The impact of stone composition on renal function

Anmar Nassir1,2,3, Hesham Saada2, Taghreed Alnajjar1, Jomanah Nasser1, Waed Jameel5, Soha Elmorsy6, Hattan Badr2
1Faculty of Medicine, Umm Al-Qura University, Makkah, 2Department of Urology, King Abdullah Medical City, The Holy Capital (KAMC-HC), 3Department of Urology, International Medical Center, 4Faculty of Medicine, King Abdulaziz University, Jeddah, 5Department of General Surgery, King Abdulaziz Hospital, Makkah, 6The Executive Administration of Research, King Abdullah Medical City, The Holy Capital (KAMC-HC), Saudi Arabia

Background: Nephrolithiasis is a common condition that has various classifications according to stone composition. Stone formation can affect renal function; it can be a strong risk factor for chronic kidney disease (CKD). The main objective of this study is to explore the association between creatinine clearance and different stone compositions.

Methods: This is a retrospective cohort study conducted in a tertiary center in Jeddah, Saudi Arabia, between 2005 and 2014. Renal function was assessed by the estimating glomerular filtration rate (eGFR) by the Cockcroft-Gault equation. Stone composition was determined by urinary calculi analysis with infrared spectrometry.

Results: Stones of 365 patients, with a mean age of 48.2 ± 13.6 years and a male to female ratio of 3.2:1, were analyzed. Stage 2 CKD has been documented. It involved oxalate, struvite, cystine, and uric acid stones. The worst eGFR was reported for stones containing uric acid. The eGFR was least affected with apatite stones followed by brushite stones.

Conclusion: Stone disease can affect renal function. Different stone compositions show factor for renal impairment, and this should be considered in patient management. A special precaution should be considered for higher risk groups. Multidisciplinary patient care and immediate referral to a nephrologist are strongly advised.

Keywords: Estimated glomerular filtration rate, renal stones, stone composition

INTRODUCTION

Renal calculi are a common condition. The prevalence rate in the Middle East region is estimated to be between 1% and 20%.1 The incidence of developing the first kidney stone is between the age of 30 and 70 years (peak age between 50 and 60 years) with a worldwide male to female ratio of 2:1.2 The male to female ratio of the incidence of renal calculi in Saudi Arabia was 5:1 in 2001, making Saudi males 2.5 times more likely to develop renal stones as compared to non-Saudis.3

Different types of renal calculi exist. In a previous study, 80% of patients with nephrolithiasis were found to form calcium stones, most of which were composed primarily of calcium oxalate and less frequently of calcium phosphate. The other main types include uric acid,
struvite (magnesium ammonium phosphate), and cystine stones. The same patient may have more than one type of stone concurrently (e.g., calcium oxalate and uric acid). In Saudi Arabia, it was found that the majority of the stones were composed of calcium (78%) followed by uric acid (19%) and phosphate (3%). Cystine stones were not reported in that paper.

Different forms of urolithiasis are known to be associated with renal insufficiency and can lead to chronic kidney disease (CKD), but renal insufficiency (creatinine clearance of <60 ml/min by Cockcroft-Gault) is not proven to be a cause of stone formation. The relationship between stone formation and renal insufficiency can sometimes be indirect. The objective of this study is to explore the presence of a possible association between stone composition and renal function and to determine which type of stone has a possible association with diminished creatinine clearance.

**METHODS**

This is a retrospective cohort study conducted in the International Medical Center in Jeddah, Saudi Arabia. It includes adult patients who had stones that either passed spontaneously or with assistance and had all their stones analyzed in the center between 2005 and 2014. Patients with missing data of renal function or stone type were excluded from the study.

**Procedures**

All of the data were extracted from the hospital information system (age, gender, weight, height, and serum creatinine), on the same week of the stone analysis. Renal function was assessed using the estimated glomerular filtration rate (eGFR) and it was calculated by the Cockcroft-Gault equation using age in years, weight in kg, and serum creatinine in mg/dl.

Cockcroft-Gault Equation:

\[
\text{Serum creatinine in mg/dl} = K \times \left(\frac{[140 - \text{age year}] \times \text{weight kg}}{\text{[serum creatinine mg/dl} \times 72]}\right)
\]

Where K = 1 for men and 0.85 for women

Ideal body weight (IBW) were calculated for all patients:

\[
\text{IBW for men} = 50 + (2.3 \times [\text{weight kg} - 150 \div 2.5])
\]

\[
\text{IBW for women} = 45.5 + (2.3 \times (\text{weight kg} - 150 \div 2.5))
\]

The weight used in Cockcroft-Gault equation varied as follows: if the actual body weight was less than the IBW, the actual body weight was used; if the actual body weight was 25% greater than the IBW, the adjusted body weight was used; and the IBW was used for the remainder of patients.

Adjusted body weight = IBW + 0.3 (actual body weight – IBW)

For all patients, over 65 years of age, if the serum creatinine was <1 mg/dl, it was recorded as 1 mg/dl.

After the eGFR was measured, it was adjusted to 1.73 m² of the body surface area (BSA) by multiplying the measured GFR by 1.73/BSA. The BSA was calculated using Du Bois and Du Bois equation.

\[
\text{BSA} = (\text{body weight kg} ^ 0.425 \times \text{height cm} ^ 0.725) \times 0.007184
\]

**Stone analysis and classification**

The first stone for each patient was analyzed and stone composition was determined at the center using DiaSys urinary calculi analysis with infrared spectrometry. Stone composition was recorded as a percentage of the following components in each individual stone: calcium oxalate, brushite (calcium hydrogen phosphate), uric acid, cystine, apatite (tri-calcium hydrogen phosphate), and struvite (magnesium ammonium phosphate).

The compositions were categorized in the following sequential order so that each stone was placed in one unique group: (1) any stone that contained magnesium ammonium phosphate was classified in the struvite category; (2) any stone that contained cystine was classified in the cystine category; (3) any stone that contained uric acid was classified in the uric acid category; (4) any stone that contained calcium hydrogen phosphate was classified in the brushite category; (5) stones that contained ≥50% calcium oxalate were classified in the oxalate category; and (6) stones that contained ≥50% tricalcium hydrogen phosphate were classified in the apatite category.

Patients were classified according to their eGFR in to the following: Stage 1 CKD with eGFR >90 ml/min, Stage 2 CKD with eGFR = 60–89 ml/min, Stage 3 CKD with eGFR = 30–59 ml/min, Stage 4 CKD with eGFR = 15–29 ml/min, and Stage 5 CKD with eGFR <15 ml/min.

**Statistical analysis**

Statistical analysis was performed using SPSS 21.0 Windows (IBMInc, New York, USA). Numerical data were
presented as means ± standard deviation and categorical data were presented as percentages. The Student’s t-test was used to compare the eGFR according to gender and the presence or absence of any component of urinary stones; and a two-side alpha was set at 0.05.

RESULTS

Of the 365 patients included in the study, the youngest patient was 18 and the oldest patient was 89-year-old with a mean of 48.2 ± 13.6 years. Male to female ratio was 3.2:1. The mean eGFR value for males and females was 79.7 ± 24.6 and 79.7 ± 29.9 ml/min/1.73 m², respectively, P value = 0.990 [Table 1].

Table 2 shows the categories of renal function for each stone type. It can be noted that brushite had the highest percentage of the patients with normal renal function followed by the highest percentage of the patients with Stage 3 was noted in uric acid stones.

Table 3 showed compassion of numeric eGFR values according to present or absent of each stone type. Findings agree with those in Table 2 as uric acid stones can be seen to be associated with significant lower eGFR.

DISCUSSION

Renal stone disease is a serious health problem, with a progressive increase in incidence and prevalence in Saudi Arabia. Some authors suggest a strong correlation between living in a warm region and the formation of renal stones. This may explain the increasing incidence of renal stones in Saudi Arabia.

Renal stones are a risk factor for many diseases, including CKD. In our research, we found that patients who had struvite, cystine, and uric acid stone composition had lower eGFR as compared to patients with other stone categories, corresponding to stage 2 of CKD. This may indicate that stone formation is an independent risk factor of CKD. In this present study, a substantial property of patients with stones had affecting renal as less than two-third had lowered eGFR.

To understand the mechanism of insult, CKD can be divided into functional and mechanical risk factors. Functional risk factors for developing CKD in renal stone patients are recurrent urinary tract infection (UTI), neurogenic bladder, ileal conduit, solitary kidney, hydronephrosis, certain stone components, etc. The mechanism of affecting renal function may be based on characteristics of stones obstructing the ureter and thus causing hydronephrosis, leading to an elevation in creatinine. As a complication of renal stones pyelonephritis can develop, resulting in creatinine elevation. These two mechanisms may lead to acute kidney injury, which may subsequently result in chronicity. Other causes related to infection and inflammation with fibrosis are linked to certain types of stones, such as brushite and some hereditary forms of renal stones. Such factors may partially explain the decrease in renal function with struvite, cystine, and uric acid stones.

Open surgery, extracorporeal shock-wave lithotripsy, and percutaneous nephron lithotripsy are methods to treat renal stones. Such methods may lead to improvement in renal function by relieving the obstruction; but simultaneously,
it may result in mechanical renal tissue injury that subsequently may cause mild decrease in renal function.[17]

A group of researchers studied around 2 thousand patients over 5 years and reached a similar conclusion that stone composition can predict the liability of developing renal disease. Their group of population studied was higher in mean age group and lower in male to female ratio. The stones were analyzed by Fourier transform infrared spectroscopy and eGFR was measured using the modification of diet in renal disease formula ml/min/1.73 m².[18] In their study, different categories of stones were categorized and cystine was not mentioned. The creatinine clearance in patients with oxalate and phosphate containing stones was in an opposite order to our finding. Despite the differences in both studies, the uric acid stones have the worst prognosis on renal function.

Risk factors for CKD include hypertension, diabetes, aging, chronic UTI, and some nephrotoxic medications.[7] According to our data, stone composition should also be considered a risk factor in patient management.

CONCLUSION

Stone analysis is very important for predicting renal function in urolithiasis patients. More precautions should be taken for those in higher risk groups. Multidisciplinary patient care and immediate referral to a nephrologist are strongly advised.

The limitation of current studies is the lack of information about other risk factors that may affect renal function, so we aim to conduct a bigger prospective study in the future to confirm current finding.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Hosseini MM, Shakeri S, Manaheji F, Aminsharifi A, Ezatzadegan S, Pakfetrat M, et al. Stone composition in patients who undergo renal stone surgery: Review of 423 stone analyses in Southern Iran. Iran J Med Sci 2014;39:75‑6.
2. Abbagani S, Gundimeda SD, Varre S, Ponnala D, Mandluru HP. Kidney stone disease: Etiology and evaluation. Int J Appl Pharm Technol 2010;1:175‑82.
3. Khan AS, Rai ME, Gandapur AS, Pervaiz A, Shah AH, Hussain AA, et al. Epidemiological risk factors and composition of urinary stones in Riyadh Saudi Arabia. J Ayub Med Coll Abbottabad 2004;16:56‑8.
4. Pandeya A, Prajapati R, Panta P, Regmi A. Assessment of kidney stone and prevalence of its chemical compositions. Nepal Med Coll J 2010;12:190‑2.
5. Rule AD, Bergstralh EJ, Melton LJ 3rd, Li X, Weaver AL, Lieske JC, et al. Kidney stones and the risk for chronic kidney disease. Clin J Am Soc Nephrol 2009;4:804‑11.
6. Kang HW, Seo SP, Kim WT, Kim YJ, Yun SJ, Lee SC, et al. Effect of renal insufficiency on stone recurrence in patients with urolithiasis. J Korean Med Sci 2014;29:1132‑7.
7. Global RPH the Clinician’s Ultimate Reference. Creatinine Clearance Methods. Available from: http://www.globalrph.com/clearance.htm. [Last accessed on 2016 May 21; Last updated 2016 Mar 11].
8. World Health Organization. Global Database on Body Mass Index. Available from: http://wwwapps.who.int/bmi/index.jsp?introPage=intro_3.html. [Last accessed on 2016 May 21; Last updated 2016 May 21].
9. Du Bois D, Du Bois EF. A formula to estimate the approximate surface area if height and weight are known. Arch Intern Med 1917;17:863‑71.
10. Maurer C, Götz W. Harn stein analyse. Urol B 1979;16:226‑8.
11. Thomas L. Laboratory and Diagnosis 5. Germany, Frankfurt: TH-Books Publishing Company; 1998. p. 411‑5.
12. Hesse A, Bach D. Stone analysis by infrared, spectroscopy. In: Rose A, editor. Urinary Stones. Baltimore: Aspects: University Park Press; 1982. p. 87‑105.
13. Lieske JC, Rule AD, Krambeck AE, Williams JC, Bergstralh EJ, Mehta RA, et al. Stone composition as a function of age and sex. Clin J Am Soc Nephrol 2014;9:2141‑6.
14. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. Am J Kidney Dis 2002;39 2 Suppl 1:S1‑266.
15. Alkhunaizi AM. Urinary stones in Eastern Saudi Arabia. Urol Ann 2015;8:6‑9.
16. Mira T Keddis AD. Nephrolithiasis and loss of kidney function. Curr Opin Nephrol Hypertens 2013;22:390‑6.
17. Wood K, Keys T, Mufarrij P, Assimos DG. Impact of stone removal on renal function: A review. Rev Urol 2011;13:73‑89.
18. Chou YH, Li CC, Hsu H, Chang WC, Liu CC, Li WM, et al. Renal function in patients with urinary stones of varying compositions. Kaohsiung J Med Sci 2011;27:264‑7.