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# Dietary approaches to stop hypertension, mediterranean dietary pattern, and diabetic nephropathy in women with type 2 diabetes: A case-control study

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SUMMARY

*Background and aims:* The association between dietary habits and kidney function in patients with type 2 diabetes (T2D) has been poorly investigated. We aimed to test the relationship between adherences to the Dietary Approaches to Stop Hypertension (DASH) diet and the Mediterranean dietary pattern (Med diet) and likelihood of diabetic nephropathy (DN) in women with T2D.
*Methods:* In a case–control study, 105 women with T2D and DN (albumin-creatinine ratio $\geq$ 30 mg/g, mean age: 55.3 $\pm$ 7.0 years; diabetes duration: 7.6 $\pm$ 2.2 years), and 105 controls with T2D and without DN (mean age: 55.4 $\pm$ 7.1 years; diabetes duration: 7.6 $\pm$ 2.1 years) who attended at Kowsar diabetes clinic in Semnan, Iran were matched for age and diabetes duration. Dietary intakes were assessed using a validated 147-item semiquantitative food frequency questionnaire. The DASH and Med diet scores were calculated using the methods developed by Fung and Trichopoulou, respectively. A generalized estimating equation model was used to examine the relationship between dietary scores and odds of DN across tertiles of dietary patterns scores.
*Results:* Type 2 diabetic women with moderate and high Med diet scores had 62% and 86% lower odds of DN in comparison with low adherent (ORs: 0.38, 95%CI: 0.20, 0.73; and 0.14, 95%CI: 0.06, 0.33; respectively). A moderate adherence to the DASH diet was not associated with risk of DN, but a significant inverse relationship was found in those with high adherence (OR: 0.71, 95%CI: 0.57, 0.90).
*Conclusions:* Adherence to the DASH and Med diets was inversely and dose-dependently associated with risk of DN. Further observational studies are needed to confirm the present results.


## 1. Introduction

Prevalence of type 2 diabetes (T2D) has been spread all over the world during the recent decades. It is estimates that the number of people with T2D will increase from 451 million at 2017 (age 18–99 years) up to 693 million by 2045 [1]. In 2017, approximately 5 million deaths worldwide were attributable to diabetes in the 20–99 years age range [1]. This prevalence is accompanied by a huge socio-economic burden in both developing and developed countries [2]. Diabetic nephropathy (DN), defined as increased urinary albumin excretion (UAE) [3], is one of the most frequent microvascular complications of T2D and is one of the main causes of chronic kidney disease (CKD) [4]. It is estimated that about 40% of people with T2D develop CKD [5]. Both albuminuria and low estimated glomerular filtration rate (eGFR) are associated with higher risk of all-cause and cardiovascular disease (CVD) mortality and morbidity in patients with T2D [6,7].

It has been shown that higher levels of cardio-metabolic risk factors including higher blood pressure, hyperlipidemia, and

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hyperglycemia are associated with a higher risk of developing DN [3]. Considering the substantial link between dietary habits and cardio-metabolic risk factors [8–12], it is possible that higher diet quality and better compliance with dietary guidelines may be associated with a lower risk of DN. Two cross-sectional analyses in the general population and in patients with T2D showed that a higher adherence to posterior-defined, healthy dietary patterns was associated with lower levels of albumin-creatinine ratio (ACR) and better eGFR [13,14]. In addition, results from cross-sectional and longitudinal investigations have indicated that a higher adherence to the Dietary Approaches to Stop Hypertension (DASH) diet and the Mediterranean dietary pattern (Med diet) was associated with better kidney function and lower likelihood of CKD in the general population [15–21].

Results from randomized clinical trials have indicated that higher adherence to the DASH and Med diets is associated with better inflammatory status, lower levels of cardio-metabolic risk factors, better glycemic control, and better endothelial function in patients with T2D [22–29]. But, to our knowledge, only one observational study in the US has assessed the association between priori-defined dietary patterns and risk of microalbuminuria and eGFR decline in patients with T2D [19]. The prevalence of CKD is high in Iran [30,31] and is estimated that to be about 15% in the Iranian general population [32]. Thus, investigating the potential association of dietary habits and kidney function in patients with T2D may provide valuable information to prepare more effective strategies in order reduce the burden of CKD. Therefore, the aim of this study was to examine the potential relationship between adherence to priori-defined dietary patterns, represented by the DASH diet score and the Med diet score, and likelihood of DN in women with T2D in a case–control study in Iran.

## 2. Materials and methods

### 2.1. Study population

This case–control study was conducted among women with existing T2D who attended at Kowsar diabetes clinic in Semnan, Iran, from July to December 2016. Women with prevalent T2D, aged between 30 and 65 years, and with a history of 3–10 years of T2D were considered eligible for inclusion in this study. T2D was defined as one the following criteria: self-reported previous diagnosis of T2D by a clinician (excluding gestational diabetes mellitus and type 1 diabetes); glycosylated hemoglobin (HbA1c) $\geq$ 6.5%; fasting blood glucose (FBG) $\geq$ 126 mg/dl; or 2-hours post-load blood glucose (2hrBG) $\geq$ 200 mg/dl (American Diabetes Association's new diagnostic criterion for undiagnosed diabetes) [33]; or medication treatment. Exclusion criteria were defined as: previous history of cancer, myocardial infarction, hepatic disease, autoimmune disorders, stroke, and coronary angiography. To conduct a case–control study, new-diagnosed cases of DN were considered eligible for enrollment when they were admitted to the clinic from July 2016 to December 2016. A total of 120 patients with DN were considered eligible for inclusion in this study. We contacted with patients, and of those, 105 patients agreed to participate in the study. We selected matched controls from among the other patients who attended in clinic, but had no previous history of DN. We contacted with 136 patients, and of these, 105 patients agreed to participate in the study as controls. Finally, 105 controls were selected by a 1:1 frequency-matching to 105 cases by age at 1-year intervals and diabetes duration at 6-month intervals. The selected cases and controls were confirmed based on a one-sample urine test. DN was defined as urinary albumin/creatinine ratio (ACR) $\geq$30 mg/g in a random spot urine sample [34], and values < 30 mg/g were considered as normal. All patients received written information concerning the background and procedures of the study, and the patients gave written informed consent prior for entering the study.

### 2.2. Data collection

At recruitment, individual participant's data including age, diabetes duration, cigarette smoking status and current use of medications were obtained. Height (m) and weight (kg) were measured while subjects were wearing light clothing without shoes. Body mass index (BMI, kg/m2) was calculated as weight in kilograms divided by the square of height in meters. Systolic and diastolic blood pressure was measured once on the left arm, while sitting after a resting period of $\geq$5 min using a manual sphygmomanometer. Physical activity was assessed using the International Physical Activity Questionnaire (IPAQ) [35]. IPAQ scores were categorized as 'low physical activity' (point score <600 metabolic equivalent (MET)/h per week), 'moderate physical activity' (point score between 600 and 3000 MET/h per week) and 'high physical activity' (point score >3000 MET/h per week).

### 2.3. Laboratory tests

Blood samples were collected after an overnight fasting (at least 8 h). Venous blood samples were drawn with minimal stasis from an antecubital vein. The serum 25 (OH)D concentration was measured by using the ELISA kits (AccuBind, Monobind Inc., USA). Other biochemical variables including FBG, 2hrBG, Hb A1c, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG), total cholesterol (TC), serum creatinine (Cr) and blood urea nitrogen (BUN) were obtained from participant's medical records during the past three month. The UAE was determined in a random spot urine sample by enzyme-linked immunosorbent assay [sensitivity 0.001 mg/L; coefficient of variation (CV) 4.5–7.6%].

### 2.4. Dietary assessment

Dietary information was obtained by interview using a validated 147-item, semi-quantitative food-frequency questionnaire (FFQ) [36], which measured the previous year's food intake. Participants were asked to report their intake of food or food items as daily, weekly, monthly or yearly. To estimate daily food intake, obtained information were converted to g/day. The mean daily consumption of each food group was calculated by multiplying the consumption frequencies and portion sizes. Dietary intake was adjusted for energy intake by using residual method [37].

**Med diet score**. The Med diet scores were calculated using the recommendations of Trichopoulou et al. [38]. Accordingly, for vegetables, fruits, whole grains, legumes, nuts, fishes, and ratio of Monounsaturated to saturated fatty acids; intakes equal or greater than median were assigned a value of 1, and for intakes lower than median a value of 0. An inverse scoring was used for meat (red and processed meats, poultry), and dairy products. Finally, participants were categorized according to the tertiles on the basis of their scores.

**DASH score**. The DASH scores were calculated using the recommendations of Fung et al. [39] that includes 8 components in the DASH diet. All eight component were categorized in quintiles, in which for fruits, vegetables, whole grains, nuts and legumes combined, and low-fat dairy products; 1 points assigned to the lowest intake (quintile 1), and five points assigned to the highest intake (quintile 5). An inverse scoring was used for red and processed meat, sugar-sweetened beverages (SSBs), and sodium. In final, participants were categorized according to the tertiles on the basis of their scores.

### 2.5. Statistical analysis

Characteristics of cases and controls were compared using χ2 for categorical variables and independent $t$ test for continuous variables. Participants were categorized on the basis of tertiles of the DASH and Med diet scores. Higher and lower dietary pattern scores represented higher and lower adherence, respectively. Characteristics of participants were compared across tertiles of dietary pattern scores using χ2 for categorical variables and one-way analysis of variance (ANOVA) for continuous variables. The Mantel-Haenszel test was used to calculate $P$ values for trends across the tertiles of dietary patterns. A generalized estimating equation model was used to calculate odds ratios and 95% confidence intervals for DN. Model 1 was used to calculate crude OR; and model 2 was adjusted for body mass index, hemoglobin A1c, and total energy intake. Forward stepwise selection method was used to enter the variables to final model. Any variable in univariate model which had a $P$ value less than 0.2 was candidate for the final model. Criteria for variable selection was Likelihood of models. All analyses were conducted undertaken using SPSS v.18.0 (IBM Corp., Armonk, NY, USA) and $P < 0.05$ was considered as significant.

## 3. Results

The general characteristics and biochemical measurements of cases and controls are provided in Table 1. In recruitment, cases and controls were matched for age and diabetes duration. Women with DN had significantly lower adherence to the DASH diet (23.25 ± 4.63 vs 24.96 ± 5.46, $P < 0.008$), and Med diet (4.13 ± 1.62 vs 5.39 ± 1.46, $P < 0.0001$) in comparison with controls. They had significantly higher levels of ACR, FBG, Hb A1c, TC, LDL, and Serum Cr ($P < 0.05$), but in terms of other biochemical variables, no statistically significant differences were found between cases and controls (Table 1) All participants were nonsmoker. The general characteristics and biochemical measurements of participants across tertiles of dietary patterns scores are shown in Table 2. Participant's age, BMI, diabetes duration, and history of CVD did not differ across tertiles of the DASH and Med diet scores. Women in the top tertile of Med diet score had significant lower levels of ACR. A nonsignificant trend toward better glycemic control was found with increasing adherence to the Med diet. In comparison with first tertile, participants in the third tertile of the DASH diet score had higher levels of ACR ($P = 0.08$), and lower levels of Hb A1C ($P = 0.09$), TC ($P = 0.06$), and LDL ($P = 0.07$).

Dietary intakes of women across categories of the DASH and Med diet scores are presented in Table 3. Intakes of fruits, vegetables, whole grains, nuts, legumes, fishes and poultry increased significantly along with the increase in the Med diet score, whilst no differences were found in total energy intake, red meat and dairy products. In terms of the DASH diet, a significant trend toward higher intake of fruits, vegetables, whole grains, fishes, poultry, and low-fat dairy products was found with increasing the DASH diet score ($P < 0.05$). They also had lower intake of high-fat dairy products and red meat ($P < 0.05$).

**Table 1**
Characteristics of participants across case and control groups (mean ± SD/n (%)).

| Variables[a] | Nephropathy (n = 105) | Controls (n = 105) | $P$[b] |
|---|---|---|---|
| Age (years) | 55.3 ± 7.0 | 55.4 ± 7.1 | 0.94 |
| Weight (kg) | 73.4 ± 13.8 | 71.6 ± 11.5 | 0.30 |
| Height (cm) | 160.7 ± 6.3 | 161.2 ± 5.9 | 0.56 |
| BMI (kg/m$^2$) | 28.7 ± 4.7 | 27.5 ± 4.4 | 0.06 |
| Energy intake (kcal/day) | 1407.0 ± 64.0 | 1452.3 ± 320.0 | 0.26 |
| Diabetes duration (years) | 7.6 ± 2.2 | 7.6 ± 2.1 | 0.88 |
| ACR | 232.2 ± 114.1 | 18.7 ± 5.9 | <0.001[d] |
| SBP (mmHg) | 126.6 ± 17.3 | 129.0 ± 98.9 | 0.80 |
| DBP (mmHg) | 82.8 ± 13.1 | 80.1 ± 11.8 | 0.12 |
| Hb (mg/dl) | 12.6 ± 1.4 | 12.6 ± 1.2 | 0.91 |
| FBG (mg/dl) | 167.1 ± 50.6 | 154.2 ± 45.0 | 0.05[d] |
| 2hrBG (mg/dl) | 217.7 ± 53.2 | 207.1 ± 54.3 | 0.15 |
| Hb A1c (%) | 8.7 ± 1.4 | 8.0 ± 1.3 | 0.001[d] |
| Vit D3 (nmol/lit) | 26.8 ± 17.5 | 28.4 ± 18.5 | 0.50 |
| Total cholesterol (mg/dl) | 185.1 ± 38.1 | 175.4 ± 32.4 | 0.05[d] |
| TG (mg/dl) | 167.3 ± 65.7 | 162.3 ± 57.9 | 0.56 |
| LDL (mg/dl) | 106.9 ± 31.8 | 94.6 ± 29.5 | 0.004[d] |
| HDL (mg/dl) | 45.0 ± 9.3 | 46.4 ± 9.3 | 0.30 |
| Serum Cr (mg/dl) | 0.92 ± 0.2 | 0.87 ± 0.2 | 0.03[d] |
| Serum BUN (mg/dl) | 15.8 ± 4.5 | 15.2 ± 3.9 | 0.29 |
| Physical activity[c] (%) | | | |
| Low | 38 (35.0) | 48 (31.7) | |
| Moderate | 39 (28.5%) | 47 (39.2%) | |
| High | 50 (36.5%) | 35 (29.2%) | |
| History of CVD | 26 (19.0%) | 30 (25%) | 0.30 |
| Medications | | | |
| ARBs | 63 (46.0%) | 68 (56.7%) | 0.10 |
| ACEIs | 28 (20.4%) | 53 (44.2%) | <0.001[d] |
| Beta blockers | 23 (16.8%) | 25 (20.8%) | 0.40 |
| Metformin | 135 (98.5%) | 119 (99.2%) | 1.00 |
| Sulfonylureas | 81 (59.1%) | 81 (67.5%) | 0.20 |
| Insulin | 41 (29.9%) | 32 (26.7%) | 0.60 |

Abbreviations: ACEIs, angiotensin converting enzyme inhibitors; ACR, albumin creatinine ratio; ARBs, angiotensin receptor blockers; BMI, body mass index; 2hrBG, 2-hour blood glucose; BUN, blood urea nitrogen; CVD, cardiovascular disease; DBP, diastolic blood pressure; FBG, fasting blood glucose; Hb, hemoglobin; HDL, high density lipoprotein; LDL, low density lipoprotein; SBP, systolic blood pressure; TG, triglycerides.

[a] Variables are presented as mean ± SD for continuous variables and n (%) for categorical variables.

[b] Independent $t$ test for continuous variables and $\chi^2$ test for categorical variables.

[c] <600 MET/h per week: ‘low’, 600–3000 MET/h per week: ‘moderate’, >3000 MET/h per week: ‘high’.

[d] Statistically significant.

**Table 2**
General and biochemical characteristics of participants across tertiles of dietary pattern scores.

| Variables[a] | Med score | | | | DASH score | | | |
|---|---|---|---|---|---|---|---|---|
| | Tertile 1 | Tertile 2 | Tertile 3 | $P_{trend}$[b] | Tertile 1 | Tertile 2 | Tertile 3 | $P_{trend}$[b] |
| Age (y) | 54.7 ± 6.8 | 55.7 ± 7.5 | 54.9 ± 7.5 | 0.73 | 54.7 ± 2.1 | 54.9 ± 7.3 | 56.7 ± 6.3 | 0.25 |
| Diabetes duration (y) | 7.4 ± 2.0 | 7.7 ± 2.2 | 7.6 ± 2.3 | 0.81 | 7.8 ± 2.1 | 7.4 ± 2.1 | 7.6 ± 2.3 | 0.42 |
| History of CVD | 19.70 | 26.80 | 18.20 | 0.31 | 22.20 | 26.80 | 15.20 | 0.18 |
| Body weight (kg) | 72.3 ± 12.4 | 71.9 ± 11.9 | 73.23 ± 13.9 | 0.81 | 72.0 ± 11.7 | 72.3 ± 14.8 | 73.3 ± 10.6 | 0.84 |
| BMI (kg/m$^2$) | 27.9 ± 5.1 | 27.6 ± 4.4 | 28.7 ± 4.5 | 0.35 | 27.5 ± 4.6 | 28.7 ± 3.8 | 28.7 ± 3.8 | 0.38 |
| ACR (mg/gr) | 199.4 ± 138.5 | 139.7 ± 139.0 | 60.7 ± 89.2 | <0.001 | 144.1 ± 133.6 | 133.0 ± 140.3 | 93.2 ± 121.0 | 0.08 |
| SBP (mmHg) | 126.3 ± 14.6 | 124.6 ± 17.9 | 132.0 ± 114.5 | 0.79 | 125.0 ± 15.2 | 124.0 ± 16.8 | 126.3 ± 131.5 | 0.55 |
| DBP (mmHg) | 83.0 ± 12.0 | 82.3 ± 13.2 | 79.5 ± 11.9 | 0.22 | 83.5 ± 11.9 | 81.4 ± 13.5 | 79.0 ± 11.4 | 0.13 |
| Hemoglobin (gr/dl) | 12.6 ± 1.4 | 12.5 ± 1.1 | 12.8 ± 1.4 | 0.19 | 12.6 ± 1.3 | 12.4 ± 1.2 | 12.9 ± 1.3 | 0.04 |
| FBG (mg/dl) | 165.0 ± 45.3 | 157.9 ± 43.7 | 160.4 ± 54.4 | 0.71 | 160.4 ± 35.8 | 167.5 ± 55.1 | 151.3 ± 49.5 | 0.14 |
| 2hrBG (mg/dl) | 207.8 ± 45.7 | 216.1 ± 53.5 | 211.8 ± 59.5 | 0.68 | 214.5 ± 53.7 | 214.3 ± 51.4 | 207.3 ± 58.1 | 0.69 |
| Hb A1c (%) | 8.6 ± 1.4 | 8.4 ± 1.3 | 8.2 ± 1.5 | 0.26 | 8.4 ± 1.1 | 8.5 ± 1.6 | 8.0 ± 1.4 | 0.09 |
| TC (mg/dl) | 184.7 ± 36.8 | 184.5 ± 35.6 | 173.0 ± 34.1 | 0.07 | 181.5 ± 29.8 | 185.6 ± 38.6 | 171.3 ± 36.2 | 0.06 |
| TG (mg/dl) | 169.3 ± 58.0 | 163.3 ± 55.2 | 163.1 ± 70.7 | 0.83 | 170.3 ± 57.7 | 162.0 ± 54.2 | 162.0 ± 75.6 | 0.67 |
| LDL (mg/dl) | 104.8 ± 34.3 | 102.1 ± 31.6 | 96.6 ± 28.2 | 0.30 | 102.7 ± 28.6 | 104.6 ± 35.0 | 92.9 ± 27.0 | 0.07 |
| HDL (mg/dl) | 45.5 ± 8.9 | 46.8 ± 10.2 | 44.7 ± 8.8 | 0.38 | 45.1 ± 8.5 | 46.2 ± 10.2 | 45.7 ± 8.8 | 0.78 |
| Serum Cr (mg/dl) | 0.93 ± 0.17 | 0.89 ± 0.16 | 0.88 ± 0.17 | 0.11 | 0.91 ± 0.14 | 0.90 ± 0.18 | 0.87 ± 0.17 | 0.39 |
| BUN (mg/dl) | 15.6 ± 4.0 | 16.2 ± 4.4 | 14.7 ± 4.2 | 0.10 | 15.6 ± 3.9 | 16.0 ± 3.9 | 14.6 ± 4.8 | 0.16 |
| Vit D3 (nmol/lit) | 26.7 ± 18.5 | 27.0 ± 16.7 | 28.8 ± 18.9 | 0.75 | 25.7 ± 15.4 | 27.9 ± 20.8 | 29.3 ± 16.6 | 0.51 |
| Physical activity (%) | | | | 0.95 | | | | 0.62 |
| Low | 32.80 | 30.90 | 36.40 | | 28.40 | 38.10 | 32.90 | |
| Moderate | 34.40 | 35.10 | 31.30 | | 35.80 | 28.90 | 36.70 | |
| High | 32.80 | 34.00 | 32.30 | | 35.80 | 33.00 | 30.40 | |
| Medications (%) | | | | | | | | |
| Metformin | 98.40 | 97.90 | 100.00 | 0.37 | 100.00 | 97.90 | 98.70 | 0.44 |
| Sulfonylureas | 70.50 | 64.90 | 56.60 | 0.18 | 70.40 | 56.70 | 63.30 | 0.17 |
| Beta blockers | 23.00 | 20.60 | 14.10 | 0.23 | 16.00 | 19.60 | 20.30 | 0.69 |
| Insulin | 21.30 | 26.80 | 34.30 | 0.18 | 22.20 | 30.90 | 31.60 | 0.33 |
| ACEIs | 37.70 | 32.00 | 27.30 | 0.38 | 35.80 | 34.00 | 24.10 | 0.22 |
| ARBs | 52.50 | 53.60 | 47.50 | 0.67 | 58.00 | 52.60 | 41.80 | 0.11 |

Abbreviations: ACEIs, angiotensin converting enzyme inhibitors; ACR, albumin creatinine ratio; ARBs, angiotensin receptor blockers; BMI, body mass index; 2hrBG, 2 h blood glucose; BUN, blood urea nitrogen; CVD, cardiovascular disease; DBP, diastolic blood pressure; FBG, fasting blood glucose; Hb, hemoglobin; HDL, high density lipoprotein; LDL, low density lipoprotein; SBP, systolic blood pressure; TG, triglycerides.
[a] Variables are presented as mean ± SD for continuous variables and n (%) for categorical variables.
[b] Anova test for continuous variables and $\chi^2$ test for categorical variables.

Multivariate adjusted odds ratios of DN across tertiles of the DASH and Med diet scores are indicated in Table 4. In the crude model, a moderate and high adherence to the Med diet was associated with a 67% ($OR_{second\ vs\ first\ tertile} = 0.33$, 95%CI: 0.16, 0.69; $P = 0.001$), and an 88% ($OR_{third\ vs\ first\ tertile} = 0.12$, 95%CI: 0.08, 0.35; $P < 0.001$) lower likelihood of DN, respectively. Adjustment for BMI, Hb A1c, and total energy intake did not change the results materially (Table 4). In the multivariate model, a moderate adherence to the DASH diet was not associated with likelihood of DN ($OR_{second\ vs\ first\ tertile} = 1.32$, 95%CI: 0.93, 1.88; $P = 0.12$), but a significant inverse association was found in women in the top tertile of the DASH diet score ($OR_{third\ vs\ first\ tertile} = 0.71$, 95%CI: 0.57, 0.90, $P = 0.005$).

## 4. Discussion

The present study provided further evidence regarding the beneficial effects of adherence to a healthy diet in patients with T2D, and indicated that better compliance with a healthy dietary pattern such as DASH and Med diets may be associated with a

**Table 3**
Dietary intakes of participants across tertiles of dietary patterns scores.

| Variables[a] | Med score | | | | DASH score | | | |
|---|---|---|---|---|---|---|---|---|
| | Tertile 1 | Tertile 2 | Tertile 3 | $P_{trend}$ | Tertile 1 | Tertile 2 | Tertile 3 | $P_{trend}$ |
| Energy (kcal/day) | 1432.5 ± 234.1 | 1426.3 ± 258.2 | 1438.7 ± 351.0 | 0.94 | 1456.7 ± 240.4 | 1453.6 ± 293.7 | 1365.8 ± 328.8 | 0.13 |
| Carbohydrate (% of total energy) | 71.1 ± 3.5 | 69.8 ± 3.1 | 70.0 ± 3.3 | 0.04 | 70.6 ± 2.4 | 69.6 ± 3.9 | 70.3 ± 3.3 | 0.13 |
| Protein (% of total energy) | 12.8 ± 1.1 | 13.2 ± 1.2 | 13.4 ± 1.2 | 0.01 | 12.98 ± 0.91 | 13.3 ± 1.3 | 13.4 ± 1.3 | 0.04 |
| Total fat (% of total energy) | 20.2 ± 3.5 | 21.0 ± 2.9 | 20.8 ± 2.7 | 0.28 | 20.45 ± 2.29 | 21.1 ± 3.5 | 20.7 ± 2.9 | 0.29 |
| Fruits (gr/day) | 183.2 ± 56.9 | 232.1 ± 74.4 | 264.9 ± 59.7 | <0.001 | 207.8 ± 76.7 | 236.1 ± 72.4 | 253.9 ± 57.7 | 0.001 |
| Vegetables (gr/day) | 183.7 ± 64.7 | 230.8 ± 60.2 | 285.2 ± 73.1 | <0.001 | 208.1 ± 73.1 | 232.5 ± 69.3 | 284.3 ± 72.3 | <0.001 |
| Whole grains (gr/day) | 73.8 ± 55.4 | 115.9 ± 65.3 | 112.3 ± 57.0 | <0.001 | 76.8 ± 38.9 | 103.6 ± 64.2 | 135.6 ± 66.9 | <0.001 |
| Nuts (gr/day) | 18.9 ± 8.2 | 23.8 ± 10.4 | 27.4 ± 7.6 | <0.001 | 22.7 ± 9.9 | 24.2 ± 9.9 | 24.9 ± 8.1 | 0.39 |
| Legumes (gr/day) | 73.9 ± 28.4 | 94.6 ± 43.9 | 103.6 ± 40.6 | <0.001 | 93.2 ± 39.6 | 92.4 ± 41.1 | 92.8 ± 42.3 | 0.99 |
| Red meat (gr/day) | 22.2 ± 8.0 | 20.0 ± 9.7 | 20.9 ± 14.0 | 0.55 | 24.9 ± 6.8 | 22.8 ± 12.7 | 13.5 ± 9.3 | <0.001 |
| Fish (gr/day) | 2.9 ± 7.2 | 5.1 ± 8.6 | 7.3 ± 11.9 | 0.02 | 3.3 ± 4.5 | 6.4 ± 10.1 | 6.9 ± 12.8 | 0.04 |
| Poultry (gr/day) | 16.8 ± 26.0 | 33.4 ± 35.8 | 38.9 ± 35.9 | <0.001 | 13.6 ± 23.7 | 29.2 ± 33.9 | 52.8 ± 34.1 | <0.001 |
| Low-fat dairy (gr/day) | 114.2 ± 46.5 | 126.9 ± 42.9 | 132.1 ± 55.8 | 0.12 | 104.3 ± 48.9 | 127.5 ± 48.7 | 147.6 ± 39.6 | <0.001 |
| High-fat dairy (gr/day) | 122.2 ± 45.5 | 125.0 ± 52.3 | 118.2 ± 48.5 | 0.68 | 134.0 ± 6.8 | 124.3 ± 50.8 | 104.2 ± 47.4 | 0.002 |

Abbreviations: DASH, dietary approaches to stop hypertension; MED, Mediterranean diet.
[a] Energy adjusted dietary intakes.

**Table 4**
Association between priori-defined dietary patterns scores and diabetic nephropathy in women with type 2 diabetes (Odds ratios and 95% confidence intervals).

| Variables | Categories of dietary patterns (n = 210) | | | *P* for trend |
|---|---|---|---|---|
| Med score | 0–3 | 4–5 | 6–9 | |
| No. cases/controls | 41/12 | 42/37 | 22/56 | <0.001 |
| Crude | 1.00 (ref) | 0.33 (0.16–0.69) | 0.12 (0.08–0.35) | |
| Adjusted[a] | 1.00 | 0.38 (0.20–0.73) | 0.14 (0.06–0.33) | |
| DASH score | 11–21 | 22–26 | 27–37 | |
| No. cases/controls | 40/28 | 42/41 | 23/36 | 0.005 |
| Crude | 1.00 (ref) | 1.40 (0.99–1.96) | 0.75 (0.62–0.96) | |
| Adjusted* | 1.00 | 1.32 (0.93–1.88) | 0.71 (0.57–0.90) | |

Abbreviations: DASH, dietary approaches to stop hypertension; Med, Mediterranean dietary pattern.
[a] Adjusted for body mass index, hemoglobin A1c, and total energy intake.

lower likelihood of DN in women with T2D. Additionally, there were some indications of a better glycemic control along with the increase in healthy dietary patterns scores.

Evidence regarding the relationship between diet and kidney function in patients with T2D is scarce, and mainly is from Western countries. To our knowledge, only one study examined the association between diet quality indices and kidney function in patients with T2D. A subgroup analysis within the Nurse's Health Study after 11 years of follow-up indicated that older white women in the top quartile of the DASH diet score had a 47% lower odds of microalbuminuria (ACR 25 to 355 mcg/mg), compared with the first quartile in the age and energy adjusted model [19]. However, no relationship was found in the multivariate model. Additionally, top versus bottom quartile of the DASH diet score was associated with a significant reduction in the risk of eGFR decline (OR: 0.55, 95%CI: 0.38, 0.80) in the multivariate analysis. A subgroup analysis in women with T2D yielded nearly similar results. A cross-sectional analysis within a cohort of patients with T2D in Taiwan indicated that a better adherence to a healthy dietary pattern, characterized by high intake of fish and vegetables, was inversely associated with serum Cr, and marginally and positively associated with eGFR [13].

Such relationship in the general populations has been more investigated. A cross-sectional analysis of 365 adolescences 12–17 years of age included in the Leontio Lyceum Albuminuria Study indicated that a greater adherence to the Med diet was inversely associated with ACR [20]. A cohort of elderly Swedish men showed that a higher adherence to the Med diet was associated with a 42% lower likelihood of CKD at baseline (OR: 0.58, 95%CI: 0.38, 0.87), and with a 23% lower risk of mortality in patients with existing CKD, after a median follow-up of 9.9 years [17]. A cross-sectional analyses of 2408 community-dwelling elderly participants in the Korean National Health and Nutrition Examination Survey suggested that a higher adherence to the DASH diet was associated with a lower odds of CKD in elderly Koreans (OR = 0.78, 95%CI 0.65, 0.94) [18]. Also, three prospective cohort studies confirmed that better compliance with DASH and Med diets was inversely associated with the subsequent risk of CKD (eGFR < 60 ml/min per 1.73 $m^2$) [15,21,40]. Our results are in line with these findings, and indicated that a greater adherence to the DASH and Med diets was associated with a lower likelihood of DN in women with T2D. However, A post-hoc analysis in a cohort of patients with T2D participating in the PREDIMED trial showed that the Med diet interventions, compared with a low-fat control diet, did not reduce the risk of DN after a median follow-up of six years [41].

Generally, the potential positive relationship between greater adherence to the DASH and Med diets and kidney function has been mainly attributed to favorable effects of these diets on levels of traditional cardiometabolic risk factors including blood pressure [29,42,43], glycemic control [23,44], and lipid profile [22,45]. Also, considering the proposed link between oxidative stress and kidney injury [46,47], the anti-inflammatory and antioxidant properties of the DASH and Med diets [24,48,49] might have a contributing role to protect against DN.

In the present study, we found that, in comparison with poor adherents, those in the third tertile of the DASH and Med diets had lower levels Hb A1c. These findings are in accordance with those of randomized controlled trials which have indicated that dietary interventions with the DASH and Med diets could improve glycemic control in patients with T2D [23,44].

The present study was accompanied with some strengths and limitations which should be noted. For the first time, we tested the relationship between the two well-known healthy dietary patterns and likelihood of DN in women with T2D. In addition, evidence regarding the association between dietary features and kidney function are mainly from Western societies. We tested such relationship in a region with distinct different properties from the original DASH and Med diets trial populations, which may be helpful to generalize the beneficial effects of these healthy dietary patterns [50]. Third, cases and controls were selected from the same source, and at the same period of time. Finally, we used a validated and relatively detailed FFQ to assess dietary intakes. We also were faced with some limitations. First, we tested the associations in a case–control design. Thus, some limitations of this type of studies including recall bias and selection bias should be considered. Second, although our controls were selected from the same source and at the same period of time and cases and controls were matched for age and diabetes duration, the existence of some differences between cases and controls including better glycemic control and lower levels of LDL among cases might affect the results. Third, the numbers of cases and controls were relatively low, which might result in a weak statistical inference.

## 5. Conclusions

The present study added new evidence to the relatively scarce investigations on the relationship between dietary features and risk of DN. We showed that higher adherence to a DASH-style diet and the Med diet was inversely associated with the risk of DN in women with T2D. Some indications of a better glycemic control were observed along with the increase in the DASH and Med diet scores. Well-designed prospective cohorts may be needed to test the longitudinal relationship between dietary features and risk of kidney impairment in patients with T2D.

## Statement of authorship

KM and AJ designed the research; KM, AJ, MSZ and MRA conducted the research; KM, AJ, MSY, and ARP performed statistical analysis; all authors contributed to write, review and revise the paper. MRA is the guarantor. All authors have read and approved the final manuscript. All authors had full access to all the data and take responsibility for the integrity of the data and the accuracy of the data analysis.

## Ethical statement

This research was conducted according to the Declaration of Helsinki. The study protocol was approved by the ethics committee of Tehran University of Medical Sciences (Ethic Number: IR.TUMS.REC.1395.2644), and by the ethics committee of Semnan University of Medical Sciences (Ethic Number: IR.SEMUMS.REC.1395.66). Informed consent was obtained from all subjects.


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## Declarations of interest

None.


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