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Clinical and Biological Characteristics of Childhood Urolithiasis in Tunisia: A Study of 300 Cases

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ABSTRACT

Background: Urolithiasis is a common disease in both developed and developing countries. Over the past few decades, this pathological condition has become more common in children as a result of the rapid variations in dietary habits and the increasing standard of living.
Objectives: Since the 1980s, the clinical and biological characteristics of urolithiasis in Tunisian children have been continuously evolving. This retrospective study defines the current status of urolithiasis among children and adolescents in Tunisia.
Patients and Methods: Between 2003 and 2010, we retrospectively reviewed the records of 300 children and adolescents (age: 6 months to 19 years) with urolithiasis. A first-line metabolic, urine, and plasma work-ups were performed in all patients. Physical and chemical analyses of the stones were performed, respectively, by stereomicroscopy and infrared spectroscopy. Statistical analysis of the results was performed using SPSS 11.0 software. Chi-square test was used for comparing the percentages.
Results: Our study shows male predominance of urolithiasis with a male/female ratio of 1.54/1. Stones were located in the upper urinary tract in 69.0% of cases, and calcium oxalate was the predominant constituent in 53.0% of stones. The prevalence of calcium oxalate stones increased with age in both genders (48.5% in infants vs 67.9% in teenagers [$P < 0.01$]). Struvite stones were most commonly detected in patients aged 2 to 9 years ($P < 0.02$), and they were significantly more prevalent in boys than in girls ($P < 0.001$). Ammonium urate stones were observed in 14.0% cases, and were more commonly detected in infants.
Conclusions: Our results suggest a high percentage of calcium oxalate stones and a low percentage of struvite stones in infants. Hence, patient age is an important factor that must be taken into account during etiopathogenic work-up of urolithiasis.

Implication for health policy/practice/research/medical education:
Pediatric urolithiasis Is An important Encountered kidney disorder in clinical practice. The Epidemiological features of this pathology continues to evolve over time. Stones analysis is the best method to ESTABLISH year effective Treatment for this pathology.

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1. Background

Urolithiasis is a common disease in both developed and developing countries. Over the past few decades, this pathological condition has become more common in children as a result of the rapid variations in dietary habits and the increasing standard of living. Changes in

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socioeconomic conditions over time have affected not only the incidence but also the site and chemical composition of calculi (1). Bladder stones, composed of ammonium urate and calcium oxalate, have been reported to be endemic in Asia, whereas renoureteral calculosis with mainly calcium oxalate and phosphate stones is currently frequent in economically developed countries (2).

Tunisia is one of the endemic countries, but there is little documentation of recent characteristics of the disease in Tunisian children (3-5). In this paper, we report the results of stone analysis of 300 patients less than 20 years of age. All children were treated in public hospitals in the central coast region of Tunisia and the stones were analyzed by infrared spectroscopy.

2. Objectives

The aim of the study was to determine stone composition by using a reliable physical method and to define the current status of urolithiasis in children in Tunisia.

3. Patients and Methods

Three hundred patients aged 6 months to 19 years (mean age, 8.3 ± 1.2 years) suffering from urinary calculi were admitted between 2003 and 2010 to the department of pediatric surgery and urology of University Hospital of Monastir. We recorded the age, sex, stone location, family history, and clinical presentation in each case. Informed consent was obtained from each patient included in the study, and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki.

Clinical investigation was performed in all cases. Interpretation was based on ratios (x over creatinine) derived from healthy Swiss children (6, 7). Briefly, the upper limits of normal (mol/mol) used for the age groups 1 to 3/3 to 5/5 to 7 and > 7 years are shown in *Table 1*. If more than 1 specimen was obtained, the average ratio was used. Ratios exceeding twice the upper limits of normal were considered strongly abnormal. All stones were documented radiologically by ultrasound and intravenous urography. Urine culture was performed in 280 cases. Calculi from the kidney or ureter, and those spontaneously passed, were classified as upper urinary tract stones. Bladder or urethral calculi were considered as lower tract stones. All stone samples obtained by means of open operation, extracorporeal shock-wave lithotripsy (ESWL), or spontaneous passages were sent for analysis.

Next, we established the structure of each calculus. The morphology of the stone was determined by stereomicroscopy, and its molecular and crystalline composition was determined by infrared spectroscopy to select its representative parts (nucleus, internal section, and external surface) (8). The proportion of each component was assessed by infrared analysis of the powder made from the whole stone. The results were expressed according to the main crystalline phase found in the stones, and named as follows: whewellite (calcium oxalate monohydrate), weddellite (calcium oxalate dihydrate), carbapatite (carbonated calcium phosphate crystallized in a hexagonal pattern), struvite or infection-related stones (magnesium ammonium phosphate hexahydrate), and calcite (anhydrous calcium carbonate). The stone component was considered to be the main component if it exceeded 75% of the total composition of the calculus. Stones, formed by a single component, were classified as pure stones, and those with more than one component, were considered as mixed stones.

Statistical analysis of the data was performed using SPSS 11.0 for Windows. Statistical significance was determined by using the chi-squared test. *P* values < 0.05 were considered significant.

4. Results

Our findings show that 60.7% of patients were male, and the male to female ratio was 1.54/1. The male to female ratio was the highest in infants and children (male/female: 1.7/1), whereas, it was the lowest in teenagers (male/female: 0.87/1). Thirty-three patients (11.0%) of the study group were ≤ 2 years of age (infants), and children (age groups, 2 to 9 years) represented 70.3% of cases. Children's age at presentation ranged from 6 months to 19 years (mean age 8.3 ± 1.2 years).

Upper urinary tract was most frequently affected by this pathology (kidney, 51.3% and ureter, 17.7%). Bladder stones were noted in 27.7% of cases. However, no significant difference was noted according to gender (30.8% in boys

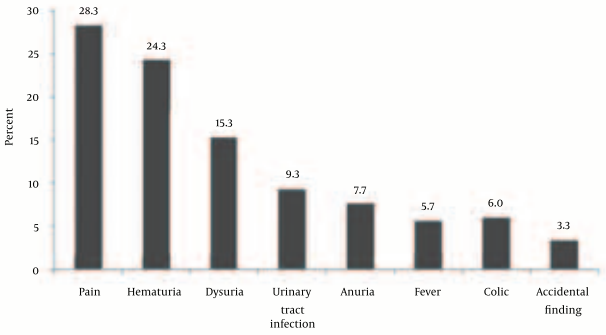

Figure 1. Clinical Presentation of 300 Tunisian Children With Urolithiasis.

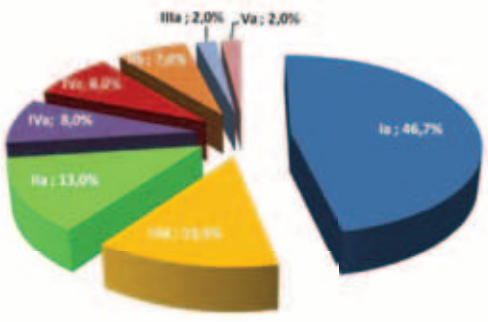

Figure 2. Most Frequent Morphology Type of Pediatric Calculi (n = 300).

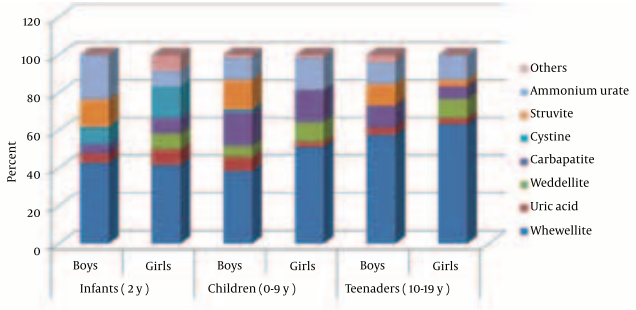

Figure 3. Main Stone Component According to Age and Sex (n = 300).

vs. 25.4% in girls). Infants appear to be more affected by bladder stones (42.4%) than teenagers (16.1%) ($P < 0.001$) (*Table 2*). A clear male predominance was pronounced in infants (male/female ratio: 1.86). Family history of renal stones was reported in 25 patients (8.3%). The most common symptom on admission was abdominal pain in 28.3% of cases (*Figure 1*). A history of urinary tract infection (UTI) was observed in 52 patients, whereas 29 had UTI on admission. Infants appear to be more affected by urinary tract infection than others ($P < 0.01$). The bacteria isolated were *Proteus* in 12 cases, *Escherichia coli* in 11, *Klebsiella pneumoniae* in 4, and *Streptococcus* and *Staphylococcus aureus* in 1 case each.

Thirty-four patients (11.3%) had an underlying anatomic abnormality, including uretero-pelvic junction obstruction in 14 cases, vesicoureteral reflux in 8 cases, neuropathic bladder in 4, and posterior urethral valves and dumb kidney in 3 each, and horseshoe kidney in 2 cases. Metabolic disorders were recorded in 8.7% of patients (hypercalciuria in 14 cases, hypercystinuria and hyperoxaluria in 6 each).

Treatments for this pathology were as follows: (1) Stones were eliminated spontaneously in 8 patients. (2) A specific treatment with D-penicilliamine (urine pH in the low alkaline range) was used in 6 cystinic patients. However, this treatment was successful in only 2 patients. (3) Surgical treatment was performed in 284 cases, and (4) endoscopy-associated ballistic lithotripsy was used in 6 cases.

In all cases, calcium oxalate stones were the most common (53.0%). It was the most abundant component of stones in all age classes (*Table 3*). There was an increasing prevalence of calcium oxalate stones with regard to age in both genders (48.5% in infants *vs.* 67.9% in teenagers ($P < 0.01$). The microscopic stone analysis has shown

Table 1. Upper Limits of Normal Ratios (x Over Creatinine) (mol/mol) Used for the Age Groups.

Age Groups, y	Calcium/Creatinine (mol/mol)	Oxalate/Creatinine (mol/mol)	Uric Acid/Creatinine (mol/mol)
1 ≤ age ≤ 3	1.4	0.12	1.3
3< age ≤5	1.1	0.08	1.1
5< age ≤ 7	0.8	0.07	0.8
5< age ≤ 7	0.7	0.06	0.55

Table 2. Stone Localization According to Age

Stone Localization	Infant 0 to 2 y (n = 33)	Children 2 to 9 y (n = 211)	Teenagers 10 to 19 y (n = 56)
Kidney, No.(%)	15(45.5)	107(50.7)	37(66.1)
Ureter, No.(%)	4(12.1)	41(19.4)	10(17.9)
Bladder, No.(%)	14(42.4)	63(29.9)	9(16.1)

Table 3. Main Component in the Whole Stones (n = 300) and in the Nucleus (n = 151) According to Age

Main Stone Component	Infants (≤ 2, y), %		Children (0 to 9, y), %		Teenagers (10 to 19, y), %		Total, %	
	Nucleus	All Stones	Nucleus	All Stones	Nucleus	All Stones	Nucleus	All Stones
Whewellite	16.7	42.4	42.7	42.7	60.9	62.5	42.4	46.3
Uric acid	5.6	6.1	0.9	5.7	0	3.6	1.3	5.3
Weddellite	5.6	6.1	5.5	7.1	8.7	5.4	6	6.7
Carbapatite	11.1	6.1	18.2	17.5	8.7	8.9	15.9	14.7
Cystine	11.1	6.1	3.6	1.9	0	0	4	2.0
Struvite	5.6	9.1	10.9	10.0	8.7	7.1	9.9	9.3
Ammonium urate	38.9	21.1	15.5	13.6	8.7	10.7	17.2	14.0
Vaterite	5.6	3.0	0.9	0.5	0	0	1.3	0.7
Aragonite	0	0	0.9	0.5	4.3	1.8	1.3	0.7
Calcite	0	42.4	0.5	0	0	0.7	0.3	

the prevalence of whewellite type Ia with the absence of type Ic. (*Figure 2*). With regard to the crystalline species, calcium oxalate monohydrate (whewellite) was the main component in every age class (Figure 3). The proportion of whewellite progressively increased from 42.4% in infants to 62.5% in the age class 10 to 19 years. Weddellite was more abundant in girls (10.2%) than in boys (4.4%) in the first 2 decades. Struvite was more frequent in patients aged 2 to 9 years ($P < 0.02$) and significantly more prevalent in boys than in girls ($P < 0.001$). Ammonium urate stones were observed in 14.0% cases, and were more frequent in infants.

The nucleus of stone was found in 151 cases (50.3%), and its main component whewellite was found in 42.4% of the cases (*Table 3*). Ammonium urate was the second most abundant chemical component in the stone nucleus and was predominant in infants ($P < 0.001$).

5. Discussion

Studies from different geographical areas show that characteristics of urolithiasis among children vary widely in terms of prevalence, site of formation, stone composition, and predisposing etiological factors. The results of sex preponderance in this pathological condition have been conflicting, but male predominance has been most commonly reported (9, 10). In Tunisia, men were shown to be the predominately affected sex (4, 11). The male preponderance was more pronounced in infants under 2 years, and especially in those presenting with bladder calculi.

Metabolic abnormalities and infectious stones prevail in most pediatric series (10, 12-15). However, contrary to our expectations, metabolic and infectious stones are rare. These findings differ from those of other studies conducted in Europe [England: 44%, 30% (10); Greece: 48%, 28.8% (16)], in the Middle East [Kuwait: 83%, 29% (17); Saudi Arabia: 10.6%, 17.6% (18); Iraq: 52%, 25.5% (19)], and in the Northern region of Tunisia (28.2% in each case) (20). However, this result indicates a decrease in the infection rate as compared to that obtained in our first study in 1986 (57% of cases) (21).

Stone composition has changed substantially over the past decades, with a progressive increase in the frequency of calcium oxalate even in the eastern hemisphere (1). Recent epidemiology studies from different continents and countries suggest that calcium oxalate is the most frequent chemical compound at present (22-24). According to Daudon *et al.* (22), calcium oxalate stones in patients from developing countries are observed primarily in North Africa and Minor Asia. In our study, the frequency of calcium oxalate stones was similar to that reported in Algerian (25), Moroccan (26), Chinese (24), and Turkish (27) studies. With regard to the crystalline species, whewellite was the abundant compound of stones in children, and its prevalence increased with age. The absence of whewellite type Ic, excludes primary hyperoxaluria origin of whewellite stones.

Ammonium urate was predominant in infants. It was the main component of the nucleus in 17.2% of our stones, whereas a frequency of 29.5% was noted in our neighboring country (25) in comparison to an 11% frequency reported in France (28). The high proportion of stones with ammonium urate nucleus in infants suggests that hyperuricosuria, low phosphorus intake, low diuresis, and chronic diarrhea are the risk factors (20) involved in stone nucleation in our region, which is confirmed by the predominance of the ammonium urate type IIId (9).

Struvite or infection-related stones, which were very common in children until the last century, are rarely seen today in industrialized countries (29). Nevertheless, epidemiological studies from various countries continue to report a frequency of struvite stones between 25% and 38% (22, 30, 31). As reported by Daudon *et al.* (9), we found a relatively low frequency of infection-related stones as compared to that reported in previous reports from our region (21). This result is probably due to, firstly, early detection of urinary infections, and secondly, the close attention paid to their treatment in recent years.

Our results indicate a high percentage of calcium oxalate stones and a low percentage of struvite stones. They also show the increase of calcium oxalate stones in teenagers and the decrease of purine stones. These results confirm the change in the etiology of urolithiasis according to age.

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