Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/0qdmvh32

PREVALENCE OF CHRONIC KIDNEY DISEASE IN OBSTRUCTIVE UROPATHY SECONDARY TO UROLITHIASIS

Anwar Shahzad[1], Sumera Kazmi[2], Raja Asim Shafique[3], Muhamad Usman Zia[4], Kafeel Azhar[5], Sofia Shoukat[6*]

[1]Associate Professor, Community Medicine, Abbottabad International Medical Institute Abbottabad, Pakistan
[2]Associate Professor, Internal Medicine, Abbottabad International Medical Institute, Abbottabad, Pakistan
[3]Consultant Urologist, Urology, Pakistan Kidney Center, Abbottabad, Pakistan.
[4]Registrar, Nephrology, Abbottabad International medical Institute, Abbottabad, Pakistan
[5]Senior Registrar, Urology, Abbottabad International medical Institute, Abbottabad, Pakistan
[6*]Assistant Professor, Biochemistry, Ayub Medical College, Abbottabad, Pakistan

***Corresponding author:** Dr. Sofia Shoukat,
*Assistant Professor, Biochemistry, Ayub Medical College, Abbottabad, Pakistan
Email: shoukatumar3@gmail.com

ABSTRACT

Recent population research has indicated that individuals with symptomatic kidney stones are at a heightened risk for chronic kidney disease (CKD). While kidney stones are not typically recognized as the primary cause of end-stage renal disease (ESRD), they may still play a significant role as contributing factors. Interestingly, CKD can offer some protection against the formation of kidney stones due to a marked decrease in urinary calcium excretion. Among those who form stones, individuals with rare genetic disorders (such as cystinuria, primary hyperoxaluria, Dent disease, and 2,8 dihydroxyadenine stones), recurrent urinary tract infections, struvite stones, hypertension, and diabetes appear to be at the greatest risk for developing CKD. The primary pathway through which kidney stones lead to CKD is generally linked to obstructive uropathy or pyelonephritis; however, crystal plugs in the ducts of Bellini and parenchymal damage resulting from shockwave lithotripsy may also play a role. The historical transition towards less invasive surgical techniques for managing kidney stones has likely positively influenced the risk of CKD. In potential kidney donors, a history of symptomatic kidney stones, but not those identified through radiographic imaging on computed tomography scans, was correlated with albuminuria. Additionally, kidney stones identified via ultrasound screening have been linked to CKD within the broader population. There is a need for further research that more accurately classifies CKD, better characterizes stone formers, thoroughly addresses potential confounding factors related to comorbidities, and employs active follow-up methods to mitigate detection bias.

Key Words: Chronic kidney disease, kidney stones, ultrasound, urinary tract infections.

INTRODUCTION

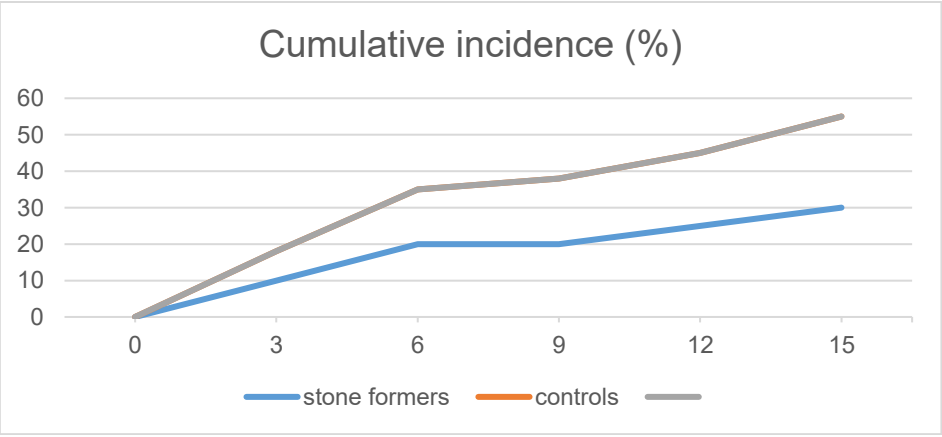
Intuitively, one might assume that kidney stones pose a risk factor for chronic kidney disease (CKD). The kidneys play a crucial role in excreting metabolic wastes such as calcium and oxalate at supersaturated levels while preventing the formation of crystals [(1)]. Therefore, the development of stones could be viewed as a manifestation of "impaired kidney function" and an indicator of kidney disease [(2)]. In cases where patients present with symptomatic kidney stones, it is standard practice to measure serum creatinine levels and evaluate for acute kidney injury (AKI) resulting from obstructive uropathy [(3)]. Following surgical or conservative

interventions to remove the stone, serum creatinine levels typically return to baseline as the AKI resolves. However, the long-term effects of kidney stones on renal health remain uncertain [4]. Are individuals with a history of stone formation at a heightened risk for CKD, and if so, which specific types of stone disease correlate with this increased risk? Furthermore, do stone formers face a greater likelihood of developing end-stage renal disease (ESRD)? What mechanisms connect kidney stones to CKD? [5].Additionally, do asymptomatic (incidental) stones present the same risk for CKD as symptomatic stones? This latter inquiry is particularly significant when assessing potential living kidney donors. [6] This review compiles existing literature that addresses these pertinent questions. We conducted an Ovid Medline search spanning from 1950 to August 2010 to locate articles for review. We combined English articles that included the terms "kidney/renal stone(s)/calculi/calculus" or "nephrolithiasis/urolithiasis" with those that contained the phrases "chronic kidney disease," "chronic renal failure," "chronic renal insufficiency," or "dialysis [7]." We further scrutinized the abstracts of the articles identified through this search for relevant content. Additional articles were discovered by examining reference lists and consulting with experts in the field [8]. One review article published in 2001 assessed the risk of CKD in individuals with a history of stone formation. Consequently, a significant portion of this review focuses on pertinent literature from the past decade [9].

Nephrolithiasis as chronic kidney disease risk factor

Numerous studies have investigated the risk of chronic kidney disease (CKD) among individuals who form stones. Nevertheless, there is a notable absence of population-based prospective cohort studies with active follow-up [10]. A historical cohort study conducted in Olmsted County, MN, evaluated the risk of CKD over several decades among all stone formers. These individuals were identified through diagnostic codes, while CKD was determined using two distinct criteria: Diagnostic codes and elevated serum creatinine levels (or estimated glomerular filtration rate [eGFR] <60 ml/min per 1.73 m2) maintained for a duration of three months or more. When compared to matched control subjects, stone formers exhibited a 51% to 68% heightened risk for CKD based on diagnostic codes (Figure 1) and a 25% to 44% increased risk for CKD based on elevated serum creatinine levels [11]. The stronger association with CKD identified through diagnostic codes may be attributed to a correlation with proteinuria (one of the diagnostic codes) that was not captured by serum creatinine levels or could stem from detection bias associated with diagnostic codes. Notably, there was an increased risk for CKD linked to kidney stones, whether the analysis included all patients or was restricted to those with follow-up serum creatinine levels. Additionally, the heightened risk for CKD associated with kidney stones could not be accounted for by several other CKD risk factors, such as diabetes, hypertension, and obesity, which are prevalent among stone formers [12]. Recently, Hippisley-Cox et al. conducted a significant population-based historical cohort study and discovered that female stone formers in England and Wales had a 27% increased adjusted risk for moderate to severe CKD (eGFR <45 ml/min per 1.73 m2 or CKD diagnosis). No association was observed in men; however, only 0.7% of the cohort had a diagnosis of stone former, which is significantly lower than the 5% prevalence typically reported for kidney stones (13) . A limitation of these studies was the dependence on diagnostic codes to adjust for comorbidities, as certain comorbidities, particularly metabolic syndrome, are not sufficiently identified through diagnostic codes (14).

Figure 1.



Risk for a clinical diagnosis of CKD between stone formers and control subjects
X-axis is years. Reprinted from reference 2, with permission.

Besides cohort studies, several other population-based studies have assessed for an association between kidney stones and CKD. Gillen *et al.* used the Third National Health and Nutrition Examination Survey (NHANES III) of the US population to compare eGFR between the 6% who reported a history of kidney stones and the 94% who did not report a history of kidney stones. Among individuals who were overweight or obese, a history of kidney stones was associated with an eGFR that was 3.4 ml/min per 1.73 m^2 lower after multivariable adjustment. A similar association in normal-weight individuals was not evident. Another population-based survey in Thailand found the 5% with a reported history of kidney stones to have an increased adjusted risk for CKD (odds ratio [OR] 2.7) (15) . However, the definition of CKD included microhematuria, in addition to the more standard criteria that require an eGFR <60 ml/min per 1.73 m^2 or albuminuria. Therefore, it is unclear the extent that microhematuria caused by direct stone injury confounded this association. Vupputuri *et al.* found that patients who had CKD and were identified by diagnostic codes and elevated serum creatinine levels were more likely to report a history of kidney stones on telephone interview when compared with matched community control subjects (OR 1.9). (16) Interestingly, the association was strongest in individuals without hypertension and in individuals who were identified by CKD diagnostic codes for interstitial nephritis or diabetic nephropathy. Because cases were identified via hospital record review, they may have had more unidentified comorbidities than control subjects did (17).

Kidney Stones as Risk Factors for ESRD

Epidemiologic association studies usually seek to identify risk factors that predict a disease. The situation is arguably reversed when assessing kidney stones (a symptomatic disease) as a predictor for a largely asymptomatic disease/risk factor (CKD) that does not always progress to clinically important outcomes. Thus, it is of particular interest also to evaluate kidney stones as a predictor for clinically important outcomes related to CKD, in particular ESRD. In their cohort study, Hippisley-Cox *et al.* reported an increased risk for ESRD with women (hazard ratio 2.1) but not men stone formers (18). The Olmsted County cohort study did not find evidence of increased risk for ESRD with stone formers, but the study had relatively few events Stankus *et al.* surveyed 300 black hemodialysis patients for a history of kidney stones and compared findings with the 5341 black individuals who participated in NHANES III. The likelihood of self-reported past kidney stones was higher for patients with ESRD than for the population control subjects (8% *versus* 3%). Of the 25 patients with ESRD and past kidney stones, only five had a stone episode within 5 years of starting dialysis and only two had ESRD that was primarily attributed to the stone disease (19).

It is important to distinguish stone formers in whom stones are the primary cause of ESRD from those in whom they are a contributing risk factor but not the primary cause. Jungers *et al.* specifically investigated ESRD cases that had been attributed to kidney stones by reviewing the case histories of 1391 consecutive patients with ESRD in France. Forty-five (3.2%) had ESRD attributed primarily or exclusively to kidney stones, with struvite stones in 19, calcium stones in 12, uric acid stones in eight, and rare hereditary stones in six (four primary hyperoxaluria, two cystinuria). (20) Tosetto *et al.* identified a history of kidney stones in only 3.2% of 1901 patients who had ESRD and were on hemodialysis, two thirds of whom (2.1%) had ESRD attributed to the kidney stones. The US Renal Data System reports only 0.2% (908 or 546,878) of all incident patients with ESRD from 2004 through 2008 had kidney stones as the primary cause, although these data are based on the ESRD Medical Evidence form (CMS 2728) and not chart review (21) .

The study by Jungers *et al.* found that 40% of stone formers who develop ESRD had a solitary functioning kidney before developing ESRD. Worcester *et al.* evaluated the cause of a solitary functioning kidney among 115 stone formers (3.5% of the patients seen in a stone clinic). The top three causes of loss for function in one kidney were staghorn calculi or high stone burden (29%), infection (23%), and ureteral obstruction (21%), whereas surgery was responsible for kidney loss in only 8%. There was a historical shift in the surgical management of kidney stones from open lithotomy to less invasive shockwave lithotripsy (SWL) and endourology, and this has likely had a beneficial impact on ESRD risk in stone formers [(21)].

Although kidney stones are predictive of future CKD, paradoxically, there is reason to believe that CKD is protective against formation of kidney stones. When GFR declines, there is an associated fall in urine calcium excretion, an important risk factor for stone formation. Indeed, evidence suggests that stone recurrence rates

may be lower in stone formers with a reduced GFR. Therefore, and ironically, if kidney stones lead to CKD, which in turn improves stone disease, then under recognition of the contribution of kidney stones to the development of ESRD may occur [15].

Disclosures

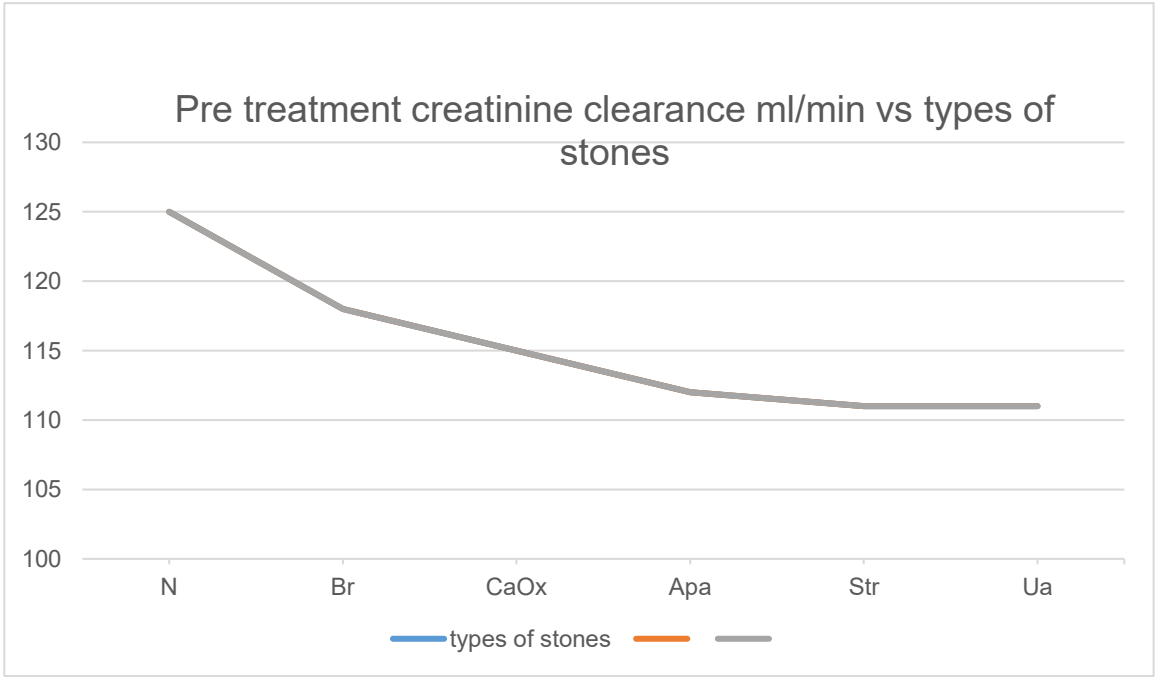
Before the development of ESRD, it is often assumed that CKD, regardless of cause, leads to a higher risk for cardiovascular morbidity and mortality. Whether this is true in stone formers who develop CKD requires further study. In Olmsted County, increased risk for mortality among stone formers was not evident. However, an increased risk for myocardial infarction among stone formers was detected, although this was *not* explained by CKD in stone formers.

Risk for CKD by Stone Type

There is evidence that the risk for CKD varies by stone type, but more studies are needed. Population-based studies often lack the granular detailed data to characterize stone type because many stone formers never have their stones analyzed or urine chemistries evaluated, and, even if so, this information often is not available in the databases available for study. Saucier *et al.* studied community stone formers in Olmsted County, MN, and identified 53 who developed CKD and were matched with 106 who did not develop CKD. Hypertension, diabetes, six or more urinary tract infections, allopurinol therapy, and struvite stone type were identified as risk factors for CKD. The association with allopurinol could either reflect treatment of hyperuricosuria for stone prevention or treatment of hyperuricemia secondary to CKD. Only half of the participants had stone type determined, and even fewer had urine chemistry data. Number of stone episodes, surgical procedures, and stone passage symptoms were not associated with CKD, although there was limited statistical power in this study [20].

Stone formers who present to specialty clinics are likely to have more severe disease than those in the general population but also have better characterized stone disease because of a more comprehensive evaluation. Worcester *et al.* reviewed urinary creatinine clearance data from 1856 stone formers with stone analyses at the University of Chicago and compared the findings with 153 normal individuals (adjusted for age, gender, and weight). Cysteine stone formers had a much lower creatinine clearance than other types of stone formers or nonstone patients. Uric acid, calcium oxalate, apatite, and struvite stone formers also had lower creatinine clearance than normal individuals (22).(Figure 2). When examined in regard to diseases that cause kidney stones, those with stones from bowel disease, intestinal bypass for obesity, and renal tubular acidosis also had lower creatinine clearance than normal individuals.

Fig: 2



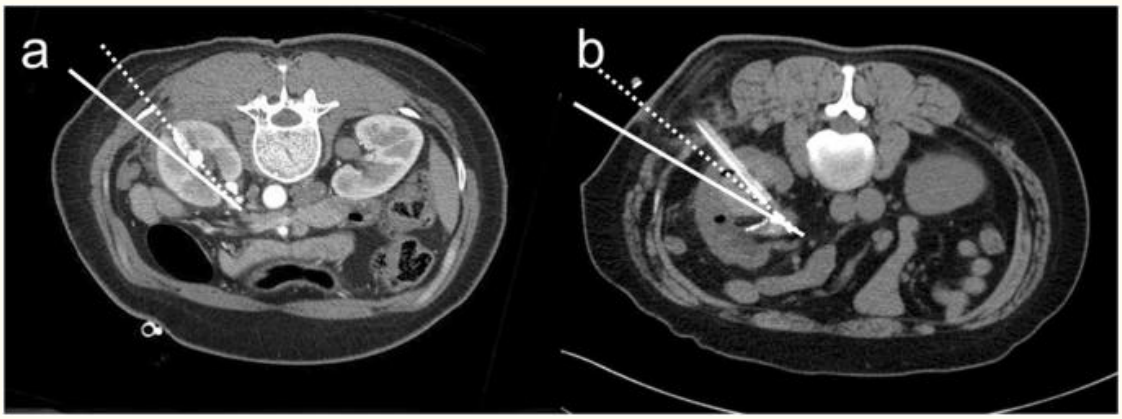
Pretreatment urinary creatinine clearance in normal control subjects (N) and different types of stone formers: Brushite (Br), calcium oxalate (CaOx), apatite (Apa), struvite (Str), uric acid (Ua), and cystine (Cys). Reprinted from reference 17, with permission.

Presumed Mechanisms for CKD in urolithiasis

Kidney stones could potentially lead to CKD *via* multiple pathways. Obstructive uropathy from a stone can cause acute injury but could also produce irreversible chronic injury. The mechanism by which any obstructive uropathy causes CKD is not completely understood. Renal vasoconstriction and inflammation can occur in response to increased intratubular pressure. The resulting fall in renal perfusion normalizes intratubular pressure but can also cause ischemia. If this ischemia persists long enough, glomerulosclerosis, tubular atrophy, and interstitial fibrosis occur Complete unilateral obstruction for 24 hours in a rat model leads to irreversible loss of function in 15% of the nephrons of the affected kidney. Therefore, if kidney stones caused recurrent episodes of obstructive uropathy, then there could be substantial loss of functional nephrons. Initially, the remaining functional nephrons may hypertrophy and hyperfilter to compensate and cause no change in the overall GFR. However, long-term, these "overworked" nephrons may fail, leading to detectable CKD (1).

Some pathways leading to CKD may be specific to certain stone types. Among predominantly calcium phosphate stone formers, approximately one third (5% overall) are brushite stone formers. Evan *et al.* studied stone formers with renal biopsies and video imaging during a percutaneous nephrolithotomy and found plugs at the ducts of Bellini in brushite stone formers as well as intestinal bypass stone formers (23). However, glomerulosclerosis, tubular atrophy, and interstitial fibrosis were particularly common among brushite stone formers (Figure 3) . Because there are only approximately 100 ducts of Bellini in each kidney (each represents the confluence of many collecting ducts), the investigators hypothesized that obstruction of these ducts could explain the increased chronic parenchymal injury (nephrosclerosis) on the cortical biopsy. Hypercalciuria and SWL treatments are common in brushite stone formers, and it is possible that these factors contributed to the development of CKD .

Figure 3.



A stone obstructing the duct of Bellini in a brushite stone former during a percutaneous nephrolithotomy. (Inset) Tubular atrophy and fibrosis score on cortical biopsy by stone type. Reprinted from reference 27, with permission.

Extracorporeal SWL is widely used to treat renal stones <2 cm in diameter . SWL has been shown in animal models to induce parenchymal injury that increases with the number of shocks, with level of energy, and with smaller kidneys. There is also an acute reduction in GFR and renal blood flow from vasoconstriction. Evaluation of treated kidneys with magnetic resonance imaging, excretory urogram, and nuclear scintigraphy reveals that 74% of patients have abnormal findings consistent with a renal contusion from the SWL. However, a long-term effect of SWL on kidney function has not been shown (15). Eassa *et al.* found no change in eGFR at approximately 4 years of follow-up or in the differential renal function of the treated kidney as assessed by nuclear scintigraphy. Even longer-term follow-up suggests that the risk for an elevated serum creatinine level is not increased with SWL compared with percutaneous nephrolithotomy or conservative management.

Hypertension has been described as a complication of SWL in many but not all studies. A recent population-based study did not find an increased risk with developing hypertension, suggesting that this complication is not common with most stone formers who undergo SWL. Pretreatment with low-energy shockwaves seems to be protective against renal injury from the high-energy shockwaves needed to treat stones.

Unique pathways may lead to CKD among struvite and uric acid stone formers. Chronic pyelonephritis from an infected struvite stone will lead to inflammation and eventual destruction of renal parenchyma Struvite stones can lead to ESRD either from obstructive nephropathy with staghorn calculi or from recurrent pyelonephritis. The urease enzyme and resultant high urine pH caused by microorganisms in struvite stone formers may also contribute to kidney injury. Large staghorn calculi may also cause papillary necrosis The risk for CKD in uric acid stone formers may be related to the concurrent hyperuricemia often seen in addition to the stones themselves. Uric acid crystals can deposit in the interstitial leading to inflammation (similar to gout) followed by interstitial fibrosis and CKD. Several general population studies have identified serum uric acid as an independent risk factor for incident CKD but did not adjust for kidney stones. Alternatively, diabetic nephropathy may link uric acid stones to CKD, given the increased risk for uric acid stones in patients with diabetes (24).

Chronic Kidney Disease in Rare Hereditary Stone Formers

Patients with rare hereditary forms of kidney stones that cause marked excretion of minerals important in stone formation, including primary hyperoxaluria, cystinuria, Dent disease, and adenine phosphoribosyl transferase (APRT) deficiency, are an important subgroup of stone formers. Patients with these disorders experience recurring stones often starting in childhood and are at high risk for CKD. ESRD is common in primary hyperoxaluria, Dent disease, and APRT deficiency, with usually less aggressive CKD in cystinuria. Cystinuria is also the most common of the rare hereditary kidney stone diseases (25).

Patients with primary hyperoxaluria have deficiencies of hepatic enzymes important in the metabolic pathways for detoxification of glyoxylate. Deficiency of either alanine glyoxylate aminotransferase (type 1) or glyoxylate hydroxy pyruvate reductase (type 2) results in marked overproduction of oxalate by the liver. Recently, a third genetic cause of primary hyperoxaluria was also identified, although the mechanism of oxalate overproduction in this subgroup has not yet been elucidated. Among patients with primary hyperoxaluria, urine oxalate excretion rates are typically two to eight times the upper limit of normal, such that the urine is markedly supersaturated for calcium oxalate. ESRD may occur as early as the first 6 months of life or may not occur until mid-adulthood. By the sixth decade of life, 90% of those with type 1 primary hyperoxaluria will have reached ESRD (10).

Cystinuria is an autosomal recessive disorder as a result of abnormal cystine transport in gut and kidney. Marked cystinuria is the hallmark of the disease. Because cystine is relatively insoluble in urine, cystine crystals and stones develop, most often beginning in childhood. The clinical course is characterized by recurring stone formation and repeated surgical procedures for extraction of stones from the urinary tract. Crystal plug obstruction of the ducts of Bellini occurs with increased glomerulosclerosis and interstitial fibrosis in the cortex. By adulthood, GFR may be reduced and CKD is more common than found in the usual stone former.

APRT deficiency, occurring as an autosomal recessive trait, leads to marked overproduction of 2,8 dihydroxyadenine by many body tissues, leading to excess excretion of this relatively insoluble compound in urine. ESRD is a widely recognized complication. Dent disease (X-linked recessive nephrolithiasis), caused by mutations of the *CLCN5* chloride channel, is associated with variable degrees of hypercalciuria and proximal renal tubule dysfunction (low molecular weight proteinuria) with CKD and ESRD occurring in affected males, usually between the ages of 15 and 45 years. Recently, it was observed that mutations in the gene associated with Lowe syndrome (*OCRL1*) can also present with a Dent disease phenotype.

Each of these inherited inborn errors of metabolism produces high concentrations of poorly soluble mineral salts in the urine, favoring the formation of crystals and kidney stones. The resulting crystals can be incorporated into the kidney parenchyma and incite an inflammatory reaction. Direct cell toxicity from high concentrations of molecules such as oxalate, injurious effects of crystals (either direct or related to a secondary inflammatory response), crystal plug obstruction of the ducts of Bellini, and consequences of stone formation such as ureter obstruction, repeated procedures, or infection are all potential factors for the development of

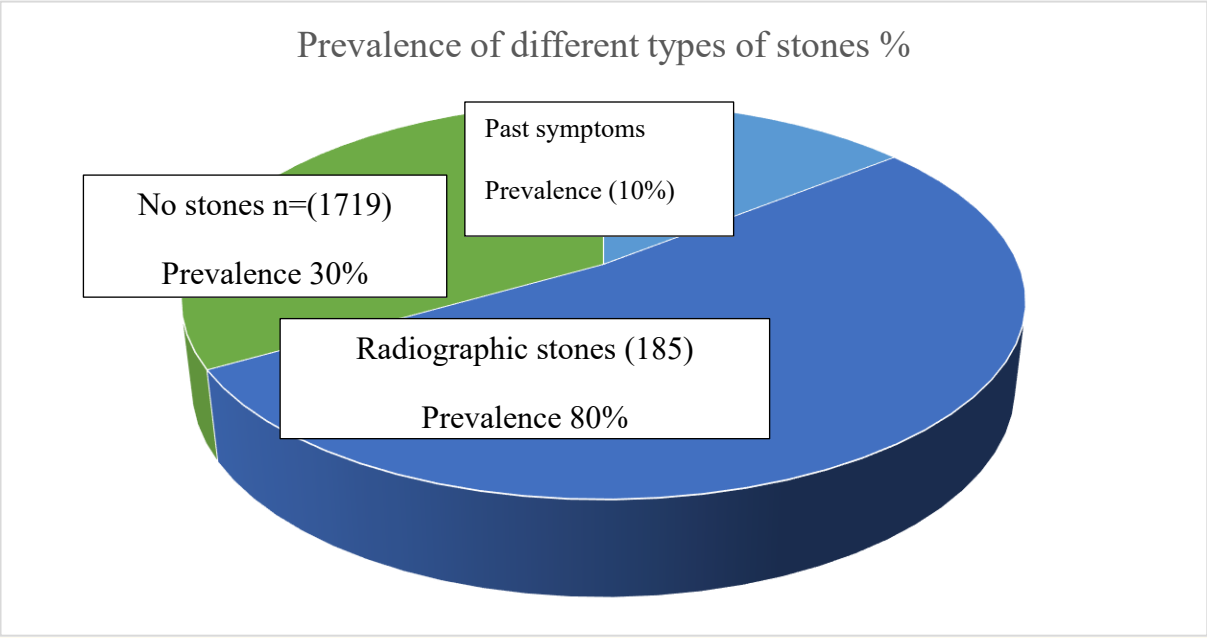
CKD and eventual ESRD. It is unclear which of these factors is most injurious. It is also unclear whether the same factors are responsible for CKD in each of the four diseases. If these diseases are recognized early and treated effectively, then CKD may be preventable. However, delay in diagnosis is the rule because of lack of familiarity with these diseases and availability of diagnostic tests.

Asymptomatic Stone Formers

With the increased use of computed tomography (CT) and other radiographic imaging, incidental asymptomatic kidney stones often are detected without pain or gross hematuria being present. Are these patients at increased risk for CKD? Lorenz *et al.* recently found that 11% of potential kidney donors at the Mayo Clinic have at least one kidney stone. Although the finding of a radiographic stone did not lead to exclusion from donation in most (76%), kidney stone was the most common radiographic kidney abnormality and the radiographic kidney abnormality that contributed most to nondonation (39% of exclusions). Strang *et al.* found that the increased sensitivity of CT angiograms compared with other imaging methods led to twice as many potential kidney donors being excluded for radiographic kidney abnormalities (including stones).

In a transplant program in which stone formers with severe disease were excluded from donor evaluations, potential donors with a history of symptomatic stones that were evaluated were still more likely to have albuminuria than those without stones (Figure 4) . However, albuminuria was not more common in potential donors with asymptomatic radiographic stones. Notably, potential donors with past symptomatic stones had larger radiographic stones (median 4 mm) than potential donors without past symptomatic stones (median 0.5 mm). Focal renal scarring was more prevalent among both asymptomatic and past-symptomatic stone formers than potential donors with no stones. Overall, these data suggest that asymptomatic stone formers may carry a lower risk for CKD than those with past symptomatic stones. However, outcome studies of asymptomatic stone formers who donate a kidney would better inform patients and clinicians during donor evaluations.

Figure 4.



Prevalence of albuminuria among nonstone formers, asymptomatic stone formers, and past symptomatic stone formers who present to donate a kidney. The prevalence of albuminuria (>30 mg/24 h) was increased in past symptomatic stone formers compared with potential donors without past symptomatic stones ($P < 0.001$).

Chen *et al.* assessed predictors of prevalent CKD in a random sample of the Chinese adult population. This study uniquely evaluated all 2554 participants with a renal ultrasound to detect kidney stones. Ultrasound can typically detect kidney stones that are >5 mm (whereas CT scanning can detect stones as small as 0.5 to 1 mm). Sonographic kidney stones were found in 56 participants (2.2%) and were associated with an eGFR <60

ml/min per 1.73 m^2 in multivariable analysis (OR 2.6). Past symptomatic kidney stone events were not reported; thus, it is unclear whether the risk for a reduced eGFR differed between symptomatic and asymptomatic stone formers.

Limitations: Several study design limitations hamper risk estimates of CKD among stone formers. First, many studies do not make the distinction between AKI and CKD. Assessment of the kidney function after treating the acute obstruction is needed, ideally at several time points. Second, stone formers seen in urology and nephrology referral clinics are likely to have more severe stone disease than those in the general population. Identifying stone formers in the general population can be a challenge because validation of stone former status among those identified by diagnostic code or survey can be difficult. Many kidney stones are identified as incidental findings on CT or ultrasound, and the clinical conditions that lead to imaging studies rather than the kidney stone itself may contribute to risk for CKD. Third, the urine dipstick or urinalysis used to help diagnose kidney stones (hematuria) is also a test to diagnose CKD (proteinuria). Therefore, there may be a bias in historical studies that rely on passive detection of CKD through clinical care. This is further complicated by follow-up serum creatinine testing being more common among stone formers than control subjects. Fourth, recent studies often used an eGFR <60 ml/min per 1.73 m^2 to identify CKD. This threshold captures the normal age-related decline in GFR in addition to the loss of GFR from a disease such as kidney stones. Studies are needed to determine whether kidney stones lead to a GFR lower than expected with normal aging. This is better determined using age-specific eGFR thresholds or even an elevated serum creatinine level. Fifth, some studies have used microscopic hematuria as part of the composite definition of CKD (in addition to albuminuria and reduced GFR). This is problematic because kidney stones themselves cause hematuria that is not glomerular in origin, and thus, CKD is not detected. Finally, thorough and accurate assessment of potential confounders, particularly medications and comorbidities, has been inadequate in most studies (26).

CONCLUSION

Several studies have found stone formers to be at increased risk for CKD and ESRD, but more research is needed. There may be significant heterogeneity in the risk for CKD, and better characterization of the stone types and clinical factors that identify stone formers at most risk for developing CKD are needed. In particular, do common calcium stone formers with infrequent episodes of stone passage and asymptomatic stone formers have increased risk for CKD? There are effective dietary and medical treatments to prevent stone formation and growth, and aggressively treating stone formers at increased risk for CKD and ESRD may be indicated. Whether stone formers can be approved as kidney donors is a common dilemma. A clearer understanding of the risk for CKD risk among kidney stone formers would obviously have an impact on this determination. Further studies, particularly prospective studies with active instead of passive follow-up, are needed to understand the relationship between kidney stones and CKD.

REFERENCES

1. Adejumo OA, Akinbodewa AA, Okaka EI, Alli OE, Abolarin OS. Obstructive Nephropathy in a Kidney Care Hospital in Southwest Nigeria: The need for early screening and prevention. Journal of Medicine in the Tropics. 2017;19(2):98-103.
2. Alelign T, Petros B. Kidney stone disease: an update on current concepts. Advances in urology. 2018;2018(1):3068365.
3. Carbone A, Al Salhi Y, Tasca A, Palleschi G, Fuschi A, De Nunzio C, et al. Obesity and kidney stone disease. A systematic review. Minerva urologica e nefrologica. 2018:393-400.
4. Cardella JT, Byers LA, Rochon PJ. Obstructive Uropathy. IR Playbook: A Comprehensive Introduction to Interventional Radiology: Springer; 2024. p. 563-73.
5. Carvalho M, Martin RLS, Passos RC, Riella MC. Nephrectomy as a cause of chronic kidney disease in the treatment of urolithiasis: a case–control study. World journal of urology. 2013;31(5):1141-5.
6. Edvardsson VO, Goldfarb DS, Lieske JC, Beara-Lasic L, Anglani F, Milliner DS, et al. Hereditary causes of kidney stones and chronic kidney disease. Pediatric nephrology. 2013;28(10):1923-42.

7. Gambaro G, Croppi E, Bushinsky D, Jaeger P, Cupisti A, Ticinesi A, et al. The risk of chronic kidney disease associated with urolithiasis and its urological treatments: a review. The Journal of urology. 2017;198(2):268-73.
8. Gudbjartsson DF, Holm H, Indridason OS, Thorleifsson G, Edvardsson V, Sulem P, et al. Association of variants at UMOD with chronic kidney disease and kidney stones—role of age and comorbid diseases. PLoS genetics. 2010;6(7):e1001039.
9. Heyns C. Urinary tract infection associated with conditions causing urinary tract obstruction and stasis, excluding urolithiasis and neuropathic bladder. World journal of urology. 2012;30(1):77-83.
10. Hsiao C-Y, Chen T-H, Lee Y-C, Hsiao M-C, Hung P-H, Chen Y-Y, et al. Urolithiasis is a risk factor for uroseptic shock and acute kidney injury in patients with urinary tract infection. Frontiers in Medicine. 2019;6:288.
11. Kartha G, Calle JC, Marchini GS, Monga M. Impact of stone disease: chronic kidney disease and quality of life. Urologic Clinics. 2013;40(1):135-47.
12. Kim JY, Lee JK, Park JT, Chang TI. Risk of incident chronic kidney disease among patients with urolithiasis: a nationwide longitudinal cohort study. Clinical kidney journal. 2024;17(3):sfae030.
13. Klahr S. Obstructive nephropathy. Internal medicine. 2000;39(5):355-61.
14. Lee EH, Kim S-H, Shin J-h, Park SB, Chi BH, Hwang JH. Effects on renal outcome of concomitant acute pyelonephritis, acute kidney injury and obstruction duration in obstructive uropathy by urolithiasis: a retrospective cohort study. BMJ open. 2019;9(11):e030438.
15. Yang J, Sun BG, Min H-J, Son Y-B, Kim TB, Lee J, et al. Impact of acute kidney injury on long-term adverse outcomes in obstructive uropathy. Scientific reports. 2021;11(1):23639.
16. Lin S-Y, Lin C-L, Chang C-H, Wu H-C, Chen W-C, Wang I-K, et al. Comparative risk of chronic kidney diseases in patients with urolithiasis and urological interventions: a longitudinal population-based study. Urolithiasis. 2017;45(5):465-72.
17. Rule AD, Bergstralh EJ, Melton III LJ, Li X, Weaver AL, Lieske JC. Kidney stones and the risk for chronic kidney disease. Clinical Journal of the American Society of Nephrology. 2009;4(4):804-11.
18. Mishra S, Sinha L, Ganesamoni R, Ganpule A, Sabnis R, Desai M. Renal deterioration index: preoperative prognostic model for renal functional outcome after treatment of bilateral obstructive urolithiasis in patients with chronic kidney disease. Journal of Endourology. 2013;27(11):1405-10.
19. Rezaee ME, Ward CE, Pollock M, Shetty SD. Association between multiple chronic conditions and urolithiasis. International urology and nephrology. 2017;49(8):1361-7.
20. Sembiring GB, Daryanto B, Gunawan A. Profile of End Stage Chronic Kidney Disease due to Obstructive Uropathy Patients Undergoing Hemodialysis. Hypertension.23(71):88.
21. Wagner CA. Etiopathogenic factors of urolithiasis. Archivos espanoles de urologia. 2021;74(1):16-23.
22. Rule AD, Krambeck AE, Lieske JC. Chronic kidney disease in kidney stone formers. Clinical Journal of the American Society of Nephrology. 2011;6(8):2069-75.
23. Yaxley J, Yaxley W. Obstructive uropathy–acute and chronic medical management. World Journal of Nephrology. 2023;12(1):1.
24. Vupputuri S, Soucie JM, McClellan W, Sandler DP. History of kidney stones as a possible risk factor for chronic kidney disease. Annals of epidemiology. 2004;14(3):222-8.
25. Singh I, Gupta N, Hemal A, Aron M, Dogra P, Seth A. Efficacy and outcome of surgical intervention in patients with nephrolithiasis and chronic renal failure. International urology and nephrology. 2001;33(2):293-8.
26. Demirhan K, Saglam HS, Cimen HI, Elcin B, Cokluk E. Effect of the location and severity of partial ureteral obstruction on urinary system stone disease formation. Scientific Reports. 2025;15(1):11560.