Risk of Chronic and End Stage Kidney Disease in Patients with Nephrolithiasis

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Abbreviations and Acronyms

ACR = albumin-to-creatinine ratio

BMI = body mass index

CKD = chronic kidney disease

eGFR = estimated glomerular filtration rate

ESKD = end stage kidney disease

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Purpose: We examine kidney stone disease as a potential risk factor for chronic kidney disease, end stage kidney disease and treatment with dialysis.

Materials and Methods: The NHANES (National Health and Nutrition Examination Survey) 2007-2010 database was interrogated for patients with a history of kidney stones. Demographics and comorbid conditions including age, gender, body mass index, diabetes, hemoglobin A1c, hypertension, gout and smoking were also assessed. Multivariate analysis adjusting for patient demographics and comorbidities was performed to assess differences in the prevalence of chronic kidney disease and treatment with dialysis between the 2 groups. History of nephrolithiasis was assessed with the question, "Have you ever had kidney stones?" Chronic kidney disease was defined as an estimated glomerular filtration rate of less than 60 ml/minute/1.73 m^2 and/or a urinary albumin-to-creatinine ratio greater than 30 mg/gm. Statistical calculations were performed using Stata® software with determinations of p values and 95% CI where appropriate.

Results: The study included an analysis of 5,971 NHANES participants for whom data on chronic kidney disease and kidney stones were available, of whom 521 reported a history of kidney stones. On multivariate analysis a history of kidney stones was associated with chronic kidney disease and treatment with dialysis (OR 1.50, 1.10–2.04, p = 0.013 and OR 2.37, 1.13–4.96, p = 0.025, respectively). This difference appeared to be driven by women, where a history of kidney stones was associated with a higher prevalence of chronic kidney disease (OR 1.76, 1.13–2.763, p = 0.016) and treatment with dialysis (OR 3.26, 1.48–7.16, p = 0.004). There was not a significant association between kidney stone history and chronic kidney disease or treatment with dialysis in men.

Conclusions: Kidney stone history is associated with an increased risk of chronic kidney disease and treatment with dialysis among women even after adjusting for comorbid conditions. Large scale prospective studies are needed to further characterize the relationship between nephrolithiasis and chronic kidney disease.

Key Words: kidney calculi; kidney failure, chronic; dialysis; epidemiology; urolithiasis

CHRONIC kidney disease is widely recognized as a significant public health concern. The prevalence of CKD in the American population from 2005 to 2010 was estimated at 14.0%, which represents an increase from 12.3% in 1988 to 1994.[1] Concomitant with this increase in

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CKD prevalence, there has also been an increase in the prevalence of nephrolithiasis in the United States, with the lifetime prevalence of kidney stones increasing during each of the last 4 decades.[2,3] Currently an estimated 8.8% (1 in 11) of the U.S. population reports a history of nephrolithiasis compared to 5.2% in 1994.[3]

Although several studies have noted a correlation between nephrolithiasis and CKD, the last nationally representative study examining this relationship analyzed a cohort between 1988 and 1994.[4–7] Given the increase in CKD prevalence and nephrolithiasis during the last 2 decades, our objective was to further delineate the more recent relationship between these 2 disease entities on a population-wide basis. A better characterization of the relationship between CKD and kidney stones may provide the impetus for increased efforts in the primary prevention of nephrolithiasis as a means of reducing morbidity and cost secondary to CKD and end stage kidney disease.

MATERIALS AND METHODS

Study Population

We performed an analysis of data from the NHANES for the years 2007 to 2010. NHANES is a periodic survey conducted by the Centers for Disease Control and Prevention that was designed to monitor trends in the health and nutritional status of the noninstitutionalized U.S. civilian population. The survey enlists a combination of personal interviews, physical examinations and laboratory testing to generate a data set that is made available for public consumption. NHANES provides prevalence data for an array of common chronic diseases including diabetes mellitus, obesity, cardiovascular disease and CKD. Nephrolithiasis was included in the NHANES III survey (1988-1994) but was subsequently excluded from data collection until the 2007-2010 survey. The survey also offers demographic, socioeconomic and additional risk factor data such as smoking history and environmental exposures. The study population was limited to those 20 years old or older. Individuals participated in an interview conducted at home as well as an extensive physical examination performed at a mobile examination center which included blood and urine collection.

Exposure and Outcome Definitions

Survey participants who answered yes to the question, "Have you ever had kidney stones?" were considered to have a history of nephrolithiasis (1,081 of 12,110 participants). Primary outcomes were incidence of CKD and treatment with dialysis (ESKD). CKD was defined as a composite of estimated glomerular filtration rate and albuminuria. Urine albumin and creatinine concentrations were obtained from a random spot urine sample from participants examined at mobile examination centers, reported in mg/gm. Responders with an eGFR less than 60 ml/minute/1.73 m^2 and/or an ACR greater than 30 mg/gm were defined as having CKD.[1] Participants with ACR less than 30 mg/gm and eGFR greater than 60 ml/minute/1.73 m^2 were defined as not having CKD. Participants for whom only one of these values was available that was not diagnostic of CKD were not included in the analysis. eGFR was calculated using the Modification of Diet in Renal Disease Study equation, [eGFR (ml/minute/1.73 m^2) = 175 $\times$ $(S_{cr})^{-1.154}$ $\times$ $(Age)^{-0.203}$ $\times$ (0.742 if female) $\times$ (1.212 if African-American)], where S_{cr} is serum creatinine.[8] As per previous publications examining eGFR in NHANES, participants with an eGFR less than 15 ml/minute/1.73 m^2 were treated as missing (11 patients not requiring dialysis) and levels that exceeded 200 ml/minute/1.73 m^2 were truncated at that level.[9,10]

Age, gender, race (reclassified as white, black and Hispanic), a history of cigarette smoking and history of gout were self-reported. Height and weight were measured and body mass index was calculated. BMI was excluded from multivariate analysis with dialysis stratified by gender to avoid overfitting. Without BMI included there were 117 events for men and 125 events for women. BMI was not significantly associated with dialysis on multivariate overall analysis. Diabetes mellitus was defined as self-report of a previous diagnosis, not during pregnancy, with concurrent use of insulin or oral hypoglycemic medication, or a serum glucose level of 126 mg/dl or greater among participants who fasted before the study visit, or a glycated hemoglobin level of 6.5% or greater. Hypertension was defined as an average systolic blood pressure of greater than 140 mm Hg, an average diastolic blood pressure of greater than 90 mm Hg or the use of antihypertensive medication. Dialysis dependence was assessed by a response of yes (sample size 293 patients) to the question, "In the past 12 months, have you received dialysis or peritoneal dialysis?"

Statistical Analysis

NHANES analytical reporting guidelines were followed, accounting for the complex survey design. Stata/SE version 11.2 was used for all statistical analysis. Two-tailed t-tests were used to generate p values for comparisons between those with vs without kidney stone history using NHANES guidelines to calculate degrees of freedom. For regression analysis the 95% CI and SE using Taylor series linearization were used. Age standardization was performed according to NHANES guidelines using the 2000 Census population with age categories 20 to 39, 40 to 59 and 60+.

RESULTS

Of the 12,110 participants for whom kidney stone history was assessed, CKD status, as assessed by ACR and or eGFR, was available for 5,971 participants. As expected, among these participants many of the nonage adjusted baseline demographic characteristics differed between those with a history of kidney stones and those without (table 1). As seen in supplementary table 1 (http://jurology.com/), no significant differences were observed in the age standardized mean eGFR between those with vs