

Pediatric Urolithiasis in Croatia

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ABSTRACT

A retrospective review was performed of the records of 148 Croatian children with urolithiasis treated between 1989 and 2003. The study evaluated age, gender, family history, clinical symptoms, location of stone, laboratory findings, stone composition, mode of treatment and compared our results with data from higher and lower socio-economic countries. The mean age of our patients was 9.38 years (10 months to 18 years). Thirty-seven children (25%) were less than 5 years (group 1), 44 (29.7%) were between 5 and 10 years (group 2) and 67 (45.3%) were older than 10 years of age (group 3). There were 60 girls and 88 boys with overall male to female ratio of 1.47. Abdominal pain (83%) and haematuria (59.5%) were the main symptoms in the groups 2 and 3. Urinary tract infection was predominant symptom in the group 1 (62.1%). Calculi were located in the kidney in 90 children (60.8%), in the ureter in 39 (26.4%), in the bladder in 8 (5.4%). Urinary tract anomalies with or without infection were associate with a greater frequency of urolithiasis in the youngest age group and hypercalciuria was predominant cause in children over 5. Stone analysis was performed in 80 children. Predominant constituent of stones was calcium oxalate (48.7%), followed by struvite (25%), calcium phosphate (13.7%), cystine (10%) and uric acid (1.2%). Calcium oxalate stones were most common in all age groups. Struvite stones were most prevalent in the children younger than 5 years of age. Most patients (33.1%) underwent surgery for removal of their calculi. In 31.8% of children stones were passed spontaneously and the highest spontaneous passage rate was in the group 3 (37.3%). Stone composition, location and etiology in Croatian children are similar to those in developed Western countries.

Key words: urolithiasis, children, Croatia

Introduction

Characteristics of urolithiasis vary in different regions of the world. Studies showed that the composition and prevalence of urinary stones in children depend on socio-economic conditions, hygiene, geographical area and dietary habits¹⁻⁴. Pediatric urolithiasis has considerably lower prevalence, different stone composition and location within urinary tract in the Western countries as compared to the countries in Asia and Middle East^{1,3,5}. Adult urolithiasis was extensively studied in Croatia⁶⁻¹². It was found that the most frequent constituent of the calculi was calcium oxalate and that the overall ratio of male to female patients was 1.52. These data are similar to those from developed European countries⁶. There are no published studies that investigate epidemiological and clinical characteristics of urolithiasis in Croatian pediatric population. Therefore, the aim of this study was to evaluate epidemiology, etiology, composition and clinical characteristics of childhood urolithiasis in Croatia and to compare data with some other countries.

Patients and Methods

The records of 148 children with urolithiasis who were treated between 1989 and 2003 in two Croatian hospitals (Clinical Hospital Split and Children's Hospital Zagreb) were reviewed retrospectively with regard to age, gender, family history, clinical symptoms, location of stone, laboratory findings, stone composition, mode of treatment and relevant pathological factors. Metabolic evaluation was performed in 95 children (64.2%). This evaluation included plasma creatinine, bicarbonate, sodium, potassium, calcium, phosphate, magnesium, urate, urinalysis (including pH), urine culture, 24-hour urine collection for calcium, creatinine, urate and a sodium nitroprusside test for cys-

tine. In some patients oxalate, citrate and cystine in 24-hour urine were also determined. Hypercalciuria was diagnosed if the amount of 24-hour urine calcium exceeded 4 mg/kg (0.1 mmol/kg)⁸. Infrared spectroscopy was performed in 80 children and stones were classified according to the prevalent constituent exceeding 50% of the whole stone examined.

Results

Epidemiology

The mean age of our patients was 9.38 years with the range of 10 months to 18 years. The mean age in boys was 9.0 (± 4.5) years and in girls 11.0 (± 5.1) years. Thirty-seven children (25%) were less than 5 years (group 1), 44 (29.7%) were between 5 and 10 years (group 2) and 67 (45.3%) were older than 10 years of age (group 3). There were 60 girls and 88 boys with overall male to female ratio of 1.47. This ratio was 1.22 in children with upper urinary tract stones. All patients with bladder stones were male. The sex ratio in the group 1 was 1.47, in the group 2 was 2.14 and in the group 3 was 1.16. Age distribution and gender of our patients in different age groups are shown in Figure 1.

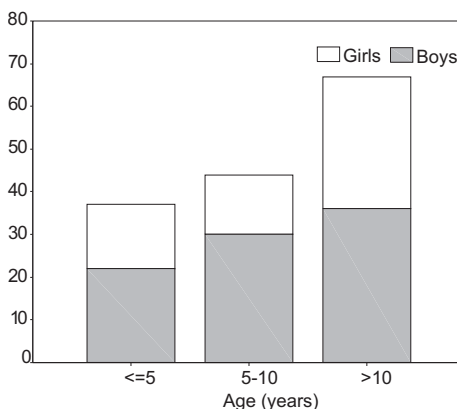


Fig. 1. Age distribution and gender of 148 patients with urolithiasis.

Clinical findings

The presenting symptoms in our patients were abdominal pain in 107 patients (72.3%), haematuria 81 (54.7%), dysuria in 9 (6%) occurring alone or in combination. Urinary tract infection (UTI) was present in 37 patients (25%). Most of the patients (62.1%) from the youngest age group presented with urinary tract infection (23/37). Abdominal pain (83%) and haematuria (59.5%) were the main symptoms in the groups 2 and 3. Seven patients were asymptomatic and presented only by spontaneous passage of stones. A positive family history was found in 37 cases (25 %).

Calculi were located in the kidney in 90 children (60.8%), in the ureter in 39 (26.4%), in the bladder in 8 (5.4%) and in both upper and lower urinary tract in 3 children (2%). The origin remained unknown in 8 children with spontaneous stone passage. Sixteen patients (10.8%) had bilateral calculi. In children with unilateral calculi more common was the right side (60.2%). In the youngest group 64.9% (24/37) of stones were in the kidney, 16.2% (6/37) in the ureter and 13.5% (5/37) in the bladder. In the groups 2 and

3 stones were in the kidney in 68,1% (30/44) and 53.7% (36/67) respectively. Only 3 children older then 5 years had bladder stones. Location of stones in different age groups is shown in Figure 2.

Stones were obtained by open surgery in 49 children (33.1%), extracorporeal shock wave lithotripsy (ESWL) in 13 (8.8 %) and endoscopic extractions in 15 (10.1%); 47 stones were passed spontaneously (31.8%). The spontaneous passage rate was 21.6% in group 1 (8/37), 29.8% in group 2 (14/44) and 37.3% in group 3 (25/67). In 18 patients stones were not obtained and in 6 patients these data are unknown.

Stone analysis

Stone analysis (infrared spectroscopy) was performed in 80 children. Predominant constituent was calcium oxalate (48.7%), followed by magnesium ammonium phosphate (struvite) (25%), calcium phosphate (13.7%), uric acid (1.2%), cystine (10%). Calcium oxalate stones were the most common in all age groups and struvite stones were most prevalent in children younger than 5 years of age. Table 1 and Figure 3 show stone analysis in different age groups.

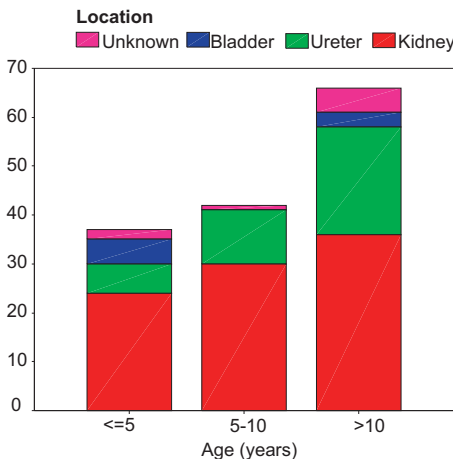


Fig. 2. Location of stones in different age groups.

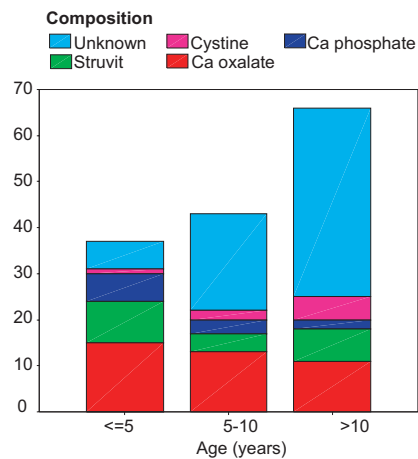


Fig. 3. Stone composition in different age groups.

TABLE 1
STONE ANALYSIS IN DIFFERENT AGE GROUPS

Component	≤ 5 years	5 – 10 years	> 10 years	Total
Calcium oxalate	15	13	11	39
Struvite	9	4	7	20
Calcium phosphate	6	3	2	11
Cystine	1	2	5	8
Uric acid	0	0	1	1
Other	0	1	0	1
Unknown	6	21	41	68

TABLE 2
ETIOLOGY OF UROLITHIASIS IN DIFFERENT AGE GROUPS

Etiology	≤ 5 years	5–10 years	> 10 years	Total
Hypercalciuria	8	10	10	28
Cystinuria	1	2	5	8
Urinary tract infection	2	5	2	9
Anomalies	10	4	5	22
Immobilization	1	0	0	1
Neurogenic bladder	2	0	2	4
Unknown	12	23	41	72

Etiology

Based on the results of metabolic evaluation, urine analysis, urine culture, imaging studies and if possible stone analysis an etiology was determined in 72 of our patients (48.6%). In 23 patients (24.2%) etiology remained unknown despite the evaluation and 53 patients had incomplete data.

Metabolic disorders were found in 36 out of 95 patients (37.9%). Hypercalciuria, confirmed by 24h urine collection, was the most common metabolic disorder and was found in 28 children (29.5%) and cystinuria in 8 (8.4%). None of our patients had primary hyperoxaluria.

Urinary tract anomalies were found in 22 patients (23.2%). Seven had hydronephrosis due to pyeloureteric junction obstruction, 8 had vesicoureteric reflux, 3 had stenosis of vesicoureteric junction, two patients had bladder diverticula, one

had kidney malrotation and one ureteropelvic duplication. Four patients had neurogenic bladder. In 12 patients with anomaly urinary stasis without infection led to formation of stones.

Urinary tract infection (UTI) was found in 37 (25%) patients. The bacteria isolated were *Escherichia coli*, *Proteus mirabilis*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*. Among patients with UTI five had also hypercalciuria, two had cystinuria and three had neurogenic bladder. Ten patients had urinary tract anomaly with UTI. In only 9 patients UTI was the only determined cause of urolithiasis.

Urinary tract anomalies were the most common cause of urolithiasis in the youngest age group and hypercalciuria was the commonest cause in children over five years of age (Table 2).

TABLE 3
COMPARISON OF STONE LOCATION AND MALE/FEMALE RATIO IN DIFFERENT COUNTRIES

	Croatia	France ¹⁵	UK ³	Tunis ⁴	Armenia ¹⁹	Turkey ¹³	Pakistan ¹
Upper u.t.	87%	93%	85%	76%	82%	65%	69%
Lower u.t.	8%	17%	15%	24%	16.6%	26%	31%
Male/female ratio	1.47	2.29	2.06	2.08	2.012	2.69	2.94

TABLE 4
CAUSES OF PEDIATRIC UROLITHIASIS IN DIFFERENT COUNTRIES

Causes	Croatia (%)	USA ²⁰ (%)	UK ³ (%)	Tunis ⁴ (%)	Armenia ¹⁹ (%)	Turkey ¹³ (%)	Pakistan ¹ (%)
Metabolic	37.9	46.5	19	25	31	34.6	25
Infection	25	13.4	60	20	20	22.2	7
Anomalies	23.2		22	7.5	4	29.6	12
Idiopathic	24.2	18.7			26		55
Others	3.2	15.3			12		1

Discussion

As the etiology and location of urinary calculi vary in different parts of the world, this retrospective study was conducted to determine the epidemiological and clinical characteristics of urolithiasis in Croatian children and to determine associated etiological factors favoring stone formation in our region. A number of studies have shown that characteristics of urolithiasis in low socio-economic conditions are bladder location, high male preponderance and frequent ammonium hydrogen urate stones^{1,13,14}. In a high socio-economic level population stones are mostly located in the upper urinary tract, the percentage of female patients is higher and calcium oxalate stones predominate^{2,15}. In this study stones were mostly located in the kidney and ureters (89%), and only 5.4% of them were in the bladder. Our results are in agreement with data from other European countries as Germany, Greece and Great Britain^{3,16,17}. In most countries urolithiasis is more frequent in boys, especially in a younger age group. The male to female ratio varies from 1.2 to 3^{1,4}. Similar to previous re-

ports, we observed higher incidence of stone formation in males (M/F 1.46) as it is clearly shown in Table 3. The male preponderance was more pronounced in younger children. According to the literature 45%–60% of children with urolithiasis are under 5 years^{2,13,15,16}. In our study 25 % of children were under 5 years, 30% between 5 and 10 years, and 45% older than 10. When compared with other studies, the low proportion of young children may be due to different etiology and possibly delayed diagnosis.

In Western countries calculi in male infants are often due to urinary tract infection. These stones are mostly located in the upper urinary tract, are composed of stuvite, and are frequent caused by Proteus. Urinary tract infection by urease-producing bacteria is responsible for 33–60% calculi in European children^{2,3,13,15,16}. Only 25% of our children had UTI, which was mostly associated with other pathological factors such as urinary tract anomalies, hypercalciuria, neurogenic bladder and cystinuria. Urinary tract infection was the only cause of urolithiasis in only 9 patients and 8 of

them had struvite stones. Additional six children with UTI had unknown etiology and stone composition. If infection related stones are not sent for analysis the frequency of struvite stones may be underestimated. Also, most published reports of the epidemiology of urinary tract stones in Europe are from 1960's to 1980's^{2,3,19}. Changing socio-economic conditions, improvement of living standard, earlier diagnosis and treatment of urinary tract infections and anomalies have generated change in the type of lithiasis in terms of both site and composition of the calculi. Recent studies show that even in lower socio-economic conditions the pattern of calculus disease changed from a predominantly lower tract site in the 1970's and 1980's to the upper tract in the 1990's^{1,5,19}. In the latest studies from Pakistan, Turkey and Armenia metabolic stones were found more frequently than infection ones and calcium oxalate became predominant constituent in pediatric urolithiasis in these countries^{1,5,19}. In adults calcium stones also predominate and account for almost 70% of all renal stones observed in economically developed countries⁶. Dietary intake, lifestyle and genetic predisposition seem to influence calcium stone formation. Stone analysis was performed in 80 of our patients and also showed a predominance of calcium oxalate calculi. Hypercalciuria, the most common metabolic cause of stones in Western children, was diagnosed in almost 30% of our children. In our patients hypercalciuria was most commonly idiopathic as neither hyperparathyroidism nor renal tubular acidosis were found. In older publications from 1979 to 1986 from North America metabolic conditions accounted for 52% of nephrolithiasis, while infection and idiopathic conditions represented 13.4% and 18.7%, respectively¹⁸. These data are similar to the data for 221 children evaluated at the Mayo Clinic between 1965 and 1987²¹. Latest North

American data of analyzed stones show that the most common component is calcium oxalate (70–80%), followed by calcium phosphate (5–10%), uric acid (5–10%), struvite (5–10%) and cystine (1–5%)²². Although predominant constituent in all age groups of our children was calcium oxalate (48.7%), struvite stones (25%) are more common in our patients than in American children, especially in the children younger than 5 years of age. It is difficult to compare our data with other Western countries, as there are no recent reports of the epidemiology of urinary tract stones in Europe. In older reports urinary tract infection was the major cause of urolithiasis outside of North America^{2,3,23,24}. In Polinsky's review of the European literature, infection accounted for 43.5% of the episodes of nephrolithiasis²⁵. According to Basaklar, nearly 75% of the pediatric stones in Europe were associated with infection or urinary anomalies¹³. Urinary tract anomalies led to formation of stones in 23% of our patients which is similar to other western countries^{3,15} (Table 4). Etiology was not determined in almost 25% of our children, which is in accordance with other reports^{19,21}. This percentage would probably decrease if the urinary citrate and oxalate had been determined in all patients. Additional 53 children had incomplete data, so the cause of stone formation in these patients also remained unknown. If more detailed investigations are undertaken it is possible that the number of »idiopathic« cases will decrease.

The clinical features in children with urinary calculi vary with age. In infants stone symptoms may be confused with colicky abdominal pain. The predominant symptoms at presentation in our children were abdominal pain (72.3%) and/ or haematuria (53.4%). Although, abdominal pain and haematuria were the most predominant symptoms in older children, our patients below 5 years of age pre-

sented mostly (62%) by urinary tract infection. These data are in accordance with some other reports^{2,3,21}. Therefore, calculus disease should always be considered in differential diagnosis when these symptoms are present.

Stones in the present study were still mainly removed by open surgery because no adequate litotripter was always available. However, this situation has been changing during the last years and open surgery procedures are being replaced by less invasive techniques²⁶. Open surgery is still necessary, especially in children with urinary tract anomalies, and those with staghorn calculi. In almost 32% of our children stones were passed spontaneously. Older children were more likely to pass the stones spontaneously than children less than 5 years old probably due to relatively larger stone burden in younger children. This fact could be important for the therapeutic approach. It would be interesting to further investigate the size of stone in relation to the diameter of the urinary tract. It could be speculated that the possibility of spontaneous passage depends on the diameter of the urinary tract. In order to confirm this the exact size of stones should be analyzed in each age group. But, it is well known that the size of stone is not the only factor that determines the possibility of spontaneous passage. For instance, the stone with sharp and rough surface, regardless of the size, is much less likely to pass spontaneously than larger stone with smooth surface. Also, the diameter

of urinary tract, especially of ureteropelvic and ureterovesical junctions, and anomalies of the upper and lower urinary tract determine the possibility of spontaneous passage. In this study we could not measure the diameter of stone because many patients had only fragments or did not bring stones at all. Therefore, further studies should determine the correlation of the stone diameter with morphology and diameter of urinary tract.

In conclusion, stone composition indicates that urolithiasis in Croatian children is heterogenic, but metabolic disorders and urinary tract anomalies are the most common causes. Urinary tract anomalies are associated with greater frequency of urolithiasis in the youngest age group and hypercalciuria is predominant cause in children over five years of age. Stones are mostly located in the upper urinary tract, the overall male to female ratio is 1.47 and calcium oxalate stones predominate, which are characteristics similar to other industrialized countries. Presenting symptoms are variable, but abdominal pain and/or haematuria are present in most children older than 5 years of age. Symptoms in younger children are presented mostly with urinary tract infection. In order to prevent renal damage, all children with these symptoms should be investigated, the nature of calculi should be determined to establish appropriate management. More effort should be made for early detection and therapy of urinary tract infections and anomalies.

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PEDIJATRIJSKA UROLITIJAZA U HRVATSKOJ

SAŽETAK

Napravljena je retrospektivna studija koja je uključila 148 djece s urolitijazom koja su bila liječena između 1989. i 2003. Studija je procijenila dob, spol, obiteljsku anamnezu, kliničke simptome, lokalizaciju kamenca, laboratorijske nalaze, sastav kamena, način liječenja i usporedila rezultate s podacima drugih država kako onih višeg tako i nižeg socio-ekonomskog stanja. Srednja dob bolesnika bila je 9,38 godina (u rasponu od 10 mjeseci do 18 godina). 37 djece (25%) bilo je mlađe od 5 godina (skupina 1), 44 (29,7%) bilo je u dobi od 5 do 10 godina (skupina 2), te 67 (45,3%) djece bilo je starije od 10 godina (skupina 3). Među ispitivanom djecom bilo je više dječaka (60 djevojčica i 88 dječaka) te je omjer dječaka naprema djevojčicama iznosio: 1,47. Bol u trbuhu (83%) i hematurija (59,5%) bili su najčešći simptomi u skupinama 2 i 3. Infekcija urinarnog trakta bila je najčešći simptom u skupini 1 (62,1%). Kamenci su bili smješteni u bubregu u 90 djece (60,8%), u ureteru u 39 (26,4%), u mokraćnom mjehuru u 8 (5,4%). Anomalije urinarnog trakta sa ili bez infekcije bile su najčešći uzrok urolitijaze u najmlađoj dobnoj skupini te hiperkalcurija je bila najčešći uzrok u djece starije od 5 godina. Analiza kamenaca napravljena je u 80 djece. Najčešći sastojak kamenaca bio je kalcijev oksalat (48,7%), potom struvit (25%), kalcijev fosfat (13,7%), cistin (10%) i mokraćna kiselina (1,2%). Kamenci kalcijevog oksalata bili su najčešći u svim dobnim skupinama. Kamenci struvita bili su najčešći u djece mlađe od 5 godina. Najviše bolesnika (33,1%) kirurški je liječeno kako bi se otklonio kamenac. U 31,8% djece, kamenci su spontano izlučeni s najvišom stopom u skupini 3 (37,3%). Sastav, smještaj i etiologija kamenaca u djece u Hrvatskoj, slična je onoj u razvijenim državama.