Original Article

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Kidney Stones in Children and Teenagers in the Central Coast Region of Tunisia

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Abstract

Objective: Since 1980s, the clinical and biological characteristics of urolithiasis in Tunisian children have continuously evolved. This retrospective study defines the current status of urolithiasis among children and adolescents in Tunisia.

Methods: We retrospectively reviewed the records of 310 children and adolescents (age: 3 months - 19 years) between 2003 and 2010, holding urolithiasis. A first-line metabolic, urine and plasma work-up was performed in all patients. Physical and chemical analysis of the stones was performed respectively by stereomicroscopy and infrared spectroscopy. Statistical analysis of the results was performed with SPSS 11.0 software. The Chi-square test was used for comparison of percentages.

Findings: Our study shows a male predominance of urolithiasis with a sex ratio of 1.5. Stones were located in the upper urinary tract in 70.7% of cases. Calcium oxalate was the predominant constituent in 52.6% of stones. There was an increasing prevalence of calcium oxalate stones according to age in both genders (48.6% in infants vs 68.5% in teenagers (P<0.01)). Struvite was more frequent in patients aged 2-9 years (P<0.02) and significantly more prevalent in boys than in girls (P<0.001). Ammonium urate stones were observed in 14.2% and were more frequent in infants.

Conclusion: Our results emphasize a high percentage of calcium oxalate stones and a low percentage of struvite stones. The persistence of urate stones reflects the particular eating habits and the infectious risk factors. The patient's age is an important factor that must be taken into account during etiopathogenic work-up.

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Key Words: Urolithiasis; Teenagers; Infants; Kidney; Tunisia

Introduction

Urolithiasis is a common disease in both developed and developing countries. This pathology has become more common in children over the past few decades as a result of the rapid variations in dietary habits and the increasing standard of living. Changes in 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

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oxalate, have been reported to be endemic in Asia, whereas renoureteral calculosis featuring mainly calcium oxalate and phosphate is currently more 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 310 patients, less than 20 years of age. All patients were treated in public hospitals in the central coast region of Tunisia and the stones were analyzed by infrared spectroscopy. The aim of the study was to determine stone composition using a reliable physical method and to investigate the etiology of urolithiasis in Tunisian children and teenagers.

Subjects and Methods

A total of 310 stone-forming children and teenagers, with ages ranging from 3 months to 19 years (mean age 8.6±1.2 years), had been admitted over the 8-year period (2003 to 2010) to the department of pediatric surgery and urology of University Hospital of Monastir. We recorded in each case the age, sex of the patient, stone location, family history and clinical presentation. Informed consent was obtained from each patient included in the study and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

Clinical exploration was performed in all cases. Interpretation of urine chemicals 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 1-3/3-5/5-7 and >7 years were, respectively, for calcium 1.4/1.1/ 0.8/0.7, oxalate 0.12/0.08/0.07/0.06, and uric acid 1.3/1.1/ 0.8/0.55. If more than one 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 carried out 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.

The structure of each calculus was established using a stereomicroscope to define the morphology of the stone and to select its representative parts (nucleus, internal section, and external surface), in order to determine its molecular and crystalline composition by infrared spectroscopy[8]. The proportion of each component was assessed by infrared analysis of the powder of 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 (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, mixed stones.

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

Findings

Of the 310 children with urolithiasis, 59.4% were males, with a male to female (M:F) ratio of 1.5. The M:F ratio was the highest in infants and children (M/F=1.7), whereas, it was the lowest in teenagers (M/F=0.83). Thirty five patients (11.3%) of the study group were ≤2 years of age (infants), while children (age groups 2–9 years) represent 70.3% of cases. Children's age at presentation ranged

Table 1: Stone localization according to age

Localisation	Infants 0-2 years (n=35) Number (%)	Children 2-9 years (n=218) Number (%)	Teenagers 10-19 years (n=57) Number (%)
Kidney	16 (45.7)	109 (50.0)	37 (64.9)
Ureter	4 (11.4)	43 (19.7)	10 (17.5)
Bladder	15 (42.9)	66 (30.3)	10 (17.5)
Total	35 (100)	218 100	57 100

from 3 months to 19 years (mean age 8.6 years). Upper urinary tract was most frequently affected by this pathology (kidney 52.3% and ureter 18.4%). Bladder stones were noted in 29.4% of by this pathology (kidney 52.3% and ureter 18.4%). Bladder stones were noted in 29.4% of cases. But, no difference was noted according to gender (29.7% in boys vs 28.8% in girls). Infants seemed to be more frequently affected by bladder stones (42.9%) than teenagers (17.5%) ($P< 0.001$) (Table 1). A clear male predominance was pronounced in infants (M/F = 2.75).

Family history of renal stones was reported in 27 patients (8.7%). The most common symptom on admission was abdominal pain in 28.7% of cases. This was accompanied by hematuria in 24.2%, dysuria in 15.5%, urinary tract infection in 9.4%, anuria in 7.4%, accidental finding in 3.2%, fever and colic each one in 5.8% of cases. Abdominal pain was predominant in school age children (Table 2).

A history of urinary tract infection (UTI) was observed in 54 patients, whereas twenty nine had UTI on admission. Infants seem to be more frequently 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, Streptococcus and Staphylococcus aureus in 1 case each.

Thirty four patients (11.0%) 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 6.5% of patients (hypercalciuria in 14 cases, hypercystinuria and hyperoxaluria in 6 each).

Treatments for this pathology were as follow: i) Stones were eliminated spontaneously in eight patients (2.6% of cases). ii) 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 two patients. iii) Surgical treatment was performed in 294 cases, and iv) endoscopy associated ballistic lithotripsy was used in six cases.

Overall, calcium oxalate was the commonest stone encountered (52.6%). 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

Table 2: Clinical presentation of 310 Tunisian children with urolithiasis

Clinical Presentation	Infant 0-2 years (n=35) Number (%)	Children 2-9 years (n=218) Number (%)	Teenagers 10-19 years (n=57) Number (%)	Total Number (%)
Pain	6 (17.1)	57 (26.1)	26 (45.6)	89 (28.7)
Hematuria	11 (31.4)	49 (22.5)	15 (26.3)	75 (24.2)
Urinary tract infection	8 (22.9)	18 (8.3)	3 (5.3)	29 (9.4)
Dysuria	3 (8.6)	43 (19.7)	2 (3.5)	48 (15.5)
Anuria	3 (8.6)	16 (7.3)	4 (7.0)	23 (7.4)
Fever	4 (11.4)	14 (6.4)	0	18 (5.8)
Colic	0	12 (5.5)	6 (10.5)	18 (5.8)
Accidental finding	0	9 (4.1)	1 (1.8)	10 (3.2)

Table 3: Main component in the whole stones (n=310) and in the nucleus (n=151) according to age

Main component	Infants (Age ≤ 2 years		Children (0-9 years)		Teenagers (10-19 years)		Total	
	All stone (%)	Nucleus (%)	All stone (%)	Nucleus (%)	All stone (%)	Nucleus (%)	All stone (%)	Nucleus (%)
Whewellite	42.9	16.7	41.7	42.7	63.2	60.9	45.8	42.4
Uric acid	8.6	5.6	6.0	0.9	3.5	0.0	5.8	1.3
Weddellite	5.7	5.6	7.3	5.5	5.3	8.7	6.8	6.0
Carbapatite	5.7	11.1	17.0	18.2	8.8	8.7	14.2	15.9
Cystine	5.7	11.1	1.8	3.6	0.0	0.0	1.9	4.0
Struvite	8.6	5.6	10.6	10.9	7.0	8.7	9.7	9.9
Ammonium urate	20.0	38.9	14.2	15.5	10.5	8.7	14.2	17.2
Vaterite	2.8	5.6	0.5	0.9	0.0	0.0	0.6	1.3
Aragonite	0.0	0.0	0.5	0.9	1.8	4.3	0.6	1.3
Calcite	0.0	0.0	0.5	0.9	0.0	0.0	0.3	0.7

genders (48.6% in infants vs 68.5% in teenagers (P<0.01). The microscopic stone analysis has shown the prevalence of whewellite type Ia (Table 4).

With regard to the crystalline species, calcium oxalate monohydrate (whewellite) was the main component in every age class (Table 5). The proportion of whewellite progressively rose from 42.9% in infants to 63.2% in the age class 10–19 years. Weddellite was more abundant in girls (10.4%) than in boys (4.3%) in the first two 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 14.2% and were more frequent in infants.

The nucleus of stone was found in 151 cases (48.7%) and its main component was whewellite in 42.4% of cases (Table 3). Ammonium urate was the second more abundant chemical component in stone nucleus and was predominant in infants (P<0.001).

Discussion

The geographical pattern of childhood urolithiasis varies widely in terms of prevalence, site of formation, stone composition and predisposing etiological factors. Reports of sex preponderance

Table 4: Most frequent morphology type of pediatric calculi (n=310)

Pure type		Percent
I	Ia	22.3
II	IIa	7.7
	IIb	8.7
III	IIIa	6.8
	IIId	11.9
IV	IVa	7.7
	Ivc	6.1
V	Va	1.9
Main mixed morphology	Ia +IIId	7.4
	Ia+II (a or b)	7.4
	IVc + IIId	2.9
	Ia + Iva	3.9
	IIa + IVa	3.9
	Others	1.6

Table 5: Main stone component according to age and sex (n=310)

Main stone component	Infants (Age ≤ 2 years)		Children (2<age<10 years)		Teenagers (10-19 years)	
	Male (%)	Female (%)	Male (%)	Female (%)	Male (%)	Female (%)
Whewellite	45.5	30.7	38.1	48.1	61.7	64.5
Ammonium urate	22.7	15.4	12.4	17.3	7.7	12.9
Carbapatite	4.5	7.7	17.5	16.0	11.5	6.5
Struvite	13.6	0	15.3	2.5	11.5	3.2
Weddellite	0.0	15.4	5.8	9.9	0.0	9.7
Uric acid	4.5	7.7	8.0	2.5	3.8	3.2
Cystine	9.2	15.4	1.5	2.5	0.0	0
Others	0	7.7	1.4	1.2	3.8	0
Total	100	100	100.0	100.0	100.0	100

in this pathology are varying but the male predominance was the most reported [9,10]. In Tunisia, boys were shown to predominate [4,11]. Our study shows a sex ratio of 1.5. The male preponderance was more pronounced in young children under 2 years, and especially in those presenting with bladder calculi (sex ratio = 2.75).

Metabolic abnormalities and infectious stones prevail in most pediatric series[10,12-17]. However, contrary to our expectations, metabolic and infectious stones were rare (6.5% and 9.4% respectively). These findings differ from studies in Europe (England: 44%; 30%[10], Greece: 48%; 28.8%[18]), in Middle East (Kuwait: 83%; 29%[19], Saudi Arabia:10.6%; 17.6%[20], Iraq: 52%; 25.5%[21] and in the Northern region of Tunisia (28.2% in each case)[22], but it shows a decrease of the infection rate with regard to our first study in 1986 where we found a 57% of cases[23].

Stone composition has changed substantially over the past decades, with a progressive increase in frequency of calcium oxalate even in the eastern hemisphere[1]. Recent epidemiology studies from different continents and countries report that calcium oxalate is the most frequent chemical compound at present[16,24-26]. According to Daudon et al[24], calcium oxalate stones in patients from developing countries are seen primarily in North Africa and Minor Asia. In our study, calcium oxalate stones were found in 52.6% of all cases. This rate is similar to those reported by Algerian[27], Moroccan[28], Chinese[26] and Turkish[29] studies. With regard to the crystalline species, whewellite was more abundant compound in children stones. Its prevalence increased with age from 48.6% in infants to 68.5% in the age class 10–19 years. The absence of whewellite type Ic, excludes primary hyperoxaluria origin of whewellite stones.

Epidemiologic observations leave no doubt that diet plays a major, if not the most important, role in the pathogenesis of urolithiasis[1]. As we previously published[30], teenagers were more likely to develop food-born hyperoxaluria in our region. These data can be mentioned to explain the high frequency whewellite stones in our study. However, further investigation must be conducted to confirm this hypothesis.

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 neighbouring country[27] in comparison to an 11% frequency reported in France[31]. The high proportion of stones, in infants, nucleated on ammonium urate (38.9%) suggests that hyperuricosuria, low phosphorus intake, low diuresis, and chronic diarrhea are risk factors[22] involved in stone nucleation in our region, which is confirmed by the predominance of the ammonium urate type IIId[9].

It has been reported that about 10–20% of children with urolithiasis have underlying anatomical abnormality of urinary tract[32,33]. Anatomical abnormalities are conducive to stone formation by allowing urine stasis as well as predisposing to infection[34].

Struvite or infection-related stones, very common in children until the last century, are rarely seen today in industrialized countries[35]. Nevertheless, epidemiological studies from

various countries continue to report a frequency of struvite stones of between 25% and 38%[24,36,37]. As it was reported by Daudon et al[9], we found a relatively low frequency of infection stones (9.7%) compared with the early publication in our region[23]. This is probably due, first, to earlier detection of urinary infections and, secondly, the greater attention paid to their treatment in recent years.

Conclusion

Our results emphasize a high percentage of calcium oxalate stones and, in contrast, a low percentage of struvite stones in Tunisia. They also show the increase of calcium oxalate stones in teenagers and the decrease of purines ones. These results confirm the change on the etiology of urolithiasis according to age. The persistence of urate stones reflects particular eating habits and infectious risk factors specific of the rural population.

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Conflict of Interest: None

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