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Pediatric Urinary Stone Disease: A 10-Year Single-Center Experience from Türkiye

Utku Dönger[1], Caner İncekaş[2], Kaan Savaş Gülleroğlu[3], Esra Baskın[3]

[1]Department of Pediatrics, Başkent University Faculty of Medicine, Ankara, Türkiye
[2]Department of Biostatistics, Başkent University, Ankara, Türkiye
[3]Department of Pediatric Nephrology, Başkent University Faculty of Medicine, Ankara, Türkiye

What is already known on this topic ?

- *Urinary system stone disease is a disease that occurs with stone formation in the kidneys, ureters, and bladder, and many factors such as hereditary, environmental, nutritional, and medications play a role.*
- *Urinary tract stones are an important health problem with an increasing prevalence worldwide in the last 20 years.*

What this study adds on this topic ?

- *In children, unlike adults, most patients have a metabolic abnormality that predisposes them to stone formation. While hypercalciuria was the most common metabolic abnormality in children in most studies, hypocitraturia was the most common in this study.*
- *Citrate helps prevent the formation of kidney stones by binding directly to calcium or by inhibiting the formation and aggregation of calcium oxalate and calcium phosphate crystals. Low levels of citrate in the urine, especially in children, can lead to the formation of calcium stones.*

Corresponding author:
Utku Dönger
✉ utkudonger@gmail.com
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ABSTRACT

Objective: Urinary stone disease (USD) is characterized by stone formation in the urinary system with an approximate prevalence of 5%–10% in children. In thisr study, the authors investigated the metabolic abnormalities that play a role in stone formation in pediatric patients with USD admitted to the authors' pediatric nephrology clinic during the last 10 years, the demographic characteristics of the patients, and the presenting symptoms.

Materials and Methods: A total of 325 pediatric patients, 166 boys (51.1%) and 159 girls (48.9%), who presented to the Pediatric Nephrology outpatient clinic of the authors' center with a prediagnosis of USD were retrospectively analyzed.

Results: Of 325 patients, 159 (48.9%) were female and 166 (51.1%) were male. The median age at diagnosis was 29 (0–229) months. 188 (57.9%) of the patients had a positive family history of USD and 22 (6.8%) had parental consanguinity. Hypocitraturia was found in 26.2% and hypercalciuria in 17.5% of patients. Stones were detected in 198 patients (60.9%) in the initial ultrasonography (USG) evaluation. Stones were most commonly located in the renal pelvis (75.8%) followed by the ureter (10.1%) and both renal pelvis and ureter (3%). About 40.4% of the stones were located in the left side, bilaterally in 37.8%, and 21.2% in the right side.

Conclusion: Urinary stone disease is common in children. Unlike adult patients, patients with a positive family history of USD and parental consanguinity necessitate further metabolic evaluation and should be investigated for underlying urinary tract infection. Identifying stone disease early in childhood can help us detect urinary tract and metabolic abnormalities earlier.

Keywords: Childhood stone disease, kidney stones, urinary stone disease, urolithiasis.

INTRODUCTION

Urinary stone disease (USD) is characterized by stone formation in the kidneys, ureters, and bladder due to multiple factors, i.e., hereditary, environmental, nutritional, and medications. Urinary stone disease is common in children, with an approximate prevalence of 5%–10% during childhood.[1-3] USD is more common in boys than girls.[4] Advances in diagnostic methods have significantly contributed to the increased incidence of USD in recent years. Aside from advances in diagnostic methods, the increased incidence of USD is attributed to changes in dietary habits. Decreased fluid intake, consumption of high sodium and high fructose, and calcium-poor diets predispose individuals to stone formation.[5] Multiple factors such as race, geographical region, socioeconomic status, and dietary habits may affect the incidence and location of urinary tract stones. In the Near/Middle East and North Africa, nephrolithiasis is an endemic disease affecting 10%–20% of the population. The higher prevalence of USD in this region can be explained by the hot and dry climate, high ambient temperatures, and dehydration.[6] Türkiye is an endemic country in terms of USD, with an

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approximate prevalence rate of 10%. Although there is limited data regarding the incidence of pediatric USD in Türkiye, it is known that 17% of USD patients are children. Hereditary factors, dietary habits, obesity, and climatic factors are thought to impact the prevalence of USD in Türkiye.[7]

Pediatric USD is often accompanied by urinary tract anomalies and metabolic abnormalities, with high stone recurrence rates. In this study, the authors investigated demographic characteristics and presenting symptoms in pediatric USD patients admitted to their pediatric nephrology clinic in the last 10 years.

MATERIALS AND METHODS

Between January 2012 and December 2022, a total of 989 patients between 0 and 18 years of age who were admitted to the pediatric nephrology outpatient clinic with a prediagnosis of USD were retrospectively analyzed. Patients in the 0-18 age group with calcium and citrate levels in spot urine or 24-hour urine and simultaneous urinary system USG at the first presentation were included in the study. Patients who were older than 18 years of age, who did not have spot or 24-hour urine calcium and citrate tests, or who did not have urinary tract USG were excluded from the study. Of the 989 patients examined from the electronic database, 662 patients were excluded from the study because of insufficient test results, and 2 patients were excluded because USG results were not available. As a result, 325 patients who met the criteria were included in the study. Patients' data were retrieved from the hospital's electronic database. Renal calculus was defined radiologically by the presence of an echogenic focus ≥ 2 mm with posterior acoustic shadowing.[8] Urine metabolic tests were evaluated according to age-appropriate reference intervals.[9] History of recurrent urinary tract infection (UTI) was defined as the presence of a positive urine culture ≥ 3 times prior to the presentation with USD. This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Başkent University (approval number: KA23/40; date: January 24, 2023). Informed consent was not required for this study as it was retrospective in nature and involved the use of anonymized data.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 25.0 (IBM Corp., Armonk, NY, USA). The conformity of the variables to normal distribution was examined by the Shapiro–Wilk test. Mean, SD, median, minimum, and maximum values were used for descriptive statistics in quantitative variables. Frequency and percentage values of the variables were used when presenting categorical variables. The Mann–Whitney *U* Test was used to evaluate variables that did not show a normal distribution between 2 groups. *P*-values below .05 were accepted as statistically significant results.

RESULTS

General Characteristics of the Patients

A total of 325 children were included in this study. Of them, 166 (51.1%) were male and 159 (48.9%) were female. Upon presentation, stones were detected in the first ultrasonography (USG) in 198 (60.9%) patients. The median age at diagnosis was 29 (0-229) months. A positive history of consanguinity was present in 6.8% of the patients, and 57.9% had a positive family history of calculi. Sixty-two (19.1%) patients had a concomitant systemic disease.

Clinical and Laboratory Findings

Thirty-two percent of the patients presented to the clinic after the incidental detection of kidney stones and crystalloids on USG. Out of 325 patients, 14.8% presented with UTIs, 13.2% with hematuria and vomiting, 12% with abdominal pain, and 5.8% with dysuria.

Children with a younger age at diagnosis presented more frequently with restlessness and UTI symptoms, while older children presented with hematuria and vomiting. The median age at diagnosis was 7 months for those presenting with restlessness and UTI, while the median age at diagnosis was 38 months for those presenting with complaints such as hematuria and vomiting ($P < .001$). Thirty-six percent of the patients were using medication at admission.

Hypocitraturia was identified in 26.2% of cases, followed by hypercalciuria (17.5%). Metabolic abnormalities at initial presentation are summarized in Table 1.

Underlying urinary system disorder was present in 39.1% of the patients. Fifty-one (15.7%) patients had a history of recurrent UTI. Forty-eight (14.7%) patients had hydroureteronephrosis (HUN), while 12 (3.7%) patients had medullary sponge kidney, 9 (2.7%) patients had ureteropelvic junction (UPJ) stenosis, 8 (2.5%) patients had vesicoureteral reflux (VUR), and 7 (2.1%) patients had Nutcracker Syndrome.

Urine culture was positive in 14.5% of the patients. The most common microorganism detected was *E. coli*. Stones were detected in 60.9% of the patients with USG at the initial presentation. The most common location of the stones was the renal pelvis (75.8%) followed by the ureter (10.1%). Three percent of the patients had stones in both the renal pelvis and ureter. About 40.4% of the stones were detected on the left side, 21.2% on the right side, and 37.8% on both sides. About 78.3% of the stones were < 5 mm in diameter. The localization and size of the stones are summarized in Table 2.

Treatment

Ten patients were treated with surgical interventions: 5 patients underwent extracorporeal shock wave lithotripsy (ESWL), 3

Table 2. Stone Characteristics and Localization

		n = 198 (%)
Localization	Renal pelvis	150 (75.8%)
	Ureter	20 (10.1%)
	Renal pelvis and ureter	6 (3.0%)
	Unspecified	22 (11.1%)
Right/left/bilateral	Left	80 (40.4%)
	Bilateral	75 (37.8%)
	Right	43 (21.2%)
Size	< 5 mm	155 (78.3%)
	5-10 mm	39 (19.7%)
	> 10 mm	4 (2%)

Table 1. Demographic Characteristics of the Patients, Clinical Presentations, and Metabolic Abnormalities

	n = 325 (%)	
Gender (male/female)	159/166 (48.9/51.1)	
Systemic disease	62 (19.1)	
Underlying urinary tract disorder	127 (39.1)	
Consanguinity	22 (6.7)	
Family history of stones	188 (57.8)	
	Mean ± SD	**Med (Min-Max)**
Age at diagnosis (month)	48.1 ± 51.5	29 (0-229)
Body weight (kg)	17.1 ± 15.1	11.2 (1.9-102)
Clinical presentation		**n = 325 (%)**
	Incidental kidney stones and crystalloids on USG	123 (37.8)
	Urinary tract infection	48 (14.8)
	Hematuria	43 (13.2)
	Vomiting	43 (13.2)
	Abdominal pain	39 (12.0)
	Dysuria	19 (5.8)
	Restlessness	15 (4.6)
	Change in urine color	15 (4.6)
	Spontaneous stone dropping	14 (4.3)
	Other	14 (4.3)
	Fever	13 (4.0)
	Urinary incontinence	8 (2.4)
	Glycosuria and polyuria	3 (0.9)
Metabolic abnormalities	Hypocitraturia	85 (26.2)
	Hypercalciuria	57 (17.5)
	Hyperoxaluria	53 (16.3)
	Hypomagnesuria	44 (13.5)
	Hyperuricosuria	36 (11.1)
	Cystinuria	4 (1.2)

patients underwent surgery, 1 patient underwent percutaneous nephrolithotomy (PNL), and 1 patient had ureteroscopy (URS). Open surgery for USD was preferred in 1 patient with HUN and UPJ stenosis because he had to undergo pyeloplasty surgery, whereas open stone surgery had to be performed in the other 2 patients because of mixed renal or ureteral anomalies and large stone size. Three patients were stone-free after open surgery. The remaining 315 patients were managed by medical and conservative approaches. Recommendations commonly included increasing fluid intake and reducing dietary salt. Additionally, pyridoxine was used in 34 patients, potassium citrate in 8 patients, and Sholl solution in 4 patients. Twenty-one patients were recommended to adhere to an oxalate-restrictive diet.

DISCUSSION

Urinary stone disease is an important health problem with an increasing incidence in both adult and pediatric populations and a tendency to recur in recent years. The annual incidence of USD in children has increased from 6% to 10% in the last 25 years.[10] In Türkiye, USD accounts for 8% of chronic kidney disease cases in children.[11] Compared to adults, children with USD are more likely to have underlying metabolic abnormalities or congenital urinary system anomalies.[1,12] Early recognition of childhood stone disease, screening for underlying metabolic abnormalities, and urinary system anomalies reduce morbidity and prevent progression to chronic kidney disease.

Male gender predominance has been reported in pediatric USD cases; however, there are fewer studies where USD was reported predominantly in girls.[13-15] In recent years, an increased incidence of USD has been reported in female patients.[14,16] In this study, the authors found that male patients were predominant (51.1%).

Bladder stones are seen in patients with low meat consumption and higher rice and cereal consumption. Urinary tract infections also increases bladder stone formation. Recent studies have shown that the stones are more frequently detected in the upper urinary tract.[14,17]

Clinical presentation of USD varies according to age. While young children and infants present with non-specific symptoms such as restlessness, nausea, and vomiting, older children present with more specific complaints such as abdominal pain, flank pain, macroscopic or microscopic hematuria, and dysuria.[5,18] In this study, 32.6% of the patients were referred to us with suspicion of kidney stones and crystalloids on USG of an external center. Younger children presented more frequently with restlessness and UTI symptoms, whereas older children presented more often with hematuria and vomiting.

Structural anomalies of the urinary system are among the most important predisposing factors to stone formation. In children, rates of underlying functional/structural anomalies in USD are variable. In Turkey, Bak et al[19] reported anatomical anomalies of the urinary system in 29.1% of children with USD, and UPJ stenosis was the most common anomaly reported. In a study by Öner et al[20] anatomical anomalies were reported in 30.4% of cases. In this study, 39.1% of the patients had concomitant underlying urinary system anomalies.

The prevalence of UTI in USD patients varies between 10% and 46% in Turkey.[14,17,21] In this study, UTI was detected in 14.5% of the patients at the time of initial presentation. UTI and USD may be seen together. Therefore, patients presenting with USD should be investigated for underlying UTI.

Identification of the metabolic abnormalities in USD is crucial for effective treatment, minimizing recurrence, and promoting long-term renal survival.[22] Hypocitraturia and hypomagnesemia are the most important risk factors for stone formation in pediatric USD followed by hypercalciuria.[23,24] In this study, hypocitraturia (26.2%) was the most common metabolic abnormality detected. Citrate helps prevent kidney stone formation by directly binding to calcium or by hindering the development and clustering of calcium oxalate and calcium phosphate crystals. When urinary citrate levels are low, it can significantly contribute to the development of calcium stones, especially in children.[28]

Children with urinary calculi frequently have a family history of USD. Ertan et al[25] reported that 68.2% of USD patients had a positive family history of USD. In another study by Melek et al,[14] 67.9% of USD patients had a family history of USD. Ramya et al[26] found that 41.7% of patients with kidney stones had a positive family history. Medairos et al[27] reported a positive family history of USD in 37.5% of the patients in the USA. In this study, the family history of USD was compatible (57.9%) with previous reports.

Studies have reported a 10-year recurrence rate of kidney stones ranging from 12% to 56%. From a medical perspective, preventing stone recurrence can be achieved through a thorough analysis of metabolic issues.[28]

This study has some limitations. One of the main limitations of this study is that it was retrospective. In addition, as it represents the experience of a single center, it may not reflect the whole population.

CONCLUSION

In conclusion, USD is not rare in children. Unlike adult patients, children with family history of USD and parental consanguinity should undergo further metabolic evaluation and should be investigated for underlying UTI. Early recognition of childhood stone disease can help us detect urinary tract anomalies and metabolic abnormalities earlier. Although hypercalciuria is considered to be the main metabolic abnormality leading to stone formation in children, low levels of citrate in the urine can also lead to stone formation.

Availability of Data and Materials: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: This study was approved by the Ethics Committee of Başkent University (approval number: KA23/40; date: January 24, 2023).

Informed Consent: Informed consent was waived in accordance with institutional and ethical guidelines.

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