J Ped Nephrol
Journal of Pediatric Nephrology

Original Article

Etiology of Urolithiasis in Children

Afshin Ghalehgolab Behbahan[1*], Elham Emami[2]

1. Pediatric Health Research Center, Tabriz Children's Hospital, Tabriz University of Medical Sciences, Tabriz, Iran.
2. School of Medicine, Tabriz University of Medical Science, Tabriz, Iran.

Use your device to scan and read the article online

Citation Ghalehgolab Behbahan A, Emami E. Etiology of Urolithiasis in Children. Journal of Pediatric Nephrology. 2022; 10(2):74-82. https://doi.org/10.22037/jpn.v10i2.37104

https://doi.org/10.22037/jpn.v10i2.37104

Article info:
Received: 17 Dec 2021
Accepted: 25 Mar 2021
Publish: 01 Apr 2022

Corresponding Author:
Afshin Ghalehgolab Behbahan
Address: Pediatric Health Research Center, Tabriz Children's Hospital, Tabriz University of Medical Sciences, Tabriz, Iran.
E-mail: ghalehgolab@yahoo.com

ABSTRACT

Background and Aim: Urinary stones are a common problem among children that causes pain, dysuria, and other complications, including urinary tract obstruction and infection. The prevalence of urinary stones in children has been increasing in recent decades.

Since the causes of urolithiasis in children differ in various geographical regions, with diverse ethnic backgrounds and popular nutritional habits changing over time, we designed this study to update the identifiable etiologies of urinary stones in children younger than 14 years in Northwest Iran.

Methods: This cross-sectional study was conducted on 144 children with urinary stones who were referred to Tabriz Children's Hospital, Tabriz City, Iran, from March 2018 to September 2020. To determine the main causes of urolithiasis, such as metabolic disorders, urinary tract infections, and anatomical abnormalities, several variables, including age, sex, and results of ultrasound examination, urine analysis and biochemical tests, urine culture, and blood gas analysis, were collected, analyzed, and interpreted.

Results: In this study, 90 boys and 54 girls with an average age of 11.75 (ranged: 1-160) months were included. The most common causes of urolithiasis were metabolic or biochemical disorders in 67 cases (46.5%), mainly hypercalciuria followed by hyperoxaluria, anatomical abnormalities in 10 children (7%), and urinary tract infections in 3 patients (2.1%). Dehydration leading to excessive urine concentration in 87 children (60.4%) was the most common condition associated with urolithiasis in the studied children.

Conclusion: Regarding the high prevalence of metabolic disorders, especially hypercalciuria in children with urolithiasis, these disorders should be considered for preventive, diagnostic, and therapeutic measures.

Keywords: Child, Nephrolithiasis, Urolithiasis, Urinary calculi, Hypercalciuria

Introduction

Urinary stones are a common problem among children causing pain, dysuria, and some other complications, such as urinary tract obstruction and or infection, renal scar formation, hypertension, and progressive renal failure in children. The prevalence of urinary stones has been increasing in recent decades, rising from 7.9 in 1996 to 18.5 in 2007 (per 100000 children younger than 18 years in the United States); this issue can be related to the prevalence of metabolic disorders, obesity, and altered feeding habits, such as high sodium intake, reduced calcium intake, reduced water intake and increased use of antibiotics [1-5]. However, better diagnostic tools and facilities may contribute to this statistical augmentation [5-7]. In children, hypercalciuria is the most common metabolic cause of urinary stones; other known causes are urinary tract anomalies and infections, cystinuria, cystic fibrosis, hyperoxaluria, hyperuricosuria, high protein, high salt, and low carbohydrate diets, low urine volume, ketogenic diet in children with refractory seizures, and the use of certain medications. Complete management of urinary stones in a child includes not only the early diagnosis and elimination of the stone itself but also the treatment of underlying cause(s), decreasing the risk of its complications and preventing the recurrence of the stone [1, 2, 5, 8, 9]. Since urinary stones in children have different causes in different areas and eras, we designed this study to investigate the underlying etiologies of urinary stones in children younger than14 years in Tabriz City, Northwest Iran.

Materials and Methods

This research is a descriptive-analytical cross-sectional study. Since little research has been conducted on this topic, this study was designed to investigate the etiology of urinary stones in children. The research proposal was approved by Child Health Research Center and the Medical Ethics Committee of Tabriz University of Medical Sciences, to be conducted in Tabriz Children's Hospital (the main referral hospital for sick children in Northwest Iran, affiliated to Tabriz University of Medical Sciences), from March 2018 to September 2020. Due to the limited number of eligible patients, the convenience sampling method was used in this study. All 144 children referred to the Pediatric Nephrology Department in our center and eligible for the inclusion criteria were enrolled during the period mentioned above, about 30 months. The inclusion criteria included proper age (from birth to the end of 14 years), the diagnosis of urinary stone by ultrasound study of the child's kidneys and urinary tract (using a high-frequency superficial probe), confirmation of the diagnosis by a pediatric nephrologist who requested for laboratory tests and interpreted the results, and the availability of complete information required in the patient's medical file. The exclusion criteria included renal dysfunction based on the decreased Glomerular Filtration Rate (GFR) detectable by increased plasma creatinine level and lack of the required laboratory tests or the initiation of any treatment before performing them.

The required information was obtained from the patient's medical files and recorded in the data collection form. In addition to patient's personal information such as age and sex, the recorded data included the results of kidney and urinary tract ultrasound study, urine analysis and urine culture, venous blood gas analysis, and measurement of creatinine, calcium, citrate, oxalate, and cystine concentration in a fresh spot urine sample to calculate the ratio of their concentration to creatinine concentration. Since the present study sought to evaluate the most common causes of stone formation in children, the diagnosis of the following disorders, including Urinary Tract Infections (UTI), anatomical abnormalities of the urinary tract, metabolic acidosis, and biochemical abnormalities, such as hypercalciuria, hypocitraturia, hyperoxaluria, and cystinuria were reviewed and re-established in enrolled patients based on the collected data. Every patient was treated and followed up for 10 to 16 months after diagnosis of urolithiasis. Finally, the collected data were analyzed using SPSS software, version 22. The $P<0.05$ was statistically considered significant.

Results

Among the 144 studied children, 54(37.5%) were girls, and 90 (62.5%) were boys. The mean age of patients was 11.75 months in the range of 1 to 160 months. The studied children were referred to a pediatric nephrology clinic by parents or other caregivers because they complained of unreasonable episodes of intense crying, irritability during voiding, dysuria, flank or abdominal pain, direct observation of solid debris in the child's urine, reddish urine, and often requesting further evaluation and treatment of some incidental abnormal findings in child's urine laboratory test or ultrasound examination of the urinary tract for any reason (Table 1).

J Ped Nephrol
Journal of Pediatric Nephrology

Table 2 presents the results of urine analysis in the studied children. Six children with pyuria were observed with a mean White Blood Cell (WBC) count of 8.83 (per high power field). This pyuria may be the result of local inflammation caused by urinary stones. The Mean±SD of specific gravity of random urine samples in 144 children in this study was 1.0159±0.0095 (ranged: 1.005-1.030). Besides, the Mean±SD of pH of their urine was 5.8±0.08 (ranged: 5-8).

Table 3 presents a detailed description of observed urinary crystals. Three cases out of 144 studied children had 3 positive urine cultures; therefore, the relative frequency of UTI in children with urolithiasis was 2.1% in our study.

Table 4 presents the calcium/creatinine ratio (both in mg/dL) in the random urine samples of studied children divided into 3 age groups. Thirty children had hypercalciuria (20.83%), 16 girls (53.3%), and 14 boys (46.7%); therefore, no significant sex difference contributed to the prevalence of hypercalciuria (P>0.05).

The ratio of citrate (mg/dL) to creatinine (g/dL) concentration in the random urine sample of 144 children was studied. A total of 12 children (4 girls and 8 boys) with a frequency of 8.3% had urine citrate/creatinine <180 showing hypocitraturia.

The ratio of oxalate to creatinine concentration (both in mg/dL) in a random urine sample of 144 children was studied in 2 age groups (infants and children). Hyperoxaluria was observed in 16 children (7 girls and 9 boys) out of 144 studied children (11.1%). Table 5 presents the detailed data of numbers and percentages.

We found just one boy out of 144 studied children with a significant amount of cystine in his random urine samples; therefore, the relative frequency of cystinuria in this study is about 0.7%.

Urinary creatinine concentration was relatively high (Mean±SD: 40±16.8, range: 6-166 mg/dL); it was more than 25 mg/dL in 87 (60.4%) studied children, indicating hyperconcentration of urine that is a sign of relative dehydration during urinary sampling.

The Mean±SD blood pH in the studied children was 7.37±0.06 (ranged: 7-7.48), detected by venous blood gas analysis. The Mean±SD blood level of bicarbonate (HCO_3) in 144 children was 22.5±3.1. In 8 children (5.6%), the bicarbonate (HCO_3) level was less than 18 mEq/L, which means that 8 children (3 girls and 5 boys) had significant metabolic acidosis.

The most common causes of urolithiasis were biochemical abnormalities or metabolic disorders (excluding dehydration), found in 67 patients (46.5%). However, considering dehydration as a biochemical disorder predisposing the patients to urolithiasis that may accompany the other metabolic causes of urinary stones in children, some patients had two underlying risk factors for urinary stone formation. Thus more than 90% of patients had one or more biochemical disorder that made them susceptible to urinary stone disease.

Table 6 presents the biochemical disorders found as etiologic risk factors for stone formation in this study.

Two categories of findings were obtained by ultrasonographic study of the kidney and urinary tract in 144 children (using a high-frequency superficial probe); the first is the urinary stones and their characteristics, including location, number, and size of stones (Table 7).

The size of urinary stones observed in the studied children was 1 to 20 mm. The second is various anatomical abnormalities in the urinary tract of 10 children. So the frequency of anatomical disorders associated with urolithiasis in our study is about 7% (Table 8).

Discussion

Kidney stone is one of the oldest known kidney and urinary tract diseases affecting children, and if not properly treated, it can cause significant complications in this age group [1-15]. Besides, this disease is still one of the most common and vital problems in pediatrics, and its prevalence is even increasing in recent decades; that may be due to modern lifestyle, improper nutritional habits such as high salt and low fluid intake, and misuse of drugs [9-17]. However, in more than 75% of pediatric kidney stones, the underlying causes are possibly recognizable [10, 16-19]. The mean age of children in our study was 11.75 months, which is higher than the mean age of cases in similar studies conducted in Iran, where the average age of children with urolithiasis was about 4 to 9 months [7, 8, 20] and in another study reported from Pakistan which was about 7 months [11]. Urinary tract stones are more common in males than females because the male to female (M/F) ratio in adults has been reported to be 4:1. Although this ratio is slightly different in children, boys develop urinary stones 1.5-2 times more than girls [21]. Among the 144 children in this

Table 1. Chief complaint recorded at the first visit of 144 studied children in Pediatric Nephrology Clinic

Chief Complaint at the First Clinical Visit	No. (%)
Abnormal findings in urinalysis	48(33.3)
Abnormal findings in an ultrasound exam	24(16.7)
Recurrent episodes of inconsolable crying	19(13.2)
Irritability during voiding	16(11.1)
Solid debris in child's urine	12(8.3)
Flank or abdominal pain	10(6.9)
Dysuria	8(5.6)
Reddish urine	7(4.9)

Table 2. The results of urine analysis in 144 studied children

Urine Analysis	No. (%) / Mean±SD (Range)
Normal urinalysis	100(69.4)
Urine specific gravity	1.0159±0.0095 (1.005-1.030)
Urine pH	5.8±0.08 (5-8)
Crystalluria	29(20.1)
Hematuria	17(11.8)
Proteinuria	7(4.9)
Pyuria	6(4.2)

study, 62.5% were male, and 37.5% were female (M/F=1.7/1). This finding is similar to studies conducted in Qom City, Iran [8], Tunisia [22, 23], Kuwait [24], and the United States [25] since they showed that urinary stones were more prevalent in boys than in girls (M/F up to 2). However, studies conducted in Yasuj City, Iran [26], Hamadan City, Iran [27], and Turkey [12], where the prevailing climate is temperate to cold, showed more girls with urinary stones. However, this gender difference in the prevalence of urolithiasis may be due to genetic-racial and lifestyle factors in addition to the geographical or climate effects [25].

Table 3. Urinary crystals in 29 out of 144 studied children

Crystal Type	No. (%)
Calcium oxalate	13(9.0)
Calcium oxalate & amorphous urates	4(2.8)
Other calcium crystals	4(2.8)
Uric acid	3(2.1)
Amorphous urates	3(2.1)
Phosphate	1(0.7)
Cystine	1(0.7)

J Ped Nephrol
Journal of Pediatric Nephrology

Table 4. Calcium/Creatinine ratio (both in mg/dL) in the random urine samples of 144 children divided into 3 age groups

Age Groups	Hypercalciuria Definition Level	No. (%)		Ca/Cr (mg/dL)		
		Patients	Patients With Hypercalciuria	Min	Max	Mean±SD
1-7 (mon)	More than 0.8	58(40.3) Female=24, Male=34	4(6.9) Female=2, Male=2	0.027	1.716	0.365±0.312
8-12 (mon)	More than 0.6	24(16.7) Female=8, Male=16	3(12.5) Female=1, Male=2	0.009	1.447	0.331±0.338
1-14 (y)	More than 0.21	62(43) Female=22, Male=40	23(37.1) Female=13, Male=10	0.015	1.406	0.210±0.245

Ca: Calcium; Cr: Creatinine.

Table 5. Oxalate/Creatinine ratio (both in mg/dL) in the random urine samples of 144 children divided into 2 age groups

Age Groups	Hyperoxaluria Definition Level	No. (%)		Oxal/Cr (mg/dL)		
		Patients	Patients With Hyperoxaluria	Minimum	Maximum	Mean±SD
1-12 (mon)	More than 0.30	82(57) Female=32, Male=50	9(11) Female=4, Male=5	0.003	0.969	0.137±0.209
1-14 (y)	More than 0.13	62(43) Female=22, Male=40	7(11.3) Female=3, Male=4	0.008	0.621	0.069±0.104

Oxal: Oxalate; Cr: Creatinine.

Some certain metabolic disorders have been repeatedly reported as common underlying risk factors for urolithiasis in most children, including hypercalciuria, hyperoxaluria, hyperuricosuria, hypocitraturia, and cystinuria with different degrees of prevalence in different studied populations that may be related to the diversity of their diet, geographical area of residence and its climate, inherited traits and age distribution of patients [7, 27-32]. Our study showed metabolic disorders in 67 patients (46.5%) out of 144 patients, including hypercalciuria in 30 patients (44.8%), hyperoxaluria in 16 patients (23.9%), hypocitraturia in 12 patients (17.9%), metabolic acidosis in 8 patients (11.9%) and cystinuria in 1 patient (1.5%) out of 67 children. Many researchers, including Mortazavi et al. [20], Naseri et al. [33]and Sadeghi et al. [34] in Iran, Alon et al. in the United States [25], Wasson et al. in Denmark [17], Edvardsson et al. in Iceland [35], Al-Eisa et al. in Kuwait [24] and Rizvi in Pakistan [11] stated that hypercalciuria is the most common metabolic disorder causing renal stone in children. Moreover, the researchers have reported that hypercalciuria is the most common metabolic risk factor for stone formation in children, even in developed countries [6,

Table 6. Biochemical disorders as underlying causes for stone formation in this study

Disorders	No. (%)
Hypercalciuria	30(20.83)
Hyperoxaluria	16(11.1)
Hypocitraturia	12(8.3)
Metabolic acidosis	8(5.6)
Cystinuria	1(0.7)
Dehydration (urinary overconcentration)	87(60.4)

Table 7. Characters of found urinary stones

Urinary Stone Characters		No. (%)
Location	Both kidneys	59(41)
	Left kidney	47(32.6)
	Right kidney	36(25)
	Ureters	1(0.7)
	Urinary bladder	1(0.7)
Number	Less than 3	97(67.4)
	3 to 5	18(12.5)
	More than 5	29(20.1)
Size (for the largest one in each patient)	Less than 5 mm	125(86.8)
	5 mm to 10 mm	17(11.8)
	11 mm to 20 mm	2(1.4)

36]. Similarly, we detected hypercalciuria in 30 144 children (20.83%) as the most common metabolic disorder causing renal stone (Table 6). No statistically significant sex difference was observed in the prevalence of hypercalciuria in this study which was similar to those reported by Honarpisheh et al. from Kashan City, Iran [37] and Kaneko et al. from the Aral Sea region [38]. We found 16 out of 144 children (11.1%) with hyperoxaluria, who were mostly male (62.5%) and aged less than 1 year (57%). Hyperoxaluria is the main underlying metabolic disorder in about 2%-20% of kidney stones in children. The etiology of hyperoxaluria is unknown in most cases, but it is attributable to metabolic changes increasing the intrinsic production or gastrointestinal absorption of oxalate [39].

A study conducted in Pakistan showed that hyperoxaluria might be the cause of urinary stones in half of the studied children. They declared that the patients' conventional high-oxalate/low-calcium diet with small amounts of dairy products is a possible reason for this finding [11]. In another study conducted in Qom City, Iran, hyperoxaluria was detected as an underlying disorder in about 15% of children with urolithiasis [8]. Our study showed that 12 out of 144 children (8.3%) with urolithiasis had hypocitraturia; two-thirds were male. Also, 8 children (5.6%) had significant metabolic acidosis; 62.5% were boys. This study indicated that cystinuria is the rarest underlying metabolic disorder contributing to urolithiasis; this finding is consistent with the results of many other studies in Iran and other countries [8, 26, 27, 33, 34, 40]. If biochemical disorders, including dehydration, are considered as underlying causes for urinary stone formation in children, more than 90% of cases in this study have metabolic backgrounds as the cause of urolithiasis (Table 6). Dehydration results in excessive urine concentration leading to supersaturation which induces solute crystallization and then stone formation [1-4, 10, 11, 14, 28]. A significant number of children in this study had

Table 8. Anatomical abnormalities accompanying urolithiasis

Anatomical Abnormalities	No. (%)
Hydronephrosis	4(2.8)
Hydroureteronephrosis	1(0.7)
Nephrocalcinosis	2(1.4)
Nephromegaly	1(0.7)
Duplicated collecting system	2(1.4)

J Ped Nephrol
Journal of Pediatric Nephrology

some degree of dehydration detected by high urine creatinine levels. This may be caused by overheating and or over-dressing of infants or insufficient water or fluid intake in children [41]. Therefore, preventing water loss in infants and increased water intake in children can prevent the formation of urinary stones, facilitate its treatment and even decrease the risk of urolithiasis recurrence [28, 42-44].

Our study showed that most children with urolithiasis had normal urine test results (69.4%); however, the most common pathological findings in urine analysis of studied children are crystalluria (20.1%) and then, hematuria (11.8%), proteinuria (4.9%), and pyuria (4.2%), in order of decreasing frequency. In a similar study conducted in Yasuj City, Iran, the most common manifestation of urinary stones in children's urinalysis was hematuria and then UTI and urinary crystals [26]. In another study conducted in Iceland, 80% of children with kidney stones had hematuria [35].

UTIs and stones have been identified as two interrelated diseases because recurrent or chronic UTIs can cause urolithiasis; on the other hand, urinary stones as foreign bodies can cause UTIs by creating stasis [26, 29, 44, 45]. We found 3 children with positive urine cultures; thus, among the underlying causes of urolithiasis in children, about 2.1% are related to UTI. However, UTI may also be a sequel of urinary stones and not necessarily its cause.

Ultrasonographic study of kidneys and urinary tract in the present study showed 10 children with anatomical abnormalities. Therefore, we assume that 5.4% of pediatric renal stones are related to anatomical disorders. However, some anatomical abnormalities, including stenotic or obstructive events leading to hydronephrosis and or hydroureter, may also be consequences of urolithiasis and not necessarily its cause. Examining the location of stones by the ultrasonographic study of the urinary tract in our patients showed the following results: bilateral kidney stones (41%), left kidney (32.6%), right kidney (25%), ureter (0.7%), and bladder (0.7%). Other researchers reported different frequency orders for locations of stones in children's urinary tract. Emad-Momtaz et al. reported that the most common location of urinary stones was the left kidney and then both kidneys, right kidney, ureter, and bladder, respectively [27]. However, Mehrabi et al. reported the right kidney as the most common and the bladder as the rarest location of the urinary stone [26]. However, almost all studies conducted in Iran, including ours, reported the low prevalence of bladder stones in children. Since a direct relationship exists between bladder stones and poor nutritional status in children, the rarity of bladder stones in Iranian children can indicate an improvement in socioeconomic status and, consequently, nutritional status in the studied population [46].

Conclusion

Our study showed that bilateral kidney stones, less than 3 in number and less than 5 mm in size, are the most common condition in pediatric urolithiasis. Patients are often referred to pediatric nephrology clinics due to incidental findings discovered by a child's urine analysis or ultrasound examination. However, recurrent episodes of inconsolable crying are the most common clinical manifestation declared by parents or caregivers of infants with urolithiasis. Crystalluria was the most common finding in patients' urinalysis. The most common underlying cause of urinary stones in children in this study was metabolic problems (foremost hypercalciuria), which are more common in boys than girls. Dehydration is the most vital biochemical disorder that causes urolithiasis in children. At the same time, it is the easiest to treat, not only to prevent urinary stone formation but also to facilitate its treatment and even decrease the risk of urolithiasis recurrence. Anatomical abnormalities and UTI are the following underlying causes of stone in children with a significant difference compared to metabolic problems.

The inability to collect 24-hour urine in infants and young children was a critical limitation in this study that compelled us to eliminate the assessment of 24-hour urine collection for the uric acid level needed to diagnose hyperuricosuria.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

References

[1] Emadoddin Moudi, Rahman Ghaffari, Asaad Moradi. Pediatric Nephrolithiasis: Trend, evaluation and management: A systematic review. J Pediatr Rev. 2017; 5(1):e7785. [DOI:10.17795/jpr-7785]

[2] Spivacow FR, Negri AL, del Valle EE, Calviño I, Fradinger E, Zanchetta JR. Metabolic risk factors in children with kidney stone disease. Pediatr Nephrol. 2008; 23(7):1129-33. [DOI:10.1007/s00467-008-0769-2] [PMID]

[3] Sas DJ, Becton LJ, Tutman J, Lindsay LA, Wahlquist AH. Clinical, demographic, and laboratory characteristics of children with nephrolithiasis. Urolithiasis. 2016; 44(3):241-6. [DOI:10.1007/s00240-015-0827-8] [PMID] [PMCID]

[4] Dwyer ME, Krambeck AE, Bergstralh EJ, Milliner DS, Lieske JC, Rule AD. Temporal trends in incidence of kidney stones among children: A 25-year population based study. J Urol. 2012; 188(1):247-52. [DOI:10.1016/j.juro.2012.03.021] [PMID] [PMCID]

[5] Sas DJ. An update on the changing epidemiology and metabolic risk factors in pediatric kidney stone disease. Clin J Am Soc Nephrol. 2011; 6(8):2062-8. [DOI:10.2215/CJN.11191210] [PMID]

[6] Sharma AP, Filler G. Epidemiology of pediatric urolithiasis. Indian J Urol. 2010; 26(4):516-22. [DOI:10.4103/0970-1591.74450] [PMID] [PMCID]

[7] Mohkam M, Mahani F, Otoukesh B, Sharifian M, Dalirani R, Hatmian B, et al. [Epidemiology of urolithiasis among children hospitalized in Mofid hospital during 5 years (Persian)]. Pajoohande. 2010; 15(3):133-6. [Link]

[8] Akhavan Sepahi M, Heidari A, Shajari A. Clinical manifestations and etiology of renal stones in children less than 14 years age. Saudi J Kidney Dis Transpl. 2010; 21(1):181-4. [Link]

[9] Akhavan Sepahi M, Eftekhari S, Shahmoradi S, Talebizadeh M, Rashidinia S, Hejazi S. Metabolic and anatomic abnormalities associated with pediatric nephrolithiasis: A cross-sectional study. Int J Pediatr. 2017; 5(5):4833-8. [Link]

[10] DeFoor W, Minevich E, Jackson E, Reddy P, Clark C, Sheldon C, et al. Urinary metabolic evaluations in solitary and recurrent stone forming children. J Urol. 2008; 179(6):2369-72. [DOI:10.1016/j.juro.2008.01.151] [PMID]

[11] Rizvi SA, Sultan S, Zafar MN, Ahmed B, Faiq S M, Hossain K Z, et al. Evaluation of children with urolithiasis. Indian J Urol. 2007; 23(4):420-7. [DOI:10.4103/0970-1591.36717] [PMID] [PMCID]

[12] Dursun I, Poyrazoglu HM, Dusunsel R, Gunduz Z, Gurgoze M L, Demirci D, et al. Pediatric urolithiasis: An 8-year experience of single centre. Int Urol Nephrol. 2008; 40(1):3-9. [DOI:10.1007/s11255-007-9234-6] [PMID]

[13] Barr DB, Wilder LC, Caudill SP, Gonzalez AJ, Needham LL, Pirkle JL. Urinary creatinine concentrations in the U.S. population: Implications for urinary biologic monitoring measurements. Environ Health Perspect. 2005; 113(2):192-200. [DOI:10.1289/ehp.7337] [PMID] [PMCID]

[14] Min HK, Sung SA, Lee SY, Lee SW. Sub-morbid dehydration-associated glomerular hyperfiltration: An emerging reality? Kidney Res Clin Pract. 2019; 38(2):196-204. [DOI:10.23876/j.krcp.18.0147] [PMID] [PMCID]

[15] Goldfarb DS, Fischer ME, Keich Y, Goldberg J. A twin study of genetic and dietary influences on nephrolithiasis: A report from the Vietnam Era Twin (VET) Registry. Kidney Int. 2005; 67(3):1053-61. [DOI:10.1111/j.1523-1755.2005.00170.x] [PMID]

[16] Kirejczyk JK, Porowski T, Filonowicz R, Kazberuk A, Stefanowicz M, Wasilewska A, Debek W. An association between kidney stone composition and urinary metabolic disturbances in children. J Pediatr Urol. 2014; 10(1):130-5. [DOI:10.1016/j.jpurol.2013.07.010]

[17] Wason M, Hansen A. Renal and urinary calculi in children. Ugeskrift for laeger. 2005; 167(40):3786-9. [Link]

[18] Wagner U, Balzar E, Ponhold W, Khoss A, Latal D, Zwiauer K. [Urolithiasis in pediatrics: Analysis of 34 patients (German)]. Z Urol Nephrol. 1987; 80(9):505-11. [PMID]

[19] Bergsland KJ, Coe FL, White MD, Erhard MR, DeFoor W R, Mahan J D, et al. Urine risk factors in children with calcium kidney stones and their siblings. Kidney Int. 2012; 81(11):1140-8. [DOI:10.1038/ki.2012.7] [PMID] [PMCID]

[20] Mortazavi F, Mahbubi L. Clinical features and risk factors of pediatric urolithiasis. Iranian Journal of Pediatrics. 2007; 17(2):129-33. [Link]

[21] VanDervoort K, Wiesen J, Frank R, Vento S, Crosby V, Chandra M, et al. Urolithiasis in pediatric patients: A single center study of incidence, clinical presentation and outcome. J Urol. 2007; 177(6):2300-5. [DOI:10.1016/j.juro.2007.02.002] [PMID]

[22] Alaya A, Nouri A, Najjar MF. Urolithiasis in Tunisian children: A study of 100 cases. Saudi J Kidney Dis Transpl. 2009; 20(6):1096-100. [PMID]

[23] Kamoun A, Daudon M, Abdelmoula J, Hamzaoui M, Chaouachi B, Houissa T, et al. Urolithiasis in Tunisian children: A study of 120 cases based on stone composition. Pediatr Nephrol. 1999; 13(9):920-6. [DOI:10.1007/s004670050728] [PMID]

[24] Al-Eisa AA, Al-Hunayyan A, Gupta R. Pediatric urolithiasis in Kuwait. Int Urol Nephrol. 2002; 33(1):3-6. [DOI:10.1023/A:1014419830292] [PMID]

[25] Alon US, Zimmerman H, Alon M. Evaluation and treatment of pediatric idiopathic urolithiasis-revisited. Pediatr Nephrol. 2004; 19(5):516-20. [DOI:10.1007/s00467-004-1422-3] [PMID]

[26] Mehrabi S, Rezaie M, Shahbazi par M, Zoladl M, et al. [Effective factors of pediatric urolithiasis in children under 14 years old that refer to pediatric and urologic medical center of Yasuj at 2010 (Persian)]. Armaghan-e-Danesh. 2013; 18(4):315-26. [Link]

[27] Emad-Momtaz H, Asnaashari F. [Metabolic disorders in children with urinary stones in Hamedan (Persian)]. Avicenna J Clin Med. 2012; 19(2):11-5. [Link]

[28] Stitchantrakul W, Kochakarn W, Ruangraksa C, Domrongkitchaiporn S. Urinary risk factors for recurrent calcium stone formation in Thai stone formers. J Med Assoc Thai. 2007; 90(4):688-98. [PMID]

[29] Marra G, Taroni F, Berrettini A, Montanari E, Manzoni G, Montini G. Pediatric nephrolithiasis: A systematic ap-

J Ped Nephrol
Journal of Pediatric Nephrology

proach from diagnosis to treatment. J Nephrol. 2019; 32(2):199-210. [DOI:10.1007/s40620-018-0487-1] [PMID]

[30] Tohidi MR, Seyezadeh A, Seyedzadeh MS, Ahmadian R, Hookari S. Prevalence of metabolic risk factors affecting childhood nephrolithiasis: A report from a university hospital in west of Iran. Int J Pediatr. 2020; 8(7):11691-9. [DOI:10.22038/IJP.2020.49179.3936]

[31] Issler N, Dufek S, Kleta R, Bockenhauer D, Smeulders N, Van't Hoff W. Epidemiology of paediatric renal stone disease: A 22-year single centre experience in the UK. BMC Nephrol. 2017; 18(1):136. [DOI:10.1186/s12882-017-0505-x] [PMID] [PMCID]

[32] Amancio L, Fedrizzi M, Bresolin NL, Penido MG. Pediatric urolithiasis: Experience at a tertiary care pediatric hospital. J Bras Nefrol. 2016; 38(1):90-98. [DOI:10.5935/0101-2800.20160014] [PMID]

[33] Naseri M, Varasteh AR, Alamdaran SA. Metabolic factors associated with urinary calculi in children. Iran J Kidney Dis. 2010;4(1):32-8. [PMID]

[34] Sadeghi S, Fazeli F, Zarifi E. Clinical characteristics and metabolic abnormalities in pediatric urolithiasis in South East Iran. J Ped Nephrol. 2015; 3(4):149-54. [DOI:10.22037/jpn.v3i4.9344]

[35] Edvardsson V, Elidottir H, Indridason OS, Palsson R. High incidence of kidney stones in Icelandic children. Pediatr Nephrol. 2005; 20(7):940-4. [DOI:10.1007/s00467-005-1861-5] [PMID]

[36] Kit LC, Filler G, Pike J, Leonard MP. Pediatric urolithiasis: Experience at a tertiary care pediatric hospital. Can Urol Assoc J. 2008; 2(4):381-6. [DOI:10.5489/cuaj.804] [PMID] [PMCID]

[37] Honarpisheh A, Hooman N, Taghavi A. Urinary calcium excretion in healthy children living in Kashan/Iran. Iran J Pediatr. 2009; 19(2):154-8. [Link]

[38] Kaneko K, Chiba M, Hashizume M, Kunii O, Sasaki S, Shimoda T, et al. Extremely high prevalence of hypercalciuria in children living in the Aral Sea region. Acta Paediatr. 2002; 91(10):1116-20. [DOI:10.1111/j.1651-2227.2002.tb00108.x]

[39] Schwarz RD, Dwyer NT. Pediatric kidney stones: Long-term outcomes. Urology. 2006; 67(4):812-6. [DOI:10.1016/j.urology.2005.10.020] [PMID]

[40] López M, Hoppe B. History, epidemiology and regional diversities of urolithiasis. Pediatr Nephrol. 2010; 25(1):49-59. [DOI:10.1007/s00467-008-0960-5] [PMID] [PMCID]

[41] Behbahan AG, Hosseini MB, Farhangmehr T. [Evaluation of Dehydration and hypernatremia in neonates admitted to Tabriz Children's Hospital (Persian)]. Med J Tabriz Uni Med Sci. 2009; 31(2):83-8. [Link]

[42] Carvalho-Salemi J, Moreno L, Michael M. Medical nutrition therapy for pediatric kidney stone prevention, part one. J Ren Nutr. 2017; 27(1):e5-8. [DOI:10.1053/j.jrn.2016.09.004] [PMID]

[43] Manz F, Wentz A. The importance of good hydration for the prevention of chronic diseases. Nutr Rev. 2005; 63(6):S2-5. [DOI:10.1111/j.1753-4887.2005.tb00150.x] [PMID]

[44] Fontenelle LF, Sarti TD. Kidney Stones: Treatment and prevention. Am Fam Physician. 2019; 99(8):490-6. [PMID]

[45] Hulton SA. Evaluation of urinary tract calculi in children. Arch Dis Child. 2001; 84(4):320-3. [DOI:10.1136/adc.84.4.320] [PMID] [PMCID]

[46] Ansari MS, Gupta NP. Impact of socioeconomic status in etiology and management of urinary stone disease. Urol Int. 2003; 70(4):255-61. [DOI:10.1159/000070130] [PMID]