

Association of Serum Biochemical Panel with Mineralogical Composition of Kidney Stone in India

Muhammed A. P. Manzoor^{1,2}, M. Mujeeburahaman², P. D. Rekha¹

¹Yenepoya Research Centre, Yenepoya University, ²Department of Urology, Yenepoya Medical College Hospital, Yenepoya University, Mangalore, Karnataka - 575 018, India

Abstract

Purpose: The aim is to study the diversity in the composition of kidney stones and its association with the basic biochemical metabolic panel in patients with kidney stone disease (KSD). **Methods:** A cross-sectional prospective study enrolling consecutive patients with KSD attending a tertiary care hospital in Mangalore (India) was undertaken. Mineral compositions of kidney stones were analyzed using attenuated total reflection-Fourier transform infrared spectroscopy. Kidney stones were classified into different groups according to the composition. Metabolic status was assessed to analyze possible association with the kidney stone. **Results:** A total of 369 patients (male 305 and female 64) in the age group of 43.05 ± 14.3 years were included in the study and showed a high diversity of kidney stone types with >50% with mixed compositions. A significant association was found between pure stone type and gender as well with age group ($P < 0.001$). Serum calcium levels in the calcium oxalate stone formers were significantly higher ($P < 0.001$) than others. Similarly, uric acid stone formers showed higher random blood sugar, blood urea, uric acid, and serum creatinine levels ($P < 0.001$). Urine pH was also found to be a contributing factor for the stone formation ($P < 0.001$). Stone recurrence did not differ significantly concerning stone composition as well as metabolic status. **Conclusion:** The study reports a high diversity of the kidney stone types among patients. This finding highlights the increased cases of mixed stones that may be because of various lifestyle factors resulting in altered metabolic status. This finding warrants mechanistic studies to understand the etiology of stone formation. This will enable to develop novel noninvasive interventional strategies and proper preventive strategies to reduce the risk of KSDs.

Keywords: Attenuated total reflection-Fourier transform infrared spectroscopy, kidney stone disease, mixed composition stones, serum biochemical panel, urine pH

INTRODUCTION

Kidney stone disease (KSD) is one of the most common urological diseases, with high prevalence worldwide.^[1] Although most patients with early KSD are treated effectively with minor kidney injuries, about 40% experience recurrence, a few experiencing relapse up to five times.^[2] KSD is a multifactorial disorder involving biochemical, environmental, epidemiological as well as genetic risk factors for the pathogenesis.^[3,4] Changes in dietary habits, obesity, hypertension as well as metabolic syndrome contribute to rise in the prevalence and incidence of kidney stones. It has been initially thought that the prevalence of KSD is high in the developed nations, however, with the change in lifestyle the incidences are also reported from across the geographical locations.^[5,6] Synergistic effects of the components of metabolic syndrome can be increased risk for KSD.^[7] Kidney stones are found in patients with specific metabolic

abnormalities, such as hypercalcemia associated with calcium stones,^[8] primary hyperparathyroidism with calcium phosphate stones, and hyperuricosuria with uric acid stones.^[9] Similar to the complexity in the causes of KSD, certain intricacies in the formation also remains unknown.^[10]

Diagnostic workup of kidney stone usually depends on 24-h urinalysis, serum metabolic panels, and knowledge of previous episode of stone and its composition. However, in some circumstances, stone analysis is not performed in clinical practice. Although, understanding the stone composition, physiological factors, and associated metabolic abnormalities

Address for correspondence: Dr. P. D. Rekha,
Professor and Deputy Director, Yenepoya Research Centre,
Yenepoya University, Mangalore, Karnataka, India.
E-mail: rekhapd@hotmail.com

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: P. Manzoor MA, Mujeeburahaman M, Rekha PD. Association of serum biochemical panel with mineralogical composition of kidney stone in India. Acta Med Int 2017;4:26-30.

Access this article online

Quick Response Code:



Website:
www.actamedicainternational.com

DOI:
10.4103/ami.ami_24_17

involved in stone disease are essential for defining prognosis, directing medical and surgical management as well as preventing stone recurrence.^[11] Several studies have reported the association between the stone types with some metabolic diseases.^[12-15] Babilash *et al.*^[16] evaluated the differences in the metabolic panel between whewellite and weddellite stone formers and they did not find any significant difference between the two groups. Recently, Moreira *et al.*^[12] investigated the association between serum biochemical metabolic panel with stone composition and found that uric acid stone formers had the highest serum glucose, blood urea nitrogen and creatinine levels, similarly, calcium oxalate stone formers had the highest serum sodium.^[12]

With the increasing incidence of KSD in the Indian population, there is a need for the detailed characterization of the stone composition and to study its association with the metabolic panel. Hence, we investigated the morphological characterization of kidney stones to describe the possible association with the basic metabolic panel to get an insight into the etiology of the specific type of stone formation.

MATERIALS AND METHODS

Ethics statement

All the procedures performed in studies involving human participants were approved by the Institutional Ethics Committee of the Yenepoya University, Mangalore (India) (YUEC.078/12; 022/16) conducted by the ethical standards of the institutional and/or national research committee. Written informed consent was obtained from all the participants.

Study design, participants, and specimen

A prospective cross-sectional study was conducted between August 2012 and November 2016 in patients with symptomatic stone diseases admitted to Yenepoya Medical College Hospital Mangalore (India). All the patients underwent a baseline assessment, including a detailed medical history, physical examination, urinalysis, complete blood count, X-ray of kidneys, ureters, and bladder, and a noncontrast computerized tomography. Each patient had their urinary stone(s) removed following the clinical practice (ureteroscopy, percutaneous nephrolithotomy, laparoscopic or open stone surgery, and/or extracorporeal shock wave lithotripsy). Patients with active urinary tract infections before admission, and not willing to consent were excluded from the study. During the evaluation, patients were also instructed to discontinue use of any medication or supplement which could interfere with blood and urinary analysis.

Analytical procedures used in the blood and urine measurements

Blood was collected in sterile vacutainers from each patient using EDTA and/or heparin as preservative. Random blood sugar was estimated by glucose oxidase-hydrogen peroxide (Trinder) using VITROS® 5600 Integrated System (Ortho-Clinical Diagnostics NJ, USA), blood urea was estimated by

urease (calorimetric), serum creatinine was estimated by an enzymatic method (IFCC-IDMS). Serum calcium and electrolytes such as sodium, potassium, and chloride were estimated by Direct-ISE using VITROS® 5600 Integrated System (Ortho-Clinical Diagnostics NJ, US). Erythrocyte sedimentation rate (ESR) was assessed by photometry method using VES MATIC CUBE 30 (Via A. Solari, Milano Italy). The 24-h urine pH was measured using a digital pH-meter, and urinary sediment was examined by light microscopy.

Physical characteristics and identification of kidney stone composition

Kidney stones retrieved were immediately transported to the laboratory and cleaned thrice with sterile distilled water. The specimens were kept at 55°C in a laboratory hot air oven (Rotek instruments, India) to remove the moisture.

Identification of the mineral composition was made using attenuated total reflection-Fourier transform infrared (ATR-FTIR) according to previously published methods.^[17,18] For this, the samples from each layered structures were powdered and mixed using a sterile mortar and pestle. Approximately, 5 mg of samples were placed directly in the instrument (Shimadzu IR Prestige 21) and ATR-FTIR spectra were recorded at mid-frequency range (4000–400 cm⁻¹) at 4 cm⁻¹ resolution. The exact chemical compositions of the calculi were determined by comparing the recorded spectrum with the standard spectral library. A baseline correction was made before interpretation of the data. Stones were classified as mixed if two or more than two types of mineral components were present. If there was only one component, the stone was classified as a pure stone.

Statistical analysis

Statistical analysis was performed using SPSS, Version 22.0 (IBM Corp) Armonk, NY, USA. Results for categorical data are summarized using frequencies and percentages. Continuous variables are reported as means ± standard deviation. Distribution of variables was measured using Kolmogorov–Smirnov test. Association between categorical variables was carried out using Chi-square test. Comparison of continuous variables (random blood sugar, hemoglobin, blood urea, serum calcium, serum creatinine, uric acid, ESR, sodium, potassium, chloride, and urine pH) across gender was done using independent *t*-test and/or Mann–Whitney U-test (or corresponding nonparametric test). Comparison of baseline metabolic profile (random blood sugar, hemoglobin, blood urea, serum calcium, serum creatinine, uric acid, ESR, sodium, potassium, and chloride) across stone types was carried out using ANOVA or corresponding nonparametric test (Kruskal–Wallis test) for continuous variables. The value of *P* < 0.05 was considered as statistically significant unless otherwise stated.

RESULTS

Patient demographics

Of the 683 patients reviewed, 369 patients meeting the inclusion criteria were included in the study. Among the study

group, 82.7% of patients were males with male:female ratio of 4.7:1. Mean age of the study group was 43.05 ± 14.3 years (range 2–78 years). Peak age group of males was between 40 and 60 years, and that of females was between 20 and 40 years. There was a significant difference between the age among the male and female groups ($P = 0.002$) [Figure 1].

Classification of kidney stones

The kidney stones were classified into five major groups based on the mineral composition. Patient demographics and basic information are given in Table 1. They were calcium oxalate stones (whewellite and weddellite), uric acid stones (anhydrous and dihydrate), struvite, other pure types (brushite, apatite, cystine, and ammonium urate), and mixed stones. Among the study group 24.3% of patients presented with pure whewellite, 8.4% uric acid, 7.6% struvite, 2.2% weddellite, 1.6% uric acid dihydrate, 1.1% apatite, 0.8% brushite, and 0.5% with cystine and ammonium urate stones. However, a majority of the patients (52.8%) showed stones of mixed compositions. The major mixed compositions were whewellite-apatite, whewellite-uric acid, struvite-whewellite, whewellite-weddellite-apatite, and whewellite-weddellite [Table 2].

Association between patient demographics and kidney stone types

In this study, significant differences between the genders among different stone types were observed. For example, pure calcium oxalate and uric acid stones were predominantly found in males while struvite was commonly found in females. A close comparison of the mean age within the same sex across stone types revealed that in females with uric acid stone were of the highest mean age (48.6 ± 13.5 years), whereas male patients with struvite stones were of highest mean age (53.8 ± 10.1 years). Calcium stones were mainly found in males in the age group of 40–60 years and struvite stones were mostly reported from females between the ages of 20 and 40 years. There was an association between pure stone type and gender ($P < 0.001$). However, >50% of the male and female patients presented stones with mixed composition.

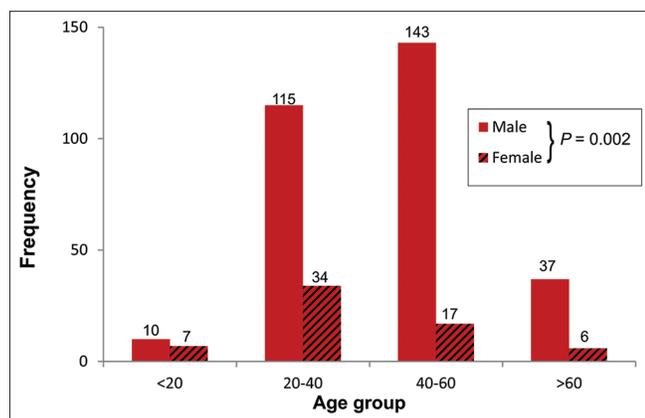


Figure 1: Distribution of patients with urolithiasis based on the age group and gender

Association between metabolic panel and kidney stone types

In the study group, differences in the basic metabolic panel across the stone types were observed [Table 3]. For example, uric acid stone formers had significantly higher random blood sugar, blood urea, serum uric acid, and serum creatinine levels. Calcium oxalate stone formers had the highest serum calcium levels. However, no significant differences were observed in the RBC, ESR, and hemoglobin levels across different stone types [Table 3]. Urine pH among patients ranged from 5.0 to 8.9, and a significant difference between urine pH and stone types was also found.

Recurrence

Among the patients, 124 (33.6%) were cases of recurrence (male, 106 and female, 18), of which 68.3% patients were reported having a recurrence after 5 years, 19.5% within

Table 1: Distribution of pure and major mixed stone types in the study cohort

Stone type	Frequency (%)		Total, n (%)	Age, mean (SD)	P*
	Female	Male			
Calcium oxalate (whewellite and weddellite)	7 (1.9)	91 (24.7)	98 (26.6)	41.5 (13.9)	<0.05
Uric acid (anhydrous and dihydrate)	3 (0.8)	34 (9.2)	37 (10)	47.5 (12.7)	
Struvite	18 (4.9)	9 (2.4)	27 (7.3)	45.6 (15.1)	
Other pure types [#]	1 (0.3)	11 (2.9)	12 (3.3)	44.9 (12.1)	
Mixed stone types	35 (9.5)	160 (43.4)	195 (52.8)	39.9 (13.7)	
Total	64 (17.3)	305 (82.6)	369 (100)	43.05 (14.3)	

Values are numbers and percentage in parenthesis. *Chi-square test (comparison between stone type and gender), [#]Brushite, apatite, cystine, and ammonium urate. SD: Standard deviation

Table 2: Distribution of major mixed stone types in the study cohort

Stone type	Frequency (%)		Age, mean (SD)	
	Female	Male	Female	Male
Whewellite-weddellite mixed	2 (1.01)	15 (7.7)	17 (9.8)	39.4 (15.9)
Uric acid-whewellite mixed	5 (2.6)	19 (9.7)	45 (16.1)	38.2 (9.6)
Whewellite-apatite mixed	11 (5.6)	55 (28.2)	32.7 (14.1)	43.6 (14.1)
Weddellite-apatite mixed	1 (0.51)	12 (6.2)	6	45.9 (16.1)
Struvite-whewellite mixed	6 (3.1)	15 (7.7)	36.6 (16.8)	44.8 (14.9)
Whewellite-weddellite-apatite mixed	2 (1.01)	16 (8.2)	35.5 (2.1)	49.6 (13.1)
Uric acid-apatite mixed	1 (0.51)	9 (4.6)	35	45.1 (7.1)
Struvite-apatite mixed	2 (1.01)	10 (5.1)	54.5 (27.5)	43 (19.4)
Uric acid-ammonium urate mixed	4 (2.1)	4 (2.1)	40.2 (11.2)	41.7 (22.1)
Whewellite-calcium carbonate mixed	-	4 (2.1)	-	55.3 (1.8)
Whewellite-protein mixed	1 (0.51)	1 (0.51)	42	53
Total	35 (17.9)	160 (8.1)	34.4 (13.9)	45.4 (13.4)

Values are numbers and percentage in parenthesis. SD: Standard deviation

Table 3: The basic metabolic panel across kidney stone types

Element	Calcium oxalate	Uric acid	Struvite	Other pure types	Mixed types	P*
Random blood sugar (mg/dL)	122.4 (53.9)	207.6 (62.5)	122.5 (51.2)	123.2 (55.2)	120.1 (53.4)	0.008 [#]
Blood urea (mmol/L)	28.1 (9.5)	33.6 (5.3)	27.9 (8.4)	27.3 (10.8)	25.2 (9.1)	0.001 [#]
Serum creatinine (mg/dL)	1.1 (0.4)	1.4 (0.33)	1.1 (0.3)	1.1 (1.1)	1.1 (0.5)	0.002 [#]
Serum calcium (mg/dL)	10.5 (0.8)	9.1 (0.9)	9.1 (0.9)	8.9 (1.8)	9.3 (1.5)	<0.001 [#]
Serum uric acid (mg/dL)	5.2 (1.5)	7.5 (2.5)	5.9 (1.6)	6.2 (2.3)	5.8 (1.5)	<0.001 [#]
Hemoglobin (g/dL)	12.7 (1.5)	13.2 (3.8)	12.7 (1.4)	12.8 (1.6)	12.8 (1.7)	0.53
ESR	24.6 (18.3)	36.7 (29.5)	28.8 (20.6)	35.3 (30.3)	23.6 (20.9)	0.12
Sodium (mmol/L)	139.7 (11.8)	137.1 (3.9)	139.7 (5.3)	138.9 (4.6)	139.4 (6.4)	0.34
Potassium (mmol/L)	4.2 (0.6)	4.3 (0.4)	4.3 (0.3)	4.7 (0.4)	4.4 (0.6)	0.41
Chloride (mmol/L)	103.3 (3.7)	100.3 (4.1)	103.1 (4.3)	105.7 (4.4)	102.5 (4.4)	0.76
Urine pH	6.7 (0.8)	6.0 (0.5)	7.4 (0.7)	6.9 (1.1)	6.6 (0.8)	<0.001 [#]

Values are mean and SD in parentheses. *Analysis of variance, [#]Statistically significant. ESR: Erythrocyte sedimentation rate, SD: Standard deviation

3 years and 12.2% within 1 year. Recurrent cases were majorly found in the age group of 40–60 years (46%), followed by 20–40 years (31.5%), and >60 years (22.6%). Statistically significant association between the age group and stone recurrence was also observed ($P < 0.001$). Nearly 50% of recurrent cases were found in mixed stone types followed by calcium oxalate (27.4%), uric acid (10.5%), and struvite (8.9%) stone formers. However, stone recurrence did not differ significantly with respect to the metabolic panel as well as stone types.

DISCUSSION

Understanding the KSD concerning stone type, the metabolic profile of the patients helps in elucidating the underlying associated medical illnesses and provides information to direct conservative measures.

In this study, a significant association of serum calcium levels in calcium oxalate stone formers ($P < 0.001$) was found. Calcium-containing stones are in general common in the majority of patients with KSD. Hypercalciuria is the most common abnormality identified in calcium stone formers.^[8] Furthermore, in the study uric acid stone formers had significantly higher glucose, blood urea, serum uric acid, and serum creatinine levels. These findings are supported by the reports showing higher risk of uric acid stone formation among patients with diabetes mellitus.^[19,20] Further, a recent study showed an increased risk of uric acid stones among poorly controlled diabetics.^[12] Serum electrolytes among different stone types did not show a significant association. However, serum chloride level was found elevated in male patients with struvite stones. Serum sodium concentration is related with the serum osmolarity, and maintained by a feedback mechanism involving antidiuretic hormone which acts on the kidney to facilitate water reabsorption. Potassium is absorbed and immediately transferred to the intracellular compartment facilitated through the stimulation of Na^+/K^+ ATPase pump by insulin. In the study group, female patients with uric acid stones had a higher level of serum potassium level. However, in many cases, the metabolic investigation does not ensure the

actual diagnosis of lithogenic disease if the stone composition does not match (e.g., in case of mixed mineral types).

Variation in the urine pH may supplement the diagnosis. In this study, a significant difference in 24-h urine pH across stone type groups was observed. For example, struvite stone formers had highest mean urinary pH, and uric acid stone formers had the lowest mean urinary pH. This observation is in accordance with the earlier report.^[21] A pH >7.5 is correlated with urinary infection, and the alkaline urine favors the formation of ammonium which turns to struvite stone formation.^[22] Higher incidence of urinary tract infection in females makes them susceptible to struvite stones. At low urine pH (<5.5), the undissociated form of uric acid predominates, leading to the uric acid stone formation. More recently, it has been reported that patients with mixed stones types showed differences in basic metabolic characteristic compared to pure stone type groups and such differences possibly be future markers for underlying metabolic abnormalities.^[23]

One of the major concerns of stone diseases is its recurrence, and in the present study, 33.6% of the cases had the previous history of KSD. Statistically significant association between the age group and stone recurrences was also observed ($P < 0.001$). The highest recurrence was found in the age group 40–60 years (57 out of 124 cases). Nearly 50% of recurrent cases were found in the mixed stone types. Recurrence cases may also present with altered stone composition^[21] and such patients may present the same metabolic urine abnormalities comparable to the first time stone formers.^[24] This is due to the other confounding factors involved in lithogenesis. Supporting evidence from the investigations on the stone is needed to define measures to decrease the incidence of recurrence.^[25] This will aid in the effective management of the disease by addressing the underlying risk factors.

With the application of infrared spectroscopy and other advanced analytical instrumentations, kidney stones are easily classified into more specific types.^[17,26,27] As KSD is a multifactorial disease with diverse chemical composition, the regional geographic factors, lifestyle practices, and the gut microbiota play a strong role in determining the formation

and composition of the stones. Even though key metabolic parameters are useful; additional parameters may also be needed for understanding the mechanisms of formation of more prevalent types of mixed stones.

CONCLUSION

It is essential to understand the precise stone composition and the metabolic panel to manage the KSD patient effectively. Furthermore, knowledge on the chemical composition and associated metabolic profile will throw light on the etiopathogenesis of stone disease in different populations. The present study suggests that the high diversity of stone types with a significant portion of mixed stone composition warrants further studies on the genesis of these compositions and strategies for preventing their recurrence.

Acknowledgments

The authors would like to acknowledge Mr. Ganesh for his support and assistance in ATR-FTIR spectroscopy, Dr. K. K. Achary and Mrs. Megha Nair for their assistance in data analysis. Authors also thank the staff in the Department of Urology, operating room and research center for their help. The authors also acknowledge Yenepoya University Seed grant (YU-Seed grant-2011/19).

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Knoll T. Epidemiology, pathogenesis, and pathophysiology of urolithiasis. *Eur Urol Suppl* 2010;9:802-6.
- Hesse A, Brändle E, Wilbert D, Köhrmann KU, Alken P. Study on the prevalence and incidence of urolithiasis in Germany comparing the years 1979 vs. 2000. *Eur Urol* 2003;44:709-13.
- Sakhaee K, Maalouf NM, Sinnott B. Clinical review. Kidney stones 2012: Pathogenesis, diagnosis, and management. *J Clin Endocrinol Metab* 2012;97:1847-60.
- Rodgers AL. Physicochemical mechanisms of stone formation. *Urolithiasis* 2017;45:27-32.
- Alatab S, Pourmand G, El Howairis Mel F, Buchholz N, Najafi I, Pourmand MR, *et al.* National profiles of urinary calculi: A Comparison between developing and developed worlds. *Iran J Kidney Dis* 2016;10:51-61.
- Rizvi SA, Sultan S, Zafar MN, Ahmed B, Aba Umer S, Naqvi SA, *et al.* Paediatric urolithiasis in emerging economies. *Int J Surg* 2016;36:705-12.
- Ramaswamy K, Shah O. Metabolic syndrome and nephrolithiasis. *Transl Androl Urol* 2014;3:285-95.
- Craven BL, Passman C, Assimos DG. Hypercalcemic states associated with nephrolithiasis. *Rev Urol* 2008;10:218-26.
- Spivacow FR, Del Valle EE, Lores E, Rey PG. Kidney stones: Composition, frequency and relation to metabolic diagnosis. *Medicina (B Aires)* 2016;76:343-8.
- Yu DS, Yang YT, Lai CH. Epidemiology and treatment of inpatients urolithiasis in Taiwan. *Formos J Surg* 2016;49:136-141.
- Ferrandino MN, Preminger GM. Basic metabolic evaluation for nephrolithiasis. *Urolithiasis: Medical and Surgical Management of Stone Disease*. London: CRC Press; 2009. p. 24-34.
- Moreira DM, Friedlander JI, Carons A, Hartman C, Leavitt DA, Smith AD, *et al.* Association of serum biochemical metabolic panel with stone composition. *Int J Urol* 2015;22:195-9.
- Pak CY, Adams-Huet B. Elucidation of factors determining formation of calcium phosphate stones. *J Urol* 2004;172:2267-70.
- Raj GV, Auge BK, Assimos D, Preminger GM. Metabolic abnormalities associated with renal calculi in patients with horseshoe kidneys. *J Endourol* 2004;18:157-61.
- Wang H, Man L, Li G, Huang G, Liu N. Association between serum Vitamin D levels and the risk of kidney stone: Evidence from a meta-analysis. *Nutr J* 2016;15:32.
- Bibilash BS, Vijay A, Fazil Marickar YM. Stone composition and metabolic status. *Urol Res* 2010;38:211-3.
- Gulley-Stahl HJ, Haas JA, Schmidt KA, Evan AP, Sommer AJ. Attenuated total internal reflection Fourier transform infrared spectroscopy: A quantitative approach for kidney stone analysis. *Appl Spectrosc* 2009;63:759-66.
- Mulready KJ, McGoldrick D. The establishment of a standard and real patient kidney stone library utilizing Fourier transform-infrared spectroscopy with a diamond ATR accessory. *Urol Res* 2012;40:483-98.
- Daudon M, Traxer O, Conort P, Lacour B, Jungers P. Type 2 diabetes increases the risk for uric acid stones. *J Am Soc Nephrol* 2006;17:2026-33.
- Chen HS, Su LT, Lin SZ, Sung FC, Ko MC, Li CY, *et al.* Increased risk of urinary tract calculi among patients with diabetes mellitus – A population-based cohort study. *Urology* 2012;79:86-92.
- Moreira DM, Friedlander JI, Hartman C, Elsamra SE, Smith AD, Okeke Z, *et al.* Using 24-hour urinalysis to predict stone type. *J Urol* 2013;190:2106-11.
- Flannigan R, Choy WH, Chew B, Lange D. Renal struvite stones – Pathogenesis, microbiology, and management strategies. *Nat Rev Urol* 2014;11:333-41.
- Cicerello E, Mangano M, Cova GD, Merlo F, Maccatrozzo L. Metabolic evaluation in patients with infected nephrolithiasis: Is it necessary? *Arch Ital Urol Androl* 2016;88:208-11.
- Eisner BH, Sheth S, Dretler SP, Herrick B, Pais VM Jr. Abnormalities of 24-hour urine composition in first-time and recurrent stone-formers. *Urology* 2012;80:776-9.
- Kok DJ. The preventive treatment of recurrent stone-formation: How can we improve compliance in the treatment of patients with recurrent stone disease? *Urolithiasis* 2016;44:83-90.
- Stoller ML, Meng MV. *Urinary Stone Disease: The Practical Guide to Medical and Surgical Management*. United States: Springer Science and Business Media; 2007.
- Scherer K, Braig E, Willner K, Willner M, Fingerle AA, Chabior M, *et al.* Non-invasive differentiation of kidney stone types using X-ray dark-field radiography. *Sci Rep* 2015;5:9527.