Original Article

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The Relationship Between Dietary Intakes and Total Kidney Volume in Patients with Autosomal Dominant Polycystic Kidney Disease Dietary Intake and Polycystic Kidney Volume

Yonca Sevim*, Egemen Cebeci**, Ozlem Persil Ozkan***, Yildiray Savas****, Savas Ozturk**, Gul Kiziltan*****

*Bahcesehir University Faculty of Health Science, Department of Nutrition and Dietetics, Istanbul, Turkey

**University of Health Sciences Turkey, Istanbul Haseki Training and Research Hospital, Clinic of Nephrology, Istanbul, Turkey

***Istanbul Arel University Faculty of Health Sciences, Department of Nutrition and Dietetics, Istanbul, Turkey

****University of Health Sciences Turkey, Istanbul Haseki Training and Research Hospital, Clinic of Radiology, Istanbul, Turkey

*****Baskent University Faculty of Health Sciences, Department of Nutrition and Dietetics, Ankara, Turkey

Abstract

Aim: There is a need to understand autosomal dominant polycystic kidney disease (ADPKD) patients' dietary habits since dietary interventions may have potential effects on ADPKD. In this study, we aimed to analyze the relationship between dietary nutrient intake and total kidney volume (TKV).

Methods: This cross-sectional study was conducted on 54 ADPKD patients recruited from the Nephrology outpatient clinic between June and July 2014. TKV was determined by magnetic-resonance imaging and general characteristics, biochemical and urinary parameters were determined. The nutrient intakes of patients were calculated using the three-day dietary records obtained on three consecutive days.

Results: The total kidney-volume median was found to be 1407 mL. Patients' total dietary energy and protein intakes were 25.8±9.4 kcal/kg, 0.9±0.3 g/kg, respectively. The percentage of carbohydrates, protein, and fat in energy was 49±7%, 14±3%, 37±7%, respectively. The mean intakes of thiamin, riboflavin, B6, calcium, magnesium, and zinc were sufficient, the mean dietary potassium intake was insufficient; and sodium intake was excessive in both sexes. In females, there was a negative but weak correlation between dietary vitamin C intake and TKV. In males, a negative but weak correlation was found between TKV and dietary intake of fiber, water, vitamin B6, vitamin K, magnesium, and iron.

Conclusions: Dietary micronutrient intake may affect TKV according to sex.

Keywords: Autosomal dominant polycystic kidney, ADPKD, kidney, nutrition, diet therapy, dietary intakes

Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is a hereditary kidney disorder characterized by renal and extrarenal involvement with cystic and non-cystic manifestations. ADPKD accounts for approximately 5% of total end-stage renal disease (1). Pharmaceutical therapies (i.e., tolvaptan and octreotide) with supportive measures such as blood pressure control, increased fluid intake, decreased salt intake, and smoking cessation are the basis of the current management of AKPD (2).

Data on dietary interventions in patients with ADPKD is still limited. The role of medical nutrition therapy hasn't been fully investigated in ADPKD (3). The lack of specific, based on strong evidence, dietary recommendations for

Address for Correspondence: Yonca Sevim
Bahcesehir University Faculty of Health Science, Department of Nutrition and Dietetics, Istanbul, Turkey
Phone: +90 212 381 00 20 E-mail: yonca.sevim@hes.bau.edu.tr ORCID: orcid.org/0000-0003-2793-1318
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ADPKD patients and the general recommendations for chronic kidney disease (CKD) patients remains important. Blood pressure control, dietary modification toward a low-protein diet, the use of antioxidants and lipid lowering agents have been investigated in PKD to reduce renal progression (4). While low protein diets are generally recommended for PKD patients, the type rather than the amount of protein may be considered more important, and omega-3 polyunsaturated fatty acids, phytochemicals, and phytoestrogens may affect PKD and cyst pathogenesis (5). Recent research with murine models of PKD showed that PKD cyst lining cells are glucose-dependent as an energy source (the Warburg effect), pointing out that defects in energy metabolism underlie the pathogenesis of PKD (6,7). Because of these findings, dietary management of ADPKD has become a focus of interest again. It's been shown that non-caloric reduction with time-restricted feeding strongly inhibits the mammalian target of rapamycin signaling, fibrosis, and proliferation in a PKD rat model (8). Conflicting results of pharmacologic and dietary strategies have been used so far to preserve renal function and slow renal damage in humans with PKD.

Data on ADPKD is mostly based on animal or human cell studies, and there is insufficient data about ADPKD patients' actual dietary consumption. This study improved the understanding of ADPKD patients' dietary behaviors and the relationship between total kidney volume (TKV) and diet, and provided evidence to support improvements in dietary recommendations and dietary interventions to reduce renal damage.

Materials and Methods

Compliance with Ethical Standards

This study was approved by the University of Health Sciences Turkey, Istanbul Haseki Training and Research Hospital, Non-Pharmaceutical Clinical Research Ethics Committee (date: 18.06.2014, protocol no: 122). Written informed consent was obtained from the patients. The privacy of the study participants was protected.

Study Population

Patients who were diagnosed with ADPKD confirmed by family history, clinical findings, and determinate kidney volume by magnetic resonance imaging (MRI) were enrolled, recruited from the Nephrology outpatient clinic during routine visits between June and July 2014, and were informed about the study. Patients who accepted to voluntarily participate in this study were screened. Patients were excluded if they used drugs affecting the cyst volume (tolvaptan, rapamycin, lithium, etc.), received renal replacement therapy, were on diet therapy for preexisting or comorbid medical conditions not related to the ADPKD standard care, those with creatinine clearance ≤15 mL/min, chronic liver or lung disease, hyperthyroidism, pregnancy, active infection, malignancy, and malnutrition (albumin less than 4 g/dL). The final number of patients was 54 (20 male and 34 female). This study is derived from Sevim's (9) doctoral thesis.

Study Design

In this study, the general characteristics, biochemical parameters, TKV, and dietary intake of patients were examined. Patients' data on general characteristics such as age, gender, height, weight, duration of illness diagnosis, chronic disease presence, and smoking status were collected through face-to-face interviews with the patients.

Height and weight are measured using a stadiometer and an electronic scale, respectively, as light as possible and without shoes. Body mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared (kg/m^2) (10). Biochemical parameters such as glucose, total protein, albumin, prealbumin, total cholesterol, very low-density lipoprotein cholesterol, low-density lipoprotein cholesterol, high density cholesterol, trigliserid, uric sit, urea, creatinine, sodium, potassium, phosphorus, calcium, iron, total iron-binding capacity, unsaturated iron-binding capacity, hemoglobin, ferritin, C-reactive protein, aspartate aminotransferase, alanine aminotransferase, urine protein level, and systolic-diastolic blood pressure, and pulse were obtained from the patient's files related visit. The estimated glomerular filtration rate (eGFR) was calculated using the creatinine equation published by The Chronic Kidney Disease Epidemiology Collaboration (11). Staging CKD was classified based on eGFR as 1, 2, 3, and 4 (12).

Total Kidney Volume with Magnetic Resonance

The MRIs of the patients were taken with a gradient-strength 48 mT ACHIEVA NOVA MRI system (Philips Koninklijke Netherlands) device with 1.5-T magnet power. The volumes of bilateral polycystic kidneys were calculated in cm^3 (mL).

Three-day Dietary Records

Patients were trained how to take three-day diet records by a dietitian using supporting materials such as photographs and replicas of various foods on the first visit. After training, dietary intakes were recorded for three consecutive days that were two weekdays and one weekend day, and the dietary records were collected and controlled by a dietitian with a face-to-face interview on the second visit. Dietary records included detailed information about all foods and beverages consumed in terms of type, amount, preparation, recipes, and ingredients. To determine the amount of food consumed, patients used an electronic food scale and/or typical volumetric

household measures. When these measurement methods were unavailable, patients were asked to estimate the portion sizes with food portion size picture books provided by a dietitian.

Evaluation of Dietary Intakes

Daily energy and nutrient intakes were calculated using the nutrition information system Ebispro for Windows, Turkish Version 2010 (BeBiS 7.2) (13). Fluid intake (water) patients was calculated as the sum of drinking water, water in beverages and food. Salt intake was also calculated as the sum of table salt (additional), the natural content of foods and beverages, and recipes.

Since there is a lack of dietary recommendations for ADPKD, the calculated energy and nutrient intakes of patients were evaluated according to the recommended dietary allowances (RDA), and adequate intakes with respect to age and gender (14). The recommendations for micronutrients, macronutrient intakes and their ratios of energy concentration are based on the acceptable macronutrient distribution range (AMDR) (15), estimated energy requirements (EER), Kidney Disease Improving Global Outcomes 2020 (16), and Turkey Nutrition Guide 2015 (TUBER) (17). The AMDR is a range of intake for macronutrient carbohydrates, protein, or fat, expressed as a percentage of total energy (kcal). To evaluate the percentage of meeting the RDA recommendations (RDA% met), a percentage of 66 or less was considered insufficient intake, and a percentage of 132 and above was considered excessive intake.

Statistical Analysis

The Statistical Package for Social Sciences (SPSS) Version 15.0 software (18) was used for the data analysis. The normality of the distribution was determined using the Kolmogorov-Simirnov test. Normally distributed continuous variables (quantitative variables) obtained by measurement are presented with mean, standard deviation (X± SD). Non-normally distributed variables were expressed as medians and interquartile ranges (M, IQR1-IQR3) and categorical data were reported as n (%). The correlations between TKV and energy, dietary nutrient intakes, salt, and caffeine were determined using the bivariate Pearson correlation coefficient for normally distributed variables and the Spearman correlation coefficient for non-normally distributed variables. The statistical significance level was 0.05 in all tests.

Results

This study was conducted on 34 female (63%) and 20 male (37%) patients with ADPKD. The general characteristics, biochemical findings, and kidney function of the patients are shown in Table 1. The eGFR median value of the patients was calculated as 53.3 mL/min/1.73 m^2 and the TKV median value was found to be 1306 mL in females and 1953 ml in males. A total of 94.4% (n=51) n of the patients had a family history of ADPKD. A total of 70.4% (n=38) n of the patients have hypertension. Most of the patients were on stage 2 and 3 CKD (Figure 1).

Dietary Intakes

Table 2 shows the daily energy, nutrient, and other intakes of the patients. Patients' mean daily energy intake was found 26.7±7.0 kcal/kg in men and 25.3±10.6 kcal/kg in women, and the results were on the lowest edge of KDIGO recommendations for energy. Simultaneously, patients' energy intakes were under the EER in both

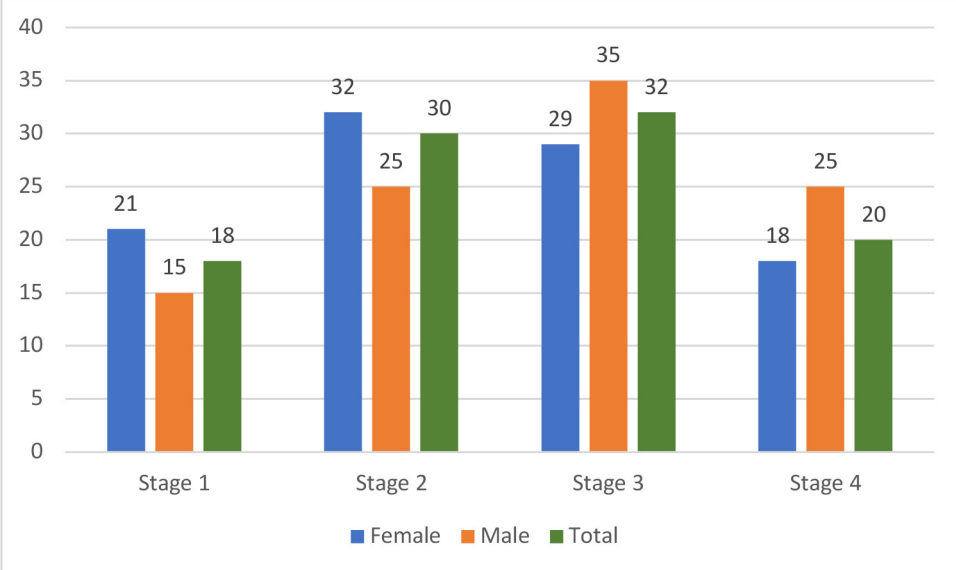

Figure 1: The percentages of patients according to chronic kidney disease stages and sex

Table 1. General characteristics of the patients according to sex									
General characteristics	Female n=34			Male n=20			Total n=54		
	$\bar{X}$±SD (M, Q1-Q3)	Min.	Max.	$\bar{X}$±SD (M, Q1-Q3)	Min.	Max.	$\bar{X}$±SD (M, Q1-Q3)	Min.	Max.
Age (year)	46±10	23	67	50±10	33	69	47±10	23	69
Duration of diagnosis (month)	122±8	4	300	86±71	4	240	108±78	4	300
BMI, kg/m^2	29.5±6.1	15.6	43.9	26.1±4.3	17.0	31.7	28.2±5.7	15.6	43.9
SBP, mmHg	133±15	100	170	148±20	115	200	138±18	100	200
DBP, mmHg	86±11	70	120	90±13	70	130	87±12	70	130
Pulse, min.	80±9	58	100	74±10	55	100	78±10	55	100
Biochemical findings									
Glucose, mg/dL	94±8	78	109	96±16	78	145	95±12	78	145
Urea, mg/dL	44±23	17	110	60±22	31	108	50±24	17	110
Uric acid, mg/dL	5.6±1.6	3.1	8.4	6.5±1.4	3.3	10.0	5.9±1.6	3.1	10.0
Creatinine, mg/dL	1.3±0.8	0.5	3.3	1.9±1.0	0.8	4.4	1.5±0.9	0.5	4.4
CRP, mg/dL	2.9 (1.3-9.0)			2.3 (1.0-6.2)			2.5 (1.2-6.6)		
Sodium, mEq/L	139±2	135	143	140±3	136	147	140±2	135	147
Potassium, mmol/L	4.6±0.5	3.6	5.8	4.6±0.5	3.7	5.5	4.6±0.5	3.6	5.8
Phosphorus, mg/dL	3.4 (3.0-3.9)			3.5 (3.0-3.6)			3.5 (3.0-3.8)		
Calcium, mg/dL	9.5±0.4	8.5	10.2	9.3±0.5	8.2	10.4	9.4±0.4	8.2	10.4
Iron, wg/dL	68±34	22	156	79±29	14	149	72±32	14	156
UIBC, wg/dL	280±55	141	407	249±59	133	390	269±58	133	407
TDBK, wg/dL	350±39	286	437	329±53	233	450	341±45	233	450
Hemoglobin, g/dL	12.5±1.3	9.5	15.1	14.2±1.5	10.7	16.8	13.1±1.5	9.5	16.8
Ferritin, ng/mL	22.8 (15.0-47.7)			66.1 (35.0-81.2)			35.3 (18.4-64.0)		
Pre-albumin, mg/dL	24.2±4.5	16.5	38.0	26.2±4.6	17.1	33.7	24.9±4.6	16.5	38.0
Albumin, g/dL	4.1±0.2	3.7	4.5	4.3±0.3	3.7	4.8	4.2±0.2	3.7	4.8
Total protein, g/dL	7.4±0.4	6.5	8.5	7.2±0.6	6.4	8.3	7.3±0.5	6.4	8.5
Total cholesterol, mg/dL	205±51	81	339	196±33	155	275	201±45	81	339
VLDL-cholesterol, mg/dL	28±14	7	65	28±13	13	57	28±13	7	65
LDL-cholesterol, mg/dL	126±41	34	232	124±28	77	170	126±36	34	232
HDL-cholesterol, mg/dL	50±12	25	78	44±6	36	62	48±11	25	78
Trigliserid, mg/dL	142±73	33	325	139±64	64	285	141±69	33	325
AST, U/L	20±6	11	45	20±5	12	32	20±5	11	45
ALT, U/L	14±4	8	25	15±4	6	25	15±4	6	25
eGFR, mL/dk/1.73 m^2	60.9 (36.9-87.1)			42.1 (25.8-74.8)			53.3 (31.8-79.5)		
Proteinuria, g/day	0.19 (0.12-0.31)			0.24 (0.14-0.98)			0.21 (0.13-0.36)		
The total kidney volume, cm^3	1306 (798-1947)			1953 (1238-3439)			1407 (939-2908)		

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, BMI: Body mass index, CRP: C-reactive protein, DBP: Diastolic blood pressure, eGFR: Estimated glomerular filtration rate, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, SBP: Systolic blood pressure, TIBC: Total iron-binding capacity, UIBC: Unsaturated iron-binding capacity, VLDL: Very low-density lipoprotein, Min.: Minimum, Max.: Maximum, SD: Standard deviation

sexes, 1176±533 kcal in females and 2058±473 kcal in male patients. The mean daily protein intake was lower than the recommendation in patients with CKD stage 2 without PKD and was higher in patients with CKD stage 3-4 without PKD. Animal and plant-based protein intakes were similar. The mean carbohydrate and protein intake contributions to the total energy according to AMDR were within the recommended range, while fat was slightly higher. An excessive fat and saturated fatty acid (SFA) intake was seen in female patients as their intakes exceeded the AMDR and TUBER. While male patients consumed lower monounsaturated FA (MUFA) than

Table 2. Daily dietary macro nutrient, caffeine and salt intake of the patients according to the sex										
	Female (n=34)			Male (n=20)			Total (n=54)			Recommendation
	$\bar{X}$±SD (M, IQR1-IQR3)	Min.	Max.	$\bar{X}$±SD (M, IQR1-IQR3)	Min.	Max.	$\bar{X}$±SD (M, IQR1-IQR3)	Min.	Max.	KDIGO[a] RDA[b], AMDR[c], TUBER[d], Other[e] (Female/Male)
Energy/Protein needs										
Energy kcal/kg	25.3±10.6	9.1	54.5	26.7±7.0	12.8	37.9	25.8±9.4	9.1	54.5	25-35[a]
Protein g/kg	0.8±0.3	0.3	1.8	0.9±0.3	0.5	0.3	0.9±0.3	0.3	1.8	Stage 1-2 0.8[a,b] 0.55-0.60 without DM Stage 3-4[a] 0.6-0.8 with DM Stage 3-4[a] Individual dietary plans[a]
CKD Stage 1	1.1±0.5	0.6	1.8	1.4±2	1.2	1.6	1.2±0.4	0.6	1.7	
CKD Stage 2	0.7±0.3	0.3	1.1	0.8±0.2	0.5	1	0.7±0.3	0.3	1.1	
CKD Stage 3	0.8±0.3	0.4	1.3	0.9±0.3	0.5	1.3	0.9±0.3	0.4	1.3	
CKD Stage 4	0.8±0.3	0.6	1.3	0.9±0.2	0.6	1	0.8±0.2	0.6	1.3	
Energy and Nutrients										
Energy, kcal	1176±533	943	2903	2058±473	1178	3147	1880±525	943	3147	2403 (EER) 3067 (EER)
Carbohydrate, g	211±79	87	465	259±69	105	418	229±79	87	465	130[b]
Carbohydrate, percentage of energy	48±7	35	67	51±7	36	65	49±7	35	67	45-65[c] 45-60[d]
Fructose, percentage of energy	3.1±1.5	0.5	6.9	2.7±2.0	0.3	7.5	2.9±1.7	0.3	7.5	
Fructose, g	13.6±8.6	3.6	36.1	14.4±12.1	1.8	49.1	13.9±9.9	1.8	49.1	
Fiber, g	21.4±8.9	5.5	41.4	26.5±9.8	15.3	44.5	23.3±9.5	5.5	44.5	25[b] 38[b]
Soluble	7.0±2.8	1.7	14.3	8.3±3	4.3	13.3	7.5±2.9	1.7	14.3	
Insoluble	13.2±5.7	3.0	24.5	16.2±5.9	9.7	28.7	14.3±5.9	3.0	28.7	
Protein, g	59±19	19	96	72±18	47	118	64±19	19	118	46[b] 56[b] 10-35[c]
Protein, percentage of energy	14±2	8	18	15±3	9	21	14±3	8	21	10-20[d]
Animal protein, percentage of protein	52±14	21	79	50±14	26	67	51±13	21	79	IE[a]
Fat, g	75±24	36	139	79±26	41	152	76±25	36	152	ND[b]
Fat, percentage of energy	38±6	20	50	34±7	21	43	37±7	20	50	20-35[c,d]
PUFA, g	0.13±0.11	0	0.50	0.25±0.20	0	0.71	0.17±0.16	0	0.71	
PUFA, percentage of energy	10±3	3	16	10±3	5	17	10±3	3	17	7-10%[d]
MUFA, g	25±9	12	46	26±8	14	41	26±9	12	46	
MUFA, percentage of energy	13±3	5	18	12±3	7	12	12±3	5	18	12-15%[d]
SFA, g	25±11	12	64	23±9	10	42	24±10	10	24	
SFA, percentage of energy	13±4	5	20	10±3	6	15	12±4	5	20	<10%[d]
Cholesterol, mg	252±101	21	498	216±87	74	426	239±97	21	498	
Omega 6 FA, g	18±7	5	36	21±11	11	53	19±9	5	53	12[b] 17[b]
Omega 3 FA, g	1.4 (1.0-1.9)			1.8 (1.3-2.9)			1.5 (1.1-2.3)			1.1[b] 1.6[b] ~2, Stage 3-4[a]

Table 2. Continued

	Female (n=34)			Male (n=20)			Total (n=54)			Recommendation
	$\bar{X}$±SD (M, IQR1-IQR3)	Min.	Max.	$\bar{X}$±SD (M, IQR1-IQR3)	Min.	Max.	$\bar{X}$±SD (M, IQR1-IQR3)	Min.	Max.	KDIGO[a] RDA[b], AMDR[c], TUBER[d], Other[e] (Female/Male)
Water, (mL)	2904±948	1439	5536	3119±987	1568	5043	2984±960	1439	5536	2700[a] 3700[a] 2000-2500[d]
Others										
Caffeine, mg	61 (39-103)			120 (65-188)			87 (50-128)			<200[e]
Salt, g	8.6±3.6	2.7	17.5	9.3±2.5	5.4	15.2	8.8±3.2	2.7	17.5	<5[d]

[a]: 16th reference.
[b,c]: Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (2002/2005).
[d]: 17th reference.
[e]: 23rd reference.
AMDR: Acceptable macronutrient distribution range, DM: Diabetes mellitus, EER: Estimated energy requirements, FA: Fatty acids, MUFA: Monounsaturated fatty acids, PUFA: Polyunsaturated fatty acids, SFA: Saturated fatty acids, vit.: Vitamin, s IE: Insufficient evidence to recommend, ND: Not determined, TUBER: Turkiye Beslenme Rehberi 2015

recommended according to TUBER, their SFA ratio was higher. Patients had a higher consumption of Omega 6 FAs than recommendations for healthy people, according to TUBER. Additionally, the mean Omega 3 FA intake was found to be 1.5 g, which is lower than the 2 gram recommendation suggested by KDIGO 2020 to lower serum triglyceride levels. Patients also did not reach the fiber RDA recommendations.

According to the KDIGO-2020 guideline, a male patient's mean water intake of 3119 mL, was insufficient, which was still below the recommended intake for healthy people. However, according to the recommendation for healthy people in the TUBER, patients meet the water needs. Patients' daily salt intake was above 5 grams.

Vitamin and mineral intake and the percentage of RDA mets are shown in Table 3. The mean intakes of thiamin, riboflavin, B6, calcium, magnesium, and zinc were sufficient in both male and female patients since the percentage of RDAs was between 66 and 132 for these nutrients. Dietary vitamin D and folate intake in female patients and only dietary vitamin D intake in male patients met the RDA insufficiently. Patients' mean dietary vitamin A and K intakes were excessive, the percentage of RDAs was above 132. In all patients, the mean dietary potassium intake was insufficient and the sodium intake was excessive.

Kidney Volume and Dietary İntake

The correlations between TKV and energy, dietary nutrient intake, salt and caffeine are shown in Table 4. In female patients there were negative but a weak correlation between dietary vitamin C intake and TKV (r=0.372, p=0.030). There were negative correlations, but not statistically significant, between energy (kcal/kg), omega 6 FA, B12, vitamin E intakes, carbohydrate /protein/ animal protein/PUFA percentage of energy and TKV in female patient. In male patients, the negative but weak correlation was found between TKV and intake of fiber (r=-0.493, p=0.027) and similar to soluble and insoluble fiber, water (r=-0.462, p=0.040), vitamin B6 (r=-0.444, p=0.050), vitamin K (r=-0.522, p=0.018), magnesium (r=-0.449, p=0.047), iron (r=-0.508, p=0.022). In male patients, there were more negative but weak correlations between TKV and dietary intake. Generally, any statistically significant correlations could not be found in all patients.

Discussion

In this cross-sectional study in patients with ADPKD, patients' total dietary energy intake was on the lowest edge of recommendations for CKD on energy need, and was under the EER value. The mean daily protein intake was lower than the recommendation for patients with CKD stage 2 without PKD and was higher for patients with CKD stage 3-4 without PKD. The mean intake of micronutrients such as thiamin, riboflavin, B6, calcium, magnesium, and zinc was sufficient, the mean dietary potassium intake was insufficient; and the sodium intake was excessive. In females, there was a negative but weak correlation between dietary vitamin C intake and TKV. In males, a negative but weak correlation was found between TKV and dietary intake of fiber, water, vitamin B6, vitamin K, magnesium, and iron.

Generally, ADPKD guidelines contain several specific dietary recommendations beyond the general CKD guidelines, or advice that is not based on strong data (19). Recent studies on protein, water, caffeine and alcohol intake, salt, BMI, and caloric restriction show that recommendations would be the same as those in CKD (4). A low protein diet (≤0.6 g/kg/day) has not been shown to delay ADPKD progression and may increase the risk of

Table 3. Daily dietary micro nutrient intake of the patients according to the sex

	Female (n=34)			Male (n=20)			Total (n:54)			Recommendation
Vitamins and Minerals	**X̄±SD (M, IQR1-IQR3)**	**Min.-Max.**	**RDA-AI % met (X̄- M)**	**X̄±SD (M, IQR1-IQR3)**	**Min.-Max.**	**RDA-AI % met (X̄- M)**	**X̄±SD (M, IQR1-IQR3)**	**Min.-Max.**	**RDA-AI % met (X̄- M)**	**RDA[a]/AI[b]/KDIGO[c] (Female/Male)**
Thiamin, mg[a]	0.7±0.2	0.2-1.6	70	0.9±0.2	0.5-1.4	73	0.8±0.2	0.2-1.6	71	1.1 1.2
Riboflavin, mg[a]	1.2±0.4	0.4-2.7	112	1.3±0.3	0.9-2.0	100	1.3±0.4	0.4-2.7	107	1.1 1.3
Vit. B12, µg[a]	2.9±1.6	0.5-6.6	122	3.3±2.0	0.9-8.2	137	3.0±1.7	0.5-8.2	128	2.4
Vit. B6, mg[a]	1.1±0.4	0.2-2.0	85	1.2±0.3	0.8-2.1	85	1.2±0.4	0.2-2.1	85	1.5 1.3-1.7
Folate, µg[a]	275±95	84-583	69	326±80	206-521	82	293±92	84-583	74	400
Vit. A, µg[a]	1160±730	263-3401	165	1019±532	325-2443	117	1108±662	263-3401	147	700 900
Vit. D, µg[b]	0.8 (0.6-1.3)		13.8	0.97 (0.5-6.6)		12.9	0.8 (0.6-1.5)		13.3	5-10
Vit. E, mg[a]	19±8	6-38	135	19.7±7.7	10.7-38.4	147	19.2±7.8	6.4-38.4	140	15
Vit. K, mg[b]	346±158	68-688	384	341±161	135-852	295	344±157	68-852	352	90 120
Vit. C, mg[a]	102±63	12-263	136	102±64	22-254	115	102±63	12-263	128	75 90
Calcium, mg[b]	759±272	275-1725	71	775±230	498-1283	71	765±255	275-1725	71	1000-1200 (800-1000 Stage 3-4)[c]
Magnesium, mg[a]	260±83	114-398	81	310±85	189-494	75	279±87	114-494	79	310-320 400-420
Potassium, mg[b]	2128±771	639-4045	46	2335±684	1437-3588	50	2205±740	639-4045	47	4700 (Individual adjust Stage 3-4)[c]
Phosphorus, mg[a]	976±313	420-1728	139	1195±283	836-1890	170	1057±318	420-1890	151	700 (Individual adjust Stage 3-4)[c]
Sodium, mg[b]	3539±1458	1192-7406	250	3821±1015	2500-6165	273	3643±1308	1192-7406	260	1500-1300 (<2300 g Stage 3-4)[c]
Zinc, mg[a]	9.9±2.9	4.7-16.3	125	12.4±3.5	8.1-21.4	114	10.9±3.3	4.7-21.4	121	8 11
Iron, mg[a]	10.8±3.6	4.3-19.3	87	12.9±3.2	8.1-18.7	161	11.6±3.6	4.3-19.3	114	18-8 8

[a,b]: Dietary Reference Intakes for Calcium, Phosphorous, Magnesium, Vitamin D, and Fluoride (1997); Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B_6, Folate, Vitamin B_{12}, Pantothenic Acid, Biotin, and Choline (1998); Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids (2000); Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc (2001); Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate (2005); Dietary Reference Intakes for Calcium and Vitamin D (2011); and Dietary Reference Intakes for Sodium and Potassium (2019).
[c]: 16th reference.
AI: Adequate intakes, KDIGO: Kidney disease improving global outcomes, RDA: Recommended dietary allowances, Vit.: Vitamin, SD: Standard deviation, Min.: Minimum, Max.: Maximum

malnutrition, and is only recommended when it's suitable (20). The general recommendation is to apply a moderate protein diet (0.75-1.0 g/kg/day) (16,21,22), and diet therapy should be planned individually for these patients. In the current study, patients' mean dietary protein intake was above 0.8 g/kg, except for those in CKD stage 2. There were several patients who had a low protein diet, which should be considered to evaluate malnutrition risk. Energy intake of 30-35 kcal/kg/day is important to maintain neutral nitrogen balance and nutritional status (16). In both sexes, patients' mean daily energy intake was under 30-35 kcal/kg/day. To achieve energy and protein intake goals for patients, it's been recommended to have counseling with a renal dietitian who will provide medical nutrition therapy (16,22).

A sodium restricted diet, ≤2.4 g/day is recommended for patients who undergo tolvaptan treatment (23), and for blood pressure and volume control improvement (16). In this study, mean salt and sodium intakes were 8.8 g and 3643 mg, respectively. The excessive intake of dietary sodium has been defined as a key modifiable factor for the enlargement of kidney cysts (24,25). Each decrease of one

Table 4. The correlation between daily dietary macronutrient, micronutrient, caffeine, salt intakes and total kidney volume of the patients according to the sex

Energy, Macro/Micronutrients, and Others	Female n=34		Male n=20		Total n=54	
	r	p	r	p	r	P
Energy, kcal	0.189	0.285	-0.156	0.511	0.124	0.371
Energy, kcal/kg	-0.001	0.997	-0.209	0.376	-0.038	0.784
Carbohydrate, g	0.143	0.420	-0.126	0.597	0.109	0.434
Carbohydrate, percentage of energy	-0.031	0.863	0.045	0.850	0.031	0.825
Fructose, percentage of energy	0.080	0.652	-0.120	0.857	-0.012	0.933
Fructose, g	0.090	0.612	-0.139	0.559	0.003	0.983
Fiber, g	0.194	0.273	-0.493	**0.027***	0.000	0.999
Soluble	0.098	0.581	-0.495	**0.027***	-0.070	0.616
Insoluble	0.240	0.172	-0.457	**0.043***	0.047	0.734
Protein, g	0.157	0.375	-0.321	0.167	0.059	0.671
Protein, percentage of energy	-0.050	0.777	-0.226	0.338	-0.088	0.527
Plant protein, percentage of protein	0.063	0.724	-0.043	0.857	0.041	0.769
Animal protein, percentage of protein	-0.063	0.724	0.043	0.857	-0.041	0.769
Protein, g/kg	-0.013	0.914	-0.326	0.160	-0.077	0.581
Fat, g	0.189	0.283	-0.073	0.759	0.107	0.440
Fat, percentage of energy	0.028	0.877	0.050	0.834	-0.018	0.895
PUFA, g	0.016	0.928	-0.135	0.569	0.011	0.939
PUFA, percentage of energy	-0.223	0.206	-0.217	0.358	-0.212	0.124
MUFA, g	0.240	0.206	-0.007	0.978	0.174	0.208
MUFA, percentage of energy	0.122	0.492	0.103	0.664	0.080	0.567
SFA, g	0.260	0.137	0.103	0.667	0.201	0.144
SFA, percentage of energy	0.154	0.386	0.262	0.265	0.113	0.939
Cholesterol, mg	0.089	0.619	-0.010	0.966	0.027	0.847
Omega 6 FA, g	-0.047	0.652	-0.197	0.406	-0.074	0.596
Omega 3 FA, g**	0.068	0.704	-0.320	0.169	-0.004	0.974
Water, (mL)	0.174	0.325	-0.462	**0.040***	-0.020	0.883
Caffeine, mg**	0.068	0.704	-0.318	0.172	-0.024	0.863
Salt, g	0.160	0.365	-0.128	0.590	0.102	0.464
Thiamin, mg	0.198	0.262	-0.267	0.255	0.090	0.515
Riboflavin, mg	0.200	0.256	-0.275	0.240	0.089	0.521
Vit. B12, µg	-0.202	0.252	-0.199	0.399	-0.177	0.201
Vit. B6, mg	0.099	0.577	-0.444	**0.050***	-0.043	0.758
Folate, µg	0.273	0.118	-0.436	0.055	0.108	0.437
Vit. A, µg	0.009	0.958	-0.287	0.220	-0.041	0.766
Vit. E, mg	-0.080	0.655	-0.114	0.631	-0.081	0.559
Vit. K, mg	0.090	0.614	-0.522	**0.018***	-0.113	0.414
Vit C, mg	0.372	**0.030***	-0.237	0.315	0.168	0.225
Calcium, mg	0.194	0.272	-0.387	0.092	0.029	0.835
Magnesium, mg	0.116	0.513	-0.449	**0.047***	-0.021	0.881
Potassium, mg	0.170	0.336	-0.430	0.058	0.012	0.929
Phosphorus, mg	0.171	0.335	-0.441	0.051	0.041	0.767
Sodium, mg	0.160	0.365	-0.143	0.546	0.099	0.475
Zinc, mg	0.034	0.848	-0.422	0.064	-0.063	0.650
Iron, mg	0.042	0.814	-0.508	**0.022***	-0.071	0.611

*p<0.05, Pearson correlation, ** Spearman correlation
FA: Fatty acids, MUFA: Monounsaturated fatty acids, PUFA: Polyunsaturated fatty acids, SFA: saturated fatty acids, vit. : Vitamin

gram of salt resulted in less kidney enlargement of 0.43% per year (24). Meijer and Gansevoort (4) advise less than 5 g/day salt intake for ADPKD (4).

A review by Picard et al. (26) stated that high potassium intake was related to lower risk, while low intake showed higher progression, and in some studies there was no relationship. Dietary potassium intake at the highest level was around >2500 mg/day, whereas the lowest was of ~1500 mg/day in studies with participants age ≥40 with CKD stage 2 and CKD patients (without CKD stage informing) (27). Unfortunately, there is no data about ADPKD patients' actual dietary mineral and vitamin intakes. In our study, patients' dietary potassium intake was found to be 2205±740 mg, which means 47% of the recommendation. dietary potassium intake levels are related to the number of fruits, vegetables, and fiber consumed in the diet. Taylor et al. (28) found that ADPKD patients' (n=11) vegetable and fruit consumption was 441 g/day, and they showed that increasing fruit and vegetable consumption from 400 g to about 1200 g daily intake was possible and well tolerated by ADPKD patients. Fruits and vegetables are rich in potassium and poor in sodium. Fruits, vegetables, nuts, and legumes, dairy, and meat products are potassium-rich foods that are also high in minerals, vitamins, and dietary fiber; it is critical to tailor dietary potassium restrictions to the nutritional status of the individual patient (16).

In this study, a negative but weak correlation between dietary vitamin C intake and TKV was seen in only female patients. The RDA percentage of vitamin C intake was found to be 136 and 115 for females and males, respectively. Since vegetables and fruits are rich in vitamin C, we may assume that female patients consumed more vegetables and fruits than males. Simultaneously, both female and male patients' dietary fiber intakes were under recommendation. A negative but weak correlation was found between TKV and fiber intake only in male patients. Fiber was discovered in legumes and grains, as well as vegetables and fruits. It can be concluded that consumption of grains and legumes is low due to patients' high intake of vitamin C but low intake of fiber. Further studies are needed to understand the possible effects of vitamin C and fiber on TKV.

In this study, patients met water intake recommendations, and only in male patients was a negative but weak correlation found between TKV and water intake. Water loading is a proposed therapy for ADPKD as it slows cyst and kidney enlargement (29). Several interventions studied increased water intake in ADPKD patients (30,31). But inconsistent results highlight the fact that randomized controlled trials are needed for ADPKD. There is no conclusion yet on how much water should be received. Individually prescribing the amount of water is a potential and viable therapeutic option. Torres et al. (32) recommended that APKD patients whose eGFR is above 30 mL/min/1.73 m^2 should have a water intake of usually 2.5-4 L per day, and for patients with an eGFR less than 30 mL/min 1.73 m^2, additional water intake should be limited to prevent hyponatremia. Patients on tolvaptan should be under dietitian supervision in terms of decreasing osmolality and sodium intake (24).

In this study, male and female patients consumed 120 and 61 mg of caffeine, respectively. Caffeine is considered to increase cAMP and contribute to disease progression by increasing renal volume in cultured cell and ADPKD mice studies. But this relationship has not been observed in human studies (4). A limit of ≤200 mg/day of caffeine, which is ≤2 cups of coffee or ≤4 cups of tea per day, is recommended to control or avoid caffeine intake (23).

Study Limitations

This study's limitations include a cross-sectional study, one center, a small sample size, and the skewness of sex. Patients had some knowledge or thoughts about nutrition, and this may have affected their dietary intake, particularly in terms of water consumption. Their dietary records may not completely reflect patients' usual dietary habits. Diet records were based on the patient's statement, and food amounts that were consumed were subjective. Therefore, the results of this study should not be generalized to the entire ADPKD population.

The most important missing part in the literature is the insufficient data about ADPKD patients' actual dietary consumption. The current study makes an important contribution to the literature, as studies examining the effect of nutrition on TKV in ADPKD patients are limited. Another strength of this study was to evaluate TKV via MRI.

Conclusion

In female patients with ADPKD, there was a negative but a weak correlation between dietary vitamin C intake and TKV. In males, a negative but weak correlation was found between TKV and dietary intake of fiber, water, vitamin B6, vitamin K, magnesium, and iron.

Ethics

Ethics Committee Approval: Ethics committee approval dated 18.06.2014 and numbered 122 was obtained from the Ethics Committee of University of Health Sciences Turkey, Istanbul Haseki Training and Research Hospital, Non-Drug Clinical Research.

Informed Consent: Informed consent was obtained.

Peer-reviewed: Externally peer-reviewed.

Authorship Contributions

Concept: Y.S., E.C., Design: Y.S., E.C., O.P.O., G.K., Data Collection, or Processing: Y.S., O.P.O., Yi.S., Analysis, or Interpretation: Y.S., E.C., S.O., G.K., Literature Research: Y.S., O.P.O., E.C., Writing: Y.S., O.P.O., S.O., G.K.

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