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The relationship of dietary antioxidant capacity with laboratory and anthropometric measurements in hemodialysis patients

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ABSTRACT

Aim: Dietary antioxidant intake correlates with blood antioxidant content and protects against oxidative damage and related inflammatory complications. This study was conducted to examine the relationship between total antioxidant capacity of diet and effective factors with laboratory and anthropometric parameters in patients undergoing hemodialysis.

Material and Method: The present case-control study consisted of 62 cases and 59 controls individuals who received hemodialysis treatment between the ages of 35-75. Dietary intake, sociodemographic data, medical history, and anthropometric measurements were collected from participants using a validated questionnaire.

Results: Examining the association between dietary components and diet's total antioxidant capacity (dTAC) reveals a positive correlation between dietary protein (kg/avg), beta carotene (mcg/day), vitamin C (mg/day), vitamin E (mg/day), and polyunsaturated fatty acids (PUFA) (g/day) (p=0.002). The serum albumin, serum neutrophil to lymphocyte ratio and HDL-cholesterol have been reported to have a positive relationship with dTAC. And body mass ındex (BMI) and other anthropometric parameters were found to have a negative connection with dTAC (p=0.007).

Conclusion: Total dietary antioxidant capacity is effective on anthropometric measurements and serum laboratory values. Increasing the antioxidant capacity of the diet in hemodialysis patients is important to prevent complications related to inflammation.

Keywords: Hemodialysis, diet total antioxidant capacity, anthropometric parameters

INTRODUCTION

There is a balance between oxygen radicals and antioxidant defense mechanisms in healthy humans. Oxidative stress (OS) is the condition that arises when this equilibrium is disrupted in favor of oxygen radicals. Uncontrollable reactive oxygen products (ROS) cause tissue damage and dysfunction in the presence of oxidative stress. Oxidative stress is involved in the pathogenesis of numerous disorders, including atherosclerosis, stroke, diabetes, preeclampsia, heart failure, cancer, and chronic kidney failure (1). Oxidative stress, which is causally related to chronic renal failure, increases with chronic renal failure and hemodialysis and increases mortality and morbidity by promoting metabolic risk factors (2). In hemodialysis patients, inflammation and oxidative stress indicators are positively correlated (3, 4). Uremia and the exposure of blood to dialysate and dialysis membrane during dialysis stimulate proinflammatory cytokines in the extracorporeal circulation (4). Free oxygen radicals (SOR) produced from polymorphonuclear cells stimulated by cytokines generates a vicious spiral between cytokines and SOR by activating nuclear factor kB (NF-kB), the transcription factor of cytokines. Activation of NF-kB induces the production of ınterleukin-1 (IL-1), tumor necrosis factor alpha (TNF-α), ınterleukin-6 (IL-6), and C-reactive protein (CRP) (5). Due to existing renal parenchymal damage and decreased glomerular filtration rate in chronic renal failure (CRF), studies have revealed that serum antioxidant capacity diminishes, free oxygen radical levels rise, and inflammation increases (6). In end-stage renal disease patients, inflammation is associated

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with insulin resistance, oxidative stress, endothelial dysfunction, and vascular calcification, and it raises cardiovascular risk factors (7). Dietary antioxidant intake correlates with blood antioxidant content and protects against oxidative damage and related inflammatory complications. Finding a correlation between dietary diversification and total antioxidant capacity is crucial for preventing serum oxidative stress and inflammatory diseases (8, 9). This study was conducted to examine the relationship between total antioxidant capacity of diet and effective factors with laboratory and anthropometric parameters in patients undergoing hemodialysis.

MATERIAL AND METHOD

Study Settings and Participants

All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. The study comprised patients who got treatment at the Hemodialysis Unit of the Malatya Turgut Özal Training and Research Hospital as well as individuals who matched the patient group in terms of age and gender and were deemed healthy by the doctor.

Exclusion Criteria

Individuals who smoke and drink alcohol, have acute inflammatory disease, use anti-inflammatory drugs, have chronic inflammation such as active hepatitis, HIV(+), have heart disease detected and symptoms by electrocardiography in the past three months, and have diabetes mellitus with a history of ischemic heart disease are at increased risk for developing ischemic heart disease. Patients who have received hemodialysis treatment for less than one month and for more than ten years, those who are scheduled for transplantation and who have recently undergone transplantation and re-entered dialysis, those who have previously received peritoneal dialysis, those who use fish oil and other antioxidant drugs, those with a cancer diagnosis, and pregnant and lactating patients who refuse to participate in the study and healthy volunteers were excluded.

Inclusion Criteria

The study included a total of 41 male and female patients who received hemodialysis treatment (6 months-10 years), entered dialysis at least 2 days a week, did not meet the exclusion criteria, aged between 35 and 75 years, and voluntarily agreed to participate in the study. The control group consisted of 41 healthy male and female volunteers aged between 35 and 75 years, who were matched with the patient group in terms of age and gender, and who visited the internal medicine outpatient clinic for routine check-ups.

Data Collection

The objectives of the study and the contents of the data collecting form were explained to the individuals who voluntarily participated in the study. In addition, they were advised that no additional measures would be taken and that they would not be required to pay any costs. By signing a consent form, individuals who consented to participate in the study were included in the study's scope.

Demographic Data: After determining the patients to be included in the study, the demographic parameters (age, gender, education level, and marital status) and health status of the patients were collected via face-to-face interviews with a questionnaire.

Laboratory Index: Blood glucose, high density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), total cholesterol, triglyceride (TG), alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine, urea, sodium, and potassium values were extracted from the hemodialysis unit records at the Malatya Turgut Özal University Training and Research Hospital. Blood samples from healthy individuals were tested in the biochemistry laboratory of Malatya Turgut Özal University Training and Research Hospital with the physician's clearance.

Anthropometric Measurements

Body weight (kg), body fat mass (kg), lean body mass (kg), body fat percentage (percent), water mass (kg), and visceral adiposity index (VAI) are all measurements of body composition. Using bioelectric impedance technology, the Tanita BC 545N portable body analyzer (bioelectric impedance device -BIA) was manufactured. The device operates on the basis of the differential in electric current permeability between lean tissue mass and fat. The impedance is measured against the method-specified weak electric current (50 kHz). The weight measurements were recorded with 0.1 kg of precision in kilograms (9). Individuals should be informed that they must fast for at least four hours prior to the measurement, not consume liquids (water, tea, coffee), not be congested with urine, refrain from engaging in strenuous physical activity for 24 hours prior, and not have any metal objects in contact with their skin during the measurement. has been made.

The height was measured using a portable stadiometer (height meter) of the Leicester brand, with the head in the Frankfurt plane, the feet next to the heels, and the back, hips, and heels touching the wall, while taking deep breaths. The measurements were taken in cm with an accuracy of 0.1 cm. Body mass index (BMI) was calculated using the formula "body weight/height2 (kg/m²)" with data of body weight and height. The resulting BMI values were assessed using the WHO classification system (10).

The waist circumference was measured with a rigid tape measure halfway between the lowest rib and the cristailiac. Before measuring the waist circumference, respondents were requested to remove any items or clothes that could obstruct the measurement. In order for the correct measurement to be taken, the individual was positioned face-to-face with the person to be measured, standing upright with a relaxed abdomen, arms at both sides, and feet together. The measurements were taken in centimeters with an accuracy of 0.1 cm. Consequently, a waist circumference of more than 80 cm in women and 94 cm in men was deemed dangerous, and a waist circumference of 88 cm or more in women and 102 cm or more in males was deemed obese (11). The individual's hip circumference was measured from the highest point on the side of the body. The waist-to-hip ratio has been linked to chronic disorders in adults. A waist-to-hip ratio of 0.85 or higher in women and 0.90 or higher in men was deemed obese (12). This measurement also determines the obesity of androids and gynoids. The waist-height ratio was calculated by dividing the waist circumference by the height, and risk classification was determined. (Waist-height ratio risk classification: for men and women; Care should be taken <0.4, normal= 0.40-0.50, precaution should be taken= 0.50-0.60, ıntervention should be done >0.60 (13).

Food Consumption Diary

In order to determine the nutritional status of the patients, 3-day food intake records were taken on successive days: the day before dialysis, the day of dialysis, and the day following dialysis. In order to determine the nutritional status of healthy individuals in the control group, retrospective 3-day food intake records were acquired. The oxygen radical absorption capacity value (ORAC) of that food was calculated by multiplying the previously reported (14) ORAC value for each food and the grams of the consumed food. The diet's total antioxidant capacity (dTAC) was estimated by adding the ORAC values calculated for each food consumed during the day. Individuals' daily calorie, macronutrient, and micronutrient intakes were determined using the "Nutrition Information System (BEBIS)" software developed for Turkey (15).

Statistical Analysis

SPSS software version 22.0. (SPSS; IBM Corp., Armonk, NY, USA). As descriptive statistics, the number, percentage, mean, standard deviation, minimum and maximum values were determined. In analytical evaluations, scale scores were analyzed using the t-test and analysis of variance. A Bonferroni analysis was performed to establish which group was responsible for the difference. As a multivariate analysis, the forward linear regression method was utilized to determine the factors influencing dORAC. Using multiple linear regression, the connections between independent variables and dORAC were determined. In binary and multivariate linear analysis, only variables with $p<0.05$ were added to the model, and only variables with $p<0.05$ were included.

RESULTS

This study was conducted with 121 people, 62 patients with a mean age of 54.8±12.60 years and 59 individuals in the control group with a mean age of 53.9±11.77 years. It was determined that hemodialysis patients received dialysis treatment for 4 years, 93.55% were married, 35.48% were primary school graduates, and 51.61% were working (**Table 1**)

Table 1. General characteristics of individuals

	Hemodialysis (n=62)	Control (n=59)	p
Age (years)	54.8±12.60	53.9+11.77	0.134
	n (%)	n (%)	
Marital status			
Married	58(93.55)	47(90.24)	0.125
Single	4(6.45)	12(9.76)	
Educational status			
Illiterate	28(45.16)	13(22.03)	0.003
Literate	4(6.45)	5(8.47)	
Primary school	22(35.48)	15(25.42)	
High school	4(6.45)	14(23.72)	
University	4(6.66)	17 (28.81)	
Working status			
Working	32(51.61)	34(57.62)	0.001
Not working	30(48.39)	25(42.37)	
CRF (years)	10.8±5.88	-	
HD (years)	4.8±3.12	-	

Abbreviations: CRF: Chronic Renal Failure, HD: Hemodialysis

Table 2 compares the laboratory results of hemodialysis and control groups according to dietary ORAC quartiles. Serum ferritin levels were found to vary between quartiles in both HD and control groups, with levels being lowest in the quartile with the greatest ORAC value ($p<0.05$). LDL-C and HDL-C values were found to differ between quartiles in the HD group. The group with the highest mean blood HDL-C level was in the quartile range with the greatest ORAC level, and the distribution of T-cholesterol levels between quartiles was significantly different in the HD group ($p<0.05$). The group with the lowest mean ORAC level in their diet had the highest total cholesterol level ($p<0.05$). In the control group, the group with the greatest ORAC level had the highest serum total cholesterol level ($p<0.05$). In the HD and control groups, the group with the highest serum ORAC level also had the greatest mean total protein level.

Table 2. The Laboratory Results Of Hemodialysis And Control Groups According To Dietary ORAC Quartiles

	Hemodialysis				Control				
	1.Quartile	2.Quartile	3.Quartile	p1	1.Quartile	2.Quartile	3.Quartile	p2	p3
CRP (mg/dL)	0.7±0.65	1.0±0.78	0.5±0.54	0.345	0.4±0.72	0.4±0.35	0.4±0.41	0.165	0.001
Lymphocyt to monocyte ratio	3.0±0.92	3.1±1.54	2.9±1.38	0.260	3.8±1.08	4.7±1.60	4.2±1.16	0.138	0.031
Neutrophil to lymphocyte ratio	3.2±2.70	3.0±1.29	3.1±1.63	0.156	2.1±0.76	1.5±0.54	1.5±0.57	0.091	0.051
Platelet to lymphocyte ratio	137.8±66.52	148.5±108.64	146.8±69.91	0.785	123.1±47.10	114.0±24.04	113.9±36.12	0.265	0.003
Ferritin (mg/dL)	344.7±222.27	460.2±259.35	302.1±181.33	0.011	109.8±90.87	111.6±95.12	98.9±62.42	0.001	0.004
Albumin (mg/dL)	3.4±0.19	3.5±0.36	3.2±0.31	0.219	3.9±0.27	4.0±0.28	4.0±0.25	0.368	0.001
LDL-Cholesterol (mg/dL)	89.0±32.33	71.4±26.59	67.5±21.41	0.001	105.9±31.35	123.4±22.30	116.1±29.40	0.001	0.009
HDL-Cholesterol (mg/dl)	42.8±11.99	45.4±11.78	57.1±25.66	0.002	48.6±9.09	50.2±13.25	52.8±14.03	0.001	0.001
Triglyceride (mg/dl)	227.2±118.39	135.1±81.98	138.3±78.27	0.001	146.7±68.21	105.3±55.90	135.9±67.46	0.002	0.001
Total Cholesterol (mg/dl)	172.0±37.15	146.7±34.98	169.7±23.94	0.003	185.5±37.50	191.9±39.21	196.2±28.42	0.001	0.029
Glucose (fasting) (mg/dl)	110.5±23.17	98.1±14.90	97.6±16.90	0.103	93.5±7.59	92.9±9.89	93.0±13.33	0.387	0.001
Hemoglobin (g/dL)	10.8+1.54	10.9+1.47	10.4+0.98	0.871	14.7±1.51	13.9±1.86	14.3±1.72	0.962	0.041
Total protein (g/dL)	6.6±0.46	6.8±0.49	6.8±0.47	0.221	7.0±0.53	7.1±0.38	7.1±0.39	0.035	0.081

p1: difference between quartiles of the patient group, p2: difference between quartiles of the control group, p3: difference between the patient and control groups' laboratory findings. Abbreviations: CRP: C-Reactive Protein, HDL: High Density Lipoprotein, LDL: Low-Density Lipoprotein

By use of linear regression, univariate and multivariate analyses of parameters associated with dietary total antioxidant capacity in hemodialysis patients were conducted (**Table 3**). In the regression analysis, it was determined that gender played a major role in all models. BMI and other anthropometric parameters were found to have a negative connection with dTAC (p=0.007). The biochemical measures HDL-C, serum albumin, and serum N/L ratio have been reported to have a positive relationship with dTAC. Examining the association between dietary components and dTAC reveals a positive correlation between dietary protein (kg/avg), beta carotene (mcg/day), vitamin C (mg/day), vitamin E (mg/day), and PUFA (g/day) (p=0.002).

Tablo 3. Univariate And Multivariate Analyzes Of Parameters Associated With Dietary Total Antioxidant Capacity İn Hemodialysis Patients

Anthropometric variables	β	p	95% CI EXP(B)		βAj	CI 95%	p
			Lower	Upper	-0.078	-0.145; 0.033	0.007
BMI (kg/m²)	-0.074	0034	-0.259	0.430			
TSFT(mm)	-0.022	0.073	-0.187	0.640			
MUAC (cm)	-0.043	0.113	-0.109	-0.008			
Waist/Hip Ratio	-0.084	0.238	-0.101	0.421			
Waist/Height Ratio	-0.050	0.091	-0.239	0.019			
Biochemical variables					0.059	0.255; 0.023	0.005
CRP(mg/dL)	-0.077	0.026	-0.098	-0.005			
LDL-Cholesterol (mg/dL)	-0.091	0.001	-0.213	-0.059			
HDL-Cholesterol (mg/dL)	0.021	0.076	-0.101	0.039			
Albumin (mg/dL)	0.757	0.050	0.202	1.254			
Neutrophil/Lymphocyte Ratio	0.242	0.072	-0.105	0.331			
Lymphocyte/Monocyte Ratio	-0.223	0.039	-0.393	-0.016			
Platelet/Lymphocyte Ratio	-0.301	0.821	-0.307	0.109			
Dietary variables					0.054	0.126; 0.013	0.002
Dietary Protein (kg/avg)	0.404	0.009	0.303	1.012			
Beta carotene (mcg/day)	0.505	0.007	0.0121	1.022			
Vitamin C (mg/day)	0.807	0.001	0.232	2.028			
Vitamin E (mg/day)	0.511	0.004	0.401	2.228			
PUFA (g/day)	0.845	0.006	0.677	2.013			

Note: β: β value simple linear regression analysis; βAj: adjusted value of β for covariates; p value: multiple linear regression analysis significance value p<0.05; gender, educational status, socioeconomic status variables were maintained constant in the final model. Abbreviations: BMI: Body Mass Index, TSFT: Triceps Skinfold Thickness, MUAC: Mid-upper Arm Circumference, CRP: C-Reactive Protein, HDL: High Density Lipoprotein, LDL-C: Low-Density Lipoprotein, PUFA: Polyunsaturated Fatty Acids

DISCUSSION

End-Stage Renal Disease (ESRD) is a complex pathology characterized by an increase in free radicals and a decrease in antioxidant defense. All patients with chronic renal failure, regardless of whether or not they receive renal replacement therapy, experience elevated oxidative stress (16). Moreover, inflammation manifests in the early stages of conical kidney failure. Nguyen–Koha et al. (17), demonstrated that the presence of inflammation and the length of time on dialysis are the most significant causes of OS in HD patients. In this study, it was determined that individuals had CRF for 10.8±5.88 years and received hemodialysis treatment for approximately 4.8±3.12 years. According to reports, low socioeconomic status and low education are risk factors for CRF (18). According to studies, hemodialysis patients have a low level of education, are married, have a moderate or low income, and are typically retired (19-21). In this study, it was established that the majority of participants were married, 53.65% of the hemodialysis patients had completed elementary school, and 41.46% of the control group had completed college.

While uremic toxins are eliminated during hemodialysis, trace elements and hydrophobic, non-protein-bound low molecular weight molecules also enter the dialysate fluid, resulting in a fall in serum levels. Trace elements having antioxidant qualities, such as vitamins C and E, copper, zinc, and selenium, enter the dialysate fluid, increasing oxidative damage in the plasma. Plasma activity of antioxidant enzymes such as glutathione-reductase (GSSG-Red), glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD) is decreased by hemodialysis treatment (22, 23) This decrease is caused by a decrease in the synthesis of these enzymes in the kidneys or by uremic toxins that alter the protein structures of these enzymes. In hemodialysis, the loss of hydrophilic free small molecular weight substances including vitamin C, trace elements, and regulating enzyme compounds, as well as the existence of malnutrition and malnutrition, are nutrition-related factors that exacerbate oxidative stress.

Serum antioxidant level is correlated with dietary antioxidant intake, and it is recognized that antioxidants protect against oxidative damage and associated inflammatory consequences (24). The intake of nutrients with antioxidant properties is very important for dietary antioxidant intake (25). Fruits and vegetables are high in fiber, bioactive compounds, and micronutrients (26). Vitamins C and E, carotenoids, and flavonoids are the most typical antioxidants present in vegetables (27). Flavonoids are the most prevalent polyphenols found in plants, and they are abundant in tea, coffee, juices, fruits, vegetables, and grains (28). However, medical nutrition therapy and restrictions in food and fluid consumption to reduce minerals such as potassium, sodium, and phosphorus cause hemodialysis patients to consume fewer of these antioxidant-rich food categories than healthy individuals (29). In addition, calcium, magnesium, and potassium intakes of CRF patients are claimed to be low, while dietary cholesterol intake is high (30). This circumstance has a negative impact on dietary antioxidant consumption and increases serum oxidative stress. Consuming foods with a high glycemic index simultaneously promotes oxidative stress and inflammation in hemodialysis users (31). In this study, the connection between dietary components and dTAC was found to be positive for dietary protein (kg/avg), beta carotene (mcg/day), vitamin C (mg/day), vitamin E (mg/day), and PUFA (gr/day) (p=0.002). In addition, this study demonstrated that these nutrients boost antioxidant capability.

There is a positive correlation between inflammation and oxidative stress marker values in dialysis patients, according to studies (32, 33). Indicators of inflammation in the hemodialysis and control groups were found to differ significantly in this investigation. In the highest quartile dTAC of serum ferritin, an essential biomarker of inflammation, was shown to be low. In addition, the inverse association between dTAC, CRP, and the ratio of lymphocytes to monocytes has been established. In HD patients, dyslipidemia and cardiovascular events are more prevalent than in the general population. Therefore, cardiovascular illnesses observed in dialysis patients are linked to antioxidant activity, and inadequate antioxidant capacity was discovered (32).

In these cases, an increase in oxidative stress in the CRF is responsible for the alteration of LDL cholesterol and the development of atherosclerosis. According to reports, oxidized LDL inhibits PON-1 by interacting with its sulfhydryl group (34). LDL cholesterol, HDL cholesterol, TG, and total cholesterol levels in the HD group were found to differ between quartiles in this investigation. It was determined that the group with the highest serum mean HDL cholesterol level was also in the quartile range with the highest dTAC level, and that a strong positive association existed between HDL cholesterol and dTAC. At the same time, it was revealed that the group with the lowest antioxidant capability had the highest overall cholesterol levels. Serum levels of total protein and albumin are significant indications of malnutrition and oxidative stress and inflammation. In the group with the greatest dTAC level, the HD and control groups had the highest mean total protein concentration. In addition, a link between serum albumin concentration and dTAC has been established.

Mild obesity and obesity have been observed to lessen the risk of mortality in hemodialysis patients (35), but the opposite has also been recorded (36). The paradoxical relationship between obesity as a risk factor for CRF and positive survival results in advanced CRF is known as the "obesity paradox." According to this paradox, overnutrition was analyzed as a long-term and undernutrition as a short-term hazard to death, and it was concluded that obesity is not a desirable model for a high survival rate in CRF patients (37, 38). Despite the obesity paradox, high BMI levels may raise the risk of atherosclerosis and cardiovascular disease, which are prevalent in CRF patients. In order to prevent obesity in patients, it is necessary to guarantee enough and balanced nutrition, encourage regular physical exercise, maintain a normal ratio of body fat, and protect muscle mass.

In a study that split dietary TAC values into five categories from least to greatest, a rise in dietary TAC value was related to a drop in BMI (39). In another study, dietary TAC values were separated into two groups based on the median of dietary TAC and BMI. There were statistically significant associations between ($p<0.05$) (40). Levels of dietary antioxidants are inversely linked to body fat percentage. In addition, larger intakes of fiber and phytochemicals, waist circumference, BMI, and plasma lipid peroxidation are inversely proportional (41). This study demonstrated that BMI and other anthropometric parameters were negatively correlated with dTAC in hemodialysis patients ($p=0.007$).

CONCLUSION

Oxidative stress, which results from an imbalance between oxidants and antioxidants, leads to the development of several problems in CRF patients. To improve serum antioxidant capacity in patients on dialysis, it is necessary to prevent uremic condition, bacterial contamination of the dialysis membrane and dialysate, and dietary inadequacies. The relationship between dietary antioxidant intake and serum antioxidant content is strong. In order to prevent complications in these people, a diet rich in antioxidants is necessary. In circumstances when enough antioxidant consumption cannot be reached by diet alone, antioxidant support therapy should be considered.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Malatya Turgut Özal University Clinical Researches Ethics Committee (Date: 01.12.2022, Decision No: 2022/61).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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