Kidney stones in Albanian children

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Abstract

Urolithiasis is already one of the oldest, even in pediatric patients. The occurrence of kidney stones is estimated to be 1:20.000 children/year. The medium age of onset is between 5-7 years. Our study aimed to see the characteristic features, predisposing factors, and therapeutic procedures for Kidney stones in children, as well as metabolic abnormalities, especially hypercalciuria. In a retrospective study, we involved 216 patients (46% of them with a family history of kidney stones) in 8 years (from 2010-2018). All patients underwent abdominal ultrasonography and laboratory examination. Male/female ratio was 2.17:1. Diagnostic medium age was 6.44 years. The most frequent symptoms were: back pain at 33.3%, abdominal pain at 19.4%, gross hematuria at 19.4%, microhematuria at 14%, urinary retention at 9.7%, dysuria at 8.3%, vomiting at 11.1%, growth retardation in 4.2%, hypertension in 1.4%, the spontaneous passage of renal calculi in 5.5%. 4.2% of patients were asymptomatic. We found infectious stones in 47.2% of cases. The chemical composition of the stone was studied only in 51% of cases, from which 56% appeared to be calcium oxalate and phosphate stones. We found metabolic abnormalities in 50% of patients. Urolithiasis is a common disease among Albanian children. 50% of patients had metabolic disorders. Calcium-oxalate and calcium-phosphate represent the most frequent types of calculi. Hypercalciuria is the most essential metabolic disorder. Hypocitraturia is the risk factor for calcium urolithiasis. We recommend estimating every child with a stone for metabolic screening.

Keywords: Abdominal ultrasonography, Gross hematuria, Kidney stones, Metabolic disorders

Introduction

Urolithiasis is already one of the oldest diseases, even in pediatric patients. More information about etiology and prevention has only been achieved in the past century [1].

Kidney stones occurs as a result of the interaction of a complex of events and particular factors (urinary saturation of electrolytes, volume, urinary pH, etc.) inducing the formation of crystals and their crescent into the urinary tract in the collector system (Urolithiasis) and parenchyma (nephrocalcinosis) [2]. Our study aimed to see the characteristic features, predisposing factors, and therapeutic procedures for kidney stones in children and to evaluate metabolic abnormalities, especially hypercalciuria, in children with kidney stones in our center during the last eight years (2007-2015).

Subjects and Methods

We included two hundred and sixteen patients with Urolithiasis in the study. This study was retrospective, and we evaluated all children who presented renal calculi during this period (2007-2015).

It evaluated the patients' age at the moment of onset of disease, sex, history, objective examination, laboratory data, clinical signs, metabolic screening, radiological examination, concomitant pathologies, and treatment.

We excluded the patients with an initial diagnosis of urinary stones made after 14 years of age and those with inadequate details

We evaluated the family history of all children. Clinical signs at the moment of presentation, associated pathologies, and treatment approaches were studied. We documented the diagnosis of kidney stones by renal ultrasonography in all patients, but direct abdominal X-ray and intravenous pyelography were performed only in selected cases.

Metabolic screening includes:

Blood: urea, creatinine, potassium, sodium, chloride, calcium, phosphate, uric acid, TCO2 (or bicarbonate), albumin, PTH.

Urine: urine stick, urine culture, pH, calcium, phosphorus, oxalate, urate, citrate, magnesium, ammonium, cystine, and creatinine. These substances were evaluated in the second-morning urine for three consecutive times for all patients.

Table 1: Normal value (95 percentile) for urinary phosphate, calcium, magnesium, urate, and oxalate excretion (solute/creatinine) in children

Age (years)	U P/Cr 95% (mmol/mmol)	U Ca/Cr 95% (mmol/mmol)	UMg/Cr 95% (mmol/mmol)	UUra/Cr 95% (mmol/mmol)	U Ox/Cr 95% (mmol/mmol)
1/12-1	19.0	2.2	2.2	1.6	0.17
1-2	14.0	1.5	1.7	1.4	0.13

2-3	12.0	1.4	1.6	1.3	0.10
3-5	8.0	1.1	1.3	1.1	0.08
5-7	5.0	0.8	1.0	0.8	0.07
7-10	3.6	0.7	0.9	0.56	0.06
10-14	3.2	0.7	0.7	0.44	0.06
14-17	2.7	0.7	0.6	0.40	0.06

UP/Cr – urinary phosphate/creatinine ratio; UCa/Cr – urinary calcium/creatinine ratio; UMg/Cr – urinary magnesium/creatinine ratio; UUra/Cr – urinary urate/creatinine ratio; UOx/Cr – urinary oxalate/creatinine ratio.

We measured cystine and other amino acids in 24-hour urine collection.

We evaluated cystine using the Nitroprusside test (Brandt's reaction).

The chemical composition of the stone was studied using the infrared spectroscopy method.

We considered the etiology of the stone infectious if the patient presents a urinary tract infection (UTI) and excluded metabolic disorders

We considered kidney stones idiopathic when we excluded UTIs, metabolic disorders, and anatomic abnormalities.

Results

Two hundred and sixteen patients with kidney stones were included, with a follow-up period of eight years; the patients were admitted to the hospital or followed in an ambulatory clinic. Two hundred sixteen, 148 male (68.5%) and 68 female (31.5%); rate M: F = 2.17:1.

The age of patients is in the range of 6 months to 14 years; the average is 6.44 years. Male patients range from 6 months to 14 years, averaging 6,86 years. Females range from 7 months to 14 years, averaging 6.12 years.

A positive family history of renal stones appeared in 99 (45.8%) patients: 24 patients had a positive history only from their parents, 21 patients from parents and grandparents, and 54 patients from grandparents and first-degree relatives.

Flank pain represents the first symptom of renal calculi in 72 (33.3%) patients and is the most frequent sign at admission. Twenty-one patients had left flank pain, 24 had right flank pain, and 27 had bilateral flank pain. Other 42 (19.44%) patients presented abdominal pain. The second sign is gross hematuria, appearing in 42 (19.44%) patients. The classic combination of renal flank pain and gross hematuria is determined only in 18 (8.33%) patients. Seventy-two (33.3%) patients have more

than one sign at diagnosis. Only nine patients had no symptoms at diagnosis (Table 2).

Table 2: Clinical symptoms at the moment of diagnosis.

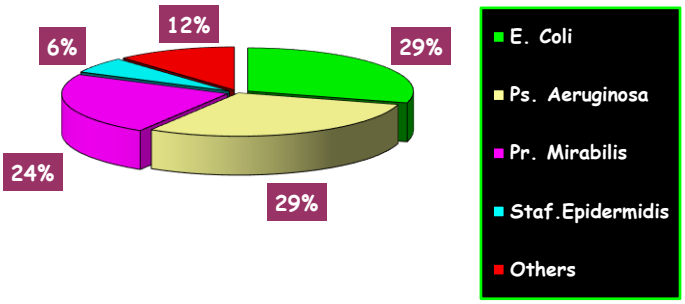
Signs and symptoms	Number of pts	%
Pain		
flank	72	33.3
abdominal	42	19.4
Gross hematuria	42	19.4
Microscopic hematuria	3	1.4
Urinary retention	21	9.7
Dysuria	18	8.3
Nausea and vomiting	24	11.1
Failure to thrive	9	4.2
Hypertension	3	1.4
Spontaneous passage	12	5.5
No symptoms	9	4.2

Infective stones were present in 102 (47.2%) patients (M: F=3,25:1).

The most infecting organisms were Escherichia Coli and Pseudomonas Aureginosa. (Figure 1)

The median age of children with infective calculi was three years.

Figure 1: Distribution of organisms



The most important examination is the abdominal ultrasonography (U.S.). One hundred and eight three (84.7%) patients were diagnosed with abdominal U.S. Abdominal X-ray and intravenous pyelography made the diagnoses in 18 patients. We made the diagnosis of only three patients by voiding cystography. In 12 patients, the calculi passed spontaneously.

One hundred and thirty-five patients had stones only in the kidneys (Figure 2).

We have analyzed 111 renal calculi (Figure 3).

Associated abnormalities were verified in 45 (20.8%) patients (Table 3).

We confirmed metabolic disorders in 108 (50%) patients. 33 (30.5%) of them presented hypercalciuria, 8 (7.4%) hyperoxaluria, 7 of them primary hyperoxaluria (type 1), and one secondary enteric hyperoxaluria to the short intestine pathology, 4 (3,7%) increased acid uric excretion, 40 (37%) hypocitraturia, 5 (4.6%) cystinuria.

In 13 patients, we associated hypercalciuria with hypocitraturia. Twelve patients with hypercalciuria have a positive family history of kidney stones. The median age of patients with metabolic disorders is 7.1 years. Ratio M: F = 2 :1.

In this group, 76 (70%) patients had bilateral renal calculi.

We performed ESWL (lithotripsy) in 38 patients. We performed open surgeryon 54 patients, the majority of them with associated malformations. We performed conservative treatment in 91 patients, and 26 had spontaneous calculi passage.

Table 3: Associated abnormalities

Associated abnormalities	**Number of patients**
Vesico-ureteric reflux (VUR)	9
Pelvic-ureteric junction obstruction	6
Duplication of the collecting system	6
Posterior urethral valves	3
Obstructed megaureter	3
Bladder exstrophy	3
Ureterocele	3
Short intestine	3
Neuropathic bladder + VUR	3
Neuropathic bladder + Arnold-Chiari syndrome	3
VUR + Ureterocele + celiac disease	3

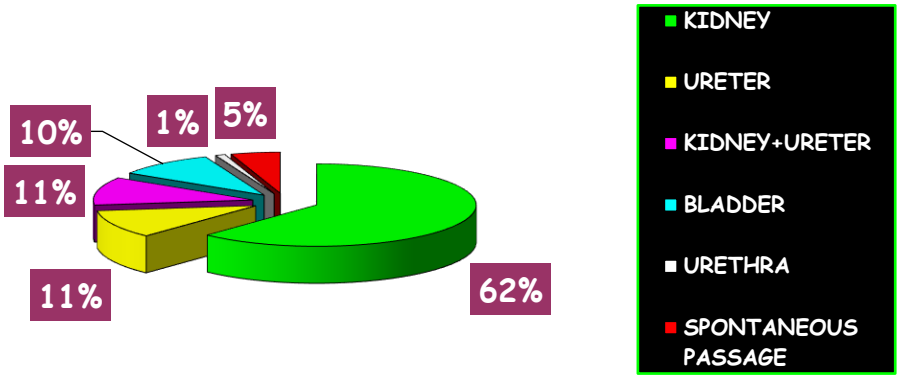


Figure 2: Stone distributions in the urinary system

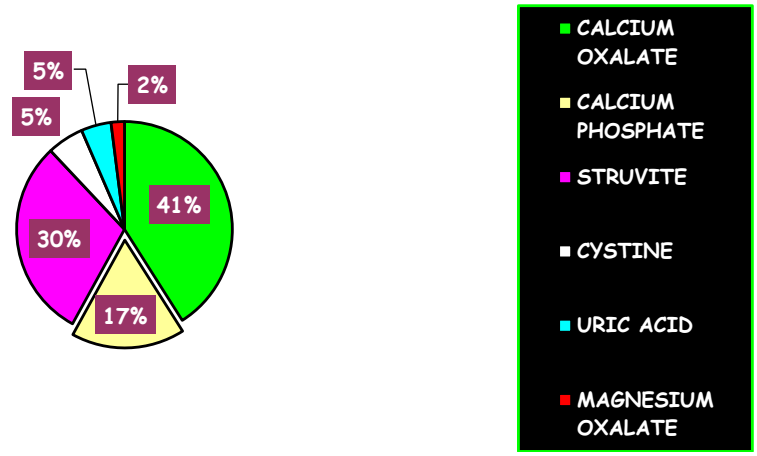


Figure 3: Stone composition

Discussion

We underestimated Urolithiasis in children because literature data consider the children admitted to the hospital. Many children have only ambulatory visits; others have a spontaneous passage of calculi; we did not identify the disease in some children, so they are not part of the statistics. However, urolithiasis prevalence in children is estimated at 1 case in 20 000 children/year [3].

Children represent about 1% of all patients with Urolithiasis. However, we considered 100% of these children with a high risk for recurrent stone formation, and they must receive therapy that will render them stone-free [4].

This pathology was identified in more than 1% of pediatric autopsies [5].

Data from studies in the United Kingdom shows 1-2 children per 1 million inhabitants per year [6].

The study of two hospitals in India evidence 600 new cases of kidney stones in children in 2 years; 60% of them had bladder calculi [7].

In contrast with the above study, an essential center in the United States found five new cases of Urolithiasis in children in 1 year; this center followed children over 20 years [8].

The data from 5 centers in the USA show that the incidence for all types of urolithiasis in children ranges from 1:3000 to 1:7500 admissions [8]. However, children with stones now report 1 in 685 pediatric hospitalizations in the United States; the majority are younger than 13 years at hospitalization [9-10].

We concluded from the data of the above studies that we do not admit all children with urolithiasis to the hospital; this influences the estimation of the frequency of this disease.

We included 180 children from the hospital and 36 others as outpatients in our study.

Literature states that pathology is more frequent in males; the ratio M: F = 2:1 to 3:1 corresponds to the type of stone [11,12,13] but not in all studies [14].

In our study, the ratio M: F is 2,17:1. The median age at diagnosis is 5-7 years [15].

Our data show an average of 6.44 years. The patient's age ranges from 6 months - 14 years.

A significant reduction in complex incidence of kidney stones primarily related to the absence of endemic calculi, is observed in developed countries [16].

This type of calculi, composed of uric acid and ammonium-urate, is determined especially in the bladder in the habitants of Turkey, the Eastern countries, especially in Thailand, by an alimentary regime characterized by a high consumption of vegetal proteins (cereal, rice). These types of stones were common in the United Kingdom [17], mostly in rural areas, but diminished in the last century, probably as a consequence of improvement in nutrition standards [18]; the same is confirmed for Turkey [19].

The data of our study showed that only 21 (9.72%) patients presented bladder stones.

In a study performed in Italy, in 432 children with kidney stones, a positive family history was reported in 33% of cases [20]. Positive family history in the U.K. study is 16% in first-degree relatives and up to 33% in first and second-degree relatives [21]. Very often, there is a positive family history of renal stone disease in first- and second-degree relatives [22].

45.83% of cases in our study comprised a positive family history of kidney stones.

The standard of calcium excretion in urine in healthy children is challenging because there is a large diversity among nations, as well as a consequence of diet or vitamin D prescription. Most literature considers the level of 4 mg/kg/die equal to 0.1 mmol/kg/die as a high limit of urinary calcium excretion. Evaluating the urinary excretion ratio of calcium/creatinine in the second voided urine in the morning is considered a valid screening method. We note a large diversity among different countries (Table 4).

Table 4: Reference values for molar ratios of urinary calcium and creatinine in children according to different authors

AGE	Matos 1996	Metropolitan Kansas City USA 2001	New Hampshire USA 2001	Stapleton USA 1987	Barratt 1999 U.K.
0–6 months	2.2	1.92	2.36	2.24	0.74
7–12months	2.2	1.37	1.65	1.68	0.74
12–18 months	1.5	1.37	1.65	-	0.74
18–24 months	1.5	0.77	1.15	-	0.74
2 – 3 years	1.4	0.77	1.15	0.56	0.74
3 – 5 years	1.1	0.77	1.15	0.56	0.74
5 – 6 years	0.8	0.77	1.15	0.56	0.74
6 – 7 years	0.8	0.55	0.6	0.56	0.74
7 – 10 years	0.7	0.55	0.6	0.56	0.74
10–14 years	0.7	0.55	0.6	0.56	0.74
14–17 years	0.7	0.55	0.6	0.56	0.74

We identified 108 (50%) patients with metabolic disorders. We identified the combination of hypercalciuria and hypocitraturia in 13 patients. We found specific urine metabolic risk factors in most children with kidney stones, and hypocitraturia is as frequent as hypercalciuria [23-25].

Clinical signs of Urolithiasis in pediatric age are huge: completely asymptomatic forms (initial nephrocalcinosis, micro-urolithiasis, spontaneous passage of calculi);

forms with essential clinical symptoms characterized by typical flank pain, especially in adolescents, recurrent UTI, urinary retention, and acute renal failure [26,27,28]. Generally, clinical manifestations do not correlate with the calculi type. The renal papilla holds most stones except struvite. During the period of stone formation or crystalluria, there must be different clinical signs of irritation of the epithelium of the urinary tract: gross hematuria and micro-hematuria, pollachiuria, dysuria, bladder contractions, incontinence, abdominal pain, and recurrent urinary tract infections [29-32].

Microhematuria and idiopathic hypercalciuria lead to Urolithiasis in children [33].

In our study, half the cases showed pain and gross hematuria, but the others presented different symptoms, and some showed no signs. Abdominal ultrasonography is a golden standard examination for urolithiasis diagnosis.

Treatment has progressed; minimally invasive treatments (ESWL, percutaneous nephrolithotomy, and endoscopy) are now employed [34], but still, in Tunisia [35] and Albania, many patients underwent open surgery.

Conclusion

Urolithiasis is a common disease among Albanian children. Nowadays, infectious calculi are common, although they are becoming less common. A positive family history of kidney stones is confirmed. Calcium-oxalate and calcium-phosphate represent the most frequent types of calculi. 50% of patients had metabolic disorders. Hypercalciuria is the most critical metabolic disorder. Hypocitraturia is the risk factor for calcium urolithiasis. Metabolic disorders can be masked by coexisting urinary tract infections. Children with kidney stones do not always present classical symptoms: pain and gross hematuria. We may treat it with mini-invasive techniques. We recommend estimating every child with a stone for a metabolic evaluation to start as soon as possible and to perform screening of brothers if necessary.

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