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Pattern of Metabolic Derangements in Patients with Urolithiasis

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ABSTRACT

Objective — *To find out current pattern of metabolic derangement in patients with urolithiasis.*

Study design — *Cross sectional study*

Place & Duration of study — *Departments of Urology and Nephrology Jinnah Postgraduate Medical Centre Karachi, from March 2016 to February 2017.*

Methodology — *All patients with urolithiasis, (kidney, ureter and bladder) meeting the inclusion criteria were included. Calculi were sent for chemical analysis. The blood samples of patients were taken for serum creatinine, calcium, uric acid, phosphates, sodium, potassium and bicarbonates. Twenty-four hours urine samples were also collected and analyzed for sodium, calcium, uric acid, phosphates, citrates and oxalates.*

Results — *Four-hundreds and ninety-six patients with the mean age of 53.44±10.36 year were included. There were 122 (24.6%) female and 374 (75.4%) male patients. Creatinine, phosphorous, urinary calcium, urinary oxalate, urinary citrate and urinary uric acid were 1.03±1.06 mg/dl, 23.9±1.98mmol/L, 333.33±141.92mg/dl, 34.57±23.41mg/dl, 263.64±205 mg/dl and 880.63±281mg respectively. In 368 (74.19%) patients there was no family history of urolithiasis, while most of the patients (n=308 - 62.09%) had current stone status. Frequency of hypercalciuria was 61%, hyperxalouria 26%, hypocitraturia 35%, and Hyperuricosuria 23% in this study.*

Conclusions — *Frequency of hypercalciuria and hypocitraturia was important observations. Male patients had more frequent metabolic derangements. Determination of metabolic derangements can help in identifying patients with high risk for recurrence and urolithiasis prophylaxis can be offered accordingly.*

Key words — *Urolithiasis, Metabolic derangements, Metabolic evaluation, Hypercalciuria.*

INTRODUCTION:

Urolithiasis is one of the common ailments. Afro-asian countries are included in a stone belt, Pakistan being one of them. The etiology of urolithiasis is multifactorial of which poor nutritional status and climate also play a role.[1] In Pakistan, highest incidence of stone disease is found in the province of Sindh and southern Punjab.[2] In Pakistan and other developing countries many patients present with acute and chronic complications as a result of long standing urinary tract calculi.[3] Moreover, urolithiasis is recurrent in nature which is up to 50% at 5 years follow-up.[4] Recurrence of disease also depends upon type of calculus.[5] Prevalence of urolithiasis is reported to be on rise globally and it is responsible for significant morbidity and adds to economic burden.[6]

Urinary tract calculi are of different composition in males and females and mostly contain calcium (Ca), 90% and 70% respectively, in combination with oxalate and phosphate. Pure uric acid, cysteine and struvite stones are among the less common types.[7] A calculus is a mixture of organic and inorganic crystals with protein, which are present physiologically

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in urine as salts. They also make complex with inhibiting agents (e.g. citrate, magnesium, glycoproteins etc). Calcium oxalate precipitation occurs in urine when its concentration is 7-11 times greater than its normal solubility. Supersaturation, aggregation crystal retention and stone formation are the series of events in lithogenesis.[8]

In patients who have recurrent stones, metabolic evaluation is found to be same as at the time of first diagnosis. Serum sodium (Na), potassium (K), chloride (Cl) and magnesium (Mg), calcium phosphate (Ca PO) and uric acid should be measured, while level of parathyroid hormones and vitamin D depend upon the serum and urine chemistry results. The cornerstone of the evaluation is the 24-hour urine collection. The variables that should be measured include volume, calcium, oxalate, citrate, uric acid, magnesium, pH and creatinine. This study was conducted to evaluate current trends in the pattern and metabolic derangements in patients with urolithiasis, This may help in taking therapeutic measures as well as planning stone prevention strategy.

METHODOLOGY:

This was a cross sectional study conducted in the Department of Urology and Nephrology Jinnah Postgraduate Medical Center Karachi, from March 2016 to February 2017. All patients with urolithiasis were included. Patients with positive urine culture or active urinary infection, malignancy, chronic kidney disease (creatinine clearance <60 ml/min), hematuria, on preventive therapy for stones, and pediatric age group were excluded.

All calculi were sent for chemical analysis. Blood samples of the patients were taken for estimation of serum creatinine, calcium, uric acid, phosphates, sodium, potassium and bicarbonates. A 24-hour urine samples were collected of all patients on random diet for measuring sodium, calcium, uric acid, phosphates, citrates and oxalates.

The data was analyzed on SPSS version 22.0, a statistical package for social science. All the quantitative variables were presented by their mean ± SD values. The qualitative variables including gender, current stone, and history of stone disease were presented by their frequencies and percentage. The observed data was classified into two groups of normal and deranged values according to their cut-off points. The final results of deranged variables of 24-hour urine in terms of frequencies and percentage were obtained. Effect modifiers like age and gender were by using Chi-square test. P-value of less than 0.05 was considered as significant.

RESULTS:

In this study 496 patients of 21 year to 69 year with the mean age of 53.44±10.36 year were included. Most of the patients were between 41-60 year (n=312 - 62.9%). There were 122 (24.6%) females and 374 (75.4%) males. Mean level of creatinine, phosphorous, urinary calcium, urinary oxalate, urinary citrate and urinary uric acid is given in table I. Most of the patients (n=308 - 62.09%) had current calculus status.

Frequency of different metabolites is given in table II. Hypercalciuria (61%) and hypocitraturia (35%) were common findings. On stratification according to age groups, frequency of hyperoxaluria was higher in age group of < 41 year and in between 41-60 years (50 % and 48.3% respectively). Chi square test showed that age group had significant effect on metabolic derangements (table III). On stratification according to gender male patients had highest frequency of metabolic derangements as compared to females which was significant (table IV).

DISCUSSION:

Urolithiasis is ranked as one of the common illnesses of kidney and its frequency is on increase. It is a systemic disorder and has multi-factorial etiology, dietary factors being the major risk factors. Metabolic workup for calculi is performed to find out underlying metabolic abnormalities that contribute to this disorder. Chemical analysis of calculus is part of basic metabolic work up.[9] This helps in classifying patients into low and high risk groups for recurrence

Table I: Mean Values of Metabolites

Metabolic Derangements	Yes	No
Hypercalciuria	304 (61%)	192 (39%)
Hyperoxaluria	130 (26%)	366 (74%)
Hypercitraturia	174 (35%)	322 (65%)
Hyperuricosuria	116 (23%)	380 (77%)

Table II: Metabolic Derangements	
Metabolites	**Mean SD**
Creatinine (mg/dl)	1.06 ±0.16
Phosphorous (mmol)	23.9 ±1.98
Urinary Calcium (mg)	333.3 ±141.92
Urinary Oxalate (mg)	34.57 ±23.41
Urinary Citrate (mg)	263.64 ±205.45
Urinary Uric Acid (mg)	880.63 ±281.50

Table III: Metabolic Derangements According To Age Group

Metabolic Derangements	<41 Year n=60		41-60 Year n=312		>60 Year n=124		P–value
	Yes	No	Yes	No	Yes	No	
Hypercalciuria	58 (96)	02 (3.3)	164 (52)	148 (47)	64 (51)	60 (48)	0.001
Hyperoxaluria	6 (10)	54 (90)	130 (41)	182 (58)	4 (3)	120 (96)	0.001
Hypocitraturia	2 (3.3)	58 (96)	172 (55)	140 (44)	2 (1)	122 (98)	0.001
Hyperuricosuria	10 (16)	50 (83)	116 (37)	196 (62)	2 (1)	122 (98)	0.001

Number (%), Chi square test applied

Table IV: Metabolic Derangements According To Gender

Metabolic Derangements	Male		Female		P–value
	Yes	No	Yes	No	
Hypercalciuria	232 (62)	142 (37.9)	54 (44.2)	68 (55.7)	0.01
Hyperoxaluria	112 (29.9)	262 (70)	20 (16.3)	102 (83.6)	0.025
Hypercitraturia	112 (29.9)	262 (70)	64 (52.4)	58 (47.5)	0.001
Hyperuricosuria	54 (28.8)	266 (71.1)	10 (8.1)	112 (91.8)	0.001

Number (%), Chi square test applied

In present study frequencies of different metabolites are similar to other reported series.[10,11] The incidence of metabolic derangement in children is different than adults. It was reported as 27%, 25%, and 31% in pediatric patients in different studies.[12-14] Males had higher frequency of calculus disease (74.40%) in present study. An American Survey of more than one million hospitalizations between 1997-2002, showed increase in number of discharge of female patients (21.0%) with renal calculi and 19.2% with ureteric stones, while the number for men remained unchanged.[15]

In present study 25.8% patients had history of urolithiasis. In a study conducted in urology clinics, 40% of the patients had first degree relatives with calculus diseae.[16] In a prospective study on males patients with positive family history of urolithiasis the risk of stone formation was doubled as compared to males who had no such history.[17] Another study conducted in Taiwan in general population, odd ratios in patients with urolithiasis whose father, mother or both parents had urolithiasis were 3.44, 4.79 and 10.40 respectively.[18] Family history must be obtained, as genetic factors have important role in urolithiasis. It is not necessary that family members who have genetic susceptibility may develop stone.

It is seen in a randomized controlled trial that higher oral fluid usage may be helpful as fewer calculi recurred.[19] Results from these observations support the protective role of higher fluid intake.[20] It has been seen that higher dietary calcium usage is associated with a lower prevalence and incidence of kidney stones in epidemiologic data since 1990.[21] It is mandatory to inquire about dietary habits, as there is significant data supporting that this is an important environmental factor influencing stone formation and dietary modifications can decrease stone disease.[22]

CONCLUSIONS:

Hypercalciuria and hypocitraturia were important observations. Frequency of hyperoxaluria was higher in middle age group and male patients had higher frequency of metabolic derangements.

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