FREQUENCY OF METABOLIC ABNORMALITIES IN URINARY STONES PATIENTS

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**Abstract:**

Objective: To determine the metabolic irregularities in the serum and urine of patients with urinary stones disease.

Methods: Fifty patients were evaluated having multiple or recurrent urinary stones, diagnosed on ultrasonography and IV urography were involved in this study. 24-hour urine sample was collected from all of the patients and got Creatinine, uric acid, calcium, phosphate, oxalate levels. Furthermore, blood sample of every participant was also taken for serum levels of urea, creatinine, uric acid, phosphate and calcium.

Results: Average age of patients was 31 ± 9.46 years with male to female ratio of almost 4:1. The chief presenting complaint was pain in lumbar region and 43 (86%) patients were found to have calcium oxalate stones on chemical analysis. Metabolic abnormalities were found in 46 (92%) patients, while there was no metabolic abnormality seen in 4 (8%) patients. 10 (20%) patients had only a single metabolic abnormality while 36 (72%) patients were having multiple metabolic abnormalities. Hyperoxaluria was commonest metabolic abnormality noted and was present in 33 (66%) patients. Other significant metabolic abnormalities were hypercalciuria, Hypercalcemia, hypocitraturia and hyperuricemia.

Conclusion: Conclusion to this study is that the frequency of metabolic abnormalities is significantly higher in patients with urolithiasis and hyperoxaluria, hypercalciuria and hypocitraturia are vital metabolic abnormalities noted in these patients.

KEY WORDS: Urolithiasis, Metabolic evaluation, Hyperoxaluria.

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INTRODUCTION:
Urolithiasis is one of the commonest issues all over the globe that affects the general populace. It is approximated that around 2% of the population suffering from renal stone disease at sometimes in their life with maximum incidence in second and third decades of their life. There are different types of urinary stones and are categorized according to their chemical composition. Calcium oxalate is the basic component of the most of stones. Different factors, such as age, gender, climate, metabolic abnormalities and heredity, are related to the development of urinary stones. Metabolic abnormalities is one of the most important factor as they can be modified to avoid the risk of urinary stones. The diagnostic tests of patients with urolithiasis include radiographic imaging along with blood and urine testing. Although there is a school of thought that a complete metabolic evaluation is compulsory in all patients with renal stones however few studies have represented that medical evaluation is not cost effective for patients who have only developed single stone.

Metabolic abnormalities such as hypercalcuiuria, hyperuricosuria, hypokalemia, hyperuricemia, hypophosphatemia and low urine volume that cause stone disease varies in different populations and depends upon environmental and genetic factors. In patients with urinary stones, diagnostic evaluation and intervention should be observed to prevent the recurrence of stone formation. Moreover, calcium stone formers, those who have recurrent stones, those who have multiple stones or bilateral stones at their first presentation and children with a stone history should always have an assessment as a correctable abnormality is usually present in these patients.

The objective of this study was to evaluate the frequency of metabolic abnormalities in urinary stones patients in local populace, so that a management policy could be formed for urinary stones patients to prevent recurrence of stone formation.

METHODS:
This cross-sectional study was done at the Department of Urology, Jinnah Hospital Lahore from June 2019 to December 2019. Total number of 50 patients with either multiple or recurrent urinary stones confirmed on ultrasonography and intravenous urography were included in this study. Patients with single urolith, urinary disorders i.e. proteinuria, recurrent UTI, congenital urinary tract obstruction and bladder outflow obstruction and with any chronic disease i.e. chronic renal failure, chronic liver disease and with history of any chronic drug usage were excluded. Patients with any known metabolic abnormality and hypo- or hyperthyroidism were also excluded from the study.

After getting informed consent and relevant history, 24 hour urine sample was collected from every patient and sent for pH, specific gravity, Creatinine, uric acid, calcium, phosphate, oxalate, citrate and magnesium. 24 hour urine samples were collected in plastic bottles, which do not react chemically by standard methods, and were stored at room temperature. In addition, blood sample of all patients were also sent for serum levels of urea, creatinine, uric acid, phosphate and calcium. The blood levels of metabolic parameters were measured by standard chemical procedures. All patients then had definitive procedure after completion of all workup and stones were sent to pathology laboratory for chemical analysis to know about the stone composition.

Statistical analysis was performed using SPSS v24. Mean and standard deviation was calculated for quantitative variables and frequency and percentage was calculated for qualitative variables. Chi square was applied and p value ≤ 0.05 was considered as significant.

RESULTS:
In this study age ranged from 20 to 50 years with mean age of 31 ± 9.46 years. Out of the 50 patients, 40 (80%) were male and 10 (20%) were females with ratio of 4:1. The chief presenting complain was pain in lumber region on the affected side i.e. in 92% patients, followed by hematuria and burning micturation. Majority of the patients i.e. 94%, were diagnosed as having renal stone or ureteric stone. Only 38% patients presented with recurrent stones while remaining 62% had stone for the first time.

Table-I: Percentage of patients according to age group (n=50).

| Age (Years) | Male | Female |
|-------------|------|--------|
| 20-30       | 14   | 02     |
| 31-40       | 17   | 05     |
| 41-50       | 09   | 03     |
Chemical analysis of stones after curative management had shown calcium oxalate stone in 86% patients. Descriptive statistics for different variables have been shown in Table-II.

| Features                                | No. of Patients | Percentage |
|-----------------------------------------|----------------|------------|
| Presenting Complaint:                   |                |            |
| • Lumber Pain                           | 46             | 92         |
| • Hematuria                             | 07             | 14         |
| • Burning Micturation                   | 04             | 08         |
| Diagnosis:                              |                |            |
| • Renal Stone                           | 32             | 64         |
| • Ureteric Stone                        | 11             | 22         |
| • Renal + Ureteric Stone                | 06             | 12         |
| • Urinary bladder stone                 | 04             | 08         |
| Recurrent stone:                        |                |            |
| • Yes                                   | 19             | 38         |
| • No                                    | 31             | 62         |
| Family history of Urolithiasis:         |                |            |
| • Yes                                   | 32             | 64         |
| • No                                    | 18             | 36         |
| Stone composition on Stone analysis:    |                |            |
| • Calcium Oxalate                       | 43             | 86         |
| • Calcium Phosphate                     | 02             | 04         |
| • Uric Acid                             | 06             | 12         |
| • Struvite                              | 01             | 02         |
| • Cystine                               | 02             | 04         |

Metabolic abnormalities were present in 46(92%) patients, while there was no metabolic abnormality in 4(8%) patients. 10(20%) patients only had one metabolic abnormality, and 36 (72%) patients had multiple metabolic abnormalities. Hyperoxaluria was the commonest observed metabolic abnormality and was found in 33 (66%) patients. Other significant metabolic abnormalities were hypercalciuria, Hypercalcemia, hypocitraturia and hyperuricemia as shown in Table-III.

| Table-III: Frequency of Metabolic abnormalities |
|-----------------------------------------------|
| Metabolic abnormality | Frequency | Percentage |
|-----------------------|-----------|------------|
| Hyperoxaluria (oxalate > 45 mg/d)             | 33        | 66%        |
| Hypercalciuria (> 250 mg/d for women and > 300 mg/d for men) | 22 | 44 |
| Hypocitraturia (citrate levels < 320 mg/d)    | 20        | 40         |
| Hypernatriuria (sodium level > 220 mmol/ day) | 15        | 30         |
| Hyperuricosuria ( > 600 mg/d in women and > 750 mg/d in men) | 11 | 22 |
| Hypomagnesuria (magnesium level < 3 mg/day)   | 05        | 10         |
| Hyperphosphaturia (phosphate level > 1.3 g/day) | 23 | 46 |
| Hypercalcemia (calcium above the normal range i.e. 8.4-10.2 mg/dl) | 17 | 34 |

**DISCUSSION:**

Advances in minimally invasive procedures have significantly altered surgical management of stone disease in the last three decades. Urolithiasis can be formed as a result of metabolic alterations, anatomical malformations of urinary tract, infections, and environmental and nutritional reasons. Therefore, not only genetic and environmental factors, but also metabolic factors are implicated in the pathogenesis of stone development. Metabolic evaluation in patients of recurrent stone formation not only identify the abnormality but also useful in determining the dosages and required drugs.

The mean age of patients in this study was 31 ± 9.46 years which was a little lower than KiracM et al5 and Majalan NN et al10 studies who calculated mean age of 42 and 43 years respectively. Urolithiasis is a illness that is known to predominantly affect males. In recent years, however, the incidence of urolithiasis in women has been increasing. A study by Scales et al11 found that the male to female ratio of urinary stone cases diminished from 1.7 to 1.3 during the last 20 years in the USA. In this study, we found a male predominance (i.e., the male to female ratio is 4:1) which is very much comparable to studies of ParvinM et al6 and KiracM et al4 who had also found predominance of male patients with urinary stones.

In our study, the chief presenting complain was pain in lumber region i.e. in 88% patients. Elfadil
GA et al\(^7\) had also discussed that lumbar pain as the main presenting complaint in his study i.e. in 67% patients. The results of this given study have shown a strong genetic predisposition to urolithiasis as 64.0% patients had family history of urolithiasis. This genetic reason is also kept up by studies done by KiracM et al\(^8\) and Majalan NN et al\(^10\) who observed a positive family history in 67.0% and 53.1% patients respectively. While, Elfadil GA et al\(^7\) had observed this in only 20% of patients. We had also found that 86% patients with recurrent urinary stones and the major stone component was calcium oxalate in our study which was also found by ElfadilGA et al.\(^8\) But in a study by Androulakakis et al\(^12\), the main components of urinary stones in Europe, in decreasing order, are struvite, calcium phosphate and calcium oxalate. In our study, metabolic abnormalities were found in 92% patients, whereas there was no metabolic abnormality in only 8% patients which is very much comparable to many previous studies.\(^6,8,10\)In a study by Amaro et al\(^8\), 62.2% of patients were having multiple metabolic abnormalities; however, the patients were not having recurrent calcium oxalate stones. Therefore, it can be presumed that multiplemetabolic abnormalities are more common in patients with recurrent calcium oxalate stones. KiracM et al\(^10\) in his study had found multiple metabolic irregularities in 71.3% patients while in our study, 72% patients had multiple metabolic abnormalities and only 20% had single metabolic abnormality.

Hyperoxaluria was the commonest metabolic abnormality seen in this study and was found in 70% patients. Interestingly, the rate of hyperoxaluria is not constant between studies that have evaluated metabolic abnormalities i.e. KiracM et al\(^1\) reported a 64.4% prevalence of hyperoxaluria, whereas Amaro et al\(^8\) found a 21% prevalence. ParvinM et al\(^10\) have also reported higher mean urinary excretion of oxalate in stone formers compared with the individuals who are not stone formers. Although hyperoxaluria was the commonest risk factors in many previous studies but it was the second commonest risk factor in the study by Hess and associates,\(^13\) and also not very common in the Thai stone formers.\(^14\)

Other significant metabolic abnormalities as observed in our study were hypercalciuria and hypocitraturia. Hypercalciuria was found in 42% patients in this study while Majalan NN et al\(^10\) and KiracM et al\(^1\) had found its prevalence as 27% and 32.8% respectively. Citrate is a natural inhibitor of stone formation, and its absence in urine causes an increase in the risk of stone formation. Various researches have revealed that the prevalence of hypocitraturia is between 19% and 63%.\(^6,10,14,15\) In the given study, the hypocitraturia was present in 40.5% patients. Hypernatriuria was present in 29.5% of participants in our study. So that, urinary sodium levels should also be evaluated along with other metabolites in patients with recurrent calcium oxalate stones. In patients with recurrent stone formation, urinary sodium has hypotriglyceride and calciumic effect.\(^4\)In a research done by Brockis et al\(^16\), hyperuricosuria and hyperuricemia were the commonest metabolic abnormality, and these conditions were frequently observed in males. In a study by KiracM et al\(^4\) the prevalence of hyperuricosuria was 14.7%. Similarly, we have observed hyperuricosuria in 21.5% patients and hyperuricemia in 29.5% patients which represents that hyperuricosuria and hyperuricemia are also common metabolic abnormalities in urolithiasis.

**CONCLUSION:**
Our study concluded that the frequency of metabolic irregularities is quite high in patients with urinary stones and hyperoxaluria, hypercalciuria and hypocitraturia are the important most metabolic abnormalities found in such patients. Therefore, we recommend that metabolic evaluation of every patient with urolithiasis should be done especially in patients who form calcium stone, those who have recurrent stones, multiple stones or bilateral stones at their first presentation and in children. It will not only help us in recognizing risk factors of development of urinary stone, but also for selection of proper medical and dietary therapies to prevent further stone formation.

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