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Original Article

Surgery Section

Correlation of Calcium, Magnesium, Uric Acid and Phosphate Levels in Serum, 24-Hour Urine, and Stone Components in Patients with Urolithiasis: A Cross-sectional Study

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ABSTRACT

Introduction: Urolithiasis is the formation of stony concretions in the bladder or urinary tract. Nearly 10% of the population suffers from urolithiasis, which has a high chance of recurring. Many resources are used to treat urinary stones globally, but the need for prevention has been neglected.

Aim: To determine the levels of Calcium (Ca), Phosphorus (P), Uric Acid (UA) and Magnesium (Mg) in the blood and urine of patients with urolithiasis, as well as in urinary stones post-procedure.

Materials and Methods: This cross-sectional study was conducted at the Department of General Surgery at the Himalayan Institute of Medical Sciences (HIMS), Swami Ram Nagar, Dehradun, Uttarakhand, India, from November 2021 to October 2022. A total of 80 patients suffering from urolithiasis were involved in the study. Serum and 24-hour urinary samples were collected for quantitative analysis of Mg, Ca, UA and Phosphate (Ph) levels. Urinary stones postsurgery were sent to the biochemistry section of the reference laboratory for semi-quantitative colorimetric determination and morphological analysis. Spearman's Rank correlation coefficient was used to correlate two quantitative variables and a p-value of <0.05 was considered statistically significant.

Results: In the study, 77.5% of the patients were males and 22.5% were females. Based on their fundamental components, a single calcium oxalate calculus was found in 39 patients. The levels of biochemical parameters associated with urinary stones were as follows: Ca component=38.13±5.53 mg/dL; Mg component=10.33±4.94 mg/dL; UA=10.13±9.04 mg/dL; and Ph=4.55±1.08 mg/dL. A strong positive correlation was observed between serum calcium and stone calcium (r=0.747, p=0.001) and between stone calcium and urine uric acid (r=0.813, p=0.001).

Conclusion: A significant relationship was observed between stone calcium and serum calcium.

Keywords: Calcium oxalate, Calculi, Renal, Serum calcium, Urinary

INTRODUCTION

Globally, urolithiasis is a complex clinical disorder that affects a significant number of people. Approximately 10% of individuals experience nephrolithiasis in their lifetimes and recurrence rates range from 50% to 70% in industrialised countries [1,2]. A 4:1 ratio of urinary calculi is seen in males compared to females and the condition is particularly prevalent in specific regions worldwide, such as Southern Asia [3,4]. A variety of modifiable dietary and lifestyle factors have been identified, such as a higher body mass index, lower fluid intake and the consumption of certain foods and beverages. Additionally, the risk of urolithiasis increases with decreased physical activity. The literature shows a consensus regarding diet and lifestyle, which has implications for patient advice [5]. Researchers have found that calcium oxalate renal stones, the most commonly diagnosed type of stone, are primarily caused by diets high in protein, salt and fructose-containing beverages [6].

Often, urolithiasis is caused by supersaturated or stagnant urine. An evaluation of metabolic function is vital following the expulsion of stones and should be repeated several times. The treatment involves blood tests, urine samples and 24-hour urine collections to determine whether any crystallisation promoters or inhibitors are present. In addition, it is crucial to analyse the composition of the expelled stones [7,8]. Citric acid excretion through the urinary system is strongly associated with urinary stones. Accordingly, high urinary uric acid levels can lead to calcification, as can chronic dehydration and persistently low urinary Ph [9,10].

As kidney stones become more prevalent in Indian populations, detailed characterisation is required [11,12]. Numerous studies have found that urinary calculi recur annually after previously treated patients experience their initial stone event. It appears that calculi should be prevented, rather than only treated, as it is a chronic disease [13,14]. The likelihood of developing urolithiasis increases when calcium, oxalate, uric acid and phosphorus are excreted in higher amounts in the urine. Therefore, it may be helpful to devise a treatment strategy based on the correlation between urine parameters in urolithiasis patients [15-17]. A wide range of minerals can be found in urine and urine biomarkers are widely used for early disease diagnosis [18-20].

The study presented here evaluates the levels of calcium, phosphorus, uric acid and magnesium in serum, 24-hour urine and urinary stones in individuals suffering from urolithiasis. It also aimed to determine the correlation of these values in serum, 24-hour urine and urinary stones among patients with urolithiasis.

MATERIALS AND METHODS

The present cross-sectional study recruited 80 participants from the Department of General Surgery at the Himalayan Institute of Medical Sciences (HIMS), Swami Ram Nagar, Dehradun, Uttarakhand, India from November 2021 to October 2022. Informed consent was obtained from the patients and ethical clearance from the institute was granted with reference number SRHU/HIMS/ETHICS/2022/335. A consecutive sampling technique was employed.

Inclusion and Exclusion criteria: Patients of both genders over 18 years old, diagnosed with renal and/or ureteric stone disease, who were undergoing surgery for stone removal during the study period, were included. The exclusion criteria comprised individuals with infection stones (matrix), a history of recurrent Urinary Tract Infections (UTIs) in the last six months, malignancy, pregnancy, metabolic syndromes including hypertension, Type 2 diabetes and obesity, Pelvic Ureteric Junction (PUJ) obstruction, renal insufficiency, or any other related diseases.

Study Procedure

Diagnosed patients with urolithiasis were reviewed on an inpatient basis in the Urology/Surgery Department and were interviewed to gather their history and undergo examination for urinary stones. Their radiological findings were recorded on a case recording form. A consultant urologist performed the surgical removal of stones using ureteroscopic lithotripsy and Percutaneous Nephrolithotripsy (PCNL). According to the enrollment conditions, serum and 24-hour urinary samples were collected for quantitative analysis of magnesium, calcium, uric acid and phosphate levels and these were taken from patients after stone removal. The urinary stones, postsurgery, were sent to the reference laboratory in the Biochemistry section for semi-quantitative colorimetric determination conducted on an autoanalyser (Unicel DXC 700AU from Beckman Coulter) and for morphological analysis using a LIIR-20 automatic analyser (Lambda Science Corporation, China).

STATISTICAL ANALYSIS

Different statistical analyses were conducted using Statistical Package for the Social Sciences (SPSS) software version 22.0. Percentages and frequencies were calculated for all the considered variables. For quantitative variables, the authors provided the mean and standard deviation. The relationship between two quantitative variables was determined using Spearman's Rank Correlation Coefficient. A p-value <0.05 was considered statistically significant, while a p-value >0.05 was considered not statistically significant.

RESULTS

In the study, 77.5% of the patients were males and 22.5% were females [Table/Fig-1]. Based on their fundamental components, a single calcium oxalate calculus occurred in 39 patients. In the mixed calcium oxalate group, 25 patients had calcium oxalate and carbonate apatite stones, calcium oxalate and anhydrous uric acid stones, or calcium oxalate and magnesium ammonium phosphate stones (struvite). The other stone group included 16 patients with uric acid stones, apatites, sodium urates, or ammonium urates.

Variables	Status	Frequency	Percentage (%)
Gender	Male	62	77.5
	Female	18	22.5
Dysuria	Yes	22	27.5
	No	58	72.5
Stone location	Upper urinary tract	54	67.5
	Lower urinary tract	19	23.7
	Both upper and lower urinary tract	7	8.75
	Distribution of investigations		
X-ray	Yes	44	55
	No	36	45
USG	Yes	69	86.3
	No	11	13.8
NCCT	Yes	67	83.8
	No	13	16.3

[Table/Fig-1]: Patient characteristics.
USG: Ultrasonography, NCCT: Non contrast computed tomography

In 44 patients, the calyces and renal pelvis stones of the urinary tract were analysed by X-ray. The stones had diameters ranging from 7 to 18 mm. An X-ray diffraction analysis was used to define pure stones as those with more than 75% of their main component. Multiple stones were present in 67 (83.8%) of the urinary tracts assessed via NCCT. Smaller stones and those located further down the ureter are less likely to be identified by ultrasound.

The level of urinary calcium was found to be 3.43±0.97 (normal range: 2.5 to 7.5 mmoL/24 hrs) and the level of phosphate was 1.69±0.47 (normal range: 0.97 to 1.45 mmoL/24 hrs). The level of serum calcium was found to be 10.28±1.00 (normal range: 8.8 to 10.6 mg/dL) and the level of phosphate was 2.68±0.52 (normal range: 2.5 to 4.5 mg/dL) [Table/Fig-2].

Levels of biochemical parameters (Urine)		
Variable	**Mean±SD**	**Normal range**
Ca	3.43±0.97	2.5-7.5 mmol/24 hrs.
Mg	2.13±0.26	1.8-2.6 mg/dL
UA	2.70±0.45	1.48-4.43 mmol/24 hrs.
Ph	1.69±0.47	0.97-1.45 mmol/24 hrs.
Levels of Biochemical Parameters (Serum)		
Variable	**Mean±SD**	**Normal range**
Ca	10.28±1.00	8.8-10.6 mg/dL
Mg	2.22±0.39	1.8-2.6 mg/dL
UA	5.98±0.84	2.6-7.2 mg/dL
Ph	2.68±0.52	2.5-4.5 mg/dL

[Table/Fig-2]: The Mean±SD values of urine and serum components in each group.

The calcium component in urinary stones was measured at 38.13±5.53 [Table/Fig-3].

Correlation analysis revealed a strong positive correlation between serum calcium and stone calcium (r=0.747, p=0.001) [Table/Fig-4].

Variable	Mean±SD (mg/dL)
Ca	38.13±5.53
Mg	10.33±4.94
UA	10.13±9.04
Ph	4.55±1.08

[Table/Fig-3]: Levels of biochemical parameters (urinary stone).

Variables		Serum Ca	Serum Mg	Serum UA	Serum Ph
Stone Ca	Correlation coefficient	0.747**	0.171	0.634**	0.604**
	p-value	0.001	0.130	0.001	0.001
Stone Mg	Correlation coefficient	0.631**	-0.024	0.366**	0.319**
	p-value	0.001	0.836	0.001	0.004
Stone UA	Correlation coefficient	0.403**	0.140	0.127	0.220*
	p-value	0.001	0.216	0.263	0.050
Stone Ph	Correlation coefficient	0.010	0.263*	0.195	-0.241*
	p-value	0.933	0.018	0.084	0.031

[Table/Fig-4]: Correlation between urinary stone and serum components.
**: A 0.01 level of significance indicates a significant correlation
*: A significant correlation exists at the level of 0.05

Additionally, there was a strong positive correlation between the amount of calcium in the stone and urinary Uric Acid (UA) (r=0.813, p=0.000) [Table/Fig-5].

DISCUSSION

Urinary stone disease is more common in men than in women. Statistically, the ratio of males to females in urolithiasis in Germany was found to be 1.4:1, as reported in an epidemiological study on urolithiasis in the country [21]. The present study observed that 77.5% of the patients were males while 22.5% were females,

Variables		Urine Ca	Urine Mg	Urine UA	Urine Ph
Stone Ca	Correlation coefficient	0.029	-0.106	0.813**	0.200
	p-value	0.800	0.350	0.001	0.076
Stone Mg	Correlation coefficient	0.163	-0.268*	0.667**	0.004
	p-value	0.149	0.016	0.001	0.974
Stone UA	Correlation coefficient	0.110	-0.287**	0.444**	-0.165
	p-value	0.331	0.010	0.001	0.143
Stone Ph	Correlation coefficient	-0.259*	0.225*	-0.246*	-0.283*
	p-value	0.020	0.044	0.028	0.011

[Table/Fig-5]: Correlation between urinary stone and urine components.
**: Significant correlation at the 0.01 level
*: Significant correlation at the level of 0.05

showing a predominance of one sex over the other, which aligns with the epidemiological findings [22]. According to the present study, the ratio of males to females was 3.4:1, which is consistent with the studies conducted by Sreenevasan G and Kant R et al., [23,24].

In a related study, a reduction in crystal inhibitors or supersaturation of urine salts has been associated with an increased risk of stone formation [25]. The prevalence of hyperoxaluria, hyperuricosuria, hypercalciuria and hypocitraturia was found to be higher in men, while urinary volume was lower in women, according to Yagisawa T et al., [26]. In our study, serum and urinary calcium, urate, magnesium and phosphate levels were observed to be within normal limits in subjects with urolithiasis.

The present analysis revealed a strong correlation (r=0.747, p=0.0001) between the calcium component of the stone and serum calcium levels. Additionally, we noted a significant positive correlation between the amount of stone calcium and serum uric acid (r=0.634, p=0.0001). This finding is in line with previous studies that indicated the biochemical irregularities associated with uric acid stone formation are primarily due to decreased urine pH, followed by higher urinary urate levels and lower urine volume [27]. Few studies have investigated the prophylactic effects of adequate fluid intake, even though urine volume is considered the most significant risk factor [6,28].

An overabundance of uric acid crystals in the urine occurs when the urine pH drops below 5.5, a condition known as hypercalciuria. Stones can form when there is excessive uric acid in the urine. Individuals with high protein intake, particularly from red meat and poultry, are more likely to develop uric acid stones. It has been found that the case group, particularly male patients, had significantly higher serum uric acid levels [28]. Some studies have documented and confirmed the role of urinary uric acid in the formation of calcium oxalate stones, highlighting the importance of treating hyperuricosuria [29-31]. Therefore, a comprehensive understanding of the pathophysiology is essential when planning treatment. The present analysis revealed a comprehensive prediction of urolithiasis based on clinical factors and urinalysis, which may aid in patient-centred diagnostic imaging decisions.

Limitation(s)

The limitation of the present experiment was that the authors did not verify the consistency between morning urine and 24-hour urine by comparing and rectifying the urine chemical data. Moreover, the present study did not consider other parameters like urine Ph, specific gravity, or biochemical parameters that reflect protein and blood status.

CONCLUSION(S)

A transparent relationship was observed between stone components and urinary and serum parameters. The most common type of stone was calcium oxalate. Moreover, a significant relationship was found between stone calcium and serum calcium, as well as between the amount of calcium in stones and urine UA in patients with urolithiasis. Hence, studies focussing on nutrition and metabolism are needed to determine modifiable factors that may facilitate better treatment planning from a clinical perspective.

Authors' contribution: PP: Surgical and medical practices and analysis or interpretation, SA: Concept, AP: Design, AS: Data collection or processing, SD: Literature search, AKD: Writing.

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