Nutritional Assessment of Renal Transplant Recipients Using DEXA and Biochemical Parameters

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Abstract

Introduction and Aims: Malnutrition is frequently encountered in patients with CKD. Despite successful renal transplantation, malnutrition ensues. We evaluated the relationship between serum albumin levels, and various indicators of nutritional status.

Methods: We did a retrospective study of 249 post-transplant patients who successfully underwent renal transplantation (between 1995-2012) at a tertiary care center. Serum parameters such as albumin (brromocresol green Method) hemoglobin, electrolytes, creatinine, prednisolone dose and presence of diabetes mellitus were analyzed. Lifestyle factors such as smoking, alcohol and diet, BMI were also looked at. We classified Serum Albumin as =<3.3, 4 g/dL, 3.5-3.9 g/dL, and more than 4 g/dL. We classified BMI as per WHO guidelines. Dual Energy X-Ray Absorptiometry was used to evaluate body composition, including lean body mass, fat body mass and fat percentage. Descriptive statistics, co-relational statistics and Pearson’s Chi-Square test was used.

Results: Among the 150 Males and 99 females, the mean age was 46 ± 13 years. The mean serum albumin value was 3.6 ± 0.6 g/dL. 10% had a normal BMI, 62% Pre Obese, 21% Class 1 Obese, 5% Class 2 Obese, and 2% Class 3 Obese. A meat-based diet was ingested by 76% of our study group, and 24% were pure vegetarians. The mean dose of prednisolone taken was 20 ± 10 mg/day. 5% of the transplant patients were deceased and 1% had a failed graft. On follow up we found a significant positive correlation between serum albumin and hemoglobin (p=0.002), Fat% (p=0.032) and a meat-based diet (p=0.032). A serum albumin value of 4g/dL was observed in 46% of those ingesting a meat-based diet, in contrast to 25% pure vegetarians. 66% of the vegetarians had a serum albumin value ranging from <3-3.6 g/dL. There were negative correlations between prednisolone dose and serum albumin (p=0.005), FM (p=0.006), Fat% (p=0.002) and serum Creatinine (p=0.013). A positive correlation between hemoglobin levels and LDL (p=0.005), FM (p=0.004), HCO3- (p=0.015) and Cl- (p=0.012), and hemoglobin levels and potassium levels (p=0.015) were observed. No significant correlation was observed between serum albumin and patient survivals.

Conclusions: Serum albumin varies with diet, and is significantly higher among those eating a meat-based diet following transplant. Post-transplant mild obesity was prevalent in 62% of our study group. A higher fat content was associated with higher serum albumin levels, which may reflect a better nutritional status. Lower maintenance doses of prednisolone may improve the Albumin Levels. A further randomized controlled trial looking at the role of protein supplementation in vegetarians following renal transplantation as well as evaluating the effect of lowered prednisolone dose is warranted.

Keywords: Protein-energy-wasting; End-stage-renal-disease; Chronic kidney disease; Maintenance hemodialysis; Dietary protein intake

Introduction

There is very less data on renal nutrition in the post-transplant period, among south-east Asian countries, including India. Nutritional status refers to the composite quantitative and qualitative assessment of visceral and somatic (muscle) protein stores and energy balance [1,2].

Among the many risk-factors that affect the outcomes of Chronic Kidney Disease (CKD), especially End-Stage-Renal Disease, and on Maintenance Hemodialysis (MHD), Protein-Energy-Wasting (PEW) of CKD plays a major role [1-5]. Evaluating nutritional status is a critical component of physiologic and fundamental to identifying PEW. Multiple studies indicate that PEW is closely associated with major adverse clinical outcomes, and is associated with increased hospitalization and death [2,6-8].

Although Serum albumin (S. albumin) is a marker of nutritional status, concerns have been expressed regarding its applicability [9]. S. albumin robustly associates with death and hospitalization, is easily and reproducibly measured, and responds to appropriate interventions [10].

Dietary Protein Intake (DPI), and diet composition has a direct influence on serum albumin concentrations, and inadequate DPI is characterized by a decrease in the rate of albumin synthesis [11].

At least 60% of adult renal transplant recipients develop dyslipidemia, which occurs within one month of the initiation of immunosuppressive therapy and continues indefinitely unless treated. Cyclosporine, sirolimus, and prednisone are mainly implicated, and the lipid profile differs between individual agents [12]. There is a growing amount of evidence suggesting that dyslipidemias contribute to the
very high incidence of cardiovascular disease after transplantation [13].

Transplant related immunosuppression can worsen the pre-existing medical conditions such as Diabetes Mellitus (DM), hyperlipidemia, hypertension and cardiovascular complications [14].

Metabolic acidosis, promotes PEW by increasing protein catabolism via suppression of insulin/insulin growth factor-1, signaling and activation of the ubiquitin-proteasome system [15].

Body Mass Index (BMI) has a very strong association with outcomes after renal transplantation independent of most of the known risk factors for patient and graft survival. The extremes of very high and very low BMI before renal transplantation are important risk factors for patient and graft survival [16].

We sought to evaluate the relationship between S. albumin levels and various indicators of nutritional status, and the variability of S. albumin among diabetics and non-diabetics, and those consuming a meat-based and pure vegetarian diets.

Methods

We studied the database of 249 post-transplant patients, selected at random, which successfully underwent renal transplantation (Between 1995-2012) at a tertiary care center, in south-India. Written consent was obtained from all the patients, enrolled in this study, and this study was approved by the ethics committee of the center.

Data was collected retrospectively. Patient demographics such as age, sex, and a proxy of indicators of nutritional status were used: Serum assays such as S. albumin, hemoglobin (hb%), High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL), Triglycerides (TG1), Serum Calcium (Ca), Inorganic Phosphate (PO4), and electrolytes: sodium, potassium, chloride, bicarbonate, and renal parameters: serum creatinine (S. Cr) were obtained from baseline blood investigation reports; lifestyle factors such as smoking, alcohol, primary diet composition, body mass index, the presence of DM and various indicators of nutritional status, and the variability of S. albumin among diabetics and non-diabetics, and those consuming a meat-based and pure vegetarian diets.

We classified our patients, as DM (defined as a fasting glucose level of ≥ 126mg/dL, or a 2-h plasma glucose ≥ 200 mg/dL, and non-diabetics (fasting glucose <126 mg/dL and 2-h post-prandial glucose level <200mg/dL). We also classified them under, Smokers (including those who stopped smoking; we considered a minimum of three cigarettes per week) and Non-smokers, and those who ingested Alcohol (minimum of 60 mL of 80-proof ethanol per-day) and Non-drinkers.

Statistics

Descriptive and co-relational coefficients, employing Pearson’s Chi-Square test (two-tailed approach), was used to determine the influence of serum albumin over all the other variables. Paired samples T-test were done, to analyze the changes in the nutritional parameters, including-S. Albumin, Hb%, HDL, LDL, S.Ca, HCO3, BMI, fat%, FM, and LBM, and prednisolone dose, before and after transplant. The results were considered to be statistically significant if the alpha error was less than 5% (p<0.05). All statistical analysis was performed using the IBM SPSS Statistics software package v. 16. 0.

Results

Among the 150 males and 99 females recipients studied, the mean age of the transplant recipients were 46 ± 13 years. Our patients were on a hemodialysis for a mean period of 7. 2 ± 8 months, before transplant. Five percent of the transplant patients, who were followed up, died.

Table 1 shows the various descriptives analyzed, along with mean and standard deviation. The mean s. albumin value was 3.67 ± 0.6 g/dL. The mean dose of prednisolone was 20 ± 10 mg/day. The mean Hb% was 10.5 ± 2gm%. The means of other serum assays and electrolytes were in the normal range, as shown in (Table 1). Fifty percent of our cohort had Hb% levels ≤ 10.9 gm%.

Fifty six percent of our study group was diabetic. 11% gave a history of consumption of Alcohol. 31% were smokers and 76% ate a meat-based diet, 24% were vegetarians.

(Table 2) shows the distribution of S. Albumin among the diabetic’s and euglycemics the mean s. albumin levels among the diabetics and non-diabetics were 3. 65 ± 0. 56 g/dL and 3. 89 ± 0. 44g/dL respectively. An s. albumin value of ≥ 4 g/dL was observed in 38% of the diabetics and 75% of the non-diabetics respectively. An s. albumin value <3- 3. 4g/dL was observed in 38% of the diabetics and 19% of the non-diabetics respectively. Twenty-four percent of the diabetics and 6% of the non-diabetics had serum albumin values ranging between 3. 5 g/dL and 3. 9g/dL (p=0. 076)

Thirty percent of our cohort had bicarbonate levels <22mEq/L.
The s. albumin values were on the lower range among the diabetics. Significant positive correlations between s. albumin and BMI Distribution, using a cross-tab, and Pearson’s chi square test. Table 3 shows the distribution of S. albumin amongst the vegetarians and those consuming a meat-based diet. s. albumin values of ≥ 4g/dL were observed among 46% of those, who ingested a meat-based diet. Only 25% of those consuming a pure vegetarian diet had s. albumin values of ≥ 4g/dL. 66% of the pure-vegetarians had s. albumin value ranging from <3-3.4 g/dL. Twenty-eight percent and 8% of the meat-based diet consumed and vegetarians (respectively) had a s. albumin value between 3.5-3.9 g/dL. (P value = 0.032).

Table 4 shows the distribution of S. Albumin and BMI. Ten percent, of our study sample had a normal BMI, 62% Pre Obese, 21% Class 1 Obese, 5% Class 2 Obese, and 2% Class 3 Obese. No significant co-relation between BMI and s. albumin was obtained (p = 0.91).

Positive correlations between Hb levels and LDL (p = 0.005), FM (p = 0.004), HCO3- (p = 0.015) and Cl- (p = 0.012) were also observed.

Negative correlations between prednisolone dose and s. albumin (p = 0.005), FM (p = 0.006), Fat% (p = 0.002) and S. Cr (p = 0.013) and between Hb% levels and potassium levels (p = 0.015) were observed.

The s. albumin values were on the lower range among the diabetics. Thirty-eight percent of the diabetics, and 75% of the non-diabetics had s. albumin values > 4 g/dL (0.076).

Table 5 shows the results of the paired samples T-test, done on various parameters, comparing the means and standard deviations, on the first follow ups and the 6th monthly follow ups. The S. albumin level at the first follow up, post-transplant, was 3.58 ± 0.43 g/dL, and at 6 months was 3.827 ± 0.507 g/dL (p value = 0.208). The mean dose of prednisolone ingested, at the first follow up and at 6 months, was 21 ± 12 mg and 10 ± 9.75, respectively. The mean HCO at baseline and 6 months was 23.38 ± 3 and 25.25 ± 2.6 (p = 0.049). The mean BMI at baseline and 6 months was 22.67 ± 10.55 kg/m² and 23.59 ± 3.4 kg/m² (p = 0.051). The fat% at baseline and 6th month follow up was 26.79 ± 10.56% and 32.44 ± 11.14% (p = 0.003). The mean FM at baseline and the 6th month was 19.48 ± 9 kg and 23.91 ± 10.70 kg (p = 0.44). The mean LBM at baseline and at 6th month was 44.21 ± 5.44 kg and 43.963 ± 5.767 kg (p = 0.763).

No significant co-relation was observed between S. albumin and DM, BMI, smoking and a history of ingesting alcohol.

**Discussion**

A number of factors affect the nutritional and metabolic status in CKD, leading to multiple adverse consequences (Figure 1) [17]. These factors may persist, despite transplantation [2,6-8].

According to other studies, S. albumin also predicts progression of co-morbid conditions like DM, hypertension, including advanced kidney disease [18,19]. For example, levels < 2.5 g/dL have been associated with a risk of death 20 times higher compared with a reference level of 4.0-4.5 g/dL in hemodialysis patients, and levels of 3.5-4.0 g/dL (considered to be within the normal range) were associated with doubling the risk of death [20,21].

**Obesity**

Weight gain, obesity, dyslipidemia and post-transplant DM and metabolic complications are common in the recipients of successful renal transplants. According to the UNOS data, approximately 34% patients who underwent renal transplant were overweight [8]. In comparison to our study, we found out that mild obesity was prevalent in 62% of our study group, the higher BMI could be attributed to post transplant increase in appetite, a sedentary lifestyle, a dietary implementation a high carbohydrate diet and steroid ingestion. They are at increased risk for post-transplant DM, hypertension, and dyslipidemia that require close monitoring [8,9].

BMI has a very strong association with outcomes after renal transplantation independent of most of the known risk factors for patient and graft survival. The extremes of very high and very low BMI

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before renal transplantation are important risk factors for patient and graft survival [16].

There are several epidemiological studies, indicating that a higher BMI, regardless of its etiology (i.e., increased LBM or adiposity) is associated with better survival in these patients [22,23]. If weight gain in one potential outcome of an intervention, gain in LBM should be a part of it, along with gain in fat mass. Fifty six Percent of our patients, were diabetic, and had a higher BMI. Increased s. albumin levels were also associated with higher fat content, reflecting a better nutrition. Diabetic patients, despite effective treatment, had lower s. albumin

| Table 5: Paired samples T-Test – Comparing the means and standard deviations of the 1st follow up and 6th month follow up of various parameters. |
|-----------------------------|---------|----------|---------|------------------------|
| Mean | Std. Deviation | N | Std. Error Mean | Significance |
| Sr. Albumin (gm/dL) (1st Follow up) | 3.583 | .4301 | 18 | .1014 .208 |
| Sr. Albumin (gm/dL) (6th month) | 3.828 | .5074 | 18 | .1196 |
| Pred. Dose (mg) (1st Follow up) | 21.355 | 12.0031 | 22 | 2.5591 .002 |
| Pred. Dose (mg) (6th month) | 10.000 | 9.7590 | 22 | 2.0806 |
| Hb (gm%) (1st Follow up) | 12.383333 | 1.4824529 | 6 | .6052089 .047 |
| Hb (gm%) (6th month) | 12.783333 | 1.3467244 | 6 | .5497979 |
| HDL (mg/dL) (1st Follow up) | 48.67 | 6.028 | 3 | 3.480 .286 |
| HDL (mg/dL) (6th month) | 42.67 | 13.051 | 3 | 7.535 |
| Ca (mg/dL) (1st Follow up) | 8.956250 | .7999740 | 16 | .1999935 .247 |
| Ca (mg/dL) (6th month) | 9.206250 | .903535 | 16 | .1226339 |
| HCO(mEq/l) (1st Follow up) | 23.380 | 3.0327 | 15 | .7830 .049 |
| HCO(mEq/l) (6th month) | 25.253 | 2.6409 | 15 | .819 |
| BMI(kg/m²) (1st Follow up) | 22.679981 | 3.6989091 | 18 | .9354808 .051 |
| BMI(kg/m²) (6th month) | 23.590380 | 3.4501668 | 18 | .8132121 |
| Fat % (1st Follow up) | 26.792000 | 10.5657434 | 25 | 2.1131487 .003 |
| Fat % (6th month) | 32.444000 | 11.1425266 | 25 | 2.2285053 |
| Fat Mass (kg) (1st Follow up) | 19.485733 | 9.0031264 | 15 | 2.3245972 .044 |
| Fat Mass(kg) (6th month) | 23.918333 | 10.7062466 | 15 | 2.7643410 |
| LBM (kg) (1st Follow up) | 44.214400 | 5.4443011 | 15 | 1.4057125 .763 |
| LBM (kg) (6th month) | 43.963133 | 5.7678948 | 15 | 1.4892640 |
| Cr (mg/dL)(1st Follow up) | 1.194118 | .3210736 | 17 | .078718 .071 |
| Cr (mg/dL)(6th month) | 1.317647 | .3107155 | 17 | .0753596 |

(S. Albumin – Serum Albumin; Pred. Dose – Prednisolone Dose ingested; Hb – Hemoglobin; HDL – High density Lipoprotein; Ca – Serum Calcium; HCO – Arterial Sodium Bicarbonate; BMI – Body mass index; Fat% - Fat percentage as quantified by DEXA; Fat Mass)

Figure 1: The conceptual model for etiology and consequences of PEW on CKD.
levels, similar to other studies [24]. We observed, in our study that as
the fat-content (fat% or FM) went higher, serum albumin levels also
increased. A higher adiposity is associated with a better outcome and
nutritional status in renal transplant recipients.

This calls for strict dietary counseling, lifestyle changes and exercise
promotion after transplantation, with repeated strict monitoring of
their nutritional status. Patients should be counseled and explained the
health benefits to ensure compliance.

Diabetes

Gama-Axelsson et al. [25] report their findings regarding the
predictive value of s. albumin as a nutritional marker in a large and
well-phenotyped cohort of incident and prevalent maintenance dialysis
patients. Their results show that serum albumin was significantly
related with DM. However, in our study, S. albumin co-related poorly
with the diabetic status, although, we observed that the diabetic
patients had a lower S. Albumin level

CKD patients often have other co-morbid diseases that can
significantly affect their nutritional status. These may persist despite
transplant, owing to some genetic component implicated in their
pathogenesis. Patients with CKD secondary to diabetes have a higher
incidence of PEW, when compared with the non-DM patients
[26]. Insulin resistance is detectable in MHD patients, even in
the absence of obesity, and is strongly associated with increased muscle
protein breakdown, even after controlling for inflammation [27-32].
Appropriate management for DM and insulin resistance is important
for preventing further loss of LBM in these patients.

Diet

Successful transplantation enables the recipient to end the dietary
restrictions imposed on them. This induces an overall sense of well-
being and an increase in appetite and subsequently, causes weight gain.
This might push the patient to become pre-obese or obese, which is
associated with increased morbidity and mortality [16,33].

Dietary protein and energy intakes of 0.6-0.8 g/kg of ideal
body weight per day and 30-35 kcal/kg of ideal body weight per day,
respectively, are able to preserve their protein stores through the
progression of kidney disease [34-36]. Accordingly, the levels of protein
and calories should be adjusted when hyper metabolic conditions like
acute illness and hospitalizations occur. Accordingly, the minimum
protein and energy requirements for patients on hemodialysis and
peritoneal dialysis are 1.2 g/kg of ideal body weight per day and 30-35
kcal/kg of ideal body weight per day based on physical activity level
[37]. Immunosuppression and steroid use, and dyslipidemia

Our cohort of patients belonged to the upper or upper middle
class, were predominantly non-vegetarians who underwent regular,
uninterrupted hemodialysis, counseled adequately by the dietician in
the dialysis unit pre and postoperatively. These patients were treated
with recombinant erythropoietin, carnitine and iron supplements
as required. The patients were on a triple drug combination of
the following, in the decreasing order of frequency: prednisolone,
cyclosporin, mycophenolate mofetil, azathioprine and sirolimus.

The hyperlipidemic effects of steroids have been well described.
Immunosuppressive therapy in renal transplant patients leads to
accumulation of triglyceride-enriched Very-Low Density Lipoprotein
(VLDL) and LDL. Triglyceride enrichment in LDL indicates the
accumulation of small, dense LDLs, which are known to bear enhanced
atherosclerotic risk. [14]. Patients who were on a prednisolone-
cyclosporin regimen, showed an improvement in the lipid profile,
after conversion to azathioprine-prednisolone regimen [38]. The
prevalence of hyperlipidemia after renal-transplantation varies from 16-60%
[12]. Causes of dyslipidemia are usually multiple, but
include immunosuppression (especially prednisone, cyclosporine and
sirolimus), graft dysfunction (reduced glomerular filtration rate and
proteinuria), and genetic predisposition [13]. We found the HDL (49.
62 ± 13.505mg/dL), LDL(90.850 ± 31.584 mg/dL) and TGI(113.8
± 57.592 mg/dL) levels in the normal limits on follow up. We also
found that the s. albumin levels were higher among those with a higher
LDL level, which may indicate a better nutritional status, among those
patients.

Hemoglobin

Fifty percent of our cohorts were anemic, with Hb% levels less
than 10.9g/dL which may be due to such as the latent malnutrition,
immunosuppressant drug use, chronic blood loss or graft dysfunction
[39]. If un-treated, it might contribute to cardiovascular events in
these patients [40]. This calls for investigations to look for substrate
deficiencies, such as iron, B12, folic acid, and the usage of erythropoietin
is warranted.

Depression

Depression, socio-economic factors, acute concurrent illness,
lifestyle and inadequate dietary prescription are the other factors that
should also be addressed as causes of post-transplant malnutrition.
Early recognition and treatment of depressive symptoms, which are
common in CKD, ESRD and the post-transplant period, are linked to
fatigue [41], and an unwillingness to eat [42], are important
components to the prevention of PEW [43-45].

Metabolic acidosis

Thirty percent of our cohort, had bicarbonate levels <22 mEq/L,
which would have a catabolic effect on the recipients, or even graft
dysfunction. Metabolic acidosis is a common electrolyte abnormality,
encountered in patients with progressive CKD; it promotes PEW by
increasing protein catabolism via suppression of insulin/insulin growth
factor-1, signaling and activation of the ubiquitin-proteasome system
[15]. In addition, acidosis stimulates the oxidation of essential amino
acids, and raises the protein requirements [46]. There are a number of
studies indicating improvement in nutritional status with oral HCO
supplementation [47]. However, data on post-transplant patients are
very limited. Metabolic studies in PD patients showed that correction
of a low serum HCO concentration will downregulate muscle proteolysis,
although no appreciable effect is observed in net protein synthesis.
HCO would have to be instituted to maintain it >22 mEq/L [48].

In our study, we found that the mean Hb%, S. Ca, HCO, BMI,
Fat% was higher at 6 months, compared to baseline, which could
be attributed to a better nutrition, or nutritional interventions and
counseling during the follow up period. The mean Cr was higher
6months later, with respect to the baseline [24].

The predicted financial gains greatly overcome any cost associated
with the various nutritional interventions for CKD, ESRD and post-
transplant patients [49]. For this reason, careful attention to the
nutritional and metabolic state of post-renal transplant patients is
warranted in developing countries, with well-trained renal nutritionists,
with appropriate follow up, and counseling.

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Conclusions

Serum Albumin varies with diet, and is significantly higher among those eating a meat-based diet following transplant. A higher fat content was associated with higher Serum albumin levels, which may reflect a better nutritional status. Lower maintenance doses of prednisolone, and steroid-sparing regimens, may improve the S. albumin Levels and the lipid profile. Protein anabolism is determined by nutritional availability and the type of diet ingested. Dietary protein intake should be adjusted to daily needs, and other factors like, infections, hospitalization’s, diabetes and insulin resistance and metabolic acidosis. Prevention of muscle-mass wasting is an important factor to be considered in nutritional counseling in the post-transplant period. Ineffective management of diabetes may lead to lower Serum albumin levels. Attention should be paid to the prevention of acidosis. This calls for a dietary counseling, and lifestyle changes advice to all transplant recipients, to prevent the development of diabetes, hypertension, and the general state of health, which may have an impact on the long term recipients, to prevent the development of diabetes, hypertension, and metabolic syndrome in chronic kidney disease. Semin Nephrol 26: 134-157.

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References


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