Research Article

J Ped. Nephrology 2018;6(1)
http://journals.sbmu.ac.ir/jpn

Metabolic Evaluation in Pediatric Urolithiasis: Our Experience

How to Cite This Article: Gadekar C, Sharma A, Parab S, Mane N, Andankar M, Pathak H. Metabolic Evaluation in Pediatric Urolithiasis: Our Experience. J Ped. Nephrology 2018;6(1).

Chetan Gadekar,
Amit Sharma,*
Sandesh Parab,
Narsing Mane,
Mukund Andankar,
Hemant Pathak

Department of Urology, TNMC & BYL Nair Hospital, Mumbai, Maharashtra, India.

*** Corresponding Author**
Amit Sharma, MD
Department of Urology, TNMC & BYL Nair Hospital, Mumbai, Maharashtra, India.
E mail: dramiturology@gmail.com

Introduction: Pediatric urolithiasis is a morbid condition that is often associated with underlying metabolic disorders. It is essential to diagnose and manage the underlying metabolic disorder along with management of urolithiasis to prevent stone recurrence and decrease the morbidity.
Materials and Methods: This retrospective observational study was conducted in 50 patients below 15 years of age with urolithiasis. Urine collection was done for 24 hours in toilet-trained children and spot samples were taken from younger children. The urinary parameters that were evaluated included calcium, oxalate, citrate, uric acid, and total urine volume. The serum levels of calcium, phosphorus, creatinine, uric acid, electrolytes, parathormone, and albumin were also measured. Stone analysis was done whenever possible.
Results: There were 32 males and 18 females. Sixty-two percent of the patients had a low calcium intake and 70% of the children had a history of low water intake and had a low urine volume over 24 hours. Half of the children had serum metabolic abnormalities, including hypocalcaemia (n=19,38%), hypocalcaemia with hyperphosphatemia (n=2, 4%), hypercalcemia (n=2, 4%), and hyperuricemia (n=2,4%). Urinary abnormalities were detected in 42% of the children (n=21). These abnormalities included hypocitraturia in 11 patients (50%), hypercalciuria in 7 patients (30%), hyperoxaluria in 1 patient (6%), and hyperuricosuria in 2 patients (12%). Stone analysis was done in 18 patients. Fifteen patients (30%) had calcium oxalate stones, two patients (4%) had uric acid stones, and one patient had a mixed stone.
Conclusions: It is important to maintain an optimal blood calcium level and increase fluid intake to prevent stone formation in children.

Keywords: Urolithiasis; Pediatric; Metabolic Disorders.

Received: June-2017
Revised: Aug-2017
Accepted: Sep-2017

Running Title: Metabolic Evaluation in Pediatric Urolithiasis

Introduction

Once rare, the incidence of pediatric urolithiasis is increasing, particularly in females [1]. The incidence of urolithiasis in children has been reported to be about 2 to 3% [2, 3]. However, there is a great variation in its incidence, composition, location, and clinical characteristics, which is related to climatic, dietary, and socioeconomic factors [2]. This condition is commoner in whites than Asians and Africans [4]. Predominantly, renal calculi are seen in western populations whereas Asians and Africans suffer from vesical calculi [4].

The predisposing factors for pediatric urolithiasis have been reported to be genetic inheritance, nutrition, metabolic abnormalities, environmental factors, anatomical characteristics, and calculus-inducing medications [2, 5]. It is important to identify children at increased risk of recurrent stone disease and target the management of biochemical derangements including management of the stone disease [2]. The compositional analysis of the extracted stones helps to diagnose the underlying pathological and biochemical derangements, guiding further work-up and

treatment [2]. Metabolic disorders are more common in children; therefore, it is mandatory to do metabolic evaluations in these patients [6]. This study was conducted to investigate the metabolic risk factors of urolithiasis in children and review the available literature in this regard.

Materials and Methods

This retrospective observational study was conducted in50 patients aged below 15 years with urolithiasis who were managed at a tertiary center from January 2014 to December 2016. After confirming a diagnosis of urolithiasis using standard imaging techniques, (ultrasonography and intravenous pyelography with computed tomography in selected cases), these children were evaluated for the presence of any underlying metabolic disorders.

Detailed history of dietary habits, average water intake per day over the last few months, and intake of medications, if any, was noted.

A detailed family history of urolithiasis was also taken. Urine collection was done for 24 hours in toilet-trained children and spot samples were collected in younger children. The urinary parameters that were evaluated included calcium, oxalate, citrate, uric acid, and total urine volume. The serum levels of calcium, phosphorus, creatinine, uric acid, electrolytes, parathormone, and albumin were also measured. Stone analysis was done whenever possible.

Patients with urinary tract infection (UTI), those who were already diagnosed with metabolic disorders, and children receiving calcium, vitamin D, and vitamin C supplementation were excluded from this study.

Results

Medical records of 50 patients over a period of two years were evaluated retrospectively. There were 32 males (64%) and 18 females (36%). Twenty-two patients (44%) were below 5 years of age. Sixty-two percent (n=31) had a low calcium intake which was related to poor milk intake or vegetarian diet in older children and top fed infants. Seventy percent (n=35) of the children had a history of low water intake and hence had a low urine volume over 24 hours.

Fifty percent (n=25) of the children had serum metabolic abnormalities, including hypocalcemia in (n=19, 38%), hypocalcaemia with hyperphosphatemia (n=2, 4%) hypercalcemia (n=2, 4%) and hyperuricemia (n=2,4%) (Table 1).

Table 1. Serum abnormalities in 25 patients

Serum Abnormality	Number of patients (n=25)
Hypocalcemia	19
Hypocalcaemia and Hyperphosphatemia	2
Hypercalcemia	2
Hyperuricemia	2

Urinary abnormalities were detected in 42% of children (n=21), including hypocitraturia in 11 patients (50%), hypercalciuria in 7 patients (30%), hyperoxaluria in 1 patient (6%), and hyperuricosuria in 2 patients (12%) (Table 2).

Stone analysis was done in 18 patients.

Table 2. Urinary abnormalities detected in 21 patients.

Urine abnormality	Number of patients (n=21)
Hypocitraturia	11
Hypercalciuria	7
Hyperoxaliuria	1
Hyperuricosuria	2

Fifteen patients (30%) had calcium acid stones, and one patient had mixed stone (Table 3).

Table 3: Stone analysis in 18 patients.

Stone Type	Number of Patients (n=18)
Calcium Oxalate	15
Uric Acid	2
Mixed	1

Table 4. Suggested management of urolithiasis caused by metabolic abnormalities.

Metabolic Abnormality	Initial Treatment	Second line Treatment
Hypercalciuria	Reduction in dietary sodium Dietary calcium at RDA Thiazides	Potassium citrate Neutral phosphate
Hyperoxaluria	Adjustment of dietary oxalate Potassium citrate	Neutral phosphate Magnesium Pyridoxine
Hypocitraturia	Potassium citrate Bicarbonate	
Hyperuricosuria	Alkalinization	Allopurinol
Cystinuria	Alkalinization Reduction of dietary sodium	Tiopronin (thiola) D – penicillamine Captopril

The family history was non-contributory in all patients.

Discussion

In children, urolithiasis is a morbid disease condition and is often associated with underlying metabolic and genitourinary anomalies [2]. Metabolic disorders can be detected in approximately half of the children with urolithiasis [4]. The morbidities and sequela of urolithiasis in children are urinary tract infection (UTI), urinary obstruction, scarring of the urinary tract, hypertension, and progressive deterioration of the renal function [2]. The incidence of UTI is approximately 8-45.9% in children with urolithiasis that increases to 62% in children below five years of age [2, 7, 8, 9, 10], which mandates screening of all children who present with stone disease to rule out any underlying metabolic disorders or risk factors and manage the condition accordingly.

Low dietary intake of calcium is one of the risk factors for pediatric urolithiasis [2]. Low calcium intake in children leads to an increase in the available intestinal oxalate and subsequently increases oxalate absorption, resulting in the super saturation of calcium oxalate [2]. Low calcium intake also stimulates calcitriol production, which leads to hypercalcemia and inhibition of parathormone production causing hypercalciuria [2, 11]. In 1997, Curhan et al conducted a large cohort study and reported a decreased incidence of nephrolithiasis in subjects who had increased levels of dietary calcium [12]. In the present study, 31 patients (62%) had a low calcium intake, hypocalcaemia was detected in 19 patients (38%), and hypercalcemia was seen in 2 patients (4%).

Low urinary volume has been reported to contribute to pediatric urolithiasis [2]. Borghi L et al reported that low urine volume is a risk factor of nephrolithiasis and recommended a high intake of water as the initial therapy [13, 14]. Gajengi et al also reported that low urine volume and low fluid intake are contributory factors for pediatric urolithiasis [2]. Therefore, the first line of management of pediatric urolithiasis is a high oral fluid intake [2]. All mothers need to be instructed to give adequate water to maintain the morning sample of urine as pale yellow or straw color [2]. Adolescents are advised to maintain a daily urine output of 2 liters [6]. In this study, 70% of the patients (n=35) had a history of low water intake.

Hypocalcemia is usually related to a low calcium intake, high intake of phosphates, and a low magnesium intake. However, it was difficult to find a correlation between hypocalcemia and urolithiasis as the majority of the children in this study had a low water intake and a low urine volume. Hypercalcemia and hyperuricemia were also found in 2 patients each, and both were idiopathic [14].

In the absence of Indian literature for normal reference values of 24-hour urinary metabolic values, the normal reference values were taken from the western literature in this study. In our study, 24-hour urinary abnormalities were found in 42% (n=21) of the patients with half of them having hypocitraturia (n=11). This finding is comparable with other studies in the literature. Naseri et al, Erbagci et al, and Gajengi et al also reported that hypocitraturia was the most common urinary metabolic abnormality detected in their studies [2, 15, 16].

Hypercalciuria is defined as excretion of more than 4mg/kg/day of urinary calcium [4]. It is found in as many as 4% of healthy children and predisposes them not only to urolithiasis but also to hematuria, dysuria, urgency, and possibly to recurrent UTI [4]. Most cases are idiopathic. Dent's disease is an X-linked genetic disorder with defects in the renal chloride channel (CLCN 5) associated with significant hypercalciuria and

urolithiasis [6].

Hyperoxaluria is found in up to 20% of the children who have nephrolithiasis [4]. Enteric hyperoxaluria may result from a diet rich in oxalate and is also seen in children with malabsorption. Foods high in oxalate include strawberry, star fruit, sweet potatoes, wheat bran, tea, cocoa, pepper, chocolate, parsley, beets, spinach, nuts, and citrus juices. Excess vitamin C is metabolized to oxalate and can lead to hyperoxaluria. Mild idiopathic hyperoxaluria is commonly identified concurrently with idiopathic hypercalciuria. In children with malabsorption, undigested fatty acids form a complex with calcium that would otherwise bind with oxalate in the intestines. The increased level of unbound oxalate leads to higher absorption of enteric oxalate. The presence of increased luminal bile salts damages the colonic epithelium, which also leads to increased oxalate absorption. Therefore, all children with chronic diarrhea, fat malabsorption, and digestive disorders are prone to hyperoxaluria and subsequent stone formation. Hyperoxaluria was seen in one case, which was lower than what is quoted in the western literature [6]. Such discrepancies may be mostly due to differences in the dietary pattern and use of western pediatric urinary standards, as we do not have reference values for Indian pediatric population.

Primary hyperoxaluria is a rare autosomal-recessive disorder of hepatic enzymes causing marked overproduction of oxalate. Type I primary hyperoxaluria is more severe. There is deficiency of alanine-glyoxylate aminotransferase (AGT) and the defect is on chromosome band 2q37.3. Type II disease is caused by a defect in the enzyme glyoxylate reductase/hydroxypruvate reductase and the defect is related to chromosome 9.

Most patients present with urolithiasis or nephrocalcinosis during infancy or childhood. Aggressive stone formation is common with progressive renal deterioration.

Hyperuricosuria is defined as excretion of uric acid more than 10mg/kg/day [5]. It has been documented in 2% to 10% of children and adolescents found to have a metabolic predisposition to kidney stone formation [4]. Uric acid is very poorly soluble in acidic urine so low pH is a necessity for stone formation.

Uric acid overproduction may result from an inborn error of purine metabolism. Lesch-Nyhan syndrome is one such disorder. There is a complete deficiency of HGPRT enzyme and the disease presents with mental retardation, spasticity, choreoathetosis, and self-mutilation along with hyperuricemia and hyperuricosuria. Urolithiasis may present early in the disease course in the first year of life. In this study, uric acid stones were seen in two patients; both of them had hyperuricemia and hyperuricosuria [5]. Stone analysis showed calcium oxalate stones in 15 patients, although hypercalciuria was seen in 7 patients and hyperoxaluria was seen in only one patient. Such findings may be due to variations in the reference values adopted from the western literature. Such contradictions are also seen in other Indian studies, highlighting the need for urinary reference values for Indian pediatric population. The suggested management plan for pediatric patients with urolithiasis who have associated metabolic abnormalities has been briefly summarized in Table 4 [17].

Conclusions

Hypocalcemia secondary to poor dietary intake is the most common serum abnormality that is correctable with simple dietary interventions and providing proper advice to parents. Hypocitraturia is the most common urinary abnormality. Poor water intake is the most common risk factor for formation and recurrence of urinary calculus. It is important to maintain an optimal blood calcium level and increase the fluid intake to prevent stone formation in children.

Acknowledgement

None declared

Conflict of Interest

None declared

Financial Support

None declared

References

1. Partalis N, Sakellaris G. Pediatric urolithiasis. Essentials in PediatrUrol 2012;79-88 ISBN:978-81-308-0511-5.
2. Gajengi AK, Wagaskar VG, Tanwar HV, Mhaske S, Patwardhan SK. Metabolic evaluation in paediatric urolithiasis: A 4-year open prospective study. J ClinDiag Research, 2016 (Feb);10(2):PC04-PC06.
3. Spivacow FR, Negri AL, del Valle EE, Calvino I, Fradinger E, Zanchetta JR. Metabolic risk factors in children with kidney stone disease. PediatrNephrol. 2008;23:1129-33.
4. Nicoletta JA, Lande MB. Medical evaluation and treatment of urolithiasis. Pediatric Clinics of North America. 2006 Jun 30;53(3):479-91.
5. Davis ID, Avner ED, Behrman RE, Kliegman RM,

Jenson HB. Nelson textbook of Pediatrics. 17 ed, Philadelphia, Saunders. 2004, pp:1822-25.
6. Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA. Campbell-Walsh Urology: Expert Consult Premium Edition: Enhanced Online Features and Print, 4-Volume Set. Elsevier Health Sciences; 2011 Aug 25.
7. Dursun I, Poyrazoglu HM, Dusunsel R, Gunduz Z, Gurgoze MK, Demirci D, et al. Pediatricurolithiasis: an 8-year experience of single centre. IntUrolNephrol. 2008;40:3-9.
8. Sternberg K, Green eld SP, Williot P, Wan J. Pediatric stone disease: an evolving experience. J Urol. 2005;174:1711-14.
9. Alpay H, Ozen A, Gokce I, Biyikli N. Clinical and metabolic features of urolithiasis and microlithiasis in children. PediatrNephrol. 2009;24:2203-09.
10. Bioci M, Saraga M, Kuzmi AC, Bahtijarevi Z, Budimir D, Todori J, et al. Pediatricurolithiasis in Croatia. CollAntropol. 2003;27:745-52.
11. Tefekli A, Esen T, Ziylan O, et al. Metabolic risk factors in pediatric and adult calcium oxalate urinary stone formers: is there any difference? Urol Int. 2003;70(4):273-77.
12. Craven BL, Passman C, Assimos DG. Hypercalcemic States Associated with Nephrolithiasis. Rev Urol. 2008;10(3):218–26.
13. Borghi L, Schianchi T, Meschi T, Guerra A, Allegri F, Maggiore U, et al. Comparison of two diets for the prevention of recurrent stones in idiopathic hypercalciuria. N Engl J Med. 2002;346(2):77-84.
14. Borghi L, Meschi T, Amato F, Briganti A, Novarini A, Giannini A. Urinary volume, water and recurrences in idiopathic calcium nephrolithiasis: a 5-year randomized prospective study. J Urol. 1996;155(3):83943.
15. Naseri M, Varasteh AR, Alamdaran SA. Metabolic factors associated with urinary calculi in children. Iran J Kidney Dis. 2010;4(1):32-38.
16. Erbagci A, Erbagci AB, Yilmaz M, et al. Pediatric urolithiasis-evaluation of risk factors in 95 children. Scand J UrolNephrol. 2003;37(2):129-33.
17. Milliner DS. Urolithiasis. In: Pediatric nephrology. Philadelphia: Lippincott Williams & Wilkins; 2004. p. 1104.