

Original Article



Dietary Total Antioxidant Capacity and Its Association with Renal Function and Progression of Chronic Kidney Disease in Older Adults: a Report from a Developing Country

Parivash Ghorbaninejad , Saba Mohammadpour , Farhang Djafari ,
Somayeh Tajik , Sakineh Shab-Bidar

Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences (TUMS), Tehran 14167-53955, Iran

OPEN ACCESS

Received: Aug 4, 2020

Revised: Oct 20, 2020

Accepted: Oct 22, 2020

Correspondence to

Sakineh Shab-Bidar

Department of Community Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, No 44, Hojjat-dost Alley, Naderi St., Keshavarz Blvd, Tehran 14167-53955, Iran.

E-mail: s_shabbidar@tums.ac.ir

Copyright © 2020. The Korean Society of Clinical Nutrition

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID iDs

Parivash Ghorbaninejad
<https://orcid.org/0000-0001-9218-684X>

Saba Mohammadpour
<https://orcid.org/0000-0002-1199-0244>

Farhang Djafari
<https://orcid.org/0000-0001-6890-8208>

Somayeh Tajik
<https://orcid.org/0000-0001-5846-6426>

Sakineh Shab-Bidar
<https://orcid.org/0000-0002-0167-7174>

Conflict of Interest

The authors declare that they have no competing interests.

ABSTRACT

While evidence exists for an association between the dietary total antioxidant capacity (DTAC), mortality, metabolic syndrome, and cardiovascular diseases, data about DTAC and renal function, and progression of chronic kidney disease (CKD) are scarce. This study aimed to determine the associations between DTAC, renal function, and progression of CKD in older adults. The present cross-sectional study consisted of 226 older adults aged ≥ 60 years old from five districts of Tehran, Iran. DTAC was estimated using the oxygen radical absorbance capacity (ORAC) method. Dietary intake, socio-demographic data, medical history, and anthropometric measurements were collected using a validated questionnaire. The estimated glomerular filtration rate (eGFR) was assessed from serum creatinine. Albumin to creatinine ratio (ACR) was calculated by dividing albumin concentration by creatinine concentration and reported as mg/g. The DTAC ranged from 112.8 to 2,553.9. Analyses indicated that DTAC was not associated with eGFR ($p = 0.35$) and ACR ($p = 0.91$) even after controlling for confounding variables. Additionally, in logistic regression, no association between eGFR < 60 mL/min/1.73 m² ($p = 0.32$) and ACR ≥ 30 mg/g ($p = 0.32$) with DTAC was observed, which was independent of confounding variables. We observed that more compliance with DTAC is not associated with renal function and CKD progression. Further studies are needed to confirm the findings of the present study in larger samples on different populations.

Keywords: Antioxidants; Oxidative stress; Kidney diseases; Albuminuria

INTRODUCTION

Chronic kidney disease (CKD)—a disease with a progressive decrease in renal function—is one of the important public health concerns which is increasing in incidence and prevalence [1]. A previous study demonstrated that the prevalence of CKD stages 3–5 was 11.6% among Iranian adults [2]. Chronic kidney disease is often related to other chronic disorders like diabetes, hypertension, and dyslipidemia [3]. This is a considerable disease, with progressive glomerular dysfunction, which is not usually reversible and results in a higher rate of

mortality [1]. Glomerular filtration rate (GFR) is a key indicator of kidney function assessing its performance. Several gold standards using direct assessment of exogenous markers such as inulin, iothalamate, ethylenediaminetetraacetic acid, diethylenetriamine pentaacetic acid, and iohexol are used for measuring GFR and renal function [4,5]. Due to several limitations to using direct methods for measuring kidney function in interventional studies with a large sample size and their high cost, estimated glomerular filtration rate (eGFR) is widely used in studies as a biomarker for assessing kidney function [6].

Despite non-modifiable CKD risk factors, such as race, gender, and family history of CKD, diabetes, obesity, physical inactivity, smoking, and dietary patterns are modifiable risk factors [7,8]. Accumulating evidence showed that lifestyle modifications including dietary manipulations may have beneficial effects on kidney function [9]. Chronic low-grade inflammation commonly expressed by a persistently elevated serum C-reactive protein (CRP) concentration is involved in the progression of kidney dysfunction. It is suggested that protective effects of healthy food groups such as vegetables, whole grains, fruit, and legumes on kidney health may be contributed to the high content of antioxidant compounds [10,11]. These valuable effects could be explained by their functions in preventing the formation of free radicals [12].

Emerging evidence using single nutrients with antioxidant potential has been shown the protective effects on kidney function, however, the overall antioxidant action of the diet measuring by a new tool called dietary total antioxidant capacity (TAC), defines synergistic actions of all antioxidants is a practical predictor of diet-disease relationships [13]. The association between dietary TAC and chronic diseases has been investigated in previous studies which showed improvements in cardiovascular risk factors [14] and lower weight and abdominal fat gain [15]. Additionally, the results of a study indicated that the habitual intake of the dietary TAC is associated with a lower risk of CKD [16]. Thus, the aim of this study was to investigate the association of habitual dietary TAC intake with kidney function.

MATERIALS AND METHODS

Participants

In this cross-sectional study, subjects were selected among healthy people aged ≥ 60 years old in five districts of Tehran, Iran. A total of 226 participants (65 men and 161 women) with an average age of 67.04 (60–83 years), were randomly selected through a 2-stage random cluster sampling for 2 years (2014–2015). For this aim, Tehran was divided into 5 regions included: North, South, East, West, and Central districts. After preparing a list of health centers in each area, 25 of them were chosen randomly (in attention to budget and time limitations). Then, an identical number of subjects were randomly chosen from each center. The sample size was attained based on mean and standard deviation in a previously published study [17]. The number of people needed for this study according to the following formula was [18]:

$$\frac{(z_{1-\alpha/2})^2 \times s^2}{d^2} = 193.$$

However, to replace patients who were excluded due to under- or over-reported food intakes, and to empower the study, we continued sampling until 250 individuals were enrolled. Subjects aged over 60 years, interested to participate in the study, and able to answer questions were included. Exclusion criteria were under or over-reporting of dietary intakes

(less than 800 kcal/d or more than 4,200 kcal/d, respectively), suffering from kidney, liver, and lung diseases and other conditions affect cardiovascular and respiratory system's health or infectious and active inflammatory diseases, pregnancy, lactation, routine supplement or drug use such as weight loss, hormonal, sedative drugs, thermogenic supplements like caffeine and green tea, conjugated linoleic acid (CLA), etc.

This study was conducted according to the guidelines laid down in the Declaration of Helsinki. All procedures were followed by the ethical standards of the Tehran University of Medical Sciences (IR.TUMS.REC.1395.2618), who approved all aspects of the study. All participants signed written informed consent before the start of the study.

Demographic data

Information on general characteristics such as age, sex, marital status, smoking and socioeconomic status, use of medications, use of mineral and vitamin supplements, and history of any diseases were asked during a face-to-face interview.

Dietary intake assessment

The habitual diet was assessed with a quantitative 147-items food frequency questionnaire (FFQ) which is validated for the Iranian population [19]. The trained interviewer asked each participant to report how often, on average, they have consumed each food item on a daily, weekly, monthly, or yearly scale over the previous year. For analyzing the energy and nutrients content of food items we used Nutritionist IV software (First Databank, San Bruno, CA, USA), modified for Iranian foods [20].

Calculation of the DTAC

DTAC was assessed by Nutrient Data Laboratory of USDA Database, using the oxygen radical absorbance capacity (ORAC) method for 100 grams of selected foods, and expressed as micromole of Trolox Equivalents ($\mu\text{mol TE}/100\text{ g}$) [21].

Biochemical assessments

Samples of 10ml of blood and at least 3 mL of urine were taken from all participants after overnight fasting (14 hours), between the hours of 8–10 am in acid-washed test tubes without anticoagulant. After 30 minutes of storing at room temperature, clot formation, and blood samples centrifuging at 1,500 g for 20 minutes, serums were put in -80°C until subsequent testing. Serum albumin and urea were assessed by a colorimetric method, using commercial kits (Pars Azmoon, Tehran, Iran) with an autoanalyzer (Selecta E; Vitalab, Holliston, The Netherlands). The concentration of CRP was assessed by enzyme-linked immunosorbent assay (ELISA) using the commercial kit (IBL international, Hamburg, Germany). Serum creatinine was measured according to the standard colorimetric Jaffe_Kinetic reaction method. Albumin to creatinine ratio (ACR) was calculated by dividing albumin concentration in milligrams by creatinine concentration in grams. We used the modification of diet in renal disease (MDRD) equation formula to express the eGFR in $\text{mL}/\text{min}/1.73\text{ m}^2$ of body surface area [22] that calculates as follows:

$$\text{eGFR} = 186 \times (\text{Serum creatinine})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \\ \times (1.210 \text{ if African-American}).$$

Subjects were classified based on their eGFR levels by the national kidney foundation guidelines: $\text{eGFR} \geq 60\text{ mL}/\text{min}/1.73\text{ m}^2$ as not having CKD and $\text{eGFR} < 60\text{ mL}/\text{min}/1.73\text{ m}^2$

as having CKD [3]. According to the American Diabetes Association, ACR ≥ 30 mg/g is represented as albuminuria [23].

Anthropometric measures, physical activity, and blood pressure

Weight was measured in light clothing to the nearest 100 g by a SECA digital weighing scale (Seca725; Seca GmbH & Co., Hamburg, Germany) and height was measured using a stadiometer (Seca GmbH & Co.) to the nearest 0.1 cm without shoes. Body mass index (BMI) was calculated as the body weight divided by height and expressed as kilograms per meter squared. Waist circumference (WC) was measured between the lower rib and iliac crest, using a tape meter. Data on physical activity was collected using the short-form International Physical Activity Questionnaire to calculate the metabolic equivalent (MET) minute per week [24]. Blood pressure (BP) was measured after an initial resting for 15 minutes while the patients were in a seated position and arms. BP was measured twice with at least a 30-second interval by a digital instrument (Beurer BP equipment, BC-08; Beurer GmbH, Ulm, Germany). The average of two measurements was used in our analyses.

Statistical methods

Participants were categorized based on the tertiles of the DTAC (≤ 741.3 , 741.3–1,185.7, and $\geq 1,185.7$ $\mu\text{mol TE}/100\text{g}$). For comparison, the general characteristics among the tertiles of the DTAC, one-way analysis of variance (ANOVA), and χ^2 tests were used for quantitative and qualitative variables, respectively. Analysis of covariance (ANCOVA) was performed to report energy-adjusted nutrient intakes across the tertiles of the DTAC. A post hoc multiple comparisons test using the Tukey method was performed across tertiles of the DTAC. We used ANOVA in the crude model and ANCOVA in three adjusted models to compare biochemical variables across the tertiles of DTAC after controlling for confounding variables such as age, sex, physical activity, socioeconomic status, systolic blood pressure, diastolic blood pressure, weight, height, potassium, phosphorus, and protein intake. The eGFR < 60 mL/min/1.73 m² and ACR ≥ 30 mg/g were classified as subjects with CKD. Odds ratio and 95% confidence intervals were obtained using logistic regression to determine the relationship between the DTAC with kidney function. The risk was reported in crude and 3 adjusted models. In this analysis, the first tertile of exposure was considered as the reference category. We considered $p < 0.05$ as the significance level, priority. For all analyses, SPSS 22 for Windows (SPSS Inc., Chicago, IL, USA) was used.

RESULTS

The demographic characteristics of all 226 participants across tertiles of DTAC are shown in **Table 1**. The mean \pm standard deviation age of the study participants was 67 ± 5.7 years (from 60 to 83 years), and 72% of participants were women. The DTAC range was from 112.8 to 2,553.9. The body weight of tertile 3 was significantly higher than that of tertile 1 ($p = 0.01$). Subjects in the highest, compared to the lowest tertile category of DTAC were more likely to be married ($p < 0.001$). Furthermore, there was a significant difference in the smoking status among the groups of DTAC ($p = 0.02$). However, we did not observe any significant differences in age, height, waist circumference, body mass index, systolic and diastolic blood pressure, sex, and physical activity across the tertiles of DTAC. Additionally, there was a significant association between the first and third tertiles of weight based on the Tukey test.

Nutrient intakes of participants across the tertiles of DTAC after adjusting for energy intake are reported in **Table 2**. The findings showed that the intake of energy ($p < 0.001$), total fat (p

Table 1. General characteristics of the participants in the study based on tertiles of DTAC

Characteristics	Tertile 1 (≤ 741.3) (n = 76)	Tertile 2 (741.3– 1,185.7) (n = 75)	Tertile 3 ($\geq 1,185.7$) (n = 75)	p value
Age (yr)	67.7 \pm 6.10	67.3 \pm 5.97	66.0 \pm 5.12	0.07
Weight (kg)	71.0 \pm 11.4 ^a	71.1 \pm 11.1 ^{a,b}	75.7 \pm 13.0 ^b	0.01*
Height (cm)	155 \pm 7.70	155 \pm 8.33	157 \pm 7.92	0.10
WC (cm)	99.0 \pm 11.4	98.9 \pm 9.20	99.6 \pm 10.4	0.71
BMI (kg/m ²)	29.3 \pm 4.15	30.2 \pm 5.05	29.6 \pm 4.38	0.65
Systolic blood pressure (mmHg)	140 \pm 19.9	144 \pm 23.5	141 \pm 22.5	0.53
Diastolic blood pressure (mmHg)	83.1 \pm 14.9	87.8 \pm 16.3	83.0 \pm 12.1	0.07
Sex				0.19
Male	19 (25.0)	20 (26.7)	26 (34.7)	
Female	57 (75.0)	55 (73.3)	49 (65.3)	
Marital status				< 0.001*
Single	0 (0)	0 (0)	3 (4.0)	
Married	49 (64.5)	53 (70.7)	59 (78.7)	
Divorced	0 (0)	2 (2.7)	2 (2.7)	
Widow	27 (35.5)	20 (26.7)	11 (14.7)	
Smoking				0.02*
None smoker	67 (88.2)	68 (90.7)	56 (74.7)	
Former and current smoker	9 (11.8)	7 (9.3)	19 (25.3)	
Physical activity				0.88
Very low	34 (44.7)	37 (49.3)	37 (49.3)	
Low	31 (40.8)	22 (29.3)	25 (33.3)	
Medium and high	11 (14.5)	16 (21.3)	13 (17.3)	

One-way analysis of variance for quantitative data and χ^2 test for qualitative data have been used. Values are presented as mean \pm standard deviations or number of subjects (%).

DTAC, dietary total antioxidant capacity; WC, waist circumference; BMI, body mass index.

*Significantly different between groups ($p < 0.05$); ^{a,b}Tukey post hoc test: means with the same letter indicate no significant difference. Any difference between 2 means carrying different letters is significant at 0.05.

= 0.03), monounsaturated fatty acids (MUFAs) ($p = 0.01$), fiber ($p = 0.04$), folate ($p < 0.001$) and vitamin E ($p = 0.04$) in people in the third tertile were significantly more than the first tertile. No significant relation was observed between other nutrient intakes across the tertiles of DTAC. A post hoc Tukey test showed the significant relations between all groups of DTAC for energy and folate intake and also the differences between the first tertile with tertile 2 and 3 in total fat and vitamin E intake. Besides, this test indicated that tertiles 1 and 2 and also tertiles 1 and 3 significantly differed for MUFAs and fiber intake, respectively.

The mean of kidney function variables reported by tertiles of DTAC is presented in **Table 3**. We did not find any significant differences in the mean of biochemical characteristics of renal function across the DTAC tertiles even after controlling for confounders.

Logistic regression was applied for assessing the association of DTAC intake and CKD progression and albuminuria in crude and adjusted models (**Table 4**). The crude result of logistic regression indicated no association of eGFR < 60 mL/min/1.73 m² with DTAC. After adjustment for confounder variables, the non-significant association remained. Regarding albuminuria, our crude findings also proposed no relationship between DTAC tertiles and the risk of ACR ≥ 30 mg/g. After controlling for confounder variables, the result did not change remarkably.

DISCUSSION

Our findings showed that the intake of energy, total fat, MUFAs, folate, fiber, and vitamin E increased significantly across tertiles of DTAC while no significant relation was observed

Table 2. Macro and micronutrients intake across tertiles of DTAC

Intake	Mean ± SD	Tertile 1 (n = 76)	Tertile 2 (n = 75)	Tertile 3 (n = 75)	p value
Energy (kcal/d)	2,775 ± 799	2,367 ± 601 ^a	2,729 ± 642 ^b	3,235 ± 879 ^c	< 0.001*
Total fat (g/d)	78 ± 36	66 ± 25 ^a	84 ± 45 ^{b,c}	85 ± 32 ^c	0.03*
SFAs (g/d)	23 ± 10	20 ± 8	24 ± 9	26 ± 11	0.16
MUFAs (g/d)	27 ± 17	22 ± 8 ^a	30 ± 26 ^b	27 ± 10 ^{a,b}	0.01*
n-3 PUFAs (g/d)	1.2 ± 0.8	1.04 ± 0.6	1.2 ± 0.7	1.4 ± 1.1	0.62
n-6 PUFAs (g/d)	13.6 ± 7.0	11.6 ± 5.6	14.8 ± 7.8	14.4 ± 6.9	0.08
Cholesterol (mg/d)	204 ± 103	179 ± 81	206 ± 102	228 ± 118	0.52
Protein (g/d)	84 ± 31	71 ± 25	84 ± 30	96 ± 33	0.76
Carbohydrates (g/d)	371 ± 137	302 ± 101	370 ± 125	441 ± 146	0.15
Fiber (g/d)	46.7 ± 24.0	40.0 ± 18.6 ^a	46.0 ± 22.9 ^{a,b}	54.1 ± 29.5 ^b	0.04*
Phosphor (mg/d)	1,640 ± 619	1,415 ± 469	1,675 ± 651	1,833 ± 654	0.11
Vitamin A (µg/d)	804 ± 444	732 ± 472	774 ± 336	907 ± 495	0.40
β-Carotene (µg/d)	5,342 ± 3,046	4,754 ± 2,569	5,179 ± 2,519	6,101 ± 3,770	0.72
Thiamin (mg/d)	2.1 ± 0.9	1.7 ± 0.6	2.2 ± 0.9	2.5 ± 0.9	0.20
Riboflavin (mg/d)	2.1 ± 0.8	1.9 ± 0.6	2.1 ± 0.7	2.4 ± 0.9	0.14
Niacin (mg/d)	25.2 ± 10.3	20.9 ± 8.7	24.8 ± 10.2	29.9 ± 10.2	0.48
Vitamin B-6 (mg/d)	2.1 ± 0.7	1.8 ± 0.6	2.1 ± 0.6	2.5 ± 0.8	0.82
Folate (µg/d)	569 ± 205	446 ± 129 ^a	570 ± 180 ^b	694 ± 216 ^c	< 0.001*
Vitamin B-12 (µg/d)	4.3 ± 3.2	4.1 ± 4.1	4.08 ± 2.5	4.8 ± 2.8	0.22
Vitamin C (mg/d)	193 ± 97	157 ± 69	184 ± 82	240 ± 116	0.33
Vitamin D (µg/d)	1.8 ± 1.7	1.5 ± 1.2	1.9 ± 1.9	2.02 ± 1.8	0.50
Vitamin E (mg/d)	12.9 ± 5.4	11.01 ± 4.3 ^a	13.9 ± 6.4 ^{b,c}	14.05 ± 4.7 ^c	0.04*
Vitamin K (µg/d)	241 ± 164	204 ± 153	251 ± 144	268 ± 188	0.60
Iron (mg/d)	18.9 ± 8.0	15.5 ± 5.9	19.2 ± 8.6	22.0 ± 8.1	0.41
Magnesium (mg/d)	481 ± 196	415 ± 140	493 ± 226	536 ± 196	0.12
Selenium (µg/d)	129 ± 68	134 ± 86	129 ± 63	124 ± 52	0.55
Zinc (mg/d)	12.3 ± 4.8	10.6 ± 4.03	12.6 ± 5.1	13.9 ± 4.7	0.37
Potassium (mg/d)	4,104 ± 1,404	3,579 ± 1,037	4,016 ± 1,297	4,725 ± 1,594	0.21
Calcium (mg/d)	1,138 ± 433	991 ± 316	1,157 ± 428	1,268 ± 496	0.11

Analysis of covariance has been used; All values are mean ± SD and adjusted for total energy intake.

DTAC, dietary total antioxidant capacity; SD, standard deviation; SFA, saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid. *Significantly different between groups ($p < 0.05$); ^{a,b,c}Tukey post hoc test: means with the same letter indicate no significant difference. Any difference between 2 means carrying different letters is significant at 0.05.

Table 3. Multivariate adjusted means for biochemical characteristics of renal function

Biochemical characteristics	Mean ± SD	Tertile 1 (n = 76)	Tertile 2 (n = 75)	Tertile 3 (n = 75)	p value	P1	P2	P3
Serum urea (mg/dL)	33.7 ± 14.4	33.6 ± 12.1	35.6 ± 19.8	31.9 ± 9.2	0.46	0.30	0.31	0.54
Serum creatinine (mg/dL)	1.1 ± 0.9	1.08 ± 0.3	1.3 ± 1.5	1.09 ± 0.3	0.98	0.09	0.13	0.33
Serum albumin (mg/dL)	4.7 ± 2.7	5.1 ± 4.6	4.6 ± 0.3	4.5 ± 0.4	0.21	0.38	0.37	0.24
Urine creatinine (mg/dL)	2.45 ± 1.4	2.3 ± 1.4	2.6 ± 1.4	2.3 ± 1.3	0.83	0.19	0.18	0.15
Urine albumin (mg/g)	83.5 ± 148	68.2 ± 68.5	101.7 ± 194	80.7 ± 153	0.61	0.32	0.40	0.28
hs-CRP (mg/L)	4.8 ± 12.8	5.9 ± 19.5	3.9 ± 8	4.7 ± 7.1	0.55	0.51	0.48	0.51
eGFR (mL/min/1.73 m ²)	77.5 ± 109	89 ± 154	64.7 ± 45.6	78.7 ± 97.7	0.56	0.44	0.44	0.35
ACR (mg/g)	34 ± 67.6	26.5 ± 20.8	36 ± 54.9	39.9 ± 104	0.24	0.74	0.78	0.91

Analysis of variance in crude model and analysis of covariance in adjusted models have been used (P1, adjusted model for age, sex, physical activity, and socioeconomic status; P2, Model 1 + systolic and diastolic blood pressure; P3, Model 2 + weight, height, potassium, phosphorus, and protein intake). All values are mean ± SD.

SD, standard deviation; hs-CRP, high-sensitivity C-reactive protein; eGFR, estimated glomerular filtration rate; ACR, albumin to creatinine ratio.

*Significantly different between groups ($p < 0.05$).

between other nutrient intakes and DTAC. We also found that DTAC had no significant relationship with the biomarkers of kidney function in crude and 3 adjusted models. Additionally, increased odds of having CKD were not significant across DTAC tertiles.

For many years the association of single antioxidant nutrient and food groups like vegetables and fruits with health and disease has been the focus of interest [25]. However, investigating the association of single antioxidant nutrient or food groups may not reflect the interaction

Table 4. Relationship of DTAC with eGFR and urine ACR

Tertiles of DTAC	ACR \geq 30 mg/g		Tertiles of DTAC	eGFR $<$ 60 mL/min/1.73 m ²	
	OR (95% CI)	p value		OR (95% CI)	p value
Crude			Crude		
Tertile 1 (n = 72)	1 reference	0.15	Tertile 1 (n = 76)	1 reference	0.99
Tertile 2 (n = 71)	2.03 (0.93–4.46)	0.07	Tertile 2 (n = 75)	0.97 (0.51–1.87)	0.94
Tertile 3 (n = 66)	1.97 (0.88–4.38)	0.09	Tertile 3 (n = 75)	0.97 (0.51–1.87)	0.94
Model 1			Model 1		
Tertile 1 (n = 70)	1 reference	0.12	Tertile 1 (n = 74)	1 reference	0.93
Tertile 2 (n = 71)	2.25 (1.00–5.09)	0.04*	Tertile 2 (n = 75)	0.96 (0.49–1.88)	0.90
Tertile 3 (n = 65)	1.94 (0.83–4.50)	0.12	Tertile 3 (n = 74)	1.08 (0.54–2.15)	0.81
Model 2			Model 2		
Tertile 1 (n = 70)	1 reference	0.13	Tertile 1 (n = 74)	1 reference	0.91
Tertile 2 (n = 71)	2.24 (0.99–5.07)	0.05	Tertile 2 (n = 75)	0.93 (0.47–1.84)	0.84
Tertile 3 (n = 65)	1.94 (0.83–4.51)	0.12	Tertile 3 (n = 74)	1.08 (0.54–2.15)	0.81
Model 3			Model 3		
Tertile 1 (n = 70)	1 reference	0.21	Tertile 1 (n = 74)	1 reference	0.43
Tertile 2 (n = 71)	2.11 (0.91–4.91)	0.08	Tertile 2 (n = 75)	0.91 (0.44–1.86)	0.80
Tertile 3 (n = 65)	1.58 (0.63–3.93)	0.32	Tertile 3 (n = 74)	1.47 (0.68–3.18)	0.32

Values are reported based on the logistic regression test (Model 1, adjusted for age, sex, physical activity, and socioeconomic status; Model 2, model 1 + systolic and diastolic blood pressure; Model 3, model 2 + weight, height, potassium, phosphorus, and animal protein intake).

DTAC, dietary total antioxidant capacity; eGFR, estimated glomerular filtration rate; ACR, albumin to creatinine ratio; OR, odds ratio; CI, confidence interval.

*Significantly different between groups ($p < 0.05$).

or synergetic effects of antioxidants in the whole diet and different mechanisms to prevent disease [13]. Therefore, DTAC was developed as an applicable tool for the assessment of the antioxidant potential of a diet [13].

We found that the intake of energy, total fat, MUFAs, fiber, folate, and vitamin E increased significantly across tertiles. The association between DTAC with the indices of the Mediterranean diet and the Healthy Eating Scores has also been reported [13]. Bonaccio et al. [26], also reported that adherence to a Mediterranean diet is along with a high intake of antioxidant components like MUFA, fiber, folate, and vitamin E. In a population-based cohort study, a higher intake of vitamin E and vitamin C had associated with reduced risk incidence of CKD. Apart from observational studies, these reported associations have been confirmed in a few intervention studies with improvement in eGFR and protein excretion following a pharmacological dose of vitamins C and E [27], which was not confirmed in others [28]. The consumption of fibers from fruits, vegetables, and whole grains, confirms a higher intake of nutrients found in these foods like folate and vitamin C. It also showed a relation between dietary fiber with a reduction of inflammation and mortality among patients with CKD [29]. Previous studies have demonstrated an age-related increase of oxidative stress [30] and the role of oxidative stress in several age-related diseases like the progression of CKD [12]. In a recent systematic review, an inverse association between TAC and the health outcomes in middle-aged and elderly populations were determined [31]. Excessive oxidative stress is a progressive mediator connecting with higher malignancy rates in end-stage renal disease (ESRD) patients and structural changes induced by reactive oxygen species in β 2-microglobulin and fibrosis which may result in inflammation [32,33]. Antioxidants with beneficial effects on inflammation and oxidative stress may influence CKD development and progression by compensating for imbalances in oxidative stress [12]. The participants in tertile 3 had higher body weight. The role of high body weight in oxidative stress and inflammation can be a justification for the lack of relationship between DTAC and the improvement of CKD markers.

We could not find any significant relation between biomarkers of kidney function across the DTAC tertiles in crude and 3 adjusted models. Our results confirmed the findings of a study done by Lin et al. [34], who reported that there was no association between the dietary approach to stop hypertension (DASH) style pattern score which is rich in antioxidant components, with eGFR and ACR. In contrast, a study conducted on 635 patients with diabetes reported that by increasing scores of “the vegetable and fish” dietary pattern which is high in antioxidants, fiber, and phytochemicals, serum creatinine decreased and eGFR increased [35]. Low sample size in our study may result in a lack of association. Moreover, the diverse results may also be related to the different assessment tools like dietary intake questionnaire (147-item FFQ vs. 45-item FFQ).

Another important finding of the present study was that a higher intake of TAC was not related to the risk of CKD. Similar to our finding, a case-control study consisted of 210 patients with type 2 diabetes, reported no significant association between DTAC and CKD risk [36]. On the other hand, a study showed that diets high in TAC were associated with a lower risk of incident CKD among subjects with hyperglycemia [17]. Contrary to our study, they included hyperglycemic patients and it is obvious that variety in health condition and the design of study is another factor that can be made controversies in findings. Moreover, the association of the Mediterranean diet, rich in antioxidants, with decreased risk of incident CKD has been reported [37]. Different food processing and cooking methods in various cultures may affect the availability and content of dietary antioxidants, which may explain these conflicting results [38].

The present study has some strengths and limitations. This study is the first study that explored the association between DTAC with kidney function in Iranian elderly with a validated FFQ and considers the controlling of confounder variables. However, this was a cross-sectional study, and therefore we could not assess the causal relationship. In addition, the assessment of dietary TAC may be affected by cultivation procedures, storage, and cooking [38]. Moreover, we did not assess serum TAC. Several studies have reported that dietary TAC has been positively associated with plasma total antioxidant capacity [39]. The low sample size was another limitation. Also, the results could not be generalized to the general population. Because we used FFQ to obtain information on participants' dietary intake and also participants were elderly, recall bias, overestimation, and underestimation of dietary intakes were possible. Moreover, it is possible that there still may be residual confounding factors, although attempts were made in our study to control all relevant cofounders.

CONCLUSION

In conclusion, we did not observe an association between DTAC, kidney function, and the odds of having CKD and albuminuria. However, further investigation, without all the limitations of this study is needed to confirm our findings.

ACKNOWLEDGEMENTS

We would like to acknowledge all participants who made this research possible.

REFERENCES

1. Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, Hogg RJ, Perrone RD, Lau J, Eknoyan G; National Kidney Foundation. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Ann Intern Med* 2003;139:137-47.
[PUBMED](#) | [CROSSREF](#)
2. Khajehdehi P, Malekmakan L, Pakfetrat M, Roozbeh J, Sayadi M. Prevalence of chronic kidney disease and its contributing risk factors in southern Iran: a cross-sectional adult population-based study. *Iran J Kidney Dis* 2014;8:109-15.
[PUBMED](#)
3. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 2002;39:S1-266.
[PUBMED](#)
4. Glasscock RJ, Winearls C. Ageing and the glomerular filtration rate: truths and consequences. *Trans Am Clin Climatol Assoc* 2009;120:419-28.
[PUBMED](#)
5. Food and Drug Administration. Guidance for industry: pharmacokinetics in patients with impaired renal function—study design, data analysis, and impact on dosing and labeling. Rockville (MD): US Department of Health and Human Services; 1998.
6. Chung SM, Lee DJ, Hand A, Young P, Vaidyanathan J, Sahajwalla C. Kidney function changes with aging in adults: comparison between cross-sectional and longitudinal data analyses in renal function assessment. *Biopharm Drug Dispos* 2015;36:613-21.
[PUBMED](#) | [CROSSREF](#)
7. Tarver-Carr ME, Powe NR, Eberhardt MS, LaVeist TA, Kington RS, Coresh J, Brancati FL. Excess risk of chronic kidney disease among African-American versus white subjects in the United States: a population-based study of potential explanatory factors. *J Am Soc Nephrol* 2002;13:2363-70.
[PUBMED](#) | [CROSSREF](#)
8. Williams RA, Flack JM, Gavin JR 3rd, Schneider WR, Hennekens CH. Guidelines for management of high-risk African Americans with multiple cardiovascular risk factors: recommendations of an expert consensus panel. *Ethn Dis* 2007;17:214-20.
[PUBMED](#)
9. Bello AK, Nwankwo E, El Nahas AM. Prevention of chronic kidney disease: a global challenge. *Kidney Int Suppl* 2005;68:S11-7.
[PUBMED](#) | [CROSSREF](#)
10. Sorensen MD, Hsi RS, Chi T, Shara N, Wactawski-Wende J, Kahn AJ, Wang H, Hou L, Stoller ML; Women's Health Initiative Writing Group. Dietary intake of fiber, fruit and vegetables decreases the risk of incident kidney stones in women: a Women's Health Initiative report. *J Urol* 2014;192:1694-9.
[PUBMED](#) | [CROSSREF](#)
11. Bernstein AM, Treyzon L, Li Z. Are high-protein, vegetable-based diets safe for kidney function? A review of the literature. *J Am Diet Assoc* 2007;107:644-50.
[PUBMED](#) | [CROSSREF](#)
12. Small DM, Coombes JS, Bennett N, Johnson DW, Gobe GC. Oxidative stress, anti-oxidant therapies and chronic kidney disease. *Nephrology (Carlton)* 2012;17:311-21.
[PUBMED](#) | [CROSSREF](#)
13. Puchau B, Zulet MÁ, de Echávarri AG, Hermsdorff HH, Martínez JA. Dietary total antioxidant capacity: a novel indicator of diet quality in healthy young adults. *J Am Coll Nutr* 2009;28:648-56.
[PUBMED](#) | [CROSSREF](#)
14. Kim K, Vance T, Chun O. Greater total antioxidant capacity from diet and supplements is associated with a less atherogenic blood profile in US adults. *Nutrients* 2016;8:15.
[CROSSREF](#)
15. Bahadoran Z, Golzarand M, Mirmiran P, Shiva N, Azizi F. 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;9:70.
[PUBMED](#) | [CROSSREF](#)
16. Opara EC, Abdel-Rahman E, Soliman S, Kamel WA, Souka S, Lowe JE, Abdel-Aleem S. Depletion of total antioxidant capacity in type 2 diabetes. *Metabolism* 1999;48:1414-7.
[PUBMED](#) | [CROSSREF](#)

17. Asghari G, Yuzbashian E, Shahemi S, Gaeini 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.
[PUBMED](#) | [CROSSREF](#)
18. Kamangar F, Islami F. Sample size calculation for epidemiologic studies: principles and methods. *Arch Iran Med* 2013;16:295-300.
[PUBMED](#)
19. Esfahani FH, Asghari G, Mirmiran P, Azizi F. Reproducibility and relative validity of food group intake in a food frequency questionnaire developed for the Tehran Lipid and Glucose Study. *J Epidemiol* 2010;20:150-8.
[PUBMED](#) | [CROSSREF](#)
20. Ghafarpour M, Houshiar-Rad A, Kianfar H. The manual for household measures, cooking yields factors and edible portion of food. Tehran: Keshavarzi Press; 1999.
21. U.S. Department of Agriculture, Agricultural Research Service. USDA database for the oxygen radical absorbance capacity (ORAC) of selected foods, Release 2. Washington, D.C.: U.S. Department of Agriculture; 2010. p. 10-48.
22. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D; Modification of Diet in Renal Disease Study Group. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. *Ann Intern Med* 1999;130:461-70.
[PUBMED](#) | [CROSSREF](#)
23. Molitch ME, DeFronzo RA, Franz MJ, Keane WF, Mogensen CE, Parving HH, Steffes MW; American Diabetes Association. Nephropathy in diabetes. *Diabetes Care* 2004;27 Suppl 1:S79-83.
[PUBMED](#) | [CROSSREF](#)
24. Hurtig-Wennlöf A, Hagströmer M, Olsson LA. The International Physical Activity Questionnaire modified for the elderly: aspects of validity and feasibility. *Public Health Nutr* 2010;13:1847-54.
[PUBMED](#) | [CROSSREF](#)
25. McMartin SE, Jacka FN, Colman I. The association between fruit and vegetable consumption and mental health disorders: evidence from five waves of a national survey of Canadians. *Prev Med* 2013;56:225-30.
[PUBMED](#) | [CROSSREF](#)
26. Bonaccio M, Di Castelnuovo A, Bonanni A, Costanzo S, De Lucia F, Pounis G, Zito F, Donati MB, de Gaetano G, Iacoviello L; Moli-sani project Investigators. Adherence to a Mediterranean diet is associated with a better health-related quality of life: a possible role of high dietary antioxidant content. *BMJ Open* 2013;3:e003003.
[PUBMED](#) | [CROSSREF](#)
27. Earle KA, Zitouni K, Pepe J, Karaflou M, Godbold J Jr. Modulation of endogenous antioxidant defense and the progression of kidney disease in multi-heritage groups of patients with type 2 diabetes: PROspective EVALuation of Early Nephropathy and its Treatment (PREVENT). *J Transl Med* 2016;14:234.
[PUBMED](#) | [CROSSREF](#)
28. Collins R, Armitage J, Parish S, Sleight P, Peto R; Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: a randomised placebo-controlled trial. *Lancet* 2003;361:2005-16.
[PUBMED](#) | [CROSSREF](#)
29. Krishnamurthy VM, Wei G, Baird BC, Murtaugh M, Chonchol MB, Raphael KL, Greene T, Beddhu S. High dietary fiber intake is associated with decreased inflammation and all-cause mortality in patients with chronic kidney disease. *Kidney Int* 2012;81:300-6.
[PUBMED](#) | [CROSSREF](#)
30. Mutlu-Türkoğlu U, İlhan E, Öztezcan S, Kuru A, Aykaç-Toker G, Uysal M. Age-related increases in plasma malondialdehyde and protein carbonyl levels and lymphocyte DNA damage in elderly subjects. *Clin Biochem* 2003;36:397-400.
[PUBMED](#) | [CROSSREF](#)
31. Nascimento-Souza MA, Paiva PG, Martino HS, Ribeiro AQ. Dietary total antioxidant capacity as a tool in health outcomes in middle-aged and older adults: a systematic review. *Crit Rev Food Sci Nutr* 2018;58:905-12.
[PUBMED](#) | [CROSSREF](#)
32. Shang W, Huang L, Li L, Li X, Zeng R, Ge S, Xu G. Cancer risk in patients receiving renal replacement therapy: a meta-analysis of cohort studies. *Mol Clin Oncol* 2016;5:315-25.
[PUBMED](#) | [CROSSREF](#)
33. Capeillere-Blandin C, Delaveau T, Descamps-Latscha B. Structural modifications of human β_2 microglobulin treated with oxygen-derived radicals. *Biochem J* 1991;277:175-82.
[PUBMED](#) | [CROSSREF](#)

34. Lin J, Fung TT, Hu FB, Curhan GC. Association of dietary patterns with albuminuria and kidney function decline in older white women: a subgroup analysis from the Nurses' Health Study. *Am J Kidney Dis* 2011;57:245-54.
[PUBMED](#) | [CROSSREF](#)
35. Hsu CC, Jhang HR, Chang WT, Lin CH, Shin SJ, Hwang SJ, Huang MC. Associations between dietary patterns and kidney function indicators in type 2 diabetes. *Clin Nutr* 2014;33:98-105.
[PUBMED](#) | [CROSSREF](#)
36. Abbasi M, Daneshpour MS, Hedayati M, Mottaghi A, Pourvali K, Azizi F. Dietary total antioxidant capacity and the risk of chronic kidney disease in patients with type 2 diabetes: a nested case-control study in the Tehran Lipid Glucose Study. *J Ren Nutr* 2019;29:394-8.
[PUBMED](#) | [CROSSREF](#)
37. Asghari G, Farhadnejad H, Mirmiran P, Dizavi A, Yuzbashian E, Azizi F. Adherence to the Mediterranean diet is associated with reduced risk of incident chronic kidney diseases among Tehranian adults. *Hypertens Res* 2017;40:96-102.
[PUBMED](#) | [CROSSREF](#)
38. Nayak B, Liu RH, Tang J. Effect of processing on phenolic antioxidants of fruits, vegetables, and grains--a review. *Crit Rev Food Sci Nutr* 2015;55:887-919.
[PUBMED](#) | [CROSSREF](#)
39. Hermsdorff HH, Puchau B, Volp AC, Barbosa KB, Bressan J, Zulet M^Á, Mart^ínez JA. Dietary total antioxidant capacity is inversely related to central adiposity as well as to metabolic and oxidative stress markers in healthy young adults. *Nutr Metab (Lond)* 2011;8:59.
[PUBMED](#) | [CROSSREF](#)