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Tanushree Banerjee

Deidra C. Crews

Donald E. Wesson

Sai Dharmarajan

Rajiv Saran

See next page for additional authors

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Authors

Tanushree Banerjee, Deidra C. Crews, Donald E. Wesson, Sai Dharmarajan, Rajiv Saran, Nilka Ríos Burrows, Sharon Saydah, Neil R. Powe, Chi yuan Hsu, Kirsten Bibbins-Domingo, Charles McCulloch, Vanessa Grubbs, Carmen Peralta, Michael Shlipak, Anna Rubinsky, Raymond Hsu, Josef Coresh, Delphine Tuot, Diane Steffick, Brenda Gillespie, William Herman, Friedrich Port, Bruce Robinson, Vahakn Shahinian, Jerry Yee, Eric Young, William McClellan, Ann O'Hare, Melissa Fava, Anca Tilea, Desmond Williams, and Mark Eberhardt

AJKD

Original Investigation

Food Insecurity, CKD, and Subsequent ESRD in US Adults

Tanushree Banerjee, PhD,[1] Deidra C. Crews, MD, ScM,[2,3] Donald E. Wesson, MD,[4] Sai Dharmarajan, MS,[5] Rajiv Saran, MD,[5,6] Nilka Ríos Burrows, MT, MPH,[7] Sharon Saydah, PhD,[7] and Neil R. Powe, MD,[8] on behalf of the CDC CKD Surveillance Team*

Background: Poor access to food among low-income adults has been recognized as a risk factor for chronic kidney disease (CKD), but there are no data for the impact of food insecurity on progression to end-stage renal disease (ESRD). We hypothesized that food insecurity would be independently associated with risk for ESRD among persons with and without earlier stages of CKD.

Study Design: Longitudinal cohort study.

Setting & Participants: 2,320 adults (aged ≥ 20 years) with CKD and 10,448 adults with no CKD enrolled in NHANES III (1988-1994) with household income ≤ 400% of the federal poverty level linked to the Medicare ESRD Registry for a median follow-up of 12 years.

Predictor: Food insecurity, defined as an affirmative response to the food-insecurity screening question.

Outcome: Development of ESRD.

Measurements: Demographics, income, diabetes, hypertension, estimated glomerular filtration rate, and albuminuria. Dietary acid load was estimated from 24-hour dietary recall. We used a Fine-Gray competing-risk model to estimate the relative hazard (RH) for ESRD associated with food insecurity after adjusting for covariates.

Results: 4.5% of adults with CKD were food insecure. Food-insecure individuals were more likely to be younger and have diabetes (29.9%), hypertension (73.9%), or albuminuria (90.4%) as compared with their counterparts ($P < 0.05$). Median dietary acid load in the food-secure versus food-insecure group was 51.2 mEq/d versus 55.6 mEq/d, respectively ($P = 0.05$). Food-insecure adults were more likely to develop ESRD (RH, 1.38; 95% CI, 1.08-3.10) compared with food-secure adults after adjustment for demographics, income, diabetes, hypertension, estimated glomerular filtration rate, and albuminuria. In the non-CKD group, 5.7% were food insecure. We did not find a significant association between food insecurity and ESRD (RH, 0.77; 95% CI, 0.40-1.49).

Limitations: Use of single 24-hour diet recall; lack of laboratory follow-up data and measure of changes in food insecurity over time; follow-up of cohort ended 10 years ago.

Conclusions: Among adults with CKD, food insecurity was independently associated with a higher likelihood of developing ESRD. Innovative approaches to address food insecurity should be tested for their impact on CKD outcomes.

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INDEX WORDS: Food insecurity; nutrient intake; dietary acid load (DAL); dietary patterns; end-stage renal disease (ESRD); incident ESRD; kidney disease progression; disease trajectory; modifiable risk factor; poverty; health disparities; socioeconomic status; food deserts; chronic kidney disease (CKD); NHANES.

As per the US Department of Agriculture,[1] food security is defined as a person's perceived ability to obtain nutritious and healthy food with essential nutrients, fruits and vegetables, and limited amounts of saturated fats, sugar, and salt for an active and healthy life. In 2013, an estimated 14.3% of American households were categorized as food insecure because they lacked the proper availability of or

From the [1]Division of General Internal Medicine, Department of Medicine, University of California, San Francisco, CA; [2]Division of Nephrology, Department of Medicine, Johns Hopkins University School of Medicine; [3]Welch Center for Prevention, Epidemiology and Clinical Research, Johns Hopkins Medical Institutions, Baltimore, MD; [4]Texas A&M College of Medicine and Scott and White Healthcare, Temple, TX; [5]Kidney Epidemiology & Cost Center and [6]Division of Nephrology, Department of Medicine, University of Michigan, Ann Arbor, MI; [7]Division of Diabetes Translation, Centers for Disease and Control and Prevention, Atlanta, GA; and [8]Department of Medicine, Priscilla Chan and Mark Zuckerberg San Francisco General Hospital, San Francisco, CA.

[*]A list of the CDC CKD Surveillance Team appears in the Acknowledgements.

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Address correspondence to Tanushree Banerjee, PhD, Priscilla Chan and Mark Zuckerberg San Francisco General Hospital, 1001 Potrero Ave, Bldg 10, Ward 13, 1311N, San Francisco, CA 94110. E-mail: banerjeet@medsfgh.ucsf.edu

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means to obtain food and frequently experienced hunger or inadequate nutrient intake.[2] In households with limited resources, adequate food cannot be bought, so sometimes cheap, energy-dense, and nutrient-poor foods that are filling are purchased instead. Thus, these individuals consume fewer servings of fruits, vegetables, and dairy products and consume higher amounts of refined grains, added sugars, and saturated and trans fats.[3]

Lack of access to fresh healthy foods can contribute to poor diet composition and higher levels of diet-related diseases. Such unhealthy dietary patterns are associated with some leading causes of chronic disease and death, including chronic kidney disease (CKD),[4] coronary heart disease,[5] diabetes,[6] hypertension,[7] and obesity.[8] Unhealthy diets are also characterized by higher dietary acid load, which often corresponds to lower consumption of fruits and vegetables. Dietary acid load is associated with risk for CKD progression.[9] Compared with persons with higher incomes, individuals with lower incomes are more likely to both be food insecure and have higher dietary acid loads.[3,9]

Prior studies have shown an association of food insecurity with chronic diseases.[3,10] In particular, food insecurity has been shown to be associated with prevalent CKD.[11] We conducted a cross-sectional analysis of lower-income participants in NHANES (National Health and Nutrition Examination Survey) 2003 to 2008 and the Healthy Aging in Neighborhoods of Diversity Across the Life Span (HANDLS) Study. We found that food insecurity might play a role in disparities in kidney disease, particularly in people with diabetes or hypertension. Despite an association between food insecurity and prevalent CKD being noted, little is known about the association of food insecurity and progression of earlier stages of CKD to end-stage renal disease (ESRD). Understanding these relationships is important given that nutritional self-care is an essential approach to the management of CKD and its complications.[12] Furthermore, emerging data suggest that certain healthy dietary patterns may slow kidney function decline.[13-15] In this study, we examined data from a nationally representative sample of US adults to determine whether food insecurity is independently associated with progression to ESRD among individuals with and without CKD.

METHODS

Study Population and Baseline Data

To test the relationship between food insecurity and CKD progression, we used data from NHANES III, a national probability sample of US noninstitutionalized civilians conducted in 1988 to 1994 by the Centers for Disease Control and Prevention (CDC) National Center for Health Statistics. We included participants 20 years or older with: (1) complete data for dietary intake obtained from a single 24-hour recall questionnaire (n = 34,955); (2) CKD, defined as estimated glomerular filtration rate (eGFR) of 15 to 59 mL/min/1.73 m^2 or urinary albumin-creatinine ratio (ACR) ≥ 30 mg/g (n = 4,234); (4) annual household income ≤ 400% of the federal poverty limit (in order to exclude higher income persons unlikely to experience food insecurity [as in previous studies[3,16]]; n = 2,794); and (4) total caloric intake per day of 800 to 4,200 kcal/d for men and 600 to 3500 kcal/d for women[17] (n = 2,349) and (5) who were not pregnant (n = 2,320). For the non-CKD group, we included participants with eGFRs ≥ 60 mL/min/1.73 m^2 and ACRs ≤ 200 mg/g, with all other inclusion criteria remaining the same (n = 10,448).

A consent form was signed by participants in the survey and participants consented to storing specimens of their blood for future research.

Sociodemographic and Clinical Measurements

Medical history and demographic data were collected through an in-person survey followed by a medical examination and laboratory testing as specified in NHANES documentation.[18]

Sociodemographic factors were assessed during the interview. Racial/ethnic categories were self-reported by participants and assigned as follows: non-Hispanic white, non-Hispanic black, Mexican American, and others (Asian, Native American, other Hispanic, and those of unknown race/ethnicity). Self-reported information for education and income was obtained during the interview portions of the surveys. We excluded participants if income was missing. Income was assessed using the poverty income ratio, which is the ratio of household income to household poverty level.[18]

Diabetes was defined by self-report or measured hemoglobin A_{1c} level ≥ 6.5%.[19] Hypertension was defined as either self-report, measured average systolic blood pressure ≥ 140 mm Hg, measured average diastolic blood pressure ≥ 90 mm Hg, or reported use of antihypertensive medications.[20] Body mass index (BMI) was calculated from anthropometric data as weight (in kilograms) divided by height (in meters) squared. Nutrient intake data derived from NHANES single 24-hour dietary recall questionnaire was used to estimate dietary acid load. Because we did not have dietary chloride levels available in NHANES, we computed dietary acid load using the simplified calculation model developed by Remer and Manz,[21] as in our previous work.[9,22] This may possibly underestimate predicted net acid excretion because the average dietary acid load of ~1 mEq/kg/d noted in the average American diet is based on Lennon's estimation. Lennon et al[23] estimate net endogenous acid by taking into account the unmeasured anion content of diet and stool (Na + K + Ca + Mg) − [Cl + (1.8 × P)]).

Measurement and Classification of Albuminuria and Kidney Function

Serum and urine samples were collected in the mobile examination center. The procedures for measuring serum creatinine and urinary albumin and creatinine have been described.[22] eGFR was calculated using the CKD-EPI (CKD Epidemiology Collaboration) creatinine equation[24] to determine baseline CKD.

Food Insecurity

We defined food insecurity in NHANES III as an affirmative response to the question, "In the last 12 months, did you or your household ever cut the size of your meals or skip meals because there wasn't enough money for food?"[25] This question was a proxy for the broader definition of food insecurity, which includes a person's ability to access nutritious food.

Follow-up Data

The primary outcome was the incidence of ESRD, defined as entry into the Medicare ESRD Registry from the time of the survey through December 31, 2006. Death was ascertained through the National Death Index.[26] We used NHANES III data because to our knowledge, this is the only nationally representative sample that is linked to the Medicare ESRD Registry and National Death Index with a long follow-up and has measures on food insecurity.

Statistical Analyses

Baseline characteristics of study participants across the food-secure and food-insecure groups in both the CKD and non-CKD groups were compared using χ^2 test for categorical and *t* test for continuous variables; Kruskal-Wallis test was used for continuous variables if the normality assumption of the residuals was not met. In the CKD and non-CKD groups, we investigated the association of food insecurity with the development of ESRD in individuals using the Fine-Gray competing-risks method to account for potential bias due to the competing risk for death before ESRD.[27] Models were adjusted for demographics (age, sex, and race/ethnicity), income, clinical risk factors (diabetes and hypertension), kidney function/damage markers (eGFR and albuminuria), and nutritional risk factors (total caloric intake per day, BMI, and dietary acid load). Both eGFR and albuminuria, along with the nutritional risk factors, were analyzed as continuous variables.

In the CKD group, we ran additional analyses for mortality as the primary end point and ESRD as a competing risk to determine whether food insecurity was also a risk factor for mortality.

Sensitivity Analyses

We carried out 5 sets of sensitivity analyses to test the robustness of our findings. First, we performed stratified analyses among participants with incomes < 200% of the federal poverty limit (based on the poverty income ratio) to study the association between food insecurity and ESRD in low-income individuals (n = 1,557). Second, we performed another analysis in the general population comprising both CKD and non-CKD adults in NHANES III, who were 20 years or older and had dietary intake data, with incomes < 400% of the federal poverty limit, to explore the association of food insecurity with risk for ESRD (n = 11,726). Third, we examined the association of food insecurity and incidence of ESRD in the CKD group using the propensity score method for covariate adjustment.[28] Propensity scores were used in 2 ways and 2 sets of results were generated: (1) propensity score as a continuous variable was entered into the final multivariable competing-risk model and (2) quintiles of the propensity score were entered into the final model. Fourth, we used the isotope-dilution mass spectrometry (IDMS)−traceable 4-variable MDRD (Modification of Diet in Renal Disease) Study equation[29] to estimate GFR in our definition of CKD and then examined the association of food insecurity with ESRD in the CKD and non-CKD groups. Fifth, we examined the association of food insecurity and development of ESRD in NHANES 2001 to 2004 (n = 1,253) because this is a more recent cohort and provides information for food insecurity based on an 18-item household questionnaire. Scored responses from the questionnaire were grouped into 4 categories: full, marginal, low, and very low food security (0, 1-2, 3-5, and 6-10 affirmative responses, respectively). We defined food security as the combined full and marginal categories and defined food-insecure participants as those who were in the low or very low categories. In NHANES 2001 to 2004, because the number of events was small due to the shorter follow-up, we used the propensity score method for covariate adjustment.[28]

Analyses included NHANES survey sample weights to account for the complex sample design following the analytical guidelines for NHANES data as proposed by the CDC.[29] For variance estimates, we used Fay's balanced repeated replication procedure, an approach for estimation of standard errors for multistage samples that consist of many sampling units.[30,31] Results were considered significant for $P < 0.05$. All analyses were performed using SAS, version 9.2 (SAS Institute Inc).

Institutional Review Board Approval

This study was approved by the University of California, San Francisco, Institutional Review Board (Committee on Human Research application #10-04162).

RESULTS

Study Participants

In our study population of NHANES III participants with CKD (n = 2,320), 4.5% had food insecurity. Baseline characteristics are presented in Table 1. Food-insecure participants compared with food-secure participants had lower incomes and were younger, less likely to be non-Hispanic black (28.8% vs 32.8%), and more likely to have diabetes (29.9% vs 25.0%), hypertension (73.9% vs 67.3%), and albuminuria (90.4% vs 77.1%; $P < 0.05$). Dietary acid load was greater for food-insecure participants, but results were of borderline statistical significance ($P = 0.05$).

Among non-CKD participants (n = 10,448), 5.7% were food insecure. In this population, food-insecure participants compared with food-secure participants were more likely to have low educational attainment (67.0% vs 41.9%) and were younger, less likely to be non-Hispanic black (27.7% vs 28.8%), and less likely to have hypertension (31.5% vs 35.8%; $P < 0.05$).

On examining incident ESRD events by eGFR groups and ACR groups, we found 115, 125, and 346 events in groups with eGFRs, 45, 45 to <60, and ≥60 mL/min/1.73 m^2, respectively, and 227, 125, and 234 events in groups with ACRs, 30, 30 to 300, and >300 mg/g, respectively.

CKD Group

During a median of 12.4 (interquartile range [IQR], 6.6-14.9) years, 120 (5.2%) NHANES III participants with earlier stages of CKD developed ESRD. Figure 1A illustrates cumulative incidence by food-security status. This was significantly different ($P < 0.001$ by log-rank test). In crude analyses, those reporting food insecurity were 2.8 times more likely to progress to ESRD than the food-secure group. Multivariable adjustment for age, sex, and race/ethnicity did not much alter the risk for ESRD (relative hazard [RH], 2.64; 95% confidence interval [CI], 1.52-5.68). On adjustment for income, results were further attenuated (RH, 2.15; 95% CI, 1.25-4.90). The risk for ESRD was substantially attenuated with adjustment for the clinical risk factors of diabetes and hypertension (RH, 1.77; 95% CI, 1.19-4.20) and then on subsequent adjustment for eGFR and albuminuria (RH, 1.39; 95% CI, 1.09-3.77). The RH was not materially different when adjusted for total caloric intake per day and BMI: 1.38 (95% CI, 1.08-3.10). When the model was further adjusted for dietary acid load, the RH was further attenuated and was of borderline significance: 1.22 (95% CI, 0.99-2.11) (Table 2).

Non-CKD Group

In a median of 14.4 (IQR, 12.8-16.2) years, 226 (2.2%) NHANES III participants developed ESRD. Figure 1B illustrates the cumulative incidence by food-security status in the non-CKD group. A multivariable model adjusted for demographics, poverty income ratio, clinical factors, kidney markers, and nutritional factors revealed that food insecurity was not associated with risk for ESRD (RH, 0.77; 95% CI, 0.40-1.49) (Table 3).

Sensitivity Analyses

CKD Population < 200% of the Federal Poverty Limit

When we examined participants with CKD and incomes < 200% of the federal poverty limit, we found our results to be similar to our primary analysis. A total of 8.8% of this sample was food insecure. The unadjusted hazard of ESRD for food-insecure participants was 3 times greater than that of food-secure participants (RH, 2.97; 95% CI, 1.68-5.18). After multivariable adjustment for demographics, income, clinical risk factors, kidney markers, and nutritional risk factors, the risk was attenuated (RH, 1.38; 95% CI, 1.07-1.98). On further adjustment for dietary acid load, the increased risk for ESRD among food-insecure individuals was nominally reduced to 25% (RH, 1.25; 95% CI, 0.995-1.81), but this result did not meet the threshold of statistical significance ($P = 0.06$).

General Population

On exploring the association between food insecurity and ESRD in the general population (n = 11,726) whose income was <400% of the federal poverty limit, 7.2% of participants were noted to be food insecure. In total, 586 (4.9%) participants developed ESRD in the general population. We did not find a significant association between food insecurity and risk for ESRD (RH, 1.10; 95% CI, 0.64-1.99).

Propensity Score Method in NHANES III

Among food-insecure participants, after adjusting the competing-risk model using propensity scores for risk factors to be food insecure, the RH for ESRD was 1.26 (95% CI, 0.98-2.04) for propensity score as a linear covariate. That is, with increasing propensity, the risk for ESRD also increased. The RH for ESRD for propensity score as quintiles was 1.27 (95% CI, 1.00-2.02).

eGFR < 60 mL/min/1.73 m^2 and ACR > 300 mg/g

When we examined the association of food insecurity with incident ESRD in participants with eGFRs < 60 mL/min/1.73 m^2 and ACRs > 300 mg/g, we found 221 of 230 participants to be food insecure. There were 97 (42.2%) ESRD events observed. In the multivariable model, the RH for incident ESRD for participants who were food insecure was 2.29 (95% CI, 0.91-5.92) when compared with those who were food secure.

Food Insecurity and Mortality

In competing-risk analyses, results were no longer significant if death was included as the end point in lieu of being treated as a competing risk. The RH for death was 1.07 (95% CI, 0.62-1.86) comparing food-insecure with food-secure participants with CKD.

MDRD Study Equation

Using the IDMS-traceable 4-variable MDRD Study equation for calibrated serum creatinine[29] level to determine baseline CKD, 6.1% of 2,369 NHANES III participants with CKD were food insecure while 7.2% were food insecure in the non-CKD group. We noted 136 (5.7%) ESRD events in participants with CKD and 214 (2.1%) ESRD events in non-CKD participants. The RH associated with ESRD in the unadjusted model for participants with CKD was 2.81 (95% CI, 1.62-5.84), while for the non-CKD participants, it was 0.50 (95% CI, 0.25-0.98). In the multivariable model, when adjusted for demographics, income, and clinical risk factors, RHs in the CKD and non-CKD groups were 1.79 (95% CI, 1.20-4.20) and 0.77 (95% CI, 0.40-1.47), respectively. The fully adjusted model showed a RH of 1.21 (95% CI, 0.99-2.10) in the CKD group and 0.76 (95% CI, 0.39-1.47) in the non-CKD group, which were similar compared with those estimated using the CKD-EPI equation.

NHANES 2001 to 2004

Baseline characteristics of participants are presented in Table S1 (provided as online supplementary material). We found 7.9% of the 1,253 participants with CKD to be food insecure in this cohort. There were 32 (2.6%) ESRD events observed. Among food-insecure participants, after adjusting the model using propensity scores for risk factors to be food insecure, the RH for ESRD was 1.07 (95% CI, 0.99-1.31) for propensity score as a linear covariate. The RH for ESRD for propensity score as quintiles was 1.09 (95% CI, 1.00-1.30; Table S2).

Table 1. Baseline Characteristics of US Adults With and Without CKD by Food-Security Status in NHANES III, 1988 to 1994

	CKD Group (n = 2,320)				Non-CKD Group (n = 10,448)			
Characteristic	**All**	**Food Secure**	**Food Insecure**	***P***	**All**	**Food Secure**	**Food Insecure**	***P***
Age, y	68.0 [50.0-78.0]	69.0 [51.0-79.0]	52.0 [34.0-68.0]	0.01	41.0 [30.0-61.0]	41.0 [30.0-61.0]	35.0 [27.0-49.0]	0.02
Age category								
20-50 y	23.5	22.5	43.6		63.2	62.4	76.2	
51-70 y	37.2	37.3	35.6		23.4	23.7	18.6	
>70 y	39.3	20.8	20.8		13.4	13.9	5.2	
Male sex	42.9	43.2	37.5	0.2	45.2	45.4	43.0	0.5
Race/ethnic groups				<0.001				<0.001
Other	3.1	3.0	4.8		4.4	4.5	3.1	
Mexican American	23.4	21.9	53.8		31.2	29.7	56.5	
Non-Hispanic black	32.5	32.8	28.8		28.7	28.8	27.7	
Non-Hispanic white	41.0	42.4	12.5		35.6	37.0	12.7	
Poverty income ratio	1.7 ± 0.9	1.8 ± 0.9	0.9 ± 0.5	<0.001	1.8 ± 1.0	1.9 ± 1.0	0.8 ± 0.5	<0.001
Education				0.02				<0.001
<HS	56.8	56.0	72.2		43.3	41.9	67.0	
HS/some college	37.0	37.5	26.7		48.5	49.6	31.0	
≥College degree	6.2	6.5	1.1		8.2	8.5	2.0	
Weight								
Male, kg	78.1 [68.5-89.9]	78.3 [68.5-89.7]	73.1 [65.8-92.3]	0.8	77.9 [68.6-88.6]	78.1 [68.8-88.8]	74.8 [65.6-85.3]	0.007
Female, kg	68.8 [59.3-81.1]	68.5 [59.0-81.1]	70.0 [61.3-81.1]	0.4	67.5 [58.4-80.3]	67.5 [58.4-80.2]	68.8 [58.8-80.7]	0.9
Height								
Male, cm	171.6 [166.6-176.6]	171.6 [166.6-176.6]	169.1 [162.2-176.2]	0.09	172.9 [168.1-178.1]	173.0 [168.3-178.2]	170.2 [165.1-175.6]	<0.001
Female, cm	158.0 [153.3-163.2]	158.0 [153.4-163.2]	156.3 [151.3-162.2]	0.2	160.0 [155.6-165.0]	160.2 [155.7-165.0]	157.9 [153.3-164.0]	<0.001
Body mass index								
Male, kg/m^2	26.8 [23.8-30.2]	26.8 [23.9-30.1]	27.0 [22.9-32.8]	0.6	26.1 [23.3-29.3]	26.1 [23.4-29.2]	25.8 [22.8-29.4]	0.6
Female, kg/m^2	27.7 [23.6-32.4]	27.6 [23.5-32.3]	28.9 [25.7-33.2]	0.1	26.5 [22.9-31.2]	26.4 [22.8-31.1]	27.5 [23.8-32.5]	0.05
Diabetes	29.7	25.0	29.9	0.001	7.2	7.2	7.4	0.5
Hypertension	73.6	67.3	73.9	0.03	35.6	35.8	31.5	0.02
eGFR, mL/min/1.73 m^2[a]	73.2 [48.0-121.9]	73.9 [50.2-117.7]	71.5 [47.1-122.5]	0.04	123.7 [99.4-151.6]	122.8 [98.4-150.5]	136.2 [110.2-165.5]	<0.001
Albuminuria > 30 mg/g	77.7	77.1	90.4	0.008	8.3	8.2	9.4	0.4
Total calories								
Male, kcal/d	1,786 [1,355-2,351]	1,790 [1,361-2,353]	1,637 [1,308-2,274]	0.4	2,272 [1,706-2,935]	2,274 [1,712.5-2,935]	2,256 [1,635-2,898]	0.3
Female, kcal/d	1,401 [1,063-1837]	1,405 [1,072-1,837]	1,327 [952-1,866]	0.4	1,640 [1,245-2,119]	1,640 [1,244-2,115]	1,644 [1,263-2,159]	0.4

(Continued)

Table 1 (Cont'd). Baseline Characteristics of US Adults With and Without CKD by Food-Security Status in NHANES III, 1988 to 1994

Characteristic	CKD Group (n = 2,320)				Non-CKD Group (n = 10,448)			
	All	Food Secure	Food Insecure	*P*	All	Food Secure	Food Insecure	*P*
Dietary acid load								
Male, mEq/d	52.8 [47.6-59.9]	52.8 [47.6-59.9]	53.5 [45.3-59.4]	0.4	57.4 [51.1-64.3]	57.5 [51.2-64.4]	56.6 [49.5-63.0]	0.3
Female, mEq/d	45.0 [39.7-50.5]	44.9 [39.5-50.5]	45.2 [39.9-50.6]	0.9	47.0 [42.0-52.8]	47.0 [42.0-52.7]	46.9 [41.8-52.9]	0.4

Note: Values for categorical variables are given as percentages; values for continuous variables, as mean ± standard deviation or median [interquartile range].

Abbreviations and definitions: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HS, high school; hypertension defined as self-reported, average blood pressure ≥140/90 mm Hg and use of medications; poverty income ratio, a ratio of family income to poverty threshold; NHANES, National Health and Nutrition Examination Survey.

[a]There were 22 participants missing data for eGFR estimation in NHANES III.

In the non-CKD group, we found 10.2% of the 4,883 participants to be food insecure. There were 16 (0.3%) ESRD events observed. The RH for incident ESRD adjusted for propensity scores for risk factors to be food insecure was not significant (Table S2).

DISCUSSION

In this population-based cohort study of adults with CKD, food insecurity was associated with a higher likelihood of developing ESRD independent of demographics, income, clinical risk factors, and kidney markers. Nutritional factors including dietary acid load explained some of the association between food insecurity and kidney failure. Food insecurity may be a heretofore unrecognized risk factor for progression to ESRD among adults with CKD. On the contrary, adults without CKD showed no association between food insecurity and incident ESRD.

Several studies have demonstrated cross-sectional associations between food insecurity and chronic diseases,[3,32,33] including one report on CKD.[11] To our knowledge, our analysis is the first report of an association between food insecurity and CKD progression to ESRD. Controlling for the potential confounders in the multivariable model attenuated the association between food insecurity and ESRD, suggesting that these confounders contributed to an increased risk for ESRD among food-insecure adults with CKD. The large RH for ESRD observed among food-insecure adults could possibly be explained on the basis of several factors, such as diabetes status, low income, and nutritional factors. We observed a 2-fold risk for ESRD when the model was adjusted for demographic factors, low income, diabetes, and hypertension. These results are consistent with previous work showing that food insecurity is associated with increased risk for type 2 diabetes and worse glycemic control,[16] and food insecurity has the strongest association with CKD in persons with either diabetes or hypertension.[11]

Food insecurity is closely linked to poverty. Among individuals living at <200% of the US federal poverty limit, it has been estimated that 45.7% are food insecure.[34] Several studies have highlighted a strong association between socioeconomic status and incidence of ESRD.[35-38] In an analysis of 1,373,454 US adult patients initiating dialysis therapy during 1995 to 2010, Garrity et al[35] found area-level poverty status (zip code−defined area in which ≥20% of households live under the federal poverty limit) to be associated with a 1.24-fold higher ESRD incidence, after taking the distribution of age, sex, and race/ethnicity within a zip code into account. Compounding the issues of poverty and food insecurity, many low-income neighborhoods lack availability of healthful foods in nearby stores and markets. In the

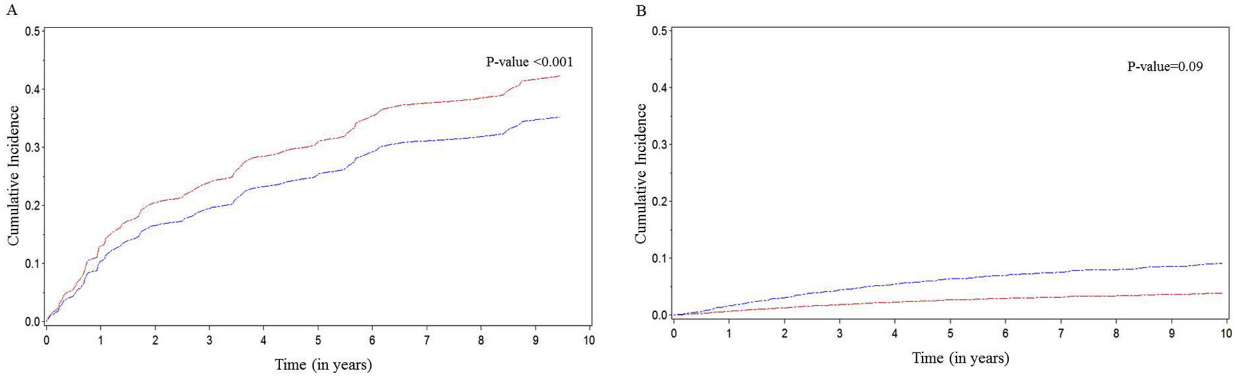

Figure 1. Cumulative incidence for risk for end-stage renal disease by food insecurity status in the (A) chronic kidney disease (CKD) group and (B) non-CKD group. Red line, food-insecure group; blue line, food secure group.

United States, stores stocking healthier options are clustered in more affluent neighborhoods as compared with those that are less affluent.[39-41] This may have contributed to observed differences in dietary acid load (a reflection of fruit and vegetable intake) between food-insecure and food-secure participants in our study.

In this study, we observed that total caloric intake per day, BMI, and dietary acid load accounted for some of the risk for ESRD associated with food insecurity. When financial or geographic restrictions become barriers for poor communities to obtain healthy foods, people from these communities are likely to eat fewer fruits and vegetables[42] and instead consume "processed foods"—lower quality and high-energy-dense foods high in starches, added sugars, and added saturated fats.[43] Consumption of energy-dense foods that are high in acid precursors and limited intake of fruits and vegetables and fiber may explain the increase in dietary acid load.[44] Furthermore, earlier studies have shown that diet composition resulting in an acid-producing diet increases the risk for progression to ESRD among adults with earlier stages of CKD.[22,45] By adding total caloric intake, BMI, and dietary acid load to explain the association of food insecurity with ESRD, the RH was attenuated to 1.21 from 1.40, the risk after adjusting for demographics, income, clinical risk factors, and kidney markers. This implies that food insecurity might lead to ESRD through direct effects of diet quality on kidney health, which has important implications for clinical practice, research, and public health. These observations reflect the difficulty addressing and interpreting the relationship of diet quality as a potential causal mechanism for the disease burden of ESRD among those of lower socioeconomic position and with food insecurity.

Our study's strengths include a large national sample of well-characterized participants from NHANES III and 12 to 18 years of follow-up. Thus, it represents one of the largest cohorts establishing that food insecurity is associated with

Table 2. RH for Risk for ESRD for Food Insecurity in NHANES III Participants With CKD

Model Adjusted for	n	No. of ESRD Events	RH (95% CI)	*P*
Unadjusted	2,320	120	2.75 (1.60-5.90)	0.01
+ Demographics	2,320	120	2.64 (1.52-5.68)	0.03
+ Income	2,320	120	2.15 (1.25-4.90)	0.04
+ Clinical factors	2,320	120	1.77 (1.19-4.20)	0.01
+ Kidney markers	2,156	101	1.39 (1.09-3.77)	0.03
+ Nutritional factors	2,156	101	1.22 (0.99-2.11)	0.06

Note: Reference group is food-secure group. Demographic factors are age, sex and, race; clinical factors, diabetes mellitus and hypertension; kidney function/damage status, estimated glomerular filtration rate and albuminuria; nutritional factors, total caloric intake/day, body mass index, and dietary acid load.

Abbreviations: CI, confidence interval; CKD, chronic kidney disease; ESRD, end-stage renal disease; NHANES, National Health and Nutrition Examination Survey; RH, relative hazard.

Table 3. RH for Risk for ESRD for Food Insecurity in NHANES III Participants Without CKD

Model Adjusted for	n	No. of ESRD Events	RH (95% CI)	*P*
Unadjusted	10,448	226	0.55 (0.32-1.02)	0.06
+ Demographics	10,448	226	0.60 (0.35-1.07)	0.06
+ Income	10,448	226	0.75 (0.40-1.39)	0.1
+ Clinical factors	10,448	226	0.79 (0.41-1.47)	0.2
+ Kidney markers	10,254	220	0.75 (0.38-1.40)	0.1
+ Nutritional factors	10,254	220	0.77 (0.40-1.49)	0.2

Note: Reference group is food-secure group. Demographic factors are age, sex and, race; clinical factors, diabetes mellitus and hypertension; kidney function/damage status, estimated glomerular filtration rate and albuminuria; nutritional factors, total caloric intake/day, body mass index, and dietary acid load.

Abbreviations: CI, confidence interval; CKD, chronic kidney disease; ESRD, end-stage renal disease; NHANES, National Health and Nutrition Examination Survey; RH, relative hazard.

poor outcomes. However, the limitations of our study deserve comment. First, we did not have laboratory follow-up data and measurements of food insecurity over time. Thus, with measurements at a single time point, misclassification is possible if levels of CKD risk factors (eg, diabetes and hypertension) or other factors (eg, eGFR, ACR, and food insecurity) change over time. The lack of longitudinal assessments further limits our ability to adequately examine mediation. Furthermore, due to the lack of follow-up data for food insecurity, we cannot consider the baseline measure of food insecurity as an indication of chronic food insecurity. Second, food insecurity in NHANES was defined at a household level, whereas ESRD was determined on an individual level. However, evidence suggests that if food insecurity is present in a household, it affects almost all adults in the household.[46] Third, the food sufficiency question that was used in NHANES III does not permit a distinction to be made between moderate and severe insecurity and also does not allow the food-security status of children and adults to be estimated separately. However, similar but not significant results from the 18-item questionnaire used in NHANES 2001 to 2004 suggest that the screening question minimizes respondent burden without substantially biasing the data. Fourth, this survey was conducted in the early 1990s; subsequent changes in public assistance and food programs may limit the applicability of results to the current situation. However, this cohort was used because it is the most recent nationally representative sample that is linked to the ESRD Registry with a long follow-up and data for food insecurity. Our sensitivity analysis using NHANES 2001 to 2004 provides more recent information on eating patterns, although with much shorter follow-up. The similarity of results from the 2 NHANES cohorts supports the validity of results.

In summary, we have observed that food insecurity in lower income individuals with earlier stages of CKD is associated with increased risk for ESRD and that this association is partially mediated by nutritional factors, including higher levels of dietary acid load. This finding may have important public health implications. Further studies might be considered to clarify whether the excess risk for ESRD apart from the traditional risk factors is confined to the nutritional factors that we measured or to other environmental factors. Better detection of food insecurity in a clinical setting and more systematic approaches to measuring food insecurity in people accessing the health care system for treatment of chronic diseases may be appropriate to determine the best ways to meet their needs and better their health outcomes. Dietary interventions to slow CKD progression that account for how the financial difficulties of participants might affect implementation of recommended dietary changes may be beneficial for low-income communities.

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Contributions: Research idea and study design: TB, NRP, DCC; data acquisition: TB; data analysis/interpretation: TB, NRP, DCC, DEW, NRB, SS, SD, RS; statistical analysis: TB; supervision or mentorship: NRP. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. TB and NRP take responsibility that this study has been reported honestly, accurately, and transparently; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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SUPPLEMENTARY MATERIAL

Table S1: Baseline characteristics of US adults with CKD by food security status in NHANES 2001-2004.

Table S2: Relative hazard for risk of ESRD for food insecurity in NHANES 2001-2004 participants.

Note: The supplementary material accompanying this article (http://dx.doi.org/10.1053/j.ajkd.2016.10.035) is available at www.ajkd.org

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