

Original Research

Nutritional Counseling Improves the Nutritional Status, Liver Function, and Serum Electrolytes of Patients with Liver TransplantationSaba Tanveer ¹, Ali Saad R. Alsubaie ², Rezzan Khan ³, Hajra Ahmed ⁴, Mahpara Safdar ⁴, Zainab Bibi ³, Sadaf Yousaf ⁵, Bismillah Sehar ⁶, Iftikhar Alam ⁷, Aiman Hadayat ⁸, Falak Zeb ^{9,10,*}

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Abstract

Nutrition counseling may assist liver transplant patients in controlling weight gain, addressing micronutrient deficiencies, and maintaining metabolic status. This study aimed to determine the effect of nutritional counseling on nutritional status, liver profile, and serum electrolytes of liver transplant patients. In this case-control study, 100 patients were recruited from Shifa International Hospital, Islamabad, who were potential liver transplant candidates. They were divided into two groups: a case group, who were given nutrition counseling (n = 50), and a control group, who were not provided nutrition counseling (n = 50). Data was collected about patients' socio-economic status, medical history, anthropometric, biochemical and dietary profiles. Independent t-tests, chi-square tests for qualitative frequency distribution, and paired t-tests were used. At baseline, the weight and BMI of the case and control were comparable, but there was a non-significant difference. Nutrition counseling was effective in improving biochemical variables (potassium at preoperative, sodium and albumin during illness; p-value < 0.05), Liver function (ALT at preoperative and postoperative, AKT at preoperative, during sickness and postoperative; p-value < 0.05) and macronutrient profile (fat intake during illness and protein intake during postoperative stage; p-value < 0.05) in case group as compared to control. Effective nutrition counseling improves liver transplant patients' nutritional status, liver function, and serum electrolytes.

Keywords

Nutritional counseling; serum electrolytes; liver function; body mass index

1. Introduction

Nutritional counseling is essential for resolving issues related to malnutrition as judged by the hospital nutrition team at the time of admission. It should be provided to patients periodically to ensure and promote food intake and enhance their knowledge of food options related to their disease condition and body requirements. An individualized protocol to diagnose, stratify the magnitude of malnutrition and follow up with customized nutrition planning for patients helped to achieve nutritional targets more successfully when compared to the standard prescription [1].

For patients with advanced chronic liver disease and the majority of patients with acute liver failure, liver transplantation has become the treatment of choice. Malnutrition is common in patients with end-stage liver disease and cirrhotic patients. Therefore, poor nutritional status is one of the predictors of increased morbidity and mortality rates after surgery [2]. The effect of malnutrition on the outcome of liver transplantation (LTx) is still being debated. Nutritional therapy is an integral part of care in all phases of LTx. Managing malnutrition before and while on the waiting list for a liver transplant and excessive weight gain/metabolic disturbances post-surgery are still challenges in LTx care [3]. The underlying etiology of malnutrition becomes more complicated as the illness advances to end-stage liver disease and may involve iatrogenic factors as well as nausea and vomiting, anorexia, increased energy expenditure, abnormal nutrient metabolism, maldigestion,

and malabsorption. There is a definitive need in patients with chronic cholestatic and or end-stage liver disease to identify nutritional deficits early and initiate nutritional therapies to both optimize development and prevent complications. Optimized pre-transplant nutrition has been reported to help in relatively faster post-transplant recovery while concurrently reducing complications [4].

Even though patients' nutritional habits vary and they are resistant to change, it is clear that a qualified and dedicated transplant nutrition team can implement perioperative nutrition protocol to obtain better healthy targets [5]. One of the risk factors for higher morbidity and mortality rates following liver transplant surgery is regarded to be poor nutritional status. Several patients may concurrently exhibit excessive potassium levels soon after the surgery. In addition, immunosuppression causes hypomagnesemia [3].

Liver transplant recipients are prone to weight gain and metabolic syndrome. This is due to several reasons, such as improved diet, immunosuppression, and reduced stress with improved catabolic state. Calcineurin inhibitors increase post-transplant hypertension and dyslipidemia, while corticosteroids increase all components of metabolic syndrome. Heimbach et al. [5] showed in their series that more than 50% of patients who had undergone liver transplantation for non-alcoholic steatohepatitis (NASH) had post-liver transplant weight gain with body mass index (BMI) > 35 kg/m², post-transplant diabetes mellitus and recurrence of NASH in the allograft. Patients often attempt to reduce weight through diet and exercise. However, this is inadequate for several patients as they usually struggle to lose weight. Combating micronutrient deficiencies, guiding regarding the role of diet in wound healing and graft retention, and advising on food safety and infection prevention [6]. Interventional programs with dietary and exercise counseling could potentially partially or fully normalize the nutritional changes brought on by LT. Specific diet and exercise regimens may help acquire an appropriate muscle mass recovery or prevent the predisposition towards becoming overweight [7]. In clinical settings, nutritional status assessment at the time of admission is of vital importance to know about the actual weight status as even many pre-transplant patients are underweight, which is masked by ascites and edema. In a study by Chaney and Heckman, eight patients were enrolled to participate in supplemental nutrition education. Patients with terminal liver disease encounter nutritional and metabolic disorders that are primarily related to the disease, influencing quality of life, morbidity, and mortality in patients on the waiting list for liver transplantation [8].

In addition, another reported that one-year intense nutritional counseling reduced visceral fat, fasting glucose, AST, ALT, triglycerides, and histologic score in patients with non-alcoholic steatohepatitis [9]. Another study also demonstrated that nutritional counseling with a specific Mediterranean diet significantly improved liver enzymes (AST, ALT, and GGT) and anthropometric indices (BMI, waist circumference, and waist-to-hip ratio) in patient's non-alcoholic fatty liver disease [10]. If an appropriate interdisciplinary approach is taken by offering adequate nutritional counseling and intervention, these derangements may be prevented or alleviated when necessary. Nutrition counseling impacts long-term outcomes as it can avoid future related morbidity and mortality, such as metabolic syndrome, and have a good effect on overall results during the perioperative period and long-term after transplantation. This study aimed to determine the effect of nutritional counseling on nutritional status and health outcomes of liver transplant patients.

2. Materials and Methods

2.1 Study Design and Location

A hospital-based observational prospective study was conducted on liver transplant patients to investigate the effect of nutritional counseling on the nutritional status and health biomarkers of the patients at Shifa International Hospital Islamabad.

Ethical and administrative approval was sought from the research ethical committee of Shifa International Hospital, Islamabad (SIHREC-0081) to conduct the study.

2.2 Sampling Technique

In this cross-over interventional study, openEPI software was used to calculate sample size, and patients with acquired liver transplantation were recruited through convenient random sampling.

2.3 Study Subjects and Group Allocation

A total of 100 patients were enrolled in the study who were potential candidates for liver transplantation at Shifa International Hospital Islamabad. They were divided into case (n = 50) and control (n = 50). Nutritional counseling was provided to the case group for 12 weeks, while the control group was not provided any dietary or nutritional counseling.

2.4 Inclusion and Exclusion Criteria

All patients (irrespective of gender) referred for liver transplantation and above 20 years of age were included. The exclusion criteria were children, patients who declined or withdrew participation, patients discharged from hospital within one week, patients who could not complete follow-up interviews, and patients with a life expectancy of less than 3 months due to complications.

2.5 Development of Nutritional Counseling Material

Nutritional counseling material for the present study was already developed and practiced for liver transplant patients. These materials were based on the hospital administration's standardized protocol, keeping in view the ESPEN and EASL guidelines and recommendations. The details of the counseling materials can be found in the Hospital Manual of Shifa International Hospital Islamabad. Briefly, Liver transplant patients were given active nutritional counseling (explanation about dietary and fluid recommendations and usage with the help of charts and pamphlets twice a week). The dietitian visited the patients in person for nutritional counseling. A sample menu for liver transplant patients was made to give awareness and should strictly follow a balanced diet during pre- and post-operation. The sample menu was designed based on the patient's daily caloric and macronutrient requirements.

2.6 Intervention of Nutritional Counseling

The selected liver transplant patients were divided into case (provided nutritional counseling) and control groups. Nutritional counseling protocol was given to the case group after counseling his/her nutritional intake was calculated by 24-hour dietary recall, while no nutritional counseling

was given to the liver transplant patients of a control group. The patients in the case group were advised to follow nutritional counseling and dietary plans till the next visit. The patients were counseled for three months to record their anthropometric, biochemical, and dietary intake.

2.7 Data Collection

2.7.1 Socioeconomic and Demographic Characteristics

The interview was conducted to collect the patients' information regarding their age, gender, education, and marital status through a standard questionnaire. Reliable information on monthly income status was either not available, or the patients did not want to disclose it.

2.7.2 Anthropometric Information

According to the WHO recommended procedures, the weight and height of cases and controls were taken. Equipment's were calibrated for anthropometric measurements. Patients were advised to remove heavy clothing and shoes before taking weight and size. Weights were taken on a beam scale with a minimum scale of up to 0.01 kg, while a height measurement height board was used with a minimum scale of up to 0.01 cm. BMI was calculated according to WHO classification, and subjects were classified as underweight, normal, overweight, and obese.

2.7.3 Biochemical Parameters

Biochemical analysis was performed on a Roche Cobas 6000 analyzer (Roche Diagnostics, Mannheim, Germany) for the study of sodium, potassium, creatinine, albumin, phosphorus, magnesium, calcium, and liver function tests (alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, total bilirubin). A 5 ml blood sample was used for the analysis. These parameters were investigated in the laboratory of Shifa International Hospital and monitored throughout the study at three time points i-e, preoperative, during illness, and postoperative. Mean reference lab values at Shifa International Hospital were used for data analysis. Most of the lab biochemical tests were repeated weekly as otherwise advised by the concerned physician. This was done as a follow-up and to make changes in the medication type and dosage. In addition to the lab tests for biochemicals above, other nutritional-related biochemical (e.g., Hb, hematocrit, ferritin; total serum protein, C-reactive protein, pre-albumin and total lymphocyte count) were also ordered as part of the treatment strategy when deemed necessary by the consultant physician in a patient with prior nutritional complications. We don't report on these because of the limited data available.

2.7.4 Dietary Assessment

A 24-hour dietary recall method was used to interview for food and beverages taken during the last 24 hours by the liver transplant patients. Food models were used to estimate the portion size of food, which was converted into the number of food & beverages consumed by the patient. The amount of food noted in the 24-hour recall questionnaire was used to calculate dietary nutrient intake using an in-house nutrient calculator in Microsoft Office Excel 2003 (Microsoft Corporation, Redmond, WA). This calculator is based on data from the food composition tables for Pakistan, as previously reported [11].

2.8 Data Entry and Statistical Analysis

Data collection was repeated daily and weekly for different variables of interest. Data on food intake and anthropometrics were available on a daily basis. Data on most of the biochemicals were available on a weekly basis. The study protocol was based on intent-to-treat. Therefore, the final data for any patients was assumed to be collected before discharge from the hospital. Data for all patients was completed within 6 months. Data regarding demographic socio-economic status, medical history, anthropometric, biochemical, and dietary of the patients were entered into the computer for error checking and statistical analysis. Data were entered using descriptive statistics, including frequency, mean, and median, which were determined and checked for data distribution to apply appropriate statistics. To a customarily distributed data independent t-test, chi-square test for qualitative frequency distribution. Furthermore, an ANOVA two-sided test was used to compare the data between the groups and determine the effect of nutritional counseling on the nutritional status and biochemical parameters of the patients. A 5% level of significance was chosen in this study.

3. Results

Table 1 shows the demographic data (age, gender, and education level) of both groups. The average age of both groups was approximately the same. The percentage of male patients was much higher (80%) in both control and intervention groups. In the control group, 78% had less than bachelor’s degree, 18% bachelor’s and 4% had advanced degrees. In the intervention group, 52% had less than bachelor’s degree, 32% had bachelor’s, and 16% had advanced degrees. Overall, most patients have less than bachelor's educational backgrounds.

Table 1 Demographic Characteristics of the Liver Transplant Patients.

		Variables	Mean ± SD/N (%)
Age	Control		48.19 ± 10.67
	Case		50.92 ± 9.51
Gender	Control	Male	40 (80)
		Female	10 (20)
	Case	Male	41 (82)
		Female	9 (18)
Education	Below bachelor	Control	39 (78)
		Case	26 (52)
	Bachelor degree	Control	9 (18)
		Case	16 (32)
	Advanced degree	Control	2 (4)
		Case	8 (16)

% = percentage, SD = Standard deviation.

Figure 1 shows the geographical distribution of the Patients. Results indicated that subjects from Khyber Pakhtunkhwa (KP) were 18%, Punjab 36%, Sindh 37%, Baluchistan 7%, and Gilgit Baltistan (GB) were 2%. However, both groups showed that most subjects were from the Punjab

province (36%) and Sindh (37%).

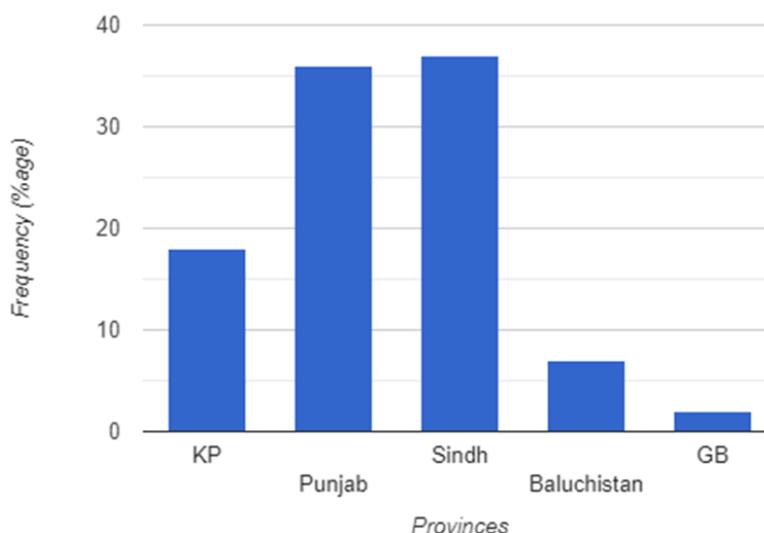


Figure 1 Geographical Distribution of the Patients.

The mean weight of the control group was 71 kg, and BMI was 26, while in the case group was 67 kg and 25.9, respectively, which indicates that they both fell into the category of overweight. There were no significant changes in the anthropometric parameters at baseline between the groups. The findings also suggested that the majority of the patients were in the category of overweight and obesity (control: 32% fat and 18% obese; Intervention: 36% overweight and 30% obese) (Table 2).

Table 2 Baseline Anthropometrics of the Patients.

Variables	Mean ± SD/N (%)		P-value
	Control	Case	
Weight	71.82 ± 13.23	67.88 ± 12.67	NS
BMI	26.06 ± 4.82	25.94 ± 4.94	NS
BMI categories	<18.5	1 (2)	0 (0)
	18.5-24.9	24 (48)	17 (34)
	25-29.9	16 (32)	18 (36)
	>30	9 (18)	15 (30)

Weight and BMI were recorded at two periods at baseline and after 12 weeks. The mean preoperative and postoperative (weight after 3 months of surgery) in the case group was 67.88 ± 12.67 and 71.98 ± 13.04 kg, respectively. The preoperative and postoperative weight in the control group was 71.17 ± 13.14 and 72.64 ± 12.30 kg, respectively. The analysis showed that weight seemed to improve as time progressed, but there was a non-significant ($p > 0.05$) difference in weight, and BMI observed between the case and control groups (Figure 2).

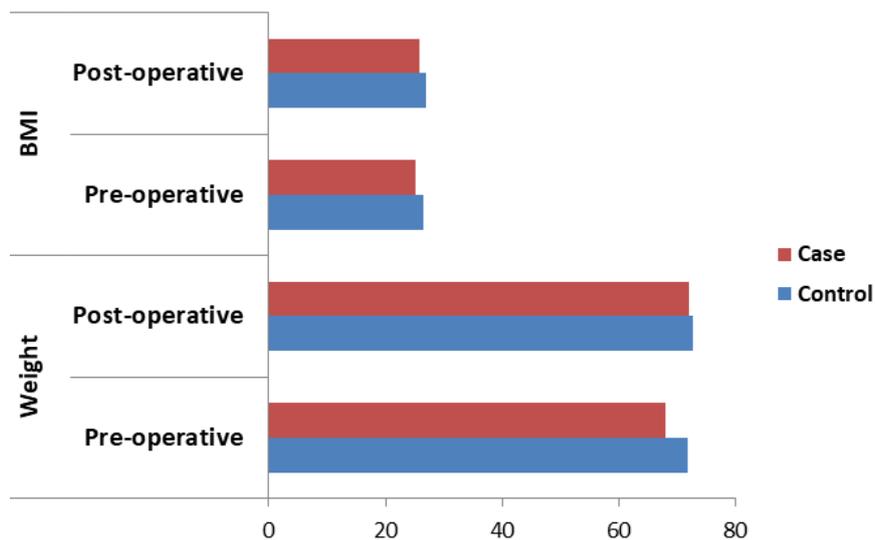


Figure 2 Effect of Nutritional Counseling on Nutritional Status of the Patients. Patients mean weight (Kg) is shown along x-axis. Note: weight shown is adjusted for ascites and/or oedema.

Table 3 shows the effect of nutritional counseling on biochemical parameters, including serum electrolytes and liver function of both groups at different intervals, including preoperative, during illness, and postoperative data. The significant findings were observed for Potassium (meq) at preoperative ($p = 0.005$), Sodium (mg) ($p = 0.041$) and Albumin (mg) ($p = 0.026$) during illness, ALT (U/L) at preoperative ($p = 0.045$) and postoperative ($p = 0.011$), Alkaline phosphatase at preoperative ($p = 0.050$), during illness ($p = 0.047$) and postoperative ($p = 0.023$).

Table 3 Effect of Nutritional Counseling on Biochemical Parameters of the Patients.

Variables	Pre operative			During illness/Hospitalized			Post operative		
	Control	Case	P-value	Control	Case	P-values	Control	Case	P-value
Sodium (mg)	132.64 ± 6.62	133.48 ± 5.33	0.509	137.40 ± 4.50	135.55 ± 3.99	0.041	138.04 ± 4.48	136.95 ± 5.413	0.298
Potassium (meq)	4.28 ± .43	3.94 ± .63	0.005	3.87 ± 0.61	4.030 ± 0.45	0.191	4.51 ± 0.58	5.01 ± 0.60	0.892
Albumin (mg)	2.68 ± 0.66	2.73 ± 0.56	0.704	2.88 ± 0.27	2.72 ± 0.36	0.026	3.61 ± 0.59	3.47 ± 0.51	0.144
Magnesium (mg)	1.96 ± 0.36	1.92 ± 0.34	0.567	1.93 ± 0.37	1.84 ± 0.26	0.173	1.82 ± 0.26	2.42 ± 0.265	0.336
Phosphorus (mg)	3.07 ± 0.97	2.98 ± 0.67	0.481	3.21 ± 1.2	3.01 ± 1.03	0.407	3.87 ± 0.56	4.07 ± 0.53	0.407
Creatine (mg)	0.91 ± 0.41	0.86 ± 0.30	0.482	0.92 ± 0.54	0.88 ± 0.49	0.692	1.02 ± 0.32	3.48 ± 15.51	0.279
Calcium (mg)	8.41 ± 0.61	8.20 ± 0.72	0.890	8.88 ± 0.56	7.73 ± 1.19	0.114	8.88 ± 0.56	8.689 ± 0.606	0.107
AST (U/L)	106.64 ± 83.4	88.95 ± 71.65	0.285	49.64 ± 58.33	62.0 ± 28.31	0.088	49.64 ± 58.33	70.48 ± 80.89	0.160
ALT (U/L)/(mg)	84.0 ± 108.40	52.73 ± 51.04	0.045	62.49 ± 68.13	118.09 ± 69.5	0.132	62.49 ± 68.13	116.05 ± 13.58	0.011
AKT (mg)	165.21 ± 94.7	133.23 ± 50.7	0.050	93.81 ± 49.0	164.75 ± 29.6	0.047	154.13 ± 41.2	289.36 ± 372.6	0.023
TB (mg)	6.32 ± 12.13	5.80 ± 8.45	0.816	1.78 ± 4.70	5.14 ± 3.94	0.950	1.78 ± 4.70	3.03 ± 8.45	0.382

AKT = Alkaline phosphatase, ALT = Alanine aminotransferase, AKT = Aspartate aminotransferase, TB = Total bilirubin.

The figure shows the effect of nutritional counseling on the energy and macronutrient intake of the patients. A significant change was observed in the fat intake ($p = 0.005$) during illness (hospitalized) and protein intake ($p = 0.043$) during the postoperative stage between the case and control group (Figure 3).

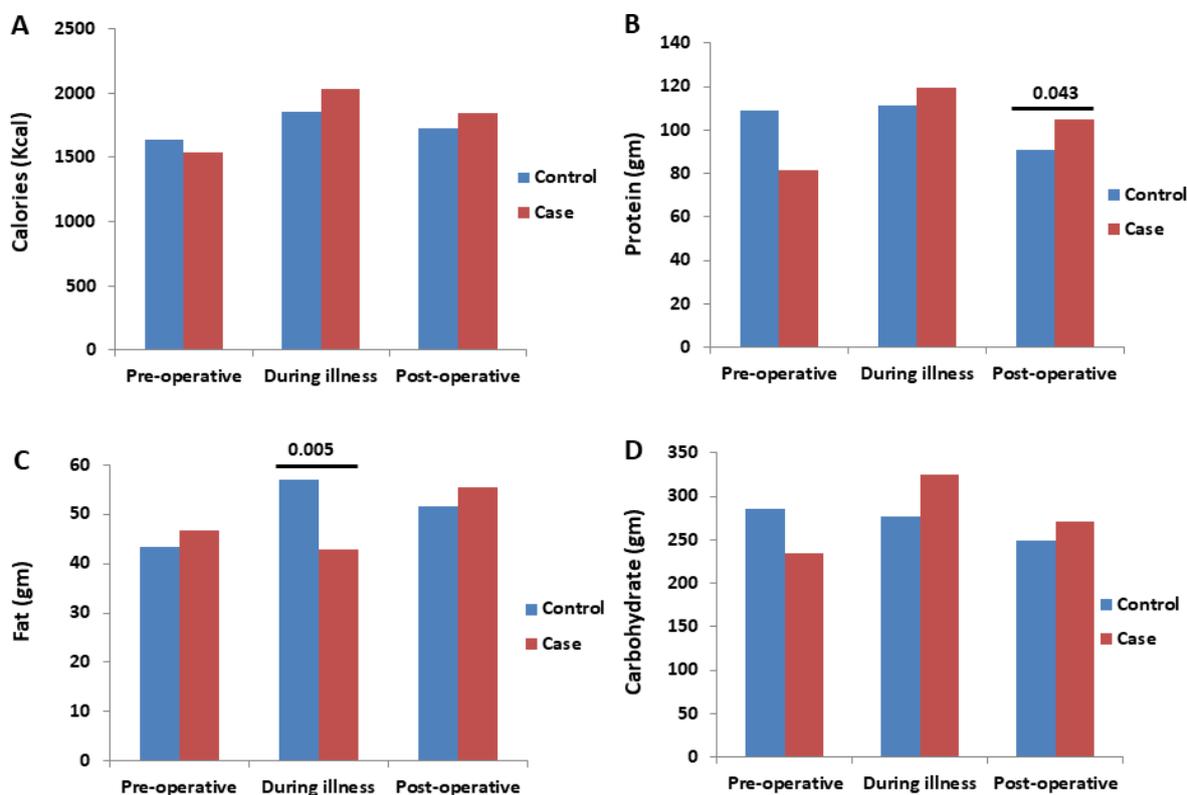


Figure 3 Effect of Nutritional Counseling on Dietary Intake of Macronutrients of the Patients.

4. Discussion

The present study investigated the effect of a structured nutritional counselling intervention on weight status and related lab biochemistry of 100 hospitalized patients admitted for liver transplantation in Shifa International Hospital, Islamabad, Pakistan. Nutritional counseling was provided to the patients (case group) with the routine hospital dietary menus. There were differences in the lab biochemistry of the selected biochemicals between the control and intervention groups. The results show that weight seemed to improve as time progressed, but a non-significant ($p > 0.05$) difference in weight and BMI was observed between case and control groups. Weight gain after liver transplantation is critical for patients with nutritional recovery. In a study of 597 patients, the average weight gain ranged from 1.8 kg to 9.5 kg six months to three years after transplantation, resulting in a prevalence of approximately 70% overweight ($BMI > 25 \text{ kg/m}^2$). The possible factors responsible for weight gain after transplant are older age, family history of being overweight, high BMI before the disease, post-transplant hypometabolism, physical inactivity, high donor BMI, being married, less sleep, and less dietary calcium intake [12].

The progressive weight gain in the result is in continuum with the study whose results showed that in 17 liver recipients' prior to transplantation and 12 months after transplantation, a

progressive weight gain was reported, and the rate of obese patients increased from 11.8 to 29.4% [13]. The excessive prevalence of overweight and obese patients who were candidates for liver transplants was also reported by Baraldi et al.. Still, he and colleagues also concluded that following a nutritional follow-up and a personalized diet, fat mass was normalized in 91% of men at the time of transplantation [14]. As a result, obesity management counseling should be initiated for both patients undergoing liver transplant evaluation and liver transplant recipients. Long-term effects of lifestyle interventions for obesity and metabolic syndrome in patients after liver transplantation have yet to be published in studies. However, dyslipidemia, along with other factors, is a risk factor for obesity and liver failure by inducing fatty liver diseases that increase the chance of liver transplantation.

Interestingly, a study revealed that dietary counseling with a prescription of a personalized diet normalized the total cholesterol and low-density lipoprotein levels in patients following liver transplantation [15]. Another study reported significant weight and BMI differences in pre and post-transplantation. The study found that in 42 long-term survivors studied between 18 and 100 months after successful liver transplantation, the mean BMI and fat mass were significantly higher in transplanted patients compared to 39 patients with liver cirrhosis and a healthy control group [16].

Electrolyte abnormalities are frequent after liver transplantation, particularly during the acute phase, and are typically associated with abdominal drains, gastrointestinal losses, and fluid overload. Not in all, but in a few patients, the serum potassium, phosphorus, and magnesium levels can be depleted during the acute post-transplant period as a result of diuretic use or refeeding syndrome and should be closely monitored. Nutrition screening, intervention, and counseling can correct the abnormalities early and prevent complications [17].

The results indicate a significant difference for sodium and potassium in cases versus control groups that is novel and is not supported by past literature as no critical studies are conducted to evidence the association of nutrition counseling in improving sodium and potassium levels, particularly in liver transplant patients. Many patients may experience high potassium levels shortly after transplantation. This is usually due to the immunosuppressive drug's nephrotoxicity. As a result, it may be critical to adjust potassium food sources and use dietary modifications that reduce potassium content in nutritional intake during the early postoperative period. This is not necessarily long-term after transplant because this transient imbalance often resolves itself [18].

Both ALT and AKT in the postoperative phase are elevated for the case group because serum ALT levels were markedly elevated immediately after transplantation, as evidenced in a longitudinal study [19]. For AKT, biliary obstruction and rejection are two of the most prominent causal factors of abnormal liver function tests (LFTs) in patients who have had a liver transplant [20]. Moreover, at postoperative, the protein intake improved in cases as compared to the control group. This is evident from the nutrition therapy effectiveness evidenced by past studies. One study concluded that a nutritional protocol with a higher enteral nutrition (EN) rate and high-protein ONS resulted in a higher protein intake early after liver transplant [21]. Similar results were reported by Bitterman et al., who concluded a marked improvement in protein intake in the group given a nutrition care plan [5]. During the illness, the fat intake was less in the case group as compared to the control group. That is the result of the nutrition therapy and is a continuum with a study reported that physician-assisted nutrition counseling can result in positive changes in diet, weight, and blood lipids [22]. Therefore, it is essential to invest resources in nutritional counseling to improve the eating habits of patients with liver disease and eliminate behavioral risk factors for

disease progression [23]. Finally, in clinical practice, while weight gain may be an issue to be taken into consideration, however, monitoring weight and the presence of ascites or oedema must be taken into consideration. Massive post-transplantation ascites is a rare but severe condition following liver transplantation. Although many etiologies are suggested as the cause of this complication, the definitive etiology remains unknown in some cases. Drug-induced post-transplantation ascites is one of the possible etiologies.

5. Strength and Limitations

The significant strength of the study was its methodology of comparing cases with the control that explicitly presented the effect of counseling in comparison. However, further large-scale research using data from various hospitals is required to corroborate these findings. Furthermore, prospective studies on the influence of counseling on health outcomes are necessary to demonstrate the long-term value of nutrition counseling. Patients' attitudes, perceptions, and beliefs were a bar to implementing counseling interventions effectively. Since this study only included individuals who had liver transplants from a single hospital, our findings may not be applicable to patient groups that may not have access to similar treatment in other hospitals. Finally, the association between progressive disease, the development of hepatorenal syndrome, and serum electrolytes was not monitored as per the Hospital protocol. In addition, the effects of diuretics on serum electrolytes couldn't be observed. These are essential aspects from both the treatment and research studies perspectives and must be considered in both settings.

6. Conclusion

The study demonstrated that nutrition counseling confers beneficial health outcomes in liver transplant patients. LT patients' nutritional status improved in macronutrient and biochemical parameters in cases versus controls. Liver function indicators, i.e., ALT and AKT, also improved significantly in the case group compared to controls.

Author Contributions

Saba Tanveer: Methodology, Formal analysis, Investigation, Writing – original draft, Writing – review & editing, Visualization. **Ali Saad R. Alsubaie:** Investigation, Methodology, Project administration. **Rezzan Khan:** Investigation, Methodology, Project administration, Funding, Writing – review & editing. **Hajra Ahmed:** Investigation, Methodology, Project administration. **Mahpara Safdar:** Conceptualization, Writing – original draft, Writing – review & editing, Supervision, Project administration. **Zainab Bibi:** Methodology, Formal analysis, Investigation, Visualization. **Sadaf Yousaf:** Supervision, Project administration, Funding acquisition. **Bismillah Sehar:** Conceptualization, Resources. **Iftikhar Alam:** Conceptualization, Resources, Investigation, Formal analysis. **Aiman Hadayat:** Supervision, Project administration. **Falak Zeb:** Conceptualization, Supervision, Project administration, Writing – original draft, Writing – review & editing.

Competing Interests

The authors declare that they no conflict of interest regarding this paper.

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