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STUDY OF CORRELATION BETWEEN SEVERITY OF UROLITHIASIS AND LABORATORY PARAMETERS AND THEIR IMPLICATIONS IN DETERMINING PROBABLE RISK PROFILES.

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Abstract

Introduction: Urolithiasis is a severe health problem and significantly increases the national health expenditures in almost all regions. During the last three decades, the incidence of urinary stones has steadily increased, suggesting that specific constant metabolic and urinary parameters are associated with stone formation. This study aims to identify parameters of the patient's serum, urinary, and radiological clinical presentations and assess the clinical severity of stone disease based on this information.

Materials and Methods: An observational study was conducted by the Department of General Surgery at the Himalayan Institute of Medical Sciences (HIMS), Swami Ram Nagar, Dehradun, for 12 months. The authors analyzed a total of 80 patients suffering from urolithiasis. The data were compiled from all serum and urinary examinations and radiological scans collected within one month before surgery after obtaining written informed consent and ethical clearance. Analysis of variance (ANOVA) was used to compare more than two categories, and the Spearman test was used to determine correlations.

Results: The multiplicity of stones was positively correlated with the side of stones in the upper tract ($r = 0.450$, $P < 0.01$), large stone volume ($r = 0.272$, $P < 0.05$), stone recurrence, and urinary parameters. Stone sides in the upper tract were positively correlated with upper tract obstruction sides ($r = 0.573$, $P < 0.01$) and large stone volume ($r = -0.242$, $P < 0.01$). Several variables were positively correlated with the number of obstructions in upper tracts with large stone volumes ($r = -0.787$, $P < 0.01$).

Conclusion: The study concluded that the serum panel and urinary profile were strongly associated with urinary tract obstructions and the total stone volume. These factors acted as harbingers of complicated stone patterns.

Keywords: Stone multiplicity, Urinary stones, urolithiasis

Introduction

Urolithiasis is an emerging pandemic affecting millions of people worldwide, especially in the developing world. The prevalence of nephrolithiasis is around ten percent, and they will recur about 50-70% of the time in their lifetime (1,2). A rise in urolithiasis prevalence was observed in both sexes and some areas of the Indian subcontinent. Managing urinary health has required capital, but the forestalling of stones has not been explored in this field. According to the National Health and Nutrition Examination Survey (NHANES), 19 percent of men and 9 percent of women will develop kidney stones during their lifetimes (3).

Numerous epidemiological arenas exist, including anatomical factors related to metabolism, diet, and urine that may lead to a condition known as urolithiasis. These different risk factors are more prevalent in patients with recurrent stone disease. Hydronephrosis and renal compromise may occur as a result of upper urinary tract stones. Nephrolithiasis incidence rates differ by geographical region of a country. Many places in the country are designated annually as Gujarat, Maharashtra, Punjab, and Rajasthan, constituting the stone belt (4,5). About seventy-five percent of patients with nephrolithiasis develop calcium stones, mainly calcium oxalate or calcium phosphate, while uric acid stones account for less than ten percent (6). A clinical decision is influenced by knowledge of the materials that make up renal stones. Urine composition analysis over 24 hours gives an idea of the possible contents of a stone but does not specify them. Although they coexist, urinary stones' most common crystalline materials contain calcium phosphate, calcium oxalate, uric acid, and struvite. The non-crystalline materials Blood and protein are found in stones (7).

This study aims to investigate the relationship between various clinical and laboratory findings of calcaneus in patients with urolithiasis. It also looks for a deeper understanding of these parameter changes and risk factors associated with this condition.

Materials and Methods

An observational study was conducted at the Department of General Surgery, Swami Rama Himalayan University, Dehradun, for a period of 12 months from November 2021 to October 2022, recruiting 80 patients undergoing surgical removal of renal and ureteric stones, which remained in follow-up for at least six months after obtaining written informed consent and ethical clearance. An evaluation and diagnosis of stone diseases was carried out using USG W/A, X-ray, non-contrast CT scans for kidney, ureter, and bladder (NCCT KUBs), and contrast-enhanced computed tomography (CECT) were performed as required. In this case, stone multiplicity or morphological analysis of stones was interpreted as the presence of multiple stones in the urinary tract, irrespective of their location. An upper urinary tract obstruction is characteristic of ureteric calculus or renal calculus-induced hydronephrosis. A large stone bulk was defined as a stone larger than 2 cm in diameter.

Patient demographics, including age at presentation, gender, co-morbidities, medical and surgical histories, were recorded. BMI was calculated based on measurements. Test results were obtained for all hematological and biochemical tests. A series of serum and urine tests were conducted to investigate calcium, magnesium, phosphorus, albumin, and uric acid levels. Urine samples were collected from patients in the morning for analysis of pH, specific gravity, protein, and bacteria. A Chi-square and Student's t-test were used to compare discrete and continuous variables. The Pearson's R analysis was used to calculate the correlation coefficient. Statistical significance was defined as a P value less than 0.05. All statistical analyses were performed using SPSS version 22.

Results

The median age across the entire patients was 52.14 ± 11.35 years despite the gender group (p-value 0.035). The median age for ureteric stones was maximum (Table 1). Multiple stones occurred in 65 % of cases and were managed in the same sitting if they were on the same side or 3 to 6 months apart when they were on the opposite side. Stone sites in the upper tract incorporated 52.5 % of cases on

one site and 33.75 % on two sites. The prevalence of hydronephrosis of the upper tract due to obstruction was 47.5% on one side and 42.5% on both sides. Large stones were observed in 35 percent of cases, but this was not significantly related to the same finding regarding the importance of presenting to the emergency department as soon as possible.

According to the biochemical parameters, median serum values of uric acid and phosphorus among the calculi groups did not reach statistical significance level (p-values 0.321 and 0.239) (Table 2). Protein metabolism was based on dietary habits and serum albumin levels in all calculi groups and was significantly associated with them (p-value 0.011). Although serum calcium concentration plays a crucial role in urolithiasis development, our analysis finds a significant association (p-value 0.012) and also for obstruction (p-value 0.002) and large stone bulk group (p-value 0.001). The presence of ureteric calculi is significantly associated with male gender and advancing age. There was an association between renal calculi and recurrence and UTI. There was a recurrence rate of one-fourth in the entire cohort following the follow-up period, with kidney stones having the highest number of cases, indicating significant association (Chi-square value 3.504, p-value 0.015) and correlation (R-value 2.07, p-value 0.041).

Table 1. Combined distribution pattern for categorical and clinical parameters.

Age (Years)	**Mean±SD**	**52.14 ± 11.35**
Gender	Male/Female	62/18
Recurrence	Present/Absent	20/60
BMI	Mean±SD	25.11±2.25
Dysuria	Present/Absent	22/58
Stone multiplicity	Present/Absent	52/28
Site of upper tract stones	0/1/2	11/42/27
Side of upper tract obstruction	0/1/2	8/38/34
Large stones in bulk.	Present/Absent	28/52

Table 2. Analysis of Continuous Variable Median Values with Correlational P-Values (Chi-Square Analysis or Pearson's R Analysis)

Variables	**Renal calculi**	**Ureteric calculi**	**Renal+ureteric calculi**	**P-Value**
Age	52.24	54.13	48.56	0.035
BMI	24.8	25.61	25.23	0.484
Serum uric acid	0.34	0.35	0.36	0.321
Serum albumin	40.24	41.12	41.54	0.011
Serum Ca	2.22	2.25	2.26	0.012
Serum Mg	1.88	1.85	1.87	0.043
Serum Ph	1.16	1.04	1.17	0.239
Urine pH	5.85	6.04	5.96	0.674
Urine specific gravity	1.022	1.018	1.018	0.487

Ca: Calcium, Mg: Magnesium, Ph: Phosphorus, and BMI: Body Mass Index.

An analysis of the correlation between stone multiplicity and other clinical variables found a positive correlation between the multiplicity of stones and stone recurrence (R-value 0.362, p-value 0.001) and urine albumin (R-value 2.89, p-value 0.012). The stone sides of the upper tract were positively correlated with age (R-value 1.32, p-value 0.02). The large stone volume was positively correlated with age (R-value 0.771, p-value 0.004), serum Calcium (R-value 0.701, p-value 0.001), serum and urine phosphorus (R-value 0.201 and 0.295, p-value 0.001 and 0.002) and Urine albumin (R-value 3.89, p-value 0.011). The upper tract obstruction sides was positively correlated with age (R-value 4.53, p-value 0.031), BMI (R-value 7.57, p-value 0.041), serum calcium (R-value 3.06, p-value

0.002), serum and urine phosphorus (R-value 3.86 and 6.75, p-value 0.041 and 0.042), urine albumin (R-value 0.092, p-value 0.002) and negatively correlated with gender (R-value -0.44, p-value 0.012) and serum and urine magnesium (R-value -2.67 and -4.67, p-value 0.037 and 0.048) (Table 3).

Table 3. A comparison of clinical parameter groups and their corresponding biochemical and epidemiological variables with their corresponding correlation values

Variables	Multiplicities		Stone sides		Large stones bulk		Obstruction sides	
	Pearson's R-value	P-value	Pearson's R-value	P-value	Pearson's R-value	P-value	Pearson's R-value	P-value
Gender	-0.47	0.071	-0.6	0.98	0.121	0.34	-0.44	0.012
Age	0.56	0.219	1.32	0.02	0.771	0.004	4.53	0.031
Recurrence	0.362	0.001	4.03	0.031	1.12	0.07	0.26	0.117
BMI	0.29	0.164	2.57	0.56	0.754	0.124	7.57	0.041
Serum albumin	1.052	0.061	1.44	0.77	0.12	0.42	7.36	0.121
Serum Ca	14.17	0.83	2.54	0.26	0.701	0.001	3.06	0.002
Serum Uric acid	4.32	0.27	3.06	0.21	0.143	0.24	0.95	0.914
Serum Mg	0.153	0.112	2.56	0.09	-0.431	0.062	-2.67	0.037
Serum Ph	0.253	0.15	0.52	0.06	0.201	0.001	3.86	0.041
Specific gravity	1.92	0.091	1.85	0.04	0.116	0.133	0.41	0.092
pH	2.12	0.085	0.33	0.084	0.1	0.12	0.575	0.1
Urine Albumin	2.89	0.012	0.337	0.952	3.89	0.011	0.092	0.002
Urine Ca	2.68	0.132	0.445	0.995	0.885	0.952	3.62	0.431
Urine Uric acid	3.63	0.088	0.445	0.012	3.55	0.442	0.091	0.098
Urine Mg	0.183	0.234	5.52	0.114	0.635	0.076	-4.67	0.048
Urine Ph	0.394	0.182	0.661	0.07	0.295	0.002	6.75	0.042

Ca: Calcium, Mg: Magnesium, Ph: Phosphorus, and BMI: Body Mass Index.

Discussion

According to our patient population, calculi in the bilateral upper tract appear to be associated with a higher serum calcium level. The amount of calcium excreted in the urine increases significantly, the pH of the urine increases, and citrate excretion decreases. Due to the abovementioned factors, urinary calcium phosphate and monosodium urate concentrations rose significantly. Moreover, we found that higher calcium and phosphate levels and lower magnesium levels are related to upper urinary tract obstruction side numbers.

Hypercalcemia and hypercalciuria are critical factors in calcium urolithiasis that need to be addressed urgently and immediately. There is hypercalcemia when the level of serum calcium increases and when the blood's or serum albumin's pH differs (8). Calcium is either bound or free of albumin in serum, depending on its bonding state to albumin. Due to the inactivity of calcium bound to albumin, ionized calcium poses the most significant concern. Patients with low albumin have a lower total calcium level on lab tests. Accordingly, patients with low serum albumin tend to have higher serum levels of calcium. During alkaline conditions, negatively charged albumin binds hydrogen ions. As a result, physiologically active calcium is reduced because these spots allow ionized calcium to bind.

Calcium stones are more likely to form with hypercalcemia and hypercalciuria, which increase calcium salt saturation in the urine and bind negatively charged inhibitors (9).
According to one study, stone patients have a nine to 18-fold higher risk of hypercalcemia and hypercalciuria than non-stone patients (10). The study indicates that only three patients (0.05%) in our cohort had real hypercalcemia by definition, in which serum calcium was greater than 2.75 mmol/l, which is in accordance with the prospective study (11). Another prospective cohort study of men found a 0.69 relative risk of stone formation (12). There is some evidence that serum phosphate levels are a significant risk factor for calcium urolithiasis (13,14). In a few studies, no compelling evidence supports an association between a patient's serum phosphate level and stone recurrence (15).
Our study found a negative correlation between the number of obstructions in the upper urinary tract and serum magnesium. According to some authors, magnesium can reduce stone formation through various mechanisms. A magnesium chelate produces a more soluble magnesium-oxalate complex than calcium oxalate, increasing urinary citrate levels (16).
Based on our analysis, older patients had a higher risk of bilateral upper urinary tract calculi and obstruction as well as a larger stone volume. It has been proven in previous studies that older patients with stone formation suffer from more metabolic syndromes than younger ones (17,18). In addition, older patients often present with peculiar presentations of urolithiasis, causing long delays in diagnosis and treatment (19). This may explain the higher bilateral upper urinary tract calculi frequency and larger stone volume in older patients. It has been observed that a few patients with high urine pH (> 7.5) may have formed infection stones (magnesium ammonium phosphate plus carbonate apatite). In urine with low pH, uric acid precipitates and leads to stone formation (20).
The present study showed that older age and disease recurrence were positively linked with kidney damage ipsilaterally. Many studies significantly correlated the history of recurrent stone formation with kidney damage on the ipsilateral side (21,22). Our study found a negative correlation between obstruction sides and serum and urine magnesium levels. A higher urine protein level was positively correlated with a greater stone bulk and a greater stone multiplicity. In a few studies, proteinuria has been identified as a surrogate outcome for CKD, indicating the disease's progression by proteinuria changes (23). As we have observed, this is in line with our findings.
According to the authors, this study has few limitations. Due to the lack of regular identification of patients in our cohort, we did not categorize few of them according to their stone composition. We also did not differentiate the invaluable serum and 24-hour urine analysis for the super-saturation profile, which includes urinary calcium, phosphate, citrate, and oxalate.

Conclusion

The results of our analysis indicate that upper urinary tract obstruction correlates more with abnormal electrolyte metabolism in terms of serum calcium, magnesium, and phosphate levels. Clinically, some urine parameters are correlated in patients with urolithiasis and this may contribute to a better treatment plan.

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