Multiple factors influencing mortality in hemodialysis patients

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Abstract. – OBJECTIVE: Both decreased food intake and elevated inflammation contribute to malnutrition in hemodialysis (HD) patients. Malnutrition, inflammation, anthropometric measurements, and other comorbidity factors were investigated in this study as potential indicators of mortality in HD patients.

PATIENTS AND METHODS: By measuring geriatric nutritional risk index (GNRI), malnutrition inflammation score (MIS), and prognostic nutritional index (PNI), 334 HD patients' nutritional status was assessed. Through the use of four different models and logistic regression analysis, the predictors of each individual's survival status were examined. The models were matched using the Hosmer-Lemeshow test. On the survival of patients, the effects of malnutrition indices in Model 1, anthropometric measurements in Model 2, blood parameters in Model 3, and sociodemographic characteristics in Model 4 were investigated.

RESULTS: Five years later, 286 individuals were still on hemodialysis. Patients who had a high GNRI value had a lower mortality rate in Model 1. The body mass index (BMI) value of the patients was found to be the best predictor of mortality in Model 2, and it was found that patients with high muscle percentage had a lower mortality risk. The difference in urea level measured at the beginning and end of hemodialysis was found to be the most potent predictor of mortality in Model 3, although C-reactive protein (CRP) level was also discovered to be one of the best predictors for this model. The final model, Model 4, revealed that mortality was lower in women than in men and that income status was a reliable predictor of mortality estimation.

CONCLUSIONS: The best indicator of mortality in hemodialysis patients is the malnutrition index.

Key Words:
Chronic kidney disease, Hemodialysis, Malnutrition, Nutrition.

Introduction

In patients with chronic kidney disease (CKD) receiving hemodialysis, malnutrition is a significant predictor of mortality. The presence of malnutrition is a sign that a person's protein and energy reserves are running low. This circumstance typically portends a decline in people's functional abilities[1]. Malnutrition develops in hemodialysis patients as a result of both reduced dietary intake and elevated inflammation brought on by CKD. Inflammation and malnutrition are two conditions that cause hemodialysis patients to lose protein-energy[2]. Therefore, it is crucial to be able to identify malnutrition early in order to lower the risk of mortality and prevent the development of further diseases. Strategic nutrition plans that could possibly prevent malnutrition are necessary in light of all of this[3]. The nutritional status of an individual can be measured using a variety of instruments. The appropriate intervention can be chosen based on the individual's disease status and the efficacy of treatment using measurement tools that determine nutritional status. However, there is not yet a measurement device that uses the gold standard method to assess the nutritional status of hemodialysis patients[4].

Especially in dialysis patients, protein-energy malnutrition (PEM), which starts in the early stages of CKD, is a significant risk factor for mortality and morbidity. Malnutrition can be identified using a variety of techniques, including the measurement of biochemical and anthropometric parameters, body composition analysis, determining nutritional status, and nutritional screening tools. No one can agree on which approach best represents PEM, though[5].

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Patients who are undernourished frequently have low body weight, low body mass index (BMI), low triceps skinfold thickness (TST), low mid-upper arm circumference (MUAC), and/or decreased muscle strength[6,7]. To screen and assess nutritional status, nutritional screening tests developed specifically for different patient groups – such as the Malnutrition Inflammation Scores (MIS), Geriatric Nutritional Risk Index (GNRI), and Prognostic Nutritional Index (PNI) – are used[8,9].

Malnutrition, inflammation, anthropometric measurements, and other comorbidity factors were investigated in this study as potential indicators of mortality in HD patients.

Patients and Methods

Sample and Ethics Committee

This study is a longitudinal prospective two center study of patients undergoing long-term HD with 60 months of follow-up. This study was conducted with CKD patients who received hemodialysis treatment between March 2016 and March 2021 in Mardin and Erzurum State Hospital. Individuals who had received or were receiving regular (3 days per week) hemodialysis treatment, had no contraindications for bioelectrical impedance analysis (BIA) (i.e., not limbless nor with a pacemaker) were included in the study. Excluded patients were those with permanent cardiac pacemaker, patients with liver cirrhosis, infections, malignancy and patients on irregular dialysis due to financial constraints. Each step of the study was carried out in accordance with the 2010 Helsinki declaration. The study protocol was approved by the Ethics Committee of Malatya Turgut Ozal University, non-interventional clinical research, with the session decision dated 10.01.2022 and numbered 2022-3.

Anthropometric measurements body weight, height, upper middle arm and upper middle arm circumference measurements of individuals were regularly taken and recorded by the responsible officers working in the hemodialysis unit. The anthropometric measurements of individuals were sourced from hospital records (Figure 1).

Blood Parameters

At the start of the study, hemoglobin (g/dL), iron (mcg/dL), iron binding capacity (mcg/dL), ferritin (ng/mL), calcium (mg/dL), total protein (g/dL), albumin (g/dL), total-cholesterol (mg/dL), high density lipoprotein (HDL) cholesterol (mg/dL), low density lipoprotein (LDL) cholesterol (mg/dL), triglyceride (mg/dL), C-reactive protein (CRP) (mg/dL), phosphorus (mg/dL), blood urea nitrogen (BUN) (mg/dL) were obtained from the patients' files. Blood parameters and blood samples were taken from hemodialysis patients before and after the hemodialysis session and allowed to clot for 10 minutes, cooled at 4°C, then centrifuged. Also, serum was obtained and stored at 4°C.

Body Composition Measurements

Bioelectrical impedance analysis has proven to be a quick, objective, simple, and noninvasive method to assess body composition. BIA measurement was performed by TANITA 780 BC (Type 780 BCN, Tokyo, Japan) body composition analyzer, which is a multifrequency bioimpedance device. The BIA measurement of dialysis patients was conducted by the responsible hospital staff 30 minutes after a hemodialysis session.

Lean tissue index (LTI), fat tissue index (FTI), and body mass index (BMI) were calculated. LTI was defined as a quotient of lean tissue mass over height squared. FTI was defined as a quotient of fat mass over height[10].

Patient Observation

Researchers followed participants in the study for 5 years while they underwent regular hemodialysis. The patients were clinically assessed at the beginning of the study, and blood was drawn for the analytical studies. At the beginning of the study, information was also gathered on demographic factors, chronic kidney disease and medical history, dialysis, anthropometric measurements, and laboratory data.

In March 2016, there were 407 hemodialysis patients, according to hospital records. 28 patients

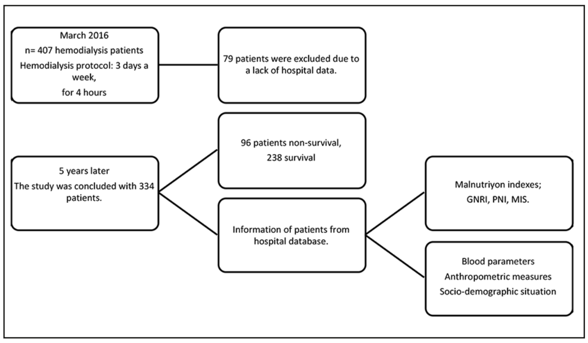

Figure 1. Flow chart of the study.

were left out of the study because they moved to a different city, 16 patients were moved to another unit for transplantation, and 29 patients were left out because there were not enough hospital records. 334 patients total were used to wrap up the study. Patients' health conditions were monitored for five years.

Geriatric Nutritional Risk Index (GNRI)

The GNRI was calculated using the formula [1.489 * serum albumin (g/L) + 41.7 * (body weight in kilograms/ideal body weight)]. The ideal body weight was calculated using the formula [22 * square of height in meters].

For the GNRI, a score of >112.3 was considered normal, scores of 103.8 to 112.3 were considered mild to moderate, and scores of <103.8 were considered severe malnutrition[11].

Prognostic Nutritional Index (PNI)

The PNI was calculated using the formula [10 * serum albumin (g/dL) + 0.005 * total lymphocyte count (mm^3)]. For the PNI, a score of >56.1 was considered normal, scores of 50.0 to 56.1 were considered mild to moderate, and scores of < 50.0 were considered severe malnutrition[12].

Malnutrition inflammation score (MIS) was applied during the assessment of malnutrition status. This scoring is determined by 10 basic questions including the evaluation of the individual's dry weight change in the last 6 months, diet status, presence of gastrointestinal symptoms, functional capacity, comorbid conditions, subcutaneous adipose tissue, muscular dystrophy, body mass index, serum albumin level and serum total iron binding capacity. Each question includes 4 steps from good to bad. The value of a total of 10 MIS questions ranges from 0 to 30, the severity of malnutrition increasing as the number increases[13].

Individuals' malnutrition inflammation status was evaluated by the researchers using the MIS form.

Statistical Analysis

Baseline differences between survival and non-survival patients were evaluated using independent samples Student's *t*-test for variables normally distributed and Mann-Whitney U test for variables not normally distributed. Based on assumptions, numerical variables in the study are given as mean±standard deviation; categorical data are given as frequency (n) and percentage (%). Statistical differences were considered $p<0.05$ statistically significant. Their significance was detected using the SPSS software version 22.0 (IBM Corp., Armonk, NY, USA). In the logistic regression analysis, the predictors of the survival of the individuals were analyzed with 4 different models. The Hosmer Lemeshow test was used to determine model suitability in the models. The effects of malnutrition indices, anthropometric measurements, blood parameters, and sociodemographic characteristics on the patients' health status, given in Model 1, 2, 3, and 4 respectively, were examined. The cases where the type 1 error level was below 5% were interpreted as statistically significant.

Results

The general characteristics of patients given in Table I, were determined by examining the hospital registry system in hemodialysis patients who have been followed for five years. The mean age of survival patients (56.21±11.22) was lower than the mean age of non-survival patients (63.19±14.13). It was observed that the frequency of cardiovascular disease was higher in both groups, and that diabetes and hypertension are among the other comorbid diseases. It was determined that 23.11% of the survival patients had low body weight, and 22.92% of the non-survival were cachectic category. The presence of regular physical activity was determined to be 15.13% in survival patients and 15.63% in non-survival. It was determined that the application of a diet specialized for the hemodialysis treatment was 61.76% in the survival patients, and the status of not following a specialized diet for hemodialysis treatment was 67.71% in the non-survival patients. In both groups where daily fluid intakes were examined, it was observed that 1 liter and less fluid consumption was 53.78% and 27.08% for each group, respectively.

The malnutrition index values and laboratory data of hemodialysis patients are listed in Table II. The diagnosis years of survival patients were found to be lower than those who died, but the duration of HD treatment was found to be higher in non-survival patients. From the blood results of the individuals, hemoglobin, iron, total protein, albumin values and blood lipid levels were found to be higher in survival patients than in non-survival patients. Ferritin, iron binding capacity, CRP and phosphorus levels of non-survival individuals were higher than survival individuals.

Table I. General characteristics of hemodialysis patients.

	Survival n = 238		Non-Survival n = 96		p
	N	%	N	%	
Age (years)	56.21 ± 11.22		63.19 ± 14.13		0.001**
[a]Comorbidities					0.001*
Diabetes	85	35.71	38	39.58	
Hypertension	98	41.18	40	41.67	
Cardiovascular disease	137	57.56	46	47.92	
BMI (kg/cm^2) BMI category					0.001*
< 18.5 and under (cachectic)	45	18.91	22	22.92	
18.5-20.00 (low body weight)	55	23.11	18	18.75	
20.01-25.00 (normal)	88	36.97	27	28.13	
25.01-30.00 (overweight)	38	15.97	23	23.96	
> 30 and upper (obese)	8	3.36	6	6.25	
Regular physical activity					0.196*
Yes	36	15.13	15	15.63	
No	202	84.87	81	84.38	
Weekly physical activity frequency					0.089*
1-2 days per week	16	6.72	9	9.38	
3 days per week	12	5.04	4	4.17	
4 days and more per week	8	3.36	2	2.08	
Diet for HD treatment					0.002*
Yes	147	61.76	31	32.29	
No	91	38.24	65	67.71	
Daily fluid intake					0.945*
1 liter or less	128	53.78	26	27.08	
1-1.5 liters	43	18.07	18	18.75	
1.5-2 liters	8	3.36	15	15.63	
2 liters or more	10	4.20	12	12.50	
No information	45	18.91	25	26.04	

*Chi-square, **Student's *t*-test, a multiple diseases have been questioned. HD: Hemodialysis, BMI: Body Mass Index.

In the binary logistic regression analysis models made to examine the mortality status in hemodialysis patients, 4 different models were created separately with the malnutrition indices, anthropometric measurements, blood parameters and socio-demographic characteristics of the individuals. Each model creates a statistically significant integrity within itself ($p<0.05$) (Table III). In Model 1, it was observed that the mortality status of individuals with high GNRI value was lower, and the best predictor of mortality status in the model was the GNRI score. When anthropometric measurements and mortality status were examined in Model 2, it was seen that individuals with high muscle percentage had a lower risk of mortality. It was determined that the best predictor of mortality in the model was the BMI value of the individuals. In Model 3, the effects of individuals' blood parameters and mortality status were examined. It was observed that the strongest predictor affecting mortality in the model was the difference in the urea level measured during entry and exit from hemodialysis treatments. However, CRP level was also found to be one of the best predictors in this model. Lastly, in Model 4, created with the socio-demographic and gender of the individuals, it was seen that the mortality of women was lower than that of men, and income status was a good predictor for mortality estimation in this model.

Discussion

Age has a significant impact on mortality risk and quality of life. Age increases mortality risk by 5% every additional year[14]. Studies[15] have revealed that patients who receive dialysis for five years or longer, experience negative effects on their life expectancy and quality of life. Another significant risk factor for cardiovascular diseases (CVD) is age increase as hemodialysis duration increases[16]. In this study, it was discovered that the individuals who passed away

Table II. The blood findings and malnutrition indices of hemodialysis patients.

	Survival (n = 238)	Non-survival (n = 96)	p
CKD (year)	9.36 ± 9.74	7.44 ± 4.06	0.001*
HD (year)	4.63 ± 4.72	5.68 ± 3.78	0.003*
BMI (kg/cm^2)	23.81 ± 3.93	21.52 ± 5.82	0.012**
Lean tissue index (kg/cm^2)	6.25 ± 0.94	4.89 ± 0.77	0.001**
Fat tissue index (kg/cm^2)	13.21 ± 2.33	11.38 ± 1.99	0.002**
Hemoglobin (g/dL)	10.92 ± 1 .82	10.71 ± 2.02	0.312**
Iron (mcg/dL)	62.27 ± 33.88	52.95 ± 25.44	0.003
Iron binding capacity (mcg/dL)	119.72 ± 46.58	134.09 ± 36.80	0.001*
Ferritin (ng/mL)	612.31 ± 466.20	617.81 ± 41.03	0.201*
Calcium (mg/dL)	8.57 ± 0.49	8.55 ± 0.69	0.803*
Total protein (g/dL)	6.80 ± 0.48	6.07 ± 0.46	0.009**
Albumin (g/dL)	3.74 ± 0.36	3.02 ± 0.31	0.112**
eGFR (mL/sec/1.73 m^2)	6.38 ± 1.35	4.24 ± 0.88	0.030**
T-cholesterol (mg/dL)	162.86 ± 46.23	159.33 ± 54.76	0.007*
HDL cholesterol (mg/dL)	32.07 ± 6.46	31.72 ± 7.45	0.004*
LDL cholesterol (mg/dL)	89.22 ± 31.78	86.28 ± 40.94	0.003*
Triglyceride (mg/dL)	176.13 ± 109.84	160.66 ± 90.30	0.008*
CRP (mg/dL)	4.71 ± 1.88	6.05 ± 1.56	0.003**
Phosphorus (mg/dL)	5.41 ± 1.24	5.66 ± 2.03	0.107**
GNRI value	102.11 ± 24.49	86.91 ± 19.29	0.001**
PNI value	48.21 ± 11.39	54.21 ± 12.47	0.006**
MIS value	4.50 ± 2.09	5.89 ± 2.19	0.008**

**Student's *t*-test and *Mann-Whitney U test. HD: Hemodialysis, GNRI: Geriatric Nutritional Risk Index, PNI: Prognostic Nutritional Index, MIS: Malnutrition Inflammation Score, BMI: Body Mass Index, CKD: Chronic Kidney Disease, CRP: C-reactive protein, HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein, Sec: Second, eGFR: Glomerular Filtration Rate.

Table III. Modeling of the factors affecting the mortality status of hemodialysis patients separately by binary logistic regression analysis.

	Beta	Wald	EXP.	p	95% CI	
Model 1						
Malnutrition Indexes						
GNRI value	0.001	29.301	3.018	0.006	4.001	1.008
MIS value	-0.207	5.101	2.111	0.009	2.802	1.201
PNI value	6.107	4.101	0.721	0.102	0.402	2.003
Hosmer Lemeshow = 0.159						
Model 2						
Anthropometric measures						
BMI (kg/cm^2)	0.107	25.101	5.123	0.006	8.406	2.001
Lean tissue index (kg/cm^2)	6.102	18.108	2.210	0.007	4.103	0.903
Fat tissue index (kg/cm^2)	-8.502	3.103	2.803	0.006	3.105	1.335
Upper middle arm circumference (mm)	0.802	12.301	0.801	0.109	16.005	7.001
Hosmer Lemeshow = 0.079						
Model 3						
Blood parameters						
CRP (mg/dL)	8.001	4.108	2.306	0.001	3.207	1.002
Hemodialysis Input-output urea difference (mg/dL)	-3.208	8.102	2.909	0.003	4.902	2.135
Hemodialysis Input-output BUN difference (mg/dL)	-3.103	23.302	0.198	0.103	0.404	0.109
Hosmer Lemeshow = 0.057						
Model 4						
Socio-demographic situation						
*Gender (1)	16.103	0.119	3.406	0.001	4.008	1.187
Monthly income	11.002	2.213	2.208	0.007	2.328	1.118
Educational status	8.122	1.107	1.036	0.107	1.404	0.986
Hosmer Lemeshow = 0.590						

*Reference category woman, $p < 0.05$; CI: Confidence Interval. HD: Hemodialysis, GNRI: Geriatric Nutritional Risk Index, PNI: Prognostic Nutritional Index, MIS: Malnutrition Inflammation Score, BMI: Body Mass Index, CRP: C-reactive protein, BUN: Blood Urea Nitrogen.

had higher mean ages and years spent receiving hemodialysis. It is well-known[15] that the main comorbidities in patients with end-stage renal disease are hypertension, diabetes, and various cardiovascular conditions (ESRD). It is acknowledged[17] that cardiovascular diseases are both the most frequent comorbidity and the most frequent cause of death. The comorbid disease status in this study was comparable to that described in the literature.

In addition to adequate dialysis and medical care, nutritional management aiming at adequate energy and protein intake through dieting is prioritized in the control and prevention of malnutrition, hyperphosphatemia, and uremic syndrome[18]. According to this study, survivors had better dietary compliance.

Patients with chronic kidney disease tend to be sedentary people with poor physical abilities. Regular exercise helps people maintain healthy body weight, blood pressure, and serum lipid levels. It also lowers CRP, a marker of inflammation, which lowers the risk of CVD mortality[19,20]. Patients with low activity levels experience a decline in their muscle power and endurance. In this study, there were no appreciable differences between the two groups' members' levels of physical activity.

The daily fluid balance for hemodialysis patients is computed based on blood pressure and urine volume. Congestive heart failure is the leading cause of death for CKD patients who do not follow the fluid restriction guidelines, and excessive fluid intake in between dialysis sessions increases the risk of developing hypertension, edema, hyponatremia, and complications from fluid withdrawal during dialysis[21].

In this study, MIS, GNRI, and PNI indices were used to identify malnutrition in hemodialysis patients. The results showed that individuals with high GNRI values had a lower mortality status, and the GNRI score was the best predictor of mortality status in the model. The clinical usefulness of the GNRI as a predictive tool was questioned in one study on hemodialysis patients, but other studies[22,23] found it to be a reliable tool for determining nutritional status in hemodialysis patients. Hemodialysis patients who participated in the study attested that GNRI is, in fact, a significant predictor of mortality[24,25]. In order to plan patient interventions and lower costs, it has been said[23] that GNRI assessments can be routinely carried out in HD patients who are at risk of malnutrition. Our study adds to the body of literature in this area.

Changes in body composition may occur in CKD due to a variety of factors, including decreased protein and energy intake, hormonal changes, deterioration of the water and sodium metabolism, and calcium-phosphorus balance. An increase in malnutrition was discovered to be associated with a decline in the fat-muscle ratio and anthropometric measurements, which define body composition in dialysis patients[26]. In line with the literature, this study discovered that a decline in BMI, fat, and muscle percentages in dialysis patients was connected to a high rate of mortality. Additionally, it has been proven that an individuals' BMI value was the best indicator of mortality.

Contrary to what is believed to be true of the general population, HD patients with high BMI (obesity) and hypercholesterolemia, a sign of overnutrition, have been found to have better clinical outcomes than those who do not, and HD patients with high BMI and body weight gain have been shown[27] to have higher survival rates. This circumstance is referred to as reverse epidemiology or paradoxical risk factors. It was discovered that the relative risk of mortality decreased by 10% for every unit increase in BMI and was significantly higher in overweight and obese HD patients with BMI 27.5 kg/m^2 compared to HD patients who were normal weight (BMI 20.0-27.5 kg/m^2) and low weight (BMI 20.0 kg/m^2).

Low cholesterol levels in ESRD patients who also have inflammation and/or malnutrition increase the risk of death from CVD[28]. However, high cholesterol was linked to death[29] even when the presence of inflammation was altered in dialysis patients. This study demonstrated that low cholesterol and triglyceride levels raise mortality over the course of a five-year observation period.

A decrease in serum proteins is caused by metabolic disorders brought on by uremia in hemodialysis patients, inadequate dietary intake, inadequate absorption, losses through medication, and dialysate. The two main serum proteins that help in determining a patient's malnutrition status are albumin and total protein. The serum albumin, total protein, hemoglobin, and iron values of the patients who died in this study were found to be lower, which has been specifically associated with increased morbidity and mortality[30-32].

The majority of dialysis patients experience a chronic inflammation as side effect. Patients who show signs of inflammation frequently exhibit erythropoietin resistance, which increases the severity of the inflammation and the mortality rate in these patients[33,34]. While serum levels of positive acute phase reactants like CRP, TNF-α, and ferritin, which are indicators, rise, serum levels of negative acute phase reactants like albumin and transferrin fall. It has been demonstrated[35] that deaths from all diseases and deaths from cardiovascular causes increase by 4.6 and 5.5 times, respectively, when the serum CRP level in hemodialysis patients rises from 3.3 mg/L to 15.7 mg/L. PEM may also manifest in these patients as a result of the ongoing inflammation process[33,36]. The main causes are the close connection between malnutrition and inflammation, decreased quality of life, increased mortality, and length of hospital stay. Albumin synthesis is quickly and effectively suppressed in the presence of inflammation[37,38]. In this study, patients who died had remarkably high serum ferritin, total iron binding capacity, and CRP values, and had low albumin levels, all of which were predictive of death.

Dietary protein intake, glomerular filtration rate, and the efficacy of dialysis therapy are the main variables influencing blood urea nitrogen levels. High plasma creatinine in hemodialysis results in a low mortality risk, and it is a measure of muscle mass and nutritional status. The inlet and outlet urea difference, a reliable indicator of adequate dialysis, is a significant predictor of mortality in this model.

Increased levels of blood phosphate, parathyroid hormone, and calcium-phosphorus products have been linked to all-cause mortality, cardiac mortality, and sudden death, according to studies[39]. The study found no distinction in the type of mortality.

According to researchers[40,41], the patients' quality of life improves as their income and educational level rise. This study has demonstrated that income level has a significant impact on survival. A significant risk factor for CKD[41] is male gender. Among the demographic factors examined in this study, gender was one of the most significant predictors of mortality. This is due to the higher BMI and body composition of female hemodialysis patients.

Limitations

The first limitation of the study is that there was little data on comorbidity included in it. Additionally, we had neither data on the medications, if any, used to treat comorbidities or their dosages, nor did we study patient adherence to therapy. Second is the lack of information on dialysis access, dialysis membrane, and numerous other known or unknown confounders. Since this research was observational, causal relationships could not be investigated.

Benefits of this study include the relatively long follow-up period (60 months), comprehensive baseline clinical assessments of the patients' states by study doctors, in-depth laboratory analyses, concurrent measurements of body composition, and the long follow-up period (60 months). Additionally, participants were chosen at random without knowing beforehand how inflammatory they were.

Conclusions

Given the overwhelming evidence demonstrating that HD patients have higher protein requirements and that maintaining adequate energy levels is essential to maximize protein intake while also maintaining energy stores, low protein and energy intakes must be especially dangerous for these patients. According to health statistics, malnutrition is not typically considered to be a leading cause of death alone, with the exception of the oldest age groups. However, HD patients have a higher mortality rate when they exhibit anthropometric and biochemical signs of malnutrition. Serum albumin levels are a particularly strong predictor of prognosis, but they may not exclusively or solely reflect protein malnutrition but also the outcomes of different diseases.

One of the few studies that examines various models of hemodialysis patients' mortality and survival rates is this one. The results of the study showed that variables, particularly those relating to nutrition, have an effect on hemodialysis patients with chronic kidney disease's death status.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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Ethics Approval

Ethics approval was obtained from the Ethics Committee of Malatya Turgut Ozal University, non-interventional clinical research, with the session decision dated 10.01.2022 and numbered 2022-3.

Informed Consent

The study was approved by the Malatya Training and Research Hospital Ethics Committee.

Authors' Contributions

Study design: N.A, H.A, B.Y, data collection: N.A, H.A and data analysis under the supervision of B.Y, N.A, H.A, data interpretation and manuscript writing: N.A, H.A, B.Y, review and editing: B.Y, N.A, H.A and supervision and project administration. All authors approved the final version of the manuscript.

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