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Dietary Fiber Intake and Its Association with Diabetic Kidney Disease in US Adults with Diabetes: A Cross-Sectional Study

Dietary Fiber and Diabetic Kidney Disease

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Abstract

BACKGROUND

Dietary fiber (DF) intake may have a protective effect against type 2 diabetes (T2D); however, its relationship with diabetic kidney disease (DKD) remains unclear.

AIM

To investigate the potential association between DF intake and the prevalence of DKD in individuals diagnosed with T2D.

METHODS

This cross-sectional study used data from the National Health and Nutrition Examination Survey (NHANES) collected between 2005 and 2018. DF intake was assessed through 24-hour dietary recall interviews, and DKD diagnosis in individuals with T2D was based on predefined criteria, including albuminuria, impaired glomerular filtration rate, or a combination of both. Logistic regression analysis was used to assess the association between DF intake and DKD, and comprehensive subgroup and sensitivity analyses were performed.

RESULTS

Among the 6,032 participants, 38.4% had DKD. With lower DF intake—T1 (≤ 6.4 g/1000 kcal/day)—as a reference, the adjusted odds ratio for DF and DKD for levels T2 (6.5-10.0 g/1000 kcal/day) and T3 (≥ 10.1 g/1000 kcal/day) were 0.97 (95%CI: 0.84-1.12, $P = 0.674$) and 0.79 (95%CI: 0.68-0.92, $P = 0.002$), respectively. The subgroup analysis yielded consistent results across various demographic and health-related subgroups, with no statistically significant interactions (all $P > 0.05$).

CONCLUSION

In US adults with T2D, increased DF intake may be related to reduced DKD incidence. Further research is required to confirm these findings.

Key Words: Dietary fiber; Diabetic kidney disease; Type 2 diabetes; National Health and Nutrition Examination Survey (NHANES); Cross-sectional study

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Core Tip: This cross-sectional analysis of NHANES data, spanning 2005 to 2018, explored the potential correlation between dietary fiber (DF) intake and the prevalence of diabetic kidney disease (DKD) in individuals diagnosed with type 2 diabetes (T2D). The study, which involved 6032 participants, reveals that higher DF intake, particularly in the tertile with ≥ 10.1 g/1000 kcal/day, is associated with a statistically significant reduction in DKD incidence. These findings suggest a potential protective effect of increased DF intake against DKD in adults with T2D in the United States. Further investigation is warranted to corroborate these observations.

INTRODUCTION

Diabetes is a collective term for ¹metabolic disorders characterized by hyperglycemia stemming from deficiencies in insulin secretion, insulin action, or both^[1]. With the continuous expansion of the global economy and improved life expectancy, the prevalence of diabetes has increased. According to data from the International Diabetes Federation Diabetes Atlas, an estimated 783.2 million individuals aged 20–79 years worldwide will be living with diabetes by 2045^[2]. Diabetic kidney disease (DKD) is a complication associated with prolonged diabetes that affects approximately 40% of individuals with type 2 diabetes (T2D) and is ¹¹one of the most prevalent diabetic complications^[3]. DKD markedly increases the risk of cardiovascular events and progression to end-stage renal disease^[4,5], culminating in the need for dialysis or renal transplantation. Existing therapeutic approaches offer only symptomatic relief and cannot impede the progression of DKD into chronic kidney disease (CKD)^[6]. Therefore, delaying or ameliorating the onset and progression of DKD is crucial.

Dietary fiber (DF) is a composite material composed of indigestible carbohydrates and lignin and resists degradation in the upper gastrointestinal tract. Their primary sources are whole grains, fruits, vegetables, and legumes^[7]. Previous studies have highlighted the multifaceted advantages of DF, including its ability to modulate blood glucose ^[8,9] and lipid levels^[9], enhance insulin sensitivity^[10], ameliorate inflammatory responses^[9], reduce the onset of diabetes^[11–13], and lower the prevalence of cardiovascular diseases^[14,15] and CKD^[16]. However, large-scale studies assessing the association between DF intake and the incidence of DKD in diabetic populations are lacking. Therefore, the current study aimed to investigate whether a higher DF intake reduces the occurrence of DKD in individuals with T2D.

MATERIALS AND METHODS

Study design and participants

The National Health and Nutrition Examination Survey (NHANES) was designed to assess the health and nutritional status of both adults and children in the United States.

This program employed a comprehensive approach that combined structured interviews and physical examinations to amass extensive datasets. NHANES operates under the National Center for Health Statistics (NCHS), in partnership with the United States Department of Agriculture, which is responsible for the compilation and dissemination of dietary and nutritional data. Prior to participating in this survey, all NHANES participants provided written informed consent, and the study was approved by the NCHS Institutional Review Board^[17]. The survey included intricate measurements, standardized interviews, and laboratory assessments to gather information related to demographics, dietary habits, physical parameters, laboratory diagnostics, and health-related parameters.

This cross-sectional investigation draws from data acquired from NHANES surveys conducted between 2005 and 2018. For more comprehensive details, individuals can access the NHANES resources *via* www.cdc.gov/nchs/nhanes. The current analysis included participants aged 20 years and older who had completed both structured questionnaire surveys and rigorous laboratory examinations. Pregnant women and individuals with missing critical variables were excluded from the analysis.

Dietary fiber intake

All NHANES participants were eligible to undergo two 24-hour dietary recall interviews. The first dietary recall interview took place at the Mobile Examination Center, and the second interview occurred *via* telephone three to ten days later. To ensure the integrity and availability of raw data, data from the first 24-hour dietary recall were utilized. Recognizing that total calorie intake may influence dietary data, the data for DF and protein intake used in this study were adjusted for total calorie intake.

Diagnosis of type 2 diabetes and diabetic kidney disease

The diagnosis of T2D was based on the criteria established by the ADA^[18] and self-reported questionnaires. Participants were classified as having T2D if they met any of the following conditions: (1) a documented previous diagnosis by a medical practitioner; (2) current utilization of insulin or oral hypoglycemic medications; (3) fasting plasma glucose (FPG) ≥ 7.0 mmol/L; (4) glycosylated hemoglobin (HbA1c) \geq

6.5%; or (5) plasma glucose ≥ 11.1 mmol/L 2 h post oral glucose tolerance test. The diagnosis of DKD in patients with T2D was established when the albumin-to-creatinine ratio (ACR) exceeded 30 mg/g and/or the estimated glomerular filtration rate (eGFR) fell below 60 mL/min/1.73 m²^[19]. ACR was computed by assessing the urine albumin-to-urine creatinine ratio, whereas eGFR was determined using the Chronic Kidney Disease Epidemiology Collaboration algorithm^[20].

Other potential variables

The current study examined variables that could influence the association between DF intake and DKD. These variables included age, sex, race/ethnicity, educational level, marital status, family income, body mass index (BMI), smoking status, daily calorie and protein intake, dietary supplement usage, history of coronary heart disease (CHD), hypertension, family history of diabetes, age at initial diabetes diagnosis, insulin and glucose-lowering drug utilization, blood pressure, and various laboratory tests including HbA1c, fasting plasma insulin (FINS), FPG, total cholesterol (TC), alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum uric acid (SUA), blood urea nitrogen (BUN), serum creatinine (sCr), hemoglobin, urine albumin, and urine creatinine. Race/ethnicity was categorized into non-Hispanic white, non-Hispanic black, Mexican American, or other ethnic groups. Educational level was stratified by the number of years of completed education as follows: < 9 years, 9–12 years, and > 12 years. Marital status was classified as being married, living with a partner, or living alone, based on questionnaire responses. Family income was determined using the family poverty income ratio and categorized as low (≤ 1.3), medium (1.3–3.5), and high (> 3.5) income levels^[17]. Smoking status was divided into three categories: never smoked, former smoker, and current smoker. Never-smokers were individuals who had smoked < 100 cigarettes in their lifetime. Former smokers were defined as those who had smoked more than 100 cigarettes in their lifetime but were not currently smoking. Current smokers were defined as individuals who had smoked at least 100 cigarettes in their lifetime and were currently smoking. The use of dietary supplements was defined as the use of dietary supplements or medications in the past month. The diagnosis of

CHD was ascertained through a questionnaire item inquiring about prior diagnosis of CHD. The diagnosis of hypertension included systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg, self-reported diagnosis with hypertension, or being informed about hypertension on two or more occasions. A family history of diabetes was determined through questions concerning close relatives with diabetes. The duration of diabetes was calculated by subtracting the age at initial diagnosis with diabetes from the age at time of the interview. Those diagnosed within the last year were categorized as having diabetes for half a year. The use of insulin- and glucose-lowering drugs was determined based on specific questionnaire responses. BMI was calculated using height and weight measurements. The homeostasis model assessment of insulin resistance (HOMA-IR), employed to evaluate insulin resistance (IR), was calculated using the formula $\text{HOMA-IR} = \text{fasting plasma insulin } (\mu\text{U/mL}) \times \text{fasting plasma glucose (mmol/L)} / 22.5^{[21]}$. Further details regarding the measurement techniques used for these variables are available at www.cdc.gov/nchs/nhanes/.

Statistical analysis

Data analyses were conducted using R Statistical Software (<http://www.R-project.org>, The R Foundation) and the Free Statistics analysis platform (Beijing, China). Continuous variables are presented as means \pm standard deviations (SD) or medians (interquartile range), while categorical variables are reported as frequencies or percentages. To compare baseline characteristics between groups based on DF intake, independent t-tests were used for continuous variables, and chi-square tests were used for categorical variables. Univariate logistic regression analysis was performed to explore the relationship between the potential factors and DKD. Subsequently, a multivariate logistic regression analysis was performed to ascertain the association between DF intake and DKD. Model 1 was adjusted for age, sex, race/ethnicity, educational level, marital status, and family income. Model 2 incorporated all the covariates from Model 1 and included additional adjustments for smoking status, CHD, hypertension, and daily calorie and protein consumption. Model 3 extended the adjustments to encompass the duration of diabetes; insulin usage; and HbA1c, HOMA-IR, TC, ALT, SUA, and

hemoglobin levels. To explore the potential nonlinear relationship between DF intake and DKD, restricted cubic splines (RCS) were applied while controlling for all covariates in the full model (Model 3). Subgroup analyses were conducted by stratifying the data into five subgroups based on age (20–60 years *vs* ≥ 60 years), sex (male *vs* female), BMI ($< 25 \text{ kg/m}^2$ *vs* $\geq 25 \text{ kg/m}^2$), HbA1c level ($< 7.0\%$ *vs* $\geq 7.0\%$), and eGFR level ($< 90 \text{ mL/min/1.73 m}^2$ *vs* $\geq 90 \text{ mL/min/1.73 m}^2$). Additionally, this study explored the interactions between DF intake and these factors. To ensure the robustness of the findings, the relationship between DF intake and DKD was re-examined after excluding extreme energy intake values ($< 500 \text{ kcal/day}$ or $> 5000 \text{ kcal/day}$). To address missing data, multiple imputation techniques were employed to fill existing gaps and facilitate a comprehensive analysis.

RESULTS

Study population

This study included 70190 participants from NHANES 2005–2018, of whom 39749 were aged 20 years or older. However, the study excluded pregnant women ($n = 708$), individuals with missing ACR and eGFR data ($n = 4476$), those lacking dietary data ($n = 2150$), and those who did not meet the diagnostic criteria for T2D ($n = 26383$). This resulted in a final sample size of 6032 participants, of which 2316 were diagnosed with DKD. The inclusion and exclusion criteria are shown in Figure 1.

Baseline characteristics

Table 1 presents the baseline characteristics of all the participants categorized into tertiles based on their DF intake. In total, 2316 (38.4%) patients had DKD. The average age of the study participants was 61.1 years, and 2892 (47.9%) were female. Individuals who consumed more DF tended to be older, female, Mexican American, married, living with a partner, or a never smoker, or have a lower educational level, lower BMI, lower daily calorie consumption, and higher protein consumption. Moreover, this group was more likely to use dietary supplements and glucose-lowering drugs and had a

longer duration of T2D. Notably, they displayed lower levels of FINS, HOMA-IR, TC, SUA, sCr, hemoglobin, and diastolic blood pressure.

Relationship between dietary fiber intake and diabetic kidney disease

Univariate analysis revealed that age; race/ethnicity; educational level; marital status; family income; smoking status; CHD; hypertension; daily calorie and DF consumption; duration of diabetes; insulin usage; and levels of HbA1c, FPG, HOMA-IR, TC, ALT, SUA, and hemoglobin were associated with DKD (Table 2).

To ascertain the independent association between DF intake and DKD, multivariate analyses were performed with adjustments in the three models. As indicated in Table 3, DF intake and DKD were inversely related, with an adjusted OR value of 0.97 (95% CI: 0.96-0.98, $P < 0.001$). Compared with individuals with a lower DF intake belonging to Tertile 1 (T1, ≤ 6.4 g/1000 kcal/day), the unadjusted OR values for DF intake and DKD in Tertile 2 (T2, 6.5-10.0 g/1000 kcal/day) and Tertile 3 (T3, ≥ 10.1 g/1000 kcal/day) were 0.97 (95% CI: 0.84-1.12, $P = 0.674$) and 0.79 (95% CI: 0.68-0.92, $P = 0.002$), respectively. Accordingly, the relationship between DF intake and DKD exhibited an inverse linear pattern (nonlinear, $P = 0.814$) in RCS analysis (Supplementary Figure 1).

Subgroup analysis

The association between DF intake and DKD was consistent across multiple subgroups. As illustrated in Figure 2, no significant interaction was detected in any subgroup after stratification by age, sex, BMI, HbA1c level, or eGFR ($P > 0.05$).

Sensitivity analysis

After excluding individuals with extreme energy intake, 5910 individuals remained, and the association between DF intake and DKD was stable. Compared with individuals with a lower DF intake, T1 (≤ 6.4 g/1000 kcal/day), the unadjusted OR values for DF intake and DKD in T2 (6.5-10.0 g/1000 kcal/day), and T3 (≥ 10.1 g/1000 kcal/day) were 1.00 (95% CI: 0.86-1.16, $P = 0.996$), and 0.82 (95% CI: 0.70-0.96, $P = 0.011$), respectively (Supplementary Table 1).

DISCUSSION

This cross-sectional study of adults with T2D in the United States revealed an inverse correlation between DF intake and the occurrence of DKD. Higher intake of DF may be associated with a reduced incidence of DKD. Subgroup and sensitivity analyses further reinforced the stability of these findings.

Numerous studies have highlighted the potential benefits of increasing DF intake in reducing the incidence of diabetes. A seven-year prospective study discovered that individuals with lower total DF intake were more susceptible to developing diabetes^[11]. Additionally, an analysis of multiple prospective cohort studies supported the association between increased daily intake of cereal fiber and decreased risk of T2D^[12]. The potential protective effects of DF intake against diabetes may be linked to its ability to enhance blood sugar control, regulate lipid levels, manage body weight, and modulate inflammatory responses^[9]. These effects were also observed in the present study. The high DF intake group exhibited lower FINS, HOMA-IR, TC, and BMI.

Research indicates that the protective effects of cereal fibers against diabetes may be attributed to their modulation of the gut microbiota through various mechanisms, including the enhancement of glucose tolerance, reduction of inflammation, and alteration of immune responses¹² via energy metabolism pathways such as colonic fermentation and production of short-chain fatty acids (SCFAs)^[22]. DF serves as the primary energy source for most gut microbiota and undergoes fermentation in the intestine, resulting in the production of active intestinal metabolites called SCFAs such as butyrate, propionate, and acetate^[23]. Studies have revealed a deficiency in SCFAs, particularly butyrate, in the gut of individuals with T2D^[24]. This insufficiency is predominantly ascribed to alterations in the composition of the gut microbiota, resulting in diminished production of SCFAs^[25]. In a randomized controlled trial, Zhao *et al* identified a distinct cohort of SCFA producers that contributed to the amelioration of T2D through augmented SCFA production^[24]. Notably, an increase in DF intake can modulate the generation of SCFA metabolites^[24]. Inflammation and fibrosis play pivotal roles in the pathophysiology of DKD. Significantly, discernible differences exist in the abundance and composition of the gut microbiota between individuals with DKD and

healthy controls [26]. Research suggests that the gut microbiota may affect DKD development by modulating endocrine functions and the composition of microbial metabolic byproducts within the gut[27]. Notably, SCFAs derived from the gut microbiota can regulate inflammation, oxidative stress, fibrosis, and energy metabolism, thus offering preventive and therapeutic potential in DKD[6]. Experimental evidence indicates a notable decrease in DKD incidence in diabetes-induced animals fed a high-fiber diet, emphasizing the potential renoprotective role of DF. This protective effect is attributed to its capacity to reshape the gut microbiota ecology, mitigate dysbiosis, and stimulate the proliferation of SCFA-producing bacteria. Consequently, SCFA concentrations increase, exerting a protective effect against DKD through the GPR43 and GPR109A pathways[28,29]. Simultaneously, *in vitro* experiments have suggested that SCFAs modulate inflammatory responses in renal tubular cells and podocytes under hyperglycemic conditions[29]. Butyrate, a SCFA, may alleviate renal inflammation and fibrosis in mice through various pathways[30,31], thereby mitigating DKD. Furthermore, research indicates that SCFAs enhance autophagic capability in renal tubular cells of diabetic mice through the histone deacetylase (HDAC2)/unc-51 Like autophagy-activating kinase 1 (ULK1) axis, thus alleviating renal fibrosis[32]. The correlation between the gastrointestinal system and the kidneys is called the “gut-kidney axis”[33]. These studies underscore the significance of gut microbiota in DKD, highlighting the interplay between DF, gut microbiota, SCFAs, and renal health.

To the best of our knowledge, this is the first study to investigate the correlation between DF intake and DKD in a large cohort of patients with T2D. However, the current study had certain limitations. First, akin to most cross-sectional investigations, it can only delineate an association between DF consumption and DKD but cannot establish causation. Second, the data on DF intake relied on 24-hour dietary recall information from the NHANES, which may be susceptible to recall bias. Third, distinct sources of DF may have different effects. Unfortunately, specific data about the sources of DF consumption in NHANES were not obtained. Future studies should consider including these factors. Finally, the current investigation focused on the adult

population with diabetes in the United States. To address this limitation, we aim to validate current findings in future studies that include a more diverse population.

CONCLUSION

In an adult population with T2D in the United States, elevated DF intake may be associated with a decreased incidence of DKD. However, further research is required to confirm this hypothesis.

ARTICLE HIGHLIGHTS

Research background

This study focused on the relationship between dietary fiber (DF) intake² and diabetic kidney disease (DKD) in individuals with type 2 diabetes (T2D). The prevalence of T2D is increasing globally. The protective effect of DF against T2D is acknowledged, but its specific impact on DKD remains unclear. DKD poses a substantial health burden, underscoring the importance of investigating modifiable factors such as DF intake for potential preventive strategies.

Research motivation

The main topics driving this research included understanding the potential protective role of DF against DKD, a complication frequently associated with T2D. Key problems to be addressed include the lack of conclusive evidence on the DF-DKD relationship and the need for targeted interventions to mitigate DKD risk in T2D patients. Solving these problems is crucial for future research on diabetes management and the prevention of kidney disease.

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Research objectives

The primary objective of this study was to investigate the association between DF intake and the prevalence of DKD in T2D individuals. Realizing these objectives contributes to filling gaps in the current knowledge regarding the role of DF in DKD prevention,

providing insights for future research to refine dietary recommendations for individuals with T2D.

Research methods

5

This study employed a cross-sectional design utilizing National Health and Nutrition Examination Survey (NHANES) data collected between 2005 and 2018. DF intake was assessed through 24-hour dietary recall interviews, and DKD diagnosis was based on predefined criteria, including albuminuria and impaired glomerular filtration rate. This study employed various statistical methods including multiple regression models, restricted cubic splines, stratified analysis with interactions, and sensitivity analysis.

Research results

Of the 6032 participants, 38.4% presented with DKD. The study reveals a significant association between higher DF intake and reduced odds of DKD, particularly in the highest intake tier (T3: ≥ 10.1 g/1000 kcal/day).

Research conclusions

This study proposes that an increased DF intake is associated with a reduced incidence of DKD in adults with T2D. These findings contribute to the field by suggesting potentially modifiable factors for DKD prevention of T2D in individuals.

Research perspectives

Future research should delve deeper into the mechanisms underlying this observed association and explore the feasibility of dietary interventions to prevent or manage DKD in T2D patients. Additionally, longitudinal studies are warranted to establish causality and inform evidence-based dietary guidelines for individuals with T2D at risk of DKD.

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