International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2013): 6.14 | Impact Factor (2014): 5.611

Urolithiasis in Children – Albanian Experience

Diamant SHTIZA[1], Enkelejda SHKURTI[2], Edmond PISTULLI[3], Maksim BASHO[4], Spiro SILA[5], Sokol BUBA[6]

[1]Department of Pediatrics, Nephrology and Dialysis Unit, University Hospital Centre "Mother Tereza" of Tirana

[2, 3]Department of Public Health, Lecturer of Statistics, Faculty of Nursing, Tirana University

[4]Department of Imaging, Pediatric Service, University Hospital Centre "Mother Tereza" of Tirana[4]

[5]Department of Anesthesiology, Infantile Surgery Unit, University Hospital Centre "Mother Tereza" of Tirana[5]

[6]Department of Pediatrics, Infantile Surgery Unit, University Hospital Centre "Mother Tereza" of Tirana[6]

Abstract: ***Background: Urolithiasis is already one of the oldest diseases even in pediatric patients. The prevalence of kidney stones is estimated to be 1:20.000 children/year. The medium age of onset is between 5-7 years. The aim of our study was to see the characteristic features, predisposing factors and therapeutic procedures for urolithiasis in children, as well as metabolic abnormalities especially hypercalciuria. Methods: In a retrospective study we involved 216 patients (46% of them with family history for kidney stones) in an 8 year period (study period from 2007 till 2015). All patients underwent abdominal ultrasonography and laboratory examination. Results: Male/female ratio was 2.17:1. Diagnostic medium age was 6.44 years. The most frequent symptoms were: back pain in 33.3%, abdominal pain in 19.4%, gross hematuria in 19.4%, microhematuria in 14%, urinary retention in 9.7%, dysuria in 8.3%, vomiting in 11.1%, growth retardation in 4.2%, hypertension in 1.4%, spontaneous passage of renal calculi in 5.5%. 4.2% of patients were asymptomatic. Infectious stone was found 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. Metabolic abnormalities were found in 50% of patients. Conclusions: Urolithiasis is common disease among Albanian children. 50% of patients had metabolic disorders. Calcium-oxalate and calcium-phosphate represents the most frequent types of calculi. Hypercalciuria is the most important metabolic disorder. Hypocitraturia is the risk factor to calcium urolithiasis. We recommend that every child with stone must be estimated for a metabolic screening.***

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

1. Introduction

Urolithiasis is already one of the oldest diseases even in pediatric patients. An apparent endemic bladder stone was found in the grave of a 16-year-old-Egyptian boy, after 6000 years [1].

Since the 4th century B.C. Hippocrates described kidney stones as "bad of stone". But, more information about etiology and prevention was achieved only in the past century [2].

Urolithiasis is occurs as a result of interaction of a complex of events and particular factors (urinary saturation of electrolytes, volume, urinary pH, etc.) inducing formation of crystals and their crescent into urinary tract, in the collector system (urolithiasis) and/or parenchyma (nephrocalcinosis) [2]. The aim of our study was to see the characteristic features, predisposing factors and therapeutic procedures for urolithiasis in children and to evaluate metabolic abnormalities especially hypercalciuria in children with kidney stones, in our centre during the last 8 years (2007-2015).

2. Subjects and Methods

Two hundred and sixteen patients with urolithiasis were included in the study. This study was retrospective and we evaluated all children who presented renal calculi during this period (study 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, as well as concomitant pathologies and treatment.

The patients who had initial diagnosis of urinary stone made after 14 years of age and those with inadequate details were excluded.

Family history is evaluated in all children.

Clinical signs at the moment of presentation, associated pathologies and treatment approach were studied.

Diagnosis of urolithiasis was documented by renal ultrasonography in all patients, but direct abdominal X-ray and intravenous pyelography was 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. The used references were suggested by Matos et al (Table 1) [30].

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.

Cystine and others amino acids were measured in 24 hour urine collection.

Cystine is evaluated by Nitroprusside test-Brandt's reaction).

Stone chemical composition was studied by infrared spectroscopy method.

Etiology of stone is considered infective, if the patient presents urinary tract infection (UTI) and metabolic disorders are excluded.

The kidney stone is considered as idiopathic in cases where the UTI, metabolic disorders and anatomic abnormalities are excluded.

3. Results

Two hundred and sixteen patients with urolithiasis were included, follow-up period 8 years; the patients were admitted in hospital or followed in 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; average is 6.44 years. Male patients have a range of 6 months to 14 years with an average of 6,86 years. Females have a range of 7 months to 14 years with average of 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; 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 the moment of admission. Twenty one patients had left flank pain, 24 had right flank pain and 27 bilateral flank pain. Others 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 the moment of diagnosis. Only 9 patients did not have any symptom at the moment of 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)
Medium age of children with infective calculi was 3 years.

The most important examination is the abdominal ultrasonography (US). One hundred and eight three (84.7%) patients were diagnosed by abdominal US. Abdominal X-ray and intravenous pyelography made the diagnoses in 18 patients. Only in 3 patients the diagnoses was occasionally made by voiding cystography. In 12 patients the calculi passed spontaneously.

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

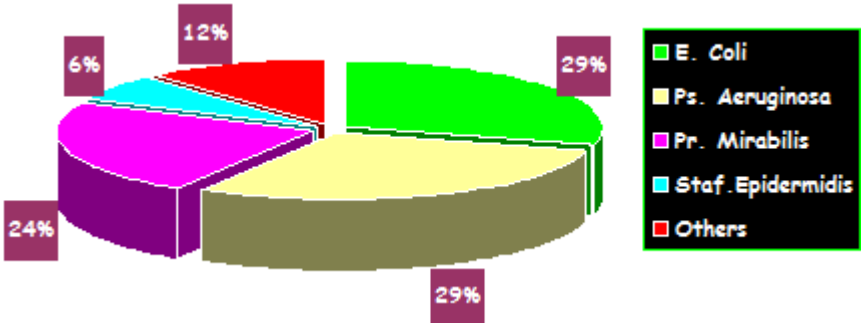

Figure 1: Distribution of organisms

We have analyzed 111 renal calculi (Figure 3).

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

Metabolic disorder was confirmed in 108 (50%) patients. 33 (30.5%) of them presented hypercalciuria, 8 (7.4%) hyperoxaluria, 7 of them primary hyperoxaluria (type 1) and 1 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 hypercalciuria is associated to hypocitraturia. 12 patients with hypercalciuria have a positive family history for kidney stones. The medium 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.

ESWL (lithotripsy) was performed in 38 patients. Open surgery was performed in 54 patients, the majority of them with associated malformations. Conservative treatment was performed in 91 patients and 26 patients had a spontaneous passage of calculi.

Table 3: Associated abnormalities

Associated abnormalities	*Number of patients*
Vesico-ureteric reflux (VUR)	9
Pelvi-ureteric junction obstruction	6
Duplication of 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

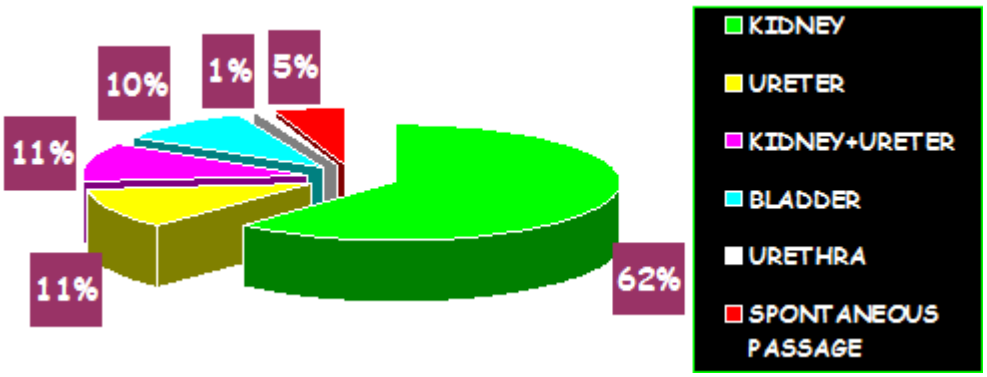

Figure 2: Stone distributions in urinary system

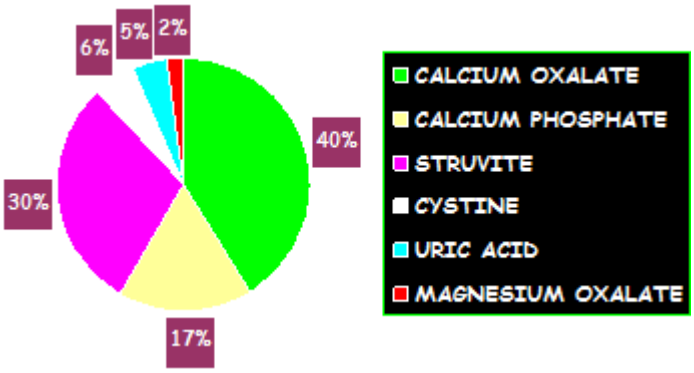

Figure 3: Stone composition

4. Discussion

Urolithiasis in children is underestimated, because literature data get in consideration the children admitted in hospital. Many children have only ambulatory visits; others have a spontaneous passage of calculi; the disease is not identified in some children, so they are not part of statistics. However, urolithiasis prevalence in children is estimated 1 case in 20 000 children/year [2].

Children represent about 1% of all patients with urolithiasis, but 100% of these children are considered high risk for recurrent stone formation, and it is crucial for them to receive a therapy that will render those stone free [3].

This pathology was identified in more than 1% of pediatric autopsies [4].

Data from United Kingdom studies evidence an incidence of 1-2 children per 1 million of habitants per year [5].

The study of two hospitals in India evidence 600 new cases of urolithiasis in children in a period of 2 years; 60% of them had bladder calculi [6].

In contrast with the above study, an important centre of United States found 5 new cases of urolithiasis in children in 1 year; this centre followed the children more than 20 years [7].

The data of 5 centers in USA show that the incidence for all types of urolithiasis in children ranges from 1:3000 to 1:7500 admissions [8]. But, children with stones now account for 1 in 685 pediatric hospitalizations in the United States; more than half of the patients are younger than 13 years at hospitalization [33].

From the data of the above studies, the conclusion is reached that not all children with urolithiasis are admitted in hospital; this influences the estimation of this disease frequency.

In our study 180 children were admitted to the hospital and the 36 others were followed as outpatients.

Literature states that pathology is more frequent in males; ratio M:F = 2:1 to 3:1 corresponding to the type of stone [9,10,11] but not in all studies [12].

In our study the ratio M:F is 2,17:1. Medium age at the moment of diagnosis is 5-7 years [13].

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

An important reduction of complex incidence of the urolithiasis, especially related to the absence of endemic calculi is observed in developed countries [14].

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 United Kingdom [5], mostly in rural areas, but in diminution in the last century, probably as a consequence of nutrition standard improvement [23]; the same is confirmed for Turkey [15].

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 urolithiasis a positive family history was reported in 33% of cases [13]. Positive family history in UK study is 16% in first degree relatives, and up to 33% in first and second degree relatives [23]. Very often there is a positive family history of renal stone disease in first- and second-degree relatives [35].
45.83% of cases comprised positive family history for kidney stones in our study.

The standard of calcium excretion in urine in healthy children is very difficult, 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 0.1 mmol/kg/die as a high limit of urinary calcium excretion. The evaluation of urinary excretion ratio 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 Harmpshire USA 2001*	*Stapleton USA 1987*	*Barratt 1999 UK*
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

Our data show that metabolic disorders were identified in 108 (50%) patients. The combination hypercalciuria-hypocitraturia was identified in 13 patients. Specific urine metabolic risk factors are found in most children with

kidney stones and that hypocitraturia is as frequent as hypercalciuria [35].

Clinical signs of urolithiasis in pediatric age are very large; forms that are completely asymptomatic (initial nephrocalcinosis, micro-urolithiasis, spontaneous passage of calculi); forms with an important clinical symptoms characterized by typical flank pain, especially in adolescents, recurrent UTI, urinary retention and acute renal failure [2,16,18]. Generally, clinical manifestations are not correlated with the calculi type. Most stones are located in renal papilla, except struvite. During the period of stone formation or cristalluria, there must be different clinical signs of irritation of epithelium of urinary tract: gross hematuria and micro-hematuria, pollachiuria, dysuria, bladder contractions, incontinence, abdominal pain and recurrent urinary tract infections [19].

Microhematuria and idiopathic hypercalciuria lead to urolithiasis in children [20].

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

Treatment has progressed, the minimally invasive treatment (ESWL, percutaneous nephrolithotomy and endoscopy) now are employed [23], but still in Tunisia [34] and in Albania a lot of patients underwent to open surgery.

5. Conclusion

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

References

[1] Belman AB, Kaplan GW: Calculus disease. In Belman AB, Kaplan GW (eds): Genitourinary problems in Pediatrics. *Philadelphia Saunders,* 1981, p 309.
[2] Khoory B.J. et al. Renal stones in Pediatrics. Med. Surg. Ped., 1998, 20: 367-376
[3] So et al. Normal urinary calcium/creatinine ratios in African-American and Caucasian children Pediatric Nephrology 2001;16:133-9
[4] Voghenzi A. Urolitiasi nel bambino. *Il pediatra* 1996: 50
[5] Ghazali S, Barratt TM, Williams DI. Childhood urolithiasis in Britain. *Arch Dis Child* 1973; 48: 291-295
[6] Nash MA: Urolithiasis. *In Edelmann CM Jr (ed):Pediatric Kidney Diseases*, Boston, Little, Brown, 1978, p 1170
[7] Bas HN, Emanuel B. Nephrolithiasis in childhood. *J Urol.* 95:749, 1966
[8] Piel CF, Roof Bs: Renal calculi. In Rubin MI, Barratt TM (eds): *Pediatric Nephrology. Baltimore, Williams and Wilkins*, 1975, p 760
[9] Bassaklar AC, Kale N. Experience with childhood urolithiasis. Report of 196 cases. *Br J Urol* 1991; 67:203-5
[10] Serkissian et al. Pediatric urolithiasis in Armenia: a study of 198 patients observed from 1991-1999. *Pediatric nephrology* 2001;16:728-32
[11] Gearhard JP, Herzborg GZ, Jeffs RD. Childhood urolithiasis: experiences and advances. *Pediatrics* 1991;87:445-50
[12] Milliner DS, Murphy ME. Urolithiasis in pediatric patients. *Mayo Clin Proc* 1993; 68:241-8
[13] Lama G, Marrone N. Urolitiasi in età pediatrica. *Rivista italiana pediatrica* 1992, 18 (Suppl. 1): 21.
[14] Pyrah LN. Epidemiology of urolithiasis. In Pyrah L.N., *Springer-Verlag*, Berlin 1979:3.
[15] Oner et al. Etiological and clinical patterns of urolithiasis in Turkish children. *Eur Urol* 1997
[16] Polinski MS, Kaiser BA, Baluarte HJ. Renal stones and hypercalciuria. *Adv Pediatric* 1993; 40:353-84
[17] Chambers TL, Moss G. Hypercalciuria, Stones and nephrocalcinosis. In: Postlethwaite R.J. (Ed), *Clin Ped Nephrology, 2nd Ed, Butterworth Heinemann,* 1994:389
[18] Barratt TM. Urolithiasis and nephrocalcinosis. *Pediatric Nephrology* 1999, p 933-941
[19] Heiliczer et al. Non calculi urinary tract disorders secondary to idiopathic hypercalciuria in children. *Ped Clin North Am* 34:711, 1987
[20] Roy SIII, Stapleton FB, Noe HN. Hematuria preceding renal calculus formation in children with hypercalciuria. *J Pediatrics* 1981 Nov;99(5):712-5
[21] Perrone HC, Schor N. Nephrolithiasis and hypercalciuria. In: Paniagua G.G., Nefrologia pediatrica, Mosby/Doyma Libri 1996:1012
[22] La Manna A, Polito C et al. Calyceal microlithiasis in children: report on 196 cases. *Pediatric Nephrology* 1998, 12:214-217
[23] Coward et al. Epidemiology of pediatric renal stone disease in the UK. *Arch Dis Child* 2003;88: 962-965
[24] Stapleton et al. Urolithiasis in children. The role of hypercalciuria. *Pediatric Ann* 1987;16:980-91
[25] Choi et al. Urolithiasis in childhood: current management. *J Pediatric Surgery* 1987;22:158-64
[26] Pak CYC. Disorders of stone formation. In Brenner BM, Rector FC (eds): The Kidney, 3rd ed. Philadelphia, WB Saunders, 1976, p 1326
[27] Coe FL, Favus M.J. Disorders of stone formation. In Brenner BM, Rector FC (eds): The Kidney, 3rd ed. Philadelphia, WB Saunders, 1986, p 1403
[28] Segal S, Their SO. Cystinuria. In: Scriver C.R., Beandet A.Z., Sly W.S., et al. (eds), The metabolic basis of inherited disease, New York, Mc Graw-Hill, 1989:2479

[29] Campfield T., Braden G., Flynn-Valone., et al. Urinary oxalate excretion in premature infants. Effect of human milk versus formula feeding. *Pediatrics*, 1994, 94:674
[30] Matos et al. Urinary phosphate/creatinine and magnesium/creatinine ratios in healthy pediatric population. *J Pediatrics* 1997;131(2):252-7
[31] Matos et al. Urinary oxalate and urate creatinine ratios in healthy pediatric population. *Am J Kidney Dis* 1999; Aug; 34(2):e1
[32] Straub M, Gschwend J, Zorn. Pediatric urolithiasis: the current surgical management. Pediatric Nephrology 2010 Feb 4 [Epub ahead of print]
[33] Bush NC et al. Hospitalizations for pediatric stone disease in United States, 2002-2007. J Urol. 2010 Mar; 183(3):1156
[34] Jallouli et al. Pediatric urolithiasis in Tunisia: a multi-centric study of 525 patients. J Pediatric Urology 2006 Dec;2(6):551-4.
[35] Spivacow FR et al. Metabolic risk factors in children with kidney stone disease. Pediatric Nephrology 2008 Jul;23(7):1129-33