

Metabolic Constituents of Urinary Stone Composition in Sudanese Children

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ABSTRACT

Objectives: The aim of this study was to show the biological characteristics of pediatric urolithiasis in Sudanese patient's population and evaluation of some metabolic risk factors.

Materials and Methods: We analyzed prospectively urinary stones from 175 consecutive children (129 males, 46 females), aged 3 months to 16 years. Patients were reviewed in Soba Teaching Hospital, Khartoum state Sudan, during the period October 2005-May 2009. The chemical analysis of stones was carried out by Urinary Calculi Analysis Kit, manufacturer DiaSys Diagnostic system GmbH.

One hundred and thirty blood samples (80 patients, 50 controls) were collected from patients with renal stone to screen some metabolic risk factors, serum calcium, serum phosphate, serum uric acid, and serum creatinine. Fifty samples, of 24 hours urine collection (30 patients, 20 controls) were collected to determine the excretion of urine calcium, phosphate and uric acid. It was analyzed by auto analyzer Cobas Integra 400 Plus.

Statistical Analysis: Statistical analysis of data was carried out using software SPSS 11.0 for Windows. Statistical significance was determined using chi-square test & Fisher exact test.

Results: The sex ratio was 2.8:1 boys to girls. Clinical presentation of this pathology was dominated by flank pain (67%), urinary tract infection (49%), hematuria (27%), and acute renal failure (6.2%). Stones were located in the upper urinary tract in 74.9% of cases. Calcium Oxalate was found more frequently in children stones than infants ($P < 0.0001$) and was the main component in 55.4% of stones constituents. Cystine stone was more frequent in infant than children ($P < 0.011$). Uric acid stones were more frequent among boy's stones than girls' (8% vs 0.6%) ($P < 0.05$).

Metabolic urolithiasis cases accounted for 6.3% of our patients, and earlier onset of symptoms, were more common in patients with positive family history of urolithiasis, increased frequency multiple and bilateral stones were observed in this group compared with the other etiologic groups. There was increase urinary calcium, uric acid excretion in patients with renal stones ($p > 0.009$, $p > 0.013$ respectively).

Conclusions: urolithiasis is a serious problem among Sudanese children with early onset of presentation. Proper management of UTI with a careful metabolic assessment of young stone formers is valuable in combating urolithiasis.

INTRODUCTION

The composition and clinical characteristics of urinary calculi in children vary greatly from one part of the world to another and from one historic

period to the next (Oner *et al.* 1997). This variation is related to climate, dietary, genetic, and socioeconomic factors (Kamoun *et al.* 1999). Urolithiasis (UL) can develop in pediatric patients as a result

of metabolic disorders, anatomical malformations of the urinary tract, infection, and environmental and nutritional factors (Gearhart *et al.* 1991).

Urolithiasis in children is a frequent disease characterized by its varied patho physiological background (Angwafo, III *et al.* 2000) Clinical investigations of a patient with urolithiasis include a careful history, radiological and biochemical evaluation. It is always important to define the cause of urinary calculi disease among children to prevent recurrence and possible impairing of renal function. (Kamoun *et al.* 1997). A numbers of publications have previously reported the high prevalence and particular patterns of stone disease among children in developing countries (Elder JS 2004). We lack data about Urolithiasis in Sudanese children.

MATERIALS AND METHODS

Between October 2005 to May 2009, 175 pediatric patients with Urolithiasis, their age between 3 months-16 years, in the pediatric Surgery Clinic, Soba Teaching Hospital in Khartoum state.

Patients were referred from different regions of Sudan State. Full documentation included recording of age, sex, residency, age of onset of symptoms, age of diagnosis of stone disease, clinical presentation, past medical and surgical history, family history of stone disease, and recurrence (which was considered if the patient had previous surgery or spontaneous passage of stone before presentation).

All stones were documented radiologically by renal ultrasonography (US), conventional X-ray of the abdomen (KUB), and intravenous pyelography (IVP). Stones were analysis by chemical analysis (DiaSys Diagnostic System GmbH, Germany) and character of the stone (unilateral or bilateral, single or multiple). Metabolic work up was done for patients suffering from multiple or bilateral renal stones. Metabolic work up included assessment of serum levels of calcium, phosphate, uric acid, and creatinine, Urinary 24-hrs collections were done for volume, calcium, phosphate, and uric acid , all

the parameter were measured by automated analyzer Cobas Integra 400 Plus.

RESULTS

Children under study were aged between three months to 16 years (mean age 4.96 ± 4 years). 30.1% of the cases were infants aged less than two years, 44% aged from 2 to 6 years, and 25% more than 6 years. Clinical presentation of this pathology was dominated by flank pain (67%), urinary tract infection (49%) hematuria (27%), and acute renal failure (6.2%). A positive family history of urolithiasis was recorded for 34 patients (20%).

Urolithiasis was more frequent among boys. The sex ratio was 2.8:1 (129 boys and 46 girls); ratio was 3.2:1 among infant patients, and 2.7:1 among children. Seventy five percent of the calculi were located in the upper urinary tract system and 25% in the lower one as in Fig.1.

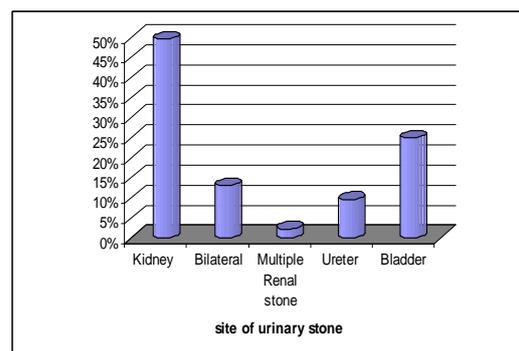


Fig. 1: distributions of urinary calculi according to stone site.

Calcium oxalate stone were the commonest constituents (55.4%), followed by ammonium urate (48.6%), Struvite (15.9%), calcium phosphate (11.4%), uric acid stones (8%), and cystine stones (5.7%). The components of the upper urinary tract calculi were calcium oxalate (40%), ammonium urate (35.4%) and calcium phosphate (21%), whereas the main components of the lower urinary tract calculi were ammonium acid urate (23%), struvite (9.1%), and calcium oxalate (10.4%).

There was significant association between upper urinary tract and calcium phosphate stones, and cystine stones $P <$

0.028, 0.045 respectively, and lower urinary tract with Struvite stones $P < 0.0001$. Cystine stones were more common in patients with positive family history $P < 0.001$.

There was no difference between the mean of total serum calcium, phosphate, serum uric acid, and serum creatinine in patients with renal stone compared to control group as in tables 1 and 2.

Table 1: Metabolic blood screen in patients with renal stone:

	Study group (Mean \pm SD)	Control group (Mean \pm SD)	Sig. (2-tailed)
S. Calcium	9.6 \pm 0.85 g/dL	9.5 \pm 0.7 mg/dL	<0.56*
S. Phosphate	4.3 \pm 0.4 g/dL	4.2 \pm 0.3 mg/dL	<0.345*
S. uric acid	3.5 \pm 1.1mg/dL	3.5 \pm 1.0 mg/dL	<0.979*
S. creatinine	0.46 \pm .24mg/dL	0.4 \pm 0.1 mg/dL	<0.089*

* P value > 0.5 no significant association

Table 2: Metabolic 24 hrs urine excretion screen in patients with renal stone:

	Study group (Mean \pm SD)	Control group (Mean \pm SD)	Sig. (2-tailed)
Calcium excretion	1.98 \pm 0.8 mg/kg/day	1.4 \pm 0.5 mg/kg/ day	<0.008*
Phosphate excretion	5.0 \pm 1.9 mg/kg/day	5.2 \pm 1.2 mg/kg/ day	<0.626
Uric acid excretion	1.0 \pm 0.5 mg/kg/day	0.6 \pm 0.4 mg/kg/ day	<0.012*

* P value > 0.5 no significant association

Evaluation of metabolic risk factors in 24-hour urine samples revealed 45 children (25.7%) with a single risk factor. Among these, hypercalciuria (1 case), cystinuria (ten cases). The stone composition, Calcium oxalate stone represent its principal component (55.4%), which was more frequent in children (64.4%) than infants (35.2%) ($P < 0.0001$). Ammonium urate represent 48.6% of stone constituents. Struvite stone frequency 15.4% of stones constituents, it was more frequent in lower urinary tract than upper one ($P < 0.0001$). Calcium phosphate stones were found in (11.4%) of stone constituents, it was more frequent in upper urinary tract than lower one ($P < 0.028$). Purine stones were (8.6%) of cases mostly observed in boys (8 vs. 0.6%% in girls) ($P < 0.043$).

DISCUSSION

Our study showed a male predominance with urinary calculi, a boys: girls ratio of

2.8:1; the ratio was 6.3 among patients with lower urinary tract stones and 2.3 among patients with upper urinary tract stones, similar result was found in Egyptian children, male more common than female ratio 2.7; the ratio was 5.3 among patients with lower urinary tract stones and 2.4 among patients with upper urinary tract stones (Aggour *et al.* 2009), also in Saudi Arabia the ratio was 2.5:1 boys to girls (Al-Rasheed *et al.* 1995), and different ratio reported by Alaya *et al* in Tunisia children found that the ratio 1.47:1 male: female (Alaya *et al.* 2009b). Patients were classified according to onset of stones into three age groups. Group I (aged < 2years) contained 33.1% of the patients; 77.8% were boys and 70% had stones in the upper urinary tract. Group II (2-6 years) contained 41.7% of the patients; 73% were boys and 71% had stones in the upper urinary tract. Group III (>6 years) contained 25.1% of the patients; 68% were boys and 86% had stones in the upper urinary tract. We hypothesize that the fact that the proportion of patients having upper urinary tract stones increases with age is most probably due to improvement of dietary habits and nutritional status of children.

Children often present with non specific symptoms, especially the younger ones, and less commonly with flank pain or hematuria. However, in this study, the main presenting symptoms were flank pain (67%), hematuria (27%) and dysuria (23%). In Tunisia children the clinical presentation of urinary calculi pathology was abdominal pain in 28%, hematuria 25.6%%, and urinary tract infection 14.3% (Alaya *et al.* 2009a). There is a variation in presenting symptoms, especially flank pain, among different countries, which may be related to the degree of awareness in the population and the onset of seeking medical advice.

In Europe, urinary stones are mainly located in the upper urinary tract and the proportion of bladder calculi does not exceed 14% (Daudon 2000), in Egypt 19% (Aggour *et al.*, 2008), and Tunisia children 20.2% (Alaya *et al.* 2009). It is absent even in other industrialized countries such as the United States of America (Stapleton 2002). Bladder stones were observed only in rural areas of

developing countries, 51.1% in Morocco (Oussama *et al.* 2000), and 71% in Cameroon (Angwafo, III *et al.* 2000a). However, in this study bladder stone frequency was 24.6% of all urinary calculi in study group, and it is more frequent in boys than girls (29.5% VS 13%) $P < 0.029$.

Several studies noted a strong association between urolithiasis and urinary tract infections (Kamoun *et al.* 1995). It is not always easy to determine if the infection is the cause or the consequence of lithiasis. The frequency of urinary tract infections was about 15 to 57% of lithiasic patients in the years 1970-1980, and does not exceed 2% in Europe at present (Jungers *et al.* 2001). In this study, infection reached 49.1% of cases comparable with that found in North America 8% (Sternberg *et al.* 2005), in England (30%), (Coward *et al.* 2003) Kuwait (29%) (Al-Eisa *et al.* 2002) and the Egypt 66% (Aggour *et al.* 2008).

The chemical analysis of the 175 stones in our study revealed that calcium oxalate is the main component, found in 55.4% of the patients' stones, followed by ammonium acid urate in 48.6%. The difference in the proportion of ammonium acid urate stones in comparison to studies from other countries and communities, including Tunisia (3%) and Armenia (5.1%), may be explained by the hotter climate and poorer dietary habits with subsequent dehydration and uric acid supersaturation.

The components of the upper urinary tract calculi were calcium oxalate (40%), ammonium urate (35.4%) and calcium phosphate (21%), whereas the main components of the lower urinary tract calculi were ammonium acid urate (23%), struvite (9.1%), and calcium oxalate (10.4%). The main components of childhood stones in Europe, in decreasing order, are struvite, calcium phosphate and calcium oxalate (Androulakakis *et al.* 1991).

The etiology and history of stone formation varies in different populations and it is represented by anatomical abnormalities, metabolic studies, dietary habits and stone composition. This study identified etiological causes in 21.7% of the 175 cases in which records were

available, including 5.7% (10/175) that were classified as cystinuria, 15.4% as infection stone, 0.5% as anatomic abnormalities and 0.5% hypercalcuria. Overall predisposing factors can be identified in 30% to 80% of the patients depending where the studies were done (Milliner and Murphy 1993; Fraser *et al.* 1999a; Pietrow *et al.* 2002a) In developing countries an idiopathic cause is reported in up to 50% of cases compared with less than 20% in developed nations (Pietrow *et al.* 2002b; Hari *et al.* 1995). The rate of anatomical abnormalities was low in this study and in other developing countries compared with 20% to 30% in developed countries (Fraser *et al.* 1999b). This result is perhaps a reflection of better diagnostic and imaging facilities in developed nations, where prenatal examination is routine. Similarly metabolic causes show wide variation from up to 50% in the United States of America, 16% in the United Kingdom, 2% in Armenia and 15% in North India.

CONCLUSIONS

Urolithiasis is a serious problem among Sudanese children with early onset of presentation. Proper management of UTI with a careful metabolic assessment of young stone formers is valuable in combating urolithiasis.

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ARABIC SUMMARY

المكونات الأيضية لحصاوى المجارى البولية عند الأطفال السودانيين

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 3 - كلية الطب - جامعة الخرطوم - السودان.

الاهداف:

الهدف من هذه الدراسة معرفة مكونات الحصاوى البولية عند الاطفال السودانيين وتقييم بعض العوامل الايضية التي تساعد في تكوين الحصاوى

الطرائق المتبعة:

تم تحليل الحصاوى المتكونة عند 175 طفل (129 اولاد، 46 بنات) تتراوح اعمارهم بين 3 شهور و 16 سنة. تم جمع الحصاوى من مستشفى سوبا الجامعي-الخرطوم-السودان خلال الفترة من اكتوبر 2005- مايو 2009. تم تحليل الحصاوى بواسطة محاليل كيميائية مصنعة بواسطة شركة المانية (GMH). ثلاثون ومائة عينة من الدم (80 مرضى - 50 عينة ضابطة) جمعت من المرضى المصابين بحصاوى الكلى للكشف عن بعض العوامل الايضية المؤدية لتكوين الحصاوى وتشمل قياس الكالسيوم ، والفوسفات غير العضوي وحمض البوليك والكرياتينين. 50 عينة من البول المجموع خلال 24 ساعة (30 مصابين - 20 عينة ضابطة) لقياس الكالسيوم والفوسفات وحمض البوليك التي تم اخراجها خلال اليوم وقد تم قياسها بجهاز (COBAS INTEGRA 400 PLUS).

التحليل الاحصائي:

تم بواسطة استخدام برنامج SPSS 11.5. الاختبارات الاحصائية التي استخدمت Chi-SQUARE AND FISHIR EXACT TEST.

النتائج:

نسبة معدل تواجد الحصاوى عند الاطفال السودانيين المصابين حسب النوع 2.8 : 1 ولد : بنت. اهم اعراض الحصاوى التي ظهرت الام جانبية عند 67% ، التهاب المجارى البولية 49%، بول دموي 27%، فشل كلوي حاد 6.2%. معظم الحصاوى وجدت في الجزء العلوي من الجهاز البولي عند 74.9% من المصابين. حصاوى الكالسيوم اوكسالات اكثر شيوعا عند الاطفال مقارنة بالرضع بدلالة احصائية $P < 0.001$ وتمثل 55.4% من مكونات الحصاوى الموجودة. حصاوى حمض الستين الاميني اكثر شيوعا عند الرضع مقارنة بالاطفال $P < 0.01$. وحصاوى حمض البوليك اكثر شيوعا عند الاولاد مقارنة بالبنات بنسبة 8% مقابل 0.6% بقيمة احصائية $P < 0.05$.

في هذه الدراسة 6.3% من الحصاوى تكونت نتيجة عوامل ايضية واهم ما يميز هذه الحصاوى ان اعراضها تظهر مبكرا وهي اكثر شيوعا عند المرضى الذين لديهم تاريخ اسري للمرض. وغالبا ما تتكون الحصاوى على جانبي الكلى ويكون حدوثها متكرر مقارنة بالانواع الاخرى من الحصاوى. هنالك زيادة في كمية الكالسيوم وحمض البوليك المخرجة خلال اليوم عند هؤلاء المرضى بدلالة احصائية ($P < 0.009$ و $P < 0.013$) على التوالي.