



RESEARCH ARTICLE



## Cross Sectional Study for Metabolic Evaluation in Pediatric Urolithiasis

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### ABSTRACT

Urolithiasis is a worldwide problem and important kidney disorder which is usually encountered in clinical practice in all age groups. The worldwide prevalence of the disease is changing with pediatric urolithiasis becoming the most incurring problem. Pediatric stone disease differs from adult in various aspects but mainly in etiology and the treatment plan. A fivefold increase in the disease occurrence has been noted in the children in the last decade. Around 7% of all stones occur in children younger than 16 years. Owing to this diversity in etiology there are many different compositions of stones. The most common underlying cause and the least understood is the metabolic derangement owing to the disease. Metabolic abnormality can be primary or secondary due to an underlying disease or pathology; hence it is an important topic of interest. This study was conducted with sole purpose of identifying metabolic derangements in pediatric patients with urolithiasis and to prevent further recurrences.

### ARTICLE HISTORY

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### Keywords

Pediatric; Urolithiasis; Metabolic

### Introduction

Kidney stone disease has now become an increasing concern in pediatric age group as well as the prevalence has been increasing since past two decades. Over the time, the cause behind the stone formation has shifted greatly from urinary infection to metabolic derangements. Hence, many consider urolithiasis more of a symptom than a disease in children. Urolithiasis is estimated to affect 2% of the pediatric population and about five times of increase in incidence of the disease has been noted in children in past decade. And the prevalence of the disease has been higher among males but few studies indicate an equal incidence among both the sexes [1,2]. It is nowadays considered a lifestyle disease as it has more incidence in developed countries where animal protein diet intake is more by the population. The prevalence of urolithiasis is 5%–19.1% in West Asia, Southeast Asia, South Asia, as well as some developed countries (South Korea and Japan), whereas it is only 1%–8% in most part of East Asia and North Asia. In India and Malaysia, the incidence was lower than 40/100000 in 1960s, but three decades later, it grew dramatically to 930/100000 and 442.7/100000, respectively [3]. Due to an observed change in civilization, dietary habits, lifestyle and increased advancement in diagnostic tools and technology an increased surge of cases has been noted in paediatric age group as well. In children, upper urinary tract stones were thought to be usually associated

with urinary tract anomalies and infection rather than with metabolic disturbances, whereas a shift in the epidemiology of paediatric renal stone disease has been observed leading to believe. Underlying metabolic causes are the most common reason, but it can be masked by coexisting urinary tract infection. Also noted, a high recurrence rate in up to 80% of the cases, whereas, unless a prophylactic treatment has been undertaken new stone formation will occur in 30-50% of the cases [4]. It is a multifactorial disease and variety of factors like gender, socio economic status, dietary habits, lifestyle, drug consumption, genetic disorder, metabolic or endocrine disorder, dehydration, chronic illness, urinary tract infections, urinary tract anomalies, lack of treatment affects the anatomical location and type of stone formation.

Family history is also one of the most overlooked causes in development of stone formation. Familial occurrence of urolithiasis is noted in about 40% of the cases [5]. Owing to this diversity in etiology there are many different compositions of stones. The most common underlying cause and the least understood is the metabolic derangement owing to the disease. We hope from this review and study to educate ourselves more on the etio-pathogenesis of the disease and how to prevent recurrence of further stone formation in later age of life as well.

## Materials and Methodology

### Inclusion criteria

A total of 30 patients were included in the study. All radiologically proven cases of Urolithiasis within age 0-15 years and with parents willing to give consent.

### Exclusion criteria

Patients not willing to give consent, those with urinary tract stones due to neurological problems, anatomical abnormalities, surgical co-morbidities. Patients in clinically morbid and septic conditions. Patients who are asymptomatic and urinary tract stone was an incidental finding.

### Methodology

A step-by-step approach was chosen. After well-informed consent from the parents, detailed history about the presenting complaints was taken and proforma was given to the guardians to fill for better analysis. General examination, complete physical examination and basic blood investigations were conducted. 24 hr urine collection was done in a sterile container with aseptic precautions and was sent for analysis and simultaneously patients were categorized according to age groups, clinical features, and distribution of stones. Surgical procedure for patient was decided and stone was sent for analysis. Urine metabolites, serum markers and type of stone were correlated, and records were maintained.

### Blood and urinary parameters

All patients with suspected stone disease underwent detailed workup Biochemical investigations [6,7].

### Complete blood count

Hemoglobin and hematocrit will be deranged if the disease process has severely affected the renal function. Total leucocyte count will be raised in the presence of infection in the body.

### Normal reference value for hemoglobin in children

6 m to 2 years -10.5 to 13.0 g/dL; 2 m to 5 years -11.5 to 13.0 g/dL

5 m to 8 years -11.5 to 14.5 g/dL; 13 m to 18 years -12.0 to 15.2 g/dL

**Table 1.** Urinary volume and solutes analysis.

Metabolite	Age	Random (mg/mg)	24-h
Calcium	6- 12m	< 0.6	<4 mg/kg/d
	>2 years	< 0.21	
Oxalate	2 - 5 years	< 0.08	< 50 mg/1.73 m <sup>2</sup>
	5 - 14 years	< 0.06	
Citrate	Up to 5 y	0.2 - 0.42	180 mg/gm in males >300 mg/gm in females
Uric Acid			250-750 mg/24 hr

### Renal function test

Creatine is a metabolic product of body which gets excreted unchanged via kidney. It helps in evaluating the renal health. Serum creatinine values in 0-1 y: <0.6 mg/dL. 1 y to adults: 0.5-1.5 mg/dL

### Serum calcium levels

New-born: 7.0 to 12.0 mg/dL; 0 to 2 years: 8.8 to 11.2 mg/dL

2 years to adults: 9.0 to 10.0 mg/dL

### Serum sodium levels

Serum sodium levels have an impact on urinary calcium excretion and thus affects incidence of kidney stones. Normal sodium levels range from 136-145 mEq/L.

### Serum uric acid

Hyperuricemia does not necessarily point toward hyperuricosuria but it surely affects the urinary uric acid excretion depending on the etiology behind it.

Normal values in males: 3.0-7.0 mg/dL; Normal values in females: 2.0-6.0 mg/dL

### Urine analysis

Color/ pH/ Specific gravity/ Presence of sugar/ proteins RBCs/WBCs cast, Pus cells, Presence of cast/crystals.

### Urine culture and sensitivity

For presence of UTIs, organism responsible and antibiotics sensitive for the respective organism. Struvite stones are quite common in infected urine especially Proteus infection.

Urinary volume and solutes analysis shown in Table 1

### Statistical analysis

Data will be entered in excel sheet and will be analyzed using SPSS software, appropriate statistical test like ANOVA, chi square, will be applied wherever necessary.

## Discussion and Results

Following results were obtained from cross-sectional study conducted among 30 patients (Tables 2-9).

**Table 2.** Age distribution of patients.

Age group	Number	Percentage
<1 year	1	3.30%
2-5 year	6	20%
5-10 year	17	56.70%
>10 year	6	20%
Total	30	100%

**Table 3.** Sex distribution of patients.

Sex	Number	Percentage
Male	18	60%
Female	12	40%
Total	30	100%

**Table 4.** Dietary habits in patients.

Diet pattern	Number	Percentage
Veg	9	30%
Mixed	21	70%

**Table 5.** Association of stones with family history.

Family history	Type of stones						Total		P-value
	Ca Oxalate	Uric Acid	Mixed	Struvite	Ca P	Cysteine	No.	%	
Yes	6	1	1	0	0	0	8	26.7	0.03
No	7	4	3	2	2	2	22	73.3	0.07
Total	13	5	4	4	2	2	30	100	

**Note:** P: Significant value

**Table 6.** Type of stones.

Type of stones	Number	Percentage
calcium oxalate	13	43.30%
Uric acid	5	16.75%
Mixed	4	13.30%
Struvite	4	13.30%
Calcium phosphate	2	6.70%
Cysteine	2	6.70%

**Table 7.** Association of stone with presenting symptoms.

Symptoms	Ca oxalate	Uric acid	Mixed	Struvite	Ca P	Cysteine	Total		P-value
							No	%	
Pain	7	4	3	4	1	1	20	66.7	0.23
Vomiting	6	2	0	1	0	0	9	30	0.3
Dysuria	7	4	2	1	0	1	15	50	0.1
Frequency	11	2	1	2	2	2	20	66.7	0.03
Haematuria	2	3	0	3	0	1	9	30	0.002
Fever	7	4	1	4	0	0	16	53.3	0.21
Sign of Sepsis	0	1	0	2	0	0	3	10	0.7

**Note:** P: Significant value

**Table 8.** Association of blood parameters with type of stone.

Urine Parameters	Range	Type of Stones						6		p-value, Chi-square Test
		Ca Oxalate	Uric Acid	Mixed	Struvite	Ca P	Cysteine	No.	%ge	
Urinary pH	<6.5	8	5	2	0	0	1	16	53.3	0.01, 12.6
	>7.5	2	0	1	3	2	1	9	30	
Urinary pH	<0.21	3	4	1	1	1	0	10	33.3	0.02, 5.87
	>0.21	10	1	3	3	1	2	20	66.7	
24h Uric Acid (250-750mg/ day)	>750	3	5	0	0	0	0	8	26.7	0.002, 19.4

**Note:** P: Significant value

**Table 9.** Association of urinary metabolites with type of stone.

Urine Parameters	Range	Type of Stones						Total		p-value, Chi-square Test
		Ca Oxalate	Uric Acid	Mixed	Struvite	Ca P	Cysteine	No.	%ge	
SERUM Na+ (mEq/L)	<135	3	1	0	1	0	0	5	16.7	0.04, 3.7
	>145	6	1	3	2	0	1	15	50	
SERUM Ca (mg/dL)	<8.5	7	1	2	3	0	0	14	46.7	6.36, 0.6
	>10.2	4	0	0	0	0	1	4	13.3	
SERUM Uric Acid (mg/dl)	>5.5	3	2	0	1	0	0	2	6.7	0.83, 0.93

**Note:** P: Significant value

### Age and sex distribution

The disease is mainly endemic in low - economic countries mostly the region known as "The Afro- Asian Stone Belt". The prevalence of stone was found to be up to 15% of children less than 15 years of age as when compared to 1-5% in developed countries. The study also suggested major predisposition of the disease among males [3]. Study conducted by Hoppe B, et al. [8] suggested diseases affecting 4% of females and 5.5% of males whereas, In the study conducted by Clayton DB, et al. also concluded that most series have shown 5-15 years of age group as the most prevalent range for pediatric urolithiasis [9]. In the study conducted by Gouru VR, et al. among total of 55 patients, again the incidence of disease was more in boys (41) and the mean age of presentation was 7.8 years the presentation was 14 children below 5 years of age, 26 between 6 to 10 years of age group and 15 children between 11 to 15 years of age group. The findings were kind of like our study [10].

### Dietary habits and family history

In the cross- sectional study conducted by Yousefichaijan P, et al. among 270 children belonging to 2-12-year age group showed higher prevalence among females (55.6%). In their study positive significant dietary association with animal protein intake (p-value 0.0001),

meals water (p-value 0.023), fluid intake (p-value 0.011), meat (p-value 0.0001) were found. On logistic regression, they also found that intake of sodium (p-value 0.0001), methionine (p-value 0.0001), animal protein (p-value 0.0002) and fat (p-value 0.0001) had significant effect on kidney stone formation [11]. Whereas, in the study conducted by Zakaria M, et al. 43 % of the study population had positive family history of stone disease. When they compared the study population with the control group they found, decreased water intake, protein intake (both vegetables and animal source), and sodium intake in the study group [12].

### Clinical features

The study conducted by Bhatt S, et al. among 58 patients with pediatric urolithiasis in Manipal the presentation of disease was more in males (65.5%) with age ranged from 1 year to 12 years (mean age group 6.85 ± 1.27 years). In their study 7 children were asymptomatic and the most common clinical presentation was Urinary tract infection (29.3%) followed by abdominal pain (24%) and least common presentation was urinary retention (2%). Among them, 82.6% patients had renal stones and 12% of them had Ureteric stones and the least common was bilateral staghorn calculi in 8.6% of the cases [13]. In the study conducted by Gouru VR, et al.

among 55 pediatric patients (<15 years of age) 91% of the patients (50/55 cases) presented with abdominal/flank pain whereas, fever and vomiting were present in 44%, 33% of the patients respectively. Dysuria, frequency, and hematuria was seen in 40%, 31%, 51% of patients, respectively. Two patients in their study presented with sepsis [10].

### **Serum chemistries, stone analysis and lithorisk profile (urinary parameters)**

Gouru, et al. in their study series had all the serum chemistries (calcium, phosphate, uric acid) levels normal in all the children. Calcium oxalate stones were most common in their study as well whereas, they had 2 cases of silicate renal stones (which are in itself a very rare variety) and the cause behind it is unknown. They found Hypernatruria as the most common urinary abnormality (65%) followed by Hyperuricosuria in 57.5% of children. Hypercalciuria and Hyperoxaluria was found in nearly 50% of the patients in their study and they had significant positive correlation between hyperuricosuria, hypercalciuria and hyperoxaluria [10]. Gajengi AK, et al. [14] in their prospective and observational study conducted over 4-year time period in KEM hospital, Mumbai found Hypocalcemia as the most common abnormality in the serum in 88% of patients and only 3% of the patient had Hyperuricemia. Gajengi AK, et al. in their study also had 54% of the patients with calcium oxalate stones and least common with cystine stones (4%) like our study and Hypocitraturia as the most common urinary abnormality followed by hypercalciuria (50% and 31%, respectively). In the study conducted by Rizvi SA and Sultan S, et al. conducted over four year period among 2618 patients out of which 2216 patients who presented with normal renal function, had mean Hb of 9.5 g/dl. (In our study, only 6.7% of the patients were anemic rest had normal hemoglobin level). The most common stone in their study was also Calcium oxalate (63%) whereas; most common metabolic abnormality was hypocitraturia (87%) of patients and hyperuricosuria in 26% of the patients [15]. Similar findings were appreciated in Mundkur S, et al. [16] study with Hypocitraturia being the most common abnormality (63.1%) followed by Hypercalciuria (14.8%). Although none of the patients had Hyperuricosuria.

### **Conclusion and Summary**

This study can be summarized as the following

Age distribution of patients stated that majority of the patients i.e., 56.7% belonged to 5-10 years of age group and only 1 patient presented from <1 year of age group. Male predominance was more (60%) than females. Majority of the patients i.e., 70% belonged to mixed dietary habit. Positive significant association found with family

history of disease with p-value 0.03 and was present in 27% of the patients. Most common clinical presentation was flank pain and increased frequency of micturition in 66.7% of patients. Hematuria was most presented in struvite stones whereas, pain and fever were the most common presenting symptom in calcium oxalate stone. Positive significant association was found between Hematuria and frequency of micturition with stone disease (p-value 0.002, 0.03 respectively). 1 patient presented with serum creatinine 2.2 and needed emergency Double J stent placement to salvage the kidney, whereas 3 patients presented with features of sepsis who improved after stone clearance. Serum Sodium levels were elevated in 50% of the patients, and the association was significant with the disease (p-value 0.04). 83.3% patients had deranged urinary pH favoring lithiasis. 67% patients had positive urine culture. Hypercalciuria was the most common urinary abnormality found in 66.7% of the patients and the association was significant with p-value 0.02. Hyperuricosuria was present in 27% of the patients and the association was significant with p-value 0.002.

As the overall incidence of Urolithiasis is increasing, need to better tackle the disease is emerging. Patients who have had at least one documented incidence of stone disease and those with family history of disease, those with recurrent episodes should undergo 24 hour urinalysis and serum chemistries. This testing is considered "standard of care" by many experts. The testing can help us find chemical risk factors responsible for stone disease that can be prevented by dietary modifications, medical therapy. American Urological Association Guidelines recommend 24-hour urine testing even for first time stone formers. The annual visit combined with imaging and urine testing can be advised in follow up of the patients. Better counselling should be done to increase the compliance of therapy after testing and investigations.

**Hypercalciuria:** If hyperparathyroidism is ruled out and serum calcium is normal, patient should be started on moderate increase in dietary calcium. Restriction of calcium should NOT be recommended. Whereas, if calcium intake is good and hypercalciuria persists, try medical therapy with diuretic. Restrict salt intake if hypernatruria is present.

**Hypocitraturia:** Try adding citrus juice in the diet and start patient on potassium citrate supplement as per the recommended dose. Sodium bicarbonate or any urinary antacid can be added if citrate consumption is not possible and urinary Ph needs to be increased. Advise patients to increase daily intake of water (at least >21/day).

**Hyperuricosuria:** Advise patients to cut down on pro-

tein intake especially animal meat and consider using allopurinol for hyperuricemia along with Vitamin B6.

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