# GENDER AND AGE DISTRIBUTION, AND URINARY METABOLIC ABNORMALITIES IN PATIENTS WITH RECURRENT URINARY TRACT STONES

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#### ABSTRACT

**Background:** Urolithiasis is one of the most common urological disorders. Patients with recurrent urinary tract stones may have underlying metabolic abnormality. The objectives of this study were to determine the gender and age distribution, and frequency of common urinary metabolic abnormalities in patients with recurrent urinary tract stones.

**Material & Methods:** This cross-sectional study was conducted in Department of Urology, Institute of Kidney Diseases, Peshawar from August 2011 to June 2012. Patients above 13 years presenting with recurrent urinary tract stones were included. 24-hour urine sample was sent for metabolic abnormalities. Gender, age in years, and age grouping were demographic while presence of hypercalciuria, hyperoxaluria, hyperuricosuria and hypocitraturia were research variables.

**Results:** Out of 70 patients, males were 45 (64.3%) and females were 25 (35.7%). Mean age was  $29.72 \pm 8.5$  (16-68) years. Hypercalciuria was noted in 34 (48.60%) patients with 20 (28.6%) males and 14 (20.0%) females. The highest number of patients i.e 21(30.0%) was noted in age group 21-30 years. Hyperuricosuria was noted in 12 (17.19%) patients. The highest number of patients i.e. nine (12.9%) was noted in age group 21-30 years. Hyperoxaluria was reported in 16 (22.90%) patients. The highest number of patients i.e. nine (12.9%) was noted in age group 21-30 years. Hyperoxaluria was reported in 16 (22.90%) patients. The highest number of patients i.e. nine (12.9%) was noted in age group 21-30 years. Hyperoxaluria was noted in 22 (31.44%) patients. The highest number i.e. 14 (20.0%) with hypocitraturia was noted in age group 21-30 years.

**Conclusion:** Recurrent stone former have high frequency of metabolic abnormalities. Prompt treatment of these abnormalities will decrease the chances of recurrent stone formation.

**KEY WORDS:** Urolithiasis, Urinary Tract Stones, Renal Colic; Hematuria; Renal Failure; Urinalysis; Hypercalciuria; Hyperoxaluria; Hyperuricosuria; Hypocitraturia.

This article may be cited as: Naeem M, Ahmad T, Khan MK, Ullah H. Common urinary metabolic abnormalities in patients with recurrent urinary tract stones. Gomal J Med Sci 2015; 13:127-30.

### INTRODUCTION

Urolithiasis is one of the most common urological disorders.<sup>1</sup> A total of 3-5% of the population in their lifetime is affected by kidney stones.<sup>2</sup> It is more common in men (13%) than women (7%) but in children both sexes are affected equally.<sup>3</sup> In the last 25 years the prevalence of kidney stone disease has increased in both genders.<sup>4</sup>

Stones are broadly divided into two types i.e. Calcium and non calcium calculi (Struvite, uric acid, cystine, xanthine, indinavir and others). Patients may be asymptomatic or present with renal colic, hematuria, infection, vomiting and renal failure.<sup>4</sup> Although

**Corresponding Author:** Dr. Muhammad Naeem Associate Professor Department of Urology, Institute of Kidney Diseases, Hayatabad Medical Complex, Peshawar E.mail: mnaeen04@yahoo.com both intrinsic and environmental factors can contribute to urinary stone formation, the exact cause is still unclear.<sup>1</sup> Multiple risk factors predispose patients to recurrence such as abnormal anatomy, family history of stone disease, environmental conditions and metabolic abnormalities such as hypercalciuria (35%), hyperoxaluria (19%), hypocitraturia (27%), hyperuricosuria (18%), and a low urinary volume (56%).<sup>5</sup> In majority of the cases of recurrent stones, thorough evaluation reveals metabolic abnormalities. If these metabolic abnormalities go untreated, the stones may recur. The recurrence rate may be as high as 50% within 5 years of presentation.<sup>2</sup>

The prevalance of recurrent renal stones may be decreaed by increased fluid intake, decreased soft drink intake, balance diet, treating infection, preventing trauma to the renal system during surgery, and identification and treatment of underlying metabolic abnormalities.<sup>6</sup> Patients with recurrent stones, family history of stones and multiple stone former with history of stone passage per urethra are the candidates for metabolic evaluation. The patient does not have to be stone free to undergo a metabolic evaluation. The only pre requisite is the absence of gross hematuria and renal obstruction.5 Single 24-hour urinalysis is sufficient to assess the risk of recurrent stones.<sup>7</sup>

The objectives of this study were to determine the gender & age distribution, and frequency of common urinary metabolic abnormalities in patients with recurrent urinary tract stones.

### **MATERIAL AND METHODS**

This cross-sectional study was carried out in the Department of Urology and Renal Transplantation, Institute of Kidney Diseases, Hayatabad Medical Complex, Peshawar, Pakistan from August 2011 to June 2012. All patients age above 13 years of either gender who presented with recurrent urinary tract stones were included in the study. Recurrent stone was defined as stone diagnosed by ultrasound or X-ray KUB six months of self passage or retrieval of stone by surgery. All pregnant ladies, first time stone formers and those patients taking antacid, indinavir or potassium sparing diuretics were excluded from the study. These conditions are associated with abnormal level of urinary ions (Ca, uric acid, oxalate and citrate) and act as confounders.

All the patients were subjected to detailed history and physical examination followed by routine investigations. From all patients, a 24-hour urine sample was collected under strict aseptic condition in a graduated jar and was sent to hospital laboratory to identify common metabolic abnormalities of the urinary tract (hypercalciuria, hyperoxaluria, hyperuricosuria and hypocitraturia). All the above mentioned investigations were conducted under supervision of a single experienced pathologist.

Gender, age in years, and age grouping were demographic while presence of hypercalciuria, hyperoxaluria, hyperuricosuria and hypocitraturia were research variables. Age was grouped as; 14-20 years, 21-30 years, 31-40 years, 41-50 years, 51-60 years, and above 60 years.

Data were analyzed using SPSS version 17 (SPSS Inc., Chicago, IL). Mean and SD were

calculated for numerical variables such as age. Frequencies and percentages were calculated for categorical variables such as gender and presence of hypercalciuria, hyperoxaluria, hyperuricosuria and hypocitraturia.

## RESULTS

Out of 70 patients with recurrent stone disease, males were 45 (64.3%) and females were 25 (35.7%) with male to female ratio of 1.89:1. Mean age of the sample was 29.72 $\pm$  8.5 (16-68) years. There were three (4.28%) patients in age group 14-20 years, 46 (65.72%) in 21-30 years, 11 (15.72%) in 31-40 years, seven (10%) in 41-50 years, zero in 51-60 years, and three (4.28%) patients in >60 years, with modal age group of 21-30 years.

Frequency and percentages of all the four urinary metabolic abnormalities cross-tabulated by age groups are summarized in Table 1. As some of the patients have more than one urinary metabolic abnormalities, hence total is 84 instead of 70 patients.

Hypercalciuria was noted in 34 (48.60%) patients with 20 (28.6%) males and 14 (20.0%) females. The highest number of patients i.e 21 (30.0%) with hypercalciuria was noted in age group 21-30 years.

Hyperuricosuria was noted in 12 (17.19%) patients with seven (10%) males and five (7.1%) females. The highest number of patients i.e. nine (12.9%) was noted in age group 21-30 years. No patient was reported in second and sixth decade.

Hyperoxaluria was reported in 16 (22.90%) patients with 13 (18.3%) males and three (4.6%) females. The highest number of patients i.e. nine (12.9%) was noted in age group 21-30 years.

Hypocitraturia was noted in 22 (31.44%) patients with equal number i.e. 11(15.7%) of males and females. The highest number i.e. 14 (20.0%) with hypocitraturia was noted in age group 21-30 years. Only one (21.4%) was noted both in second and seventh decade.

## DISCUSSION

Recurrent stone formation is associated with obstruction and infection particularly in patients with

 Table 1: Metabolic abnormalities (frequency & percentage-wise) in patients with recurrent urinary tract stones cross-tabulated by age groups (n=70).

Metabolic abnormality	14-20 years	21-30 years	31-40 years	41-50 years	51-60 years	>60 years	Total No. (%)
Hypercalciuria	2 (2.86)	21(30.0)	7 (10.0)	3 (4.29)	0 (0.0)	1 (1.43)	34 (48.60)
Hyperuricosuria	0 (0.0)	9 (12.9)	1(1.43)	1 (1.43)	0 (0.0)	1 (1.43)	12 (17.19)
Hyperoxaluria	2 (2.86)	9 (12.9)	2 (2.86)	2 (2.86)	0 (0.0)	1 (1.43)	16 (22.90)
Hypocitraturia	1 (1.43)	14 (20.0)	4 (5.72)	2 (2.86)	0 (0.0)	1 (1.43)	22 (31.44)

Gomal Journal of Medical Sciences April-June 2015, Vol. 13, No. 2

systemic diseases such as diabetes mellitus.<sup>8</sup> In addition stone treatment is costly in term of time and use of medical resources.<sup>9</sup> Prevention significantly reduces recurrence rates so it is important to evaluate metabolically a patient for underlying causes of stone formation. The assessment of the urinary pattern of promoters and inhibitors of stone formation, a suitable metabolic evaluation should also focus on the occurrence of systemic diseases potentially complicating with secondary nephrolitiasis.<sup>10</sup>

There are two types of metabolic evaluations available for stone formers: a limited metabolic evaluation and a comprehensive metabolic evaluation. A limited metabolic evaluation involves the collection of one or two random 24-hour urine samples. In a comprehensive metabolic evaluation, the patient first collects the random 24-hour urine samples and then goes on a week of a restricted calcium, oxalate, sodium, and purine diet. After the collection of a third restricted diet 24-hour urine sample, the patient undergoes a calcium load test.

In our study hypercalciuria was the most common metabolic cause of stone formation. Hypercalciuria is defined as urinary calcium excretion greater than 300 mg/d in men and greater than 250 mg/d in women. In a single 24-hour urine collections, hypercalciuria occured in almost half (48.60%) of the patients. Brian H<sup>11</sup> conducted study on 311 patients; 71 (22.8%) were first-time stone-formers and 240 (77.1%) were recurrent stone-formers. He observed hypercalciuria in 43.3% patients which were similar to our result. Similarly Park et al<sup>12</sup> reported hypercalciuria in 35 to 65% of his patients. Mustafa Kırac13 investigated the effects of dietary factors on 24-hour urine parameters in 108 patients with idiopathic recurrent calcium oxalate stones. He observed hypercalciuria in 38 (35.5%) patients both before and after the dietary intervention. Although hypercalciuria can be accompanied by diseases causing a hypercalcemic state such as primary hyperparathyroidism, myeloproliferative disease, vitamin D intoxication, or Cushing's syndrome, most hypercalciuria is idiopathic and results from hyper-absorption of calcium in the intestine or failure of calcium re-absorption in the renal tubule.<sup>14</sup> In addition, hypercalciuria may have a genetic predisposition, and about half of patients who have hypercalciuria have a family history of stone disease.15

Hyperuricosuria, defined as uric acid excretion greater than 750 mg/d, is associated with calcium oxalate stones in 20% of patients. It was found in 12 (17.19%) of patients. Our result is supported by the study of Brian H<sup>11</sup> who reported hyperuricosuria in 23.3% patients in recurrent stone formers. Uric acid is an end product of purine metabolism and serves as the nucleus of urinary crystallization to induce the formation of calcium oxalate stones. It is also responsible for urinary stone formation by reducing the activity of urinary inhibitors in the urine. Hyperuricosuria is also related to a family history. This relation can be supported by the fact that the metabolism and excretion of uric acid may be influenced by inherited factors and that men with gouty diathesis are at increased risk of stone formation.<sup>16</sup> Curhan et al<sup>17</sup> found increased urinary excretion of uric acid in a group with a family history of renal stones, but statistical significance was not reached.

Hyperoxaluria in adults is defined as oxalate excretion exceeding 40 mg/d. It was found in 16 (22.90%) patients which was slightly lower than that reported by Brian H<sup>11</sup> which was 33.3%. In contrast, Mustafa Kırac<sup>13</sup> reported hyperoxaluria in 84 (77%) of patients, which was higher than our results. In adults, hyperoxaluria is usually secondary to increased oxalate absorption from the gastrointestinal tract. This condition is frequently found in patients with inflammatory bowel disease and in patients following small bowel bypass surgery for the treatment of morbid obesity. Hypocitraturia is defined as less than 300 mg/d of urinary citrate excretion. Hypocitraturia was found in 22 (31.44%) of patients.

## CONCLUSION

Recurrent stone former have high frequency of metabolic abnormalities. Prompt treatment of these abnormalities will decrease the chances of recurrent stone formation.

## REFERENCES

- Fwu CW, Eggers PW, Kimmel PL, Kusek JW, Kirkali Z. Emergency department visits, use of imaging and drugs for urolithiasis have increased in the United States. Kidney Int 2013; 83(3): 479-86.
- Stechman MJ, Loh NY, Thakker RV. Genetic causes of hypercalciuric nephrolithiasis. Pediatr Nephrol 2009;24:2321-32.
- Pearle MS, Calhoun EA, Curhan GC. Urologic diseases in America project: urolithiasis. J Urol 2005;173:848-57.
- Sakhaee K. Recent advances in the pathophysiology of nephrolithiasis. Kidney Int 2009; 75(6):585-95.
- 5. Chandhoke S. Evaluation of recurrent stone former. Urol clin N Am 34;2007:315-22.
- Fink HA, Akornor JW, Garimella PS, MacDonald, Cutting A, Rutks IR, et al. Diet, fluid, or supplement for secondary prevention of nephrolithiasis: a systematic review and meta-analysis of randomized trials. Eur Urol 2009;56:72-80.
- Castle SM, Cooperberg MR, Sadetsky N, Eisner BH, Stoller ML. Adequacy of a single 24-hour urine collection for metabolic evaluation of recurrent nephrolithiasis. J Urol 2010;184:579-83.

- Worcester EM, Parks JH, Evan AP, Coe FL. Renal function in patients with nephrolithiasis. J Urol 2006;176(2):600-3.
- Saigal CS, Joyce G, Timilsina AR; Urologic diseases in America Project. Direct and indirect costs of nephrolithiasis in an employed population: opportunity for disease management? Kidney Int 2005;68:1808-14.
- Heilberg IP, Weisinger JR. Bone disease in idiopathic hypercalciuria. Curr Opin Nephrol Hypertens 2006;15(4):394-402.
- Pak CY, Britton F, Peterson R, Ward D, Northcutt C, Breslau NA, et al. Ambulatory evaluation of nephrolithiasis. Classification, clinical presentation and diagnostic criteria. Am J Med 1980;69:19-30.
- 12. Park C, Ha YS, Kim YJ, Yun SJ, Lee SC, Kim WJ. Comparison of metabolic risk factors in urolithiasis patients according to family history. Korean J Urol 2010;51:50-3.
- Mustafa Kıraç, Bora Küpeli, Lokman İrkilata, Özlem Gülbahar, Nur Aksakal, Üstünol Karaoğlan, et al. Effects of dietary interventions on 24-hour

urine parameters in patients with idiopathic recurrent calcium oxalate stones. Kaohsiung J Med Sci 2013;29(2):88-92.

- 14. Mandel N. Mechanism of stone formation. Semin Nephrol 1996;16:364-74.
- 15. Coe FL, Parks JH, Moore ES. Familial idiopathic hypercalciuria. Engl J Med 1979;300:337-40.
- Kwon OJ, Ahn SH. Comparison of the lithogenic risk factors for first time and recurrent stoneformers. Korean J Urol 2006;47:1093-8.
- 17. Curhan GC, Willett WC, Rimm EB, Stampfer MJ. Family history and risk of kidney stones. J Am Soc Nephrol 1997;8:1568-73.

CONFLICT OF INTEREST Authors declare no conflict of interest. GRANT SUPPORT AND FINANCIAL DISCLOSURE None declared.