Original Article

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Clinical Features and Risk Factors of Pediatric Urolithiasis

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Abstract

Objective: Urolithiasis in children although occurring less often than adults, causes considerable morbidity. The main aim of this study is to evaluate clinical features and risk factors of pediatric urolithiasis.

Material & Methods: All children with documented urolithiasis who were referred to department of pediatric nephrology between 1999 and 2005, were evaluated from the point of demographic features, family history, clinical symptoms, imaging results and laboratory findings.

Findings: We investigated 184 patients (100 females and 84 males) with urolithiasis between 2 months and 14 years of age (mean age 3.66±3.49 years). The stones' diameter was 3-27 mm (mean 8.20±5.36). In 85.8% of cases the stone was located only in kidneys and in 3.3% only in bladder. The most common causes of presentation were urinary tract infection (UTI), restlessness and gross hematuria. Positive family history was detected in 41%, UTI in 40.8%, anatomic abnormality in 13% and sterile pyuria in 18.5% of patients. Metabolic evaluation, which was carried out in 162 patients, revealed that 104 (64%) of them had a metabolic risk factor including normocalcemic hypercalciuria (42%), Hyperuricosuria (10.5%), Cystinuria (7.4%), and Hyperoxaluria (4.3%).

Conclusion: All children with urolithiasis should be completely evaluated, as most of them have an anatomic, infectious or metabolic risk factor.

Key Words: Urolithiasis, Children, Hypercalciuria, Risk factor, Hyperuricosuria

Introduction

Urinary lithiasis in children is less common than in adults and approximately 7% of urolithiasis occurs in children younger than 16 yrs of age[1]. Generally the incidence of stone disease in children is about 2-3%[2]. However its incidence, composition, location and clinical characteristics vary

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greatly from one country to another and from one historic period to the next. This wide geographic and historic variation is related to climatic, dietary and socio-economic factors. Urolithiasis in childhood accompanies with considerable morbidity such as urinary tract infection (UTI), obstruction, scarred kidney, hypertension and progressive deterioration of renal function.

All children with stone must be screened for infectious, anatomic and metabolic risk factors which significantly differ in children and adults[3]. By early diagnosis and treatment of these risk factors, future stone formation may be prevented. The aim of this study is to evaluate the demographic features, clinical presentations and risk factors of urolithiasis in children who were referred to our institution and compare them with literature.

Material & Methods

In this cross-sectional study 184 children with urolithiasis were evaluated between October 1999 and September 2005 in department of pediatric nephrology. Diagnosis of urolithiasis was confirmed by two different sonographists. In all patients demographic and clinical features, family history, size and location of stone, history of vitamin D_3 injection, results of imaging and laboratory findings were recorded. Biochemical investigations included: serum calcium, phosphorus, alkaline phosphatase, creatinine, uric acid, electrolyte levels, together with blood pH and HCO_3. Urine tests included urinalysis, urine culture, and urinary calcium, creatinine, oxalate and uric acid excretion in 24 hrs, and spot test for cystinuria. Urine samples for calcium and oxalate were acidified, and samples for urate measurement alkalized. All samples were obtained from patients without dietary and activity restrictions. In patients who had positive spot test, chromatography of urinary amino acids or stone analysis was done to confirm cystinuria. Sonography was performed in all patients to detect the size and location of stones and possible anatomic malformations. Intravenous urography, voiding cystourethrography and renal scintigraphy were performed in selected cases.

Patients who had nephrocalcinosis without stone, those whose stone diameter was less than 3 millimeter and patients with inadequate data were excluded. Normal values for urine constituents were defined as less than 4 mg/kg for calcium, less than 0.57 mg/kg for oxalate, and less than 10.7 mg/kg for uric acid[1]. SPSS software was used for data analysis.

Findings

Data from 184 patients (100 girls and 84 boys) with documented urolithiasis were evaluated. There was no significant difference between male and female frequency ($p>0.05$). The mean age at first presentation was 3.66 ± 3.49 years (range 2 months-14 years). One-hundred ten patients (59.8%) were under 2 years of age. Bilateral kidney stones were found in 85 patients (46%). In those with unilateral urolithiasis, the stone was located in 48 (26%) patients on the left and in 39 (21%) patients on the right side, without significant difference

Table 1: Location of stones in 184 children with urolithiasis at first presentation

Location of stones	Number (%)
Kidneys	158 (85.8)
Kidney and ureter	14 (7.6)
Ureter	6 (3.3)
Bladder	6 (3.3)
Total	184 (100)

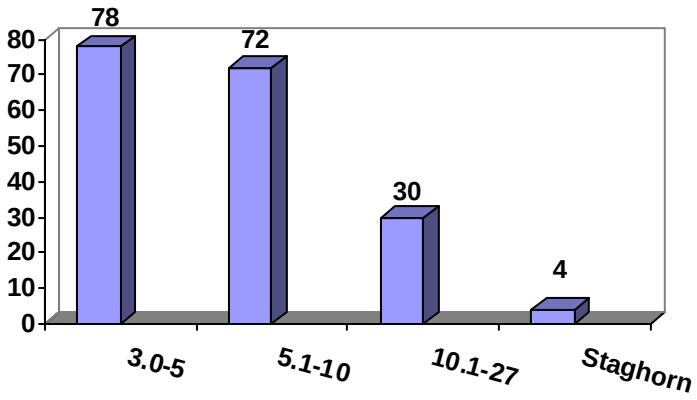

Fig 1: Distribution of stone's size (in millimeter) in 184 patients with urolithiasis.

(p>0.05). Table 1 demonstrates the location of stones. The stones' diameter was 3-27 mm (mean 8.20±5.36) (Fig. 1).

The main causes of presentation were symptoms of UTI in 46 (25%), nonspecific symptoms such as irritability and restlessness in 44 (24%), gross hematuria in 38 (20.6%), abdominal or flank pain in 28 (15.2%), and passage of stone in urine in 14 (7.6%) patients. family history of urolithiasis in the first or second degree members of family. Anatomical malformation was found in 21 children (13%) including vesicoureteral reflux in 11, uretero-pelvic junction stenosis in 6, and ectopic kidney with hydronephrosis in 2 cases. Duplex collecting system and ureterocele was encountered each in 1 case. At least one episode of UTI was detected in 75 (40.8%) patients and 34 (18.5%) cases had sterile In 10 patients (5.4%) stone was found incidentally in sonography performed for control of prenatal hydronephrosis. Four patients (2.1%) presented with anuria and renal failure due to obstruction (two of them had cystinuria and the other two had hyperurico-suria as underlying risk factor).

Evaluation for possible predisposing factors revealed that 76 (41%) patients had positive pyuria. Sixty nine patients (37.5%) had history of vitamin D_3 injection in a dose of 300.000–900.000 IU for suspected rickets and 66 of them were under 2 years old. Metabolic investigation was completed in 162 patients and metabolic risk factor detected in 104 cases (64%). Normocalcemic hypercalciuria accounted for 42% of 162 cases who were investigated for metabolic factors and 65% of identified metabolic factors (table 2).

Table 2: Results of metabolic investigation in 162 children with urolithiasis

Findings	Number	Percentage
Normocalcemic Hypercalciuria	68	42
Hyperuricosuria	17	10.5
Cystinuria	12	7.4
Hyperoxaluria	7	4.3
Normal	58	36
Total	162	100

Discussion

Incidence of bladder stones in children has been decreased in recent decades in most countries. In Pakistan the pattern of calculous disease changed from 60% in lower tract site in the mid 1980s to 15% in the mid 1990s[4]. The main factor that leads to the formation of bladder stone is a nutritionally poor diet low in animal protein, calcium and phosphate and high in cereal[5]. As nutrition improves indeveloping countries, bladder stones give way to upper urinary tract stones. In this study the majority of patients had upper urinary tract stones, which resembles that of developed countries.

Clinical symptoms of urolithiasis in children may be nonspecific and misleading. Renal colic is uncommon in younger age[6]. In some studies hematuria has been reported as main cause of presentation[7,8]. In a study performed in Croatia, most children less than 5 yrs old presented with UTI, and most patients more than 5 yrs presented with abdominal pain and hematuria[9]. In this study UTI and restlessness, were the most common causes of presentation, probably due to the lower mean age of our cases (3.66 yrs) comparing with mean age of 7-10 yrs reported in most literature[2,9,10,11].

Regarding the predisposing factors for stone formation, anatomic abnormalities were detected in 13% and UTI in 40.8% of our patients. However, the exact role of UTI in stone formation is unclear in our patients, because stone can predispose the patient for UTI and conversely UTI is a predisposing factor for stone formation. In the later situation the stone composition is a combination of magnesium, ammonium and phosphate (struvite). In a study in Tunisia, based on stone composition, UTI was involved in the nucleation or growth of a third of calculi[12].

Metabolic evaluation showed that normo-calcemic hypercalciuria, hyperuricosuria and cystinuria, in respective order were the most frequent metabolic risk factors in our patients. Uric acid stones comprise less than 5% of all lithiasis in children in America[1], but are more common in less developed areas of the world[13,14]. Cystinuria which accounts for 7.4% of our patients is a rare autosomal recessive disorder of the renal tubular amino acid transporter. Its role in kidney stones in children has been reported from 1%-12.9%[1,15,16,17]. Cystinuria often results in large rounded stones and may cause obstruction and anuria as occurred in two of our patients.

In most literature from western developed countries hypercalciuria is the most common metabolic risk factor[1,10,11] and accounts for 30%-50% of identified metabolic factors[6]. In this study hypercalciuria accounts for 65% of identified metabolic factors. Although hyper-calciuria is usually idiopathic, it may be secondary to other diseases such as vitamin D_3 excess. In this study 60% of cases were under 2 years of age and 60% of them had history of high dose vitamin D_3 injection for suspected rickets (without documented rickets).Although it is difficult to establish the diagnosis of vitamin D_3 overdose retrospectively when plasma calcium has returned to normal range, but its possibility should be considered. Recently the role of vitamin D_3 gene receptor polymorphism in pediatric nephrolithiasis has been reported[18,19]. The higher frequency of hypercalciuria in this study and the lower mean age of our patients in comparison with other studies, arises a question about the role of vitamin D_3 excess in our patients. These findings necessitate a prospective controlled study to evaluate the impression of high dose vitamin D_3 injection in urolithiasis of children in our area.

Conclusion

Pediatric urolithiasis is a serious problem in our area with early onset of presentation. Stone location and its metabolic risk factors are similar to those in developed countries except the higher frequency of hypercalciuria. All children with urolithiasis should be completely investigated because most of them have a metabolic, infectious or anatomic risk factor and some patients may have multiple risk factors.

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