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Impact of pre-transplant nutritional status on prognosis following liver transplantation

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Abstract
Malnutrition is almost universally present in patients with End Stage Liver Disease (ESLD) undergoing liver transplantation and has been associated with delayed ICU stay, increased morbidity and mortality. After liver transplant (LT), when liver function is restored, amelioration in the nutritional status is expected. After liver transplantation in fact dietary intake rapidly normalizes and fat mass is progressively regained while the recovery of muscle mass can be slower. Although there is no gold standard for the assessment of nutritional status in patients with liver disease, anthropometric measurements, such as arm muscle circumference and triceps skin fold, SGA and HGS have been utilized in large groups of patients, mainly in those awaiting LT, and proved to be useful in identifying muscle and fat depletion. In this study, the nutritional status of a group of 29 Indian and Middle East patients was prospectively analyzed prior to transplantation, at the time of discharge from the hospital (post LT) and at the completion of one month post LT, and the relationship between nutritional status and prognosis were analyzed. The statistical analysis of this data suggested that a significant proportion of patients undergoing liver transplantation are nutritionally compromised and it was found that the overall nutritional status of most subjects improved post LT, which may be possibly improved by nutritional intervention.

Keywords: End Stage Liver Disease, Liver Transplantation, nutritional status

1. Introduction
The liver has metabolic functions, and when affected by disease may cause nutritional deficiencies, leading to Protein-Energy Malnutrition (PEM). Its manifestation is caused by different factors, which include inadequate food intake, abnormal nutrient metabolism and altered digestion and absorption, together with an increased catabolism and an increase in protein-energy requirements [1].
Malnutrition is associated with progressive liver failure, as a result of which the most malnourished patients have a worse prognosis for the illness, as morbidity and mortality increases both before and after the transplant [2]. It is associated with increased hospital admissions and longer stays, raising costs both before and after the transplant [3, 6].
It is imperative that anthropometric, clinical, biochemical and nutritional assessments coupled with appropriate nutritional interventions are absolutely necessary to understand their potential beneficial effect on prognosis in patients post liver transplantation.

2. Material and Methods
2.1 Aim of the study
To study the impact of pre liver transplant nutritional status of patients on post-liver transplant prognosis assessed in terms of length of ICU stay.

2.2 Objectives of the study
1. To assess the nutritional status of patients awaiting liver transplantation using the anthropometric, biochemical, clinical, dietary, functional and SGA (Subjective Global Assessment) methods in three stages
   a. Pre transplant stage
   b. Post-transplant stage
   c. Follow up stage
2. To compare the assessments made at each stage (pre-transplantation Vs Post-transplantation Vs follow up)
3. To study the impact of nutritional status on the post transplantation prognosis assessed in terms of length of ICU stay.

2.3 Research design
Prospective research design was adopted in this study. A prospective study is one in which individuals are selected on the basis of factors that are to be examined for possible effect on some outcome. The individuals are followed for a period of time to determine the effect of factors under study on the outcome of the study [4].
This study involved a follow-up of patients registered in Hepato Pancreatic Biliary and Transplantation Department (HPB Dept.) of Global Hospitals, Chennai, who were listed in the waiting list for liver transplantation.

2.4 Sample size
Twenty nine male and female adult subjects of Indian origin awaiting liver transplantation participated in this study.

2.5 Sampling design
Purposive sampling was used to select subjects for this study.

2.6 Phases of the study
The study was conducted in three phases as shown in the table 1.

Table 1

Phase I	Phase II	Phase III
Pre-transplant (at the time of registration)	**Post-transplant (at the time of discharge from hospital)**	**Follow up (one month after transplantation)**
The following assessments were made: Anthropometric – weight, Mid arm circumference, Triceps Skin fold measurement. Biochemical - Assessment of haemoglobin, albumin and total protein Clinical- MELD - the Model for End stage Liver Disease Dietary – food diary Functional- hand grip strength. SGA- Subjective Global Assessment	All assessments repeated at the time of discharge. The length of ICU stay was recorded	All assessments were repeated after the completion of one month of the transplant.

3. Results

3.1 Degree of malnourishment predicted using subjective global assessment (sga) prior to liver transplantation

Subjective global assessment (SGA) is a technique that combines multiple elements of nutritional assessment to classify the severity of malnutrition[5]. These components are weight loss during the previous 6 months, changes in dietary intake, gastrointestinal symptoms, functional capacity, metabolic demands, signs of muscle wasting, and the presence of presacral or pedal edema. Based on this evaluation, patients in the present study were classified into three groups: well (A), moderately malnourished (B) and severely malnourished (C). According to SGA, malnutrition was present in nearly 80 per cent of the patients, and of these, 20 patients (male and female) were moderately and 8 (male and female) were severely malnourished.

3.2 Comparison of anthropometric assessments

The weight, mid upper arm circumference and Triceps skin fold thickness was assessed at the pre-transplant stage, post-transplant stage and after a follow up period of one month.

The following three comparisons were also made to see if there was any improvement in these assessments after transplantation:

1. Pre-transplant Vs Post-transplant
2. Pre-transplant Vs follow up
3. Post-transplant Vs follow up

A significant decrease in weight was observed after transplantation which was the result of significant improvement in ascites post transplantation. The weight did not improve further during the one month follow up assessment. The mid arm circumference and the triceps skin fold thickness however Showed a statistically significant increase during the post transplantation and the follow up phase.

3.3 Comparison of biochemical assessments

The hemoglobin, serum albumin and total protein levels which are direct indicators of an individual's nutritional status were assessed. The findings are tabulated in table 2

Table 2: Comparison of Biochemical Assessments (Pre Transplantation Vs Post Transplantation Vs Follow Up)

Biochemical Parameters	Stage	Mean	SD	Comparisons made	p value
Haemoglobin (g/dl)	Pre-transplant	10.31	1.58	Pre-transplant Vs Post-transplant	0.004***
	Post-transplant	9.35	1.05		
	Follow up	9.98	1.10	Pre-transplant Vs follow up	0.249 NS
				Post-transplant Vs follow up	0.000***
Albumin (g/dl)	Pre-transplant	2.79	0.48	Pre-transplant Vs Post-transplant	0.399 NS
	Post-transplant	2.69	0.48		
	Follow up	2.99	0.47	Pre-transplant Vs follow up	0.092 NS
				Post-transplant Vs follow up	0.002***
Total Protein (g/dl)	Pre-transplant	6.52	1.51	Pre-transplant Vs Post-transplant	0.007
	Post-transplant	5.58	0.86		
	Follow up	5.79	0.86	Pre-transplant Vs follow up	0.034
				Post-transplant Vs follow up	0.137

There was a statistically significant decrease in the haemoglobin levels (g/dl) post transplantation. However, a statistically significant increase in the same parameter was observed during the follow up phase. The albumin levels (g/dl) also showed a statistically significant increase in the follow up period. A similar observation was made for total protein (g/dl) as well.

Albumin denotes the functional ability of the liver and improvement in its level post transplantation signifies a normally functioning liver with good synthetic function.

3.4 Comparison of functional assessment

The handgrip strength is considered a simple and reliable method to evaluate muscle function in liver disorders and indirectly, the nutritional status in clinical setting. It is measured using the dynamometer.

Handgrip strength improved significantly at the time of discharge after liver transplantation but 1month after the transplantation, there was no statistically significant change. This might take a time period of 6 months to 1 year to improve.

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3.5 Clinical assessment using the meld system

The Model for End-Stage Liver Disease (MELD) system is a numerical scale used for adult liver transplant candidates. The range is from 9 (less ill) to 40 (gravely ill). The individual score determines how urgently a patient needs a liver transplant within the next three months. The number is calculated using the most recent laboratory tests.

Lab values used in the MELD calculation include:

1. Bilirubin, which measures how effectively the liver excretes bile.
2. INR (formally known as the prothrombin time).
3. Creatinine, which measures kidney function.

There are five levels within the MELD continuous disease severity scale. They are:

40 or more — 71.3% mortality
30–39 — 52.6% mortality
20–29 — 19.6% mortality
10–19 — 6.0% mortality
<9 — 1.9% mortality

The MELD scores for patients fell into scores ranging between 10 and 19 (6.0 per cent mortality category). The MELD score is currently accepted as a disease severity index of cirrhotic patients awaiting liver transplantation.

3.6 Comparison of dietary assessment

There was a highly significant improvement in the calorie and protein intake of patients post transplantation. This may be one reasons for improvement in the haemoglobin, serum albumin and total protein levels during the follow up phase.

Malnutrition is a well-known complication of advanced liver disease and is associated with detrimental consequences if left untreated. It is, therefore, of critical importance to assess the nutritional status of all patients with chronic liver disease and to optimize nutritional support in these patients. A structured nutritional counseling session was conducted for the patients by the researcher of the study. Separate counseling sessions were conducted for the pre-transplant and the post-transplant phase.

3.7 Correlation between specific pre-transplant nutritional Status indicators and ICU stay

The impact of pre-transplant nutritional status on prognosis post liver transplantation can be best understood by studying the length of the ICU stay. Better the nutritional status, better will be the prognosis and shorter the ICU stay. Specific nutritional status indicators such as SGA and Protein intake exhibited a positive correlation to the length of ICU stay. It was observed that when the SGA scores and protein intake was good, it reduced the length of ICU stay, thus substantially reducing the treatment cost.

4. Conclusion

Nutritional aspects are important both for patients awaiting liver transplantation and for those who live on with a liver graft. While pre-transplant patients and those in the immediate post-transplant period usually require correction of numerous nutritional deficiencies to improve their overall condition, post-transplant liver patients have to be followed up to ensure they do not develop over nutrition. Both settings require an interdisciplinary approach that integrates the expertise of physicians, surgeons, nutritionists, and nursing staff who are well-aware of these issues. Only with joint efforts can nutritional imbalances be overcome to optimize the outcome of patients in liver transplant programs.

5. References

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