



Original Article

The effects of protein intake on albuminuria in different estimated glomerular filtration rate: A population-based study

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ABSTRACT

Background: Chronic kidney disease (CKD) is a serious condition associated with early mortality, decreased quality of life, and increased health-care expenditures.

Methods: Data from the National Health and Nutrition Examination Survey (NHANES) collected from 1999 to 2012 were used. Subjects were divided into 4 estimated glomerular filtration rate (eGFR) categories: stage 1: eGFR ≥ 90 mL/min/1.73 m², stage 2: eGFR 60–89, stage 3: eGFR 30–59, and stage 4/5: eGFR < 30 , and 3 age strata (< 45 y, 45–64, 65+). Associations between protein intake and albuminuria were determined.

Results: A total of 45,259 subjects were included. Despite decreasing protein intake, there was a significant increase in the prevalence of albuminuria with decreasing levels of eGFR. Multivariable analysis showed that albuminuria was associated with daily protein intake in patients ≥ 65 years old with stage 1 disease, and that diabetes was associated with albuminuria in patients ≥ 65 years old with stage 2 and 3 diseases. Overall, albuminuria in patients with stage 1 disease was associated with hours of sitting per day and blood glucose level.

Conclusion: Albuminuria was associated with daily protein intake in patients of 45–64 years old with stage 1 CKD disease, and was associated with hours of sitting per day and blood glucose level. These data further support the importance of lifestyle changes in the management of CKD, especially in patients with early-stage disease.

1. Introduction

Chronic kidney disease (CKD) is a serious condition associated with early mortality, decreased quality of life, and increased health-care expenditures [1,2]. Deaths due to CKD have increased by approximately 82% in the past 20 years [3], and worldwide the number of patients receiving renal replacement therapy is estimated to be well over 1 million with an annual growth rate of approximately 8% [4]. CKD is more prevalent in the elderly population, and with the aging of the population the prevalence is expected to increase [5,6]. The condition is associated with a number of comorbidities including hypertension, cardiovascular disease, and end-stage kidney disease [7–9]. Management of CKD is a critical health issue.

Hallmarks of CKD are albuminuria and reduced glomerular filtration rate (GFR) with 5 recognized stages based on GFR ranging from stage 1 (kidney damage with normal or increased GFR [> 90 mL/min/1.73 m²]) to stage 5 (renal failure [GFR < 15 mL/min/1.73 m²]) [9]. The majority of the literature suggests that decreasing protein intake in

stage 1–4 CKD can delay progression to stage 5 disease [10–13], and the current Kidney Disease: Improving Global Outcomes (KDIGO) guidelines suggest a protein intake of 0.6–0.75 g of protein per kilogram of body weight per day (g/kg/d) for patients in stages 1–4 CKD [9]. By comparison, study indicates that an average healthy person in the United States consumes well above this amount [14], and that the mean dietary protein intake at different stages of CKD is higher than current guidelines recommend [15].

Protein plays a vital role in immunity, metabolism, health of bones, nerves, and much more. Although the literature suggests that restriction of protein intake can delay the progression of CKD [16–18], protein insufficiency can be extremely detrimental to general health. It is not clear if equivalent actual protein intake produces different effects in different stages of estimated glomerular filtration rate and age-related change. Thus, the purpose of this study was to use data from a national population-based database in the United States to determine the effect of protein intake on proteinuria at different stages of estimated glomerular filtration rate, and at different age strata.

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2. Materials and methods

2.1. Data source

Data from the National Health and Nutrition Examination Survey (NHANES) collected from 1999 to 2012 were used for this analysis. The NHANES program began in the early 1960s, and has been conducted as a series of surveys focusing on the health and nutritional status of the United States population. NHANES participants are randomly selected through a complex, multistage cluster design to represent the United States population of all ages. Further information about background, design, and operation of the program are available on the NHANES website (<http://wwwn.cdc.gov/nchs/nhanes>). The survey and data collection was approved by the NHANES Institutional Review Board (IRB), and the NCHS Research Ethics Review Board (ERB) (Protocol#98–12, Protocol#2005–06, and Protocol #2011–17). All of the NHANES data are de-identified and analysis of the data does not require IRB approval or subject informed consent.

2.2. Study population

Data of NHANES participants who were examined at a mobile exam center (MEC) and were not missing serum creatinine data (creatinine level can be used to determine an estimated GFR [eGFR]) or covariates of interest were included in the analysis. Pregnant women and bone cancer patients were excluded due to dramatic hemodynamic changes.

2.3. Study variables

2.3.1. Estimated glomerular filtration rate (eGFR)

GFR was estimated from serum creatinine level using the Modification of Diet in Renal Disease (MDRD) Study equation (eGFR_{MDRD}): $eGFR = 1.75 \times [(calibrated \text{ serum creatinine in mg/dL})^{-1.154}] \times age^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African-American})$ [19]. eGFR was then categorized based on the classification system established by the National Kidney Foundation Kidney Disease Outcomes Quality Initiative [9]. The categories are defined as follows: stage 1: eGFR ≥ 90 mL/min/1.73 m², stage 2: eGFR 60 to 89 mL/min/1.73 m², stage 3: eGFR 30 to 59 mL/min/1.73 m², and stage 4/5: eGFR < 30 mL/min/1.73 m². Because there were so few patients with stage 5 disease, those with stage 4 and stage 5 disease were grouped together.

2.3.2. Albuminuria

Albuminuria was calculated by the ratio of urine albumin (mg/dL)/urine creatinine (g/dL) (UACR) [20–23]. Albuminuria is defined when UACR is > 30 mg/g. A solid-phase fluorescent immunoassay for the measurement of human urinary albumin described by Chavers et al. [24] was used. Creatinine analysis was performed using the Jaffé kinetic rate reaction [25]. Detailed specimen collection and processing instructions are discussed in the NHANES Laboratory Procedures Manual [26]. According to the American Diabetes Association, the gold standard for measuring urine albumin excretion is a 24-h urine collection. Currently, the National Kidney Foundation recommends the use of spot urine ACR obtained under standardized conditions [27]. The UACR is a more convenient test for patients, and may be less prone to errors due to improper collection methods and variations in 24-h protein excretion compared with a random urine specimen [20].

2.3.3. Daily protein intake

NHANES included a 24-h dietary recall interview to obtain information from participants on their intake the types and amounts of foods and beverages from the previous day. Using detailed databases of the nutrient composition of foods from the U.S. Department of Agriculture, estimates of daily protein intake (gm) were calculated for each subject. In addition, daily protein intake may be associated with

disease as a result of confounding by total energy intake [28]. We also included total energy (kcal) for adjustment. The NHANES computer-assisted dietary interview (CADI) system is an automated data collection form that was developed using Power BuilderTM; several databases (i.e., Quick List food list, brand name food list, and food amount unit list) are linked to this system. Detailed descriptions of the dietary interview methods are provided in the NHANES Dietary Interviewer's Training Manual [29].

2.3.4. Demography

Age, sex, race/ethnicity were obtained from the NHANES database.

2.3.5. Behavioral data

Smoking was dichotomized, and defined by the question “Do you now smoke cigarettes?”. Participants who, in their entire life, never had at least 12 drinks were defined as “lifetime abstainers” by the question “In your entire life, have you had at least 12 drinks of any type of alcoholic beverage?”. Participants who had at least 12 drinks in their entire life, but had not consumed alcohol in the past 12 months were defined as “former drinkers” by the question “In the past 12 months, how often did you drink any type of alcoholic beverage?”. Participants who consumed at least 12 drinks in their entire life and drank on at least 1 day in the past year were considered current drinkers [30]. Sitting hours, such as average hours watching television or videos, and average hours computer use on a typical day were combined and obtained by the question “Over the past 30 days, on average, about how many hours per day did you sit and watch television or videos or use a computer or play computer games?”.

2.3.6. Biological data

Overweight was dichotomized, and defined by body mass index (BMI) ≥ 25 kg/m², and measurements were taken during the MEC visit. Diabetes mellitus was self-reported and patients were asked if they had ever been told by a doctor or healthcare professional that they had diabetes or sugar diabetes. Patients who responded “yes” were classified as having a diagnosis of diabetes. Hypertension was also dichotomized, and defined by the question “Have you ever been told by a doctor or other health professional that you had hypertension, also called high blood pressure?” or by asking if the participant was taking a prescription medication to lower blood pressure. Arthritis was defined as having been told by a doctor or healthcare professional that the participant had arthritis. Osteoporosis was defined as having been told by a doctor or healthcare professional that the participant had osteoporosis, sometimes called thin or brittle bones. C-reactive protein (CRP) is considered one of the best measures of an acute phase response to an infectious disease, or other cause of tissue damage and inflammation. CRP levels were determined using a Behring Nephelometer for quantitative CRP determination. Detailed specimen collection and processing instructions are discussed in the NHANES Laboratory Procedures Manual [26]. Serum glucose level was measured in a fasting subsample of persons 12 years of age and older. Glucose in mg/dL was as converted to mmol/L by multiplying by 0.05551.

2.4. Statistical analysis

Data of demographic and basic characteristics were expressed as mean $\pm$ standard deviation (SD) for continuous variables, and number (%) for categorical variables by eGFR level. Differences in categorical variables were determined using the chi-square test, and differences in continuous variables among groups were examined using the complex samples binary logistic regression model. Both univariate and multivariate regression analyses were performed to determine the significant factors associated with the risk of albuminuria (UACR > 30 mg/g). Variables having a P-value < 0.05 in univariate analysis were selected and evaluated by multivariate analysis with stepwise selection. Results were presented as odds ratio (OR) with corresponding 95% confidence

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