

**Original Article****Investigating Relationships of the Inflammatory Degrees of Malnutrition and Protein Quality with Risk Factors of Cardiovascular Diseases in Hemodialysis Patients**Mahsa Baghbani¹, Golnaz Majdizadeh¹, Zahra Mirali², Shahrzad Ossareh³, Ariyo Movahedi^{4*}

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ABSTRACT

Background and Objectives: Cardiovascular diseases are the most important causes of death in patients with chronic kidney failure, including hemodialysis patients. Inflammation is one of the major causes of increased malnutrition. An increase in the concentration of vascular inflammation factors in the blood such as the concentration of serum C-reactive protein is a strong predictor of mortality in hemodialysis patients. In this study, the relationship between the inflammatory degree of malnutrition and protein quality with risk factors of cardiovascular diseases in hemodialysis patients was assessed.

Materials and Methods: This descriptive-analytical cross-sectional study was carried out on 120 hemodialysis patients aged 20–80 y (57.43 ± 15.58) in Tehran, Iran, using simple random sampling. General characteristics and anthropometric indices were recorded. Malnutrition-inflammation was assessed using questionnaires and food intake was investigated using 24-h recalls.

Results: Demographic and anthropometric characteristics were not significantly different between groups with heart diseases ($P < 0.05$). No significant correlation was observed between the indicators of malnutrition-inflammation and suffering from heart diseases in hemodialysis patients ($P < 0.05$). No significant relationship was reported between the quality index of dietary proteins and heart diseases ($P < 0.05$).

Conclusions: No significant relationship was detected between the inflammatory degrees of malnutrition and protein quality and the risk factors of cardiovascular diseases in hemodialysis patients. Further studies are highly suggested.

Keywords: Malnutrition, Cardiovascular disease, Hemodialysis

Highlights

- To our knowledge, this research uniquely explores the relationship between malnutrition-inflammation and cardiovascular risk, employing comprehensive questionnaires and dietary recall methods to assess inflammatory levels and nutrition quality.
- The findings indicate no significant correlation between malnutrition-inflammation indicators, dietary protein quality, and the incidence of heart disease in the studied population, which challenges existing assumptions about these relationships.
- This research provides novel insights specifically related to hemodialysis patients, a group that experiences unique nutritional challenges and cardiovascular risks, contributing to the limited existing literature on this subject.

Introduction

The increase in the incidence of end-stage renal disease (ESRD) and its complications is a serious public health problem worldwide (1). Since decades ago, attentions to

the problem of protein and energy malnutrition and its effects on the quality of life of hemodialysis (HD) patients have increased. Protein deficiency has been addressed more

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than other nutritional problems, majorly because its consequences are easily assessed and extensive studies in the community have shown the adverse effects of a small decrease in serum albumin on the patient survival (2,3). Malnutrition in HD patients is multifactorial. Decreased intake of nutrients, loss of nutrients because of dialysis, changes in protein metabolism, acidosis and inflammation are known as the major causes of malnutrition in these patients. Increased metabolism during dialysis can lead to malnutrition (4). In several studies, a decrease in food intake and weight has been observed in these patients. Furthermore, the food intake pattern changes in ESRD patients, who are treated with HD (5). It is important to assess the protein status and diet in order to determine the presence of malnutrition in HD patients. In fact, the nutritional status of HD patients is one of the major elements of the clinical status of these patients (6). Inflammation can be one of the reasons for decreasing energy and protein intake in HD patients. Several signaling pathways and humeral factors have been stated to be intricate in the pathogenic mechanisms of muscle wasting in HD patients, including insulin/insulin-like growth factor-1 (IGF-1) signaling, ubiquitin-proteasome system, endogenous glucocorticoids, caspase-3, metabolic acidosis, inflammation and sex hormones (7). The most assessed inflammatory factor is C-reactive protein (CRP), which is associated with increased risk of cardiovascular diseases (CVD) and death, the two in the normal populations and in HD patients (8) as the most worldwide common disease (9) as well as these patients (10,11).

Protein-energy malnutrition (PEM) is common in HD patients and is addressed as one of the most important factors of CVDs in HD patients (12). Malnutrition is a strong predictor of mortality in HD patients, especially when it is associated with inflammation. Malnutrition inflammation score (MIS) is a simple low-cost tool that assesses the existence of malnutrition with inflammation (13). Protein-energy malnutrition and inflammation in dialysis patients (MHD) include a high prevalence. Since these two diseases often occur simultaneously in MHD patients and to emphasize their important relationship, it is addressed as malnutrition-inflammation complex syndrome (MICS) or malnutrition-inflammation atherosclerosis syndrome (MIA), which is associated with atherosclerotic CVDs (14). The MICS is a condition; in which, protein and energy reserves are lost caused by inflammatory and non-inflammatory causes in patients with chronic kidney disease (CKD). Protein and energy intake often decreases due to underlying disease, psychological, social factors and uremic anorexia (15). The low level of serum albumin is a strong predictive dangerous factor that not only majorly show protein-malnutrition, but also demonstrate effects of several other disease factors (e.g. overhydration, infection and chronic disease), which may increase the risk of death.

Low levels of serum creatinine (low muscle mass), serum cholesterol (decreased energy) and low urea levels (low protein consumption) are linked to increased mortality as well.

To prevent and treat malnutrition linked to HD, necessary assessments should be used to correct factors that decrease appetite and increase pure protein catabolism (e.g. under dialysis, acidosis, low energy intake, accompanying conditions, psychological, social and economic factors) (16). Dietary recommendations should be made with the aim of ensuring adequate consumption of protein and energy sources of foods (17). In the rapid assessment methods of nutritional status for the diagnosis and management of PEW, subjective global assessment (SGA), malnutrition inflammation score (MIS), geriatric nutritional risk index (GNRI) and PEW definition criteria can be used (18). Due to long-term HD needs usually three times a week, most patients often suffer from problems such as poor nutritional status and low quality of life (19). Inappropriate nutrition is common in HD patients and is highlighted as one of the most important factors of CVDs in HD patients. In HD patients, nutrition includes a major effect on the treatment process. Creating appropriate nutritional conditions and preventing malnutrition or its improvement are major nutritional goals in these patients. In fact, nutritional assessment is effective for improving the quality of life and health and decreasing problems and complications of diseases as well as hospitalization time and treatment costs (20).

Currently, a comprehensive study on the prevalence of energy-protein malnutrition in HD patients of Iran is not available and only a limited number of studies have shown that there is a lack of energy or protein intake in 51–70% of HD patients, (21). Results of studies on the nutritional status of HD patients referred to Sina and Amiralam Hospitals (Tehran), Shafa Hospitals (Kerman) and Shahid Beheshti Hospitals (Zanjan) show the rate of malnutrition as 38–75% (21,22). Since no study has been carried out on relationships between inflammation-malnutrition score and protein quality index with risk factors of CVDs in HD patients, the current study was carried out to fill the gap.

Materials and Methods

Study design and participants

This descriptive-analytical cross-sectional study was carried out on 120 volunteers aged 20–80 years, referred to Shahid Hashminejad Hospital of Tehran (the major center for kidney diseases), Iran, September 2022 to June 2023, using random sampling method. Sample size was calculated based on similar studies (23) using G*Power software (24). The inclusion criteria included men and women aged 20–80 years, willing to participate in the study and at least having 6 m of dialysis and permanent HD. Exclusion criteria included not suffering from specific

diseases such as cancers, AIDS and hepatitis. Medical history of all the patients, including CVDs, was collected by a medical specialist at the hospital. To ensure that CVD happened during the dialysis, medical history of the patients was checked further.

Assessments

Informed consent forms were collected from all the participants at the beginning of the study. This study was approved by the Research Ethics Committee of the Faculty of Medical Sciences, Islamic Azad University, Sciences and Research Branch, Tehran, Iran (ethical no. IR.IAU.SRB.REC.1400.251). Information linked to the basic characteristics of the participants, including age, level of education, economic status, medical history and smoking, were collected using general questionnaires. Anthropometric indices, including height, dry weight and BMI, were assessed using standard methods. Information linked to malnutrition-inflammation status was collected using valid and reliable MIS, DMS and SGA questionnaires and food intake was assessed using valid and reliable 24-h food recall questionnaires (25,26). In non-pregnant adults, thresholds indicating severe malnutrition typically included 16.0–21.0 cm with a majority included 18.0–19.0 cm. For moderate malnutrition, the range was usually wider of 18.0–23.0 cm with almost all included 21.0–23.0 cm, except for one outlier (27). To calculate quality of protein, quantity of essential and non-essential amino acids was calculated and the intake ratio of each was investigated after calculating the quantity of people's food intake using the food diary. Based on the DRI, the recommended quantity was assessed using a method by Lenis et al. (28). Despite the accuracy of 1-d 24-recall for such a study (29), it was decided to use 3-d 24-recall as two non-consecutive days and one holiday in the present study to include further tangible outcomes (30).

Statistics

Kolmogorov-Smirnov test and D'Agostino-Pearson omnibus test were used to find out normality of the variables (31). Student's t-test was used to compare the mean of quantitative (for parametric distributions) and Mann-Whitney U test (for nonparametric distributions) to compare the medians of outcomes between the two groups. Pearson's correlation test was used to assess the relationship between the quantitative variables and Spearman's correlation test was used to assess the relationship between the ordinal variables. To assess the relationship between ordinal variables with levels less than 4 or nominal variables, chi-square test was used in consensus tables. Logistic regression was used to find affecting variables and degrees of effect on the dependent

variable. Moreover, IBM SPSS Statistics for Windows v.26 (IBM, Armonk, N.Y., USA) was used for all analyses and a P-value of 0.05 or less with a confidence interval of 95% was recorded as significant.

Results

As shown in Table 1, incidence of heart diseases is higher in middle-aged and elderly people with ESRD. For economic status, 53.3% of the participants had a poor economic status, 40% had an average economic status and 6.7% had a good economic status. In HD patients who had a poor economic status, incidence rate of heart disease was 52.8% and those with moderate to good economic statuses had a total incidence rate of 47.2%. Educational status had no significant relationship with the rate of CVDs. For body mass index (BMI), 55 HD patients were overweight and obese (BMI > 25); of which; 46 patients had CVDs. Number of dialysis time included no significant relationship with the rate of CVDs in HD patients. Furthermore, 64.2% of the HD patients had high blood pressure and the rate of CVDs in HD patients with high blood pressure was 64%. In addition, 35% of the HD patients (the two groups) were diabetics and rate of CVDs in HD patients with diabetes was 38.2%.

As shown in Table 2, 73% of HD patients had moderate to severe malnutrition-inflammation index; of them, 77.5% had heart diseases. Moreover, 56.2% of HD patients with heart diseases had mild to moderate malnutrition index and 43.8% of them had severe malnutrition. Additionally, 65% of HD patients had mild to moderate DMS scores and 35% of them had severe scores. In fact, 62.9% of HD patients with heart diseases had DMS scores in mild to moderate range and 37.3% of them had DMS scores in the severe range.

Table 3 compares the quality index of proteins, macronutrients and micronutrients in HD patients without CVDs and those with CVDs. No significant relationships were seen between the variables and CVDs in HD patients.

As shown in Table 4, a significant correlation was seen between MIS index, and DSM and SGA in HD patients.

As shown in Table 5, no significant relationship was reported between MIS index and heart diseases in HD patients and malnutrition-inflammation did not increase the chance of heart diseases in HD patients even after adjusting for confounder variables.

Table 1. Comparison of demographic and hospital information in all hemodialysis patients and between the cardiac patients and healthy people separately.

Variable	Total	CVD		P value*
		Yes	No	
Gender				0.17
Male	74 (61.7)	23 (74.2)	51 (57.3)	
Female	46 (38.4)	8 (25.8)	38 (42.7)	
Age				0.41
20-40	24 (20.0)	5 (16.1)	19 (21.3)	
41-60	44 (36.7)	9 (29)	35 (39.3)	
>61	52 (43.3)	17 (54.8)	35 (39.3)	
Economic status				0.60
Good	8 (6.7)	1 (3.2)	7 (7.9)	
Average	48 (40.0)	13 (41.9)	35 (39.3)	
Weak	64 (53.3)	17 (54.8)	47 (52.8)	
Education Status				0.73
Under Diploma	30 (25.0)	7 (22.6)	23 (25.8)	
Diploma	53 (44.2)	15 (48.4)	38 (42.7)	
Bachelor and above	37 (30.8)	9 (29)	28 (35.5)	
BMI (kg/m ²)				0.42
<18.5	5 (4.2)	2 (6.5)	3 (3.4)	
18.5-24.9	60 (50.0)	17 (54.8)	43 (48.3)	
25-30	35 (29.2)	10 (32.3)	25 (28.1)	
30>	20 (16.7)	2 (6.5)	18 (20.2)	
Number of times of dialysis per week				0.60
2	2 (1.7)	0 (0)	2 (2.2)	
3	115 (95.8)	31 (100)	84 (94.4)	
4	2 (1.7)	0 (0)	2 (2.2)	
5	1 (0.8)	0 (0)	1 (1.1)	
Hypertension				0.58
Yes	77 (64.2)	20 (64.5)	57 (64)	
No	43 (35.8)	11 (35.5)	32 (36)	
Congestive heart failure				0.49
Yes	11 (9.2)	1 (3.2)	10 (11.2)	
No	109 (90.8)	30 (96.8)	79 (88.8)	
Coronary artery disease				0.18
Yes	23 (19.2)	6 (19.4)	17 (19.1)	
No	97 (80.8)	25 (80.6)	72 (80.9)	
Chronic obstructive pulmonary disease				0.39
Yes	8 (6.7)	2 (6.5)	6 (6.7)	
No	112 (93.3)	29 (93.5)	83 (93.3)	
Nervous disorders				0.10
Yes	8 (6.7)	1 (3.2)	7 (7.9)	
No	112 (93.3)	30 (96.8)	82 (92.1)	
Gastrointestinal disease				0.09
Yes	12 (10.0)	2 (6.5)	10 (11.2)	
No	108 (90.0)	29 (93.5)	79 (88.8)	
Liver failure				0.46
Yes	6 (5.0)	1 (3.2)	5 (5.6)	
No	114 (95.0)	30 (96.8)	84 (94.4)	
Diabetes				0.71
Yes	42 (35.0)	8 (25.8)	34 (38.2)	
No	78 (65.0)	23 (74.2)	55 (61.8)	
Infectious disease				0.83
Yes	15 (12.5)	4 (12.9)	11 (12.4)	
No	105 (87.5)	27 (87.1)	78 (87.6)	
Kidney transplant				0.48
Yes	16 (13.3)	2 (6.5)	14 (15.7)	
No	104 (86.7)	29 (93.5)	75 (84.3)	

BMI; Body Mass Index, SBP; systolic blood pressure, DBP; diastolic blood pressure, SGA; Subjective Global Assessment, MIS; Malnutrition Inflammation Score, DMS; Dialysis Malnutrition Score

*Using Chi-Square test

Table 2. Comparison of the indicators of malnutrition-inflammation in all hemodialysis patients to differentiate between cardiac and healthy patients.

Indicators of malnutrition - inflammation	Total	CVD		P value*
		No	Yes	
Classification of SGA				0.91
Mild malnutrition	32 (26.7)	12 (38.7)	20 (22.5)	
Moderate malnutrition	81 (67.5)	17 (54.8)	64 (71.9)	
Severe malnutrition	7 (5.8)	2 (6.5)	5 (5.6)	
Classification of MIS				0.98
Mild to moderate	64 (53.3)	14 (45.2)	50 (56.2)	
Severe	56 (46.7)	17 (54.8)	39 (43.8)	
DMS score classification				0.11
Mild to moderate	78 (65)	22 (71)	56 (62.9)	
Severe	42 (35)	9 (29)	33 (37.1)	

SGA; Subjective Global Assessment, MIS; Malnutrition Inflammation Score, DMS; Dialysis Malnutrition Score

*Using Chi-Square test

Table 3. Assessment and comparison of the quality index of proteins, macronutrients and micronutrients received by hemodialysis patients with cardiovascular diseases and healthy people

	Total	CVD		P value*
		No	Yes	
Total amino acid intake (mg)	31377±7719	30608±7677	31645±7760	0.52
Essential Amino Acids (mg)	25787±5959	25710±6654	25814±5737	0.93
Non-Essential Amino Acids (mg)	4985±2372	4541± 1931	5139±2499	0.23
CEAA (mg)	25787±5959	25710±6654	25814±5737	0.93
Branched chain amino acids (mg)	11822±2745	11769±3062	11841±2645	0.91
BCAA to Total Amino Acids	0.38±0.04	0.39±0.04	0.38±0.03	0.25
Sulfuric amino acids (mg)	2462±570	2446±607	2467±560	0.86
Conditionally essential amino acids to non-essential amino acids	6.7±6.4	7.3±5.3	6.5±6.8	0.59
Essential aromatic amino acids (mg)	1575±1918	1421±1308	1629±1475	0.93
Essential aromatic amino acids to non-essential amino acids	13.4±12.8	14.5±10.6	13.0±13.6	0.59
The ratio of essential amino acids to non-essential amino acids	3.1±2.9	3.3±2.4	3.0±3.1	0.60
Aromatic amino acids (mg)	7757±1804	7702±19.75	7777±17.52	0.84
The ratio of aromatic amino acids to the total amino acid intake	0.25±0.02	0.84±0.08	0.82±0.08	0.23
Energy (Kcal)	1589±404	1546±421	1613±395	0.39
protein (g)	66.5±16.1	65.1±16.7	67.4±15.8	0.46
Carbohydrates (g)	186.1±52.9	179.9±52.0	189.6±53.4	0.33
Fiber (g)	15.8±5.1	12.3±5.6	16.0±5.0	0.42
total fat (g)	65.6±21.2	64.4±24.5	66.4±19.3	0.65
Saturated fatty acids (g)	21.1±10.2	20.7±11.5	21.5±9.4	0.68
MUFA(g)	21.7±6.9	21.3±6.9	21.9±6.9	0.63
PUFA(g)	17.8±8.6	17.5±10.4	17.9±7.4	0.82
Cholesterol (mg)	224.2±85.9	223.3±75.0	224.7±91.8	0.93
Retinol (µg/dl)	197.7±76.7	197.5±77.5	197.8±76.7	0.98
Vitamin A, (RE)	381.7±149.6	380.7±167.9	382.4±195.5	0.95
Alpha Carotene (µg)	575±570	591±638	566±532	0.83
beta-carotene (µg)	1870±1331	1855±1456	1877±1260	0.31
Cryptoxanthine (mg)	85.5±66.3	76.8±55.9	89.6±77.8	0.33
Lycopene (mg)	1841±1832	1924±2193	1794±1610	0.71
Lutein and xanthine (mg)	879±1200	857±1013	591±1298	0.88
thiamine (mg)	1.2±0.34	1.2±0.36	1.3±0.33	0.42
riboflavin (mg)	1.3±0.33	1.3±0.31	1.3±0.34	0.52
Niacin (mg)	19.1±5.0	18.4±5.4	19.5±4.8	0.28
Pyridoxine (mg)	1.6±0.4	1.6±0.44	1.7±0.37	0.67
Folic acid (µg)	157.8±68.0	155.5±72.6	154.4±66.7	0.94
Dietary folate (µg)	186.0±64.7	182.2±70.0	187.1±61.0	0.66
Total folate, DFE	449.7±150.2	447.2±160.3	451.1±145.4	0.89
Total folate	339.7±107.6	336.9±115.3	341.5±103.8	0.82
Choline (mg)	245.2±67.5	242.3±65-6	246.8±89.9	0.73
Cobalamin (µg)	2.6±0.97	2.6±1.0	2.6±1.0	0.91
Vitamin C (mg)	55.9±29.3	56.1±33.8	55.8±26.7	0.96
Vitamin D IU	4.0±2.1	4.0±2.3	4.0±2.1	0.89
Vitamin (mg) E	8.0±5.1	8.0±5.5	7.0±4.8	0.93
Calcium (mg)	678.4±217.1	652.9±200.7	692.5±225.8	0.34
Phosphorus (mg)	1067±290	1039±297	1082±286	0.44

	Total	CVD		P value*
		No	Yes	
magnesium (mg)	229.4±67.2	218.4±62.4	235.6±70.8	0.19
Iron (mg)	10.0±2.9	9.7±3.2	10.1±2.8	0.47
Zinc (mg)	9.1±2.8	9.0±2.9	9.1±2.8	0.81
copper (µg)	0.9±0.4	0.89±0.46	0.90±0.37	0.89
Selenium (µg)	92.0±27.1	90.3±29.8	92.9±25.6	0.60
potassium (mg)	2123±523	2107±556	2132±508	0.80
Sodium (mg)	1972±550	1928±558	1997±558	0.51
Caffeine (mg)	61.5±34.3	63.5±34.0	60.4±34.6	0.64

*Analyzed by t-test. AA; Amino Acid, EAA; Essential Amino Acids, NEAA; non-essential amino acid, CEAA; Conditionally Essential Amino Acid BCAA; Branched Chain Amino Acid, MUFA; Monounsaturated Fatty Acids, PUFA; Polyunsaturated Fatty Acids, RAE; Retinol Activity Equivalent, DFE; Dietary Folate Equivalent

Table 4. Correlation of MIS index with DSM and SGA in hemodialysis patients

Variable	R	P*
DSM	0.687**	<0.001
SGA	0.540**	<0.001

* Anylysed by using Pearson correlation

Table 5. Assessment of relationships between MIS index and cardiovascular diseases in hemodialysis patients

variable	odd ratio	Confidence interval 95%	P value*
MIS			
Model 1	0.96	(0.86-1.06)	0.40
Model 2	0.99	(0.88-1.12)	0.99

Model 1: Raw model

Model 2: Adjusted for age, gender, literacy level, smoking, economic status, BMI and energy intake

*Logistic regression

Discussion

Based on the present study, a significant relationship was observed between SGA score, MIS and DSM in the entire study population. By increasing SGA score, MIS and DSM scores increased in the two groups. Results showed a significant difference between the results of the mental comprehensive index, DSM and MIS between the two groups of HD patients with and without heart diseases. According to SGA classification, more than 70% of HD patients with CVDs had moderate malnutrition. In total, nearly 90% of the entire study population had moderate malnutrition based on the SGA index and less than 6% of the entire study population (the two groups) had severe malnutrition. In fact, no significant difference was seen between the two groups (HD patients with CVDs and those without CVDs) for the scores achieved; in contrast to the previous studies. Results of data assessment in the present study showed that despite the high proportion of moderate malnutrition in the two study groups (with and without CVDs), a significant relationship was recorded between the classification scores of the mental comprehensive assessment (mild, moderate and severe), with CVDs were not observed in HD patients. Several studies such as Tayyem et al. (2008) have been carried out on HD patients in Jordanian hospitals, showing that nearly (62%) HD patients suffered from mild to severe malnutrition based on SGA (32). Similarly, Qureshi and colleagues (2006) in a study on HD patients in a hospital in Stockholm, Sweden,

showed that 51% of HD patients had mild malnutrition and 13% of them had moderate to severe malnutrition based on comprehensive mental assessments (33). However, no study has assessed relationships between SGA scores and CVDs in HD patients. In a study by Ashabi and colleagues carried out in 2017, investigating prevalence of malnutrition-energy in HD patients of Tehran, Iran, based on SGA, it was shown that nearly 60.5% of HD patients had mild to moderate malnutrition and 1% had severe malnutrition (34). However, other studies showed that a majority of patients who had kidney diseases for a longer time and were on dialysis for a longer time achieved higher scores from SGA assessment. In fact, this shows severity of malnutrition in HD patients (24,29–31). Based on MIS classification, 53.3% of the total population of HD patients (the two groups) had mild to moderate malnutrition and 46.7% of all HD patients (the two groups) were severely malnourished; similar to previous studies (25,35,36). However, no significant relationship was observed between MIS malnutrition and CVD in HD patients. In other studies such as a study by Ashabi et al., nearly 54% of the HD patients had mild to moderate energy-protein malnutrition and 1% of them had severe malnutrition based on the MIS score. Relationship between MIS malnutrition and CVDs was not significant (34). Based on the DMS classification, 65% of the total population of HD patients had normal condition and 35% of them suffered from mild to moderate malnutrition.

Normally, three types of energy-protein malnutrition can be identified in HD patients. Type I includes insufficient intake of energy or protein without inflammation, Type IIa includes insufficient intake of energy or protein accompanied by inflammation and Type IIb includes insufficient intake of energy and protein accompanied by inflammation. Comparison of non-traditional risk factors of HD patients in types of protein-energy malnutrition has shown that in HD patients suffering from Types IIa and IIb protein-energy malnutrition with inflammation, concentration of CRP and sICAM-1 was significantly higher than that in patients suffering from Type I energy-protein malnutrition. Since these two factors are risk factors for CVDs, risk of heart diseases increases if HD patients suffer from energy-protein malnutrition. Basically, Type II proteins, including IIa and IIb, can be major causes of inflammation in HD patients suffering from energy malnutrition; hence, increasing in the concentration of systemic inflammatory factor of CRP and vascular inflammatory factor of sICAM-1. In HD patients with energy-protein Type I malnutrition, the concentration of systemic and vascular inflammatory factors does not increase and as a result, these patients are not exposed to the mentioned risk factors (34).

In a study by Taghdir et al., significant relationships between inflammation and increased risks of CVDs in HD patients were seen. Inflammation can be another reason for decreasing energy and protein intake in HD patients and is the major initiator of the molecular cascade of events that causes anorexia and adverse effects in these patients. In addition, studies have stated that inflammation causes progressive breakdown of skeletal muscles. Several studies have shown that analysis of muscle mass is closely linked to the occurrence of inflammatory conditions, especially with the activation of specific proteases by inflammation. The most assessed inflammatory factor is CRP, which is associated to an increased risk of CVDs and mortality in normal populations and HD patients (37,38).

Although a study by Kalantar-Zadeh and colleagues has indicated that energy-protein malnutrition is a risk factor for CVDs, rather it seems that malnutrition with inflammation is a risk factor for CVDs in HD patients. In other words, other manifestations of malnutrition, inflammation and atherosclerosis that indicate malnutrition and inflammation, are the major reasons for increasing the risk of CVDs in HD patients (39). Based on the studies, inflammatory process promotes inflammatory cell proliferation and infiltration into the intima of arterioles, including coronary arteries, leading to atherosclerosis and stenosis of these vessels and hence causing coronary and other vascular diseases (40). In a study carried out by Afshar et al., no significant relationship was detected between malnutrition-inflammation and heart diseases in HD patients. This could be attributed to the younger age

and shorter time of dialysis of the patients, compared to another study by Kalantar-Zadeh (41).

Based on the present study, no significant association was reported between the inflammatory malnutrition index and heart diseases in HD patients. Inflammation in HD patients includes several causes, one of which is the presence of oxidative stress. Loss of antioxidants such as carnitine during HD may contribute to this disorder (34). A clear correlation is reported between inflammation and oxidative stress in HD (25). Several components of current HD can cause inflammation in the patients. It is effective in causing oxidative stress due to components of the dialysis membrane such as acetate and pyrogens during each HD session. Thus, guidelines used to assess dietary patterns of these patients are similar and all HD patients follow similar dietary guidelines (35).

Results of this study showed no significant difference between the two groups for protein quality index. In other words, no significant difference is reported between protein quality, macro and micro nutrients and risk factors of heart diseases in HD patients. Due to various reasons such as insufficient education about the diets, dietary restrictions by the patients and limitation of phosphorus and potassium intakes, quantity of protein intake from animal and vegetable sources in these patients is less than the recommended level, leading to decreases of fat and structural protein reserves and muscle breakdown in long-terms. This can lead to inflammation and hence increases in the risk of heart diseases. As previously shown, malnutrition may result in CVDs such as cardiomyopathy, heart failure, cardiac arrhythmia (42). Specifically, no relationship was seen between the ratio of amino acids and risk factors of heart diseases in HD patients. However, no study has linked the protein quality index (by separating the ratio of essential, non-essential, branched, sulfur and aromatic proteins), amino acids and risk factors of heart diseases in HD patients. It seems that interventional and prospective clinical studies should be carried out to detect such a relationship.

Conclusion

Findings of the present study showed no significant relationship between the indicators of malnutrition-inflammation and protein quality index of diets with the risk factors of heart diseases in HD patients. In fact, results of the study were contrary to the initial hypotheses of the study and thus further studies are highly recommended.

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Data availability: Data are available upon requests to the corresponding author.

Conflict of interest

Authors declare no conflict of interest.

Ethical approval: This study was approved by the Research Ethics Committee of the Faculty of Medical Sciences, Islamic Azad University, Science and Research

Branch, with the ethics number of IR.IAU.SRB.REC.1400.251.

Informed consent

Informed consents (oral or written) were collected, based on each unit policy of data management

References

- Zou Y, Hong D, He Q, Wen Y, Li G. Epidemiology investigation and analysis of patients with hemodialysis in Sichuan province of China. *Ren Fail.* 2019;41(1):644–9.
- Hakim RM, Levin N. Malnutrition in Hemodialysis Patients. *Am J Kidney Dis.* 1993;21(2):125–37.
- Morais AAC, Silva MAT, Faintuch J, Vidigal EJ, Costa RA, Lyrio DC, et al. Correlation of nutritional status and food intake in hemodialysis patients. *Clinics (Sao Paulo).* 2005;60(3):185–92.
- Iorember FM. Malnutrition in Chronic Kidney Disease. *Front Pediatr.* 2018;6:161.
- Acchiardo SR, Moore LW, Latour PA. Malnutrition as the main factor in morbidity and mortality of hemodialysis patients. *Kidney Int.* 1983;24(SUPPL. 16):1.
- Lai S, Amabile MI, Altieri S, Mastroluca D, Lai C, Aceto P, et al. Effect of Underlying Renal Disease on Nutritional and Metabolic Profile of Older Adults with Reduced Renal Function. *Front Nutr.* 2017;4(March):1–6.
- Löwbeer C, Stenvinkel P, Pecoits-Filho R, Heimbürger O, Lindholm B, Gustafsson SA, et al. Elevated cardiac troponin T in predialysis patients is associated with inflammation and predicts mortality. *J Intern Med.* 2003;253(2):153–60.
- Chait A, Chang YH, Oram JF, Heinecke JW. Lipoprotein-associated inflammatory proteins: Markers or mediators of cardiovascular disease? Vol. 46, *Journal of Lipid Research.* © 2005 ASBMB. Currently published by Elsevier Inc; originally published by American Society for Biochemistry and Molecular Biology.; 2005. p. 389–403.
- Coronado F, Melvin SC, Bell RA, Zhao G. Global Responses to Prevent, Manage and Control Cardiovascular Diseases. *Prev Chronic Dis [Internet].* 2022 Dec 8;19:220347. Available from: http://www.cdc.gov/pcd/issues/2022/22_0347.htm
- Albahr RB, Bargman JM. A Comparison of Hemodialysis and Peritoneal Dialysis in Patients with Cardiovascular Disease. Vol. 39, *Cardiology Clinics.* 2021. p. 447–53.
- Cozzolino M, Mangano M, Stucchi A, Ciceri P, Conte F, Galassi A. Cardiovascular disease in dialysis patients. *Nephrol Dial Transplant.* 2018 Oct;33(suppl_3):iii28–34.
- Borges MCC, Vogt BP, Martin LC, Caramori JCT. Malnutrition Inflammation Score cut-off predicting mortality in maintenance hemodialysis patients. *Clin Nutr ESPEN.* 2017;17(November):63–7.
- Kopple D. Award Lecture , malnutrition in maintenance. *Am J Clin Nutr.* 1997;65(May):1544–57.
- Zimmermann J, Herrlinger S, Pruy A, Metzger T, Wanner C. Inflammation enhances cardiovascular risk and mortality in hemodialysis patients. *Kidney Int.* 1999 Feb;55(2):648–58.
- Riella MC. Nutritional Evaluation of Patients Receiving Dialysis for the Management of Protein-Energy Wasting: What is Old and What is New? *J Ren Nutr.* 2013;23(3):195–8.
- Ishii H, Aoyama T, Takahashi H, Kamoi D, Tanaka M, Yoshikawa D, et al. Serum albumin and C-reactive protein levels predict clinical outcome in hemodialysis patients undergoing endovascular therapy for peripheral artery disease. *Atherosclerosis.* 2013;227(1):130–4.
- de Roij van Zuidewijn CLM, ter Wee PM, Chapdelaine I, Bots ML, Blankestijn PJ, van den Dorpel MA, et al. A Comparison of 8 Nutrition-Related Tests to Predict Mortality in Hemodialysis Patients. *J Ren Nutr.* 2015;25(5):412–9.
- Cholewa M, Madziarska K, Radwan-Oczko M. The association between periodontal conditions, inflammation, nutritional status and calcium-phosphate metabolism disorders in hemodialysis patients. *J Appl Oral Sci.* 2018;26:1–8.
- Sathvik BS, Parthasarathi G, Narahari MG, Gurudev KC. An assessment of the quality of life in hemodialysis patients using the WHOQOL-BREF questionnaire. *Indian J Nephrol [Internet].* 2008 Oct;18(4):141–9. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20142925>
- Tsai AC, Chang MZ. Long-form but not short-form Mini-Nutritional Assessment is appropriate for grading nutritional risk of patients on hemodialysis-A cross-sectional study. *Int J Nurs Stud.* 2011 Nov;48(11):1429–35.
- Tabibi H, As'Habi A, Heshmati BN, Mahdavi-Mazdeh M, Hedayati M. Prevalence of protein-energy wasting and its various types in Iranian hemodialysis patients: A new classification. *Ren Fail.* 2012;34(10):1200–5.
- Ghorbani A, Hayati F, Karandish M, Sabzali S. The prevalence of malnutrition in hemodialysis patients. *J Ren Inj Prev.* 2020;9(2).
- Liu WL, Chen YH, Duong T Van, Wong TC, Chen HH, Chen TH, et al. The Effect of Different Nutritional Education Models on Reducing Cardiovascular Disease Risk Factors by Improving Dietary Fat Quality in Hemodialysis Patients. *Nutrients [Internet].* 2022 Sep 16;14(18). Available from: <http://www.ncbi.nlm.nih.gov/pubmed/36145214>
- Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral and biomedical sciences. *Behav Res Methods [Internet].* 2007 May;39(2):175–91. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/17695343>
- Fouque D, Kalantar-Zadeh K, Kopple J, Cano N, Chauveau P, Cuppari L, et al. A proposed nomenclature and diagnostic criteria for protein-energy wasting in acute and chronic kidney disease. *Kidney Int [Internet].* 2008 Feb;73(4):391–8. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/18094682>
- Steiber AL, Kalantar-Zadeh K, Secker D, McCarthy M, Sehgal A, McCann L. Subjective Global Assessment in chronic kidney disease: a review. *J Ren Nutr [Internet].* 2004 Oct;14(4):191–200. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/15483778>
- Fiorentino M, Sophonneary P, Laillou A, Whitney S, de Groot R, Perignon M, et al. Current MUAC Cut-Offs to Screen for Acute Malnutrition Need to Be Adapted to Gender and Age: The Example of Cambodia. *PLoS One.* 2016;11(2):e0146442.
- Lenis NP, Van Diepen HTM, Bikker P, Jongbloed AW, Van Der Meulen J. Effect of the ratio between essential and nonessential amino acids in the diet on utilization of nitrogen and amino acids by growing pigs. *J Anim Sci.* 1999;77(7):1777–87.
- United States Department of Health and Human Services. Recommendations on potential approaches to dietary

- assessment for different research objectives requiring group-level estimates. *Cancer.gov* [Internet]. 2020;1–5. Available from: <https://dietassessmentprimer.cancer.gov/approach/table.html>
30. Huang K, Zhao L, Guo Q, Yu D, Yang Y, Cao Q, et al. Comparison of the 24 h Dietary Recall of Two Consecutive Days, Two Non-Consecutive Days, Three Consecutive Days and Three Non-Consecutive Days for Estimating Dietary Intake of Chinese Adult. *Nutrients*. 2022 May;14(9).
 31. D'Agostino RB, Belanger A, D'Agostino RB. A Suggestion for Using Powerful and Informative Tests of Normality. *Am Stat* [Internet]. 1990 Nov;44(4):316. Available from: <https://www.jstor.org/stable/2684359?origin=crossref>
 32. Tayyem RF, Mrayyan MT, Heath DD, Bawadi HA. Assessment of Nutritional Status Among ESRD Patients in Jordanian Hospitals. *J Ren Nutr*. 2008;18(3):281–7.
 33. Qureshi AR, Alvestrand A, Danielsson A, Divino-Filho JC, Gutierrez A, Lindholm B, et al. Factors predicting malnutrition in hemodialysis patients: A cross-sectional study. *Kidney Int*. 1998 Mar;53(3):773–82.
 34. As'habi A, Tabibi H, Hedayati M, Mahdavi-Mazdeh M, Nozari B. Association of energy-protein malnutrition with risk factors of cardiovascular diseases in hemodialysis patients. *Iran J Nutr Sci Food Technol*. 2011;6(2):1p-1p.
 35. Dukkipati R, Kopple JD. Causes and prevention of protein-energy wasting in chronic kidney failure. *Semin Nephrol* [Internet]. 2009 Jan;29(1):39–49. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/19121473>
 36. Badrasawi M, Zidan S, Sharif I, Qaisiyha J, Ewaida S, Jaradat T, et al. Prevalence and correlates of malnutrition among hemodialysis patients at hebron governmental hospital, Palestine: cross-sectional study. *BMC Nephrol* [Internet]. 2021;22(1):214. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/34098899>
 37. Taghdir M., Ashourpour M.*, Ghandchi Z., Pourghaderi M., Sepandi M. ANA, *. Assessment Of Energy And Protein Intake And Some Of The Related Factors In Hemodialysis Patients Referred To Imam Khomeini Hospital Author(s): Iran *J Endocrinol Metab MARCH* 2012. 2012;7(2):57–77.
 38. Muscaritoli M, Molfino A, Bollea MR, Rossi Fanelli F. Malnutrition and wasting in renal disease. *Curr Opin Clin Nutr Metab Care*. 2009 Jul;12(4):378–83.
 39. Kalantar-Zadeh K, Ikizler TA, Block G, Avram MM, Kopple JD. Malnutrition-Inflammation Complex Syndrome in Dialysis Patients: Causes and Consequences. *Am J Kidney Dis*. 2003;42(5):864–81.
 40. Del Fabbro E. Cachexia and Wasting: A Modern Approach. *JAMA* [Internet]. 2007;297(5):533. Available from: <https://books.google.com/books?id=IQyGxrmQ17AC>
 41. Reza Afshar SS. Assessment of Nutritional Status in Patients Undergoing Maintenance Hemodialysis: A Single-Center Study from Iran. *Fam Environ Res*. 2007;51(3):307–19.
 42. Welte JW, Barnes GM. Drinking among homeless and marginally housed adults in New York State. *J Stud Alcohol* [Internet]. 1992 Jul;53(4):303–15. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/1619924>