

URIC ACID - CREATININE RATIO IN PATIENTS WITH RENAL STONES

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ABSTRACT

The prevalence of kidney stone disease in India is 11%. Adult males are 3 times more affected than females and is a major cause of morbidity in human beings. The metabolic defects are less common cause in the patient presenting for the first time with kidney stones than the recurrent stone formers. The present study was aimed to determine the urinary levels of uric acid and creatinine. Uric acid and creatinine ratio were determined to assess the susceptibility for stone formation in such patients. In our research work we took 30 clinically diagnosed cases of urolithiasis and 30 age and sex matched healthy controls. Our results showed increased concentration of stone promoters such as uric acid and decreased concentration of stone inhibitors such as creatinine in urine of urolithiasis patients. Observations of our research work provide some evidence regarding the role of the above-mentioned ratios in the pathogenesis as well as susceptibility of such subjects for urolithiasis.

KEYWORDS: Metabolic defects, Uric acid/Creatinine Ratio, Urolithiasis.

INTRODUCTION

Urolithiasis is defined as deposition of crystalline aggregates composed of varying amounts of crystalloid and a small amount of organic matrix in the urinary tract (kidney, ureter & bladder). The life time prevalence of kidney stone disease is estimated 1% to 15% with the probability of having a stone according to age, gender, race and geographic location. Stone disease has the highest prevalence in whites followed by Hispanics, Asians and Africans. Stone disease is most common in 40-60 years of age. Hot and dry climate are some of the predisposing factors for stone formation. Seasonal variation is related to stone formation by way of increased temperature in summers leading to fluid losses through perspiration and perhaps by sunlight induced increased Vitamin D formation. Heat exposure and dehydration have a role to play even as an occupational risk factors for stone disease. Metabolic evaluation of the workers in occupations where they are exposed to high temperature showed a higher incidence of low volume and subsequent urolithiasis. Those exposed to high temperature exhibited lower urine volumes and pH which predispose to renal stone disease. Obesity and weight gain are independent risk factors for incident of stone formation. Incidence of stone disease is less in

areas with hard water supply and more in areas with soft water supply. This might be due to the urine becoming super saturated with respect to salts which actually constitute the core of the stones in urinary tract, such that ions or molecules precipitate out of solution and form crystals or nuclei either in kidney or ureters. Once formed crystals may get retained in the kidney at anchoring sites that promote growth and aggregation and leads to stone formation. In normal human urine, concentration of calcium oxalate is 4 times higher than its solubility in water. Urinary factors favoring stone formation includes low volume, hypocitraturia, increased Calcium, Uric acid and Phosphorus. Once the concentration product exceeds the solubility product crystallization can potentially occur.^[1]

Calcium and Uric acid are seen in almost all the stones in different proportions. Previous studies have shown association of uric acid containing stones with hypercalciuria and hyperuricosuria. Idiopathic hypercalciuria has been increasingly recognized as a common pathology for renal stone disease. Hypercalciuria is defined as > 4 mg/kg/day of calcium excretion in urine.^[2]

A direct positive correlation between U Calcium-Creatinine ratio in hypercalciuria has been shown by Osorio *et al.*^[3] The tubular handling of promoters and inhibitors of stone formation as well as their urinary pattern can be strongly influenced by genetic factors.^[4] Studies have shown that urine Calcium/Creatinine value is believed to be varying with climate and exposure to sunlight, mineral composition of drinking water, dietary habits, age, genetics and sex.^[5] The present study was carried out to evaluate Uric acid/Creatinine ratio in urolithiasis patients with hypercalciuria and hyperuricosuria.

MATERIAL AND METHODS

The study was conducted from July 2012 to January 2013 in Department of Biochemistry, JJM Medical College, Davangere, Karnataka, India on 30 clinically and radiologically diagnosed cases of urolithiasis from Department of Urology, JJM Medical College and on 30 age and sex matched healthy controls taken from general population of Davangere. Written informed consent was taken from patients as well as healthy controls. An approval from Institutional Ethical Committee of JJM Medical College, Davangere was also obtained before study.

The urinary calcium was estimated by ARSEZANO'S method using semi-automated analyser. The urinary uric acid was estimated by URICASE method by semi-automated analyser. Urinary creatinine was measured by rapid enzymatic method in semi-automated analyser.^[9,6]

The results were analyzed statistically and were expressed as Mean \pm Standard Deviation. A p-value of 0.05 or less was considered as statistically significant [Table-1].

RESULTS

A total of 30 urolithiasis patients with mean age of 45 years comprising and 30 controls with mean age of 45 years were investigated in this study. Study showed that the Urinary Calcium, Uric acid level were significantly increased ($p < 0.05$) but Urinary Creatinine level was not significantly decreased or increased in urolithiasis patients as compared to healthy controls. This Study also showed that Urinary Calcium/Creatinine ratio and Uric acid/Creatinine ratio was significantly increased ($p < 0.05$) as compared to healthy controls. [Table-1] Cumulative data representation shows comparison of parameters between cases and controls. [Fig-1]

Table 1: Various parameters in subjects.

Parameters	Controls	Cases	P value
U. Calcium	5.13 \pm 0.67	7.06 \pm 1.85	< 0.001
U. Uric acid	2.43 \pm 0.44	4.26 \pm 0.54	< 0.001
U. Creatinine	16.98 \pm 4.43	17.04 \pm 0.44	0.98
U. Calcium/Creatinine ratio	0.32 \pm 0.09	0.62 \pm 0.44	0.002
U. Uric acid/Creatinine ratio	0.21 \pm 0.15	0.37 \pm 0.22	0.007

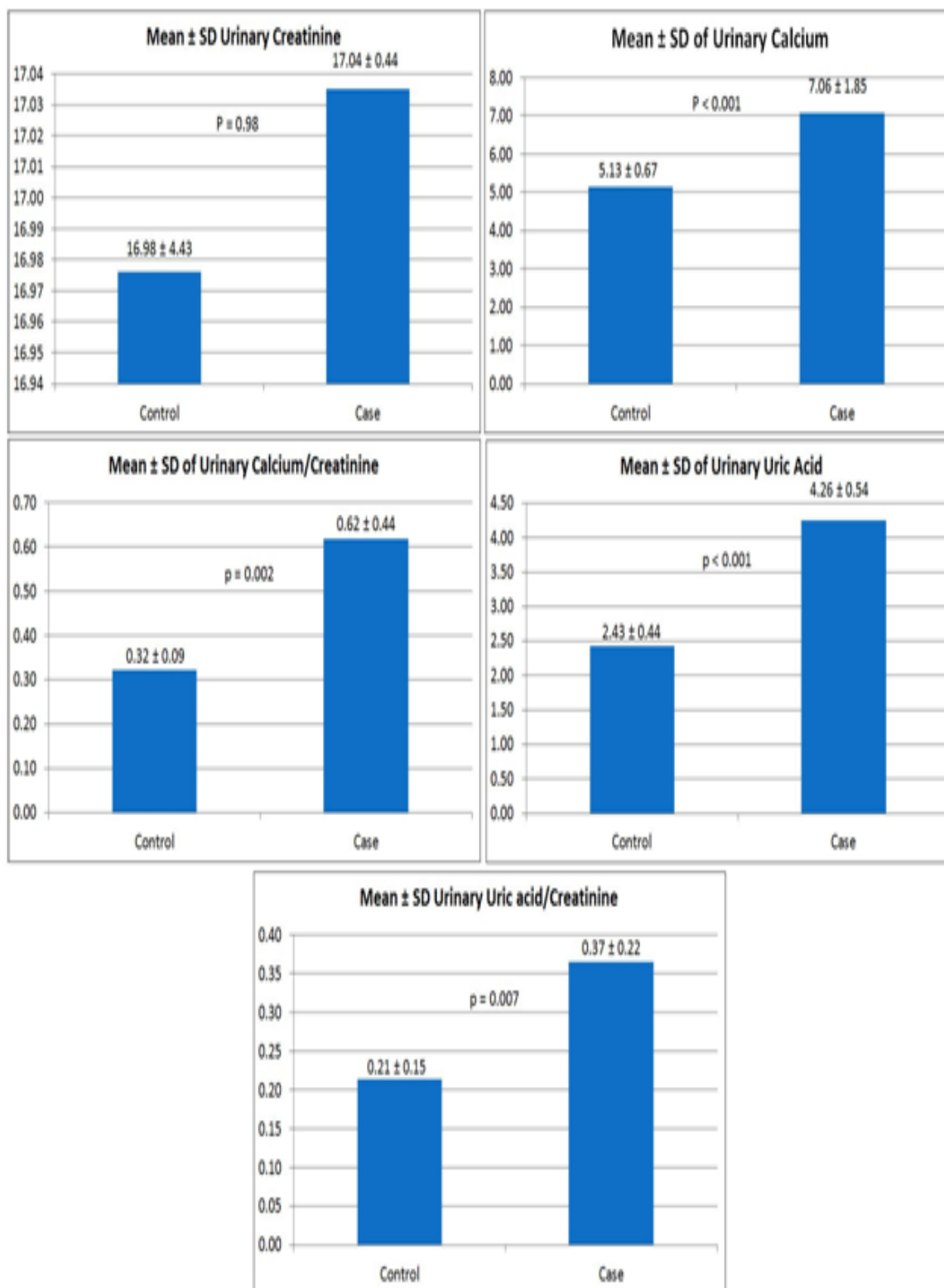


Fig. 1: Cumulative representation of various parameters.

DISCUSSION

Surgical intervention is often the management of choice for recurrent stone disease. Urolithiasis is a well-recognized clinical problem and remains the major source of morbidity in human population. It is generally

believed that metabolic defects are often not the common etiology in the patients with recurrent renal disease.

The relationship between calcium excretion and calcium intake are complex. Therefore, both diagnostic and therapeutic purposes, it appears to be more useful to get

information on the dietary dependence rather than on calcium dependence of hypercalciuria.^[2]

Various studies have shown that a low calcium diet and high uric acid diet results in an excessively negatively calcium balance in patients with idiopathic hypercalciuria and renal stone. Patients in whom calcium was best absorbed from high calcium from high calcium diet also had the greatest calcium loss on low calcium diets. Study also suggested that a sustained high flux of calcium though kidney may attenuate the calcium conservation mechanisms in the renal tubules^[3]. Moreover, two major factors that promote uric acid precipitation are a high urine uric acid concentration and an acid urine pH, which drives the following reaction converts the relatively soluble urate salt into insoluble uric acid.^[4-5] This would explain the higher calcium excretion during fasting that we found in stone formers as compared with normal subjects. Such a superfluous when the kidney is being flooded with calcium.^[6]

Values of creatinine tend to be lower in acidified or alkalinized samples than in untreated urines. This influence of pH has been predicted from studies of aqueous solutions.^[7] Moreover, several factors including geographic location, genetics, nutritional habits, source of drinking water, season, exposure to sunlight and even environmental pollutants have been postulated to explain the calcium /creatinine ratio in controls and cases.^[8-9]

Aim of the study was to assess the suitability of uric acid creatinine ratio to predict the incidence or to guide the management in urolithiasis.

Hyperuricemia is a major risk factor for urolithiasis. In some studies, hyperuricemia has been shown to contribute to calcium oxalate stone formation via heterogeneous nucleation, the primary mechanism of uric acid containing calcium stones.^[10] The solubility of urate salts is also affected by the relative concentrations of cations in the urine. Increased urinary sodium concentrations promote formation of the monosodium urate complex.^[11]

There is no established evidence that the prevalence of osteopenia is significantly increased in patients with idiopathic hyperuricemia as well as hypercalciuria.^[12]

CONCLUSION

In our study we found that urinary calcium and uric acid were found to be increased and there was no significant change in urinary creatinine level. Ratios such as calcium creatinine ratio and uric acid creatinine ratio were also increased. There was a significant co relation between the promoters and inhibitors with stone formation in the urinary tract. Calcium/creatinine ratio and uric acid/creatinine can be used as an index of stone formation but studies with higher sample size should be taken up to substantiate our findings.

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