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Research Article

Pediatric urolithiasis: What role does metabolic evaluation has to play?

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ABSTRACT

Background Pediatric urolithiasis is a perplexing problem faced by pediatricians as well as urologists across the globe. By early diagnosis and treatment of these risk factors, future stone formation may be prevented. Aim: To evaluate the clinical, biochemical and metabolic characteristics of the patients and the interventions required to prevent recurrence.
Methods: In this retrospective study, cohort of pediatric patients presenting with urolithiasis at Kasturba Medical College, Manipal formed the study population. Patient's records served as study tools. Medical records department was approached and data was collected. Metabolic evaluation was done in all children. Urine tests included urinalysis, urine culture, 24 hours urinary pH, volume, calcium, oxalate, citrate, uric acid, and creatinine. Finally a total of 58 pediatric urolithiasis cases were included in this study.
Results: Mean age of study subjects was 6.85±1.27 years. Top three presentations of pediatric urolithiasis were symptoms of Urinary tract infection (UTI), abdominal pain and flank pain in 29.3%, 24.1% and 17.2% children respectively. Gross hematuria was observed in 15.5% of cases. 82.6% of stones were renal stones. Calcium oxalate stone was most common (50%) variety found. Hyperoxaluria was the most common (79.3%) metabolic abnormality detected. 31% had stone recurrence during follow up and 8 of these had >1 metabolic abnormality. Only 6/28 (21.4%) patients managed conservatively had stone recurrence whereas 12/30 (40%) managed with a procedure had stone recurrence.
Conclusions: Metabolic evaluation for urolithiasis helps us to identify children those at increased risk for recurrent stone disease. Thus metabolic evaluation is a must in all pediatric patients as it helps in segregating patients needing medical therapy.

Keywords: Urinary calculi, Child, Metabolic evaluation, Urological abnormalities

INTRODUCTION

Pediatric urolithiasis is a perplexing problem faced by pediatricians as well as urologists across the globe. Pediatric urolithiasis is a significant medical problem, which has seen an increasing incidence in developing countries.[1] Pediatric urolithiasis are associated with considerable morbidity and commonly associated with metabolic abnormalities.[2] By treating these abnormalities stone formation can be prevented. By early diagnosis and treatment of these risk factors, future stone formation may be prevented.

Genetic inheritance, nutrition, metabolic abnormalities, environmental factors, anatomical characteristics, and calculus- inducing medication are the factors predisposing for urolithiasis in children. Clinical and metabolic patterns of urolithiasis have changed over the

years.[3] As most children with stone disease have an underlying metabolic abnormality, it is necessary that these children should be cautiously evaluated so that the etiology of their disorder can be obtained.[4]

At present there is an evident paucity of literature for metabolic evaluation of renal stones in pediatric population in India. The present study was therefore conducted with an objective to evaluate the clinical, biochemical and metabolic characteristics of the patients and the interventions required to prevent recurrence. An additional objective was to find out association of metabolic abnormality and management modality with recurrence of urinary calculi.

METHODS

The present retrospective study was planned and executed by the Department of Pediatrics in collaboration with Department of Urology, Kasturba Medical College, Manipal. Retrospective cohort of pediatric patients presenting with urolithiasis during 1st January 2007 to 31st December 2013 at this tertiary care health center formed the study population. Only confirmed cases of pediatric urolithiasis were included in this study. Diagnosis of stone disease was confirmed by Ultrasonography and Intravenous pyelography and Computed Tomography in selected cases.

Study tools were records of the patients such as information from Medical Records Department (MRD) and information from Pediatrics and Urology departments. Medical records were reviewed for clinical and laboratory data including gender, age at diagnosis, presence of urinary tract anomalies, and Urinary Tract Infections (UTI) in the form of urinalysis, urine culture and complete blood count. Metabolic evaluation was done in all children. In children with UTI, metabolic evaluation was performed after treatment and only after confirmation of clear urinalysis and culture report they were included in the study. Urine tests included urinalysis, urine culture, 24 hours urinary pH, volume, calcium, oxalate, citrate, uric acid, creatinine. Biochemical investigations included Serum calcium, Serum phosphorus, Serum creatinine, Serum uric acid, Serum electrolytes, Serum Parathyroid hormone and Serum albumin. In case family history of Urinary Calculi was captured in records, trained personnel contacted families to gather the information. Finally a total of 58 pediatric urolithiasis cases were included in this study.

The study adhered to the tenets of the Declaration of Helsinki for research in humans. Permission of Institutional ethics committee (IEC) was sought before the commencement of the study. All the proforma were manually checked and edited for completeness and consistency and were then coded for computer entry. After compilation of collected data, analysis was done using Statistical Package for Social Sciences (SPSS), version 20 (IBM, Chicago, USA). The results were expressed using appropriate statistical methods. The chi-square (χ^2) test or Fisher's exact test was used to compare different groups. A two tailed $p<0.05$ was considered statistically significant.

RESULTS

Out of total studied subjects, there were 20 girls (34.5%) and 38 boys (65.5%) with age ranged from 1 year to 12 years (mean±S.D, 6.85±1.27 years). Seven children (12.1%) were asymptomatic and the urinary calculus was diagnosed when ultrasonography was performed for other reasons. Top three presentations of pediatric urolithiasis were symptoms of Urinary tract infection (UTI), abdominal pain and flank pain in 29.3%, 24.1% and 17.2% children respectively. Gross hematuria was observed in 15.5% of cases (Table 1).

Table 1: Clinical features of urinary calculi among study subjects.

Presentation	Number	Percentage
Symptomatic children		
Urinary tract infection	17	29.3
Abdominal pain	14	24.1
Flank pain	10	17.2
Gross hematuria	9	15.5
Nausea and vomiting	5	8.6
Dysuria	3	5.2
Lower urinary tract symptoms (Difficult voiding)	3	5.2
Frequency	2	3.4
Urinary retention	1	1.7
Asymptomatic children		
Diagnosed by ultrasonography for different reasons	5	8.6
Microscopic hematuria or crystal on urine analysis	2	3.4

Stone analysis revealed that majority (82.6%) of stones were renal stones. Vesicle calculus was least common. On the other hand, Calcium oxalate stone was most common variety found in half of the study participants. Least common variety (3.4%) was cystine type of stones. (Table 2).

Metabolic evaluation was done in all children. Hyperoxaluria was the most common (79.3%) metabolic abnormality detected. 24% had high urinary uric acid levels whereas 25.9% had Hypercalciuria (Table 3).

Twenty-five children had no family history of nephrolithiasis, whereas 33 children had a positive family history. There were no significant differences regarding the types of metabolic abnormalities between the children with and without a positive family history of urinary calculi (Table 4).

Table 2: Types and distribution of urinary calculi among study participants.

Stone analysis- types and distribution	N	%age
Distribution of stone		
Renal	48	82.6
Ureteric	7	12.1
Vesicle calculus	2	3.4
B/L Renal calculi	10	17.2
B/L Staghorn calculi	5	8.6
Types of stone		
Calcium oxalate	29	50
Calcium phosphate	8	13.8
Uric acid	10	17.2
Cystine	2	3.4
Struvite	9	15.6

Table 3: Pattern of urinary metabolic abnormality.

Urinary metabolic abnormality	Number	Percentage
Hypercalciuria	15	25.9
Hyperoxaluria	46	79.3
Hypocitruria	13	22.4
Hyperuricosuria	14	24.1

Table 4: Association of family history of urinary calculi with urinary metabolic abnormality.

Urinary metabolic abnormality	Children with urinary calculi		P value
	Positive family history	Negative family history	
Hypercalciuria	3	2	0.63*
Hyperoxaluria	26	20	0.91**
Hypocitruria	2	1	0.60*
Hyperuricosuria	2	2	0.58*

Chi-square test**, Fisher exact test*

Management of study subjects based on metabolic evaluation

48.3% (n=28) were managed conservatively, 34.5% (n=20) underwent PCNL, 20.7% (n=12) had URS, whereas 2 each had pyelolithtomy and cystolithotomy. Potassium citrate was administered to all the patients, 14 patients with high urinay uric acid levels received allopurinol, 44 patients (75.9%) were on pyridoxine and 10 patients (17.24%) received thiazides.

31% (n=18) had stone recurrence during follow up and 8 of these had more than one metabolic abnormality. Only 6/28 (21.4%) patients managed conservatively had stone recurrence whereas 12/30 (40%) managed with a procedure had stone recurrence. Association of metabolic abnormality and management modality with recurrence of urinary calculi was found statistically insignificant (Table 5).

Table 5: Association of metabolic abnormality and management modality with recurrence of urinary calculi.

Variable	Recurrence		P value*
	Yes	No	
Number of metabolic abnormalities in a single case			
One (n=58, Recurrence rate=17.2%)	10	48	0.29
More than one (n=30, Recurrence rate= 26.6%)	8	22	
Type of management			
Conservative (n=28, Recurrence rate= 21.4%)	6	22	0.12
Surgical (n=30, Recurrence rate= 40%)	12	18	

Chi-square test*

DISCUSSION

Urolithiasis is less common in children than in adults. The incidence in children is generally about 2-3%.[5] However its incidence, composition, location and clinical characteristics vary greatly from one country to another. This wide geographic variation is related to climatic, dietary and socioeconomic factors.

As per literature, the major symptoms of urolithiasis in childhood are abdominal colic and gross hematuria.[6] Similarly, in the current study top three presentations of pediatric urolithiasis were symptoms of Urinary tract infection (UTI), abdominal pain and flank pain in 29.3%, 24.1% and 17.2% children respectively. Gross hematuria was observed in 15.5% of cases. Our findings also revealed that stones could predispose to UTI; conversely, UTI itself may be important in the formation of stones. In children below five years of age, UTI accounts for 62% of urolithiasis.[7]

When urinary infections are the primary cause, it produces calculi composed of struvite (magnesium-ammonium-phosphate) and carbonate apatite. These stones form as a result of the bacterial enzyme urease, which hydrolyzes urinary urea to ammonia and carbon dioxide. This produces an alkaline urinary environment and favors the formation of struvite calculi. Organisms known to produce urease include Proteus, Klebsiella, and Pseudomonas.[8]

In this study it was observed that stone analysis revealed that majority (82.6%) of stones were renal stones. Vesicle calculus was least common. On the other hand, calcium oxalate stone was most common variety found in half of the study participants. Least common variety (3.4%) was cystine type of stones. Hyperoxaluria was the most common (79.3%) metabolic abnormality detected. 24% had high urinary uric acid levels whereas 25.9% had

Hypercalciuria. Thus we can say hyperoxaluria seemed to be the most important metabolic factor of calculus forming in our pediatric series. Erbagci et al., in his series of 95 patients found urinary metabolic abnormality in 90% of patients with hypocitruria most common abnormality.[3] To best of my knowledge, there is no Indian literature on normal reference 24 hour urinary metabolic value. The cause of this contradictory observation may be normal reference 24 hour urinary metabolic value which was taken according to western literature.

We observed that there were no significant differences regarding the types of metabolic abnormalities between the children with and without a positive family history of urinary calculi. Rates of a positive family history in children with urolithiasis were as high as 54% in other studies conducted in Turkey.[3] Rates as high as 78.7% were reported in Argentina, along with comparable numbers (69-78%) in Italy.[5]

In this study, only 6/28 (21.4%) patients managed conservatively had stone recurrence whereas 12/30 (40%) managed with a procedure had stone recurrence. Association of metabolic abnormality and management modality with recurrence of urinary calculi was found statistically insignificant.

When pediatric patients form calculi, they usually do so in recurrent fashion (65% life- long risk of recurrence), and because of potential morbidity of the disease, metabolic evaluation is indicated in all children with urolithiasis.[9,10] Metabolic evaluation can lead to identification of metabolic abnormalities present in patients and help one to establish effective therapy. Type and extent of evaluation depends on the severity and type of calculus, presence and absence of systemic diseases, risk factors of recurrent calculus formation, and family history of nephrolithiasis (considered as a significant risk factor of relapse).[11]

CONCLUSION

The findings of the study highlight the patients having a metabolic abnormality are more likely to have stone recurrence. The metabolic evaluation for urolithiasis helps us to identify children those at increased risk for recurrent stone disease and also to diagnose specific treatable metabolic derangements. Thus metabolic evaluation is a must in all pediatric patients as it helps in segregating patients needing medical therapy.

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