ORIGINAL ARTICLE

EFFECT OF MEDICAL NUTRITION THERAPY ON NUTRITIONAL STATUS OF CHRONIC KIDNEY DISEASE UNDER HAEMODIALYSIS ASSESSED BY MIS TOOL: A PRE-POST INTERVENTIONALSTUDY IN TERTIARY HOSPITAL OF NEPAL

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ABSTRACT

Chronic kidney disease (CKD) remains a major global public health challenge, accounting for approximately 1.48 million deaths worldwide in 2023 and ranking as the ninth leading cause of death globally. The global prevalence of CKD is estimated at 9.1%, with advanced disease being less common, as CKD stage 5 affects about 0.07% of the population and 0.041% requiring dialysis.The estimated annual incidence of end-stage kidney disease in Nepal is approximately 2,900 new cases, highlighting the growing need for effective prevention and management strategies. Thisstudy aims to evaluate the prevalence of Protein-Energy Wasting (PEW) using serum albumin, C-reactive protein (CRP) for inflammation, and the Malnutrition Inflammation Score (MIS) both before and after medical nutrition therapy intervention. It also explores the relationship between Malnutrition Inflammation Score, C - reactive protein, and serum albumin in patients undergoing haemodialysis. The study involved 83 chronic haemodialysis patients from Kist Medical College and Teaching Hospital, Imadol, Gwarko, Nepal.Patients were divided into two categories: adequately nourished and malnourished. Initially, only 22% of patients were adequately nourished, while 78% were classified as malnourished. Following dietary counselling, monitoring and evaluation, the proportion of adequately nourished patients on haemodialysis increased significantly to 80%.Paired sample t-test were used to compare pre and post intervention values, and results are interpreted as mean differences with 95% confidence intervals.MIS scores significantly decreased (mean difference=9.76;95%CI:8.4 to 11.2;p<0.001) at twelve months. The study found a strong negative correlation between MIS and albumin levels (r = -0.661, p = 0.01). Furthermore, moderate positive correlation was detected between CRP and MIS in haemodialysis patients (r = 0.454, p = 0.01). This study highlights that dietary counselling and regular monitoring help increase protein intake, enhance serum albumin levels, reduce inflammation, and decrease muscle wasting, leading to improved nutritional status in patients.

Keywords: *nutritional status, chronic kidney disease, MIS tool, CRP, haemodialysis*

INTRODUCTION

The most recent global estimate shows that chronic kidney disease (CKD) was responsible for approximately 1.48 million deaths worldwide in 2023, making it the ninth leading cause of death globally according to the Global Burden of Disease Study 2023[1]. The global prevalence of CKD was estimated at 9.1%, where in CKD 5 stage is 0.07% and dialysis is 0.041% of the population[2]. Chronic Kidney Disease (CKD) is also a major public health concern in Nepal. The prevalence of CKD is almost 10.6% in urban chronic kidney disease Society of Nephrology's Kidney Disease Data Centre has revealed numerous CKD among cohorts in Nepal[1]. The estimated new cases of terminal kidney disease was 2,900 patients[3]. A nationwide cross-sectional study in Nepal from 2016 to 2018 among 12,109 Nepalese adults found that 6.1% had Chronic Kidney Disease[4]. In 2016, Nepal's Ministry of Health introduced free lifetime haemodialysis program. The number of haemodialysis centres reached 42, marking a 22.3% increase since 2010 and there were 1,975 patients in the same year[3].

Dialysis has undoubtedly prolonged the lives, however, there are certain side effects. Nutritional abnormalities can occur even before dialysis begins, as renal function is impaired which causes poor nutritional status during initial phase of dialysis. This is often associated with negative outcomes[5].In haemodialysis patients, protein-energy malnutrition can result from increased protein catabolism caused by metabolic acidosis, reduced appetite, nutrient deficiencies, insulin resistance, and inflammation. Poor nutrition results in reduction in weight and modifications in fat mass and lean mass[6].Haemodialysis patients are often malnourished[7]. Nutritional status can be assessed through weight monitoring and blood tests. However, blood test results can be influenced by chronic inflammation and fluctuating iron levels. Additionally, weight can be impacted by fluid intake and the frequency of haemodialysis sessions. Research indicates that along with malnutrition, chronic low-grade inflammation plays an important role in Protein Energy wasting [8&9].

The Malnutrition–Inflammation Score (MIS) is a comprehensive assessment tool that integrates dietary intake, weight changes, gastrointestinal symptoms, functional capacity, comorbidities, physical examination findings, and laboratory parameters, offering a more holistic evaluation of nutritional and inflammatory status in this population. Despite its recognised clinical utility, there are limited studies in Nepal utilising the MIS system to assess nutritional status among haemodialysis patients. Furthermore, there is a paucity of literature examining the relationship between MIS scores and biochemical as well as inflammatory markers, such as serum albumin and C-reactive protein. Additionally, few studies have investigated the impact of dietary intervention on anthropometric, biochemical, clinical, and dietary outcomes in haemodialysis patients.

The study was conducted to assess the nutritional status of haemodialysis patients using the Malnutrition Inflammation Score (MIS) both before and after diet therapy, to examine the correlation between MIS scores and the biochemical marker of malnutrition, serum albumin, and to explore the relationship between MIS scores and the inflammatory marker, C-reactive protein (CRP).

METHODOLOGY

Study design and sampling method

This is a single centre, single arm pre-post interventional study. The study population comprises outpatient chronic kidney disease (CKD) patients undergoing haemodialysis at KIST Teaching Hospital; a 300-bed tertiary hospital in Nepal. A Purposive sampling was employed. The study was conducted in accordance with ethical guidelines approved by the Cyberjaya University Research Ethics Committee (CREC) with Reference Number as UOC/CEREC/Al-External (04/2023), the Nepal Health Research Council (MOH, Nepal) with Reference number as 458 and the Institutional Review Committee of KIST Medical College and Teaching Hospital. Written informed consent was obtained from all participants after explaining the study. All participants received structured medical nutrition therapy with pre- and post-intervention assessments; however, as no control group was included, the study was not designed to establish causality.

Study sample and sample size

Inclusion criteria: Participants aged 18 years and above who had been undergoing maintenance haemodialysis for a minimum duration of three months were eligible for inclusion. Only patients receiving regular twice-weekly haemodialysis sessions were selected. Among these, patients were included if they were classified as malnourished, defined by at least one of the following criteria: serum albumin level ≤3.5 g/dL, unintentional dry weight loss of ≥5% over the preceding three months, or a body mass index (BMI) <20 kg/m^2. To minimise potential confounding factors, only clinically stable haemodialysis patients were enrolled, and a within-subject pre–post comparison design was employed.

Exclusion criteria: Patients with evidence of acute infection, chronic inflammatory diseases, or those who had undergone surgery within the preceding three months or during the follow-up period were excluded. In addition, individuals who had been hospitalised within the past three months, experienced major cardiovascular events, or died during the follow-up period were excluded from the analysis. Other exclusion criteria included nephrotic syndrome, a history of malignancy, and chronic liver disease.

The sample size was calculated using G*Power 3.1.9.7 software, based on a dependent (paired) sample design for continuous data with an a priori power analysis. The parameters included an effect size of 0.3, a significance level (α) of 0.05, and a statistical power (1–β) of 0.85. Based on these inputs, the required sample size was 75. Accounting for an expected dropout rate of 10%, the final sample size was adjusted to 83 participants.

Data Collection and Nutritional Assessment

Several methods have been identified to evaluate the severity of malnourished chronic kidney disease patients but none of these methods have proven to be easy to implement in clinical practice or consistently reproducible. Currently there is no single tool available to effectively identify protein-energy wasting[10&11]. According to the International Society of Renal Nutrition and Metabolism, the recommended approach to diagnosing protein-energy wasting involves analyzing serum chemistry, body composition, signs of muscle wasting, and decreased appetite. Subjective Global Assessment (SGA) is used to diagnose Protein Energy Wasting[10&12]. The updated KDOQI guidelines regarding nutrition focuses on assessment of nutritional status, diet therapy, monitoring and evaluation, dietary protein and calories intake, nutrition supplements, micronutrients, and electrolytes[13].Nutritional status is also measured using the Modified Quantitative Subjective Global Assessment (MQSGA)[14&15].To more effectively identify inflammation in protein-energy wasting (PEW) the same group modified the criteria for the seven components of the MQSGA ,introducing three new factors and this revised scoring system is called the Malnutrition-Inflammation Score (MIS)[16&17].

The demographic information of the patients, such as age, duration of haemodialysis and the presence of co morbid conditionwas gathered at baseline. Height and weight were recorded post dialysis to calculate the body mass index (BMI, kg/m^2). Pre-dialysis biochemical parameters were

taken from the patients' medical records. Nutritional status was evaluated using the Malnutrition Inflammation Score (MIS) tool. The tool includes change in weight, diet consumed, symptoms related to gastrointestinal system, patients' ambulatory condition, co morbidity, subcutaneous fat, muscle wasting, BMI, serum albumin, and TIBC. Each component was graded on a four-level severity scale, with the total score ranging from 0 (normal) to 30 (severely malnourished). Based on the MIS score, patients were categorized into adequately nourished (AN) and malnourished (MN), with a cutoff score of below 7 for AN and above or equal to 7 for MN[18]. Nutrition assessments were conducted at two time point, before intervention at the start of research and post intervention, in the twelfth month.

Nutrition Intervention

All patients received structured dietary counselling and were followed up regularly throughout the study period, with each consultation conducted by a trained dietitian. Individualised meal plans were prescribed to ensure a daily protein intake of 1.2 g/kg body weight and an energy intake ranging from 25 to 40 kcal/kg body weight. Dietary potassium, sodium, and fluid intake were restricted to 1,500–2,000 mg/day, 2–4 g/day, and 500–1,500 mL/day, respectively, based on patients' urine output and serum electrolyte levels. The primary objectives of the dietary intervention were to improve anthropometric, biochemical, and dietary parameters; prevent fluid imbalance and accumulation of metabolic waste products; and reduce the risk of metabolic complications associated with haemodialysis. Follow-up visits were scheduled every three days and documented in a dietitian-maintained logbook. Dietary adherence was monitored using repeated dietary recalls and counselling records.

Statistical Analysis

Following data collection, all study records were systematically reviewed to ensure completeness, consistency, and accuracy. Any missing or inconsistent data were cross-checked against hospital records and field notes to minimise errors and potential bias. The validated data were subsequently coded, categorised, and entered into SPSS software (version 20), with double-entry verification and random cross-checks performed to reduce data entry errors. Paired t-tests were used to compare pre- and post-intervention values, and results are presented as mean differences with 95% confidence intervals. Continuous variables are expressed as mean ± standard deviation. The strength and direction of the associations between MIS scores and biochemical or inflammatory markers were assessed using Pearson's correlation coefficient. Statistical significance was set at a p-value <0.05. Assumptions of normality were assessed prior to conducting inferential analyses.

RESULTS

Table 1: Baseline demographic, clinical, nutritional, and biochemical characteristics of haemodialysis patients (n = 83)

Characteristics	Mean ± SD
Age	46.30±14.60
Haemodialysis duration, months	21.66±18.00
MIS	13.79±5.63
Albumin	2.82±0.34
Urea	154.51±26.36
Creatinine	8.22±3.09
CRP	9.09±1.51

The average age of participants is approximately 46 years. The average duration of haemodialysis for the participants is 21.66 months with high standard deviation. This shows that some patients were on dialysis for less than a year, while others are on dialysis for several years. The MIS score average is 13.79, with a standard deviation of 5.63. Malnutrition and inflammation is quite high among this study population as the MIS score is at higher side. This suggests that the participants are at increased risk for malnutrition associated complications.

Serum albumin average is 2.82 g/dl. Hypoalbuminemia is considered as one of the factors of malnutrition, and for patients under

haemodialysis, it can also be due to inflammation or fluid imbalance. This result also aligns with the fact that the study participants are malnourished. In this study population, the average serum urea level is 154.51 mg/dl, a poor kidney function and may reflect the severity of the disease. The average serum creatinine level is 8.22 mg/dl which signifies impaired kidney function and is used to determine the progression of renal disease. C - reactive protein levels rise in response to inflammation. In this study, elevated CRP levels indicate a possible ongoing inflammatory response in these patients, which is often seen in CKD and may contribute to malnutrition and other complications. The large variation in CRP levels may indicate differing degrees of inflammation among the patients.

Table 2. Nutritional status of haemodialysis patients at baseline based on the Malnutrition-Inflammation Score (MIS)

MIS Scoring	Adequately nourished	Malnourished
	18	65
	22%	78%

The MIS data shows that 18 individuals fall into the adequately nourished category, and 65 individuals are classified as malnourished. This indicates that a significant majority (78%) are malnourished, while only a small portion (22%) is adequately nourished.

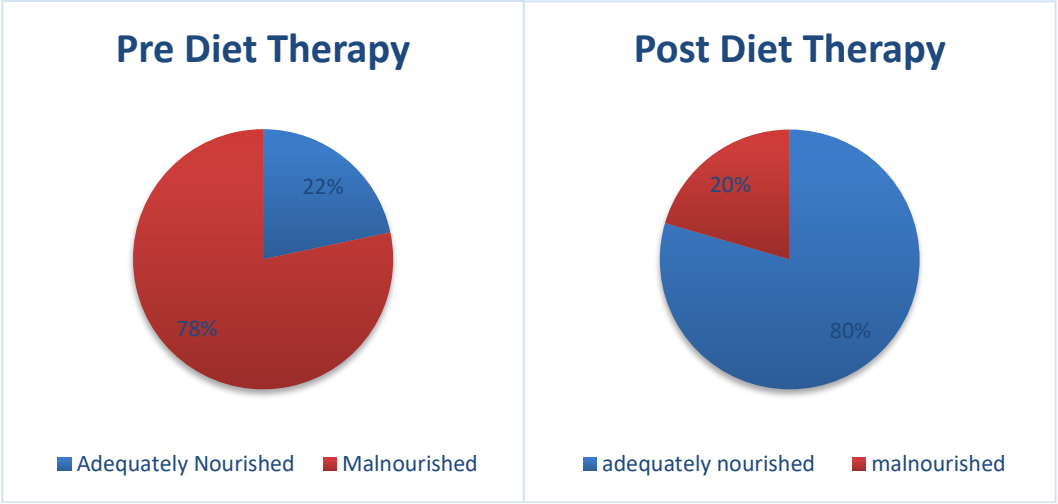

Figure 1. Comparison of nutritional status pre and post dietary intervention.

The MIS data indicates that at baseline, a large majority (78%) of patients are malnourished while a small percentage (22%) is adequately nourished. However, after receiving medical nutrition therapy, the majority (80%) are adequately nourished.

Malnutrition Inflammation Score (MIS) decreased significantly from a baseline of 13.79 ±5.63 to 4.03 ±2.55 at the 12th month, indicating improved nutritional status. Albumin levels showed a noticeable improvement, rising from 2.82 ±0.34 at baseline to 3.75 ±0.32 after 12 months, suggesting better protein status. Haemoglobin levels slightly increased from 9.89 ±8.12 at baseline to 10.19 ±0.78 after 12 months, indicating a marginal improvement in blood oxygen-carrying capacity. Urea levels significantly decreased from 154.51 ±26.36 at baseline to 92.03 ±17.95 in the 6th month, suggesting improved kidney function and reduced waste accumulation. Creatinine levels also dropped from 8.22 ±3.09 at baseline to 4.81 ±2.20 after 12 months, indicating better renal function. C-reactive protein (CRP) levels decreased from 9.09±1.51 at baseline to 6.37 ±1.01 at the 12th month, reflecting a reduction in inflammation.

Table 3. Changes in measured parameters over the study period. Values are presented as mean ± SD.

Characteristics	Baseline	12th month
MIS	13.79±5.63	4.03±2.55
Albumin	2.82±0.34	3.75±0.32
Haemoglobin	8.99±1.17	10.19±0.78
Urea	154.51±26.36	92.03±17.95
Creatinine	8.22±3.09	4.81±2.20
CRP	9.09±1.51	6.37±1.01

Table 4: Changes in Nutritional, Biochemical, and Inflammatory Parameters Following Medical Nutrition Therapy – Pre and Post Intervention.

Pair	Mean	Standard deviation	Mean Difference	95% CI of Difference	T	P value Sig (2tailed)
MIS	13.79	5.63			14.35	< 0.001
PIMIS	4.03	2.55	9.76	(8.4,11.2)		
Urea	154.51	26.36			17.414	0.001
PI urea	92.03	17.95	62.48	(54.1,68.2)		
Creatinine	8.22	3.09			10.44	0.001
PI creatinine	4.81	2.20	3.41	(2.61, 3.84)		
Sodium	138.23	3.6			6.27	0.001
PI sodium	134.50	4.26	3.73	(11.8, 13.5)		
CRP	9.09	1.51		(2.2,3.1)	12.21	0.001
PI CRP	6.37	1.01	2.72			
Albumin	2.82	0.34		(-1.0,-0.81)	-16.99	0.01
PI Albumin	3.75	0.32	-0.93			

Paired samples t-test analysis demonstrated significant improvements in nutritional and biochemical parameters following medical nutrition therapy. The Malnutrition-Inflammation Score (MIS) decreased significantly (mean difference = 9.76; 95% CI: 8.4–11.2; p < 0.001). Serum urea and creatinine levels also showed significant reductions. In addition, inflammatory status improved, as indicated by a significant decrease in C-reactive protein (CRP) levels (mean difference = 2.72; 95% CI: 2.2–3.1; p = 0.001).

Table 5: Spearman/Pearson correlation of serum albumin and C-reactive protein (CRP) with Malnutrition-Inflammation Score (MIS). Negative correlations indicate an inverse relationship, while positive correlations indicate a direct relationship. p-values denote statistical significance.

Parameter	R	Significance
Albumin	- 0.661	0.001
CRP	0.454	0.01

The correlation between Albumin and MIS is represented as R = -0.661 at p-value 0. 001.This shows that there is a significant negative correlation between Albumin and MIS. The correlation coefficient (R = 0.454) indicates a moderate positive correlation between CRP and MIS. Since the significance value (p = 0.01) is less than the standard threshold of 0.05, this result is statistically significant. In summary, higher albumin levels are associated with lower MIS scores and higher CRP levels are associated with higher MIS.

DISCUSSION

Renal patients often experience a heightened catabolic and inflammatory state, leading to the breakdown of muscle and other tissue proteins,

which can result in malnutrition. Personalized nutrition plans can help mitigate malnutrition and reduce associated morbidity and mortality [19].In this study, the intervention led to reductions in serum urea, creatinine, and CRP levels. Although the KDOQI guidelines recommend 25–35 kcal/kg body weight, providing higher caloric intake to selected malnourished patients produced positive outcomes.

In this study, based on the MIS score, only 22% of patients were adequately nourished at baseline, while 78% were malnourished. After Medical Nutrition Therapy (MNT), the percentage of adequately nourished patients on haemodialysis increased significantly to 80%. The mean MIS score improved notably, rising from 13.79 ± 5.63 at baseline to 4.03 ± 2.55post-intervention. This differs from the study by In Young Jo et al., which showed only a slight increase in the number of nourished patients, with the MIS score changing marginally from 5.33 ± 2.78 at baseline to 5.31 ± 2.56 after six months of intervention. This suggests a notable improvement in nutritional status in the present study after diet therapy, in contrast to the more limited changes seen in the other study[6].Various studies have reported differing findings on the relationship between MIS, CRP, and albumin in haemodialysis patients. Serum albumin is a widely used marker for malnutrition nevertheless its levels can be affected by factors like inflammation and fluid balance, potentially limiting its reliability in nutritional assessment.

MIS assessments were conducted by trained dieticians using a standardized protocol. The absence of formal inter-rater reliability testing is considered as limitation. Due to the exploratory nature of the study, formal multiplicity correction was not applied. Although this was a single-centre study with a relatively small sample size, the adequacy of the sample is supported by an a priori calculation based on a dependent-sample design for continuous data. Using an effect size of 0.3, a significance level of 0.05, and a statistical power of 0.85, the sample size was sufficient to detect meaningful changes following the intervention, thereby strengthening the validity of the findings.

We found a negative correlation between MIS and albumin ($r = -0.661$, $p = 0.001$), suggesting that a higher MIS score is associated with lower serum albumin levels. This aligns with the findings of K. Tur et al., as they also had a negative correlation between MIS and albumin ($r = -0.511$, $p = 0.005$). Both studies emphasize the impact of factors such as inflammation and fluid balance on albumin levels, which can influence the assessment of nutritional status in haemodialysis patients[20]. Similar negative correlation was observed in other studies[21].

We observed a significant relationship between CRP and MIS, with a correlation of $r = 0.454$ and $p = 0.01$. The result is consistent with that of Aggarwal, which shows a positive correlation between MIS and CRP. This shows that inflammation and malnutrition co exists in haemodialysis patients[21]. Nevertheless, In a study by Pisetkul et al., no significant correlation was found between CRP and MIS in haemodialysis patients ($r = 0.08$, $p = 0.44$)[22].In conditions like CKD, where both malnutrition and inflammation coexists, high CRP level often correlates with a higher MIS so patients usually have severe malnutrition and inflammation.

In patients with CKD on haemodialysis, inflammation and malnutrition are closely interrelated, often described together in syndrome such as Malnutrition Inflammation complex syndrome. Chronic inflammation driven by uremia, pro-inflammatory cytokines ,oxidative stress and dialysis related factors suppress appetite ,increase protein catabolism and contributes to protein energy wasting thereby promoting malnutrition .Likewise poor nutritional status can impair immunity and may further exacerbate systemic inflammation in a vicious cycle[11.23.24].

This study is among the first in Nepal to explore the use of diet therapy in haemodialysis patients while employing the Malnutrition-Inflammation Score (MIS) as a nutritional assessment tool in an interventional setting. While globally there have been several dietary intervention studies using nutraceuticals as high protein source in haemodialysis patients but there is a lack of evidence of examining how structured Medical Nutrition Therapy (MNT) with locally available foods can improve nutritional outcomes among hemodialysis patients, particularly in resource-limited settings like Nepal, where dietary patterns, cultural practices, and economic constraints differ significantly. These findings emphasize the importance of incorporating systematic dietary evaluation and therapeutic approaches into the management of haemodialysis patients to mitigate malnutrition and its related complications.

CONCLUSIONS

This study underscores the profound role of diet therapy in enhancing the holistic health of patients undergoing chronic haemodialysis. Utilizing the Malnutrition-Inflammation Score (MIS), the prevalence of Malnutrition was effectively evaluated, revealing a significant improvement post-intervention. The proportion of well-nourished patients rose markedly from 22% to 80%, accompanied by a substantial reduction in the mean MIS score over twelve months.A strong negative correlation between MIS and serum albumin levels underscores the importance of addressing hypoalbuminemia in combating malnutrition in this population. Additionally, significant correlation was observed between MIS

and CRP, the study demonstrates the potential of dietary counselling and regular monitoring to enhance protein intake, improve serum albumin levels, reduce inflammation, and mitigate muscle wasting. Medical Nutrition therapy was associated with significant improvements in nutritional and inflammatory markers among haemodialysis patients. This research marks an important progression in comprehending and addressing malnutrition in haemodialysis patients, stressing the necessity of organized nutritional interventions as a vital element of patient care.

ACKNOWLEDGEMENTS
I am deeply grateful to Nephrology department doctors and nurses for their support and contribution to this research.

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