

The Dietary Inflammatory Index Is Associated With Diabetes Severity

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Objective: The Dietary Inflammatory Index (DII) is a recently developed dietary inflammation assessment tool. The current study examined the association between DII and the presence and severity of diabetes in adults age ≥ 20 years.

Research Design and Methods: Cross-sectional analysis of 4434 adult participants in the National Health and Nutrition Examination Survey (NHANES 2013 to 2014). The DII was calculated based on 24-hour dietary recall data. Linear and logistic regression models were used to estimate the relationship and control for possible confounding factors.

Results: Among 4434 participants, mean age was 49.4 years, mean BMI (body mass index) was 29.3 kg/m², and mean DII (higher is more inflammatory) was 0.65 (range, -3.41 to +9.05). The mean DII scores in participants with and without diabetes were 0.79 and 0.50, respectively ($P = .0098$). Participants with Hemoglobin A1c (HgbA1c) $>9\%$ had higher DII scores than those with 6.5% to 9% HgbA1c (1.37 vs 0.54, $P = .0002$) and those with $<6.5\%$ HgbA1c (1.37 vs 0.50, $P < .0001$). With 1 point increase in the DII score, odds of having diabetes increased by 13% (95% CI, 1.02 to 1.24). Among the individuals with diabetes, we also observed a significant association between severity of diabetes and DII scores; with 1 point increase in DII score, the odds of having HgbA1c higher than 9% increased by 43% (95% CI, 1.21 to 1.68).

Conclusions: The DII had a significant association with diabetes and a stronger association when HgbA1c $>9\%$. Further research will help clarify the association between inflammation and diet and the utility of the DII as a tool in risk assessment and management of patients with diabetes. (J Am Board Fam Med 2019;32:801–806.)

Keywords: Biomarkers, Body Mass Index, Cross-Sectional Studies, Diabetes Mellitus, Diet, Inflammation, Logistic Models, Nutrition Surveys, Risk Assessment

The Dietary Inflammatory Index (DII) has emerged as a possibly important tool in assessing diet quality and inflammation in the setting of high-

risk medical conditions. The DII is a measure derived from analysis of multiple databases to measure the impact of 45 specific types of food on inflammatory biomarkers including IL-1 β , IL-4, IL-6, IL-10, TNF- α , and C-reactive protein (CRP).¹ Following the initial study that described the DII, subsequent studies have explored the association of the DII and a variety of chronic medical conditions, including chronic kidney disease,² cardiovascular disease,³ depression,⁴ and metabolic syndrome.⁵

Diabetes has not been studied extensively in relation to the DII, but it represents an important medical condition that has been associated with inflammation^{6–9} and diet^{10–12} in a variety of studies. Determining further information about the DII and diabetes could facilitate its use in the clinical setting, and might provide a tool for the assessment of the risk of diabetes. However, there has been

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limited experience in studying the association of the DII and diabetes.

The goal of this study was to evaluate the relationship between DII and the presence of diabetes in a nationally representative sample of adults in the U.S population. A second goal was to explore the relationship between DII and the severity of diabetes.

Methods

Study population

The present study was a retrospective cross-sectional study using data from the continuous National Health and Nutrition Examination Survey (NHANES 2013 to 2014). The NHANES is a series of complex and multistage surveys, conducted by the National Center for Health Statistics (NCHS), designed to assess the health and nutritional status of the noninstitutionalized US population. Since 1999, the continuous NHANES¹³ collected demographic, socioeconomic, dietary, and health-related information through 2 components, an in-home interview and a medical examination, on selected participants in 2-year cycles. Informed consents were obtained from all participants and the protocol for conducting the NHANES survey was approved by the NCHS Research Ethics Review Board. Details on survey design and response rate can be found on the NHANES Web site.¹³ Analyses for this study were limited to adults ≥ 20 years of age (the customary classification cutoff in the NHANES) with nonmissing information for variables of interest. The NHANES uses ≥ 20 years as the cutoff for adults, and we have used it to be consistent with many previous NHANES studies. The focus of the study was adults with diabetes because the role of inflammation in diabetes, while well established in adults, is not as well established in children.¹⁴ West Virginia University Institutional Review Board approved this study to be exempt.

Definition of Nondiabetes, Prediabetes, Diabetes, and Severe Diabetes

To define diabetes status of a participant, we followed the guideline from the American Diabetes Association using measured HgbA1c as a diagnostic criterion: without diabetes treatments, participants with HgbA1c less than 5.7%, between 5.7% to 6.4%, or 6.5% or greater would be categorized as

having no diabetes, prediabetes, or diabetes respectively; 9% or greater HgbA1c would be defined as having severe diabetes.¹⁵ We also added those people who answered positively to the question, "Were you told by a doctor that you have diabetes?" to identify additional individuals with diabetes.

The DII and NHANES 2013 to 2014

The DII is a tool, created to examine the inflammatory potential of individuals' diets. A description of the design and development of the original DII can be found elsewhere.¹

The current study incorporated the latest version of DII, which represents an improved scoring algorithm based on extensive review of the literature and a world food consumption data from several countries.¹⁶ Briefly, a total of 45 food parameters (types of food and nutrients) derived from dietary data were assigned inflammatory effect scores based on the research findings from 1943 selected articles, examining the role of the food parameters on the 6 established inflammatory biomarkers (IL-1 β , IL-4, IL-6, IL-10, TNF-a, and C-reactive protein), published from 1950 to 2010. World food consumption data, based on 11 diverse populations around the world, was used to generate a mean and standard deviation for each food parameter. An individual's diet was then linked to the world food database as a z-score, calculated by subtracting the "standard global mean" and dividing its standard deviation. This z-score was then converted to a centered percentile score to minimize the risk of "right skewing." The product of the centered percentile score and the respective article generated inflammatory effect score for each food parameter was then summed to create an overall DII score for an individual. A total DII score could be positive or negative. Higher positive DII scores indicate more proinflammatory diets and more negative scores imply more anti-inflammatory diets.

In this study, we utilized a total of 28 out of the 45 food parameters, for which we had dietary intake data available from the 2 24-hour dietary recalls data in the NHANES 2013 to 2014 to calculate DII scores. These parameters include total calories, total fat, saturated fat, monounsaturated fat, polyunsaturated fat, omega-3 fatty acids, omega-6 fatty acids, protein, carbohydrate, fiber, alcohol, cholesterol, niacin, thiamin, vitamin A, vitamin B2, vitamin B6, vitamin B12, vitamin C, vitamin D,

vitamin E, iron, magnesium, selenium, zinc, folic acid, β carotene, and caffeine. We calculated the total DII scores per 1000 calories of food consumed to control for the effect of different amounts of total energy intakes.

Population Covariates

We extracted population characteristics including age, gender, race, BMI (body mass index), physical activity, smoking status, alcohol use, and socioeconomic status (education level, health insurance status) as potential covariates. Age was divided into 3 groups: 20 to 44 years, 45 to 64 years, and 65 years and older. We examined race in 4 race groups of non-Hispanic white, non-Hispanic Black, Hispanic, and Other race, as they are categorized in the NHANES.¹³ There were 4 BMI categories combined as underweight (<18.5 kg/m²), normal (18.5 to 24.9 kg/m²), overweight (25 to 29.9 kg/m²), and obese (≥ 30 kg/m²) based on the Center for Disease Control and Prevention breakdown. Participants' education level was grouped into 2 categories of " $<$ High school" and " \geq High school." Health insurance status was defined as "Yes" for having health insurance and "No" for not having health insurance. Two levels of physical activity were defined as " ≥ 150 " or " < 150 " minutes moderate-intense recreational physical activity per week. Smoking status was coded as "smoke" for current smokers and "not smoke" for current nonsmokers. For alcohol use, the cutoff for "alcohol use" and "no alcohol use" was at least 12 alcohol drinks in the past year.

Statistical Analysis

All analyses in this study were conducted using SAS (version 9.4, 2013, SAS Institute Inc. Cary, NC). To account for the complex survey design (including oversampling, survey nonresponse, and post-stratification), we incorporated 2-year sampling weights and SAS survey analysis procedures following NHANES survey methods and analytic guidelines.¹³

Population characteristics of the study sample were compared across diabetes status using χ^2 test. Regression analyses were performed to determine the differences in DII scores between diabetes status and between the severity levels of diabetes. To examine the relationship between diabetes and DII scores adjusted for all covariates included age, sex, race, socioeconomic status, BMI categories,

alcohol use, smoking status, and physical activity, we estimated multivariable adjusted odds ratios (ORs) using logistic regression models. There were no missing values for DII, and only 108 for HgbA1c. Missing values were addressed by the assumption of missing at random. All tests were 2 tailed, and P-values less than .05 were considered statistically significant.

Results

Based on the inclusion criteria, a total of 4434 subjects, 46.5% men and 53.5% women, were included from NHANES 2013 to 2014 for this study. The percentages of subjects with no diabetes, prediabetes, and diabetes were 59.4%, 26.5%, and 14.1% respectively. As showed in Table 1, subjects who were black, older, nonsmoker, not alcohol user, and having higher BMI, less education, health insurance, and less than 150 minutes exercise per week, were more likely to have diabetes.

Table 2 presents the comparison in mean DII scores between people with no diabetes, prediabetes, and with diabetes. Mean (SD) DII for the whole sample were 0.65 (1.50), with ranges between -3.41 to 9.05 (higher number is more inflammation). The least square means of DII scores for the no diabetes, prediabetes, and diabetes participants were 0.50, 0.50, and 0.79, respectively. The results of the regression analyses indicated that subjects with diabetes had significantly higher DII scores than those without diabetes ($P = .01$) and those with prediabetes ($P = .03$). Among individuals with diabetes, those who had higher HgbA1c ($>9\%$) had higher DII scores than those with lower HgbA1c between 6.5% and 9% (1.37 vs 0.55, $P = .0002$).

After adjusting for age, sex, race, BMI, physical activity, smoking status, alcohol use, and socioeconomic status, we found a significant association between the incidence of diabetes and DII scores (Table 3). With 1 point increment in the DII score, odds of having diabetes increased by 13% (95% CI, 1.02 to 1.24).

We also examined severity of diabetes. Among the individuals with diabetes, we observed a significant association between severity of diabetes and DII scores, using a linear regression and continuous variables for HgbA1c and DII ($P < .04$). For each 1-point increment in DII score, the odds of having HgbA1c higher than 9% increased by 43%

Table 1. Population Characteristics by Diabetes Status in NHANES 2013 to 2014 (N = 4434)

Characteristic	Overall*	No Diabetes (n = 3810), % (95% CI)	Diabetes (n = 624), % (95% CI)	P-Value†
Age (years)				
20 to 44	1862	96.4 (95.2 to 97.5)	3.6 (2.5 to 4.8)	<.0001
45 to 64	1562	86.0 (83.3 to 88.8)	14.0 (11.2 to 16.7)	
65+	1010	78.8 (76.6 to 81.0)	21.2 (19.0 to 23.4)	
Sex, %				
Male	2060	88.4 (86.8 to 89.9)	11.6 (10.1 to 13.2)	.08
Female	2374	89.9 (88.6 to 91.3)	10.1 (8.7 to 11.4)	
Race				
Non-Hispanic white	1988	90.0 (88.7 to 91.1)	10.0 (8.8 to 11.3)	.0005
Non-Hispanic Black	884	85.0 (82.5 to 87.4)	15.0 (12.6 to 17.5)	
Hispanic	979	89.2 (86.7 to 91.7)	10.8 (8.3 to 13.3)	
Other	583	88.4 (85.7 to 91.0)	11.6 (9.0 to 14.3)	
Education				
≥High school	3524	90.1 (88.8 to 91.4)	9.9 (8.6 to 11.2)	<.0001
<High school	847	83.6 (81.3 to 86.0)	16.4 (14.0 to 18.7)	
Health insurance				
Yes	3533	88.3 (87.0 to 89.6)	11.7 (10.4 to 13.0)	.0006
No	896	93.4 (91.2 to 95.6)	6.6 (4.4 to 8.8)	
Physical activity				
≥150 Minutes/week	1400	93.2 (91.3 to 95.2)	6.7 (4.8 to 8.7)	<.0001
<150 Minutes/week	3034	87.0 (86.0 to 88.0)	13.0 (11.9 to 14.0)	
Body mass index				
Underweight (<18.5 kg/m ²)	68	97.9 (94.7 to 100)	2.1 (0.0 to 5.3)	<.0001
Normal (18.5 to 24.9 kg/m ²)	1208	96.4 (95.3 to 97.5)	3.6 (2.5 to 4.7)	
Overweight (25 to 29.9 kg/m ²)	1418	92.3 (91.0 to 93.6)	7.7 (6.4 to 9.0)	
Obese (≥30 kg/m ²)	1707	81.3 (79.3 to 83.3)	18.7 (16.7 to 20.7)	
Smoking				
Yes	833	91.9 (89.7 to 91.2)	8.1 (5.9 to 10.3)	.03
No	3600	88.6 (87.2 to 90.0)	11.4 (10.0 to 12.8)	
Alcohol use				
Yes	3081	90.5 (89.6 to 91.4)	9.5 (8.6 to 10.4)	<.0001
No	1174	83.9 (80.5 to 87.4)	16.1 (12.6 to 19.5)	

NHANES, National Health and Nutrition Examination Survey; CI, confidence interval.

*Unequal sample sizes due to missing values from subjects.

†P-value for comparison of difference in proportion between diabetic and non-diabetic subjects, using χ^2 test.

(95% CI, 1.21 to 1.68). When examining DII and HgbA1c as continuous variables, each 1 point increase in DII score was associated with an increase of 0.03 in HgbA1c ($P = .04$). There was negative correlation (-0.57) between DII scores and dietary fiber intake.

Discussion

The results of the current study demonstrate a significant association between the DII and diabetes, and between the DII and severity of diabetes, with greater inflammation (higher DII) making diabetes and higher diabetes severity more likely.

The results remained significant after adjustment for possible confounders including age, sex, race, BMI, smoking status, alcohol use, physical activity, and socioeconomic status. The odds of having a HgbA1c higher than 9% increased by 43% with a >1.0 DII score toward a more inflammatory diet.

The study is consistent with previous literature on the association of inflammation and diabetes.⁶⁻⁹ Ridker and colleagues,⁶ for example, demonstrated that individuals with elevated levels of the inflammatory biomarker high-sensitivity CRP are at increased risk of mortality and morbidity from diabetes and other conditions, including myocardial

Table 2. Means (Least Square) of Dietary Inflammatory Index (DII) Scores by Diabetes Status and Severity of Diabetes

Diabetes Status	LS Mean	Std Error	P-Value
No diabetes (n = 2634)	0.50 [§]	0.05	.03 [‡]
Pre-diabetes (n = 1176)	0.50 [†]	0.06	
Diabetes (n = 624)	0.79* [†]	0.10	
Severity of Diabetes			
Mild (HgbA1c 6.5% to 9%) (n = 375)	0.55	0.11	.0002 [§]
Severe (HgbA1c > 9%) (n = 94)	1.37	0.14	

The range of the DII scores was -3.41 to 9.05. Positive scores are pro-inflammatory and negative scores are anti-inflammatory.

* $P < .05$ for comparison of difference between non-diabetic and diabetic subjects.

† $P < .05$ for comparison of difference between pre-diabetic and diabetic subjects.

‡ P -value for comparison of mean difference in DII scores between non-diabetic, pre-diabetic, and diabetic subjects using regression analysis.

§ P -value for comparison of difference in DII scores between subjects with different levels of severity of diabetes using regression analysis.

Table 3. Odds Ratio (OR) and 95% CI for the Relation Between the Diabetes Severity and Dietary Inflammatory Index (DII) Scores in NHANES 2013 to 2014

Model	OR	95% CI	P-Value*
Model I [†]	1.13	1.02 to 1.24	.02
Model II [‡]	1.43	1.21 to 1.68	.0003
Model III [§]	1.37	1.27 to 1.46	<.0001
Model IV [¶]	0.99	0.85 to 1.15	.85

CI, confidence interval; DII, Dietary Inflammatory Index; NHANES, National Health and Nutrition Examination Survey.

* P -values from logistic regression analysis for association between diabetes and DII scores, between severity of diabetes and DII scores, adjusted for age, sex, race, health insurance status, education level, BMI, smoking status, alcohol use, and physical activity.

†Model I comparing diabetes to no diabetes.

‡Model II comparing severe diabetes (HgbA1c > 9) to mild diabetes (6.5 ≤ HgbA1c ≤ 9).

§Model III comparing severe diabetes (HgbA1c > 9) to no diabetes.

¶Model IV comparing mild diabetes (6.5 ≤ HgbA1c ≤ 9) to no diabetes.

infarction and stroke. King and colleagues⁸ previously showed in analysis of a national cohort, after controlling for age, race, sex, smoking, length of time with diabetes, insulin, and BMI, that HgbA1c was significantly associated with an increased likelihood of elevated CRP for HgbA1c >9.0% (75 mmol/mol) (OR, 2.15; 95% CI, 1.07 to 4.32). Such results support the findings of the current study that diet-induced inflammation (suggested by a dietary index based on self-reported intake) and diabetes are related, and that a more inflammatory diet

profile is associated with a higher risk of severity of diabetes according to HgbA1c.

More recent studies have provided further support for the association. A recent British study investigated the cross-sectional association between an anti-inflammatory dietary pattern and diabetes in the National Diet and Nutrition Survey¹⁷. A total of 1531 survey members provided dietary data. A regression analysis was used to derive an anti-inflammatory dietary pattern. Overall, 52 survey members had diabetes. The derived anti-inflammatory pattern was inversely related to CRP, and was associated with lower odds of diabetes (adjusted OR for highest compared with lowest quintile: 0.17; 95% CI, 0.04 to 0.73). In research done by Kolovertou and colleagues¹⁸, adherence to a low inflammatory Mediterranean diet was associated with a decreased risk of developing diabetes of 49% (95% CI, 0.30 to 0.88) as well as lower levels of TNF- α , CRP, and IL-6. Wholegrain cereals, fruits and legumes had the greatest predictive ability, which supports the current study finding of a high correlation of the DII and fiber intake (-0.57).

The study has some limitations that should be considered. The time of diabetes diagnosis is not known for the cohort, and the study is cross-sectional, limiting the results to an association and not causality. Further, dietary intake data are limited to 2-day recall of intake, thus misclassification of DII could occur due to memory lapses or that the 24-hour recall of diet is not representative of the person's overall diet. However, 24-hour recall of di-

etary intake as a method of collecting diet history is considered a reasonable estimate for populations.¹⁹ In addition, one third of the DII parameters were missing from the NHANES database. However, the DII is based on a global database of foods, while the foods included in the NHANES are the common foods consumed in the United States. The strengths of the study include a national sample and the consistency of results when controlling for possible confounding factors.

In conclusion, the implications of the current study are consistent with previous research regarding the importance of inflammation in the diet as a factor in diabetes and its severity. A higher DII score for higher inflammation was associated with a higher likelihood of diabetes and severe diabetes (>9% HgbA1c). Further research is needed to determine whether the DII tool could be useful in practice, and whether a diet that specifically targets the DII parameters could be used to reduce the development of diabetes or its severity.

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