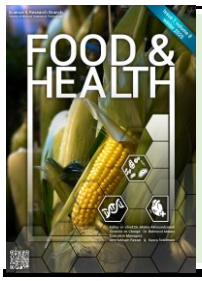

Food & Health Journal

Journal homepage: sanad.iau.ir/journal/fh

Exploring the link between dietary characteristics and diabetic kidney disease: a literature review

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ARTICLE INFO

Original Article

Article history:
Received 29 January 2025
Revised 17 February 2025
Accepted 10 March 2025
Available online 25 March 2025

Keywords:
Diabetic neuropathies
Diet
Diabetes complications
Diet therapy

ABSTRACT

Diabetic kidney disease is a major health issue and its prevalence is rising rapidly. This microvascular complication of diabetes finally leads to end-stage renal disease and kidney transplantation. Several factors increase the risk of progression to kidney disease, but nutrition and diet are the most modifiable ones. In this review, we aimed to assess different dietary characteristics and their association with diabetic kidney disease. Electronic literature searches were conducted on PubMed and Google Scholar. In general, the findings suggested that lower inflammatory properties of a diet and greater compliance with healthy dietary patterns, including the DASH, Mediterranean diet, plant-based dietary index, etc., were associated with reduced albuminuria, preserved eGFR, and reduced tubular injuries in individuals with diabetes. Greater adherence to anti-inflammatory, anti-oxidative, plant-based, and low-carbohydrate dietary characteristics might be a beneficial approach in delaying nephropathy progression and preserving kidney function in diabetic patients.

1. Introduction

Diabetes is considered a prevalent chronic disease, as its prevalence was 830 million in 2022, and it is predicted to increase rapidly in the future (1). Diabetic kidney disease (DKD) is one of the most debilitating complications of diabetes, which can lead to end-stage renal disease (ESRD) and the need for dialysis or kidney transplantation (2). According to the latest data from the World Health Organization (WHO), both diabetes and kidney diseases are among the top 10 causes of death (3). The worldwide impact of DKD is a significant health issue, as well as an economic one, due to the considerable rise in healthcare expenses it causes (4).

DKD pathogenesis is multifactorial involving hyperglycemia, hypertension, and hyperlipidemia. Its pathogenesis can be summarized as an increase in inflammation and oxidative stress (5).

As far as we know, the primary proven strategies for preventing nephropathy in diabetic patients are controlling blood glucose and blood pressure (6). Previous research on nutrition and DKD primarily focused on individual nutrients or specific foods and their effects on DKD, while this attitude has some limitations. In this study we aimed to review the association between the different properties of a diet and the risk of diabetic kidney disease.

2. Diabetic Kidney Disease Diagnosis

DKD is a major microvascular complication of diabetes, which is defined by a decline in renal function, a reduction in the GFR, usually the occurrence of diabetic retinopathy, and the presence of proteinuria. The key diagnostic markers for DKD include persistent albuminuria, which appears alongside diabetic retinopathy and is noted in the absence of other kidney disorders. Kidney function should be evaluated using serum creatinine-based eGFR calculations, ideally with the chronic kidney disease epidemiology collaboration (CKD-EPI) formula, due to its enhanced accuracy in the eGFR range of 60–90 mL/min/1.73 m² (7).

3. DKD Risk factors

Numerous risk factors contribute to the development and progression of diabetic nephropathy (DN), modifiable risk factors include poor blood pressure and poor glycemic control, increased HbA1c, proteinuria, obesity, smoking, high serum

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cholesterol, use of oral contraceptives, hyperuricemia, while the others are not modifiable including family history, male gender, and specific ethnic backgrounds. (8, 9).

4. Oxidative stress, Inflammation, and Diabetic Kidney Disease

Persistent high blood sugar level induces oxidative stress and leads to higher production of reactive oxygen species (ROS), while reducing the body's antioxidant capacity, causing oxidative stress-related damage to DNA and proteins, and triggering the immune system to produce inflammatory mediators and cytokines that impact glomerular capillaries. This, in turn, alters the structure and functionality of renal tubules, intensifying both renal and systemic damage (10). Figure 1 shows different factors that contribute to the pathogenesis of diabetic kidney disease.

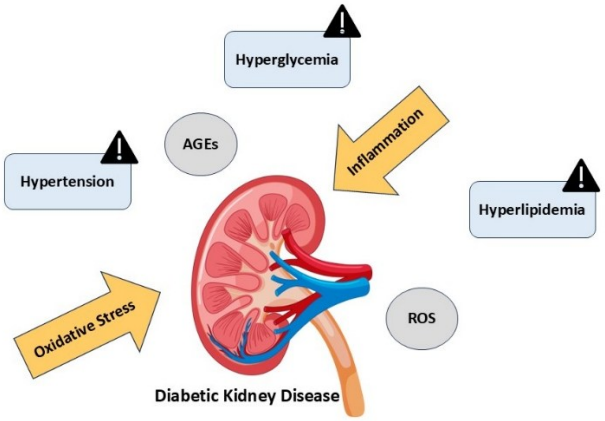

Figure.1. Different factors contribute to the pathogenesis of diabetic kidney disease—the central role of inflammation and oxidative stress. Abbreviations: AGEs, advanced glycation end products; ROS, reactive oxygen species.

5. Inflammatory/Anti-inflammatory Diet

5.1. Dietary Inflammatory Index

The Dietary Inflammatory Index (DII) was created to offer a measurable way to evaluate how diet affects health outcomes, which can include everything from levels of inflammatory cytokines in the blood to various chronic diseases (11). DII shows how much a diet is inflammatory or anti-inflammatory; a higher DII shows the more pro-inflammatory aspects of a diet. An analysis of 2712 subjects indicated that higher DII was associated with a higher risk of DKD in patients with diabetes (12). In a study on 7974 diabetic individuals, patients in second and third tertiles of DII had an increased frequency of CKD (13). A cross-sectional study on 4264 diabetic patients showed that higher DII increased the risk of DKD (14). Another cross-sectional study on 2644 females found that there was an inverse association between E-DII (DII that is adjusted for energy) and eGFR in diabetic females (15). It has been observed that an anti-inflammatory diet, defined as DII less than 0, was associated with higher eGFR in comparison with a pro-inflammatory diet, defined with DII more than or equal to 0, in diabetic patients with CKD, but there were no significant differences between cardiovascular risk factors as well as pulse wave velocity, C-reactive protein (CRP), systolic and diastolic blood pressure, triglycerides, total cholesterol, LDL-cholesterol, HDL-cholesterol, and HbA1C (16).

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5.2. Mediterranean Diet

The Mediterranean diet (MED) is a broad term that refers to the eating habits of people residing in the nations bordering the Mediterranean Sea. This diet mainly emphasizes plant-based foods, with animal-based products primarily limited to fish and poultry and only a small amount of dairy. Food choices within the Mediterranean diet are largely made up of green leafy vegetables, a variety of legumes, and nuts, along with fresh fruits and whole grains. Olive oil, which consists of monounsaturated fat and contains alpha-linoleic acid—an essential omega-3 fatty acid- serves as a fundamental part of this diet (17).

In a case-control study on women, it has been shown that higher adherence to MED could reduce the odds of diabetic nephropathy to 76% (18). Also, another study on the mentioned subjects showed that high and moderate adherence to the Med diet was associated with 86% and 62% reduction of DN risk respectively (19). In another longitudinal study, lower levels of MDS were associated with diminished kidney function and a decrease in health-related quality of life but did not correlate with other indicators of cardiovascular risk factors (20). Results of a cross-sectional study revealed that higher adherence to MED did not have any significant association with biomarkers of renal function, including creatinine, BUN, eGFR, and cardiovascular disease indicators, as well as triglyceride, total cholesterol, LDL, HDL, FBG, and HbA1c (21).

6. Dietary Oxidative and Antioxidative Factors

6.1. Dietary Total Antioxidant Capacity

Dietary total antioxidant capacity (DTAC) reflects the overall intake of antioxidants obtained from one's diet (22). Findings from a population study which was conducted on 1179 individuals with dysglycemia showed that after 3 years, higher DTAC was associated with 39% reduction in the risk of CKD (23). However, two other studies found no significant association between DTAC and eGFR (24) or CKD in patients with type 2 diabetes (25). One of them was a cross-sectional study on 240 patients (24), and the other one was a case-control study on 210 patients (25).

6.2. Composite Dietary Antioxidant Index and Dietary Antioxidant Quality Score

In a study on 5676 diabetic patients, it was observed that a higher composite dietary antioxidant index (CDAI) was

associated with a 26% reduction of DKD and a 33% all-cause mortality risk (26) but, the study conducted by Omid et al. could not find any significant association between dietary antioxidant quality score (DAQS) and DAI and kidney function in type 2 diabetic patients (24). It should be mentioned that in the latter study, in addition to vitamin A, vitamin C, vitamin E, zinc, selenium, and carotenoids, magnesium was also considered in the calculation of DAI.

6.3. Oxidative Balance Score

Oxidative Balance Score (OBS) considers BMI, total iron intake, total fat, smoking status, and alcohol consumption status as pro-oxidants and carotenoids, dietary fiber, total folate, riboflavin, niacin, vitamin B6, vitamin B12, vitamin C, vitamin E, calcium, magnesium, copper, selenium, zinc, and physical activity as antioxidants (27). Liu et.al in a cross-sectional study on 5389 diabetic participants, showed that there was a reverse association between OBS and eGFR, albuminuria, and DKD (28).

7. Plant-based Dietary Pattern

In previous studies, it has been shown that vitamins, fatty acids, flavonoids, and antioxidant minerals play a role in reducing inflammation and oxidative stress in DN patients (29). Higher consumption of whole grains, vegetables, fruits, nuts, legumes, fibers, unsaturated fats, and plant-based proteins can be a proper approach in DKD (30). In a study, foods were categorized into three groups: healthy (legumes, nuts, whole grains, fruits, vegetables, vegetable oils, tea/coffee), unhealthy (fruit juices, SSBs, refined grains, sweets or desserts, potatoes), and animal foods. The results of this study indicated that a higher overall plant-based dietary index (PDI) and a higher healthy PDI (hPDI) were associated with a 71% and 70% reduced risk of DN (31). In another study on diabetic patients, higher adherence to a plant-based dietary pattern was associated with a lower risk of kidney disturbances (32).

8. Dietary Approaches to Stop Hypertension (DASH)

The DASH diet promotes the consumption of fruits, vegetables, whole grains, lean proteins, and low-fat dairy while limiting sodium, sugary drinks, and processed foods. Following these dietary guidelines helps individuals reach and sustain healthy blood pressure levels. These food items are generally rich in minerals like potassium, calcium, and magnesium, along with protein and dietary fiber (33). In a case-control study on 210 diabetic women, higher adherence to the DASH diet was associated with reduced risk of DN (34). In another analysis of the mentioned population, it has been shown that high adherence to the DASH 29% lowered the risk of DN but moderate adherence was not associated with the risk of DN (19).

9. Phytochemical Index

The protective role of dietary flavonoids against diabetic nephropathy has been proposed in some studies (35, 36). In a study of 1949 individuals, increased dietary flavonoid intake was associated with reduced odds of DN (37). The “Phytochemical Index” (PI) is characterized as the proportion of dietary calories obtained from foods abundant in phytochemicals. The calories included in this index come from fruits, vegetables (excluding potatoes), legumes, whole grains, nuts, seeds, fruit and vegetable juices, and soy products, as well as wine, beer, and cider, along with any foods made from these items (38). In a study of 210 women with diabetes, higher PI was associated with a lower risk of DN (39).

10. Micronutrient content

The effect of different dietary micronutrients, including vitamins and minerals, on DN prevention or management has been investigated in different studies. In a research conducted on 210 diabetic women, vitamins and minerals were categorized into three groups; higher fat-soluble vitamins and minerals pattern reduced odds of DN by 47% and 49% respectively, while water-soluble vitamins pattern was not associated with the risk of DN (40).

11. Dietary Diversity Score

Kant et al. established the Dietary Diversity Score (DDS) to assess the variety and balance of dietary intakes (41). In a study by Rezazadegan et al., foods were categorized into five main groups: fruits, vegetables, grains, dairy products, and meats. The results of this study showed that higher DDS, fruit, and vegetable adherence were associated with a reduced risk of DN (42).

12. Low-carbohydrate Diet

An analysis of 210 diabetic women showed that higher adherence to a low-carbohydrate diet score (LCD) was associated with a 71% reduced risk of DN (43), while results of a meta-analysis which included 12 trials and 942 individuals, showed that LCD had no significant effect on kidney function biomarkers including eGFR, creatinine clearance, urinary albumin, serum creatinine, and uric acid, but it should be noted that duration of intervention varied widely from 5 weeks to 24 months (44).

13. Conclusion

Diabetic kidney disease (DKD) is a growing concern that significantly impacts the quality of life of individuals with diabetes. It often progresses to end-stage renal disease, necessitating dialysis or kidney transplantation and resulting in substantial medical costs. Managing DKD is a complex challenge, requiring a combination of dietary interventions and medication. Nutritional status is identified as a modifiable factor influencing the development of DKD, emphasizing the importance of preventing malnutrition while adhering to dietary restrictions essential for controlling the condition.

This review highlights that various dietary factors can affect the risk of DKD in patients with diabetes. Different dietary characteristics and their relationship with DKD are summarized in table 1. Higher adherence to anti-inflammatory, antioxidant, Mediterranean, DASH, DDS, and predominantly plant-based dietary patterns may lower the risk of DKD. Figure 2 shows the effect of different healthy dietary patterns on the risk of diabetic kidney disease progression. However, due to some inconsistencies in findings, conducting larger and more comprehensive prospective studies is recommended to establish clearer insights.

Table.1. Summary of different dietary patterns and their relationship with DKD

Dietary Pattern	Author. year	Study design	Study population	Results
Dietary Inflammatory Index (DII)	Rui et.al. 2024	Case-control	2712 subjects	Direct association between DII and DKD risk.
	Guo et.al. 2023	Cross-sectional	7974 diabetic participants	Direct association between DII and frequency of CKD.
	Wang et.al. 2022	Cross-sectional	4264 subjects	Direct linear dose–response association between DII and DKD risk.
	Lin et.al. 2021	Cross-sectional	2644 diabetic and prediabetic women	Direct association between DII and decreased eGFR and arterial stiffness.
	Herbert et.al. 2021	Cross-sectional	241 diabetic participants	Anti-inflammatory group (DII < 0) had a higher eGFR than pro-inflammatory (PID; DII ≥ 0) group.
Mediterranean Diet (MED)	Noori et.al. 2022	Case-control	210 diabetic women	Reverse association between MED and DN.
	Picard et.al. 2021	post-hoc analysis of an RCT	50 patients with type 1 or T2DM and Stage 1-4 CKD	Reverse association between MED and kidney function.
	Moradi et.al. 2020	Cross-sectional	270 DN patients	No significant association between MED and renal function and cardiovascular risk factors.
	Jayedi et.al. 2019	Case-control	210 diabetic women	Reverse association between moderate and high MED score and DN.
Dietary total antioxidant capacity (DTAC)	Omid et.al. 2024	Cross-sectional	240 T2DM patients	No significant association between DTAC and eGFR.
	Abbasi et.al. 2019	Case-control	210 T2DM patients	No significant association between DTAC and CKD in T2DM patients.
	Asghari et.al. 2018	prospective population-based study	1179 individuals with dysglycemia	Reverse association between DTAC and risk of incident CKD
Composite dietary antioxidant index (CDAI)	Zhang et.al. 2023	Prospective study	5676 DM patients	Reverse association between CDAI and DKD and all-cause mortality.
	Omid et.al. 2024	Cross-sectional	240 T2DM patients	No significant association between DAI and eGFR.
Dietary antioxidant quality score (DAQS)	Omid et.al. 2024	Cross-sectional	240 T2DM patients	No significant association between DTAC and eGFR.
Oxidative balance score (OBS)	Liu et.al. 2024	Cross-sectional	5389 T2DM patients	Reverse association between OBS and albuminuria, DKD, and decreased eGFR.
Plant-based dietary patterns	Mirzababaei et.al. 2024	Case-control	210 T2DM women	Reverse association between overall PDI and healthy PDI and DN risk.
	Ding et.al. 2024	Cross-sectional	1522 diabetic patients	Reverse association between plant-base dietary pattern and renal impairment.
Dietary Approaches to Stop Hypertension (DASH)	Mirzababaei et.al. 2023	Case-control	210 T2DM women	Reverse association between DASH and DN risk.
	Jayedi et.al. 2019	Case-control	210 diabetic women	Reverse association between high adherence to the DASH and DN.
Dietary flavonoid intake	Liu et.al. 2023	Cross-sectional	1949 individuals	Reverse association between dietary flavonoid intake and DN risk.
Phytochemical index (PI)	Bahrampour et.al. 2023	Case-control	210 T2DM women	Reverse association between PI and DN risk.

Micronutrient pattern	Bahrampour et.al. 2023	Case-control	210 T2DM women	Reverse association between fat-soluble vitamins and mineral pattern and DN risk. No significant association between water-soluble vitamin pattern and DN risk.
Dietary Diversity Score (DDS)	Rezazadegan et.al. 2022	Case-control	210 T2DM women	Reverse association between DDS and DN risk.
Low-carbohydrate diet (LCD)	Hajishirazi et.al. 2023	Case-control	210 T2DM women	Reverse association between LCD and DN risk.
	Suyoto et.al. 2018	Meta-analysis of 12 controlled trials	942 T2DM participants	No significant effect of LCD on renal function markers.

Abbreviations: CDAI, Composite Dietary Antioxidant Index; DAQS, Dietary Antioxidant Quality Score; DASH, Dietary Approaches to Stop Hypertension; DDS, Dietary Diversity Score; DII, Dietary Inflammatory Index; DKD, Diabetic Kidney Disease; DN, Diabetic Nephropathy; DTAC, Dietary Total Antioxidant Capacity; eGFR, estimated Glomerular Filtration Rate; LCD, Low-carbohydrate diet; MED, mediterranean diet; OBS, Oxidative Balance Score; PDI, Plant-based dietary index; PI, Phytochemical Index.

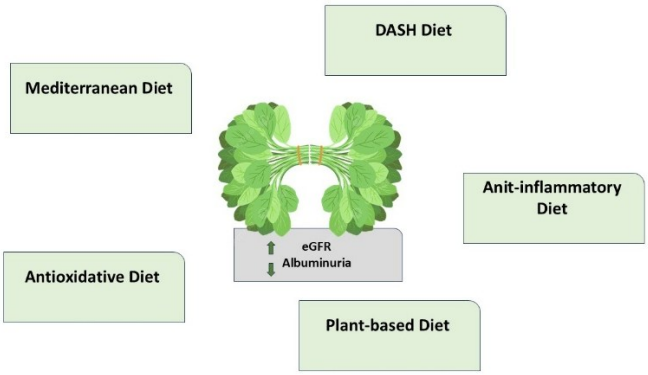

Figure.2. Effect of different healthy dietary patterns on the risk of diabetic kidney disease progression. They are associated with reduced albuminuria, increased eGFR, improved biomarkers of renal function, and lower risk of DKD.

14. Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

14. Conflict of interest

The authors declare no conflict of interest.

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