The Association between Plant-Based Dietary Index and Odds of Diabetic Nephropathy in Women: A Case-Control Study

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Abstract

Recent research has suggested that adherence to plant-based dietary index (PDI) may reduce the risk of type 2 diabetes and related complications like DN. Therefore, the aim of this study was to investigate the possible association of PDI with the odds of DN. We enrolled 105 eligible women with DN and 105 controls (30–65 years) who were referred to the Kowsar Diabetes Clinic in Semnan, Iran. A 147-iteme food frequency questionnaire (FFQ) was used to evaluate an overall PDI, healthy plant-based diet index (hPDI), and unhealthful plant-based diet index (uPDI). Biochemical variables and anthropometric measurements were assessed for all patients using the pre-defined protocols. According to our final analyze, after controlling for potential confounders, participants with greater adherence to overall PDI (OR: 0.29; 95% CI: 0.15–0.56; P < 0.001) and hPDI (OR: 0.30; 95% CI: 0.15–0.56; P < 0.001) had 71% and 70% lower odds of DN compared to those with a low adherence. Conversely, subjects with a higher adherence to the uPDI were positively associated with increased odds of DN (OR = 5.00; 95% CI = 2.78–8.98; P < 0.001) and (OR = 4.27; 95% CI = 2.24–8.14; P < 0.001) in the crude and adjusted models, respectively. The result of this study showed that greater adherence to overall PDI and hPDI was inversely associated with the odds of DN. However, further prospective studies are warranted to confirm these results. Plant-based diet; Diabetic nephropathy; Diabetes; case-control

1. Introduction

Diabetic nephropathy (DN) is a microvascular complication caused by diabetes mellitus and mainly induced by chronic hyperglycemia and high blood pressure (BP) (1). The early stage of DN begins with microalbuminuria and gradually progresses to macroalbuminuria, severe proteinuria, decreased glomerular filtration rate (GFR), chronic renal failure, and finally end-stage renal disease (ESRD) (1). This progressive condition can be identified by pathological changes in renal biopsies and glomerular lesions (2).

DN often occurs in 20–40% of diabetic patients with a peak incidence after 10–20 years of diabetes onset and also can be a factor contributing to cardiovascular disease (CVD). Patients with DN have a 30 times higher risk of the all-cause mortality as compared with those without nephropathy (3). In 2017, the global prevalence of DN among men and women was 15.48/1000 and16.50/1000, respectively and also the estimated number of deaths due to DN was 219,451 (4). The prevalence of DN in low- and middle-income countries is 3 to 6 times higher than in some high-income countries and also it is in the range of 7%-35% with a median of 15% (5). Indicator which is commonly used to diagnose DN is albuminuria (urinary albumin to creatinine ratio ≥ 30 mg/g) and can also decline the estimated glomerular filtration rate (eGFR) (< 60 ml/min/1.73 m2) (6). There could be various risk factors of DN, such as age, gender, ethnicity, and family background which are the susceptible factors. Systemic conditions like sustained hyperglycemia, hypertension, and obesity could be both initiating and progressing factors. Smoking, acute kidney injury (AKI) and dietary factors are the other putative risk factors (7).

The treatment strategy of DN is to preclude the kidney from further malfunction and the development of microalbuminuria to macroalbuminuria. Good glucose control, optimal BP, and lipid profile can play a major role in demanding multifactorial interventions and following a healthy lifestyle (8). Among these, diet therapy is considered as an important approach in the treatment of DN. For instance, restricting dietary protein and salt intake can slow DN progression and help maintain renal function (9, 10). In contrast, a higher intake of sugar, salt, and fats is associated with hyperglycemia, hypertension, and dyslipidemia which exacerbates DN (11). The American Diabetes Association suggests that delaying or preventing diabetes complications can be attainable with a higher intake of vegetables, fruits, legumes, and whole grains, and consuming lower glycemic-load foods (12). On the other hand, the substitution of soy and other vegetable proteins instead of animal proteins results in reduced renal hyperfiltration, acid load, and proteinuria, leading to a lower risk of DN (13). Recent studies have suggested that there is an inverse association between following a plant-based diet (PBD) and the risk of T2DM and its secondary outcomes. In addition, several high-quality dietary strategies, such as Dietary Approach to Stop Hypertension (DASH), Diet Diversity Score (DDS), and Mediterranean dietary pattern (MDP) containing less processed food and rich in plant-based food are associated with delayed progression of DN (14–16). PDI are the newly graded dietary patterns which consist of 3 indices: an overall plant-based diet index (PDI), a healthful plant-based diet index (hPDI), and an unhealthful plant-based diet index (uPDI). These indices are categorized as healthy vs less healthy plant foods through their association with type 2 diabetes mellitus (T2DM), CVD, hypertension, and other outcomes (17). Some studies have revealed an inverse association between higher adherence to PDI and lower fasting blood sugar (FBS), 2-h postprandial glucose (2hrBG), and lower risk of T2DM (17, 18). Therefore, we hypothesized that higher adherence to these PBDs may be associated with the odds of DN. To the authors' knowledge, no study has been conducted to investigate the association between PDI with the odds of DN. Therefore, the aim of this case-control study was to examine this association.

2. Materials & Methods

2.1. Subjects

This case-control study was conducted on 210 patients (including 105 cases and 105 controls) aged 30–65 years with a history of 3 to 10 years of diabetes who were referred to Kowsar Diabetes Clinic in Semnan, Iran, from July to December 2016. Woman with T2DM were enrolled in this study according to recent American Diabetes Association's diagnostic criteria: 1) fasting blood glucose (FBG) ≥ 126 mg/dl, 2) glycated haemoglobin (HbA1c) ≥ 6.5%, and 3) 2hrBG ≥ 200 mg/dl. While, DN was considered as Urinary albumin-to-creatinine ratio (ACR) ≥ 30 mg/g in a random spot urine sample.

Patients with a history of cancer, autoimmune disorders, coronary angiography, myocardial infarction, stroke, and hepatic disease were excluded from the study. In addition, over- and under-reporting of total energy intake (< 500 kcal/day or > 3500 kcal/day), and implausible responses to the FFQ (food frequency questionnaire) were regarded as the study exclusion criteria. Each participant was completely informed about the study protocol and provided written informed consent before taking part in the study. Ethical

approval for this study was obtained from the Committee of Tehran University of Medical Sciences (Ethics number: IR.TUMS.REC.1395.2644) and the Ethics Committee of Semnan University of Medical Sciences (Ethics number: IR. SEMUMS. REC.1395.66). Besides, all methods were performed in accordance with the relevant guidelines and regulations.

2.2. Demographic, Anthropometric, and Blood Biomarkers Assessment

Socio-demographic variables including age, diabetes duration, medical history, and medications were obtained by the expert interviewers. Bodyweight (kg) was recorded while participants wore light clothes without shoes. Height (m) was measured to the nearest 0.1 cm using a non-stretchable tape in a standing position with shoes removed. BMI was calculated by dividing weight (kg) by the square of height (kg/m²). Systolic blood pressure and diastolic blood pressure (SBP and DBP, respectively) were measured on the left arm after ≥ 5-min rest in the sitting position using a manual sphygmomanometer.

Biochemical parameters, including blood glucose (FBS, 2hrBG, HbA1c,), kidney function tests (blood urea nitrogen (BUN), total serum creatinine (Cr)), and lipid profile (total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides (TG)) were obtained from an individual's medical records over the last 3 months.

Information on physical activity was collected using a validated International Physical activity Questionnaire (IPAQ) (19). Based on the IPAQ scoring protocol, the participants' physical activity was categorized into three levels of low (score < 600 Metabolic Equivalents/Week), medium (score between 600 and 3,000 MET/h/Week), and high (score > 3,000 MET/h/Week) (20).

2.3. Dietary assessment

Patients' dietary intake was collected using the 147-item semi-quantitative food frequency questionnaire (FFQ), with the approved validity and reliability via face-to-face interviews (21). Frequencies of consumption of food items (per day, week or month) were assessed based on standard serving sizes commonly used by Iranians during the preceding year. Final portion sizes were converted into g/day. Nutritionist 4 software (modified for Iranian foods) was used to evaluate the average daily intake of energy and nutrients.

2.4. Calculating PDI scores

According to recent epidemiological knowledge concerning the association between food items and chronic complications (T2DM, disease cardiovascular, and certain cancers) alongside intermediate outcomes (obesity, hypertension, lipids, and inflammation), we categorized plant-based foods into the overall, healthy, and less or unhealthy groups (4). First, FFQ data were classified into 18 food groups **(Supplementary Table S1)** based on culinary and nutrient similarities, within greater categories of healthy plant foods (whole grains, fruits, vegetables, nuts, legumes, vegetable oils, tea/coffee), unhealthy plant foods (fruit juices, SSBs, refined grains, potatoes, sweets/desserts), and animal foods (butter/lard, dairy,

egg, fish/seafood, meat, miscellaneous animal-based foods). Margarine and hydrogenated vegetable oil were excluded from the index due to fatty acid composition changing over time from high trans-fatty acid to high unsaturated fat (17). After adjusting all food groups for total energy intake, each was divided into quintiles and also each quintile was assigned a score between 1 and 5 (1 for the lowest quintile and 5 for the highest quintile). To create the PDI, all plant foods were scored positively, while animal food groups were given inverse scores. For hPDI, positive scores were allocated to healthy plant food items and revers scores to unhealthy plant and animal food groups. Finally, for uPDI, positive scores were assigned to less healthy plant food items and in contrast, inverse scores to healthy plant food and animal food groups. The collective sum of scores represented the conformity to a PBD pattern with a theoretical range of 18 (as the lowest adherence) to 90 (as the highest adherence).

2.5. Statistical analysis

The normal distribution of quantitative variables was assessed using the Kolmogorov–Smirnov test. General quantitative characteristics and dietary intakes were estimated as mean ± SD, while categorical characteristics were expressed as frequency (percentage). To examine differences in continuous and categories variables PDI groups including (the overall PDI, hPDI, and uPDI) among participants, we used the independent sample t-test and Chi-square, respectively. ANCOVA analysis was performed for adjustment model (adjusting for age, energy intake, margarin, hydrogenated vegetable oil, diabetes duration, and PA). In addition, binary logistic regression was performed to investigate the association between adherence to the PDI and the odds of DN in two different models (Model1: unadjusted, Model2: adjusted for age, energy intake, margarin, hydrogenated vegetable oil, diabetes duration, and PA. The test results were represented as odds ratios (OR) and 95% confidence intervals (CI). All the statistical analyses were performed using SPSS version 25(SPSS Inc., Chicago, IL, USA). P-values of less than 0.05 were considered to characterize significant results.

3. Results

3.1. Study population characteristics

The general characteristics of the 210 eligible subjects according to low and high adherence to the overall PDI, hPDI, and uPDI are displayed in Table 1. The median (interquartile range) of the age, weight, height, and body mass index (BMI) were 57 years, 72 kg,160 cm, 27.52 kg/m2, respectively. Moreover, 32.7% of total participants had low PA. No statistically significant differences were investigated in terms of sociodemographic characteristics and anthropometric variables between adherences to overall PDI, hPDI, and uPDI scores. According to the result, greater adherence to overall PDI and hPDI was associated with lower Alb ($P = 0.004$ and $P = 0.009$), BUN ($P = 0.004$ and $P = 0.009$), Cr, and ACR ($P < 0.001$ for both). In contrast, in individuals with higher adherence to uPDI were associated with increased kidney function tests including Alb ($P = 0.004$), Cr, and ACR ($P < 0.001$for both). Besides, 62.9 and 70 precent of participants with decreased adherence to the overall PDI and hPDI respectively, were more likely to have nephropathy ($P < 0.001$).

Also, an individual with higher adherence to overall PDI and hPDI had lower percentage of ACIE usage (P = 0.02 and P = 0.005). Conversely, a lower percentage of ACIE usage was observed in patients with higher adherence to uPDI (P = 0.03). Moreover, high adherence to hPDI was associated with decreased FBS, 2hBG, HbA1c, TC, LDL and improved HDL. Also, high adherence to uPDI was correlated with evaluated FBS, 2hBG, HbA1c, TG, TC, LDL. However, these associations were not statistically significant (P > 0.05).

3.2. Association between characteristics dietary intake among adherence of PDI scores

Nutrient and food intakes of individuals with low and high adherence to PDI are displayed in **Table 2.** After controlling for potential cofounders, subject with greater adherence to the overall PDI showed a lower intake of energy, carbohydrate, protein, fat, total fiber, cholesterol, Saturated Fatty Acid (SFA), Monounsaturated Fatty Acid (MUFA), oleic, linoleic, lutein, α-carotene, vitamin E, vitamin C, vitamin K, B1, B2, B9, B12, phosphorous, calcium, magnesium, iron, zinc, selenium, animal fat but inversely they consumed higher total fiber, Polyunsaturated Fatty Acid (PUFA), linolenic, vitamin A, β-carotene, vegetable oils, fruits, nuts, legumes, and tea/coffee (P < 0.001). They also decreased intake of miscellaneous animal-based foods (P = 0.02), B8 (P = 0.003), and sodium (P = 0.02), while increased the consumption of vegetables (P = 0.02), fruit juices (P = 0.01), and sweets/desserts (P = 0.01). Additionally, the intake of energy, protein, fat, total fiber, SFA, MUFA, PUFA, oleic, linoleic, linolenic, lutein, α-carotene, β-carotene, vitamin E, vitamin C, vitamin K, B1, B8, B9, potassium, phosphorous, magnesium, iron, zinc, selenium, vegetables, vegetable oils, fruits, legumes (P < 0.001 for all), and nuts (P = 0.006) significantly increased with increasing hPDI adherence, whilst decreased consumption of cholesterol, vitamin A, calcium, potato, egg, animal fat (P < 0.001), and dairy (P = 0.004) was associated with higher adherence to hPDI. In comparison with lower adherence, participants with greater adherence to the uPDI had significantly higher intake of energy, carbohydrate, fat, total fiber, SFA, MUFA, PUFA, oleic, linoleic, linolenic, vitamin A, lutein, α-carotene, β-carotene, vitamin C, vitamin K, B1, B2, B9, sodium, potassium, phosphorous, calcium, iron, selenium, refined grains, SSB, animal fat (P < 0.001), and fruit juices (P = 0.02). In contrast, they decreased the consumption of protein, cholesterol, B8, B12, magnesium, zinc, whole grains, vegetables, vegetable oils, fruits, legumes, sweets/desserts, dairy, fish/seafood, meat, and miscellaneous animal-based foods (P < 0.001).

3.4. Associations between adherence to PDI scores

The associations between adherences to the overall PDI, hPDI, uPDI and odds of DN in crude and adjusted model are presented in Table 3. In the crude model, a significant association was observed between higher adherence to the overall PDI (OR: 0.32; 95% CI: 0.18–0.56; P < 0.001) and hPDI (OR: 0.22; 95% CI: 0.12–0.40; P < 0.001) with odds of DN compared to those with the lowest adherence, reducing the odds of DN by 68% and 78% respectively. Contrastingly, participants with a greater adherence to the uPDI were 100% more likely to have increased odds of DN (OR = 5.00; 95% CI = 2.78–8.98; P < 0.001). After adjusting for potential confounders for age, energy intake, margarin, hydrogenated vegetable oil, diabetes duration, and PA, relationship between the odds of DN and PDI remined significant.

Binary logistic regression was conducted to investigate the associations between PDI components in the crude and adjusted models. Significant association was seen between high consumption of vegetables (OR: 0.37; 95% CI: 0.21–0.66; P = 0.001), vegetable oil (OR:0.16; 95% CI: 0.08–0.29; P < 0.001), fruits (OR: 0.27; 95% CI: 0.15–0.48; P < 0.001), nuts (OR: 0.52; 95% CI: 0.30–0.90; P = 0.02), legume (OR: 0.21; 95% CI: 0.11–0.37; P < 0.001), whole grain (OR: 0.44; 95% CI:0.25–0.77; P = 0.004) and reduced odds of DN. Besides, individuals with higher intake of refined grain (OR: 1.92; 95% CI: 1.11–3.32; P = 0.02), animal fat (OR: 7.94; 95% CI: 4.42–14.69; P < 0.001), eggs (OR: 2.64; 95% CI: 1.51–4.60; P = 0.001), and meats (OR: 0.36; 95% CI: 0.20–0.63; P < 0.001), Fish/seafood (OR: 0.39; 95% CI: 0.22–0.68; P = 0.001) increased the odds of DN. The significant association remained (P < 0.05) even after controlling for cofounders, except for fish/seafood and refined grain. Moreover, participants with more intake of miscellaneous animal-based foods (OR: 0.49; 95% CI: 0.27–0.91; P = 0.02) had 51% enhanced odds of DN in the adjusted model.

4. Discussion

This was the first study investigating the relationship between plant-based and DN among women. According to our findings, higher adherence to the PDI might reduce the odds of DN. In addition, our findings revealed the possible beneficial effects of PDI on DN and kidney function tests in both crude and adjusted models. Our findings were in line with the studies that investigated the association of PBD patterns including the MDP, DASH diet, and higher DDS with reduced odds of DN (14–16). Although there was no significant association between adherence to PDI and other biochemical markers, our findings proposed the possible beneficial effects of overall PDI and hPDI on the reduction of FBS, 2hBG, HbA1c, TC, LDL and the improvement of HDL. Also, elevated FBS, 2hBG, HbA1c, TG, TC, and LDL were showed by higher adherence to uPDI.

the term PBD refers to mainly as “vegan” or “vegetarian” or dietary patterns with an emphasis on the intake of plant foods, such as vegetables, fruit, whole grains, nuts, seeds, oils, legumes, and beans and the exclusion of some or all animal-based foods or byproducts. Basically, the potential positive association between the consumption of diverse foods, especially higher vegetables, fruits, legumes, and whole grain, lower intake of red or processed meats, or greater adherence to the DASH, MDP, and PBD with improved kidney function has been mainly assigned with optimal efficacies of these high-quality dietary approaches on levels of CVD risk factors, such as glycemic control, lipid profile, and BP range (22–26).

Our results showed that a greater intake of vegetables, vegetable oils, fruits, whole grains, and legumes might reduce the odds of DN, while higher consumption of dairy, animal fat, egg, meat, miscellaneous animal-based food, fish/seafood might increase the odds of DN. Studies recommend shifting away from the intake of animal-derived protein and moving towards plant-based rich foods may be beneficial for diabetes and chronic kidney disease (CKD) prevention (17, 27). Similarly, the several prospective studies have also suggested that increasing the intake of whole grains, vegetables, fruits, and dairy and reducing consumption of SSB, egg, and red and processed meat can significantly reduce the risk of insulin

resistance (IR), prediabetes, and T2DM (28, 29). A prospective cohort after the 23-year follow-up reported that red and processed meat increased the risk of CKD by 23%, while higher intake of nuts and legumes decreased CKD by 19% and 17%, respectively (30). A subgroup analysis within the Nurse's Health Study after the 11-year follow-up period showed that individuals with adherence to a western dietary pattern (higher intake of red and processed meat, saturated fats, and sweets) had 2.17 times higher odds ratio for microalbuminuria and a 77% higher risk for rapid eGFR decline, as compared with those with adherence a prudent diet (high in vegetables, fruits, legumes, and whole grains). Therefore, diets enriched in vegetables, fruits, legumes, and whole grains but low in red and processed meat, saturated fats, and sweets may be protective against eGFR decline (31). The results of a review concluded that animal proteins are significantly associated with several DN clinical abnormalities, including IR, proteinuria, microalbuminuria, and accelerated progression of kidney failure, while a vegan diet reduced eGFR decline, decreased microalbuminuria, enhanced insulin sensitivity, and delayed the rate of DN progression (32). Conversely, Li XF et al reported that a low-protein diet is significantly effective for declaring proteinuria and ACR (33). In addition, Nettleton et al conducted an observational study on 5042 elders (aged 45–84 years) and the results demonstrated that high consumption of vegetables, fruits, whole grains, and low-fat dairy foods was correlated with 20% lower ACR across quintiles. Moreover, greater intake of non-dairy animal food was positively associated with 11% higher ACR level (34). Protein overload induces renin-angiotensin system (RAS) and vasoactive modulators activation (glucagon and insulin-like growth factor-1), leading to glomerular hypertension and hyperfiltration. It is well established that a low-protein diet (LPD) is linked to RAS inhibition. On the other hand, LPD may declare similar reno-protective and antiproteinuric efficacies as RAS inhibitors like Angiotensin-Converting Enzyme Inhibitors (ACIEs) and Angiotensin Receptor Blockers (ARBs) (35, 36). As mentioned above, PBD (a model for the LPD) is strongly favorable to slowing the progression of the DN and renal insufficiency by reducing glucagon activation, lowering net acid production, and enhancing the anti-protein uric effect (32, 37). In conclusion, modification in dietary protein sources instead of protein amount and restriction may be a more appropriate approach and long-term treatment of chronic renal failure (30).

The global burden of disease proposed that a greater intake of fruits, nuts/seeds, vegetables, and whole grains could prevent 4.9, 2.5, 1.8, and 1.7 million death per year via remarkable effects on decreased CVD risk factors (38). Due to the absence of cholesterol in the vegetable domain, vegan dietary patterns rich in fibers and soy proteins reduce TC compared to dietary patterns that contain animal derivatives (32). Azadbakht et al. revealed that participants in higher quartile of the DDS for vegetables decreased the probability of hypertension, hypercholesterolemia, and elevated level of serum LDL (25). Also, more studies reported lower serum TG and higher HDL in those with greater adherences to the MDP (22). Furthermore, a systematic review and meta-analysis of RCTs reported that increased adherence to DASH diet was associated with a 2.4 mm Hg lower DBP and 4.3 mm reduced Hg SBP (39). In addition, we investigated a direct association between high adherence to the uPDI and increased DBP. However, we found no statistically significant association between different adherences to overall PDI and hPDI with BP. Adversely, a cross-sectional analysis of 4680 adults ages 40–59 years enrolled in the INTER national study on MAcro/micronutrients and blood Pressure showed that a greater adherence to the overall PDI

and hPDI was associated lower BP, whereas a higher score of uPDI was positively associated with SBP. In the other hand, intakes of whole grains and vegetables contributed to reverse associations of hPDI with BP. Furthermore, intakes of refined grains, SSB, and total meat illustrated the positive associations of uPDI with BP (40). The failure to observe these inconsistent findings may be due to different dietary assessment tools, several analysis models, type of study design, and a relatively low sample size.

Hyperglycemia-induced oxidative stress (OS), results in to a range of metabolic, biochemical and hemodynamic alteration in kidney tissues. OS also could be promoted by other accompanied hyperglycemia complications, such as the formation of advance glycation end products (AGEs), generation of reactive oxygen species (ROS), and reactive nitrogen species (RNS) (41, 42). The sustained production of ROS and RNS or inhibition of antioxidant systems underlying the mechanism of glucose toxicity can lead to renal fibrosis, IR, endothelial dysfunction, and alterations in functions β cells of the pancreas and gradually toward micro- and macro-vascular abnormalities (43). Also, it has been proposed that the production of angiotensin II via hyperglycemia exerts proliferative, pro-fibrotic, and pro-inflammatory effects, including tumor activation of alpha-tumor necrosis factor (TNF-α), interleukin 6 (IL-6), and C-reactive protein (CRP). Furthermore, AGEs have been suggested to amplify inflammatory response, endothelial dysfunction, and subsequent CKD in individuals with CKD through pro-inflammatory molecules release, such as IL-IA, IL-6, and TNF-α (44). AGEs are found in foods with high content of fat and protein, such as processed meats and meat substitutes. Besides, types of cooking methods, such as frying, broiling, roasting, baking as well as cooking at high temperatures and longer time format high amounts of AGEs. Contrary to this, carbohydrate-rich foods, such as grains, legumes, bread, vegetables, and fruits, were among the lowest items in AGEs due to higher content of water, antioxidants, and vitamins which may diminish new AGE production even after cooking (45, 46). In light of this, different dietary patterns, composition, and diversity of plant-based foods enriched in fibers, vitamins, micro-nutrients, and healthy phytochemical bioactive compounds including dietary antioxidants, phenolics, and carotenoids are beneficial to counter chronic OS, improve glycemic control and dyslipidemia and help prevent the progression and pathogenesis of T2DM (47). In a systematic review on efficacy of fruits and vegetables consumption on inflammatory biomarkers and immune cell populations explored greater intake of fruits and vegetables conduct to decreased pro-inflammatory biomarkers (CRP, TNF-α, and IL-6) and also enhanced immune cell populations (48). Previous study showed that increased hPDI score was associated with decreased hs-CRP concentration. Additionally, those with higher uPDI scores had higher levels of hs-CRP and IL-6 serum. A cross-sectional study reported that higher hPDI score was associated with lower hs-CRP and Also uPDI scores had significant increases in hs-CRP and IL-6 concentration (49). Similarly, another cross-sectional study reported that greater adherence to PBD was associated with higher insulin sensitivity, lower CRP, and IL-6 serum level (50). Antioxidant-based therapy has been recommended as a dietary treatment for OS damages and enhancing antioxidant capacities. Recent studies demonstrated that flavonoids, which are widely distributed in plants including fruits, nuts, seeds, vegetables, and plant products (coffee, chocolate, and tea) have several biological and pharmacological activates including anti-oxidant, anti-apoptotic, anti-inflammatory, anti-tumor, and cardio-protective efficacy (51, 52). A systematic review and meta-analysis

of 28 RCTs revealed that flavonoids intake had statistically significant effects on insulin sensitivity, glucose and lipid metabolism in intervention group compared to placebo. Also, this study concluded a significant reduction in T2DM key biomarkers, such as FBS, HbA1c, TG, TC, LDL-C, and homeostasis model assessment of IR (53).

Many gut microbiome species ferment amino acids/proteins (tryptophan, tyrosine, and phenylalanine) into metabolic uremic toxins which may lead to kidney function decline. Uremic toxins retention, such as indoxyl sulfate (IS), *p*-Cresyl sulfate (*p*CS), and trimethylamine-N-oxide (TMAO) have been associated with chronic CKD progression, and clinical CKD-related complications that could responsible for an acceleration in CVD-related mortality and uremic bone disease. Dietary patterns (animal versus plant) may influence gut microbiota composition and gradually change them from potentially beneficial gut bacteria (including families *Bacteroides-Prevotella* and *Lactobacillus-Lactobacillaceae*) to potentially harmful bacteria (e.g., from the family *Fermicutes-Ruminococcus* and *Enterobacter-Enterobacteriaceae*). Therefore, different approaches including dietary modification may be considered as a novel therapeutic strategy for reducing the gut-derived toxins (54).

Studies have documented that poor microbial diversity or dysbiosis can play a significant role in the fast progression of low-grade inflammation and IR in T2DM (54). Resistant starches derived from wheat, corn, nuts, vegetables, and fruits are utilized by intestinal gut flora and produced short chain fatty acids (SCFAs). SCFAs provide energy and nutrients to the colonocytes and also are associated with epithelial barrier integrity, decreasing gut permeability, and preventing toxic byproducts release to blood stream circulation, thereby alleviating and preventing chronic inflammation (55). A recent cross-sectional study indicated that greater adherence to the overall PDI was significantly associated with the relative abundance of the majority of species (*Haemophilus parainfluenzae*) that were related to reduced generation of IS. In contrast, higher consumption of uPDI was significantly associated with bacteria linked to increased IS and *p*CS (free and total) levels (56). Meanwhile, another study showed that a higher hPDI score was positively and significantly linked with a greater relative abundance (%) of *Bacteroides-cellulosilyticus and Haemophilus-parainfluenzae*, etc. alongside, the enrichment of pathways, contributing to amino acid biosynthesis, pyruvate fermentation, and the depletion of pathways is involved in processing the components from animal-based food groups. Conversely, a lower hPDI score was correlated with the enrichment of pathways that contributed to the metabolism of animal-based food items (57). Additionally, Gretchen et al. reported that elevated TMAO serum level was associated with an enhanced risk of CVD and mortality in patients with CKD. Moreover, a higher level of TMAO has been associated with increased intake of animal-based food items in omnivorous diet consumers (a diet high in animal protein including meat, eggs, fish, and dairy). Hence, a PBD has been proposed as an intervention and useful approach to delay the progression of CKD and reduce the risk of CVD (58).

The present study had multiple strengths and limitations. To the best of our knowledge, this is the first study investigating the association between adherence to the PDI and the odds of DN among women with T2DM. Moreover, our cases and controls were from the same location in period of time, and we used a detailed FFQ that was validated and reliable to assess dietary intakes. Despite the strengths, we also

acknowledge some limitations that should be considered. First, due to study design, some limitations of this type of studies, such as recall and selection biases of case-control studies are not unavoidable. In addition, although we matched cases and controls based on age and diabetes duration, other related factors, such as BMI, better glycemic control and low serum levels of LDL among cases might affect the results. Third, urine albumin without urine Cr level is subject to false-negative and false-positive determinations because the hydration status affects urine concentration. Finally, the relatively small number of cases and controls may result in a weak statistical inference.

In conclusion, the result showed that a greater adherence to overall PDI and hPDI was inversely associated with the odds of DN. Convergingly, a higher adherence to uPDI was positively associated with odds of DN. In the other words, participants with increased intake of vegetable, fruit, whole grain, nut, legume decreased the odds of DN, while more consumption of refined grain, meat, animal fat, fish/seafood, and miscellaneous animal-based food was associated with high odds of DN through the mentioned mechanisms. Kidney faction tests including ACR, BUN, and Cr improved as the adherence to overall PDI and hPDI. According to the mentioned limitations, further well-designed prospective studies should be conducted to investigate the longitudinal relationship between dietary features and risk of kidney impairment in patients with T2DM.

Declarations

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Data Availability Statement

The data supporting the findings of this study are available from Dr Khadijeh Mirzaei, but restrictions are applied for the availability of these data, which were used under license for the current study, and so are not publicly available. However, data are, available from the authors upon reasonable request and with permission of Dr.Khadijeh Mirzaei.

Conflict of interest

None to be mentioned.

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Tables

Table 1. Characteristics of the study population among adherence of the plant-based indices

		PDI				hPDI				uPDI			
		Low adherence (n= 105) Mean±SD	High adherence (n= 105) Mean±SD	P-value	P-value*	Low adherence (n= 107) Mean±SD	High adherence (n= 103) Mean±SD	P-value	P-value*	Low adherence (n= 110) Mean±SD	High adherence (n= 100) Mean±SD	P-value	P-value*
Quantitative Variables[a]													
Demographic characteristics and anthropometry													
Age (year)		54.63±7.39	56.11±6.68	0.12	0.12	54.86±7.33	55.90±6.78	0.28	0.25	55.30±7.40	55.45±6.72	0.87	0.87
Weight (kg)		71.32±13.69	73.66±11.60	0.18	0.22	72.33±12.38	72.66±12.13	0.85	0.46	71.70±12.89	73.36±12.53	0.34	0.36
Height (m)		161.39±5.70	160.46±6.45	0.26	**0.004**	161.25±5.59	160.58±6.58	0.42	**0.004**	160.68±6.04	161.19±6.16	0.54	**0.004**
BMI (kg/m2)		27.63±4.82	28.56±4.32	0.14	0.58	27.77±4.89	28.43±4.26	0.30	0.70	27.97±4.19	28.23±5.01	0.67	0.86
Blood parameters													
FBS (mg/dl)		169.92±53.89	151.37±39.59	**0.005**	0.06	164.45±45.89	156.70±50.46	0.24	0.31	156.62±50.42	165.08±45.52	0.20	0.34
Postprandial BS (mg/dl)		219.25±53.85	205.60±53.38	**0.06**	0.28	213.52±47.33	211.28±60.23	0.76	0.57	208.75±53.67	216.47±54.18	0.30	0.47
HbA1c (%)		8.69±1.42	7.99±1.25	**<0.001**	**0.003**	8.48±1.27	8.20±1.48	0.76	0.11	8.18±1.45	8.52±1.29	**0.07**	0.11
Serum cholesterol (mg/dl)		185.15±33.48	175.38±37.18	**<0.001**	0.27	187.08±35.32	173.18±34.72	**0.004**	**0.05**	174.75±35.38	186.33±35.08	**0.01**	0.12
TG (mg/dl)		161.27±59.38	168.24±64.25	0.41	0.46	164.26±55.90	165.26±67.63	0.97	0.61	157.48±65.13	172.75±57.21	**0.07**	0.23
LDL (mg/dl)		107.88±30.41	93.58±30.41	**0.001**	**0.03**	105.05±32.05	96.23±29.73	**0.04**	0.32	96.05±29.91	105.87±31.87	**0.02**	0.28
HDL (mg/dl)		44.88±9.54	46.54±8.93	0.19	0.63	44.27±9.22	47.20±9.09	**0.02**	0.28	45.84±9.64	45.57±8.85	0.8	0.94
Hb (g/dl)		12.58±1.39	12.65±1.19	0.71	0.95	12.69±1.30	12.54±1.28	0.38	0.91	12.77±1.30	12.44±1.27	**0.06**	0.52
Alb (mg/dl)		13.86±11.30	8.92±8.14	**<0.001**	**0.02**	12.89±8.61	9.83±11.34	**0.02**	**0.009**	9.36±11.16	13.62±8.38	**0.002**	**0.004**
Cr (mg/dl)		0.90±0.16	0.88±0.17	0.36	0.001	0.91±0.16	0.88±0.17	0.15	**0.001**	0.87±0.16	0.92±0.17	**0.01**	**<0.001**
BUN (mg/dl)		16.16±4.58	14.81±3.71	**0.02**	**0.04**	162.11±130.80	87.31±126.92	**0.007**	**0.02**	14.87±4.29	16.15±4.05	**0.02**	0.08
ACR (mg/g)		166.44±135.96	84.41±119.06	**<0.001**	**<0.001**	16.25±4.85	14.69±3.28	**<0.001**	**<0.001**	81.70±120.85	173.52±131.68	**<0.001**	**<0.001**
Vit D (ng/ml)		26.17±17.78	29.05±18.16	0.24		25.69±18.47	29.60±17.33	0.15	0.47	28.85±18.00	26.25±17.96	0.29	0.57
Blood pressure													
SBP (mmHg)		125.78±16.50	129.85±98.98	0.67	0.54	125.39±16.03	130.33±99.98	0.61	0.46	129.35±96.77	126.12±16.47	0.74	0.46
DBP (mmHg)		81.21±12.89	81.69±12.11	0.78	0.85	82.06±12.83	80.82±12.13	0.47	0.75	78.56±10.90	84.62±13.36	**<0.001**	**0.009**
Qualitative variables[b]													
Nephropathy	No	39 (37.1)	66 (62.9)	**<0.001**	**<0.001**	35 (33.3)	72 (68.6)	**<0.001**	**<0.001**	75 (71.4)	30 (28.6)	**<0.001**	**<0.001**
	Yes	66 (62.9)	39 (37.1)			70 (66.7)	33 (31.4)			35 (33.3)	70 (66.7)		
Drugs user (%)													
ARB	Yes	56 (53.3)	49 (46.7)	0.33	0.35	59 (56.2)	46 (43.8)	0.12	0.13	52 (49.5)	53 (50.5)	0.47	0.48
	No	49 (46.7)	56 (53.3)			48 (45.7)	57 (54.3)			58 (55.2)	47 (44.8)		
ACIE	Yes	40 (61.5)	25 (38.5)	**0.02**	**0.02**	42 (64.6)	23 (35.4)	**0.008**	**0.005**	27 (41.5)	38 (58.5)	**0.03**	**0.03**
	No	65 (44.8)	80 (55.2)			65 (44.8)	80 (55.2)			83 (57.2)	62 (42.8)		
Beta-blocker	Yes	22 (57.9)	16 (42.1)	0.32	0.32	22 (57.9)	16 (42.1)	0.38	0.47	17 (44.7)	21 (55.3)	0.38	0.21
	No	82 (48)	89 (52)			85 (49.1)	87 (50.0)			93 (53.8)	79 (46.2)		
Metformin	Yes	103 (49.5)	105 (50.5)	0.15	0.11	105 (50.5)	103 (49.5)	0.16	0.16	110 (52.9)	98 (47.1)	0.13	0.15
	No	2 (100)	0 (0)			2 (100)	0 (0)			0 (0)	2 (100)		
Sulfonylurea	Yes	68 (51.1)	65 (48.9)	0.66	0.56	68 (51.1)	65 (48.9)	0.97	0.86	68 (51.1)	65 (48.9)	0.63	0.56
	No	37 (48.1)	40 (51.9)			39 (50.6)	38 (49.4)			42 (54.5)	35 (45.5)		
Insulin	Yes	32 (52.5)	29 (47.5)	0.64	0.63	29 (47.5)	32 (52.5)	0.52	0.47	34 (55.7)	27 (44.3)	0.53	0.53
	No	73 (49)	76 (51.0)			78 (52.3)	71 (47.7)			76 (51)	73 (49)		
Physical activity (%)													
Low		30 (44.1)	38 (55.9)	0.47	0.45	35 (51.5)	33 (48.5)	0.98	0.88	38 (55.9)	30 (44.1)	0.77	0.78
Moderate		38 (54.3)	32 (45.7)			35 (50.0)	35 (50.0)			36 (51.4)	34 (48.6)		
Moderate		37 (51.4)	35 (48.6)			37 (51.4)	35 (48.6)			36 (50.0)	36 (50.0)		

a Mean±SD, b n (%)

*Significant items with a p-value≤0.05 are bolded. p-value reported after adjusting for age, energy intake, margarine, hydrogenated vegetable oil, diabetes duration, and PA.

Independent sample t-test for quantitative data and %2 test for qualitative data have been used. Subjects with low adherence to overall PDI, hPDI, and uPDI had a score (<18); high adherence: (≥54). Overall PDI, plant-based dietary index; hPDI, healthy plant-based dietary index; uPDI, unhealthy plant-based diet index. BMI, body mass index; ACIE, angiotensin-converting enzyme inhibitors; ACR, albumin-to-creatinine ratio; ARB, angiotensin receptor blockers; BMI, body mass index; BS, blood sugar; CVD, cardiovascular disease; DBP, diastolic blood pressure; FBS, fasting blood sugar; HB, hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; SD, standard deviation

Table 2. Dietary intake of nutrients among adherence of the plant-based indices

	PDI				hPDI				uPDI			
	Low adherence (n= 105)	High adherence (n= 105)	P-value	P-value*	Low adherence (n= 107)	High adherence (n= 103)	P-value	P-value*	Low adherence (n= 110)	High adherence (n= 100)	P-value	P-value*
	Mean±SD	Mean±SD			Mean±SD	Mean±SD			Mean±SD	Mean±SD		
Macronutrients and energy												
Energy (Kcal/d)	1516.38±312.44	1343.52±236.822	**<0.001**	**<0.001**	1419.69±261.93	1440.61±317.13	0.60	**<0.001**	1399.69±309.15	1463.24±264.47	0.11	**<0.001**
Carbohydrate (g/day)	267.11±59.82	235.48±47.45	**<0.001**	**<0.001**	251.19±50.97	251.40±61.32	0.97	**<0.001**	245.40±61.55	257.78±49.02	0.11	**<0.001**
Total fiber (g/day)	37.99±8.94	38.84±8.31	0.47	**<0.001**	37.88±8.08	38.97±9.17	0.36	**<0.001**	36.31±7.19	40.73±9.47	**<0.001**	**<0.001**
Protein (g/day)	48.89±9.52	45.08±8.52	**0.003**	**<0.001**	45.78±7.63	48.23±10.50	0.05	**<0.001**	47.11±9.53	46.85±8.90	0.84	**<0.001**
Fat (g/day)	34.68±9.49	31.25±5.68	**0.002**	**<0.001**	32.34±7.45	33.62±8.50	0.24	**<0.001**	32.22±7.07	33.79±8.86	0.15	**<0.001**
Micronutrients												
Chol (mg/day)	8.06±7.25	5.41±8.89	**0.01**	**<0.001**	7.01±7.84	6.44±8.58	0.61	**<0.001**	8.05±10.35	5.28±4.46	0.11	**<0.001**
SFA (g/day)	6.53±1.78	5.88±1.44	**0.004**	**<0.001**	6.01±1.45	6.41±1.81	0.07	**<0.001**	6.06±1.63	6.36±1.66	0.19	**<0.001**
MUFA (g/day)	11.70 ±3.67	10.40±2.26	**0.002**	**<0.001**	10.90±2.79	11.21±3.42	0.47	**<0.001**	10.66±2.70	11.48±3.46	**0.05**	**<0.001**
PUFA (g/day)	10.64±2.89	10.46±1.71	0.58	**<0.001**	10.16±3.42	10.95±1.93	**0.01**	**<0.001**	10.48±2.52	10.62±2.21	0.69	**<0.001**
Oleic (g/d)	11.38±3.57	10.05±2.05	**0.001**	**<0.001**	10.61±2.67	10.82±3.28	0.60	**<0.001**	10.32±2.57	11.15±3.33	**0.04**	**<0.001**
Linoleic (g/d)	9.57±2.72	9.31±1.45	0.37	**<0.001**	9.10±1.68	9.80±2.56	**0.01**	**<0.001**	9.41±2.39	9.48±1.93	0.81	**<0.001**
Linolenic (g/d)	0.88±0.30	0.95±0.26	**0.05**	**<0.001**	0.88±0.27	0.96±0.30	**0.05**	**<0.001**	0.90±0.30	0.94±0.27	0.36	**0.003**
Vitamin A (RAE/day)	20.34±15.82	24.64±9.82	**0.01**	**<0.001**	22.72±15.33	22.25±10.89	0.79	**0.008**	20.81±14.44	24.34±11.75	**0.05**	**0.002**
Lutein (µg/day)	288.64±118.97	261.77±89.42	0.06	**<0.001**	270.90±99.57	279.67±112.31	0.54	**<0.001**	265.39±98.49	286.00±112.90	0.15	**<0.001**
α-Carotene (RAE/day)	1.22±4.00	0.52±2.12	0.11	**<0.001**	0.85±2.84	0.89±3.57	0.92	**<0.001**	0.56±2.07	1.20±4.10	0.14	**<0.001**
β-Carotene (RAE/day)	15.47±8.86	17.06±5.88	0.12	**<0.001**	15.18±7.05	17.39±7.90	0.03	**<0.001**	15.82±5.23	16.75±9.46	0.37	**<0.001**
Vitamin C (mg/day)	10.53±5.24	10.27±6.27	0.74	**<0.001**	10.67±5.14	10.12±6.37	0.49	**<0.001**	9.59±5.67	11.29±5.77	**0.03**	**<0.001**
Vitamin E (mg/day)	4.19±1.55	3.94±1.39	0.21	**<0.001**	3.98±1.32	4.15±1.62	0.41	**<0.001**	4.06±1.58	4.08±1.36	0.93	**<0.001**
Vitamin K (mg/day)	13.19±5.73	12.98±4.15	0.27	**<0.001**	12.82±4.31	13.35±5.63	0.04	**<0.001**	12.10±3.43	14.16±6.12	0.87	**<0.001**
Vitamin B1 (mg/day)	1.77±0.36	1.59±0.26	**<0.001**	**<0.001**	1.66±0.28	1.70±0.37	0.38	**<0.001**	1.64±0.33	1.73±0.31	0.07	**<0.001**
Vitamin B2 (mg/day)	1.03±0.20	0.90±0.14	**<0.001**	**<0.001**	0.96±0.18	0.97±0.20	0.71	**<0.001**	0.94±0.18	0.99±0.19	0.08	**<0.001**
Vitamin B6 (mg/day)	0.77±0.15	0.75±0.11	0.27	**<0.001**	0.77±0.12	0.75±0.15	0.41	**<0.001**	0.75±0.14	0.77±0.13	0.30	**<0.001**
Vitamin B8 (µg/day)	18.54±6.69	16.57±3.68	**<0.001**	**0.02**	17.82±5.79	17.29±5.14	0.48	0.2	18.04±6.11	17.03±4.66	0.18	**<0.001**
Vitamin B9 (µg/day)	390.55±112.65	377.45±74.92	0.39	**<0.001**	366.19±79.65	402.50±107.14	0.03	**<0.001**	373.15±93.18	395.94±97.38	0.08	**<0.001**
Vitamin B12 (µg/day)	0.17±0.12	0.11±0.15	**0.007**	**<0.001**	0.15±0.14	0.13±0.14	0.42	**<0.001**	0.16±0.18	0.12±0.08	0.09	**<0.001**
Sodium (mg/day)	3665.81±1095.78	3384.35±876.50	**0.04**	**0.003**	3696.74±1071.07	3346.76±890.59	**0.01**	**<0.001**	3389.63±1021.15	3674.08±958.93	**0.03**	**0.001**
Potassium (mg/day)	1678.44±396.37	1737.13±383.82	0.27	**<0.001**	1653.77±299.68	1763.90±461.09	**0.04**	**<0.001**	1703.74±412.63	1712.24±366.24	0.87	**<0.001**
Phosphorous (mg/day)	938.00±156.25	875.68±166.96	**0.006**	**<0.001**	899.26±129.60	914.71±194.27	0.49	**<0.001**	903.06±174.93	911.00±152.54	0.72	**<0.001**
Calcium (mg/day)	420.87±77.07	386.84±64.47	**0.001**	**<0.001**	405.39±74.99	402.25±71.01	0.75	**<0.001**	389.86±73.34	419.25±69.58	**0.003**	**<0.001**
Magnesium (mg/day)	357.67±82.22	353.67±65.12	0.70	**<0.001**	341.59±49.38	370.29±92.76	**0.005**	**<0.001**	355.77±86.02	355.56±61.37	0.98	**<0.001**
Iron (mg/day)	15.48±2.53	14.31±2.11	**<0.001**	**<0.001**	14.74±2.04	15.06±2.72	0.32	**<0.001**	14.68±2.50	15.13±2.27	0.18	**<0.001**
Zinc (mg/day)	8.41±2.83	7.96±1.44	0.14	**<0.001**	7.79±1.23	8.60±2.92	**0.009**	**<0.001**	8.37±2.78	7.99±1.45	0.22	**<0.001**
Chromium (µg/d)	0.22±0.07	0.21±0.06	0.18	**<0.001**	0.21±0.06	0.21±0.07	0.79	**0.04**	0.22±0.07	0.21±0.06	0.52	**<0.001**
Selenium (µg /day)	130.06±31.12	113.91±21.11	**<0.001**	**<0.001**	121.11±21.91	122.90±32.79	**0.64**	**<0.001**	120.91±32.20	123.18±21.90	0.55	**<0.001**
PDI Components												
Whole grains (g/day)	114.71±97.58	120.14±80.87	0.66	0.64	107.31±88.09	127.93±90.06	0.09	0.09	148.37±105.21	83.39±49.69	**<0.001**	**<0.001**
Vegetables (g/day)	313.15±204.22	370.34±163.49	**0.02**	**0.02**	287.14±135.21	398.47±214.68	**<0.001**	**<0.001**	426.02±207.76	249.05±97.64	**<0.001**	**<0.001**
Fruits (g/day)	379.79±113.04	504.64±232.50	**<0.001**	**<0.001**	386.01±148.68	500.60±215.50	**<0.001**	**<0.001**	518.63±220.18	358.16±107.13	**<0.001**	**<0.001**
Nuts (g/day)	30.69±25.71	36.00±11.31	**0.05**	**0.04**	29.64±9.38	33.34±19.99	**0.006**	**0.006**	35.73±26.05	30.73±9.14	0.07	0.06
Legumes (g/day)	94.47±57.95	148.70±73.25	**<0.001**	**<0.001**	98.59±67.61	145.47±67.29	**<0.001**	**<0.001**	142.21±63.68	83.39±49.69	**<0.001**	**<0.001**
Vegetable oil (g/day)	2.59±2.74	6.50±2.81	**<0.001**	**<0.001**	2.81±2.98	6.35±2.81	**<0.001**	**<0.001**	6.10±3.17	2.84±2.76	**<0.001**	**<0.001**
Tea and coffee (g/day)	659.13±430.71	882.54±461.17	**<0.001**	**<0.001**	731.25±495.89	811.95±415.67	0.20	0.20	717.05±419.51	830.00±494.22	0.07	0.07
Refined grains (g/day)	561.33±154.30	593.22±174.08	0.16	0.14	595.50±188.78	558.34±133.98	0.10	0.10	542.91±211.33	615.08±73.87	**0.001**	**0.001**
Potato (g/day)	56.80±39.01	54.87±23.99	0.66	0.65	65.25±15.79	46.05±15.79	**<0.001**	**<0.001**	53.44±24.45	58.47±39.17	0.26	0.25
Sweets/desserts (g/day)	419.87±222.10	482.42±173.43	**0.02**	**0.01**	450.43±199.83	451.89±203.66	0.95	0.95	477.00±194.02	422.70±206.12	**0.05**	**0.05**
SSB (g/day)	47.94±21.86	47.09±34.70	0.83	0.82	51.07±21.67	43.82±34.64	0.06	0.07	40.99±29.67	54.69±26.43	**0.001**	**0.001**
Fruits juice (g/day)	56.33±95.97	106.77±175.70	**0.01**	**0.01**	70.87±106.33	92.64±173.82	0.27	0.26	60.41±107.43	104.79±172.44	**0.02**	**0.02**
Dairy (g/day)	504.12±133.44	462.47±226.14	0.10	0.09	519.19±211.34	446.01±148.39	**0.004**	**0.004**	540.81±211.07	420.02±128.75	**<0.001**	**<0.001**
Fish/seafood (g/day)	10.25±11.33	11.00±12.96	0.65	0.63	11.06±12.41	10.17±11.93	0.59	0.59	14.45±13.77	6.42±8.30	**<0.001**	**<0.001**
Eggs (g/day)	30.97±14.65	27.00±20.56	0.10	0.09	33.35±20.30	24.45±13.75	**<0.001**	**<0.001**	30.65±20.01	27.15±15.19	0.15	0.15
Meats (g/day)	78.35±27.15	81.94±40.18	0.44	0.42	82.51±41.09	77..69±25.26	0.30	0.31	92.07±39.28	67.03±21.14	**<0.001**	**<0.001**
Animal fat (g/day)	62.56±18.18	45.85±22.69	**<0.001**	**<0.001**	64.98±21.70	43.01±16.37	**<0.001**	**<0.001**	47.28±24.19	61.28±16.75	**<0.001**	**<0.001**
Miscellaneous animal-based foods (g/day)	56.22±21.94	49.59±21.16	**0.02**	**0.02**	54.92±18.95	50.82±24.25	0.17	0.17	57.74±25.57	47.59±14.99	**0.001**	**0.001**

*Significant items with a p-value≤0.05 are bolded. P-value reported after adjusting for energy intake.

The P-value obtained from independent sample t-test. Subjects with low adherence to overall PDI, hPDI, and uPDI had a score (<18); high adherence: (≥54). Overall PDI, plant-based dietary index; hPDI, healthy plant-based dietary index; uPDI, unhealthy plant-based diet index; Chol, cholesterol; SFA, saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid.

Table 3. Association between PDI indices adherence, their components, and odds of DN

	Crude models			Adjusted models*		
	β	OR (0.95% CI)	P-value	β	OR (0.95% CI)	P-value
Overall PDI[a]						
(Low adherence) [b]	–	–	–	–		–
(High adherence)	-1.13	0.32 (0.18-0.56)	**<0.001**	-1.21	0.29 (0.15-0.56)	**<0.001**
hPDI						
(Low adherence) [c]	–	–	–	–		–
(High adherence)	-1.47	0.22 (0.12-0.40)	**<0.001**	-1.20	0.30 (0.15-0.56)	**<0.001**
uPDI						
(Low adherence) [d]	–	–	–	–		–
(High adherence)	1.60	5.00 (2.78-8.98)	**<0.001**	1.45	4.27 (2.24-8.14)	**<0.001**
PDI Components						
Vegetables (g/day)	- 0.97	0.37 (0.21-0.66)	**0.001**	- 0.83	0.43 (0.23-0.80)	**0.008**
Vegetable oil (g/day)	-1.83	0.16 (0.08-0.29)	**<0.001**	- 2.01	0.13 (0.06-0.29)	**<0.001**
Fruit (g/day)	- 1.30	0.27 (0.15-0.48)	**<0.001**	- 1.20	0.30 (0.16-0.55)	**<0.001**
Nuts (g/day)	- 0.65	0.52 (0.30-0.90)	**0.02**	- 0.73	0.47 (0.25-0.89)	**0.02**
Whole grains (g/day)	- 0.81	0.44 (0.25-0.77)	**0.004**	-0.87	0.41 (0.23-0.74)	**0.003**
Legumes (g/day)	- 1.56	0.21 (0.11-0.37)	**<0.001**	-1.41	0.24 (0.12-0.45)	**<0.001**
Tea and coffee (g/day)	0.26	1.30 (0.75-2.24)	0.33	0.32	1.38 (0.76-2.53)	0.28
Fruits juice (g/day)	0.57	0.37 (1.02-3.07)	0.03	0.51	1.66 (0.93-2.97)	0.08
SSB	0.76	1.07 (0.62-1.85)	0.78	-0.30	0.73 (0.40-1.36)	0.33
Sweet/dessert (g/day)	- 0.38	0.68 (0.39-1.75)	0.16	-0.45	0.63 (0.32-1.25)	0.19
Potatoes (g/day)	0.57	1.77 (1.02-3.07)	0.03	0.47	1.61 (0.88-2.94)	0.30
Refined grains (g/day)	0.65	1.92 (1.11-3.32)	**0.02**	0.30	1.36 (0.74-2.48)	0.31
Dairy (g/day)	- 0.19	0.82 (0.48-1.42)	0.49	-0.29	0.74 (0.41-1.34)	0.33
Animal fat (g/day)	2.07	7.94 (4.42-14.69)	**<0.001**	2.24	9.39 (4.13-21.32)	**<0.001**
Eggs (g/day)	0.97	2.64 (1.51-4.60)	**0.001**	0.99	2.70 (1.45-5. 05)	**0.002**
Meats (g/day)	- 1.01	0.36 (0.20-0.63)	**<0.001**	-0.89	0.40 (0.22-0.73)	**0.003**
Fish/seafood (g/day)	- 0.93	0.39 (0.22-0.68)	**0.001**	-0.33	0.71 (0.39-1.29)	0.27
Miscellaneous animal-based foods (g/day)	- 0.22	0.79 (0.46-1.36)	0.40	-0.70	0.49 (0.27-0.91)	**0.02**

[a] The PDI indices score was for low adherence (18), and high adherence (54) [b,c,d] as a reference group, d The β coefficient. Overall PDI, plant-based diet index; hPDI, healthful plant-based diet index; uPDI, unhealthful plant-based diet index has been reported; SSB, sugar-sweetened beverages *Adjusted for age, energy intake, margarine, hydrogenated vegetable oil, cardiovascular diseases history, diabetes duration, and PA.

Supplementary Files

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- SupplementaryTable1.docx