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African American ESRD patients have a high pre-dialysis prevalence of kidney stones compared to NHANES III

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Abstract If nephrolithiasis (NL) promotes progression to end stage renal disease (ESRD), requiring renal replacement therapy, one might expect a higher prevalence of pre-ESRD stones among ESRD versus non-ESRD subjects. We compared the prevalence of pre-ESRD stones in an African-American (AA) hemodialysis (HD) population to the estimated stone prevalence in a nationally representative cohort of AA persons as obtained by the Third National Health and Nutrition Survey (NHANES III). Face-to-face questionnaires were administered to a sample of 300 AA HD patients undergoing dialysis therapy at the University of Chicago to determine pre-ESRD NL prevalence. All data on pre-ESRD stone prevalence was confirmed by documented medical history, radiology and laboratory findings, where available. Prevalence of pre-ESRD NL in AA HD patients was 8.3% versus 2.8% in the age, race and sex adjusted NHANES III population ($P < 0.001$). After adjustment for age and sex, it was estimated that the prevalence of pre-ESRD kidney stones among AA HD patients is significantly higher than the prevalence of kidney stones found in the general AA population.

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Introduction

The prevalence of kidney stones in patients with end stage renal disease (ESRD) has been reported to be as high as 5.3% [1]. Stone prevalence in the general US population is almost the same—5.2% [2]. However African-Americans (AA), who constitute more than 30% of ESRD patients [3] normally have a threefold lower prevalence of kidney stones [2, 4] than the remainder of the US population within which they are a minority (12.9%). Lower overall prevalence of kidney stones has also been documented in black South Africans, compared to their white counterparts [5]. Since AA people in the US population are at a higher than usual risk for ESRD and demonstrate higher rates of progression from chronic renal insufficiency to ESRD [4], stone formation may be of special importance in that an added burden of transient obstruction and need for urological instrumentation procedures could lead some to ESRD who might otherwise have maintained adequate renal function. In addition, recent data suggests that stone formation is often accompanied by renal histopathological changes that may lead to scarring and affect renal function [6–8]. This would enrich the AA ESRD population with stone formers. Our goal here is to test the hypothesis that AA ESRD patients have a higher pre-ESRD stone prevalence than that found in a nationally representative cohort of AA persons as obtained by the Third National Health and Nutrition Survey (NHANES III).

Materials and methods

Dialysis population

ESRD patients in the three geographically separate HD facilities of the University of Chicago arise from our emergency room and clinic populations, and are 95% AA. Although the Kidney Stone Program at the University of Chicago is a major referral center, its patients are drawn from a wide geographic area and have rarely contributed to the ESRD population at these three facilities. Our facilities provide care for patients in the surrounding communities, and are not targets of specific referral per se.

Interview protocol

All prevalent AA ESRD patients aged 18 years and older at the University of Chicago outpatient HD facilities were eligible to participate, except for those with advanced dementia and those who first manifested kidney stones while already on dialysis. A face-to-face screening questionnaire was administered by the medical director of each facility to determine presence or absence of history and symptoms consistent with NL. This was done once in each facility. Specifically, patients were asked: "Have you ever had a kidney stone? Has a doctor ever told you that you had a kidney stone?" Affirmative answer to either of these questions was taken to indicate a history of kidney stones. AA ESRD patients who self reported that their first stone occurred prior to starting dialysis were included into this analysis as pre-ESRD stone formers (pre-ESRD SF). Self-reported history of pre-ESRD stones was confirmed by written medical records and radiology reports in four patients, and by medical records alone in another four patients. An additional five patients reported passing a stone. Seven patients had undergone cystoscopy or other surgical stone-related procedure, including one nephrectomy.

General population

Data from the Third National Health and Nutrition Examination Survey (NHANES III) were used to estimate the prevalence of NL in the general AA population. A detailed description of the methods used in the NHANES III survey is available elsewhere [9]. Briefly, the survey was designed to provide national estimates of health and nutritional status in the civilian non-institutionalized US population aged 2 months and older. Data collected in NHANES III included, but was not limited to, socio-demographic factors, medical history, and medication use. Although subsequent surveys have been conducted, NHANES III is the most recent to include questions regarding nephrolithiasis (NL). In total, 33,994 persons were interviewed for NHANES III. In this study we restrict our attention to AA survey participants aged 18–90 years with information on the lifetime occurrence of kidney stones ($N = 5{,}341$). All eligible participants who answered "yes" to the question "Have you ever had a kidney stone?" ($N = 108$) were considered to have a history of NL.

Statistical analyses

The prevalence of kidney stones was estimated as the total number of pre-ESRD SF divided by the number of patients included in the study. Confidence intervals for the estimated prevalence of stones were based upon the normal approximation to the binomial distribution. All point estimates and standard errors reported for the general AA population incorporate the NHANES III survey weights that account for unequal probability of selection into the NHANES sample and survey non-response. Variance estimates were computed via the method of linearization [10]. Age and sex adjusted estimates of the prevalence of NL using NHANES III data were estimated via logistic regression. All statistical analyses were performed using standard software (Stata Corp. 2003, Stata Statistical Software, Release 8.0, College Station, TX, USA). The study protocol and informed consent were approved by the University of Chicago Institutional Review Board.

Results

Prevalence of pre-ESRD SF in our ESRD population

Our three dialysis facilities contained a total of 303 AA patients. Of these, 300 (140 males) were eligible to participate (three were demented). Twenty-five patients (15 males) (8.3%: 95% CI = 5.2–11.5%) were pre-ESRD SF. They and the 275 other ESRD patients did not differ in age (60 ± 16 vs. 64 ± 14 and 59 ± 18 vs. 61 ± 14, Pre-ESRD SF vs. ESRD, females and males respectively, $P > 0.05$ for both comparisons). Time from the first presentation of kidney stone to the start of dialysis ranged from 3 months to 50 years. Five patients experienced an episode of kidney stones within 3 years prior to the initiation of dialysis. Kidney stones were direct cause of ESRD in two patients: one due to hereditary RTA and another due to recurrent obstruction of a single kidney. There were no cases of

staghorn stones, primary hyperoxaluria or cystinuria. Three patients suffered from gout. No stones were due to bowel disease.

Of six retrieved stones, complete analyses were available in three patients. One stone was composed of uric acid in a patient with prior history of gout; one stone consisted of 80% calcium oxalate monohydrate and 20% protein, a third stone was calcium phosphate from a patient with RTA. Another acute nephrolithiasis episode was attributed to indinavir therapy in a patient with HIV. There were no patients who reported stones prior to dialysis who also formed a stone while on dialysis. Medical records and radiology reports of a random sample consisting of 20 ESRD patients who did not have history of kidney stones were reviewed to exclude underreporting of kidney stones. No such cases were identified.

Comparisons to NHANES III

For reference we considered the prevalence of stones among AA participating in NHANES III. The age and sex adjusted stone prevalence (adjusted to the mean age of 60 years in the ESRD sample with an equal proportion of females) was estimated to be 2.8% (95% CI: 2.2–3.3%) among AA participating in the NHANES III survey, significantly lower than the prevalence of stones prior to ESRD found in our patient sample ($P < 0.001$). Pre-ESRD prevalence of stones estimated in our ESRD sample is higher than that found in any of the reported subgroups in the NHANES III AA population, regardless of age or sex (Fig. 1). In fact, the only overlap in confidence intervals appears in the highest age groups, where the variability of such estimates is high. We should emphasize once again that only pre-ESRD stone formers are included in this analysis.

We repeated our analysis after excluding two patients (one male with indinavir stone and one female patient with RTA and recurrent calcium phosphate stone formation). In spite of that, our observed proportion of patients with nephrolithiasis was still significantly higher than that of NHANES [7.7% (95% CI: 4.7%, 10.7%) vs. 2.8% (95% CI: 2.2–3.3%), UC ESRD patients vs. NHANES, $P < 0.001$]. Thus, re-analysis of our data, using stricter criteria to eliminate cases in which stone disease was directly related to the cause of ESRD, still strongly supports our finding of a much higher stone prevalence in our AA pre-ESRD population compared to the NHANES III population. Within NHANES III there is no link between diabetes and stones, and we have not separated patients by diabetes in this work. However, we modeled the NHANES III data to account for a prevalence of 40% diabetes as found in our ESRD cohort, and the point estimate for stone prevalence increased by only 0.2% (to 3.0%, 95% CI = 2.4–3.5%). Thus, the high prevalence of DM in the ESRD patients is not likely to explain the increased numbers of stones found in this population.

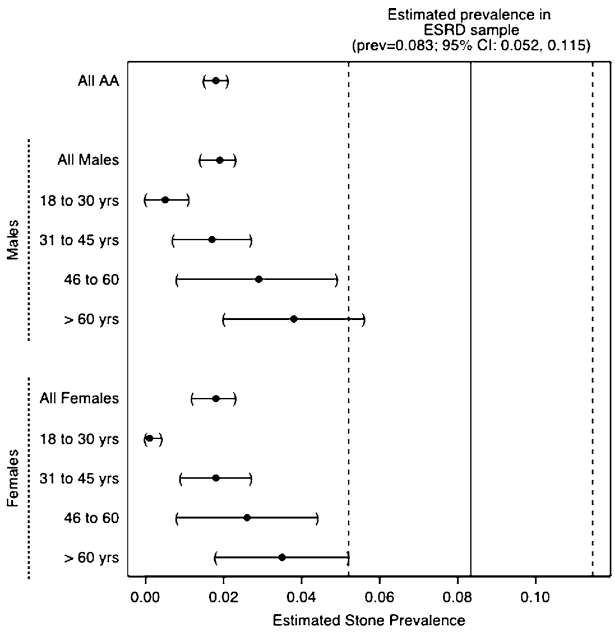

Fig. 1 Comparison of AA from NHANES III and the Chicago dialysis sample with respect to the prevalence of reported stones. All point estimates and confidence intervals for the NHANES III sample were adjusted for the survey design using sampling weights provided by NHANES

Discussion

The 8.3% prevalence of pre-ESRD kidney stones in our AA hemodialysis population is nearly three times higher than would be expected in a general AA population of similar age, sex and race. Using the estimated prevalence of stones obtained from NHANES III, only nine of our cohort of 300 patients would be expected to have a history of kidney stones prior to renal failure, but we identified 25 such cases. Nephrolithiasis or gouty nephropathy as a sole cause of ESRD is reported in 1.2% of incident patients in the US [3] and 3.2% in France [11], with a trend for decline over the past 2 decades; clearly our reported number of cases is far in excess of this number, and few of the stones were directly related to the need for dialysis in these patients.

This finding supports recently published data that kidney stones may play a role in the development of chronic kidney disease [12]. In a case-control study, comparing hospitalized patients newly diagnosed with chronic kidney disease (CKD) to matched community

controls, Vupputuri et al reported an overall odds of CKD being associated with a history of kidney stones to be 1.9 (95% CI; 1.1, 3.4). Almost 50% of their cases were AA. The prevalence of pre-ESRD stones (15 and 10% in men and women, respectively) was higher than we found, but 54% of their population was white. Their findings bolster our conclusion that kidney stones may contribute to loss of kidney function. If our two studies can be confirmed, clinicians will need to pay special attention to stone disease in chronic kidney disease.

Although the present data arise only from AA patients in the Chicago area, our dialysis units serve an unselected population drawn from three predominantly AA urban communities. Our comparison to the general AA population using NHANES III data prohibits the adjustment of many potential confounding factors, but age and gender are two of the largest predictors of stone disease [2] and we were able to adjust for these covariates in our comparison. An increased prevalence of ailments known to predispose to stones and renal failure, such as cystinuria, bowel disease, or primary hyperoxaluria was not present among our dialysis patients, and only three patients reported a history of gout. Reported stone prevalence analyzed by geographic region (West, Northeast, Midwest, and South) using the NHANES dataset demonstrated that overall prevalence in the Midwest was $4.6 \pm 0.70\%$, compared with $5.2 \pm 0.34\%$ for the country as a whole, thus our data cannot be explained by a higher regional prevalence [2].

Elsewhere we have suggested that renal function loss with age may be accelerated in stone formers [13]. Using the NHANES III data set, we have also found reduced renal function among stone forming versus non-stone forming people in those with BMIs above 27 [14]. Biopsy studies of patients who form brushite stones show obvious nephron loss in excess of appropriate controls [6]. These results are compatible with the present work in suggesting that stone formation is not completely benign with respect to renal disease and loss of renal function. None of these prior papers has specifically concerned AA populations.

Our analysis has limitations: it is a cross-sectional study, which limits its ability to establish temporal relationships. However, most pre-ESRD SF had kidney stones that would not have directly caused kidney failure except in two cases mentioned earlier. Our sample was limited in both its size and generalizability, but our observations are consistent with published data. Many possible confounders that are likely to differ between sicker pre-ESRD population and generally healthy participants in NHANES could not be controlled for, such as blood pressure, weight, dietary patterns. This could potentially lead to higher differences in the prevalence of stones. Nevertheless, more than half (56%) of our pre-ESRD SF manifested kidney stones more than 10 years before initiating dialysis. The nature of the association between CKD and kidney stones, also noted by Vupputuri [12], remains to be clarified.

Summary

Our main new finding is a high rate of pre-ESRD stone formation in AA people. If confirmed this should increase the clinical significance of stone formation in AA patients, especially if other risk factors for ESRD, such as hypertension and diabetes, are present. We have no data concerning mechanisms that might link stones to renal failure, and therefore presume as a first hypothesis that stone passage, infection, and urological procedures may contribute to renal injury in susceptible people, and thereby enrich the ESRD population with stone formers. Future prospective studies would further strengthen this relationship and should be given attention.

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