Diet Quality and Kidney Outcomes in Adolescent and Adult American Indians: The Strong Heart Family Study

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Abstract

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Background: The burden of chronic and end stage kidney disease (CKD and ESKD) is exceedingly high amongst American Indians (AI). We sought to examine the relationship of diet quality, a modifiable risk factor, and kidney outcomes in AI adolescents and young adults, hypothesizing that healthier diets are associated with lower odds of incident albuminuria and eGFR decline in this population.

Methods: This is a secondary analysis of data from the Strong Heart Family Study, a longitudinal study of cardiovascular disease and its risk factors among AIs from Arizona, North and South Dakota, and Oklahoma (n=1721, mean age 39 +/- 16 years, 16% adolescents 14-21 years old, 61% female, 28% with hypertension, 13% with diabetes, 52% with obesity, 4% with CKD at baseline). Participants completed two exams (baseline: 2001-2003; follow-up: 2007-2009). The primary exposure (at baseline) was the Alternative Healthy Eating Index 2010 (AHEI), a measure of diet quality on a 110-point scale (assessed using a 119-item Block food frequency questionnaire). The primary outcomes (at follow-up) were: 1) incident albuminuria (albumin to creatinine ratio 30mg/g or greater); 2) eGFR decline of 30% or greater. Generalized estimating equations were used to examine the association of AHEI (in quartiles) with incident albuminuria and eGFR decline.

Results: In total, 10% of participants (6% of adolescents) had incident albuminuria and 6% of participants (10% of adolescents) had eGFR decline of 30% or greater. Median AHEI for the least healthy diet quartile was 34 compared to 56 for the healthiest diet quartile. For those with normal fasting glucose levels, the odds ratio (OR) for incident albuminuria comparing extreme quartiles of diet quality (least healthy [reference] versus healthiest quartiles) was 0.48 (95%CI 0.28, 0.81) after adjustment for demographics and comorbidities.

Discussion: These results suggest an association of diet quality and incident albuminuria in AI with normal fasting glucose levels. Given the high burden of CKD in this population, further research is required to determine whether interventions to improve diet quality may improve kidney outcomes, particularly in those with normal fasting glucose levels such as adolescents and young adults.

Background and Significance

The burden of end stage kidney disease (ESKD), defined as requiring dialysis or kidney transplant, largely secondary to diabetes mellitus is exceedingly high amongst American Indians (AI).[1,2] Furthermore, there are gross racial disparities in the prevalence of diabetes and ESKD in AIs.[2–4] In 2018, the prevalence of ESKD among AIs compared to white people was 3,163 vs 1,704 per million respectively.[3] The prevalence of chronic kidney disease (CKD) amongst AIs, which can ultimately progress to ESKD, is unknown, but estimated to be as high as double that of the national average.[5]

Given the disproportionate impact of CKD and ESKD in AIs, it is important to better understand potential modifiable risk factors for CKD and ESKD, including diet. Multiple studies suggest a healthy diet is associated with a lower incidence of CKD[6–10] and albuminuria[6,11–13] when compared to those whose diet is less healthy. Furthermore, a healthy diet is associated with less estimated glomerular filtration rate (eGFR) decline in some cohorts.[12,14] Unfortunately, to date, most studies comprised older white adults, and whether findings are generalizable to younger and/or non-white populations is unclear. To date, there are no studies examining the relationship of diet and CKD or kidney function amongst AI young adults or adolescents.

The purpose of this study is to examine the relationship of diet quality and kidney function in AI adolescents and adults who participated in the Strong Heart Family Study. We hypothesize a healthier diet will be associated with lower odds of kidney dysfunction such as albuminuria and eGFR decline when compared to a less healthy diet.

Methods

Data Source and Study Design: The Strong Heart Family Study (SHFS) is a longitudinal study of cardiovascular disease (CVD) and its risk factors among AI from 12 communities in Arizona, North Dakota, South Dakota and Oklahoma. The SHFS comprised 2 examinations over 8 years: a baseline exam occurred during 2001-2003 and a follow-up exam occurred during 2007-2009. The cohort comprised adolescents and adults 14 years of age or older from 90 large families. Details of the SHFS design were published previously.[15] Written informed consent was obtained from all participants at each examination. The study was approved by the institutional review boards of each Indian Health Services region and all 12 communities.

This is a secondary data analysis of data from the SHFS. Each SHFS examination included an in-person interview, physical exam, and laboratory work-up. The in-person interview included a Block98 food frequency questionnaire (FFQ) with AI ethnic foods supplement to ascertain “usual” dietary intake over the past year. Smoking status, alcohol consumption, anthropometrics including weight, height, and blood pressure, and laboratory data for blood and urine studies were also collected. Brief details on data collection and measurements are reported below; further details were published previously.[15]

Study Population: The SHFS consists of 90 families and 2,404 total participants. For the purposes of these analyses, participants with missing data that precluded calculation of the Alternative Healthy Eating Index 2010 (AHEI) (n = 316), or who were missing urine albumin to creatinine ratio or eGFR at baseline and/or follow up (n = 99), pregnant at the time of the study (*n* = 1), or had albuminuria at baseline (n= 267) were excluded. In total, 1,721 participants from 89 families were included in the analytic sample. A total of 255 participants were 21 years old or younger at baseline. Participants excluded from the analytic sample had more diabetes mellitus (31% vs 13%), hypertension (36% vs 28%) and cardiovascular disease (15% vs 8%), but were otherwise similar to those included in the sample.

<u>Study Exposure</u>: The primary exposure was diet quality calculated using AHEI, a commonly used diet index based on daily intakes of vegetables, fruit, whole grains, sugar-sweetened beverages, nuts and legumes, red or processed meat, trans-fats, long-chain fatty acids, polyunsaturated fats, sodium and alcohol. To calculate AHEI, each individual food and nutrient component is scored 0-10 based on daily intake determined from the FFQ, and then summed for all foods.[16] See Supplementary Material for AHEI calculation.[16,17] AHEI scores range 0-110 with higher AHEI scores associated with healthier diet. We chose AHEI as the diet quality measure of interest because previous research has demonstrated that higher AHEI scores are associated with lower risk of chronic disease, such as coronary heart disease, diabetes, stroke and cancer.[16]

<u>Outcomes:</u> Primary outcomes included (1) incident albuminuria and (2) 30% or greater decline in eGFR. Incident albuminuria was defined as a random urine albumin to urine creatinine ratio of 30mg/g or greater at follow up. Decrease in eGFR by 30% or greater at follow-up defined decline in eGFR. There is no clinical or research standard for decline in eGFR, but the threshold of 30% decrease in eGFR has been used in prior studies of diet and kidney outcomes in the general population[11,12] and among CKD patients.[18–20] Urine was collected at each exam to measure urine albumin to creatinine ratio. eGFR at each exam was calculated using the MDRD equation; the MDRD is the most widely used equation to estimate eGFR in adults and uses serum creatinine, sex and age as part of the calculation. Decline in eGFR was calculated by the following equation:

$$eGFR\ decline = \frac{(baseline\ eGFR) - (follow\ up\ eGFR)}{baseline\ eGFR} * 100$$

Decline in eGFR was then dichotomized by those with 30% or higher.

<u>Covariates</u>: Covariates were selected a priori based on potential associations with diet and kidney outcomes, and included age (years), sex (male/female), site (Arizona, Oklahoma, North Dakota/South Dakota), education (years), current smoker (yes/no), physical activity (steps per day), eGFR (ml/min/1.73m2), hypertension (yes/no), body mass index (BMI) (kg/m^2), CVD (yes/no), and diabetes status (normal fasting glucose/ impaired fasting glucose/ prevalent diabetes mellitus) at baseline. Smoking status was dichotomized as current smoker vs non-smoker based on answering yes as a current smoker and smoked at least 100 cigarettes in lifetime. Physical activity is a continuous measure of the average steps taken per day (assessed via a pedometer). Hypertension is defined as taking an antihypertensive drug, or taking diuretic, beta blocker, vasodilator or cardiac medication and history of hypertension, or systolic blood pressure measurement greater than 140, or diastolic blood pressure measurement greater than 90. BMI was calculated from weight and height obtained during the exam and reported in kg/m^2. Diabetes status was categorized as prevalent diabetes mellitus, impaired fasting glucose and

normal fasting glucose based on fasting blood glucose levels per the American Diabetes Association 1997 criteria. Cardiovascular disease is defined as those with fatal or non-fatal definite coronary heart disease, myocardial infarction or probable myocardial infarction.

Statistical Analyses: AHEI was assessed categorically using quartiles. Descriptive analyses were used to examine baseline characteristics of study participants stratified by AHEI quartile with continuous factors described using mean (standard deviation) and categorical factors described using proportions. We examined the association of AHEI quartile with each outcome of interest (i.e., incident albuminuria, eGFR decline) using generalized estimating equations (GEE). The general form of the models is given by:

$$\text{Logit}(p)=\alpha + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_4 x_4 + \ldots$$

This method of analysis was selected since GEE methods allow for clustering/correlation within the data. Since our data are comprised of extended families, the GEE methods are most appropriate. GEE allows estimations of the effects of the factor of interest (x_1) on probability of outcome (y or logit (p)), while controlling for other factors (x_2, $x_3\ldots$). GEE models were structured as binomial with an independence working correlation for the primary outcomes. GEE was used to determine the beta coefficients of the AHEI quartiles for the primary outcomes of albuminuria and decline in eGFR adjusted for covariates mentioned below. Odds ratios for each outcome were calculated by exponentiating the beta coefficient for each AHEI quartile and 95% Confidence Intervals (CI) were calculated using the beta coefficients and robust standard errors.

The reference group was Quartile 1 (lowest 25^{th} percentile) for AHEI score. Model 1 is unadjusted. Model 2 is adjusted for age, sex, site, education, smoking status, and physical activity. Model 3 adjusted for all covariates in Model 2 in addition to morbidity factors including baseline eGFR (for albuminuria analyses), hypertension, BMI and CVD. Tests for interactions between all covariates were performed a priori due to the potential influence of each covariate on diet quality and albuminuria and decline in eGFR. Due to evidence of significant interaction ($p < 0.05$) of AHEI quartile with diabetes status on renal outcomes, all analyses were stratified by diabetes status (prevalent diabetes mellitus, impaired fasting glucose and normal fasting glucose) at baseline. Prior to excluding participants based on exclusion criteria, missingness was explored to assess for differences between included and excluded groups. Sensitivity analyses that further adjusted Model 3 for total daily caloric intake was performed. Secondary analyses were performed to assess associations of individual dietary components of AHEI with incident albuminuria and eGFR decline. All analyses were performed using R statistical software (r-project.com).

Results

The total analytic cohort of 1,721 participants was 61% female, mean AHEI score was 44 (range: 19-78), mean age was 39 years (range: 14-86 years old) and 16% of participants were 14-21 years old at baseline. Baseline characteristics of study participants according to AHEI, and outcomes of incident albuminuria and eGFR decline are presented in Table 1A and Table 1B, respectively. The overall range of AHEI scores is limited in the cohort. The mean AHEI score for quartile 1 (least healthy diet quality) was 34 (range: 19-38) and 56 (range: 50-78) for quartile 4 (healthiest diet quality) (Table 1A). Mean age increased and proportion of those 21 years old and younger decreased with increasing AHEI quartile. AHEI quartile 4 had more participants with prevalent diabetes, hypertension and cardiovascular disease than other quartiles. Participants in AHEI quartile 4 consumed more fruits and vegetables and less sugar sweetened beverages than participants in other quartiles.

Incident Albuminuria

As shown in Table 1B, 10% of the cohort (n=170) developed albuminuria during follow-up. A total of 9% of participants (n=16) who developed albuminuria were 21 years of age or younger. When compared to participants who did not develop albuminuria, those with incident albuminuria were more likely to have diabetes (36% vs 11%), hypertension (38% vs 26%), and cardiovascular disease (15% vs 7%). Participants who developed albuminuria were also more likely to smoke cigarettes (44% vs 37%) and accumulated less physical activity per day (5095 steps/day vs 6256 steps/day) when compared to those who did not develop albuminuria. Number of participants, mean AHEI scores and odds ratios of incident albuminuria for each AHEI quartile overall and stratified by diabetes status is shown in Table 2. Among those with normal fasting glucose levels, AHEI quartiles 2, 3 and 4 were associated with lower odds of incident albuminuria 0.24 (95% CI 0.11, 0.49), 0.43 (95% CI 0.23, 0.81), and 0.48 (95% CI 0.28, 0.81) respectively in the fully adjusted model. We did not find an association between AHEI quartile and incident albuminuria for those with diabetes mellitus or impaired fasting glucose levels.

eGFR Decline

As shown in Table 1B, 6% of the cohort (n=96) had eGFR decline ≥30%. A total of 27% of participants (n=26) with eGFR decline were 21 years of age or younger. When compared to participants who did not have eGFR decline, those with eGFR decline were more likely to have diabetes (33% vs 12%), hypertension (36% vs 27%), and cardiovascular disease (13% vs 7%), but accumulated less physical activity per day (5065 steps/day vs 6204 steps/day).
Number of participants, mean AHEI scores and odds ratios of eGFR decline for each AHEI quartile overall and stratified by diabetes status is shown in Table 3. There were no participants with eGFR decline and impaired fasting glucose in quartile 1. We did not observe an association of AHEI quartile and eGFR decline overall or stratified by diabetes status.

Sensitivity analyses adjusting for total calories were performed and did not attenuate odds ratios for AHEI score and incident albuminuria or eGFR decline. Secondary analyses were performed to assess associations of individual components of AHEI with incident albuminuria and eGFR decline and there were no significant associations.

Table 1A. Baseline characteristics of Strong Heart Family Study participants stratified by AHEI quartile

		AHEI Quartile			
Characteristic	**Total**	**1**	**2**	**3**	**4**
Participants, n	1721	431	430	430	430
AHEI score, mean (SD) (range)	44 (9)	34 (3) (19-38)	41 (2) (38-44)	47 (2) (44-50)	56 (5) (50-78)
Age, mean (SD), y	39 (16)	33 (13)	38 (16)	41 (16)	45 (17)
< = 21, n (%)	282 (16)	111 (26)	74 (17)	58 (13)	39 (9)
> 21, n (%)	1439 (84)	320 (74)	356 (83)	372 (87)	391 (91)
Sex, n (%)					
Male	671 (39)	194 (45)	164 (38)	160 (37)	153 (36)
Female	1050 (61)	237 (55)	266 (62)	270 (63)	277 (64)
Education, mean (SD), y	12 (2)	12 (2)	12 (2)	13 (2)	13 (2)
eGFR < 60 mL/min/1.73m2, n (%)	75 (4)	12 (3)	18 (4)	20 (5)	25 (6)
BMI, mean (SD), kg/m2	31 (7)	31 (8)	31 (7)	31 (7)	32 (7)
Diabetes, n (%)	227 (13)	35 (8)	47 (11)	70 (16)	75 (17)
Hypertension, n (%)	475 (28)	82 (19)	109 (25)	130 (30)	154 (36)
Cardiovascular Disease, n (%)	130 (8)	25 (6)	35 (8)	26 (6)	44 (10)
Smoke Cigarettes, n (%)	651 (38)	177 (41)	165 (38)	164 (38)	145 (34)
Physical Activity, mean (SD), steps/day	6140 (4000)	6414 (3900)	6176 (3971)	5806 (3403)	6168 (4632)
Laboratory Data, mean (SD)					
LDL, mg/dL	100 (30)	98 (32)	103 (30)	99 (30)	99 (29)
HDL, mg/dL	52 (14)	51 (13)	51 (13)	52 (15)	52 (16)
Triglycerides, mg/dL	159 (149)	144 (91)	153 (103)	160 (99)	181 (244)
Total Cholesterol, mg/dL	182 (36)	177 (38)	184 (36)	183 (33)	184 (38)
eGFR, mL/min/1.73m2	91 (21)	95 (20)	92 (22)	91 (20)	88 (22)
Diet, mean (SD)					
Total energy, kcal/day	2441 (1342)	2442 (1086)	2305 (1233)	2338 (1362)	2680 (1605)
Total Fat, %kcal	38 (7)	38 (7)	38 (8)	39 (7)	39 (7)
Total Carbohydrate, %kcal	49 (9)	49 (9)	50 (9)	48 (8)	48 (9)
Fruit, servings/day	1.0 (0.8)	0.7 (0.6)	0.9 (0.7)	1.0 (0.8)	1.4 (1.1)
Vegetables, servings/day	2.6 (2.1)	1.9 (1.3)	2.2 (1.7)	2.8 (2.1)	3.7 (2.7)
Sugar sweetened beverages, servings/day	3.0 (2.7)	3.9 (2.7)	3.2 (2.6)	2.7 (2.4)	2.3 (2.7)
Processed meat, servings/ day	0.9 (0.8)	1.1 (0.8)	0.9 (0.8)	0.8 (0.7)	0.8 (1.0)

Table 1B. Baseline characteristics of Strong Heart Family Study participants stratified by incident albuminuria and eGFR decline

Characteristic	Total	Incident Albuminuria	No Albuminuria	eGFR Decline	No eGFR Decline
Participants, n (%)	1721	170 (10)	1551 (90)	96 (6)	1625 (94)
AHEI score, mean (SD)	44 (9)	45 (10)	44 (9)	45 (8)	44 (9)
Age, mean (SD), y	39 (16)	44 (16)	39 (16)	43 (21)	39 (16)
< = 21, n (%)	282	16 (9)	266 (17)	26 (27)	256 (16)
> 21, n (%)	1439	154 (91)	1285 (83)	70 (73)	1369 (84)
Sex, n (%)					
Male	671 (39)	63 (37)	608 (39)	29 (30)	642 (40)
Female	1050 (61)	107 (63)	943 (61)	67 (70)	983 (60)
Education, mean (SD), y	12 (2)	12 (2)	12 (2)	11 (2)	12 (2)
eGFR < 60 mL/min/1.73m2, n (%)	75 (4)	9 (5)	66 (4)	8 (8)	88 (5)
BMI, mean (SD), kg/m2	31 (7)	34 (8)	31 (7)	31 (7)	31 (7)
Diabetes, n (%)	227 (13)	62 (36)	165 (11)	32 (33)	195 (12)
Hypertension, n (%)	475 (28)	65 (38)	410 (26)	35 (36)	440 (27)
Cardiovascular Disease, n (%)	130 (8)	26 (15)	104 (7)	12 (13)	118 (7)
Smoke Cigarettes, n (%)	651 (38)	74 (44)	577 (37)	32 (33)	619 (38)
Physical Activity, mean (SD), steps/day	6140 (4000)	5095 (3382)	6256 (4047)	5065 (3285)	6204 (4031)
Laboratory Data, mean (SD)					
LDL, mg/dL	100 (30)	96 (30)	100 (30)	87 (28)	101 (30)
HDL, mg/dL	52 (14)	50 (15)	52 (14)	51 (14)	52 (14)
Triglycerides, mg/dL	159 (149)	170 (103)	158 (153)	183 (251)	158 (141)
Total Cholesterol, mg/dL	182 (36)	179 (34)	182 (37)	170 (34)	183 (36)
eGFR, mL/min/1.73m2	91 (21)	94 (25)	91 (21)	104 (30)	91 (20)
Diet, mean (SD)					
Total energy, kcal/day	2441 (1342)	2357 (1238)	2451 (1353)	2501 (1409)	2438 (1338)
Total Fat, %kcal	38 (7)	38 (7)	38 (7)	38 (7)	38 (7)
Total Carbohydrate, %kcal	49 (9)	49 (9)	49 (9)	50 (9)	49 (9)
Fruit, servings/day	1.0 (0.8)	1.0 (0.9)	1.0 (0.9)	1.3 (0.9)	1.0 (0.8)
Vegetables, servings/day	2.6 (2.1)	2.6 (1.9)	2.7 (2.2)	2.8 (2.2)	2.6 (2.1)
Sugar sweetened beverages, servings/day	3.0 (2.7)	2.7 (2.5)	3.1 (2.7)	3.4 (2.8)	3.0 (2.8)
Processed meat, servings/ day	0.9 (0.8)	0.9 (0.8)	0.9 (0.8)	1.0 (1.0)	0.9 (0.8)

Table 2. Odds Ratios of incident albuminuria for each AHEI quartile stratified by diabetes status in Strong Heart Family Study

		AHEI Quartile (Score Mean, Range 0-110)			
		1 (34, 19-38)	2 (41, 38-44)	3 (47, 44-50)	4 (56, 50-78)
	Incident Albuminuria n (%)	51 (11%)	25 (6%)	46 (11%)	48 (11%)
Model 1	Overall	1.00 (ref)	0.46 (0.29, 0.74)	0.89 (0.59, 1.35)	0.94 (0.60, 1.46)
	DM	1.00 (ref)	0.59 (0.24, 1.47)	1.00 (0.40, 2.46)	0.74 (0.32, 1.72)
	IFG	1.00 (ref)	0.95 (0.23, 3.96)	2.05 (0.62, 6.79)	2.53 (0.78, 8.19)
	NFG	1.00 (ref)	0.30 (0.15, 0.59)	0.46 (0.26, 0.84)	0.56 (0.34, 0.95)
Model 2	Overall	1.00 (ref)	0.41 (0.25, 0.66)	0.76 (0.50, 1.16)	0.73 (0.46, 1.16)
	DM	1.00 (ref)	0.55 (0.22, 1.40)	0.93 (0.37, 2.33)	0.69 (0.31, 1.56)
	IFG	1.00 (ref)	0.87 (0.20, 3.85)	2.02 (0.57, 7.14)	2.77 (0.76, 10.08)
	NFG	1.00 (ref)	0.27 (0.14, 0.53)	0.44 (0.23, 0.82)	0.53 (0.31, 0.91)
Model 3	Overall	1.00 (ref)	0.39 (0.24, 0.64)	0.73 (0.47, 1.13)	0.66 (0.41, 1.07)
	DM	1.00 (ref)	0.56 (0.21, 1.48)	0.96 (0.40, 2.31)	0.73 (0.33, 1.64)
	IFG	1.00 (ref)	0.97 (0.22, 4.26)	1.79 (0.44, 7.31)	2.43 (0.68, 8.65)
	NFG	1.00 (ref)	0.24 (0.11, 0.49)	0.43 (0.23, 0.81)	0.48 (0.28, 0.81)

Model 1: unadjusted

Model 2: adjusted for age, sex, site, education level, physical activity, smoking status

Model 3: Model 2+ BMI, baseline eGFR, hypertension, cardiovascular disease

DM = Diabetes Mellitus; IFG = Impaired fasting glucose; NFG = normal fasting glucose

AHEI = Alternative healthy eating index 2010

Table 3. Odds Ratios of eGFR decline for each AHEI quartile stratified by diabetes status in Strong Heart Family Study

		AHEI Quartile (Score Mean, Range 0-110)			
		1 (34, 19-38)	2 (41, 38-44)	3 (47, 44-50)	4 (56, 50-78)
	eGFR Decline n (%)	20 (21%)	18 (19%)	31 (32%)	27 (28%)
Model 1	Overall	1.00 (ref)	0.90 (0.47, 1.72)	1.60 (0.87, 2.93)	1.38 (0.72, 2.61)
	DM	1.00 (ref)	0.73 (0.18, 2.92)	1.99 (0.50, 7.93)	2.67 (0.68, 10.41)
	IFG	n = 0	-	-	-
	NFG	1.00 (ref)	0.67 (0.31, 1.48)	1.27 (0.630, 2.58)	0.43 (0.19, 0.98)
Model 2	Overall	1.00 (ref)	0.84 (0.42, 1.70)	1.56 (0.84, 2.89)	1.26 (0.65, 2.43)
	DM	1.00 (ref)	0.40 (0.08, 1.95)	1.13 (0.24, 5.29)	1.27 (0.26, 6.24)
	IFG	n = 0	-	-	-
	NFG	1.00 (ref)	0.64 (0.27, 1.48)	1.49 (0.75, 2.99)	0.49 (0.21, 1.11)
Model 3	Overall	1.00 (ref)	0.85 (0.42, 1.73)	1.46 (0.78, 2.74)	1.20 (0.62, 2.32)
	DM	1.00 (ref)	0.36 (0.07, 1.71)	1.10 (0.24, 5.04)	1.24 (0.26, 5.85)
	IFG	n = 0	-	-	-
	NFG	1.00 (ref)	0.65 (0.28, 1.51)	1.49 (0.75, 2.97)	0.49 (0.21, 1.15)

Model 1: unadjusted

Model 2: adjusted for age, sex, site, education level, physical activity, smoking status

Model 3: Model 2+ BMI, hypertension, cardiovascular disease

DM = Diabetes Mellitus; IFG = Impaired fasting glucose; NFG = normal fasting glucose

AHEI = Alternative healthy eating index 2010

Discussion

Among participants with normal fasting glucose, those who reported higher quality diets had a 52-76% lower odds of incident albuminuria when compared to participants who reported the least healthy diet quality (i.e., lowest 25th percentile of AHEI). There was no association with diet quality and incident albuminuria among participants with prevalent diabetes mellitus or impaired fasting glucose. There was also no association with diet quality and eGFR decline regardless of diabetes status.

To our knowledge, this is the first study that has assessed the association of diet quality and kidney outcomes in AIs. Prior studies that explored the relationship of diet quality with kidney outcomes in other populations have mixed results likely related to varying diets, cohort demographics and comorbidities.[6,8,10,12–14] Synthesizing findings from previous studies is challenging due to heterogeneity in categorizing "healthy diet" across studies. Some studies use data driven assessments such as factor analysis to create "Western", "Prudent" and "Fish-Vegetable" patterns; while others use external goals such as DASH (Dietary Approaches to Stop Hypertension), DGAI (Dietary Guidelines Adherence Index), AHEI (Alternative Healthy Eating Index), etc.[6,8,10,12–14] Despite these challenges, a meta-analysis of various dietary patterns (such as Mediterranean, DASH) and diet quality measures (such as AHEI, HEI, Life's Simple Seven) with kidney outcomes reported that compared to lower quality diet, a healthier diet was associated with overall a 23% lower odds of incident albuminuria and a 30% lower odds of incident CKD; similar to the findings reported herein, there was no association of diet quality with eGFR decline.[6] Our findings of higher diet quality associated with lower odds of incident albuminuria are also consistent with results of the CARDIA (Coronary Artery Risk Development in Young Adults) study and the Nurses' Health Study. Findings from the CARDIA Study, a study comprised of American Black and White young adults, suggest that participants who reported the poorest quality diet (based on DASH (Dietary Approach to Stop Hypertension)) had a two-fold higher risk of albuminuria compared to those who reported the healthiest diet quality.[13] Similarly, elderly white females in the Nurses' Health Study who reported a diet comprised of largely Western foods (i.e., red and processed meat, saturated fats and sweets) had a higher odds of albuminuria when compared to participants whose diets did not include these foods.[12] However, findings from Ma et al (predominantly elderly white adults in the Framingham Heart Study) and Chung et al (predominantly elderly Taiwanese adults with Type 2 Diabetes Mellitus) did not find an association of DGAI (Dietary Guidelines Adherence Index) and Fish-vegetable diet respectively and albuminuria.[8,14] The results of this study build on this work by highlighting the association of diet quality and albuminuria among primarily young and middle-aged American Indians, and highlight effect modification according to diabetes status.

Accounting for diabetes status in the relationship of diet quality and kidney outcomes is complex since diabetes may be a confounder, mediator or an effect modifier. Prior studies of diet and kidney outcomes often adjust for diabetes in multivariable analyses,[12–14] but this may be an over adjustment if diabetes is on the causal pathway such that diet quality influences risk of diabetes, and diabetes is a known risk factor for CKD. Lin et al report that stratification by diabetes status did not meaningfully change results of diet quality and albuminuria in their cohort of elderly white females, although analyses may have limited power given the small number of cases in each diabetes status and diet quartile.[12] Chung et al cohort was comprised of Taiwanese elderly adults with Type 2 Diabetes and they did not find an association of diet with albuminuria.[8] Similarly, we did not find an association with diet quality and incident albuminuria among participants with diabetes mellitus or impaired fasting glucose levels. These results suggest that diet quality may be more important for those with normal fasting glucose levels than those with diabetes and impaired fasting glucose. For individuals with diabetes and impaired fasting glucose, other factors such as medications may play a more significant role in preventing kidney complications than diet. Our findings suggest that targeted interventions to reduce kidney dysfunction could focus on improving the diet of those with normal fasting glucose, particularly young individuals with poor diet quality who may be at high risk of future CKD. This is also supported by a report from the CDC that highlights adolescence as a sensitive period for interventions to improve diet in order to prevent kidney disease and other chronic diseases.[21]

Prior studies exploring diet quality using AHEI and kidney outcomes show higher AHEI scores are associated with a lower odds of incident CKD[22] and reduced hazard of death due to kidney disease.[23] To our knowledge, this is the first study to examine the association of AHEI with incident albuminuria and eGFR decline. Among those with normal fasting glucose, our findings were most consistent with a threshold effect. Participants in AHEI quartiles 2-4 had a 52-76% lower odds of incident albuminuria compared to participants in AHEI quartile 1 (i.e., least healthy diet) with observed linear trend. This finding is difficult to explain and may be due to limited power given the small number of cases in each diabetes status and AHEI quartile, rather than variability of AHEI scores. Prior studies in young adult and middle-aged populations have mean AHEI scores (44 and 47)[24,25] similar to our cohort (mean AHEI 44), but our AHEI scores had higher variability (range 19-78). Analyses for individual AHEI components were performed and none of the components were associated with albuminuria or decline in eGFR which suggests that overall dietary pattern and quality among American Indians may be more important than individual foods.

Findings from studies that have assessed the association of diet quality with eGFR decline report conflicting results. This may be due to differences in cohort demographics and varying definitions of eGFR decline.[7,12,14,26] Lin et al and Ma et al reported associations of DASH and DGAI with eGFR decline in elderly white men and women.[12,14] On the other hand, Khatri et al and Liu et al did not find an association of Mediterranean diet or DASH diet and eGFR decline in their racially diverse cohorts.[7,26] Consistent with Khatri et al and Liu et al, we did not find an association with diet quality and eGFR decline in a diverse sample of AIs from 4 states. However, our follow up period of 6-8 years may not be long enough to observe decline in eGFR in our cohort of primarily young and middle-aged adults. Additionally, the definition of eGFR decline varies across studies (e.g., percentage decrease (such as 25% or 30%)[7,12] between baseline and follow up and/or an annual decline of 2.5 or 3 mL/min/ 1.73m^2 or more)[7,12,14,26] which may also contribute to opposing findings across studies.[7,12,14,26] A standard definition of eGFR decline among the general population is needed.

The physiologic mechanisms behind low quality diet leading to kidney dysfunction may be related to increased dietary acid load to the kidney[9,27,28] and increased net endogenous acid production.[29] In the Atherosclerosis Risk in Communities (ARIC) study and Jackson Heart Study, high dietary acid load (low quality diet) was associated with a higher likelihood of developing CKD.[9,28] In cohorts of participants with CKD, higher dietary acid load and net endogenous acid production has been consistently associated with CKD progression.[27,29]

To our knowledge, this is the first study to assess the association of diet quality and kidney outcomes in AIs, a population with a high burden of diabetes and kidney disease. Other strengths of this study include the availability of comprehensive and validated data measures which maximized our capacity to adjust for potential confounders. Diet quality was measured using a FFQ with an ethnic foods supplement which allowed us to more accurately characterize diet quality than use of an FFQ alone. The Strong Heart Study is a large multi-tribal cohort study of 12 different American Indian communities across Arizona, Oklahoma, South Dakota and North Dakota which increases external validity and generalizability while appreciating that American Indian communities are not homogenous and each has unique traditions, practices and beliefs. A limitation of this study is diet quality was assessed using a FFQ which is prone to recall bias due to over-or-underreporting of food type, portion size, or frequency of consumption. A second limitation is the small sample size and limited power. Residual confounding by poorly measured (or unmeasured) factors is possible, including factors such as access to healthy food and structural racism.

The results of this study suggest that for American Indians with normal fasting glucose, higher diet quality decreases the odds of developing albuminuria. These findings have important implications for future intervention and prevention work for those with normal fasting glucose levels such as adolescents and young adults.

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