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Research Article

Characteristics of Presentation and Metabolic Risk Factors in Relation to Extent of Involvement in Infants with Nephrolithiasis

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Abstract

Objectives: To evaluate the characteristics of presentation and metabolic risk factors in relation to the extent of involvement in infants with nephrolithiasis.

Methods: A total of 111 infants (age range 0.3–11.8 months, 58.6% were girls) diagnosed with nephrolithiasis in the first year of life were included in this retrospective study. Data on age at diagnosis, gender, family history of nephrolithiasis, parental consanguinity, symptoms on admission, urinary abnormalities, surgery, size of renal calculi, and metabolic risk factors (hypercalciuria, hyperuricosuria, hyperoxaluria, hypocitraturia, cystinuria, hypercalcemia) were recorded for each patient and compared with the number of kidneys affected (bilateral vs. unilateral), the number of kidney stones (multiple vs. single), and the kidney stone size (microlithiasis vs. larger stones).

Results: Overall, 58.6% of the infants were girls. Irritability was the most common symptom on admission (34.2%). Microlithiasis (62.2%), bilateral kidney involvement (61.3%), multiple kidney stones (73.9%), and metabolic risk factors (45.0%, hypercalciuria in 31.5%) were commonly noted. Bilateral nephrolithiasis was associated with significantly higher rates of hypercalciuria than unilateral nephrolithiasis (39.7% vs. 18.6%, respectively; p=0.022). The presence of multiple kidney stones was associated with a significantly higher rate of hyperuricosuria than the presence of a single kidney stone (20.7% vs. 0.0%, respectively; p=0.006). Larger kidney stone size was associated with a significantly higher rate of hyperoxaluria than microlithiasis (100.0% vs. 0.0%; respectively; p=0.002).

Conclusion: In conclusion, our findings revealed the association of nephrolithiasis in the first year of life with identifiable metabolic abnormalities in a considerable portion of patients. Our findings emphasize the association of identifiable metabolic abnormalities with the extent of nephrolithiasis and a higher likelihood of bilateral kidney involvement, multiple kidney stones, and larger kidney stones in cases of hypercalciuria, hyperuricosuria, and hyperoxaluria, respectively.

Keywords: Infant, kidney stone, metabolic risk factor, microlithiasis, nephrolithiasis

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Nephrolithiasis is a rare but serious condition that is associated with significant morbidity in the pediatric population, and its incidence has increased in recent years.[1–4] Due to its association with significant feeding and growth problems and detrimental long-term effects on kidney function, it is important to gain an understanding of the epidemiology and metabolic underpinnings of nephrolithiasis in pediatric patients in order to provide adequate treatment and develop preventive strategies.[1, 5, 6] Recognition of nephrolithiasis in infants is particularly

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important given the potential role of early detection in preventing the progression of kidney failure and the recurrence of stones.[6, 7]

Although recent studies have suggested potential roles for predisposing metabolic risk factors, the precise reasons underlying the increasing incidence and demographic discrepancies in pediatric nephrolithiasis are not clear.[6, 7] Moreover, because nephrolithiasis in the first year of life has not been specifically addressed in most studies on pediatric nephrolithiasis, data on clinical and metabolic patterns of nephrolithiasis in infancy are scarce and the mechanism of early stone formation throughout the urinary tract remains largely unknown.[1, 7–11]

This retrospective study was designed to evaluate the characteristics of presentation and metabolic risk factors in relation to the extent of involvement in infants with nephrolithiasis.

Methods

Study Population

A total of 111 infants below 1 year of age (range 0.3–11.8 months; 58.6% girls) who were diagnosed with nephrolithiasis over a 4-year period (between April 2015 and January 2018) at a tertiary-care pediatric surgery and urology center were included in this retrospective study.

The study was conducted in full accordance with local Good Clinical Practice (GCP) guidelines and current legislations, and permission was obtained from our institutional ethics committee for the use of patient data for publication purposes.

Study Parameters

Data on age at diagnosis, gender, family history of nephrolithiasis, parental consanguinity, symptoms on admission, urinary abnormalities, surgery, size of renal calculi (microlithiasis, nephrolithiasis), comorbidity, and metabolic risk factors (hypercalciuria, hyperuricosuria, hyperoxaluria, hypocitraturia, cystinuria, hypercalcemia) were recorded for each patient and compared according to number of kidneys affected (bilateral vs. unilateral), the number of kidney stones (multiple vs. single), and the size of kidney stones (microlithiasis vs. larger stones).

The concentrations of metabolites from spot urine samples were standardized by dividing them by the urine creatinine concentration. In addition, the tubular reabsorption of phosphate was calculated. Urolithiasis was diagnosed based on the passing of stones at admission or the detection of stones >3 mm in diameter on plain abdominal radiography or ultrasonography of the urinary tract. Microlithiasis was defined as the presence of hyperechogenic structures with a diameter of <3 mm in renal calyces.

Patients without stones on admission but who spontaneously passed stones before surgery or from whom stones were surgically removed were evaluated for a history of urolithiasis.

The upper limit of the calcium/creatinine ratio in spot urine samples for hypercalciuria was set at 0.8 mg/mg for ages 0–12 months. For detection of hyperuricosuria, the upper limit of the uric acid/creatinine ratio in urine was set to 2.2 mg/mg for ages 0–12 months. For the definition of hyperoxaluria, the upper limit of the urinary oxalate/creatinine ratio was set to 288 mg/g for ages 0–6 months and at 139 mg/g for ages 7–12 months.[7] Cystinuria was defined as >573 µmol/g for ages 0–2 months, >461 µmol/g for ages 3–8 months, and >186 µmol/g for ages 9–12 months. Hypocitraturia was defined as a urinary citrate/creatinine ratio <0.20 for ages 0–1 year. Hypomagnesuria was defined as a urinary magnesium/creatinine ratio between 0.1 and 12 for ages 0–12 months. The limit for tubular reabsorption of phosphate was the standard limit of >90%.[7] Any urinary system stones obtained were sent for chemical analysis.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows version 25.0 (IBM Corp., Armonk, NY). Pearson's Chi-square test (Monte Carlo and Exact), Fisher–Freeman–Halton test (Monte Carlo), and Fisher's exact test were used for comparison of categorical data. The independent-samples t test (bootstrap) was used to analyze parametric variables. Data are expressed as the mean±standard deviation (SD), minimum–maximum, or percentage (%) where appropriate. In all analyses, $p<0.05$ was taken to indicate statistical significance.

Results

Demographic and Clinical Characteristics (n=111)

Overall, 58.6% of the infants in the study population were girls. A family history of nephrolithiasis, parental consanguinity, and urinary abnormalities were positive in 55.0%, 48.6%, and 15.3% of the infants, respectively. The manifestation was symptomatic in 60.4% of infants, and irritability was the most common symptom on admission (34.2%) (Table 1).

Microlithiasis (62.2%), bilateral kidney involvement (61.3%), and multiple kidney stones (73.9%) were commonly noted (Table 1).

Metabolic risk factors were evident in 45.0% of infants (single factor in 32.4%), with hypercalciuria (31.5%) as the most

Table 1. Demographic and clinical characteristics in the overall study population (n=111)

Age at diagnosis (months), mean±SD (min/max)	6.8±3.1 (0.3/11.8)
Gender, n (%)	
Girl	65 (58.6)
Boy	46 (41.4)
Family history of nephrolithiasis, n (%)	
No	50 (45.0)
Yes	61 (55.0)
Parental consanguinity, n (%)	
No	57 (51.4)
Yes	54 (48.6)
Symptoms on admission, n (%)	
No	44 (39.6)
Yes	67 (60.4)
Irritability	38 (34.2)
UTI	9 (8.1)
Vomiting	7 (6.3)
Diaper staining	5 (4.5)
Blood in urine	3 (2.7)
Failure to gain weight	5 (4.5)
Urinary abnormalities, n (%)	
No	94 (84.7)
Yes	17 (15.3)
Surgery, n (%)	
No	107 (96.4)
Yes	4 (3.6)
Size of renal calculi, n (%)	
Microlithiasis	69 (62.2)
Nephrolithiasis	42 (37.8)
Comorbidity, n (%)	
No	101 (90.9)
Yes	10 (9.1)
Kidney involvement	
Unilateral	43 (38.7)
Bilateral	68 (61.3)
Number of kidney stones	
Single	29 (26.1)
Multiple	82 (73.9)
Metabolic risk factors, n (%)	
Absent	61 (55.0)
Present	
Total	50 (45.0)
Single	36 (32.4)
Multiple	14 (12.6)
Hypercalciuria, n (%)	
No	76 (68.5)
Yes	35 (31.5)
Hyperuricosuria, n (%)	
No	94 (84.7)
Yes	17 (15.3)
Hyperoxaluria, n (%)	
No	105 (94.6)
Yes	6 (5.4)
Hypocitraturia, n (%)	
No	106 (95.5)
Yes	5 (4.5)
Cystinuria, n (%)	
No	110 (99.1)
Yes	1 (0.9)
Hypercalcemia, n (%)	
No	107 (96.4)
Yes	4 (3.6)

commonly identified metabolic risk factor followed by hyperuricosuria (15.3%) (Table 1).

Study Parameters According to the Number of Affected Kidneys

Bilateral nephrolithiasis was associated with a significantly higher rate of hypercalciuria and a higher likelihood of multiple metabolic risk factors, compared to unilateral nephrolithiasis (39.7% vs. 18.6%, OR 2.9, 95% CI 1.2–7.1, p=0.022; 17.6% vs. 4.7%, OR 6.2, 95% CI 1.3–30.1, p=0.010; respectively) (Table 2).

There were no significant differences between infants with unilateral and bilateral nephrolithiasis in terms of age at diagnosis (7.3±3.1 vs. 6.5±3.1 months, respectively), gender (51.2% vs. 63.2% girls, respectively), family history of nephrolithiasis (48.8% vs. 58.8%, respectively), parental consanguinity (39.5% vs. 54.4%, respectively), presence of symptoms at admission (62.8% vs. 58.8%, respectively), presence of urinary abnormalities (11.6% vs. 17.6%, respectively), size of renal calculi (65.1% vs. 60.3% with microlithiasis, respectively), or metabolic risk factors other than hypercalciuria (Table 2).

Study Parameters According to Number of Kidney Stones

The presence of multiple kidney stones, in comparison with a single kidney stone, was associated with higher likelihood of asymptomatic presentation at initial diagnosis (45.1% vs. 24.1%, respectively; p=0.041), a significantly higher rate of hyperuricosuria (20.7% vs. 0.0%, respectively; p=0.006), and a higher likelihood of multiple metabolic risk factors (17.1% vs. 0.0%, respectively, OR 17.7, 95% CI 1.01–310.8, p=0.004) (Table 3).

There were no significant differences between infants with single and multiple kidney stones in terms of age at diagnosis (6.6±3.1 vs. 7.4±3.0 months, respectively), gender (61.0% vs. 51.7% girls, respectively), family history of nephrolithiasis (56.1% vs. 51.7%, respectively), parental consanguinity (53.7% vs. 34.5%, respectively), the presence of urinary abnormalities (15.9% vs. 13.8%, respectively), the size of renal calculi (62.2% vs. 62.1% with microlithiasis, respectively), or metabolic risk factors other than hyperuricosuria (Table 3).

Metabolic abnormalities with respect to size of renal calculi

With the exception of a lower likelihood of hyperoxaluria (n=6) in patients with microlithiasis compared to those with nephrolithiasis (0.0% vs. 100.0%, respectively; p=0.002), there was no significant relationship between the likelihood of metabolic abnormalities with respect to the size of renal calculi (Table 4).

Table 2. Study parameters according to the number of affected kidneys

	Nephrolithiasis Unilateral (n=43), %	Bilateral (n=68), %	p
Age at diagnosis (months), mean±SD (min/max)	7.3±3.1 (0.3/11.8)	6.5±3.1 (0.4/11.4)	0.148[a]
Gender			
Girl	22 (51.2)	43 (63.2)	0.239[b]
Boy	21 (48.8)	25 (36.8)	
Family history of nephrolithiasis			
No	22 (51.2)	28 (41.2)	0.332[b]
Yes	21 (48.8)	40 (58.8)	
Parental consanguinity			
No	26 (60.5)	31 (45.6)	0.172[b]
Yes	17 (39.5)	37 (54.4)	
Symptoms on admission			
No	16 (37.2)	28 (41.2)	0.696[b]
Yes	27 (62.8)	40 (58.8)	
Symptoms on admission			
None	16 (37.2)	28 (41.2)	0.425[c]
Irritability	11 (25.6)	27 (39.7)	
UTI	4 (9.3)	5 (7.4)	
Vomiting	4 (9.3)	3 (4.4)	
Diaper staining	3 (7.0)	2 (2.9)	
Blood in urine	2 (4.7)	1 (1.5)	
Failure to gain weight	3 (7.0)	2 (2.9)	
Urinary abnormalities			
No	38 (88.4)	56 (82.4)	0.433[b]
Yes	5 (11.6)	12 (17.6)	
Surgery			
No	42 (97.7)	65 (95.6)	-
Yes	1 (2.3)	3 (4.4)	
Size of renal calculi			
Microlithiasis	28 (65.1)	41 (60.3)	0.689[b]
Nephrolithiasis	15 (34.9)	27 (39.7)	
Comorbidity			
No	38 (88.4)	63 (92.6)	0.506[b]
Yes	5 (11.6)	5 (7.4)	
Metabolic risk factors			
Hypercalciuria			
No	35 (81.4)	41 (60.3)	0.022[b]
Yes	8 (18.6)	27 (39.7)	
Hyperuricosuria			
No	40 (93.0)	54 (79.4)	0.062[b]
Yes	3 (7.0)	14 (20.6)	
Hyperoxaluria			
No	42 (97.7)	63 (92.6)	0.402[d]
Yes	1 (2.3)	5 (7.4)	
Hypocitraturia			
No	41 (95.3)	65 (95.6)	0.999[d]
Yes	2 (4.7)	3 (4.4)	
Cystinuria			
No	43 (100.0)	67 (98.5)	-
Yes	0 (0.0)	1 (1.5)	
Hypercalcemia			
No	42 (97.7)	65 (95.6)	-
Yes	1 (2.3)	3 (4.4)	
Number of metabolic risk factors			
None	31 (72.1)	30 (44.1)	0.010[e]
Single	10 (23.3)	26 (38.2)	
Multiple	2 (4.7)	12 (17.6)	

SD: standard deviation; [a]Independent samples t test (Bootstrap); [b]Pearson's Chi-square test (Exact); [c]Fisher–Freeman–Halton test (Monte Carlo); [d]Fisher's exact test (Exact); [e]Pearson's Chi-square test (Monte Carlo).

Table 3. Study parameters according to the number of kidney stones

	Number of kidney stones		
	Multiple (n=82)	Single (n=29)	p
Age at diagnosis (months), mean±SD (min/max)	6.6±3.1 (0.3/11.8)	7.4±3.0 (0.5/11.2)	0.198[a]
Gender, n (%)			
Girl	50 (61.0)	15 (51.7)	0.511[b]
Boy	32 (39.0)	14 (48.3)	
Family history of nephrolithiasis, n (%)			
No	36 (43.9)	14 (48.3)	0.828[b]
Yes	46 (56.1)	15 (51.7)	
Parental consanguinity, n (%)			
No	38 (46.3)	19 (65.5)	0.087[b]
Yes	44 (53.7)	10 (34.5)	
Symptoms on admission, n (%)			
No	37 (45.1)	7 (24.1)	0.076[b]
Yes	45 (54.9)	22 (75.9)	
Symptoms on admission, n (%)			
None	37 (45.1)	7 (24.1)	0.041[c]
Irritability	30 (36.6)	8 (27.6)	
UTI	5 (6.1)	4 (13.8)	
Vomiting	3 (3.7)	4 (13.8)	
Diaper staining	3 (3.7)	2 (6.9)	
Blood in urine	2 (2.4)	1 (3.4)	
Failure to gain weight	2 (2.4)	3 (10.3)	
Urinary abnormalities, n (%)			
No	69 (84.1)	25 (86.2)	0.999[b]
Yes	13 (15.9)	4 (13.8)	
Surgery, n (%)			
No	79 (96.3)	28 (96.6)	-
Yes	3 (3.7)	1 (3.4)	
Size of renal calculi, n (%)			
Microlithiasis	51 (62.2)	18 (62.1)	0.999[b]
Nephrolithiasis	31 (37.8)	11 (37.9)	
Comorbidity, n (%)			
No	75 (91.5)	26 (89.7)	0.719[d]
Yes	7 (8.5)	3 (10.3)	
Metabolic risk factors, n (%)			
Hypercalciuria, n (%)			
No	52 (63.4)	24 (82.8)	0.065[b]
Yes	30 (36.6)	5 (17.2)	
Hyperuricosuria, n (%)			
No	65 (79.3)	29 (100.0)	0.006[d]
Yes	17 (20.7)	0 (0.0)	
Hyperoxaluria, n (%)			
No	77 (93.9)	28 (96.6)	0.999[d]
Yes	5 (6.1)	1 (3.4)	
Hypocitraturia, n (%)			
No	77 (93.9)	29 (100.0)	0.324[d]
Yes	5 (6.1)	0 (0.0)	
Cystinuria, n (%)			
No	81 (98.8)	29 (100.0)	-
Yes	1 (1.2)	0 (0.0)	
Hypercalcemia, n (%)			
No	79 (96.3)	28 (96.6)	-
Yes	3 (3.7)	1 (3.4)	
Number of metabolic risk factors, n (%)			
None	38 (46.3)	23 (79.3)	0.004[c]
Single	30 (36.6)	6 (20.7)	
Multiple	14 (17.1)	0 (0.0)	

SD: standard deviation; min: minimum; max: maximum; [a]Independent samples t test (Bootstrap); [b]Pearson's Chi-square test (Exact); [c]Fisher–Freeman–Halton test (Monte Carlo); [d]Fisher's exact test (Exact).

Table 4. Metabolic abnormalities with respect to renal calculi size

	Renal calculi size Microlithiasis (n=69)	Nephrolithiasis (n=42)	p
Hypercalciuria			
No (n=76)	49 (64.5)	27 (35.5)	0.529[a]
Yes (n=35)	20 (57.1)	15 (42.9)	
Hyperuricosuria			
No (n=94)	60 (63.8)	34 (36.2)	0.424[a]
Yes (n=17)	9 (52.9)	8 (47.1)	
Hyperoxaluria			
No (n=105)	69 (65.7)	36 (34.3)	0.002[b]
Yes (n=6)	0 (00)	6 (100.0)	
Hypocitraturia			
No (n=106)	66 (62.3)	40 (37.7)	0.999[b]
Yes (n=5)	3 (60.0)	2 (40.0)	
Cystinuria			
No (n=110)	68 (61.8)	42 (38.2)	-
Yes (n=1)	1 (100.0)	0 (0.0)	
Hypercalcemia			
No (n=107)	66 (61.7)	41 (38.3)	-
Yes (n=4)	3 (75.0)	1 (25.0)	
Number of metabolic risk factors, n (%)			
None (n=61)	41 (67.2)	20 (32.8)	0.092[c]
Single (n=36)	23 (63.9)	13 (36.1)	
Multiple (n=14)	5 (35.7)	9 (64.3)	

[a]Pearson's Chi-square test (Exact); [b]Fisher's exact test (Exact); [c]Pearson's Chi-square test (Monte Carlo).

Discussion

The findings of this study indicate that symptoms of irritability on admission, microlithiasis, bilateral kidney involvement, multiple kidney stones, and metabolic risk factors (hypercalciuria in particular) were evident in a considerable portion of infants with nephrolithiasis. The presence of multiple metabolic risk factors, particularly hypercalciuria, hyperuricosuria, and hyperoxaluria, was significantly associated with a higher likelihood of bilateral involvement, multiple kidney stones, and larger kidney stones, respectively.

The high ratio of girls (46:55 M:F) in our cohort emphasizes the greater likelihood of kidney stone formation in girls in the first year of life. This is consistent with reported changes in current trends in pediatric nephrolithiasis in recent population-based studies, as characterized by a significant increase in the number of girls affected, particularly in adolescents.[1, 8, 12–14] Notably, in a previous study of 50 infants from Turkey, boys and girls were reported to be equally affected (M/F: 26/24).[7]

The identification of irritability as the most common symptom on admission in our cohort supported the concept of a very early onset of nephrolithiasis presenting with nonspecific symptoms in the first year of life.[6, 7, 15, 16] Similarly, data from a previous study in 50 infants with nephrolithiasis in Turkey indicated restlessness/irritability (20%/50%) as the most common symptom on admission.[7]

In our cohort, parental consanguinity and a positive family history for renal stones favored a genetic component to urolithiasis. This finding is in agreement with those of previous studies of pediatric nephrolithiasis in Turkey, which indicated that 27–41% of parents had consanguineous marriages and 50.0–76.5% had a positive family history.[7, 17–20]

The presence of an identifiable underlying metabolic risk factor in pediatric patients with nephrolithiasis has been estimated to be present in 33–93% of patients; younger patients are thought to have a greater likelihood of an identifiable metabolic risk factor.[1] Hypercalciuria (range, 7–34%) is the most prevalent metabolic abnormality in children with urolithiasis,[5, 9, 21, 22] including infants.[7, 23, 24] Metabolic abnormalities were identified in almost half of the infants in our cohort, with hypercalciuria (31.5%) as the most common, followed by hyperuricosuria (15.3%) and hyperoxaluria (5.4%).

Along with identification of bilateral kidney involvement in two-thirds of infants, the rates of metabolic abnormalities in our cohort were consistent with data from a previous study in Turkey that found bilateral involvement in 33 of 50 infants and at least one metabolic abnormality in 46% of infants with urolithiasis in the first year of life.[7] The authors also reported hypercalciuria in nine of 47, hyperoxaluria in five of 39, hypocitraturia in four of 31, and cystinuria in two of 50 infants.[7] In another study, 76% of Turkish children with nephrolithiasis were reported to have metabolic disorders, with hypercalciuria, hypocitraturia, hyperoxaluria, hyperuricosuria, and cystinuria seen in 41%, 39%, 22%, 9%, and 4% of the patients, respectively.[24]

The rate of microlithiasis (62.2%) in our cohort is consistent with the results of previous studies, in which microcalculi were detected in 57% of children with idiopathic hypercalciuria[15] and in 38 of 50 kidneys of infants with nephrolithiasis,[7] emphasizing the likelihood of microlithiasis as the first step in stone formation.[7, 15, 25]

Notably, in children with idiopathic hypercalciuria, a normal urinalysis was reported to be significantly more frequent in those with microcalculi.[15] We found no significant differences in the likelihood of metabolic abnormalities with respect to renal calculi size, except for a lower likelihood of hyperoxaluria (n=6) in those with microlithiasis compared to those with nephrolithiasis. This is notable given that hyperoxaluria is a neglected but important risk factor that is

associated with a higher likelihood of stone persistence in pediatric urolithiasis.[18, 26]

In our cohort, similar rates of bilateral involvement and multiple stones were noted in infants with microlithiasis or larger stones, whereas the presence of hypercalciuria was associated with a higher likelihood of bilateral involvement and the presence of hyperuricosuria was associated with a higher likelihood of having multiple stones. Similarly, bilateral stone disease has been suggested to predict the presence of metabolic abnormalities in children with nephrolithiasis as well as more severe stone disease requiring targeted medical and surgical treatment.[5] In addition, in a previous study of children with nephrolithiasis, the rates of multiple stone formation, infection, and recurrence were reported to be significantly higher in the 0–2-year age group, whereas the size of the stones was reported to be larger in patients with hyperuricosuria than in those with other metabolic disorders.[24]

Accordingly, our findings emphasize the risk of developing nephrolithiasis beginning from the first year of life, with those stemming from epidemiological characteristics and metabolic underpinnings as possibly separate clinical entities.[1, 19] Therefore, careful consideration of nephrolithiasis in relation to identifiable metabolic abnormalities in infants presenting with nonspecific symptoms for kidney stones and a positive family history is important for targeted and appropriate treatment.[1, 5, 7, 19]

This study had limitations. First, due to the retrospective single-center design of the present study, it is not possible to establish any cause-and-effect relationship or to generalize our findings to the overall pediatric stone disease population. Second, we did not perform morphological analysis of stones, which would have extended the knowledge obtained in the present study. Despite these limitations, given the paucity of solid information available on this topic, our findings represent a valuable contribution to the literature.

Conclusion

In conclusion, the findings of the present study revealed associations between nephrolithiasis in the first year of life and certain demographic characteristics, nonspecific presentation, and a positive family history along with the presence of microcalculi and identifiable metabolic abnormalities in a considerable portion of the patients. Our findings emphasize the association of identifiable metabolic abnormalities with the extent of nephrolithiasis, with a higher likelihood of bilateral kidney involvement, multiple kidney stones, and larger kidney stones in cases of hypercalciuria, hyperuricosuria, and hyperoxaluria, respectively. Future larger-scale studies in infants with nephrolithiasis are needed to gain a better understanding of the epidemiological characteristics and metabolic underpinnings in this age group to facilitate the development of appropriate prevention strategies.

Disclosures

Ethics Committee Approval: The Ethics Committee of Harran University Medical School provided the ethics committee approval for this study (02.08.2018/08).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – M.E.D.; Design – M.E.D.; Supervision – M.E.D.; Materials – K.Y.; Data collection &/or processing – K.Y.; Analysis and/or interpretation – M.E.D.; Literature search – M.E.D.; Writing – M.E.D.; Critical review – M.E.D.

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