mass Kg							
High	0	0	11	68.8	0	0	0.008*
Low	0	0	0	0.0	1	50	
Normal	2	100	5	31.3	1	50	
Total	2	100	16	100	2	100	
BIA (ffm) Kg							
High	0	0	0	0	1	50	0.005*
Low	0	0	12	75	0	0	
Normal	2	100	4	25	1	50	
Total	2	100	16	100	2	100	
BIA (mus. Mass) Kg							
High	0	0	0	0	1	50	0.008*
Low	0	0	11	68.8	0	0	
Normal	2	100	5	31.3	1	50	
Total	2	100	16	100	2	100	
BIA (body fat %)							
High	0	0	12	75	0	0	0.005*
Low	0	0	0	0	1	50	
Normal	2	100	4	25	1	50	
Total	2	100	16	100	2	100	

BIA: Bioelectrical impedance analysis, wt: weight, ffm: Fat free mass, *significant (p<0.05), **highly significant (p<0.01), N: No. of patients, percentage, Kg: Kilograms

prevalence of malnutrition and gradual deterioration of ESLD patient condition[5,6], it is important to acknowledge and rectify various nutritional complications in ESLD[13-17] which can be attained by an in-depth nutritional assessment using SGA. The present study used SGA as nutrition status indicator because a previous publication by Bakshi and Singh[25], has already shown that only SGA had moderate agreement with phase angle of the body ($\kappa = 0.444$) among various other nutrition assessment methods and was associated with various clinical and prognostic variables of patients undergoing LT.

Various prognostic factors reflected the prevalence and extent of malnutrition among ESLD patients (Table 4). The data showed significantly higher malnutrition in ESLD patients irrespective of the aetiology (p<0.05). Also previous studies have documented malnutrition in ESLD patients is independent of the varied aetiology of liver disease[15,20,25,35-40]. The present study demonstrated significantly higher (p = 0.01) prevalence of malnutrition in higher CTP grades which is comparable to various studies that have associated a higher CTP and MELD grade (higher degree of disease severity) with malnourished ESLD patients[35-38]. Malnutrition in ESLD patients has been associated to degree/severity of ascites as a major symptom of liver disease[35,41,42]. In the present study also SGA showed malnourished patients were significantly having tense ascites than mild/no ascites (p<0.01). Among the various laboratory parameters, a significantly lower (p = 0.02) haemoglobin levels were reported among malnourished patients. Other laboratory factors did not show any significant difference in the malnourished ESLD patients. The findings from the present study thus clearly show a negative impact of malnutrition on prognosis of the ESLD.

Performance Status (PS) assessment of the patients is to analyze the actual level of ability of self-care. Several major surgeries have repeatedly demonstrated that PS is an important prognostic factor for survival[5,6,43]. There are very few studies[44-46] focusing on PS of ESLD patients. But, there is dearth of information on association of malnutrition and PS in ESLD patients. In the present study, lower PS grades are depicted in Table 2 which is comparable to the already existing studies that have used ECOG-PS scale to assess the functional ability of the ESLD patients[44-46]. The association of ECOG-PS of the patients with nutrition status, showed significantly lower PS grades in malnourished patients (moderate and severe) as compared to normal patients (p<0.05). Also, there was significantly higher (p<0.05) functional inability to perform daily routine activities and

fatigue in malnourished patients than the normal patients (Table 5). Various studies have individually focused on the urgency of interventions focusing on improving malnutrition and PS[43-50]. But, the present study presents the only data on the association of PS and malnutrition. No significant results were observed between nutrition status and Quality of Life (QoL) scales of ESLD patients (Table 5).

The present study showed significantly normal triceps levels in moderately malnourished patients (Table 6). Anthropometric parameters like MUAC and Triceps skin-fold thickness and MAMC are simple, useful and recommended methods to assess muscle and fat mass in ESLD patients[37,38]. But, the present study showed that only physical examination by anthropometric measurements might not be reliable as a nutritional assessment tool for ESLD patient. A combination of nutritional assessment tool is therefore recommended for nutrition evaluation of ESLD patients[21].

Nutrition issues usually occur in liver disease due to decreased intake[3]. To our knowledge, there is a paucity of data on effect of nutrition status on various nutrition related factors like appetite, calorie intake, advice given to improve intake and dietary supplements etc. The present study showed significantly lower ($p<0.05$) calorie intake and higher weight loss prior to 1 month of assessment among malnourished patients (Table 7). The possible reasons for low intake could be early satiety because of ascites, increase in Resting Energy Expenditure (REE) before paracentesis and, dietary restrictions like low sodium and fluid intake which can reduce the palatability of food[3,4,51-53]. Hence, aggressive nutrition support with a focus to improve the calorie intake and body weight among ESLD disease patients can be expected to improve the nutrition state.

Due to altered metabolism in ESLD patients, there is altered body composition (Fig. 3). The present study in Table 8 showed significantly higher ($p<0.05$) fat mass and higher body fat% and significantly lower FFM and Muscle Mass among malnourished ESLD patients ($p<0.05$). In ESLD increased REE has also been observed during complications of liver disease, such as acute hepatic failure[51], high volume ascites[41], or presence of hepatocellular carcinoma. The diagnosis of malnutrition in ESLD is marked by muscle wasting and subcutaneous fat loss. Even in stable patients, protein depletion is prevalent in approximately 20% cirrhotics[1]. Hence, the body composition analysis in ESLD provides crucial information on the overall nutritional health of the ESLD patient.

According to the present study malnutrition assessed by SGA showed association with various nutritional and non-nutritional factors. Although the present study has limitations of small sample size and there is need for larger prospective studies on the impact of malnutrition in ESLD with various factors that can pave the way for formulating nutrition therapy plan at the earliest which can directly affect the prognosis and further treatment of these patients.

CONCLUSION

Though nutritional status assessment could be challenging task for patients with ESLD, the importance of this assessment cannot be overlooked. Malnutrition was found to be significantly associated to higher CTP Scores, aetiology, tense ascites, lower haemoglobin levels, decreased calorie intake, weight loss, lower Performance Status, inability to perform daily functions, lower fat free mass, muscle mass, higher fat mass and body fat% among ESLD patients in the present study. Hence, the study underscores an immediate need of nutrition intervention focusing on improving the nutrition status of the ESLD patients for better treatment and holistic wellbeing.

SIGNIFICANCE STATEMENT

This study discovers the effect of malnutrition on various nutritional and non-nutritional factors that can be beneficial for planning nutrition interventions for ESLD patients. This study has uncovered the critical areas of association of various factors with ESLD malnutrition that many researchers were not able to explore. Thus a new theory on nutrition protocol for ESLD may be arrived at for the holistic wellbeing of patients.

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