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URINARY STONES IN SOUTHERN INDIA: BIOCHEMICAL ANALYSIS AND ITS CLINICAL IMPLICATIONS

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ABSTRACT

Background: Urinary stones are the most common cause of acute and chronic urinary failure with an estimated prevalance of 20%. Studying the chemical composition of urinary stones forms an integral part of managing patients with urinary stones. Limited data is available about the urinary stone composition in patient populations in Southern India.

Methods: Clinical charts of patients who were admitted and later underwent surgery for urinary stones, between May 1, 2009 and April 30, 2010, at Amrita Institute of Medical Sciences, Kochi, were included in the study. Data were collected from the Clinical Biochemistry Laboratory. All blood paramters were analysed in Chemistry-Immuno Analyzers Olympus AU680 and Olympus AU2700.

Results: In 176 patients, who were included in the study, mean age 38.7 years, renal stones were most common, followed by ureteric and bladder stones. Calcium and oxalate were the most common constituents of urinary stones. 32% of the patients had above normal serum creatinine values and 36% of the patients had above normal uric acid levels. The second most common stone composition was calcium phosphate. Extremely high values of serum calcium (>12mg/dL) were found in only 3% of the patients.

Conclusion: Apart from chemical analysis of urinary stones, obtainig various blood parameters also would help clinicians in managing a patient in a holistic manner. Data presented in this study may help healthcare policy makers to look through the risk factors for urinary stone formation in this particular geographical area.

KEYWORDS: Biochemical Analysis, Southern India, Stone Composition, Urinary Stone

MANUSCRIPT

Background

The term urolithiasis refers to the formation of stones in the urinary system, primarily in the kidney (nephrolithiasis) or ureter (ureterolithiasis), and may also form or migrate in to the lower urinary system (bladder or urethra). Urolithiasis may present with painful hematuria or may remain asymptomatic.

Urolithiasis is a common problem with a worldwide estimated prevalence of 20% and a 5-year recurrence rate of 50%.[1] Almost three million visits to health care providers have been attributed to urianry stones.[2] It is one of the most important cause of acute and chronic urinary failure and thus results in high morbidity and enoromous socio-economic burden. Urolithiasis is seen mainly in younger age groups, with higher preference in males. Different epidemiological factors like age, gender, industrial development, socioeconomic status, diet and environment have been thought to play a

role in urinary stone formation.[3] Urinary stones are usually unilateral, common sites being urinary pelvis, calyces and in the urinary bladder. Protocol based metabolic evaluation in high risk patients would reveal several metabolic abnormalities, including hypercalciuria, hyperoxaluria, hyperuricosuria, hypocitraturia, and hypomagnesuria.[4] Although these metabolic disturbances are responsible for most cases, stone formation may occur in the absence of any of these risk factors as well.

Previously various studies have analysed the chemical composition of urianry stones in India.[5],[6],[7] Studying and understanding the chemical composition of urinary stones form an integral part of managing patients with urinary stones. It becomes all the more important in recurrent stone formers. Stone composition also helps us in selecting the treatment modality and in providing a clinician with the information which may help the patient in avoiding future stones.[8] Stone type and size is based on many local environmental factors like climate, dietary habits, drinking water quality etc and therefore it becomes important that we study the chemical composition of stones in different parts of the world. However, limited data is available about the urinary stone composition in Southern India. This study is aimed at analysing urinary stones and serum biochemical parameters in urolithiasis of patients coming to a tertiary level hospital in Southern India.

METHODS

Study Design

After obtaining Institutional Review Board approval, we reviewed, retrospectively, the clinical charts of patients who were admitted with a diagnosis of urolithiasis and underwent surgery for urinary stones at Amrita Institute of Medical Sciences (AIMS), Kochi from May 1, 2009 to April 30, 2010. Only this center was chosen to conduct the study as we had access to clinical charts of patients admitted here. Admitted patients underwent standard clinical examinations, routine biochemical and hematological investigations and recieved treatment as decided by their treating physician. Patient identifiers like name, age, date of birth and medical record number were used to generate the data for analysis.

Setting

Kochi, a major port city on the west coast of India, is one of the most densly populated city in the state of Kerala, with approxiamtely 2.1 million residents. With Malayalam as its official language and widespread understanding of English language, 59% of Kochi's population is in 20-59 years age group.[9] AIMS, a 1400 plus bedded academic tertiary level hospital, is an important healthcare provider in the region with an annual 6, 00, 000 outpatients and 54, 000 inpatients approximately.[10]

Patient Population

All patients who were admitted at AIMS with a diagnosis of urolithiasis and underwent surgery for urinary stones, 18 years or above, during the above said period, were included in the study.

Data Collection and Analysis

Various biochemical parameters were obtained from the Clinical Biochemistry Laboratory at AIMS. Urinary stones were crushed and analyzed for its composition. The blood parameters collected were serum calcium, creatinine, albumin, uric acid, inorganic phosphate, cystatin C, magnesium, total protein, sodium, potassium and C-reactive protein (CRP). All blood paramters were analysed in Chemistry-Immuno Analyzers Olympus AU680 and Olympus AU2700. The data obtained from the laboratory were cross-checked for accuracy and relevance. Additional data like patient demographics, appropriate past medical history and vitals were collected as well. Data regarding patients' dietary habits

and body mass index were not available. The data was analysed for various patient variables using IBM SPSS Statistics version 21. The data were analysed in comparison with 32 normal controls that came for corporate check up.

RESULTS

184 patients were found to be eligible for the study. Of these 184 patients, data of 8 patients were not available in usable form; hence 176 patients were included in the analysis. Patient characteristics have been described in Table 1. Mean age of male patients was 38.5 years and that of female patients was 40 years. Majority of the stones were renal (74%), rest being ureteric (16%) and urinary bladder (10%). Among the stones analyzed, biochemical composition has been described in Table 2. The proportion of stone components were in the order as oxalate > calcium > uric acid > phosphate > cystine > ammonium. Magnesium was not found in any patient. 35 patients had a family history of urinary stones, 78 patients were taking antihypertensive medications and 68 patients have had urinary stones in the past. None of the patients had a history of bowel diseases/surgeries or immobilization. Refer to Figure 1 for various blood parameters in these patients. 32% of the patients had above normal serum creatinine values, of which 15% had values more than 2mg/dL. 3% patients had serum albumin level above 700mg/dL.

DISCUSSIONS

Chemically analysing urinary stones, especially in recurrent stone formers, is an important step in the management of such patients.[4],[11]

Calcium and oxalate were found to be a major urinary stone constituent in our patients (Table 2), as has been previously described in other parts of India.[12] Calcium oxalate is the main constituent of urinary stone at physiological pH, oxalate forms soluble salt with sodium and potassium but it forms insoluble salts in combination with calcium, leading to stone formation.[13] Higher calcium levels seen in metabolism abnormailties are important causes of stone formation but decrease in dietary calcium also increases the risk of stone formation due to tubular reabsorption.[14] Extremely high values of serum calcium (>12mg/dL) were found in only 3% of the patients.

Rich dietary sources of oxalate like spinach, beets, nuts, chocolate, tea and wheat bran can lead to stone formation.[15] Small increases in urinary oxalate can have a major effect on calcium oxalate crystal formation.[16] However, further studies did not support this assumption.[17, 18] Therefore, restricting dietary oxalate may be a relatively ineffective intervention to reduce urinary oxalate excretion. A major source of urinary oxalate is derived from vitamin C.[19] Traxer et al demonstrated that ingestion of 2 gm vitamin C daily results in no change in urinary pH but a statistically significant increase in urinaryoxalate in normal subjects.[20] Therefore, a myriad of factors play a role increasing urinary oxalate excretion, of which dietary habits are the most important. However, dietary history is not commonly collected by physicians in India. Further investigation of factors influencing urinary oxalate as a new approach to prevent calcium urinary stones is needed.[18]

Prevalance of uric acid uric acid urolithiasis is higher in patients with type 2 diabetes mellitus and those with obesity. Main etiologic factors for the development of uric acid urolithiasis are low urinary pH, hyperuricosuria and low urinary volume.[21] Higher serum uric acid levels are usually seen in metabolic syndromes. Pure uric acid crystals are radiolucent but can be visualized by ultrasound. In our dataset, approxiamtely every one in three patients had higher than normal serum uric acid levels. Although ammonium urate urolithiasis is a rare condition, it is relatively common in Asia.[22] Purine metabolism releases both uric acid and ammonium, and almost all of our cases of ammonium stones had urate as a

constituent as well. Higher serum C-reactive protein, an acute phase reactant, levels are associated with a higher lifetime risk of urinary stones.[23],[24] Underlying inflammation, or conditions like gout may be responsible for this association. In our data set, 5% of the patients had higher than normal serum C-reactive protein levels (Figure 3). Some investigators have pointed towards the possibility of using serum CRP levels to predict ureteric stone expulsion rate. [25, 26] Patients with higher serum CRP values (> 21.9 mg/L) have low stone expulsion rates and it is recommended that these patients be managed with an immediate, minimally invasive ureteroscopy.[25]

Higher intake of magnesium has been associated with lower risk of urinary stones.[27] Magnesium inhibits calcium oxalate crystallization in human urine and also inhibits absorption of dietary oxalate from the gut lumen. No traces of magnesium were reported in urinary stones in our patient population (Table 2). 32% of the stone forming patients in our dataset had below normal serum magnesium levels. 40% of the patients had above normal serum phosphate levels. The presence of pure calcium phosphate urinary stone disease should prompt a review of the serum electrolytes (to rule out complete distal renal tubular acidosis) and the serum calcium (to exclude primary hyperparathyroidism). Less than 3% of the patients had cystine stones. Most of the cystine stones were pure cystine stones, consistent with previous data.[28]

LIMITATIONS

We relied on chemical composition of urinary stones using conventional methods. Ideally, X-ray crystallography should be used, where both the chemical composition and structure of the stones can be ascertained. Additionally, we conducted this study at only one centre in India. Therefore, the results of this study cannot be generalized to other parts of the world.

CONCLUSIONS

A clinician can customize treatment modalities for a patient according to the size and chemical composition of urinary stones. Apart from chemical analysis of urinary stones, obtainig various blood parameters would also help a clinician in managing a patient in a holistic manner. Data presented in this study may help the healthcare policy makers to look through the risk factors for urinary stone formation in this part of India.

Table 1: Baseline Patient Characteristics Included in Analysis

Patient Variables	Total	Male	Female
n	176	112	64
AVERAGE AGE (years)	38.7	38.5	40
MEDICAL HISTORY			
Family history of urinary stones	35	25	10
Past history of urinary stones	68	46	22
Hypertension	78	51	27
Urinary Tract Infection in past 5 years	112	61	51

Table 2: Average Percentage Composition of the Constituents of Urinary Stones

Stone Constituents	Percentage
Calcium	38.15
Oxalate	47.27
Ammonium	0.36
Phosphate	2.97
Uric acid	9.45
Cystine	2.32
Magnesium	0.00

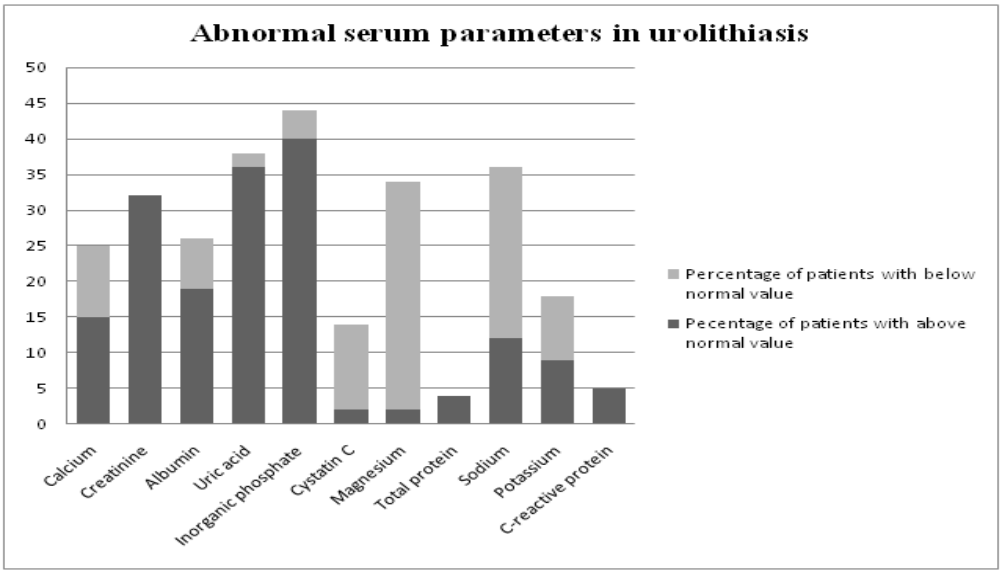

Figure 1: Blood Parameters in Patients with Urolithiasis

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