

Pediatric Urolithiasis

An Experience of a Single Center

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Introduction. The aim of this study was to evaluate the clinical features and metabolic and anatomic risk factors of urolithiasis in children.

Materials and Methods. Between 2004 and 2009, a total of 84 children (35 girls and 49 boys) had been treated because of urolithiasis. Clinical presentation, urinary tract infection, calculus localization, family history, presence of anatomic abnormalities, and urinary metabolic risk factors were evaluated, retrospectively.

Results. The children were between 6 months and 16 years of age (mean age, 5.25 ± 3.61 years). The calculus diameter was 3.2 mm to 31 mm (mean, 7.31 ± 4.64 mm). In 90.6% of the cases, the calculus was located only in the kidneys and in 2.4% it was only in the bladder. The most common presentations were urinary tract infection, restlessness, and abdominal pain. A positive family history of urinary calculi was detected in 27.3%; urinary tract infection, in 23.8%; and anatomic abnormality, in 10.7% of the patients. Metabolic evaluation, which was carried out in 78 patients, revealed that 52.6% of them had a metabolic risk factor including normocalcemic hypercalciuria (21.7%), hyperuricosuria (11.5%), cystinuria (3.8%), and hyperoxaluria (5.1%).

Conclusions. We think that urolithiasis remains a serious problem in children in our country. Family history of urolithiasis, urologic abnormalities, especially under the age of 5 years, metabolic disorders, and urinary tract infections tend to be associated with childhood urolithiasis.

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INTRODUCTION

The true incidence of urolithiasis in childhood might be higher than previously observed. Its prevalence has been increasing recently, even in regions not endemic for urinary calculus disease.¹⁻³ This may be due to increased awareness of the entity or to the extension of ultrasonography to routine practice in children presenting specific or nonspecific symptoms for urolithiasis. Approximately, 7% of urinary calculi occur in children younger than 16 years of age.^{4,5} Generally, the incidence of urinary calculi in children is about 2% to 3%.⁶

The wide geographic variations in the incidence of lithiasis in childhood appears related to climatic, dietary, and socioeconomic factors.^{4,5} Predisposing factors for lithiasis in children are genetic inheritance, nutrition, metabolic abnormalities, environmental factors, anatomical characteristics, and calculus-inducing medication. Metabolic and genitourinary anomalies which predispose to urolithiasis often coexist in pediatric patients. Early recognition of the problem and prevention of both calculus formation and its recurrence would be the main goals.^{5,7,8} In this retrospective study,

we evaluated the demographic details, metabolic risk factors, clinical presentation, anatomical abnormality, and family history of 84 children with kidney calculi who were referred to our institution for evaluation.

MATERIALS AND METHODS

We prospectively analyzed 84 consecutive patients with urinary calculi referred to the pediatric nephrology clinic of 17 Shahrivar Hospital between 2004 and 2009. For all patients, calculi greater than 3 millimeters in diameter with posterior shadow were documented through renal ultrasonography and intravenous urography or spiral computed tomography in selected cases. Ultrasonography was performed using 7.5-MHz and 10-MHz probes.

Medical records were reviewed for clinical and laboratory data including gender, age at diagnosis, presence of urinary tract anomalies, and urinary tract infections (UTIs). In children with UTI, metabolic evaluation was performed after treatment. Serum levels of calcium, magnesium, phosphate, creatinine, uric acid, sodium, potassium, chloride, and alkaline phosphatase, together with arterial blood gas measures were collected. In infants and non-toilet-trained patients, a random urine sample had been checked for creatinine, calcium, uric acid, and oxalate levels. In toilet-trained patients, 24-hour urine had been collected for the measurements. Hypercalciuria was documented if the amounts of calcium in the urine exceeded 4 mg/kg per 24 hours. Normal daily values for other urine constituents were defined as values less than 0.5 mmol/0.73 m²/24 h for oxalate, 815 mg/1.73 m²/24 h for uric acid, and 88 mg/1.73 m²/24 h for magnesium. Normal values of the urine random

parameters are summarized in Table 1. Voiding cystourethrography was performed in children with coexisting UTIs in order to determine the presence of vesicoureteral reflux. In patients who had a positive spot test for cystinuria, sodium nitroproside test and urinary amino acid chromatography had been done to confirm cystinuria. Twenty-four-hour urine specimens for oxalate and citrate were obtained in acid medium and in neutral or alkaline media for uric acid.

The SPSS software (Statistical Package for the Social Sciences, version 14.0, SPSS Inc, Chicago, Ill, USA) was used for data entry and analysis. Data were tested for statistical significance using the chi-square test, the Mann-Whitney U test, and the Spearman rho correlation coefficient test, where appropriate. *P* values less than .05 were considered significant.

RESULTS

Our sample consisted of 84 patients with ages ranged from 6 month to 16 years (mean age, 5.25 ± 3.61 years). They were 35 girls (41.6%) and 49 boys (58.4%; *P* = .13). Forty-seven of the children (58.3%) were 5 years old or younger. Sixty-eight of the children (80.9%) had one kidney calculus and 16 (19.1%) had more than one. In those with unilateral urolithiasis, the calculus was located in the left kidney in 27 (35.1%) and in the right kidney in 42 (50.0%; *P* = .24). The mean calculus diameter was 7.31 ± 4.64 mm (range, 3.2 mm to 31.0 mm). Table 2 demonstrates the location of the calculi. There was no significant differences in calculus size between the girls and the boys (*P* = .43). However, a positive correlation between calculus size and patient's age was observed (*P* < .001; Figure).

The main cause of presentation was symptoms of UTI in 20 children (23.8%), and the urinary calculus was diagnosed during imaging studies for UTI follow-up. In addition, in 3 children (3.6%), UTI was diagnosed during laboratory evaluation for urinary calculi. Other symptoms consisted of abdominal pain in 16 (19%), flank pain in 11 (13.0%),

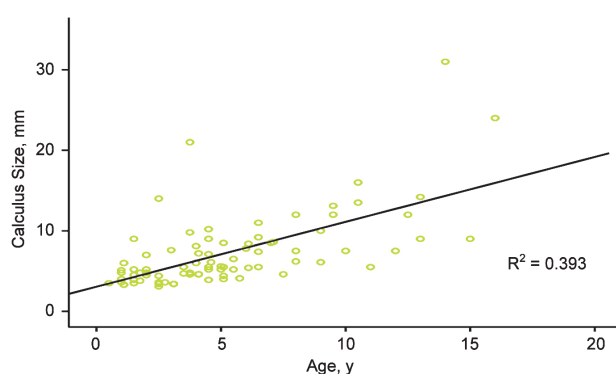
Table 1. Abnormal Values for Random Urine Factors for Children*

Abnormality	Definition
Hypercalciuria	
< 7 months	Calcium/creatinine > 0.8 mg/mg
7 to 12 months	Calcium/creatinine > 0.6 mg/mg
> 1 year	Calcium/creatinine > 0.2 mg/mg
Hyperuricosuria	
Term infant	Uric acid > 3.3 mg/dL GFR
> 3 years	Uric acid > 0.53 mg/dL GFR
Hyperoxaluria	
< 1 year	Oxalate/creatinine > 0.26 mmol/mmol
1 to 5 years	Oxalate/creatinine > 0.12 mmol/mmol

*GFR indicates glomerular filtration rate.

Table 2. Location of Calculi in 84 Children With Urolithiasis

Calculus Location	Number (%)
Kidney	76 (90.6)
Ureters	3 (3.6)
Kidney and ureters	3 (3.6)
Bladder	2 (2.4)



Scatter plot of calculus size according to the patient's age ($r = 0.642$, $P < .001$).

restlessness in 13 (15.4%), gross hematuria in 12 (14.2%), and failure to thrive in 6 (7.1%). Seven children (8.3%) were asymptomatic and the urinary calculus was diagnosed when ultrasonography was performed for other reasons (eg, failure to thrive, lack of appetite, etc). In 3 patients, the calculus was diagnosed after spontaneous calculus passage.

Some patients underwent additional imaging studies to exclude associated anatomical abnormalities. Anatomical malformation was found in 12 children (14.3%) including vesicoureteral reflux in 3, ureteropelvic junction stenosis in 5, bilateral duplex system in 2, horseshoe kidney and ureterovesical junction obstruction each in 1. Twenty-three children (27.4%) had a positive family history, including 6 (26.5%) cases in the parents, 1 (4%) in the siblings, and 16 (69.5%) in close relatives (grandparents, uncles, or aunts).

In 6 patients, urine collection data were not available. In the remaining 78 patients who underwent metabolic evaluation, the underlying metabolic disorders were found in 41 (52.6%). Normocalcemic hypercalciuria accounted for 21.7% of cases who were investigated for metabolic factors. Metabolic evaluation showed that normocalcemic

Table 3. Metabolic investigations in 84 Children with Urolithiasis

Metabolic Disorder	Girls	Boys	Total (%)
Normocalcemic hypercalciuria	5	12	17 (21.7)
Hyperoxaluria	1	3	4 (5.1)
Hyperuricosuria	3	6	9 (11.5)
Cystinuria	0	3	3 (3.8)
Hypocitraturia	3	5	8 (10.2)
Hypercalciuria and hyperuricosuria	2	4	6 (7.7)
All metabolic disorders	12	29	41 (52.5)
No metabolic disorder	12	25	37 (47.4)

Table 4. Urine Parameters in Patients With a Family History of Calculus Versus Those Without a Family History

Urine Parameters	Family History of Calculus		P
	Yes	No	
Hypercalciuria	10	7	.82
Hyperuricosuria	6	3	.88
Hyperoxaluria	3	1	.24
Hypocitraturia	2	6	.43
Cystinuria	2	1	.56
Mixed abnormalities	2	4	.18

hypercalciuria, hyperuricosuria, and hypocitraturia, were the most frequent metabolic risk factors in our patients. Table 3 shows abnormal urinary parameters in the patients. No metabolic risk factors were identified in 37 patients (47.4%). Children with and without a family history of urinary calculi were not significantly different in terms of metabolic disorders (Table 4).

DISCUSSION

Urinary calculi are a considerable childhood problem. Delay in the diagnosis of calculi or inadequate treatment may cause damage to the renal parenchyma and kidney failure by obstruction. Although the true incidence of urolithiasis in Iranian children has not been identified, pediatric urolithiasis seems to be common in Iran.

The mean age of our pediatric patients with urinary calculi was 5.25 ± 3.61 years, and 58.3% of the children were younger than 5 years old. The wide geographic variations in the age distribution appear to be related to climatic, dietary, and socioeconomic factors.⁹⁻¹³ In our study, urolithiasis was detected more commonly in boys, and the male-female ratio was 1.4. Reports of sex preponderance in childhood urolithiasis are various,^{1,10} but in most of literature, pediatric urolithiasis is more common in males (1.2:1 to 4:1).^{1,4,5,9,10,14,15} Urolithiasis in childhood has a different pattern of presentation from that in adults.^{4,5} While nonspecific symptoms such as restlessness and irritability are frequently seen in infancy, loin pain is predominantly in adulthood. In some studies, abdominal disturbance has been reported in up to 50% of children.^{1,16,17}

In this study, UTI, abdominal pain, and flank pain were the most common causes of presentation. The incidence of UTI in children with urolithiasis has been reported to be 8% to 70% in the literature.^{10,17} The rate of UTI in our patients seems to be much

lower than other reported series which have reported UTI in patients with urolithiasis. However, the exact role of UTI in calculus formation is unclear because urinary calculi can predispose the patient to UTI and conversely UTI is a predisposing factor for calculus formation.

In this case series, the location of calculi was comparable to that reported from developed countries, and 90.4% of the calculi were in the upper urinary tract and 2 patients had a primary bladder calculus. Similar to our results, recent studies from other countries have reported much lower rates of lithiasis in the lower urinary tract. During the past two decades, the pattern of calculus disease has changed in many developing countries, and incidence of bladder calculi in children has been decreased. The pattern of calculus disease has changed in many developing countries, such as Turkey, Pakistan, and Kuwait, from a predominantly lower tract site towards the upper tract.^{7,10,12,15,16}

In different studies from other countries, positive familial history of urolithiasis was reported in 11.8% to 21.9% of patients.^{1,5,6,7,9,11,16,18} In our series, 23 children (27.4%) had a positive family history, including. In countries like Iran, in which consanguineous marriages are often seen, it is very important to keep in mind metabolic diseases that may cause nephrolithiasis. It has been reported that about 10% to 19% of children with urolithiasis have underlying malformation of the urinary tract.^{2,3,5,7,11,16,17} We found urological abnormalities in 12 patients (14.3%). However, the true incidence of urological abnormalities such as vesicoureteral reflux might be higher in our patients, because urinary tract imaging studies were not done in all patients.

We found metabolic abnormalities in 42.7% of our patients; the most common etiologic factors of calculus formation were hypercalciuria (21.7%) and hyperuricosuria (11.5%). Cystinuria accounted for 3.8% of nephrolithiasis cases in our patients. Of these patients, 11.5% had hypocitraturia. Serum calcium, phosphorous, and alkaline phosphatase levels were normal in all. Metabolic abnormalities have been reported in 30% to 86% of children with urolithiasis, depending on the location of the studies.^{4,5,17,19} Over the past decades, the etiology of nephrolithiasis in children has shifted from predominantly infectious to metabolic causes. The prevailing abnormality among children with

calcareous calculi is hypercalciuria, accounting for 17% to 50% of those with an identifiable metabolic etiology.^{17,19} Although hypercalciuria is usually idiopathic, it may be secondary to other diseases such as vitamin D3 excess. In this study, only 2 of the children under 2 years of age had a history of high-dose vitamin D3 injection for suspected rickets. Although it is difficult to retrospectively establish the diagnosis of vitamin D3 overdose when plasma calcium has returned to normal range, its possibility should be considered. Recently, the role of vitamin D3 gene receptor polymorphism in pediatric nephrolithiasis has been reported.²⁰

CONCLUSIONS

Hypercalciuria and hyperuricosuria seemed to be the most important metabolic factors of calculus forming in our pediatric series. Also, we proved anatomical urinary abnormality at least in 12 of 84 pediatric patients with nephrolithiasis. It is plausible to consider that better understanding of the causes of pediatric urolithiasis may lead to earlier diagnosis and appropriate treatment of the metabolic diseases, and hence, prevention of renal damage and recurrences may be possible. In conclusion, urolithiasis should be suspected in young infants presenting with UTI and toddlers presenting with hematuria. In addition, atypical urinary symptoms may indicate urinary calculi in areas where they are endemic, so that a high index of suspicion is important for diagnosis.

CONFLICT OF INTEREST

None declared.

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