



## RESEARCH

# The relationship between dietary antioxidant capacity and serum oxidative stress index of hemodialysis patients

Hemodiyaliz hastalarında diyetin antioksidan kapasitesi ile serum oksidatif stres indeksi arasındaki ilişki

Hacer Alataş<sup>1</sup>, Mendane Saka<sup>2</sup>, Nurgül Arslan<sup>3</sup>, Bülent Yaprak<sup>4</sup>, Önder Otlı<sup>5</sup>, İrem Pembegül<sup>6</sup>

<sup>1</sup>Department of Nutrition and Dietetics, Malatya Turgut Ozal University Training and Research Hospital, Malatya, Turkey  
<sup>2</sup>Department of Nutrition and Dietetics, Faculty of Health Sciences, Başkent University, Ankara, Turkey  
<sup>3</sup>Department of Nutrition and Dietetics, Atatürk Faculty of Health Sciences, Dicle University, Diyarbakır, Turkey  
<sup>4</sup>Malatya Turgut Ozal University, Department of Internal Medicine, <sup>5</sup>Department of Medical Biochemistry, <sup>6</sup>Department of Nephrology, Malatya, Turkey

### Abstract

**Purpose:** Oxidative stress increases in uremic conditions such as kidney failure and during hemodialysis. In this study, it was aimed to examine the relationship between the total antioxidant capacity of the diet and the serum oxidative stress (sOSI) index in hemodialysis patients.

**Materials and Methods:** In this study conducted with 82 individuals (41 patients and 41 controls). Demographic characteristics and anthropometric measurements of the individuals were taken by researchers. In order to determine the nutritional status of the individuals, 3-day food consumption records were taken and the total antioxidant capacity of the diet was calculated.

**Results:** The mean age of the individuals participating in the study was found to be 54.01±2.24 years. Hemodialysis treatment mean for 4.8±3.12 years. While 41.46% of hemodialysis patients were moderately malnourished. Dietary Oxygen Radical Absorption Capacity (dORAC) (µmol) measurement result was found to be 2415.3±1073.45, 5468.4±2393.85 in the hemodialysis and control groups, respectively. In the multiple logistic regression analysis performed, the decrease in body mass index (OR 2.21 95% CI 1.050-2.317) and triceps skinfold thickness values (OR 3.22 95% CI 1.722-4.001) in hemodialysis patients led to an increase in the sOSI value. It has been observed that when dietary protein (OR 1.23 95% CI 1.003-3.189), vitamin C (OR 2.88 95% CI 1.004-3.106) and dTAC (OR 2.04 95% CI 1.967-2.001) increase, the sOSI value decreases in hemodialysis patients.

**Conclusion:** There is a positive relationship between diet total antioxidant capacity and serum antioxidant level, and

### Öz

**Amaç:** Oksidatif stres böbrek yetmezliği gibi üremik durumlarda ve hemodiyaliz sırasında artar. Bu çalışmada hemodiyaliz hastalarında diyetin toplam antioksidan kapasitesi ile serum oksidatif stres (sOSI) indeksi arasındaki ilişkinin incelenmesi amaçlanmıştır.

**Gereç ve Yöntem:** Bu çalışmaya 82 birey (41 hasta ve 41 kontrol) dahil edilmiştir. Bireylerin demografik özellikleri ve antropometrik ölçümleri araştırmacılar tarafından alınmıştır. Beslenme durumlarını belirlemek için 3 günlük besin tüketim kayıtları alınmış ve diyetin toplam antioksidan kapasitesi hesaplanmıştır.

**Bulgular:** Çalışmaya katılan bireylerin yaş ortalaması 54,01±2,24 yıl olarak bulundu. Hemodiyaliz tedavisi süresi ortalama 4,8±3,12 yıldır. Hemodiyaliz hastalarının %41,46'sı orta derecede malnütrisyonlu. Diyet oksijen radikal soğurma kapasitesi (dORAC) (µmol) ölçüm sonucu hemodiyaliz ve kontrol gruplarında sırasıyla 2415,3±1073,45, 5468,4±2393,85 olarak bulundu. Yapılan çoklu lojistik regresyon analizinde hemodiyaliz hastalarında beden kütle indeksi (OR 2.21 %95 CI 1.050-2.317) ve triseps deri kıvrım kalınlığı değerlerindeki (OR 3.22 %95 CI 1.722-4.001) azalma sOSI değerinde artışa neden olmuştur. Hemodiyaliz hastalarında diyetle alınan protein (OR 1.23 %95 CI 1.003-3.189), C vitamini (OR 2.88 %95 CI 1.004-3.106) ve dTAC (OR 2.04 %95 CI 1.967-2.001) arttığında sOSI değeri düşmektedir.

**Sonuç:** Diyet total antioksidan kapasitesi ile serum antioksidan düzeyi arasında pozitif bir ilişki vardır ve hemodiyaliz hastalarının diyet antioksidan kapasitesinin sağlıklı bireylere göre anlamlı derecede düşük olduğu

Address for Correspondence: Hacer Alataş, Department of Nutrition and Dietetics, Malatya Turgut Ozal University Training and Research Hospital, Malatya, Turkey E-mail: [hacer\\_alatas@hotmail.com](mailto:hacer_alatas@hotmail.com)

Received: 24.09.2022 Accepted: 20.12.2022

it was determined that the dietary antioxidant capacity of hemodialysis patients was significantly lower than that of healthy individuals. According to the results of the study, it is recommended to monitor the food consumption status of hemodialysis patients in order to increase the dietary antioxidant capacity.

**Keywords:** Chronic renal failure, hemodialysis, diet total antioxidant capacity, serum oxidative stress index

belirlenmiştir. Çalışma sonuçlarına göre diyet antioksidan kapasitesinin artırılması için hemodiyaliz hastalarının besin tüketim durumlarının takibi önerilmektedir.

**Anahtar kelimeler:** Kronik böbrek yetmezliği, hemodiyaliz, diyet total antioksidan kapasitesi, serum oksidatif stres indeksi

## INTRODUCTION

Chronic kidney disease (CKD) is a disease in which the fluid-solute balance and metabolic-endocrine functions of the kidney deteriorate over time as a result of a decrease in the glomerular filtration rate (GFR)<sup>1</sup>. When the ratio of antioxidants to oxidants shifts in favor of oxidants, oxidative stress is the result. Oxidative stress rises in uremic conditions like kidney failure and hemodialysis, and by supporting unconventional cardiovascular risk factors, increased oxidative stress raises mortality and morbidity rates<sup>2</sup>. According to the studies investigating the antioxidant system in chronic kidney disease patients, the total antioxidant capacities (T-AOC) and enzymes in the antioxidant system such as glutathione peroxidase, copper and zinc dismutase enzymes decrease their antioxidant activity, T-AOC value is lower compared to healthy individuals and dialysis type has an effect on T-AOC levels in patients with<sup>3,4</sup>. Regardless of whether they receive renal replacement therapy or not, all patients with chronic renal failure experience elevated oxidative stress. Additional factors that contribute to oxidative stress in dialysis patients include uremic state, dialysate contamination by bacteria, and bacterial contamination of the dialysis membrane. Superoxide radicals (SOR) are thought to form as a result of dialysis in circulating neutrophils and monocytes, and vitamin deficiency weakens antioxidant defenses, increasing oxidative stress in dialysis patients<sup>5</sup>.

The low levels of antioxidant enzymes in patients with chronic renal failure, together with the inadequacy of their dietary intake of antioxidant-rich foods in comparison to healthy individuals causes the defense of antioxidant defense systems to weaken against oxidative damage<sup>6</sup>. The presence of studies showing that there is a significant relationship between the antioxidant content of the diet and the plasma total antioxidant capacity<sup>7,8</sup>. The presence of a relationship between the nutritional diversity of the diet and the total antioxidant capacity has led to the

conclusion that the nutritional diversity of the diet and the total antioxidant capacity of the diet are important and should be investigated<sup>9</sup>.

Hemodialysis patients consumed less total dietary antioxidants overall and had lower serum antioxidant parameters, whereas healthy individuals had higher serum oxidant parameters. Total antioxidant capacity is a useful parameter for assessing the quality of the diet and is a useful value. Therefore, measurement of the antioxidant capacity of the diet in these patients is important and should be evaluated.

The aim of this study was to investigate the relationship between the total antioxidant capacity of the diet and the serum oxidative stress index in hemodialysis patients.

## MATERIALS AND METHODS

Study was conducted between May and September 2021 Malatya Turgut Ozal University, Malatya Training and Research Hospital Hemodialysis Unit. Healthy participants who visited the internal medicine polyclinic for routine check-ups. The researchers collected the study data with great care. Informed consent was obtained from all individuals participating in the study. All steps of the study were carried out according to the Helsinki 2013 Declaration. Ethical Approval "Ethics Committee Approval" of Başkent University Medical and Health Sciences Research Board dated 24/04/2021 and numbered 21/83. Malatya Turgut Ozal University hemodialysis unit and laboratories are monitored by the Ministry of Health. Hemodialysis unit is a unit with ISO 22000 certificate.

## Sample

The sample of the study was calculated using the G\*power 3.1 program. The power of the study was calculated as 56 with 0.80 effect size, 0.05 margin of error, 0.90 confidence level and 0.90 population

representation. Considering that data may be missing and data may be lost during the study process, 82 people were included in the study.

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.

Those who use cigarettes and alcohol, those with acute inflammatory disease, use anti-inflammatory drugs, individuals with chronic inflammation such as active hepatitis, HIV (+), diabetes mellitus with a history of ischemic heart disease, hemodialysis treatment for less than 6 months and for more than 10 years, those who use vitamins other than folic acid, those who use fish oil and other antioxidant drugs.

### Procedure

After selecting the patients for the study, the researcher collected data on their demographic parameters (age, gender, education level, marital status), as well as their health status, using a face-to-face interview method and a questionnaire.

### Laboratory evaluation

Ferritin and albumin values evaluated within the scope of the study were taken from the patient's file. The serum total oxidant status (TOS) and total antioxidant capacities (T-AOC) measurement of individuals included in the study was studied with using the elisa kit (Shanghai Sunred Biological Technology Co., Ltd) and sandwich model double antibody enzyme-linked immunosorbent method. The serum oxidative stress index (sOSI) was calculated by dividing the total oxidant status by the total antioxidant capacities<sup>10</sup>.

TOS, T-AOC and sOSI values were determined twice, before and after dialysis, in the hemodialysis group, and once in the control group.

### Anthropometric measurements

After dialysis, patients' body weights, heights, waist and hip circumferences, triceps skinfold thickness (TSFT), and mid-upper arm circumference (MUAC) were measured. The researcher measured the waist circumference, hip circumference, and mid-upper

arm circumference with a non-flexible tape measure, the heights with a stadiometer, and the triceps skinfold thickness with a caliper. Body mass index (BMI) was calculated for all individuals from body weight / height length (kg/m<sup>2</sup>) equation. The classification of the World Health Organization (WHO) was used to classify individuals according to their BMI<sup>11</sup>. The waist-hip ratio of the individuals was calculated by dividing the waist circumference measurement with the hip circumference measurement. National Center for Health Statistics (NCHS) 18-74 age values were used as reference values for triceps skinfold thickness and mid-upper arm circumference<sup>12</sup>.

### Food consumption diary

In the dialysis unit, the hemodialysis diet was given to the patients by the doctor and dietitian. 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 (ORAC) of food was calculated by multiplying the previously reported ORAC value for each food and the grams of the consumed food<sup>13</sup>. The diet's total antioxidant capacity (dTAC) was estimated by adding the ORAC values calculated for each food consumed during the day<sup>14</sup>. Individuals' daily calorie, macronutrient, and micronutrient intakes were determined using the "Nutrition Information System (BEBIS)" software developed for Turkey<sup>15</sup>.

### Subjective global assessment

The Subjective Global Assessment (SGA) form was used to assess the risk of malnutrition in dialysis patients, which is a significant predictor of morbidity and mortality. The assessment is divided into 3 categories as follows: A: adequate nutrition; B: risk of malnutrition or moderate malnutrition; and C: severe malnutrition. The researcher evaluated the individuals who participated in the study using the SGA form.

### Statistical analysis

SPSS 25.0 for windows was used for analysis at 95% confidence interval with 0.05 significance level. The dietary TAC capabilities of the hemodialysis and control groups were classified into quartiles. Quantitative variables were expressed using the mean

standard deviation (S), while qualitative variables were expressed using percentage (%) values. The eligibility of continuous variables for normal distribution was determined using parametric (Student's t) or non-parametric (Mann-Whitney U) tests. Chi-square Test or Fisher's Exact Test was applied for qualitative variables when the expected values in the cross tables were less than 5. The relationship between dORAC level and sOSI was analyzed by Spearman correlation analysis. Kruskalwallis H test was used to compare Quartiles of dietary ORAC levels. For the multivariate analysis, the possible factors identified with univariate analyses were further entered into logistic regression analysis to determine independent predictors of hemodialysis patient outcome. Hosmer-lemeshow goodness of fit

statistics were used to assess model fit. In all statistical tests, the significance level was accepted as 0.05.

## RESULTS

This study was conducted with 82 individuals, 41 patients with a mean age of  $54.8 \pm 12.60$  years and 41 individuals in the control group with a mean age of  $53.9 \pm 11.77$  years. Male individuals made up 58.54% of the control group and those receiving hemodialysis treatment. It has been determined that the patients have been receiving hemodialysis treatment for  $4.8 \pm 3.12$  years. While 41.46% of hemodialysis patients were moderately malnourished, all of the individuals in the control group were well-nourished (Table 1).

**Table 1. General characteristics of individuals**

Variable	Hemodialysis (n=41)	Control (n=41)	p
Gender	n (%)	n (%)	
Female	17(41.46)	17(41.46)	0.196
Male	24(58.54)	24(58.54)	
Age (years)	$54.8 \pm 12.60$	$53.9 \pm 11.77$	0.134
SGA			
A: Well Feeding	24(58.53)	41(100)	0.001
B: Moderate malnutrition	17(41.46)	-	
C: Severe malnutrition	-	-	
CKD (years)	$10.8 \pm 5.88$	-	
HD (years)	$4.8 \pm 3.12$	-	
Hemodialysis duration (hour)	4	-	
Dialysis frequency (week/day)	3	-	

SGA: Subjective Global Assessment, BMI: Body Mass Index, CKD: Chronic Kidney Disease, HD: Hemodialysis,  $p < 0.05$

Anthropometric characteristics of the individuals are presented in Table 2. The mean BMI values of the individuals in the hemodialysis and control groups were found to be  $26.3 \pm 4.28$  and  $27.8 \pm 5.03$  kg/m<sup>2</sup>, respectively ( $p = 0.044$ ). It was determined that the control group had a larger proportion of overweight individuals. Both men and women had waist-hip ratios that were more than the maximum value. The middle- upper arm circumference and triceps skinfold thickness values were found to be significantly lower in hemodialysis patients than in the control group.

The energy, macronutrient and micronutrient intakes of the hemodialysis and control groups are shown in Table 3. The calorie, protein, dietary fiber,

cholesterol, and micronutrient intakes, as well as the dORAC values, of patients undergoing hemodialysis were significantly lower compared to the control group ( $p < 0.05$ ).

The serum oxidative stress and antioxidant indicators based on dietary ORAC values of individuals are shown in Table 4. According to ORAC quartiles in hemodialysis patients, the difference between pre- and post-hemodialysis values of T-AOC was statistically significant, and the T-AOC value of the control group was higher than that of hemodialysis patients ( $p < 0.05$ ). The TOS value reduced before and after hemodialysis in correlation with the rise in ORAC uptake value ( $p < 0.05$ ). The sOSI value decreased significantly before and after dialysis in

hemodialysis patients when compared to the ORAC level ( $p<0.05$ ). In healthy individuals, the increase in T-AOC and the decrease in TOS and sOSI values were found to be significant when compared to the ORAC level ( $p<0.05$ )

**Table 2. Anthropometric characteristics of individuals**

Variable	Hemodialysis (n=41)	Control (n=41)	p
BMI kg/m <sup>2</sup> ( $\bar{X} \pm SS$ )	26.3±4.28	27.8±5.03	0.044
BMI classification (kg/m <sup>2</sup> )	n (%)	n(%)	
Underweight (<18.5)	1 (2.43)	-	0.125
Normal weight (18.5-24.9)	18 (43.92)	9(21.42)	
Overweight (25.0-29.9)	12 (29.03)	21 (51.23)	
Obese ( $\geq 30.0$ )	10(24.42)	11(26.85)	
Waist to hip ratio			
Female ( $\bar{X} \pm SS$ )	0.93±0.08	0.89±0.08	0.003
<0.85	4(23.53)	6(35.29)	0.235
$\geq 0.85$	13(76.47)	11(64.71)	
Male ( $\bar{X} \pm SS$ )	0.96±0.084	0.95±0.06	0.109
$\leq 0.90$	6(25.00)	3(12.50)	0.158
$\geq 0.90$	18(75.00)	21(87.50)	
MUAC (cm)			
Female ( $\bar{X} \pm SS$ )	27.9±3.71	30.1±3.74	0.001
<22 cm	1(5.88)	-	
$\geq 22$ cm	16(94.12)	17(100.00)	
Male ( $\bar{X} \pm SS$ )	25.4±3.03	29.7±2.38	0.009
<22 cm	4(16.67)	-	
$\geq 22$ cm	20(83.33)	24(100.00)	
TSFT (mm)			
Female ( $\bar{X} \pm SS$ )	6.4±3.16	15.1±6.75	0.001
<16.5	14(82.35)	2(11.76)	
$\geq 16.5$	3(17.65)	15(82.24)	
Male ( $\bar{X} \pm SS$ )	12.4±5.62	22.0±6.54	0.002
<12.5	24(100.00)	16(66.69)	
$\geq 12.5$	-	8 (33.33)	

BMI: Body Mass Index, MUAC: Mid-upper Arm Circumference, TSFT: Triceps Skinfold Thickness,  $p<0.05$

**Table 3. Mean and standard deviation values of energy, macro and micronutrient intakes and dORAC value of hemodialysis and control group individuals**

Variable	Hemodialysis (n=41)	Control (n=41)	p*
Daily intakes	$\bar{X} \pm SS$	$\bar{X} \pm SS$	
Energy (kcal/d)	1324.9±178.75	1681.2±501.36	0.001
Protein(g/d)	56.4±8.35	66.8±19.64	0.001
Protein (% energy)	17.3±1.02	16.4±2.35	0.023
CHO (% energy)	48.2±3.95	48.1±8.17	0.188
Total fat (% energy)	34.3±4.58	35.3±7.59	0.068
PUFA (% energy)	4.5±1.92	5.6±2.26	0.034
MUFA (% energy)	13.0±4.92	13.5±7.08	0.001
SFA (% energy)	9.4±3.71	11.7±7.71	0.001
Total cholesterol	248.8±60.45	317.8±132.78	0.001
Total fiber	14.5±2.16	21.2±8.91	0.001
Soluble fiber	4.6±0.79	6.7±3.11	0.001
Insoluble fiber	8.5±1.93	13.9±6.09	0.001
Vitamin C (mg)	94.6±32.36	104.0±56.73	0.001
Vitamin E (mg)	6.8±1.72	10.2±3.46	0.001
Thiamin (mg)	0.6±0.07	0.7±0.28	0.001
Riboflavin (mg)	1.1±0.15	1.4±0.53	0.001
Niacin (mg)	7.5±1.72	11.0±3.48	0.001
Vitamin B <sub>5</sub> (mg)	4.0±0.54	5.4±1.58	0.001
Vitamin B <sub>6</sub> (mg)	0.7±0.16	1.0±0.38	0.001
Biotin (mg)	34.9±3.83	46.4±17.11	0.001
Folate (mcg)	218.8±27.46	311.2±115.01	0.001
Vitamin B <sub>12</sub> (mcg)	2.9±0.48	5.3±3.46	0.001
Iron (mg)	5.9±0.71	9.6±3.52	0.001
Zinc (mg)	6.5±0.89	9.7±3.05	0.001
Potassium (mg)	1690.5±252.54	2360.6±377.84	0.001
Calcium (mg)	717.5±82.90	829.3±277.84	0.017
Phosphorus (mg)	808.1±101.81	1051.4±326.37	0.001

\*It was adjusted according to gender and whether the individuals were hemodialysis patients or not. p<0.05, CHO: Carbohydrate, PUFA: Polyunsaturated Fatty Acids, MUFA: Monounsaturated Fatty Acids, SFA: Saturated Fatty Acids, dORAC: Dietary Oxygen Radical Absorption Capacity

**Table 4. Mean and standard deviation values of serum oxidative stress and antioxidant values according to dietary ORAC quartiles of hemodialysis and control group individuals**

	Hemodialysis			Control			p*	
dORAC( $\mu$ mol)	2415.3 $\pm$ 1073.45			5468.4 $\pm$ 2393.85			0.001	
Quartiles of dietary ORAC								
	Hemodialysis			p**	Control			p**
	1.Quartile	2.Quartile	3.Quartile		1.Quartile	2.Quartile	3.Quartile	
	<1765 n=14	1765-1998.99 n=14	>1998.99 n=13		<3288 n=14	3288-3541.88 n=14	>3541.88 n=13	
T-AOC								
Input	17.4 $\pm$ 15.45	24.6 $\pm$ 16.36	28.7 $\pm$ 20.83	0.087	21.8 $\pm$ 13.29	25.5 $\pm$ 13.30	33.8 $\pm$ 25.30	0.001
Output	18.0 $\pm$ 13.10	29.7 $\pm$ 19.63	33.2 $\pm$ 19.30	0.001	-	-	-	
TOS								
Input	162.1 $\pm$ 120.73	163.3 $\pm$ 113.83	97.6 $\pm$ 83.65	0.001	166.7 $\pm$ 98.15	124.6 $\pm$ 115.19	112.0 $\pm$ 77.23	0.001
Output	161.7 $\pm$ 119.95	136.9 $\pm$ 111.43	89.7 $\pm$ 66.11	0.001	-	-	-	

: T-AOC: Total Antioxidant Capacities, TOS: Total Oxidant Status

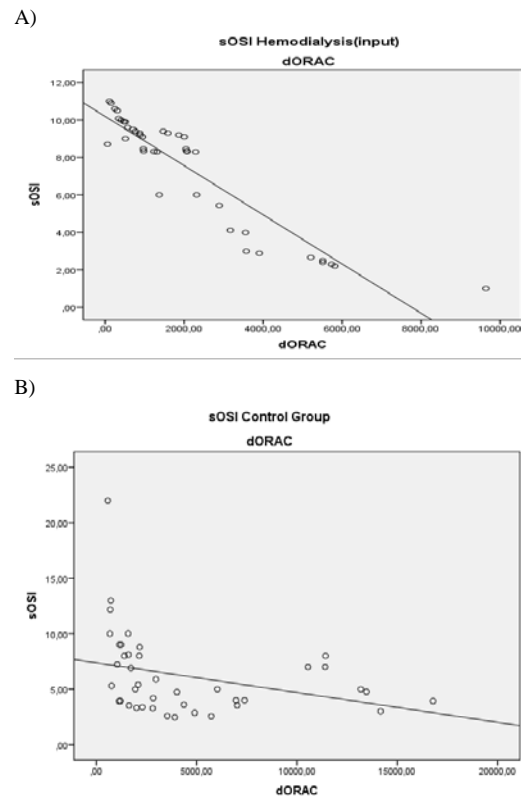
p\*: Mann Whitney U test,  $p < 0.05$ . p\*\*: Kruskal wallis H test,  $p < 0.05$ .

A negative and significant correlation was found between sOSI and dORAC in the hemodialysis group ( $p=0.003$ ,  $r=-0.485$ ). Similarly, a negative but statistically insignificant correlation was observed in the control group ( $p=0.256$ ,  $r=-0.109$ ) (Figure 1).

Multiple logistic regression analysis was used to analyze the factors affecting sOSI, a measure of oxidative stress in hemodialysis patients (Table 5).

Multiple logistic regression analysis of hemodialysis patients revealed that the risk of increasing the sOSI value is 3.12 times greater in individuals with moderate malnutrition compared to well-nourished individuals (OR 3.12 95% CI 2.101-4.302), 2.21 times greater in individuals with a BMI greater than 25 kg/cm<sup>2</sup>, and 2.21 times greater in individuals with TSFT < 50.th percentile (OR 3.22 95% CI 1.722-4.001).

One (1) unit increase in ferritin value results in a 2.11 fold increase (OR 2.11 95% CI 1.742-2.890), 1 unit increase in albumin value results in a 1.75 fold decrease (OR 1.75 95% CI 1.031-2.221), 1 gram increase in dietary protein results in a 1.23 fold decrease (OR 1.23 95% CI 1.003-3.189), 1 unit increase in ORAC value results in a 2.04 fold decrease (OR 2.04 95% CI 1.967-2.001), 1 unit increase in vitamin C (mg/day) intake results in a 2.88 fold decrease (OR 2.88 95% CI 1.004-3.106), and 1 unit increase in dietary MUFA (%) in diet results in a 1.92 fold decrease (OR 1.92 95% CI 1.345-2.467), respectively.



**Figure 1. Correlation between sOSI and dORAC of hemodialysis and control group individuals: A) Correlation between sOSI and dORAC of hemodialysis, B) Correlation between sOSI and dORAC of control group.**

:sOSI: Oxidative Stress Index, dORAC: Dietary Oxygen Radical Absorption Capacity

**Table 5. Odds ratio values of factors affecting the sOSI level in hemodialysis patients**

Variable	OR	p	%95 CI	
			Lower	Upper
SGA (Moderate malnutrition) (Well fed) (ref.)	3.12	0.001*	2.101	4.302
BMI<25 (kg/cm <sup>2</sup> ) BMI>25(ref.)	2.21	0.001*	1.050	2.317
TSFT<50.th TSFT>50.th(ref.)	3.22	0.002*	1.722	4.001
Ferritin (mg/dL)	2.11	0.028*	1.742	2.890
Albumin (mg/dL)	1.75	0.043*	1.031	2.221
Dietary protein (0.8 g/kg/day)	1.23	0.003*	1.003	3.189
dORAC(day)	2.04	0.001*	1.967	2.001
Vitamin C (90 mg/day)	2.88	0.008*	1.004	3.106
MUFA (%)/(day)	1.92	0.018*	1.345	2.467

\*SGA, BMI and TSFT data were categorized and binary logistic regression analysis was used. \*\*The intake of albumin, ferritin, daily protein, dORAC, vitamin C and MUFA were analyzed by linear regression analysis.

SGA: Subjective Global Assessment, BMI: Body Mass Index, MUFA: Monounsaturated Fatty Acids, TSFT: Triceps Skinfold Thickness, dORAC: Dietary Oxygen Radical Absorption Capacity

## DISCUSSION

Oxidative stress is linked to a number of diseases, such as diabetes, cancer, and renal diseases. Numerous diseases have been shown to have low serum antioxidant activity and high levels of oxidative stress<sup>16,17</sup>. Increased oxidative stress increases the risk of mortality and morbidity in hemodialysis patients by supporting unconventional cardiovascular risk factors<sup>18</sup>.

It has been found that patients with chronic kidney disease have higher levels of superoxide radicals (SOR) and lower antioxidant system activity, which can lead to anemia, accelerated aging, atherosclerosis, cataracts,  $\beta_2$  microglobulin arthropathy, increased hemolysis, and platelet dysfunction<sup>19,20</sup>.

Age has a significant impact on both the quality of life and the risk of mortality<sup>21</sup>. A one-year increase in age increases the risk of mortality by 5%. Free radical production has been determined to increase with age, and antioxidant defense mechanisms become insufficient. But, it is unknown whether the increase in free radicals is the cause or the result<sup>22</sup>. However, many studies have shown that oxidative stress increases with age<sup>23,24</sup>. Therefore, the age range was limited in this study. And individuals of similar ages in the hemodialysis and control groups were compared. In this study, the mean age of hemodialysis patients was found to be  $54.8 \pm 12.60$  years and  $53.9 \pm 11.77$  years in control.

During chronic renal failure, antioxidant capacity falls

and oxidative stress rises due to uremic condition. It has been demonstrated that replacement therapy makes oxidative stress worse. Studies show that people who have been receiving dialysis for five years or longer experience a decline in their quality of life and life expectancy<sup>25</sup>. Patients in this study got dialysis for an average of  $4.8 \pm 3.12$  years.

Obese people have more chronic inflammation in their bodies. It has been demonstrated that increases in body mass index (BMI), a crucial indicator of obesity, improve subcutaneous fat tissue and muscle mass in hemodialysis patients, preventing malnutrition<sup>27</sup>. While it has been observed that mild obesity and obesity reduce the risk of mortality in hemodialysis patients<sup>28</sup>, the contrary has also been reported<sup>29</sup>. According to Kazory et al.<sup>30</sup>, a BMI over 25 kg/m<sup>2</sup> was associated with atherosclerotic findings and cardiovascular mortality risk in hemodialysis patients. It was observed that the majority of healthy and hemodialysis patients participated in this study were obese and had high waist-hip ratios.

While an increase in muscle mass with an increase in BMI increased the patients' life expectancy, it was found in a study looking at the impact of body composition on survival in hemodialysis patients that an increase in body fat mass with an increase in BMI increased the release of proinflammatory cytokines from adipose tissue, leading to the development of atherosclerosis. As a result, it has been reported that having a high BMI and a high fat mass has an atherogenic effect associated with inflammation and oxidative stress, thereby increasing cardiovascular



disease (CVD) mortality, whereas having a high BMI and a high muscle mass reduces CVD related mortality and results in the lowest mortality rate<sup>31</sup>.

Patients on hemodialysis tend to eat less because of anorexia and appetite loss. In comparison to healthy individuals, this scenario leads to the consumption of fewer calories and specific nutrients. Due to the increased requirements brought on by the loss of nutrients like protein and water-soluble vitamins during dialysis, as well as the limitations imposed by the disease-specific medical nutrition therapy, hemodialysis patients' energy and nutritional needs cannot be adequately met in these patients. This situation exposes patients to an increased risk of malnutrition and vitamin-mineral deficiencies. In this study, the daily intake of calorie, protein and micronutrients was found to be lower than the individuals in the control group. However, the nutritional intake of hemodialysis patients is not at low levels. According to the SGD assessment performed during this study, most of the patients were found to be well-nourished.

In a study examining the dietary antioxidant content, the dietary antioxidant content of CKD patients was shown to be lower than that of healthy individuals<sup>6</sup>, while the food consumption and dietary antioxidant content of elderly individuals were found to be lower than those of young individuals<sup>32</sup>. Another study determined that including antioxidant-rich foods in the diet increases serum antioxidant levels and may aid in the process of healthy aging<sup>33</sup>. The determination of dTAC is critical because assessing the antioxidant capacity of a single antioxidant component in the diet does not reflect the diet's total antioxidant capacity, and interactions or synergistic effects with other antioxidants are possible<sup>34</sup>.

In studies involving a variety of diseases and age groups, it was determined that elderly individuals consumed less nutritionally than those in the dietary TAC and flavonoid group<sup>32</sup> and that a high dietary TAC value resulted in body weight gain and a decrease in abdominal obesity<sup>35</sup> in the group with high inflammation of dietary TAC content calculated using the FRAP, ORAC, TEAC, and TRAP methods.

While some studies<sup>36-38</sup> demonstrate a relationship between dietary total antioxidant capacity or dietary antioxidant compounds and serum T-AOC or other antioxidant compounds and suggest that these compounds may be beneficial in improving

pathological status in diseases, there are also studies that demonstrate no relationship between dTAC and oxidant/antioxidant conditions<sup>39,40</sup>. In this study, the dietary antioxidant capacity of hemodialysis patients calculated by the ORAC method was found to be significantly lower when compared to the control group. However, in both groups, as the dietary antioxidant level of the individuals increased, the antioxidant level in the blood increased, on the other hand, there was a decrease in the TOS level and the sOSI value decreased considerably.

Along with research demonstrating an increase in oxidative stress in CKD patients undergoing hemodialysis, there are also studies demonstrating an increase in antioxidant enzymes and a decrease in oxidation indicators after hemodialysis<sup>41</sup>. It was observed that the serum OSI value decreased significantly.

oxidative stress, which is common in CKD patients, creates a causal relationship with chronic inflammation and malnutrition. Proinflammatory cytokines are produced in response to oxidative stress caused by protein-energy deficiency. Prolonged inflammation results in the development of a chronic acute phase reaction and a number of systemic effects, including decreased appetite, increased protein degradation in skeletal muscle, muscle and adipose tissue loss, hypercatabolism, endothelial damage and impaired albumin synthesis. In the presence of inflammation, serum levels of markers such as ferritin, which are positive acute-phase reactants, increase, while serum levels of negative acute-phase reactants, such as albumin, decrease<sup>42</sup>. In this study, it was found that the serum OSI value increased 3.12 times (OR 3.12 95% CI 2.101-4.302) in individuals with malnutrition, and 3.22 times (OR 3.22 95% CI 1.722-4.001) in individuals with TSFT<50.th percentile. A 1-unit increase in ferritin, a significant predictor of inflammation, increased the serum OSI value 2.11 times (OR 2.11 95% CI 1.742-2.890), whereas a 1-unit decrease in albumin value increased the serum OSI value 1.75 times.

Increasing the antioxidant capacity of the diet increases the antioxidant capacity, which gives the ability to neutralize free radicals in tissues and body fluids<sup>43</sup>. In this study, it was observed that increasing the total antioxidant value of the diet by one unit decreased the sOSI value by 2.04 times (OR 2.04 95% CI 1.967-2.001).

Vitamin C, a soluble in water antioxidant, protects

against lipid peroxidation by scavenging reactive oxygen species (ROS) in the aqueous phase<sup>44,45</sup>. In this study, it was observed that increasing dietary vitamin C consumption by one unit (mg/day) decreased the sOSI value by 2.88 times.

Lipoprotein oxidation is affected by the fatty acid content of the lipoprotein. Polyunsaturated fatty acids are more vulnerable to oxidation than monounsaturated fatty acids<sup>46</sup>. In this study, it was determined that a 1-unit increase in dietary MUFA (g) may reduce the sOSI value 1.92 times (OR 1.92 95% 1.345- 2.467).

Increased mechanical load and cardiac metabolism, combined with obesity, result in an increase in oxygen consumption, resulting in an increase in the generation of respiratory superoxide, hydroxyl radicals and hydrogen peroxide<sup>47</sup>. Increased oxidative damage in cells occurs when the balance between free radicals and antioxidant defense systems is disrupted. Obesity is connected with increased oxidative stress for these reasons. Despite the general population's increase in comorbidities associated with BMI, slightly overweight and obese hemodialysis patients have a lower mortality risk than patients with normal or low BMI. This suggests that there is a protective relationship between obesity and mortality, especially in hemodialysis patients<sup>28</sup>. In this study, it was observed that individuals with a BMI value above 25 kg/m<sup>2</sup> had 2.21 times higher sOSI value.

Insufficient daily protein intake results in a decrease in blood albumin levels, inflammation, and malnutrition in hemodialysis patients<sup>48</sup>. In this study, it was determined that increasing dietary protein by 1 gram resulted in a 1.23-fold drop in the sOSI value (OR 1.23 95% CI 1.003-3.189).

Hemodialysis patients consume less energy and nutrients than healthy individuals. Malnutrition, which results from an insufficient intake of energy and protein, increases oxidative stress in these patients. There is a positive relationship between dietary total antioxidant capacity and serum antioxidant level, and hemodialysis patients' dietary antioxidant capacity is much lower than that of healthy individuals. This scenario is closely related to the serum oxidative stress index of individuals undergoing hemodialysis. To reduce morbidity and mortality associated with oxidative stress and inflammation in these patients, it is necessary to increase dietary antioxidant capacity or to propose antioxidant supplementation.

Future research will be guided by this study. One of the study's most significant findings was the discovery of a link between dietary antioxidant intake and serum oxidative stress. Subsequent research will focus on reducing serum oxidative stress by increasing the intake of antioxidants.

**Limitations of the study:** The limitations of the study are as follows: The single center of the study is the biggest limitation of the study. Another limitation was the difficulty of taking measurements from individuals after hemodialysis. One of the limitations is that individuals are usually above a certain age.

**Yazar Katkıları:** Çalışma konsepti/Tasarımı: HA, MS; Veri toplama: HA, ÖO; Veri analizi ve yorumlama: NA, HA, MS; Yazı taslağı: HA, NA, BY; İçerigin eleştirel incelenmesi: IP, MS; Son onay ve sorumluluk: HA, MS, NA, BY, ÖO, IP; Teknik ve malzeme desteği: ÖO, IP; Süpervizyon: NA, IP; Fon sağlama (mevcut ise): yok.

**Etik Onay:** Bu çalışma için Başkent Üniversitesi Tıp ve Sağlık Bilimleri Araştırma Kurulundan 06.05.2021 tarih ve 31968 sayılı kararı ile proje onayı alınmıştır.

**Hakem Değerlendirmesi:** Dış bağımsız.

**Çıkar Çatışması:** Yazarlar çıkar çatışması beyan etmemişlerdir.

**Finansal Destek:** Yazarlar finansal destek beyan etmemişlerdir.

**Author Contributions:** Concept/Design : HA, MS; Data acquisition: HA, ÖO; Data analysis and interpretation: NA, HA, MS; Drafting manuscript: HA, NA, BY; Critical revision of manuscript: IP, MS; Final approval and accountability: HA, MS, NA, BY, ÖO, IP; Technical or material support: ÖO, IP; Supervision: NA, IP; Securing funding (if available): n/a.

**Ethical Approval:** For this study, project approval was obtained from the Başkent University Medical and Health Sciences Research Council with the decision dated 06.05.2021 and numbered 31968.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** Authors declared no conflict of interest.

**Financial Disclosure:** Authors declared no financial support

## REFERENCES

1. Levey AS, Coresh J. Chronic kidney disease. *Lancet*. 2012;379:165-80.
2. Rysz J, Franczyk B, Lawiński J, Gluba-Brzózka A. Oxidative stress in ESRD patients on dialysis and the risk of cardiovascular diseases. *Antioxidants*. 2020;9:1079.
3. Stepniwska J, Golembiewska E, Dolegowska B, Domanski M, Ciechanowski K, Science P. Oxidative stress and antioxidative enzyme activities in chronic kidney disease and different types of renal replacement therapy. *Curr Protein Pept Sci*. 2015;16:243-8.
4. Stepniwska J, Dolegowska B, Popińska M, Salata D, Budkowska M, Golembiewska E et al. Prooxidative-antioxidative balance of cells in different types of renal replacement therapy. *Blood Purif*. 2014;37:4-11.
5. Liakopoulos V, Roumeliotis S, Gorny X, Dounousi E, Mertens PR. Oxidative stress in hemodialysis patients: a review of the literature. *Oxid Med Cell Longev*. 2017;2017:3081856.

6. Sahni N, Gupta K, Rana S, Prasad R, Bhalla AK. Intake of antioxidants and their status in chronic kidney disease patients. *J Ren Nutr.* 2012;22:389-99.
7. Wang Y, Yang M, Lee SG, Davis CG, Koo SI, Chun OK et al. Dietary total antioxidant capacity is associated with diet and plasma antioxidant status in healthy young adults. *J Acad Nutr Diet.* 2012;112:1626-35.
8. Wang Y, Yang M, Lee SG, Davis CG, Kenny A, Koo SI et al. Plasma total antioxidant capacity is associated with dietary intake and plasma level of antioxidants in postmenopausal women. *J Nutr Biochem.* 2012;23:1725-31.
9. Narmaki E, Siassi F, Koohdani F, Qorbani M, Shiraseb F, Ataie-Jafari A et al. Dietary diversity as a proxy measure of blood antioxidant status in women. *Nutrition.* 2015;31:722-6.
10. Harma M, Harma M, Kocyigit A, Erel O. Increased DNA damage in patients with complete hydatidiform mole. *Mutat Res.* 2005;583:49-54.
11. WHO. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet.* 2004;363:157-63.
12. Scott BJ. Frame size, circumferences, and skinfolds. 2010.
13. Haytowitz DB, Bhagwat S. USDA database for the oxygen radical absorbance capacity (ORAC) of selected foods. 2010;3:10-48.
14. Carlsen MH, Halvorsen BL, Holte K, Bohn SK, Dragland S, Sampson L et al. The total antioxidant content of more than 3100 foods, beverages, spices, herbs and supplements used worldwide. *Nutr J.* 2010;9:1-11.
15. Dehne LI, Klemm C, Henseler G, Hermann-Kunz E. The German food code and nutrient data base (BLS II. 2). 1999;15:355-8.
16. Chao C-T, Chiang C-K. Uremic toxins, oxidative stress, and renal fibrosis: an intertwined complex. *J Ren Nutr.* 2015;25:155-9.
17. Gupta RK, Patel AK, Shah N, Choudhary AK, Jha UK, Yadav UC et al. Oxidative stress and antioxidants in disease and cancer: a review. *Asian Pac J Cancer Prev.* 2014;15:4405-9.
18. 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;42:864-81.
19. Russa DL, Pellegrino D, Montesanto A, Gigliotti P, Perri A, Russa AL et al. Oxidative balance and inflammation in hemodialysis patients: biomarkers of cardiovascular risk? *Oxid Med Cell Longev.* 2019;2019:8567275.
20. Ebert T, Neytchev O, Witasp A, Kublickiene K, Stenvinkel P, Shiels PG et al. Inflammation and oxidative stress in chronic kidney disease and dialysis patients. *Antioxid Redox Signal.* 2021;35:1426-48.
21. Vashistha T, Mehrotra R, Park J, Streja E, Dukkupati R, Nissenson AR et al. Effect of age and dialysis vintage on obesity paradox in long-term hemodialysis patients. *Am J Kidney Dis.* 2014;63:612-22.
22. White SL, Chadban SJ, Jan S, Chapman JR, Cass AJ. How can we achieve global equity in provision of renal replacement therapy? *Bull World Health Organ.* 2008;86:229-37.
23. Karaouzene N, Merzouk H, Aribi M, Merzouk S, Berrouiguet AY, Tessier C et al. Effects of the association of aging and obesity on lipids, lipoproteins and oxidative stress biomarkers: a comparison of older with young men. *Nutr Metab Cardiovasc Dis.* 2011;21:792-9.
24. Wonisch W, Falk A, Sundl I, Winklhofer-Roob BM, Lindschinger M. Oxidative stress increases continuously with BMI and age with unfavourable profiles in males. *Aging Male.* 2012;15:159-65.
25. Rambod M, Bross R, Zitterkoph J, Benner D, Pithia J, Colman S et al. Association of Malnutrition-Inflammation Score with quality of life and mortality in hemodialysis patients: a 5-year prospective cohort study. *Am J Kidney Dis.* 2009;53:298-309.
26. Turin TC, Tonelli M, Manns BJ, Ravani P, Ahmed SB, Hemmelgarn BR. Chronic kidney disease and life expectancy. *Nephrol Dial Transplant.* 2012;27:3182-6.
27. Aydin Z, Uzun S, Karadag S, Gursu M, Doner B, Sevim Y et al. Anthropometric measurements in hemodialysis patients. *Turkish Nephrology.* 2015;24:61-7.
28. Kittiskulnam P, Johansen KL. The obesity paradox: A further consideration in dialysis patients. *Semin Dial.* 2019;32:485-489.
29. Griffin KA, Kramer H, Bidani AK. Adverse renal consequences of obesity. *Am J Physiol Renal Physiol.* 2008;294:F685-96.
30. Kazory A, Klein A, Chalopin J-M, Ducloux D, Courivaud C. Obesity and atherosclerotic events in chronic hemodialysis patients: a prospective study. *Nephrol Dial Transplant.* 2013;28:iv188-iv94.
31. Garofalo C, Borrelli S, Minutolo R, Chiodini P, De Nicola L, Conte G. A systematic review and meta-analysis suggests obesity predicts onset of chronic kidney disease in the general population. *Kidney Int.* 2017;91:1224-35.
32. Zujko ME, Witkowska AM, Waśkiewicz A, Mirończuk-Chodakowska IJ, Longevity C. Dietary antioxidant and flavonoid intakes are reduced in the elderly. *Oxid Med Cell Longev.* 2015;2015:843173.
33. Khalil A, Gaudreau P, Cherki M, Wagner R, Tessier DM, Fulop T et al. Antioxidant-rich food intakes and their association with blood total antioxidant status and vitamin C and E levels in community-dwelling seniors from the Quebec longitudinal study NuAge. *Exp Gerontol.* 2011;46:475-81.
34. Pisoschi AM, Negulescu GP. Methods for total antioxidant activity determination: a review. *Biochem Anal Biochem.* 2011;1:106.
35. Bahadoran Z, Golzarand M, Mirmiran P, Shiva N, Azizi FJN, metabolism. Dietary total antioxidant

- capacity and the occurrence of metabolic syndrome and its components after a 3-year follow-up in adults: Tehran Lipid and Glucose Study. *Nutr Metab (Lond)*. 2012;9:1-9.
36. Rautiainen S, Lindblad BE, Morgenstern R, Wolk A. Total antioxidant capacity of the diet and risk of age-related cataract: a population-based prospective cohort of women. *JAMA Ophthalmol*. 2014;132:247-52.
  37. Asghari G, Yuzbashian E, Shahemi S, Gacini Z, Mirmiran P, Azizi F. Dietary total antioxidant capacity and incidence of chronic kidney disease in subjects with dysglycemia: Tehran Lipid and Glucose Study. *Eur J Nutr*. 2018;57:2377-85.
  38. Pantavos A, Ruiter R, Feskens EF, de Keyser CE, Hofman A, Stricker BH et al. Total dietary antioxidant capacity, individual antioxidant intake and breast cancer risk: the Rotterdam study. *Int J Cancer*. 2015;136:2178-86.
  39. Zujko ME, Witkowska AM, Waśkiewicz A, Piotrowski W, Terlikowska KM. Dietary antioxidant capacity of the patients with cardiovascular disease in a cross-sectional study. *Nutr J*. 2015;14:1-13.
  40. Henríquez-Sánchez P, Sánchez-Villegas A, Ruano-Rodríguez C, Gea A, Lamuela-Raventós RM, Estruch R et al. Dietary total antioxidant capacity and mortality in the PREDIMED study. *Eur J Nutr*. 2016;55:227-36.
  41. Tajbakhsh R, Qorbani M, Mehrpour G, Rahimzadeh M, Azimzadeh MM, Mirmiranpour H et al. Effect of hemodialysis on oxidants and antioxidant factors in chronic renal failure. *Saudi J Kidney Dis Transpl*. 2017;28:507.
  42. da Silva BR, Gonzalez MC, Cereda E, Prado CM. Exploring the potential role of phase angle as a marker of oxidative stress: A narrative review. *Nutrition*. 2022;93:111493.
  43. Harasym J, Oledzki R. Effect of fruit and vegetable antioxidants on total antioxidant capacity of blood plasma. *Nutrition*. 2014;30:511-7.
  44. Tsuruya K, Eriguchi M, Yamada S, Hirakata H, Kitazono T. Cardiorenal syndrome in end-stage kidney disease. *Blood Purif*. 2015;40:337-43.
  45. Giarretta AG, Schulz M, Silveira TT, de Oliveira MV, Patrício MJ, Gonzaga LV et al. Apple intake improves antioxidant parameters in hemodialysis patients without affecting serum potassium levels. *Nutr Res*. 2019;64:56-63.
  46. Delmastro-Greenwood M, Freeman BA, Wendell SG. Redox-dependent anti-inflammatory signaling actions of unsaturated fatty acids. *Annu Rev Physiol*. 2014;76:79.
  47. Furukawa S, Fujita T, Shimabukuro M, Iwaki M, Yamada Y, Nakajima Y et al. Increased oxidative stress in obesity and its impact on metabolic syndrome. *J Clin Invest*. 2017;114:1752-61.
  48. Friedman AN, Fadem SZ. Reassessment of albumin as a nutritional marker in kidney disease. *J Am Soc Nephrol*. 2010;21:223-30.