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METABOLIC EVALUATION FOR PEDIATRIC RENAL STONES- A STITCH IN TIME

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ABSTRACT

Objectives: To evaluate the pediatric patients with renal calculi in terms of bio-metabolic profile.
Study Design: Cross sectional study.
Place and Duration of Study: Department of pediatric nephrology the Children's Hospital and the Institute of Child Health Lahore over a period of 10 months from Nov 2016 to Sep 2017.
Material and Methods: A total 85 patients with urolithiasis up to the age of 14 years were enrolled for study. Structured history and tailored investigations were collected from all the patients. Results of the physical examination, blood chemistry, and urinary excretion of metabolites (urinary calcium, citrate, magnesium and oxalate) were recorded.
Results: Out of 85 patients; 65% were males and 35% were females (2:1); mean age at presentation was 8.15 ± 5.04 years. Hypertension was documented in 57% patients. Mean level of urea and creatinine was 73.02 ± 59mg/dl and 4.435 ± 4.024mg/dl respectively. Vitamin D level was 37 ± 15.6ng/ml while serum PTH level was 51.2941 ± 26.067pg/l. Serum calcium and phosphorus was 8.54 ± 1.18 and 5.0224 ± 0.885 respectively. Among all patients, 95% were found to have metabolic abnormalities. The most common was hypercalciuria (54%) followed by hyperoxaluria in 28% patients. Hypocitraturia was seen in 21% patients. Distal renal tubular acidosis was found in 6% children. Only 5% children were having low magnesium level in their urine.
Conclusion: Majority of the children with stone disease had underlying metabolic risk factor and in our setting, hypercalciuria is the most common one.

Keywords: Distal renal tubular acidosis, Hypercalciuria, Hypocitraturia, Metabolic workup, Urolithiasis.

INTRODUCTION

Urolithiasis is endemic in certain regions like middle east and southeast asia. Pakistan is included in the 'stone belt' having renal calculus in 2% to 3% of pediatric population[1]. Worldwide, the prevalence of the disease has been reported as 1-15%. The incidence rate of the disease in children has increased over the past few years[2]. The stone is not a disease itself but it may be one of the serious signs of other systemic illnesses. Therefore, thorough early and comprehensive diagnostic evaluation is mandatory for children with first stone event[3]. High rate of recurrence up to 26% to 53% within 10 years of first episode has been documented. Etiology of stone formation depends upon anatomical abnormalities, metabolic disorders and dietary habits[4]. Systemic diagnostic assessment starts with detailed medical history and laboratory workup. Approximately 40% of the children with calculi have positive history of stones in the family members[5]. In children, other risk factors and metabolic derangements usually co-exist. The outcome is determined by not only the presence of renal stones but also the type of concurrent disease[6]. In order to decrease the long term mortality and morbidity, it is necessary to determine the characteristics and etiology of the stone appropriately. The rationale of this study was to conduct metabolic evaluation of the children with renal calculi which will help in early diagnosis of underlying metabolic cause and treatment. This will be helpful in halting the progression of disease. We lack the local data as no such study has been previously conducted in our setup. The results of this study will be useful in decreasing mortality and morbidity.

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PATIENTS AND METHODS

A total of eighty five consecutive patients were included in this cross sectional study. Sample size was calculated with WHO sample size calculator, keeping power of test 80%, level of significance at 5% and expected percentage at 2% of urolithiasis in pediatric population[1]. The study was conducted in the nephrology department at The children's Hospital Lahore and Institute of Child Health Lahore. Patients up to the age of 14 years both from indoor and outdoor departments were included in the study. The study was approved by ethical review committee of the institution. Informed written consent was taken from all the parents.The inclusion criteria were; documented episode of renal colic or hematuria due to renal stone or on imaging either by ultrasonography or enhanced computerized tomography in either kidney. Exclusion criteria were solitary kidney, presence of congenital anomaly of kidney or urinary tract, primary or secondary reflux disease or isolated bladder calculi. Patients on therapeutic dosages of vitamin D, calcium, antacid, diuretic, potassium citrate and vitamin C were also excluded. Metabolic evaluation was performed after treating active urinary tract infection. During first visit, history regarding dietary habits, stone formation and metabolic causes were elicited. Blood pressure was recorded in all the patients. A 5cc non-EDTA serum sample was taken for the measurement of calcium, phosphorus, urea, creatinine, uric acid, PTH, vitamin D, while heparinized arterial sample was taken for blood gases. The patients presenting with acutely impaired renal functions secondary to complications of calculus were stabilized until normalization of renal functions and then considered for study. Twenty four hours urine samples for calcium, oxalate, and citrate were collected. In patients having suspicion of renal tubular acidosis, anion gap was also calculated. The relevant information and results were entered on a predesigned proforma. Criteria for labeling various metabolic abnormalities are given in table-I. Data was analyzed in SPSS version 21. Mean and standard deviations were determined for the biochemical parameters observed e.g. calcium, phosphorus, urea etc. (table-II). Percentages were calculated for various metabolic risks factors as hypercalciuria, hyperoxaluria, hypocitraturia and renal tubular acidosis were detected from laboratory work up.

RESULTS

Out of 85 patients, 55 (65%) were males and 30 (35%) were females. The mean age of presentation was 8.15 ± 5.04 years. Hypertension was documented in 57% of patients while rest of them were having normal blood pressure at time of presentation. Mean levels of different serum biochemical parameters are shown in table-II. Hypercalciuria was observed in 46 (54%) children; among them forty one were having idiopathic hypercalciuria, while in four patients it was associated with distal renal tubular acidosis (RTA) and in one with increased urinary oxalate level. Hyperoxaluria was found in twenty four children (28%). Hypocitraturia was found in 18 (21%) patients which was associated with hypercalciuria, distal RTA and hyperoxaluria (10,6,2 patients respectively). Low urine magnesium level was seen in 4 children (5%). Distal renal tubular acidosis was present in six (6%) patients while four (5%) had no identifiable cause of calculus disease. Thus an underling metabolic cause was found in 95% of patients (table-III).

DISCUSSION

The frequency and etiology of renal calculi shows marked diversity. The overall life time risk for renal calculi is estimated as 1 in 15 percent[7]. The pediatric patients with renal stones should be thoroughly evaluated as it is very likely that there are predisposing factors. Early and accurate diagnosis is necessary for decreasing morbidity and mortality[8]. Majority of the participants of study (95%) were having one or more underlying metabolic pathology. Male patients were almost double than that of female which is almost similar to the studies conducted previously[9]. We found hypercalciuria as most common cause (54%) of stone disease. Sepahi *et al* in their study

documented almost 28% patients with hyper-calciuria[10]. Rellum found in their research that 47% patients were having high urinary output of calcium[11]. Second common metabolic defect observed is hyperoxaluria; our incidence is slightly higher (28%)as compared to that mentioned by Elmaci *et al* which is 11.4% in their larger group of patients[12]. Team of Alpay diagnosed 87% patients with metabolic derange-ment in their study group and found 33.1% of them with hypocitraturia while in our study, hypocitraturia was documented in 21% patients[13] found signifantly[15,16]. Although the uric acid stones are present in significant number in adult population, but they are less frequent in pediatric patients (11% vs 2%)[17]. Similarly, cysteine stones are seen rarely in our region[18,19]. It is very unfortunate that stone disease in pediatric population has not been considered as significant previously and comparable data is missing. This topic always has conflictory issues as metabolic workup and its interpretation is cumbersome and expensive and sometime has no clear answer. The training of clinicians is insufficient regarding

Table-I: Diagnostic criteria for metabolic disorder[14].

Metabolic abnormality	**Criteria**
Hyper-calciuria	>4mg/kg/day
Hyper-oxaluria	>44mg/kg/day
Hypo-citraturia	<320mg/day
Low urine magnesium level	<0.8mg/kg/24hr
Renal tubular acidosis	urine pH >5.5 with non-anion gap metabolic acidosis

Table-II: Serum biochemical parameters for study patients.

Biochemical parameters	**Mean (Standard Deviation)**
Serum Calcium (mg/dl)	8.54 ± 1.18 (6.10-10.3)
Serum Phosphorus (mg/dl)	5.0224 ± 0.885 (3.2-6.8)
Serum urea (mg/dl)	73.02 ± 59.42 (14-317)
Serum creatinine(mg/dl)	4.44 ± 4.02 (0.4-16.5)
Serum 25(OH) 2D3 (ng/dl)	8.4 ± 1.81 (6.1-10.3)
Serum PTH (pg/l)	51.2941 ± 26.06
Serum uric acid (mg/dl)	4.7 ± 1.035 (2.4-6.8)

Table-III: Urinary metabolic risk factors.

Urinary Findings	Patients (%)
Hypercalciuria	46 (54%)
Hyperoxaluria	24 (28%)
Hypocitraturia	18 (21%)
Low urine magnesium level	4 (5%)
Distal Renal tubular acidosis	7 (6%)
Un-identified etiology	4 (5%)

Joshi *et al* diagnosed 5% patients with distal renal tubular acidosis while in our study 6% were fulfilling the criteria[14]. Low urinary magnesium level was found in 5%. Although the incidence of renal calculus and its etiology varies significantly with genetic, ethnic, geographical and environ-mental background. But various studies signifi-cantly provide evidence about underlying metabolic cause of calculus disease even among infants, in whom extrinsic factors are considered less influencing; the metabolic problems were metabolic and genetic diseases. Though screening can be helpful but due to high prevalence and recurrent nature enormous financial and human resources are needed[20]. Our study has very small sample size and conducted at single center with limited laboratory facilities. The less common metabolic defects (uric acid and cysteine) should also be studied comprehensively. Secondly, this research is incomplete without collaborative participation of urologists as composition of calculi should be considered to support the

diagnosis. Finally, no diagnosis is complete now a days until the genetic confirmation is there so we need a larger trial involving all departments.

CONCLUSION

Majority of the children with stone disease had underlying metabolic risk factor and in our setting, hypercalciuria is the most common one.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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