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Long-Term Follow-up Results of Children with Urolithiasis Followed in Our Clinic

Kliniğimizde İzlenen Ürolitiyazisli Çocukların Uzun Dönem Takip Sonuçları

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Öz

Giriş ve Amaç: Ürolitiyazis, Türkiye'de çocuklarda sık rastlanan bir hastalıktır. Bu çalışmada, ürolitiyazisli çocukların klinik, radyolojik ve metabolik özellikleri üzerine bir değerlendirme yapılmıştır.
Gereç ve Yöntemler: 2010 ile 2020 yılları arasında Celal Bayar Üniversitesi Pediatrik Nefroloji Anabilim Dalı'na ürolitiyazis ve mikrolitiyazis şüphesiyle sevk edilen 158 çocuğun kayıtları geriye dönük tarandı. Olguların hastaneye başvurudaki şikayetleri ve yaşları, özgeçmiş öyküleri ve taşların lokasyonu belirlendi. Tüm hastalardan tam idrar tetkiki, spot idrar elektrolitleri, idrar kültürü, serum elektrolitleri, böbrek fonksiyon testleri, ürik asit, albümin ölçümleri ve üriner ultrasonografi istenildi. İdrar toplayabilen hastalarda 24 saatlik idrar elektrolitleri çalışıldı. Taş elde edilebilen hastalara X ışını ile difraksiyon yöntemiyle taş analizi yapıldı.
Bulgular: Çalışmada yer alan 158 çocuğun 88'i (%55.7) erkek, 70'i (%44.3) kız olup, erkek/kız oranı 1.25/1 olarak belirlendi. Ortalama tanı yaşı 89.82 ± 57.35 ay olarak saptandı. Bu hastaların 108'inde (%68.3) ailede ürolitiyazis öyküsü bulunmaktaydı. Ayrıca, 46 hasta (%29) akraba evliliğinden doğmuştu. Tanı anında 32 hastada (%20) idrar yolu enfeksiyonu tespit edildi. Hastaların 129'unda (%81.6) taşlar üst üriner sistemde bulunuyordu. Bunların 123'ünde (%77.8) taşlar tek taraflı iken, 35'inde (%22.2) bilateral taşlar mevcuttu. Taş analizi yapılan hastaların çoğunda (%80) kalsiyum oksalat taşları bulundu. En yaygın üriner metabolik risk faktörü ise hiperkalsiüri olarak belirlendi. Takip süresince 67 hasta taş hastalığından kurtulurken, 14 hastada nüks gözlendi.
Sonuç: Ülkemizde çocuklarda ürolitiazis ciddi bir sorun olarak devam etmektedir. Çocuklarda taş hastalıklarında erişkinlerden farklı olarak yüksek rekürrens oranı ve altta yatan metabolik bozuklukların daha sık olması nedeniyle metabolik değerlendirme ve taş analizi yapılmalı, ömür boyu takip gereği vurgulanmalıdır.

Anahtar Kelimeler: Çocuk, Ürolitiyazis, Mikrolitiyazis, Metabolik Risk Faktörleri

Abstract

Aim: Urolithiasis is a prevalent condition frequently observed in childhood within the Turkish population. The aim of this study was to evaluate the metabolic, radiological, and clinical features of pediatric patients with urolithiasis.
Method: Records of 158 children referred to the Pediatric Nephrology Department of Celal Bayar University between 2010 and 2020 with suspected urolithiasis and microlithiasis were retrospectively reviewed. The complaints and ages of the cases during hospital admission, their medical histories, and the location of the stones were determined. All patients underwent complete urine analysis, spot urine electrolytes, urine culture, serum

electrolytes, kidney function tests, uric acid, albumin measurements, and urinary ultrasonography. 24-hour urine electrolytes were studied in patients capable of urine collection. Stone analysis using X-ray diffraction was performed on patients from whom stones were obtained.

Results: Out of the individuals, 88 (55.7%) were male, and 70 (44.3%) were female, resulting in a male-to-female ratio of 1.25:1. The average age at the time of diagnosis was determined to be 89.82 ± 57.35 months. A family history of urolithiasis was reported in 108 (68.3%) patients, and 46 individuals (29%) were born from consanguineous marriages. At the time of diagnosis, 32 patients (20%) had a urinary tract infection. Stones were predominantly situated in the upper urinary system in 129 patients (81.6%), with 123 (77.8%) having unilateral stones and 35 (22.2%) having bilateral stones. Calcium oxalate stones were the most commonly observed (80%) in patients who underwent stone analysis. Hypercalciuria emerged as the most frequently identified urinary metabolic risk factor. At the end of the follow-up period, 14 patients experienced a recurrence, while 67 patients remained free of stones.

Conclusion: Urolithiasis continues to be a significant concern among children in our nation. Due to the higher recurrence rate and more frequent underlying metabolic disorders in children with stone diseases compared to adults, metabolic assessment and stone analysis are recommended procedures, emphasizing the need for lifelong monitoring in these cases.

Keywords: Child, Urolithiasis, Microlithiasis, Metabolic risk factors

1. Introduction

Urolithiasis progressing to end-stage renal disease (ESRD), causing significant costs in diagnosis and treatment, and having high morbidity, is a fundamental health issue [1]. Geographical variations in the incidence and composition of childhood stone diseases seem to be associated with climate, diet, genetic, and socioeconomic factors [2,3]. Changes in the composition of stones and recent increases in cases of paediatric urolithiasis may be related to dietary variations like fast food and high-protein diets, as well as the rise in obesity worldwide and sedentary lifestyles [4]. Multifactorial aetiology paediatric urolithiasis is endemic in Turkey and occurs widely throughout Asia, the Far East, and the Middle East [5, 6]. In patients younger than 14 years old, the incidence has been reported to be 17% [7]. A different study carried out in Turkey found that 0.8% of school-age children had urolithiasis [8]. Metabolic reasons (20-30%) and anatomical factors have been reported as the most common etiological factors for urolithiasis in Turkey [7, 9, 11]. Pediatric nephrolithiasis caused by metabolic abnormalities usually results in recurrence, requiring comprehensive research into the metabolic aspects of stone formation in children [12]. In a study conducted in Turkey, it was shown that stones disappeared spontaneously in 28.6% of cases of microlithiasis [13]. Therefore, it is suggested that children diagnosed with microlithiasis should be monitored for spontaneous disappearance before planning advanced metabolic investigations [14]. This research retrospectively investigated the demographic information, clinical manifestations, radiological and metabolic results, and recurrence frequencies associated with different stone compositions among children diagnosed with urolithiasis at our hospital catering to the Western region of Turkey.

2. Materials and Methods

We conducted a retrospective review of 158 pediatric patients diagnosed with urolithiasis and monitored between 2010 and 2020 at the Pediatric Nephrology Department of Manisa Celal Bayar University. The review encompassed various medical records, including demographic details, symptoms upon presentation, laboratory and imaging findings, prior medical and surgical history, family history of urinary stone-related issues, stone sizes and locations, recurrence indications, associated urinary tract infections (UTIs) and anomalies, metabolic irregularities, and medical interventions. Urolithiasis diagnosis relied on either the spontaneous passing of a stone or the detection of a stone through imaging techniques such as ultrasonography or computed tomography (CT). Stones smaller than 3 millimeters were termed microlithiasis. [15, 16]. Patients were periodically monitored post-diagnosis through ultrasound examinations, defining spontaneous remission as the permanent disappearance of stones during these checks. Stone locations were categorized as upper (kidney or ureter) or lower (bladder or urethra) urinary system. We assessed serum electrolytes (calcium, phosphorus, uric acid), hormone levels (vitamin D, parathyroid hormone), renal function (urea, creatinine levels, glomerular filtration rates), and blood gases. Furthermore, various tests were conducted to examine metabolic risk factors such as excessive calcium in urine (hypercalciuria), low citrate levels (hypocitraturia), cystine presence in urine (cystinuria), elevated oxalate levels in urine (hyperoxaluria), high uric acid in urine (hyperuricosuria), and decreased magnesium in urine (hypomagnesuria). Hypercalciuria was identified if the urinary calcium amount exceeded 4 mg/kg within 24 hours or if the ratio of calcium to creatinine in spot urine exceeded 0.8 mg/mg for 0-6 months, 0.6 for 7-12 months, and 0.2 for 1-18 years

[17]. Cystinuria was diagnosed when the 24-hour urinary cystine excretion surpassed >0.5 mmol/1.73 m2 or if the cystine/creatinine ratio in spot urine samples was over 35 mmol/mol [18]. Normal citrate levels were determined as >1.6 mmol/1.73 m2 in 24-hour urine or a spot urine citrate/creatinine ratio >0.1 mol/mol [19]. Expectedly, normal uric acid excretion was below <10.57 mg/kg/day in 24-hour urine or below the age-adjusted value in spot urine [20]. Hypomagnesuria was defined as <0.8 mg/kg/day in 24-hour urine or less than 0.63 mol/mol in spot urine. Patients exhibiting clinical indications and symptoms of UTIs underwent screenings for diagnosis. If recurrent UTIs occurred during subsequent monitoring, a voiding cystourethrogram (VCUG) was conducted to explore potential vesicoureteral reflux (VUR). Stone composition analysis was performed using the X-ray diffraction (XRD) technique at the General Directorate of Mineral Research and Exploration (MTA) laboratory. Samples submitted for analysis were acquired through spontaneous passage, extracorporeal shock wave lithotripsy (ESWL), or surgical procedures.

2.1 Statistical Analysis

The information was presented as mean ± standard deviation and percentages. The Mann-Whitney U test was applied to compare the average ages at diagnosis between males and females. For the analysis of categorical variables, the Chi-square test and Fisher's exact test were utilized. A significance level of p <0.01 was considered statistically meaningful. All statistical computations were conducted using Statistical Package for the Social Sciences 25.0 (IBM SPSS Statistics 24; Armonk, NY, USA) software. Approval for this study was granted by the Celal Bayar University Faculty of Medicine Ethics Committee (record number 60116787-020/35545, dated 22/05/2019).

	n (%)
Patients	158 (100)
Male	88 (55.7)
Female	70 (44.3)
Male/Female	1.25
Mean age at diagnosis (months)	89.82 ± 57.35
Follow-up duration (months)	18.9 ± 1.7
Family history	108 (68.3)
Consanguinity	46 (29)
Presenting symptoms	
Abdominal pain	36 (23)
Flank pain	16 (10)
Macroscopic hematuria	41 (26)
Dysuria	27 (17)
Nausea and/or vomiting	45 (28)
Restlessness	38 (24)
Spontaneous stone passage	13 (8)
Incidental	54 (34)
Presence of UTIs at diagnosis	32 (20)
History of recurrent UTIs	43 (27)
Urine analysis	
Microscopic hematuria	76 (48)
Persistent pyuria	49 (31)

Stone localization	***n (%)***
Left	71 (45)
Right	52 (33)
Bilateral	35 (22)
Upper urinary system	129 (81,6)
Lower urinary system	26 (16,4)
Upper and lower urinary system	3 (2)
Anatomical abnormality	52 (32)
Hydronephrosis	25 (15)
VUR	8 (5)
UPJ	2 (1)
UVJ	14 (9)
Duplex collecting system	3 (2)

Table 1 Demographic and Clinical Data of Patients
Table 2 Radiological data of patients
(VUR: Vesicoureteral reflux, UPJ: Ureteropelvic junction obstruction, UVJ: Ureterovesical junction obstruction)

3. Results and Discussion

3.1 Results

The demographic and clinical data of 158 patients with urolithiasis are presented in Table 1. Among the patients, 88 (55.7%) were male, and 70 (44.3%) were female, resulting in a male-to-female ratio of 1.25. The mean age at diagnosis for these patients was 89.82 ± 57.35 months, and the follow-up duration averaged 18.9 ± 1.7 months. A total of 108 patients exhibited a confirmed familial background of urolithiasis (68.3%). Additionally, 46 patients (29%) had a history of consanguinity. The most common presenting symptom was abdominal pain, reported by 36 patients (23%). Other prevalent symptoms included nausea/vomiting (28%), macroscopic hematuria (26%), and restlessness (24%). Urolithiasis was incidentally discovered in 34% (54) of cases during the evaluation of other medical conditions. At the time of diagnosis, 32 patients (20%) had UTIs, and 43 patients (27%) had a history of recurrent UTIs. Microscopic hematuria was found in 76 patients (48%), and 49 patients (31%) showed persistent pyuria during urine analysis. The results indicated that most stones were situated in the upper urinary system (81.6%). According to the US imaging classification, stone sizes ranged from 3 mm to 25 mm. Microlithiasis was found in 59 cases (37.3%). Congenital anomalies such as hydronephrosis, VUR, ureteropelvic junction obstruction (UPJ), ureterovesical junction

obstruction (UVJ), and duplicated collecting systems were present in 52 patients (32%) (Table 2).

The biochemical analysis of serum, including urea, creatinine, alkaline phosphatase, calcium, phosphorus, magnesium, parathyroid hormone, blood pH, and bicarbonate levels, did not show any abnormalities in any of the patients. The composition analysis of stones found in the examined patients is presented in Table 3. Calcium Oxalate was the most prevalent stone composition, accounting for 80% of the stones analyzed, indicating a high occurrence of calcium oxalate stones among the patients. Calcium oxalate dihydrate (Weddellite) represented in a smaller proportion (6.6%), suggesting a less common occurrence compared to calcium oxalate stones. Calcium oxalate monohydrate (Whewellite) was found in 20% of the cases, these stones were observed in a significant but lesser percentage compared to calcium oxalate stones. Calcium oxalate dihydrate + calcium oxalate monohydrate (mix) was detected in 53.4% of the stones, this mixed composition further highlights the variability and complexity in stone formation, showcasing a combination of different types of calcium oxalate stones. Cystine was found in 20% of the stones, indicating the presence of cystine stones, which might have specific implications for management due to their unique characteristics and potential recurrence. Among children with calcium oxalate stones, 36% had hypercalciuria, 28% had hyperoxaluria and hypocitraturia, and 38% had hyperuricosuria. Out of the 46 patients who underwent metabolic analysis, 37% exhibited multiple metabolic abnormalities. The most prevalent metabolic irregularities identified were excessive urinary calcium levels (53%) and low citrate levels (22%). Hyperoxaluria and hyperuricosuria were present in 11% and 12% of patients, respectively. Although not statistically significant, hypercalciuria was higher in males compared to females.

Table 3. Stone Analysis Results of Patients

	***n* (%)**
Calcium oxalate	12 (80)
Calcium oxalate dihydrate (weddellite)	1 (6,6)
Calcium oxalate monohydrate (whewellite)	3 (20)
Calcium oxalate dihydrate+calcium oxalate monohydrate (mix)	8 (53,4)
Cystine	3 (20)

All patients were advised to follow a low-salt diet. Antibiotic prophylaxis for recurrent UTIs and specific treatments for metabolic risk factors were recommended for 67 patients (42.4%). While shock wave lithotripsy (SWL) was preferred in 29% of cases, surgical interventions (ureterorenoscopy, retrograde intrarenal surgery, percutaneous nephrolithotomy) were performed in 57% of cases. Treatment-resistant stones were found in 27 patients (51.9%), yet successful nephrolithiasis clearance was accomplished in 48.1% of patients post-treatment. We noted an 8.8% recurrence rate in treated patients; however, all cases responded well to retreatment. 50 patients (31.6%) did not continue their follow-ups.

3.2 Discussion

Stone disease among children poses a significant health concern, particularly in specific global regions like Southeast Asia, the Middle East, India, Turkey, and Pakistan. Epidemiological studies indicate a rising incidence, attributed to shifts in social circumstances and dietary behaviors [2]. However, acknowledging the role of racial distribution and genetic susceptibility highlighted by familial occurrences of urolithiasis remains crucial. Understanding the causes of urolithiasis is pivotal for effective treatment planning and preventing recurrences. Numerous studies have noted a higher prevalence of urolithiasis in boys compared to girls during childhood [2,7,8]. The male-to-female ratio was determined to be 1.25 in accordance with the literature. A strong association has been observed between a family history of urolithiasis and both the likelihood of stone development and recurrence. The considerable percentage (68.3%) of patients with a positive family history underlines a robust genetic or familial predisposition. This underscores the importance for clinicians to inquire about family history when evaluating pediatric patients suspected of having urolithiasis, as it significantly influences diagnosis and treatment decisions [8]. Common symptoms observed among our patients include abdominal pain, nausea/vomiting, and visible blood in the urine. Nevertheless, the presence of overlapping symptoms with other conditions and a notable portion of incidental discoveries (34%) suggest that relying solely on clinical manifestations might not be definitive for diagnosis. A comprehensive assessment is crucial to distinguish urolithiasis from other potential causes. Our findings indicate that a majority of nephrolithiasis were situated in the upper urinary system (81.6%). Similarly, studies conducted in Turkey have reported a higher prevalence of upper urinary system stones [8, 9, 18]. Risk factors for urolithiasis encompass metabolic disorders, UTIs, and anatomical irregularities. Anatomical issues such as UPJ obstruction and vesicoureteral reflux (VUR) can contribute to stone formation. The reported incidence of anatomical defects in children with urinary stones ranges from 5-10% [4,6], aligning with our study where anatomical defects were detected in 32% of cases, consistent with existing literature. In Turkey, UTIs have been documented in 10-36% of children diagnosed with urolithiasis [8]. In our research, we observed a correlation between

urolithiasis and UTIs, with 20% of cases diagnosed with UTIs concurrently with urolithiasis and 27% having a history of recurring UTIs. This emphasizes the close link between these conditions and underscores the importance of addressing and managing both urolithiasis and UTIs simultaneously in affected pediatric patients. Typically, metabolic risk factors are more common in younger children diagnosed with urolithiasis. The presence of bilateral or multiple stones should raise suspicion of underlying metabolic disorders. Studies have reported metabolic disorders in 33-93% of children with urolithiasis [18, 19]. In our study, at least one metabolic abnormality was identified in 72% of patients. Prior studies conducted in our nation have emphasized that the most common metabolic irregularities observed are excessive levels of calcium in urine (hypercalciuria) and lower than normal levels of citrate in urine (hypocitraturia) [2, 6-9]. Similarly, hypercalciuria (53%) and hypocitraturia (22%) were the most frequently observed metabolic abnormalities in our study. The majority of cystinuria patients present in childhood, with around 75% diagnosed within the first decade and a mean age of first stone detection at 13 years. A strong clinical indicator of cystinuria is a positive family history, and screening should be performed in such cases or with parental consanguinity. Even without these factors, cystinuria should be suspected in patients with severe stone disease, including recurrent or bilateral renal stones or large staghorn calculi requiring surgical management. It's more common for stones to appear earlier in male patients [19]. We noted a higher occurrence of cystinuria in patients with bilateral or multiple stones. Additionally, cystinuria was more prevalent in males compared to females in our study ($p=0.9$). Our research found that multiple or bilateral stones were more frequent in cases diagnosed before one year, and this was statistically significant ($p<0.05$). Most kidney stones found in pediatric cases consist primarily of calcium oxalate (45–65%) or calcium phosphate (14–30%) [18]. In this study, consistent with the literature, 80% of cases had calcium oxalate stones. This high prevalence of calcium oxalate aligns with findings from other studies [4, 6-8]. This analysis emphasizes the critical role of understanding the composition of stones to customize treatment approaches effectively. The prevalence of calcium oxalate stones underscores the necessity for dietary adjustments and preventive measures aimed at reducing their occurrence [18]. Furthermore, the presence of cystine stones necessitates specific management protocols to ensure their effective dissolution or removal. Thorough stone analysis assists clinicians in devising targeted therapies and preventive strategies, thereby lowering recurrence rates and enhancing patient outcomes. Calcium oxalate stones are linked with various urine imbalances like hypocitraturia, hyperoxaluria, hypercalciuria, and hyperuricosuria [20-22]. In our study, 25% of children with calcium oxalate stones had hypercalciuria, 18% exhibited hyperoxaluria and hypocitraturia, while 45% had hyperuricosuria. Notably, hypercalciuria was prevalent in more than half of the cases (53%). Elevated levels of urinary calcium pose a significant risk for the formation of calcium-based stones. Addressing this imbalance through dietary modifications or medication interventions could be pivotal in preventing recurring stone formation [23]. Hypocitraturia was identified in a considerable portion of patients (22%). Reduced urinary citrate levels can lead to diminished inhibition of crystal formation, increasing the likelihood of stone development. Introducing citrate supplementation or dietary modifications may be considered to elevate citrate levels and hinder stone formation [24]. Although less common, hyperoxaluria and hyperuricosuria were present in noteworthy percentages (11% and 12%, respectively). Elevated urinary oxalate and uric acid levels contribute to specific types of stone formation. Management strategies that focus on dietary changes and medication may aid in controlling these conditions [25]. Cystinuria is observed in a small percentage of cases (2%). This condition requires specialized attention due to the unique nature of cystine stones, which are resistant to dissolution by typical methods. Specific treatments targeting cystine stone formation are necessary [26]. The presence of normal metabolic evaluations in some cases (28%) despite the occurrence of urolithiasis implies the involvement of factors beyond the assessed metabolic abnormalities. These findings highlight the multifactorial nature of stone formation, suggesting that other factors, such as genetic predispositions or environmental factors, might contribute to stone development. The significance of these metabolic evaluations lies in their potential to guide customized treatment strategies. Addressing these metabolic imbalances is pivotal in preventing stone recurrence and enhancing patient outcomes.

Regarding treatment approaches, all patients received guidance on dietary modifications, including reduced salt intake (especially processed and salty fast food), balanced fruit/vegetable consumption, minimized chocolate/cola intake, and increased fluid intake. Additional treatments encompassed medical therapy, surgical intervention and extracorporeal shock wave lithotripsy (ESWL) [27]. Therapeutic approach involved prophylactic antibiotics for recurrent UTIs and tailored treatments based on identified metabolic predispositions [28]. At the end of the monitoring period, 42% of cases did not have any stones remaining. Nephrolithiasis passage occurred spontaneously in 8% of cases, while 29% underwent SWL, and surgical intervention was necessary for 57% of cases. Preventing new stone formation is crucial,

considering reported recurrence rates ranging from 6% to 54% over intervals of 3-24 years [29]. In this study, the recurrence rate was 8.8%. Similar to findings by Alpay et al. [13], spontaneous remission in microlithiasis patients during the follow-up period was 38% in our study, compared to their reported rate of 29%. More than 25% of microlithiasis cases were found incidentally, while others initially showed symptoms like UTIs, hematuria, or discomfort. Throughout follow-ups, UTIs were present in around 48% of patients, and hematuria was observed in roughly 45% of cases. Abnormal ultrasound findings were notably less frequent in microlithiasis cases compared to larger stones. Over the follow-up period, 35% of microlithiasis patients experienced spontaneous remission, which was three times higher than in those with larger stones, although most stones persisted. The suspicion of kidney stones is essential in infants with UTIs and in young children with hematuria. Moreover, unusual urinary symptoms could suggest the presence of kidney stones in specific areas, necessitating a high level of suspicion for diagnosis. While microlithiasis primarily affects infants and seems relatively benign with higher chances of self-resolution, it shouldn't disregard familial urolithiasis history, metabolic issues, and similar symptom patterns to larger stones. Detecting microlithiasis could decrease invasive procedures for patients with nonspecific stomachache and hematuria, and addressing the underlying metabolic issues can prevent related clinical complications [13]. Medical treatment was administered to 52.3% of patients, targeting various conditions such as hypercalciuria, hypocitraturia, and cystinuria using specific medications and dietary adjustments. Surgical stone removal was conducted in 57% of patients, with SWL selected as the treatment option for 29% of patients. The limitations of our study include its retrospective nature, the inability to conduct metabolic evaluations for all children, and the inability to send all stones to the MTA. Another drawback of our study is the higher percentage of patients (31.6%) who did not continue with follow-up visits. Two likely reasons account for this inconsistent presence. Firstly, nephrolithiasis is widespread in our country, and caregivers might become desensitized to this situation due to other relatives experiencing similar issues. Secondly, the nature of investigations related to urolithiasis might cause discomfort among the families.

4. Conclusion

We consider urolithiasis to be a significant health issue affecting children. We advocate for a comprehensive assessment of children diagnosed with urolithiasis, starting with an analysis of stone composition, identifying risk factors, and conducting a thorough metabolic evaluation. It's crucial to address any anatomical irregularities and manage identified metabolic risk factors. Children experiencing poor growth ought to be assessed for potential nephrolithiasis. Those with recurring UTIs should undergo urinary tract ultrasound examinations. Educating parents about urolithiasis is essential, particularly for children with a positive family history, who require close monitoring for any potential stone recurrence.

In conclusion, the study emphasizes the importance of early diagnosis, comprehensive metabolic evaluations, suitable treatment strategies, and meticulous follow-up to prevent repetition and kidney failure associated with pediatric urolithiasis. Overall, the findings stress the multifactorial nature of pediatric urolithiasis, involving various clinical, radiological, and metabolic aspects, and highlight the significance of tailored management strategies for affected children.

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