

# Increasing Incidence of Renal Calculi with High Serum Calcium, Uric Acid Level & Hot Humid Climate.

Amit Kumar<sup>1</sup>, Saket Kumar Mishra<sup>2</sup>

<sup>1</sup>Senior Resident, Rama medical college and hospital, Hapur, UP.

<sup>2</sup>Senior Resident, Rama medical college and hospital Hapur, UP.

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## ABSTRACT

**Background:** To study and analyze the serum calcium, serum uric acid, age, sex, geographical distribution and compare the results with available literature. To study the incidence, prevalence and selected risk factor of kidney stone disease and estimate the effect of relationship between risk factor distributions and compare the results with available literature from around the world. **Methods:** All renal colic individual were scrutinized who came to a tertiary care hospital and 187 patients met the inclusion criteria made after basic investigation and ultrasonography. **Results:** Over a period of one year, all renal colic patients were scrutinized and 187 patients met the inclusion criteria. The most common age group was 31-60 years and males predominated over females 67% of males versus 33% of females. The major risk factors for developing stones are hot and humid climate in this region of Kerala associated with lack of adequate fluid intake and high intake of animal protein in diet. In this study of 187 renal calculi patients, 56% had high serum calcium and those who had raised serum calcium 58% had larger calculi. Out of 187 patients, 63% had high serum uric acid level. Out of 118 patients with raised serum uric acid, 74% were male and 26% were female. **Conclusion:** There is an increase in the prevalence of kidney stones in India and other parts of world. Many aspects of the mechanisms of kidney stone formation remain unclear at present. Diet and life style factor likely play an important role in the changing epidemiology of kidney stones. It appears that changes in two of most important environmental factors, diet and climate have the most significant impact on these trends; kidney stones are higher in warm or hot climates with poor fluid intake. The peak age group of recurrence of stones was 31-60 years. Males are more prone to develop kidney stones than females. Patients who had raised serum calcium and serum uric acid level had larger and multiple calculi bilaterally.

**Keywords:** Organophosphorus poisoning, Pesticides, Clinical features

## INTRODUCTION

Renal colic is one of the common conditions in routine clinical practice now days. Kidney stones are one of the most common urological problems worldwide. The overall prevalence of developing kidney stone differs in various parts of world. There is various data showed that the prevalence of kidney stone increasing day by day in industrialized world. Higher ratios of kidney stones are in males relative to females. The major risk factor for developing stones are hot climate, poor fluid intake, high animal protein diet and low calcium rich diet.

Kidney stones are affecting almost all geographical, cultural and racial groups. The high prevalence approximates 20 to 25% in the Middle East. There is increased risk of dehydration in hot or warm climates, a diet 50% in lower calcium compare to western diets, account for the higher risk of developing stones in the Middle East.<sup>[1]</sup>

In developed country there is very rapid increase over last 30 years.<sup>[2]</sup> The incidence of renal calculi is highest in Caucasian males.<sup>[3]</sup> Peak age between 40 to 60 years (approx 3 per 100 per year).<sup>[4]</sup> Epidemiologically, between 120 and 140 per 1000,000 will develop urinary stones each year with a male/female ratio of 3:1. In India the incidence and prevalence of kidney stones disease are higher in northern region compared to that in southern states.<sup>[5]</sup> Kidney stones are the most common cause of acute renal failure and chronic renal failure with estimated prevalence (20%), and there is a study of renal stone of 176 patients with the peak age group of 38.7 years, and renal stone were most common in Kochi, Kerala.<sup>[6]</sup> Diet, fluid and hot or warm climates have been thought to play a major risk to development of kidney stone disease.<sup>[7]</sup> In general, the belief is that India is a land of stones.<sup>[8]</sup> Kidney stone disease distribution per 100, 0000 of populations in India (1926-28).<sup>[8]</sup>

India generally -----	10
Punjabi-----	438
Hyderabad-----	266
Manipur (north east) -----	84
Saharanpur (U.P) -----	25

### Name & Address of Corresponding Author

Dr. Saket Kumar Mishra  
Senior Resident,  
Rama medical college and hospital  
Hapur, UP.

Ahmednagar (Maharashtra) ----- 13  
 Sylhat (Assam) ----- 2.8  
 Malabar (South India) ----- 0.3  
 Most of these stone compositions are made up of calcium, oxalate and phosphates.

The etiological and pathogenesis of kidney stone disease are debatable; however it is well known that drinking less water is a major risk factor for stone disease. New research by the National Kidney foundation suggests that the Nano bacteria may be the culprit. These findings are very useful and may eventually lead to new and more effective ways of treating and preventing kidney stone disease [9]. A Study on spectrum of kidney stone composition in India revealed that 93.4% were calcium oxalate stones, 1.2% having struvite, 1.80% apatite, 0.95% uric acid and 2.76% were mixed. Around 50-70% of these patients may develop a second stone if followed up to 10 years after the first episode.<sup>[10]</sup>

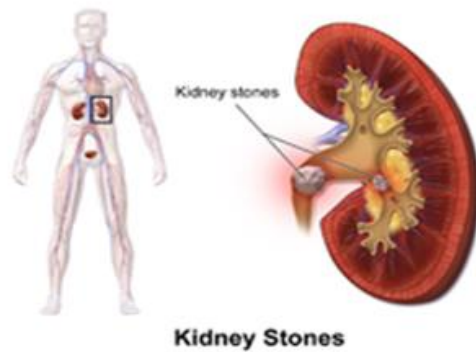
Urinary stone constitute one of the commonest diseases in our country. In India, approximately 5-7 million populations suffer from stone disease and at least 7-10 by 1000 of Indian population needs hospitalization due to kidney stone.<sup>[11]</sup>

From some experimental data, the higher prevalence of kidney stone in males can be probably due to the effect of sex hormones on lithogenic risk factors: androgen appeared to be increased, and oestrogen appeared to be decreased.<sup>[12]</sup>

Peak age of recurrence of idiopathic kidney stone is approx 35 years.<sup>[13]</sup> This indicates that hospital admission data for kidney stone disease reflects morbidity more than true prevalence.<sup>[14]</sup> A familial occurrence has been suggested for hypercalciuria which is the main risk factors for idiopathic kidney stone disease.<sup>[15]</sup> It has been proposed that comorbidity with essential hypertension, over weight and Type 2 Diabetes Mellitus predispose to kidney stone disease. Few lithogenic risk factors like urinary calcium, oxalate and uric acid excretion, are known to be influenced by rich animal protein diet, which in turn is frequently related to overweight. In female patient with basal metabolic index (BMI), 40% higher than standard, there was a (89%) increase in the prevalence of kidney stone, while corresponding figures in males was only (19%).<sup>[16]</sup> In hypertensive patients, with two to five fold increase in relative risk of kidney stone. Higher risk may be due to co-existence of risk factors for both the diseases, namely over weight and high animal protein, salt intake.<sup>[17-19]</sup> There has been much evidences of dietary factors closely related to the prevalence of stone disease in a given populations is probably due to high animal protein consumption.<sup>[20]</sup>

Drugs that may increases the risk of stone disease.<sup>[21]</sup>

- Decongestants : ephedrine, guaifensin
- Diuretics : triamterene
- Protease inhibitors : indinavir
- Anticonvulsants : felbamate , topiramate and zonisamide



**Figure 1: Location of kidney stones**

Approximately 80% of kidney stones are calcium oxalate (CaOx),<sup>[22]</sup> with a small percentage (15%) of calcium phosphate (CaP).<sup>[23]</sup>

'Red flag' sign warranting further investigation.<sup>[24]</sup>

- Episodes of first stone under the age of 25
- Bilateral or multiple renal stones, or nephrocalcinosis
- Recurrent kidney stones
- Renal stones associated with impaired renal function (eGFR < 60ml/min/1.732m<sup>2</sup>)
- Radiolucent stones may be urate or cystine
- Stone associated with underlying condition e.g. inflammatory bowel disease, gastric bypass surgery or metabolic syndrome

General measures to prevent recurrent stone formation

- Increase fluid intake is advised to maintain the urine output of 2-3l/day.<sup>[25]</sup>
- Decrease the intake of animal protein (<52g/day).<sup>[26]</sup>
- Restrict salt intake (<50mmol/day of sodium chloride).<sup>[26]</sup> Normal calcium intake (> 30 mmol/day).<sup>[26]</sup>
- Cranberry juice: decrease incidence.<sup>[27]</sup>

## MATERIALS AND METHODS

This was an analysis of data generated from the records of Ultrasonography of whole abdomen and consecutive blood samples received in the laboratory during the study period.

Renal colic is one of the common conditions in routine clinical practice in this hospital.

Kidney stones have a high prevalence in the central region of Kerala.

Kidney stones are one of the most common urological problems in Kerala.

Metabolic disorder like Type 2 DM is much higher in Kerala than other parts of India therefore may be chances of calculi is very high in this region.

Kerala known for its hot and humid climate, made me to do research in this topic as this climatic condition is one of the major risk of kidney stone disease prevalence.

Male 126 & Female 81

Patients, adolescents of 13 -19 years, adult of 20-60 years and elderly >60 years of age and both genders were included

**Sample size & sample technique**

187 Patients.

In this study, Number of patients is calculated by using the formula

$n > (Z^2 PQ) / d^2$  Where Z is the confidence coefficient at 95% = 1.96

P is the prevalence of Kidney stone which is approximately 20% Q =1- P i.e. 80%

D = the difference between estimated value and the true value, it is taken as 5.8 %

The sample size worked out to be 187 (>182.7).

Patients were approached with the Questionnaire for the assessment of Renal Colic. Complete study design with their aims and objectives were explained to patient. Patient’s history, examination, and blood sample for serum calcium & serum uric acid were noted. Informed consents were signed in local language.

The final diagnosis of Kidney stone was be done by Ultrasonographic confirmation, physician and surgeon who were blinded to the study design according to the pre-established WHO definitions after reviewing medical records.

Patients underwent standard clinical examinations, routine biochemical and haematological investigations, Ultrasonography of whole abdomen and received treatment as decided by their treating physician and surgeon. Medical record numbers were used to generate the data for analysis.

The principle of calcium estimation is by using Randox imola as it specially binds to calcium forming a coloured compound. Ca++ plus Arsenazo III coloured complex.

The Randox imola 3 uses a timed endpoint method to measure the concentration of uric acid in serum, plasma.

**RESULTS**

Over a period of year from May 2014 to April 2015 all renal colic were scrutinized and 187 patients met the inclusion criteria. Assessment of these selected patients was done in both IPD and OPD basis.

The most prevalent age group are 31-60 years of 60% had renal calculi and males predominated over female has 67% vs. 33%. In the study there is significant prevalence of renal calculi which is 95% due to poor fluid intake and about 56% in patients who had history of gout.

Out of 187 renal calculi patients 56% had high serum calcium (> 10.4 mg/dl) and 63% had high serum uric acid level (>5.7mg %). Among individual with high serum calcium and uric acid level had multiple bilateral large size of kidney stones.

A total of 187 patients 63% had past history of calculi, 45% had family history of calculi

Out of 187 patients 73% had multiple calculi, 52% had bilateral calculi and 58% had large calculi (> 6mm).

In study of total kidney calculi patients 47% had significant pus cell and 58% had RBC in urine.

Among males 57% and among females 54% had raised serum calcium level. Out of 105 patients who had raised serum calcium 58% had larger calculi.

Out of 117 patients who had past history of renal calculi 68% had large size of calculi (>6mm) and 62% had high serum calcium level.

Analysis between serum uric acid and gender was significant and out of 118 raised serum uric acid patients 87(74%) were male and 31(26%) were female. Out of 118 who had raised serum uric acid level 53% had larger calculi (> 6mm).

Among 126 males 71% were alcoholic. Out of 89 alcoholic 72% had history of gout and 74% had high serum uric acid level both had significant value in study.

Analysis between past history of renal calculi and history of gout had positive correlation and history of drug had negative correlation.

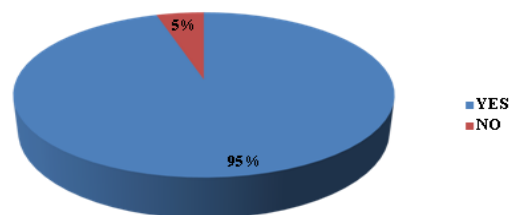
Total 105 individual with history of gout 66% had large size of calculi. Analysis of family history of calculi with history of gout (56%) and with size of calculi (45% large size) had significant.

Out of 101 patient 52 had less than 2 days of hospital stay, and patient with co morbidity like type 2 DM, hypertension and obesity have longer stay in hospital.

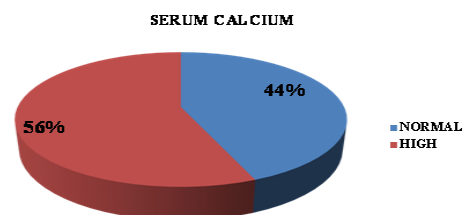
Out of total 187 patients there are 52 had history of calcium tablets while 135 have there is no history of calcium drug.

**DISCUSSION**

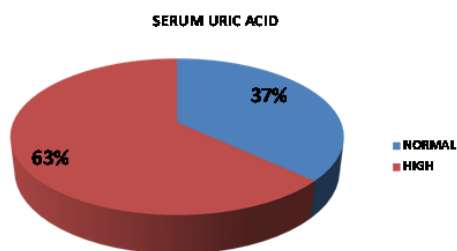
**Graph - 1 95% HAD POOR FLUID INTAKE POOR FLUID INTAKE**



**Graph - 2 OUT OF 187 RENAL CALCULI 56% HAD HIGH CALCIUM LEVELS**



Graph - 3 OUT OF 187 RENAL CALCULI 63% HAD HIGH URIC ACID LEVELS



This was an observational study with the main objective of serum calcium and serum uric acid level in individual with kidney stone in renal colic, with a focus on various risk factors for prevalence of stone disease.

Over a period of year from May 2014 to April 2015 all renal colic were scrutinized and 187 patients met the inclusion criteria. Assessment of these selected patients was done in both IPD and OPD basis.

Incidence of urinary stones was observed in the peak age of 3rd to 5th decade for the age and sex distributions in a group of 119 patients. These observations were confirmed by many others.<sup>[28]</sup>

Similarly in this study, out of 187 the most prevalent age group are 31-60 years of 60% had renal calculi.

The prevalence of kidney stones was 8.8% (95% confidence interval [CI], 8.1–9.5). Among men, the prevalence of stones was 10.6% (95% CI, 9.4–11.9), compared with 7.1% (95% CI, 6.4–7.8) among women [29].

Out of 187 renal calculi, 56% had high serum calcium (> 10.4 mg/dl), and amongst male 57% and amongst females 54% had raised serum calcium, 105 patients who had raised serum calcium 58% had larger calculi. So individual with renal stone has more chance of raised serum calcium level and large calculi.

In 117 patients who had past history of renal calculi 62% had high serum calcium level, these data shows that high level of serum calcium level in recurrent cases of kidney stone; and few study also has similar data of raised calcium level in recurrence of stone disease.

Total of 187 patients 63% had high serum uric acid level (>5.7mg %). There for individual with kidney stone diseases there is more chance of raised serum uric acid level.

Analysis between serum uric acid and gender was significant ( $p=0.01$ ), in 118 raised serum uric acid patients 87(74%) were male and 31(26%) were female and 53% had larger calculi (> 6mm).

In this study among 126 males 71% were alcoholic and analysis between alcoholic and gender was found to be significant ( $p=0.00$ ). Out of 89 alcoholic 72% had history of gout and 74% had high serum uric acid level both had significant ( $p=0.00$ ), ( $p=0.01$ ) value respectively in study.

Study on metabolic risk factors Kidney stones were more common among obese than normal-weight individuals (11.2% [95% CI, 10.0–12.3] compared with 6.1% [95% CI, 4.8–7.4], respectively;  $p < 0.001$ ). Obesity and diabetes were strongly associated with a history of kidney stones in multivariable models.<sup>[29]</sup> And one more study a report from American Journal of Kidney Diseases shows that kidney stones are associated with metabolic syndrome.

In Kerala most of them are non vegetarian (mainly beef) in diet so the intake of animal protein is high with less consumption of leafy vegetable therefore unfortunately less consuming of calcium in diet, and this plays an important role for developing kidney stone in this reason. There are various researcher mentioned in study of 864 cases of kidney stones were documented. After adjustment for potential risk factor, intake of dietary calcium was inversely associated with risk for kidney stones.<sup>[30]</sup>

## CONCLUSION

The present study demonstrates that there has been an increase in the prevalence and incidence of kidney stone in south India and other parts of world. Many aspects of the mechanism of renal stone formation remain unclear at present. Factors like diet and life style plays an important role in the changing epidemiology of kidney stone. Changes in two of most important environmental factors, diet and climate, are the significant impact on these trends. Patients who had raised serum calcium and serum uric acid level had larger and multiple calculi bilaterally. There is strong evidence that diminished fluid and dietary calcium consumption is risk factor and increase in animal protein intake has an equal impact on kidney stone risk. Kidney stone is higher in warm or hot climates, scanty fluid intake and low urine output. Co morbidity in particular Type II Diabetes mellitus may be a major factor in the development of stone. Our review demonstrated that there was a decrease in stone prevalence among older age group. The peak age groups of reoccurrence were 31-60 years and males predominance over females. History of gout and alcohol is an important risk for the development of stone formation. The study suggests that the incidence and prevalence of kidney stone is increasing globally, these increase are seen across age, sex, and race.

### Recommendations

- High fluid intake (>2.5 litre/day) and vegetarian diet are widely agreed recommendation to reduce the recurrence of kidney stone and prolong the average interval for recurrence.
- Recommendations for analgesia during renal colic First choice: start with an NSAID, e.g. diclofenac, ibuprofen.

Second choice: hydro morphine, pentazocine or tramadol.

To reduce the rate of recurrent renal colic by use a-blockers

- In patients newly diagnosed with renal stones < 10 mm, and if active removal is not indicated, observation with periodic evaluation is an optional initial treatment. Such patients may be addressed with appropriate medical therapy to facilitate stone passage during observation.
- Physicians should evaluate the need for urgent intervention and the likelihood for passage of stones, as some small stones do pass spontaneously. Metabolic risk factor for kidney stones should be addressed in recurrences cases, and also in some individual presenting for the 1st time.
- More cohort studies with large population should be done to prevent recurrent kidney stone disease.

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