ORIGINAL RESEARCH

Dietary Potential Renal Acid Load and Risk of Albuminuria and Reduced Kidney Function in the Jackson Heart Study

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Objective: Diets high in sulfur-rich protein and low in fruit and vegetables affect human acid-base balance adversely and may have a harmful effect on progression of chronic kidney disease (CKD). Little is known about the relationship of participant characteristics, dietary acid load (DAL), and kidney injury in African-Americans with high risk of CKD progression.

Design and methods: We examined the association of DAL with CKD in 3,257 African-Americans aged >20 years in Jackson Heart Study. DAL was measured with nutrient intakes assessed with a food frequency questionnaire, using a model described by Remer and Manz. We tested associations of participant characteristics with DAL using median regression, and associations of DAL with albuminuria (>17 mg/g for men, >25 mg/g for women), reduced kidney function (eGFR <60 mL/minute/1.73 m^2), or CKD defined as albuminuria or reduced kidney function using logistic regression. We further explored whether endothelin and aldosterone production in participants with hypertension mediated risk of albuminuria or reduced kidney function due to the intake of an acid-inducing diet.

Results: Younger adults, men, and those with higher body mass index had higher DAL. Higher DAL, compared with lower, was associated with greater odds of reduced kidney function (OR [95% CI]: 2.82 [1.40-4.75]). Higher DAL was also associated with greater risk of CKD, and this persisted after adjustment for confounders. Results were similar in adults with hypertension; the OR [95% CI] for highest, versus lowest, tertile of DAL with albuminuria was 1.66 [1.01-2.59]. Aldosterone and endothelin mediated the association between DAL and albuminuria; the OR [95% CI] in the highest tertile was no longer significant 1.53 [0.97-2.40] after their inclusion.

Conclusions: Higher DAL was associated with higher prevalence of CKD and with reduced kidney function. DAL may be an important target for future interventions in African-Americans at high risk of CKD.

Introduction

THERE IS INCREASING evidence that acid-base status can affect chronic kidney disease (CKD) progression as defined by the estimated glomerular filtration rate (GFR).[1,2] Recent research, including animal studies, observational epidemiology, and small clinical trials, has examined the impact of chronic metabolic acidosis on decline in GFR in individuals with moderately impaired eGFR. Acid-producing diets led to endothelin-mediated GFR decline, and that oral alkali slowed GFR decline, better preserved GFR, and lowered kidney endothelin production in rats with reduced nephron mass.[2] Dietary acid-induced kidney injury in rats with intact or reduced nephron mass is mediated by tubulointerstitial injury, through endothelin receptors. Tubulointerstitial injury is a component of hypertensive nephropathy and its increased severity may indicate nephropathy progression. Moreover, target organ damage including hypertensive nephropathy and end-stage renal disease has been shown to be more common and severe in African-Americans, than among non-Hispanic whites. An observational study by Scialla et al.[3] showed that high net endogenous acid production was associated with low

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serum bicarbonate concentration and with declines in GFR. To our knowledge, no observational study has examined the role of high acid load due to unhealthy dietary patterns on risk of albuminuria and impaired kidney function in African-Americans.

Poverty, neighborhood violence, anger, and family stress can have significant impact on the individual's dietary habits. Prolonged exposure to environments that evoke vigilance, threat, and alarm, may be an important and modifiable contributor to the intake of high-acid–producing diet.[4,5] How individuals cope with untoward environments, including the impact of religious affiliation on diet, could buffer the impact of dietary acid intake on renal function.

The Jackson Heart Study cohort provides a unique opportunity to determine the impact of diet, particularly dietary acid load, on renal function in a high-risk population in the Southern Unites States where dietary patterns may be very important. The comprehensive battery of sociocultural measures further provides the opportunity to identify possible covariates leading to high dietary acid load. The purpose of the present study is to investigate (1) the association between participant characteristics (sociodemographic characteristics, cultural, behavioral determinants, violence, coping inventory, global stress, and anger) and dietary acid load, and (2) the association between dietary acid load and impaired kidney function and albuminuria in the participants of the Jackson Heart Study (age >20 years).

Materials and Methods

Study Sample

The Jackson Heart Study recruited 5,301 African-Americans from the Jackson, Mississippi area between September 2000 and March 2004. Participants were between the ages of 21-84 years when they enrolled in the study, and nearly two-thirds were women (64%).

Dietary Assessment

Usual dietary intake was assessed for all participants using a food frequency questionnaire (FFQ) developed from a longer questionnaire previously designed for the USDA Delta Nutrition Intervention Research Initiative (Delta-NIRI).[6] This FFQ was designed specifically for a southern U.S. population to capture their regional dietary patterns and foods and was based on 24-hour dietary recall data.[7] We calculated the dietary acid load of dietary intake, based on the nutrients obtained from analysis of the FFQ that were answered in Exam 1 (September 2000-March 2004), using the model developed for prediction of net acid excretion (NAE) from nutrient intake data developed by Remer and Manz.[8,9] Intake of nonbicarbonate anions (protein, phosphorus) and mineral cations (potassium, magnesium, calcium) was derived from dietary intake data. Potential renal acid load (PRAL) was calculated, using the model [PRAL (mEq/day) = 0.49 ⋆ protein (g) +0.037 ⋆ phosphorus (mg)] − 0.021 ⋆ potassium (mg) − 0.026 ⋆ magnesium (mg) − 0.0125 ⋆ calcium (mg)].[8] NAE was estimated as NAEes (mEq/day) = PRAL + organic acids, where organic acids was calculated as OA (mEq/day) = (body surface area [m^2] ⋆ 41[mEq/day/1.73 m^2])/ 1.73(m^2).[8] The unit for all the 3 measures was mEq/day. This calculation methodology, based primarily on PRAL, allows an appropriate prediction of the effects of diet on the acidity of urine. This method of calculation of NAE_{es} was experimentally validated in healthy adults and showed that acid loads and renal NAE can be reliably estimated from diet composition.[8-10]

Covariates

All covariates were defined using baseline data. Age, sex, education, smoking status, annual income, and church support were obtained by self-report. Age was a continuous variable. Education was categorized as a high school diploma or general education development certificate or lower, some college, and bachelor's degree or higher; annual income as poor or lower middle and upper middle or affluent; church support was categorized as high support, moderate support, or least support; and smoking status was defined as "never" (reference) or "former/current". Physical activity was expressed as a summary score of the intensity, frequency, and duration of activities associated with active living, including transportation and leisure time activities.[11] Body mass index (BMI, defined as kg/m^2) was calculated from measurements of height and weight using standardized procedures. Insulin resistance was assessed using the following index: homeostasis model assessment: insulin resistance (HOMA-IR) = (glucose [nmol/L] ⋆ insulin [lU/mL]/22.5). A higher HOMA-IR is indicative of insulin resistance.[12]

Hypertension was defined as a baseline systolic blood pressure of 140 mm Hg or higher, a diastolic blood pressure of 90 mm Hg or higher, or self-reported use of antihypertensive medication.[13] Diabetes was defined as baseline fasting glucose of 126 mg/dL or higher, self-reported physician diagnosis of diabetes, or self-reported use of oral hypoglycemic medication or insulin.[14]

Kidney Function Outcome Assessment

eGFR and urinary albumin-to-creatinine ratio (ACR) were our primary outcomes. eGFR was calculated from serum concentration of creatinine measured at baseline using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.[15] Serum creatinine was measured using the Jaffe method and calibrated to measurements traceable to isotope dilution mass spectrometry.[16] Reduced kidney function was defined as eGFR lower than 60 mL/minute/1.73 m^2.[17] The urinary ACR was obtained from either 24-hour urine collections or spot urine samples.[18] Albuminuria was defined as ACR higher than or