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Clinical characteristics and metabolic abnormalities in preschool-age children with urolithiasis in southeast Anatolia

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Abstract *Objective:* Data on urolithiasis in preschool-age children are limited. The aim of this study was to investigate the metabolic etiology and clinical findings of preschool-age children with urolithiasis.
Methods: The medical records of 143 preschool-age children (81 boys, 62 girls, aged 2—6 years) with urolithiasis were retrospectively analyzed. Results of physical examination, serum biochemistry, and urine metabolic evaluation (including urinary citrate, oxalate, calcium, uric acid, cystine, and magnesium) were recorded.
Results: The mean age at diagnosis was 3.7 ± 1.3 years. A family history of stone disease was found in 79.7% of patients, and 37% of parents had consanguineous marriages. The most common presenting symptoms were hematuria (33%) and urinary tract infection (UTI; 29%). Metabolic abnormalities were found in 119 (83.2%) patients, including hyperuricosuria in 24.5%, hypocitraturia in 23.8%, hyperoxaluria in 21.7%, hypercalciuria in 21.0%, cystinuria in 7.7%, and hypomagnesuria in 1.4%. Multiple metabolic abnormalities were found in 24 (16.8%) patients. Results of 28 stone analyses revealed calcium oxalate or phosphate, cystine, and uric acid in 15, nine, and four of the patients, respectively. ^{99m}Technetium—dimercaptosuccinic acid renal scintigraphy revealed that 27.8% of the children with UTI had renal parenchymal scarring, with only four of them having vesicoureteral reflux.
Conclusion: The most frequent metabolic abnormalities in preschool-age children with urolithiasis were hyperuricosuria and hypocitraturia. A comprehensive investigation of stone disease in children presenting with hematuria and UTI is important to prevent the development of renal parenchymal scarring.

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Introduction

Urolithiasis in childhood is different from adults regarding etiology, presentation, incidence, and natural history. Urolithiasis in children is a disease that is painful, sometimes necessitates invasive procedures, and may lead to harmful effects on kidney. Although there are few data about childhood urolithiasis, recent reports have indicated the rising incidence of urolithiasis in children [1]. Because childhood urolithiasis is usually associated with metabolic abnormalities, which may result in recurrent stone formation, epidemiologic and metabolic characteristics of stone-former children deserve further investigation [1,2].

Worldwide, major variations have been reported among occurrence of urolithiasis in children. Prevalence of urolithiasis widely varies depending on geographic location, as well as hereditary and economic factors. Stone disease is endemic in Turkey, Pakistan, and Saudi Arabia, in addition to some South Asian and African countries [3]. In the USA, the geographic variation in the prevalence of kidney stone disease showed higher prevalence in the southeast than the northwest [4]. Urolithiasis was found to represent 8% of the underlying etiological factors for development of chronic kidney disease in Turkish children [5,6].

Although urolithiasis may affect children of all ages, little information is available regarding preschool-age children [7,8]. The prevalence of urinary stones in Turkey is high, particularly in the southeast. In this study, we evaluated the clinical characteristics and metabolic risk factors of urolithiasis in preschool-age children living in southeastern region of Turkey.

Patients and methods

This study was conducted in preschool-age pediatric patients aged 2–6 years with the diagnosis of urolithiasis at Diyarbakır Children's Hospital. Medical records of patients were reviewed for the following clinical and laboratory data: gender, age at diagnosis, family history of urolithiasis, parental consanguinity, presenting symptoms, accompanying urinary tract infection (UTI), urinary tract abnormalities, and metabolic abnormalities. Stone composition of spontaneously passed or surgically removed stones was also recorded. Ethical approval was obtained from the local ethics committee. All patients were followed up bimonthly with urinalysis and ultrasound examination.

The diagnosis of urolithiasis was made after passage of a stone, by ultrasound (US), and/or, in suspicious cases, by computed tomography (CT). CT examinations were performed on patients who presented with macroscopic hematuria, renal stones leading to obstructive uropathy, and flank pain. All cases were reevaluated with repeated US examination by a second sonographer to exclude artefactual images. Urinary calculi with an ultrasonographic diameter of $\leq$3 mm were defined as microlithiasis, and urinary calculi $>$3 mm in diameter were diagnosed as urolithiasis [9]. However, we evaluated both microlithiasis and urolithiasis as a whole. Following the diagnosis of urolithiasis, the patients were re-examined repeatedly by US. Voiding cystourethrography and ^{99m}-technetium dimercaptosuccinic acid (^{99m}Tc–DMSA) were performed on patients with history of recurrent UTIs or if recurrent UTI was detected during follow-up visits. The diagnosis of a UTI was done based on the presence of pyuria (defined as $>$5 white blood cells per high-power field), urinary nitrite and leukocyte esterase positivity, and positive urine culture (i.e., $>10^5$ colony-forming units per ml of a microorganism).

Serum sodium, potassium, calcium, magnesium, phosphate, uric acid, and parathormone levels were measured by standard methods. After treatment of the symptomatic stone episode and UTI, the levels of urinary calcium, oxalate, citrate, uric acid, cystine, magnesium, and creatinine were measured for metabolic evaluation from a 24-h urine in cooperated children, or from spot urine mineral-to-creatinine ratio in younger patients. Absolute urine concentrations of metabolic variables in 24-h urine sample and/or spot urinary mineral-to-creatinine ratios were determined and compared with reference values to define metabolic abnormalities (Table 1) [10,11].

All urine samples were collected in clean plastic bottles, with 10 ml of 6 N hydrochloric acid added as a preservative for 24-h urine samples. No preservative was added to spot urine samples. Each collected spot urine sample was immediately centrifuged at 1258 *g* at 4 °C for 3 min and then transferred into plastic tubes. The pH levels were measured by a dipstick analysis with LabStrip U11Plus (77 Elektronika Kft, Budapest, Hungary) and the biochemical parameters were determined by colorimetric method with Architect 1600c (Abbott Laboratories, Irving, TX, USA). Phosphorus, magnesium, calcium, uric acid, and creatinine levels were determined with Abbott kits, but citrate and oxalate levels were determined with different manufacturer kits (Abcam, Cambridge, UK), which were adapted to the same autoanalyzer.

The patients with metabolic risk factors were managed according to the underlying metabolic abnormality. An X-ray diffraction method was implemented to determine if the stone surgically removed or if the stone had spontaneously passed. The X-ray diffraction method is based on

Table 1 Normal values for urinary solute excretion.

Metabolite	Age	Random (mg/mg)	24-h (All ages)
Calcium	<12 mo	<0.81	<4 mg/kg
	1–3 y	<0.53	
	3–5 y	<0.40	
	5–7 y	<0.30	
	>7 y	<0.21	
Oxalate	0–6 mo	<0.28–0.26	<45 mg/1.73 m^2
	7–24 mo	<0.11–0.14	
	2–5 y	<0.08	
	5–14 y	<0.06–0.065	
	>16 y	<0.032	
Citrate	0–5 y	>0.20–0.42	>0.14 g/1.73 m^2
	>5 y	>0.14–0.25	
Cystine	1–6 mo	<0.112	<50 mg/1.73 m^2
	>6 mo	<0.038	
Uric acid	>2 y	<0.56 mg/dl per GFR	<815 mg/1.73 m^2
Magnesium	>2 y	>0.13	>0.8 mg/kg

GFR = glomerular filtration rate.