Metabolic Disorders in Turkish Children With Urolithiasis

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OBJECTIVE To review metabolic disorders in Turkish children with urinary tract stone disease.

MATERIALS AND METHODS The medical records of 308 pediatric patients with the diagnosis of urolithiasis between 1996 and 2008, whose disease progression was followed in a single tertiary-care center, were reviewed retrospectively. Two hundred forty-eight patients whose metabolic analyses were performed were included in the study.

RESULTS Of the 248 patients participating in the study, 142 (57%) were men and 106 (43%) were women. The median age of the patients was 48 months (minimum-maximum, 2-180 months). Seventy-six percent of the patients had metabolic disorders. Of all patients, 44% had 1, 23% had 2, and 7% had 3 metabolic disorders. Hypercalciuria, hypocitraturia, hyperoxaluria, hyperuricosuria, and cystinuria were detected in 41%, 39%, 22%, 9%, and 4% of the patients, respectively. The rate of multiple stone formation, infection, and recurrence was significantly higher in the 0-2 years age group ($P = .030$, $P = .001$, $P = .019$, respectively). The median age of patients was greater ($P = .001$) in patients with hyperoxaluria in comparison with other metabolic disorders. Compared with other metabolic disorders, multiple stones and recurrence were more frequent in patients with cystinuria ($P = .022$ and $P = .008$, respectively). The size of the stones was greater in patients with hyperuricosuria in comparison with other metabolic disorders ($P = .009$).

CONCLUSION The majority of children with urinary tract stone disease exhibited ≥1 metabolic risk factors. Metabolic risk factors should be evaluated in all children with urinary stone disease to provide appropriate treatment. UROLOGY 85: 909–913, 2015. © 2015 Elsevier Inc.

Urolithiasis is a condition resulting in a crystallized mass mixed with protein and lipid found in the kidney and the urinary tract, resulting from metabolic, endocrinologic, and urologic causes.[1] Pediatric urolithiasis is less common than in adults, and its characteristics, incidence, etiology, and localization vary greatly by geographic region.[2] The actual incidence of urolithiasis in children is unknown with a prevalence of 1%-5% in the developed countries and 5%-15% in developing countries.[3] The prevalence of urolithiasis in Turkey has been reported as 14.8%.[4] Although there are insufficient data in children, an incidence of urolithiasis in Turkish school-age children as 0.8% was reported by Remzi et al.[5]

In the majority of pediatric patients with urolithiasis, a metabolic cause for stone formation can be identified and several metabolic disorders are well-defined (eg, cystinuria or primary hyperoxaluria type 1). There is a large subgroup of patients showing a subtle increase of urinary lithogenic factors (calcium, oxalate) or a reduction of stone inhibitory substances, like urinary citrate.[6]

In Turkey, the rate of metabolic disorders in the studies on childhood urinary tract stone disease was reported to be 33.0%-83.2%.[7-9] The recurrence rate of stones due to metabolic abnormalities in children is high, and this rate can be up to 50%, if medical treatment protocol is not followed.[10] Children exhibit more ambiguous signs and symptoms of urolithiasis than adults, leading to delayed diagnosis, resulting in chronic pyelonephritis and end-stage renal failure.[1] The aim of this research was to review metabolic risk factors in urolithiasis patients whose progress was investigated at our clinic.

MATERIALS AND METHODS

In this study, the medical records of 308 patients, whose progress was investigated at the İstanbul Bakırköy Maternity and Children's Diseases Training and Research Hospital, Division of Pediatric Nephrology, with the diagnosis of urolithiasis, were evaluated retrospectively. The patients whose urinary metabolic screens showed anomaly were included in the study. The patients who did not have any metabolic screens were excluded.

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Also, patients with renal anatomic anomalies and those who developed urinary stone disease owing to the use of high-dose vitamin D were excluded from the study. For the remaining 248 patients, data related to age, gender, family history, and consanguineous marriage were extracted from the medical records of the patients. Data for urea, creatinine, uric acid, sodium, potassium, chlorine, magnesium, calcium, phosphorus, alkaline phosphatase, parathyroid hormone, the sodium-nitroprusside test, blood gases, the 3-day spot urinary calcium-to-creatinine ratio, the 24-hour metabolic stone analysis, and, if available, biochemical analysis results of the stone were obtained from the medical records of the patients. Ultrasonographic findings were also collected from the medical records. Stones <3 mm in diameter were defined as microcalculi, and those >3 mm in diameter were defined as macrocalculi.[11] Hypercalciuria was defined as urinary calcium excretion >4 mg/kg/d; hyperoxaluria as urinary oxalate >40 mg/1.73 m^2/d; hyperuricemia as urinary urate >815 mg/1.73 m^2/d; hypocitraturia as urinary citrate <400 mg/g creatinine; and cystinuria as urinary cystine >75 mg/1.73 m^2/d.[12] Urinary calcium-to-creatinine ratio 95th percentile values from the same area by age were used for hypercalciuria; 0.76, 0.60, 0.69, and 0.24 values were used for the 0-7 months, 8-18 months, 19 months to 6 years, and 7-14 years age groups, respectively.[13] The relationship between the each of the metabolic disorders (eg, hypercalciuria and hypocitraturia) and age, sex, consanguinity, recurrence, family history, bilaterality, multiplicity, stone localization, and stone size was compared.

We performed statistical analysis using Statistical Package for Social Sciences 15.0 software (SPSS Inc., Chicago, IL). Descriptive statistics were expressed as frequency and percentage for categorical variables, whereas quantitative data were expressed as median for non-normally distributed data. We used the Mann-Whitney *U* test to compare quantitative data and used the chi-square test (Fisher exact test, when needed) to compare the categorical variables. We considered 2-sided $P < .05$ as statistically significant.

RESULTS

Of the 248 patients participating in the study, 142 (57.3%) were men and 106 (42.7%) were women. The median age of the patients was 48 months (minimum-maximum, 2-180 months). A familial history of urolithiasis was found in 131 of 240 patients (54.6%). This percentage was obtained by omitting the 8 cases for which the family history of urolithiasis was not specified in the medical records. This rate was found in 55 of 240 patients (22.9%) in the first-degree relatives and in 76 of 240 patients (31.7%) in the second-degree relatives. Consanguinity was found in 28 of 119 patients (23.5%). Information regarding consanguinity was absent for 129 patients. Macrocalculi and microcalculi were present in 186 (75.0%) and 62 (25.0%) of the cases, respectively. Multiplicity and bilaterality at initial presentation were identified in 119 (48.0%) and 61 (24.6%) of the cases, respectively. An analysis of the locations of the stones revealed that 229 patients (92.3%) had upper urinary tract stones and 19 patients (7.7%) had lower urinary tract stones. All patients had at least a partial metabolic study. Hypercalciuria, hypocitraturia, hyperoxaluria, hyperuricosuria, and cystinuria were detected in 41.5%, 39.5%, 21.8%, 9.3%, and 4.4% of the cases, respectively. Table 1 shows the demographics of patients with urolithiasis. Of the patients, 189 (76.2%) had metabolic disorders; 44.2% had 1, 23.1% had 2, and 7.6% had 3 metabolic disorders. One patient had 4 metabolic disorders (Fig. 1). In patients with metabolic disorders, combined hypercalciuria and hypocitraturia in 38 of 189 patients (20.1%) was the most common metabolic disorder with multiple components. One patient had chronic renal insufficiency at the time of the diagnosis. A stone composed of uric acid was detected in this patient. No relationship was observed between the metabolic disorders and the incidence of bilaterality, multiplicity, recurrence, sex, macrocalculi, microcalculi, stone localization, consanguinity, family history of urolithiasis, and infection ($P = .118$, $P = .614$, $P = .926$, $P = .504$, $P = .438$, $P = .438$, $P = .158$, $P = .418$, $P = .400$, and $P = .431$, respectively). The rate of multiple stone formation, infection, and recurrence was significantly higher in the 0-2 years age group ($P = .030$, $P = .001$, and $P = .019$, respectively). History of stones in family was significantly higher in the >2 years group ($P = .034$; Table 2). The median age of patients was higher ($P = .001$) in patients with hyperoxaluria in comparison with other metabolic disorders. Relationship was observed between the history of stones in family and hypocitraturia ($P = .040$). Compared with other metabolic disorders, multiple stones and recurrence were more frequent in patients with cystinuria ($P = .022$ and $P = .008$, respectively). Lower urinary tract stones were significantly higher in patients with cystinuria ($P = .012$). The size of the stones was

Table 1. Demographics of patients with urolithiasis

Variables	N (%)
Age, median (min-max), mo	48 (2-180)
Male	142 (57.3)
Consanguinity	28/119 (23.5)
Family history of urolithiasis	131/240 (54.6)
First degree	55/240 (22.9)
Second degree	76/240 (31.7)
Infection	51 (20.6)
Bilaterality	61 (24.6)
Multiplicity	119 (48.0)
Stone localization	
Upper urinary system (pelvis, calyces, ureter)	229 (92.3)
Lower urinary system (bladder, urethra)	19 (7.7)
Size of stone	
Microcalculi (≤3 mm)	62 (25.0)
Macrocalculi (>3 mm)	186 (75.0)
Metabolic disorders	189 (76.2)
Hypercalciuria	103 (41.5)
Hypocitraturia	98 (39.5)
Hyperoxaluria	54 (21.8)
Hyperuricosuria	23 (9.3)
Cystinuria	11 (4.4)
Total	248 (100.0)

max, maximum; min, minimum.