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Prevalence and Clinical Characteristics of Pediatric Cystinuria in Ahvaz, Southwest Iran

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Abstract

Objective: This retrospective hospital-based study is aimed at investigating the six-year prevalence and clinical characteristics of pediatric cystinuria in Ahvaz, southwest Iran.

Method: The demographic and clinical data of children referred to nephrology wards with kidney stone disease (KSD) were obtained from the medical records. Data were statistically analyzed and compared for two groups of children with non-cystine kidney stones and those with cystinuria.

Results: From a total of 415 patients with KSD, 45 cases (10.8%) had cystinuria and 370 (89.2%) had non-cystine kidney stones. Overall, the incidence rate of KSD was higher in boys (53.7%) than girls (46.3%, p=0.03). However, no significant difference in age and gender was observed between the two groups (p>0.05). Parental consanguinity (OR [95%]:4.1 [2.15_7.8], p=0.0001) and bilateral renal involvement (OR [95%]: 2.38 [1.25_4.53], p=0.01) were more frequent in children with cystinuria. The number and size of cystine stones were significantly higher than non-cystine stones (p=0.0001). Hypercalciuria (60.72%) and hyperuricosuria (40.1%) were the most frequent metabolic disorders and were significantly more frequent in patients with non-cystine stones (p<0.01). The rate of complete recovery in cystinuria patients was significantly lower than in patients with non-cystine stones (51% vs. 83.2%, p=0.0001).

Conclusion: Parental consanguinity may increase the risk of cystinuria development. Also, the notable prevalence of symptomatic cystinuria at younger ages highlights the importance of metabolic assessment in early childhood. Bilateral renal involvement, the large number/size of cystine stones, and their recurrent nature may make cystinuria patients more vulnerable to renal parenchymal damage and more resistant to treatment.

Keywords: pediatric, kidney disease, cystinuria, recurrence, consanguinity

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INTRODUCTION

Kidney stones are one of the most common nephro-urology complications, causing frequent hospital visits and potentially leading to major problems, such as severe kidney failure [1]. Kidney stones in children are less common than in adults and their prevalence is reported to be 1.8 cases per 1,000 children [2]; however, their incidence in children has been increasing over the years [3]. The cause of this increase has not been precisely identified, but it seems that climate and dietary changes, genetic factors, and possibly other environmental factors play a role in increasing the prevalence of pediatric kidney stones [4].

The mechanism of kidney stone formation is not precisely known, but the main factor in the formation of urinary stones is a disturbance in the balance between the precipitation and dissolution of crystals [5]. Certain anatomical problems (such as urethral stricture and vesicoureteral reflux), infections, endocrine disorders, environmental factors, oliguria and some metabolic disorders can cause kidney stones, and the attraction and repulsion of ions and pH alteration may also play a role. The crystallization of calcium- and phosphate stones mostly occurs in alkaline pH, whereas acidic urine pH promotes uric acid or cystine stones [6–8]. Metabolic disorders promote kidney stone formation by increasing the crystalluria and/or reducing stone inhibiting factors, such as magnesium, citrate, pyrophosphate, osteopontin, calgranulin, uromodulin, urokinase, and albumin [7, 8]. The rate

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of recurrence of kidney stones varies from 16-67%. Metabolic disorders can lead to the recurrence of stones in the urinary tract [9]. Diagnosis of the metabolic abnormalities helps in detecting appropriate drug choices and dosages to prevent recurrence [10].

Cystinuria is a rare genetic disorder of tubulopathy (an autosomal recessive disorder) characterized by defects in cystine metabolism, leading to cystine stone formation. Cystinuria can cause recurrent kidney stones and a risk of kidney failure [11]. This disorder is caused by mutations in the genes encoding two amino acid transporter subunits, which leads to impaired reabsorption of cystine and other dibasic amino acids, including lysine, ornithine, and arginine, in the proximal tubules; this clinically manifests as cystine stones [12]. Cystine stones are clinically important due to the fact they do not dissolve in normal urinary pH, and the high probability of cystine stones becoming crystalline and causing kidney stones to recur [11, 12]. Moreover, the risk of chronic kidney disease in patients with cystinuria is much higher than in those with common stones, such as calcium oxalate [13]. Cystine kidney stones are more clinically important in children than adults due to their higher prevalence in children (3–10%) and recurring nature. If the underlying complications are not well-diagnosed and cured, these stones can increase the risk of kidney failure and chronic kidney disease [13].

Accordingly, this descriptive study, based at the children's hospital in Ahvaz, southwest Iran, investigated the six-year prevalence and clinical characteristics of children referred to the nephrology ward with cystine stones.

METHODS

Study design and population

This retrospective and six-year hospital-based study adhered to the Helsinki declarations and was approved by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran (Ethical Code: IR.AJUMS.REC.1399.196). The study data were obtained from the medical records of children referred to nephrology ward with kidney stone disease (KSD). The ward is located in the Abozar Children's Hospital, which is the main pediatric care center in Khuzestan province.

Sampling was performed using the census method, and the sample size included all recorded files of children with kidney stones who had been referred to the nephrology ward during the last ten years. The inclusion criteria encompassed children under 15 years of age with KSD, who had been followed up for at least a year. Cases with incomplete documentation were excluded.

Study procedures

Demographic and clinical data, including age, gender, parental consanguinity, degree of kidney involvement (unilateral/bilateral), clinical symptoms, kidney stone size and number, and therapeutic implications, were collected from patients' files. Then, the data from two groups of children with non-cystine stones and cystine stones were statistically compared.

A 24-hour urine metabolic workup had been created for all patients. In older children, cystinuria is defined as >315 mg cystine/gram creatinine. However, given that 24-hour urine collection is hardly feasible in younger children, the age-related standards for first-morning urine cystine concentration per gram of creatinine had been used; the normal cystine concentrations for the younger group were as follows: less than 80 mg cystine/gram creatinine for age <1 month, less than 52 mg cystine/gram creatinine for age range one month to one year, and less than 35 mg cystine/gram creatinine for age > 1 year [14].

Regular analysis of 24-hour urine had been performed to assess the metabolic risk and monitor therapy outcomes. Improvement was defined as: the elimination of clinical symptoms, a normal appearance, biochemical characteristics in 24-hour urine, and clearance of the stone on imaging following laparoscopic and robotic-assisted surgeries and/or spontaneous stone passage. Improvement may be partial and/or complete based on the degree of improvement. KSD recurrence is defined as the reappearance of clinical and biochemical signs, including pain and/or vomiting, with a new stone on ureteroscopy or ultrasound and urine abnormalities, i.e., low urine volume (<1cc/kg/hr × 24hrs), hypercalciuria (>4mg/kg), hyperoxaluria (>40 mg/1.7 3m2), and hypocitraturia (<130 mg citrate/gr creatinine and <300 for girls) [15, 16].

Statistical analysis

The qualitative variables were compared between the two groups using a Chi-square test, whereas the quantitative variables were evaluated using an independent *t*-test and/or Mann-Whitney test based on their normality status. A *p-value* of < 0.05 was considered statistically significant and the data were analyzed with SPSS version 26 (SPSS Inc., Chicago, Ill., USA).

RESULTS

Of a total of 415 patients with kidney stones, 45 cases (10.8%) had cystine stones and 370 (89.2%) had non-cystine stones (i.e., calcium oxalate (CaOx) and uric acid stones).

Demographics and clinical manifestations

Overall, the incidence of KSD was higher in boys (53.7%) than girls (46.3%, p=0.03). However, no significant difference was observed between the two groups in terms of mean age and gender (p>0.05). As shown in Table 1, parental consanguinity was more prevalent among children with kidney cystine stones (p=0.0001, OR [95%]: 4.1 [2.15_7.8]). Moreover, bilateral renal involvement was more frequent in the children with cystine kidney stones than those with non-cystine stones (p=0.01, OR [95%]: 2.38 [1.25_4.53]). The number and size of the cystine stones were significantly higher than the non-cystine stones (p=0.0001). The rate of clinical complications, such as abdominal pain, dysuria, urinary tract infection (UTI), and hypomagnesuria, was higher in the children with cystine v. non-cystine stones, but not significantly so (p>0.05). However, hyperuricosuria and hypercalciuria were significantly more frequent in the non-cystine group (p<0.01) (Table 1).

Table 1. Demographic data and clinical features of two groups of children with cystine and non-cystine kidney stones

Variable	Children with non-cystine stones (n=370)	Children with cystine stones (n=45)	*p*-value
	Mean ±SD /range and or frequency% %		
Current age (year)	8.07±4.11 (1_21)	7.93±4.30 (2_20)	0.64
Age of diagnosis (year)	2.86±3.08 (1_14)	3.24±3.05 (0.3_12)	0.08
Gender (n, %)			
Boy	199 (53.8)	24 (53.3)	0.96
Girl	171 (46.2)	21 (46.7)	
Parental consanguinity (n, %)			
Yes	106 (28.6)	28 (62.2)	0.0001
No	264 (71.4)	17 (37.8)	OR (95%): 4.1 (2.15_7.8)
Degree of kidney involvement (n, %)			0.01
Unilateral	210 (56.8)	16 (35.5)	OR (95%): 2.38 (1.25-4.53)
Bilateral	160 (43.2)	29 (64.5)	
Stone size (mm)	3.03±1.76 (1-14)	5.13± 2.98 (1.2_12)	0.0001
Stone number	2.8 ±2.41 (1-15)	5.51±3.64 (1-15)	0.0001
Abdominal pain (n, %)	278 (75.13)	36(80)	0.58
Dysuria (n, %)	153 (41.3)	24 (53.3)	0.15
Enuresis (n, %)	13 (3.5)	0	0.37
UTI* (n, %)	108 (29.2)	15 (33.3)	0.6
Hypocitraturia (n, %)	87 (23.5)	5 (11.1)	0.06
Hyperoxaluria (n, %)	78 (21.1)	5 (11.1)	0.16
Hyperuricosuria (n, %)	161 (43.5)	9 (20)	0.002 OR (95%): 3.08 (1.44_6.58)
Hypercalciuria (n, %)	236 (71.1)	16 (35.5)	0.0003 OR (95%): 3.19 (1.67_6.09)
Hypomagnesuria (n, %)	84 (22.7)	5 (11.1)	0.08
Complete improvement (n, %)	308 (83.2)	23 (51)	0.0001
Partial improvement (n, %)	0	14 (31)	
Not improved (n, %)	19 (5.2)	4 (9)	
Recurrence (n, %)	43 (11.6)	4 (9)	

* UTI: urinary tract infection

Treatments and outcomes

In this study, 24 patients (53.3%) with cystine stones were treated with D-penicillamine, 17 (37.8%) underwent surgical treatment, and four (8.9%) were treated by hydration, dietary changes (sodium restriction), and alkalization. The recovery status of cystinuria patients is presented in Figure 1. A total of 51% (n=23) of the cystinuria patients made a complete recovery, while 31% (n=14) made a partial recovery, 9% (n=4) experienced no recovery, and the remaining 9% (n=4) relapsed. Of those with non-cystine stones, the rates of complete recovery, no recovery, and recurrence were, respectively, 83.2% (n=308), 5.2% (n=19), and 11.6% (n=43). Although the rate of recurrence was not significantly different between the two groups (p=0.8), the rate of improvement or good response to treatment in the patients with cystinuria was significantly lower than those with non-cystine kidney stones (p=0.0001) (Table 1, Figure 1).

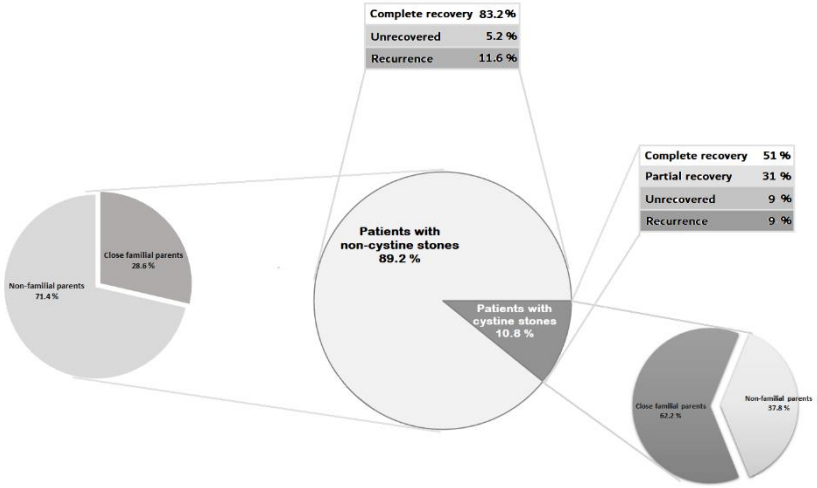

Figure 1. Prevalence and characteristics of children's kidney stones and related clinical outcomes

As shown in Table 2, out of the 24 cystinuria patients treated with D-penicillamine, 15 cases (62.5%) and six cases (25%) achieved a complete and partial recovery, respectively, but three cases (5.12%) did not recover. Moreover, three cases (12.5%) became afflicted with leukopenia. On the other hand, out of the 21 patients who did not receive D-penicillamine, eight (38.1%) completely recovered, and another eight (38.1%) partially recovered, but five (23.8%) did not recover. After comparing the two groups, no significant relationship was found between the type of treatment and the recovery rate (p=0.26). Furthermore, the recovery of cystinuria patients was evaluated based on their stone size. As shown in Table 3, no statistically significant association was found between the recovery rate and the size of the kidney stone (p=0.74). Also, no significant relationship was found between the size of cystine kidney stones and the incidence of abdominal pain (p=0.6) and/or hypercalciuria (p=0.41) (Table 4).

The average number of cystine stones in patients with a UTI (5.66±3.24) was not significantly different from that in patients without ([5.30±3.88], p=0.6), implying that there was no significant correlation between the number of stones and the incidence of a UTI.

Table 2. Association between recovery rate and D-penicillamine treatment in patients with cystine stones

Treatment with D-penicillamine	Complete improvement n (%)	Partial improvement n (%)	Not improved/ Recurrence n (%)	*p*-value
Yes (n=24)	15 (62.5)	6 (25)	3 (12.5)	0.26
No (n=21)	8 (38.1)	8 (38.1)	5 (23.8)	

Table 3. Association between recovery rate and D-penicillamine treatment in patients with cystine stones

Stone size (n)	Complete improvement n (%)	Partial improvement n (%)	Not improved/ Recurrence n (%)	*p*-value
<5 mm (n=29)	16 (55.2)	8 (27.6)	5 (17.2)	0.74
>5 mm (n=16)	7 (43.8)	6 (37.5)	3 (18.7)	

Table 4. Association between abdominal pain and hypercalciuria with cystine stones

	Stone size (mean±SD)	*p*-value
Abdominal pain		
Yes (n=35)	4.85 ± 2.89	0.6
No (n=10)	5.47 ± 3.24	
Hypercalciuria		
Yes (n=16)	5.53 ± 2.31	0.41
No (n=29)	4.72 ± 3.21	

DISCUSSION

The occurrence of cystinuria differs according to geographical area. In this study, the six-year prevalence of pediatric cystinuria in Ahvaz, southwest Iran, was 10.8%. KSD was more prevalent in boys (53.7% vs. 46.3% in girls), which is consistent with a similar report by Rizvi et al. [13]. No significant correlation was found between gender and the kind of kidney stone. Overall, 75.6% of patients were under four years old at the time of diagnosis, and 24.4% were over four years old. Also, no significant difference in mean age was observed between patients with cystinuria and those with non-cystine kidney stones. However, 73% of cystinuria patients were under five years old, indicating that the cystine stones were more likely to develop at younger ages. The average age of diagnosis for cystinuria was 38.9 months, with even a three-month-old baby being diagnosed with cystinuria. Seyedzadeh et al. reported an average age of 34 months for a diagnosis of cystinuria [17]. These results emphasize the importance of assessing metabolic status as a predisposing factor for cystinuria in early childhood.

In the present study population, parental consanguinity was significantly more frequent among the patients with cystinuria (62.2%) than those with non-cystine stones (28.6%). A study by Aydogdu et al. in Turkey reported a family history of KSD in 50% of children with cystinuria [18]. In other studies, about 40–85% of children with KSD had a family history of the disease [6, 19, 20]. According to the results of previous studies on genetic mutations causing cystinuria [21], it seems that genetic factors may also have played a role in the development of cystinuria in our study population.

In our study, bilateral renal involvement and the number and size of cystine stones were more frequent in children with cystinuria, which is consistent with the results of previous studies [13, 22, 23]. Other studies have also reported cystine stones to be larger than non-cystine stones, and occurring in the younger age range, with these patients requiring urological treatment [24–27].

The rates of abdominal pain, dysuria, UTI, and hypomagnesuria were higher in the children with cystinuria than those with non-cystine stones, but not significantly so. However, hyperuricosuria and hypercalciuria were notably more frequent in patients with non-cystine kidney stones. In the Asi et al. study, the incidence rates of abdominal pain, nausea/vomiting, and UTI in children with cystinuria were 87%, 39%, and 25%, respectively [23]. Seyedzadeh et al. found, in the city of Kermanshah, Iran [17], that UTI was observed in 31.8% of children with cystinuria, and 59.1% of children had non-specific symptoms and were diagnosed by sonography. [28] found that abdominal pain, renal colic, and UTI were the main symptoms, and metabolic abnormalities were diagnosed in 93.2% of the children with KSD, and hypercalciuria (74.6%) and hypocitraturia (44.1%) were the most common urinary complications. In the present study's population, hypercalciuria (60.72%) and hyperuricosuria (40.1%) were the most frequent metabolic disorders in children with KSD, followed by hypocitraturia (22.2%), hypomagnesuria (21.5%), and hyperoxaluria (20%). Rizvi et al. reported that the most common metabolic abnormalities in children with KSD from Asian countries are, respectively, hypocitraturia (63–87%), hyperoxaluria (40–43%), hypocalciuria (40%), and hyperuricosuria (27%) [13]. These slight differences in the rate and type of metabolic disorder may be due to genetic and nutritional differences in different geographical areas, demanding further genetic investigation.

This study's findings show that the rate of complete recovery or appropriate response to treatment in cystinuria patients was significantly lower than in patients with non-cystine kidney stones (51% v. 83.2%), which may be due to the higher rate of bilateral renal involvement in cystinuria patients and the higher number/size of cystine compared to non-cystine stones. Nevertheless, the recurrence rate was not significantly different between the cystine and non-cystine groups (9% vs. 11.6%). The study of Seyedzadeh et al. reported that excellent and poor responses to hydration and urinary alkalinization were, respectively, observed in 54.5% and 27.2% of children with cystinuria. Captopril was prescribed for five patients, but was effective only in one. D-penicillamine produced no favorable responses. Extracorporeal shockwave lithotripsy was successful in five cases but failed in four. Surgical interventions were used for 13 patients, with six patients (27.3%) needing more than one operation [17]. In the present study, out of 24 patients treated with D-penicillamine, three (12.5%) developed leukopenia, and the rest recovered completely (62.5%) or partially (25%). Out of the other cystinuria patients, 17 cases were undergoing surgical treatment, and four were treated by hydration, dietary changes, and alkalization; no significant correlation was found between the type of treatment and the recovery rate.

Asi et al. found the recurrence rate for children with cystinuria was significantly higher (71.4%) than the rate found for those in our study (9%), and the recurrence of the disease was observed after 27.9 months, on average. Their therapeutic options included alkalization plus a thiol drug for all patients, tiopronin and captopril for 52/70 and 18/70 cases, respectively [23]. Other studies have also reported a higher percentage of recurrence in patients with cystinuria compared to patients with non-cystine kidney stones [29, 30]. Such a notable contradiction with the present findings may be due to the minor differences in treatment options and/or patients' genetic characteristics in different geographical areas.

Despite the previous reports from Knoll et al. [30], the present study found no significant association between the size of cystine stones and the rates of recovery, recurrence, abdominal pain, hypercalciuria, and UTI. Therefore, the size of cystine stone seems not to be an important risk factor for cystinuria-related adverse outcomes. Nonetheless, in comparison to patients with non-cystine kidney stones, the lower recovery rate in cystinuria patients implies that the high rate of bilateral renal involvement and the large number and size of cystine stones, along with their recurrent nature, may make these patients more vulnerable to renal parenchymal damage.

Strengths and limitations of the study

The evaluation of the maximum number of eligible patients was an advantage of the current research. Moreover, considering that the data were obtained from the main pediatric care center of Khuzestan province (southwest Iran), the present findings can effectively be said to reflect the prevalence and features of KSD in the childhood population in this region. However, due to the retrospective nature of the study, investigating the level of cystine, urine pH, the effect of the disease on the quality of life, and genetic analysis of patients was not possible.

CONCLUSION

The six-year prevalence of pediatric cystinuria in Ahvaz, southwest Iran, was 10.8%. Hypercalciuria (60.72%) and hyperuricosuria (40.1%) were the most common metabolic disorders in children with KSD. Cystinuria mostly develops at younger ages (73%), highlighting the importance of metabolic assessment in early childhood. In comparison to children with non-cystine kidney stones, parental consanguinity was more frequent among children with cystinuria, implying that genetic factors may play a role in their development. The rate of complete recovery in cystinuria patients was significantly lower than those with non-cystine kidney stones (51% vs. 83.2%), which may be due to the higher rate of bilateral renal involvement in cystinuria patients and the larger number/size of cystine compared to non-cystine stones. Nevertheless, further investigations, especially multicenter genetic analyses, are recommended to detect the main risk factors of adverse outcomes in children with KSD.

REFERENCES

1. Chuang TF, Hung HC, Li SF, Lee MW, Pai JY, Hung CT. Risk of chronic kidney disease in patients with kidney stones—a nationwide cohort study. *BMC Nephrol*. 2020; 21(1): 292.
2. Bhat D, Shankar R, Shenoy RD, Rai S. Cystine Urolithiasis in Early Childhood. *Indian J Clin Biochem*. 2019; 34(3): 361–362.
3. Amancio L, Fedrizzi M, Bresolin NL, Moreira MG, Penido G. Pediatric urolithiasis: experience at a tertiary care pediatric Hospital. *J Bras Nefrol*. 2016; 38(1): 90–98.
4. Shin S, Srivastava A, Alli NA, Bandyopadhyay BC. Confounding risk factors and preventative measures driving nephrolithiasis global makeup. *World J Nephrol*. 2018; 7(7): 129–142.
5. Williams JC Jr, Gambaro G, Rodgers A, Asplin J, Bonny O, Costa-Bauzá A, et al. Urine and stone analysis for the investigation of the renal stone former: a consensus conference. *Urolithiasis*. 2021; 49(1): 1–16.
6. Tasdemir M. Metabolic Abnormalities in Children with Urinary Stone Disease and The Influence of Gender. *The Medical Bulletin of Sisli Etfal Hospital*. 2017; 51(3): 218–24.
7. Spivacow FR, Del Valle EE, Boailchuk JA, Sandoval Díaz G, Rodríguez Ugarte V, Arreaga Álvarez Z. Metabolic risk factors in children with kidney stone disease: an update. *Pediatr Nephrol*. 2020; 35(11): 2107–2112.
8. Velásquez-Forero F, Esparza M, Salas A, Medeiros M, Toussaint G, Llach F. Risk factors evaluation for urolithiasis among children. *Bol Med Hosp Infant Mex*. 2016; 73(4): 228–236.
9. Wang K, Ge J, Han W, Wang D, Zhao Y, Shen Y, Chen J, Chen D, Wu J, Shen N, Zhu S, Xue B, Xu X. Risk factors for kidney stone disease recurrence: a comprehensive meta-analysis. *BMC Urol*. 2022; 22(1): 62.
10. Ahmad I, Pansota MS, Tariq M, Tabassum SA. Frequency of metabolic abnormalities in urinary stones patients. *Pak J Med Sci*. 2013; 29(6): 1363–6.
11. Andreassen KH, Pedersen KV, Osther SS, Jung HU, Lildal SK, Osther PJ. How should patients with cystine stone disease be evaluated and treated in the twenty-first century? *Urolithiasis*. 2016; 44(1): 65–76.
12. Sahota A, Tischfield JA, Goldfarb DS, Ward MD, Hu L. Cystinuria: genetic aspects, mouse models, and a new approach to therapy. *Urolithiasis*. 2019; 47(1): 57–66.
13. Rizvi SA, Sultan S, Zafar MN, Ahmed B, Aba Umer S, Naqvi SA. Paediatric urolithiasis in emerging economies. *Int J Surg*. 2016; 36(Pt D): 705–712.
14. Leslie SW, Sajjad H, Bashir K. 24-Hour Urine Testing for Nephrolithiasis: Interpretation Guideline. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023. https://www.ncbi.nlm.nih.gov/books/NBK482448/
15. Turk C, Petřík A, Sarica K, Seitz C, Skolarikos A, Straub M, et al. EAU Guidelines on Diagnosis and Conservative Management of Urolithiasis. *Eur Urol*. 2016; 69(3): 468–74.
16. Daga S, Palit V, Forster JA, Biyani CS, Joyce AD, Dimitrova AB. An Update on Evaluation and Management in Cystinuria. *Urology*. 2021; 149: 70–75.
17. Seyedzadeh A, Momtaz HE, Moradi MR, Moradi A. Pediatric cystine calculi in west of Iran: a study of 22 cases. *Urol J*. 2006; 3(3): 134–7.
18. Aydogdu SD, Kirel B, Coskun T, Kose S. Prevalence of cystinuria among elementary schoolchildren in Eskisehir, Turkey. *Scand J Urol Nephrol*. 2009; 43(2): 138–41.
19. Celiksoy MH, Yilmaz A, Aydogan G, Kiyak A, Topal E, Sander S. Metabolic disorders in Turkish children with urolithiasis. *Urology*. 2015; 85(4):

909–13.

20. Alpay H, Gokce I, Özen A, Bıyıklı N. Urinary stone disease in the first year of life: is it dangerous? *Pediatr Surg Int*. 2013; 29(3): 311–6.
21. Martell HJ, Wong KA, Martin JF, Kassam Z, Thomas K, Wass MN. Associating mutations causing cystinuria with disease severity with the aim of providing precision medicine. *BMC Genomics*. 2017; 18(Suppl 5): 550.
22. Bhat D, Shankar R, Shenoy RD, Rai S. Cystine Urolithiasis in Early Childhood. *Indian J Clin Biochem*. 2019; 34(3): 361–362.
23. Asi T, Dogan HS, Bozaci AC, Citamak B, Altan M, Tekgul S. A single center's experience in pediatric cystine stone disease management: what changed over time? *Urolithiasis*. 2020; 48(6): 493–499.
24. Reinstatler L, Stern K, Batter H, Scotland KB, Ardekani GS, Rivera M, et al. Conversion from Cystine to Noncystine Stones: Incidence and Associated Factors. *J Urol*. 2018; 200(6): 1285–1289.
25. Yang Y, Albanyan H, Lee S, Aloysius H, Liang JJ, Kholodovych V, et al. Design, synthesis, and evaluation of l-cystine diamides as l-cystine crystallization inhibitors for cystinuria. *Bioorg Med Chem Lett*. 2018; 28(8): 1303–1308.
26. Usawachintachit M, Sherer B, Hudnall M, Tzou DT, Taguchi K, Hsi RS, et al. Clinical Outcomes for Cystinuria Patients with Unilateral Versus Bilateral Cystine Stone Disease. *J Endourol*. 2018; 32(2): 148–153.
27. Friedlander JI, Antonelli JA, Canvasser NE, Morgan MSC, Mollengarden D, Best S, et al. Do Urinary Cystine Parameters Predict Clinical Stone Activity? *J Urol*. 2018; 199(2): 495–499.
28. Amancio L, Fedrizzi M, Bresolin NL, Penido MG. Pediatric urolithiasis: experience at a tertiary care pediatric hospital. *J Bras Nefrol*. 2016; 38(1): 90–8.
29. Onal B, Dogan C, Citgez S, Argun B, Onder AU, Sever L, Caliskan S, Canpolat N, Tasdemir M, Erozenci A. Percutaneous nephrolithotomy in children with cystine stone: long-term outcomes from a single institution. *J Urol*. 2013; 190(1): 234–7.
30. Knoll T, Zollner A, Wendt-Nordahl G, et al. Cystinuria in childhood and adolescence: recommendations for diagnosis, treatment, and follow-up. Pediatr Nephrol. 2005; 20: 19–24.

الانتشار والخصائص السريرية لداء البيلة السيستينية لدى الأطفال في الأهواز، جنوب غرب إيران

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الملخص

الخلفية والأهداف : تهدف هذه الدراسة الاسترجاعية المستندة إلى المستشفى إلى التحقيق في انتشار (6) سنوات والخصائص السريرية البيلة السيستينية لدى الأطفال في الأهواز، جنوب غرب إيران.

منهجية الدراسة : تم الحصول على البيانات الديموغرافية والسريرية الخاصة بالأطفال المصابين بمرض حصوات الكلى (KSD) الذين أشاروا إلى أجنحة أمراض الكلى من السجلات الطبية. ثم تم تحليل البيانات إحصائياً ومقارنتها بين مجموعتي الأطفال المصابين بحصوات الكلى غير السيستين وأولئك الذين يعانون من بيلة سيستينية.

النتائج: من إجمالي 415 مريضًا مصابًا بمرض KSD ، كان لدى 45 حالة (10/8٪) بيلة سيستينية و 370 حالة (89/2٪) مصابون بحصى الكلى غير السيستين .بشكل عام، كان معدل حدوث KSD أعلى في الأولاد (53/7 ٪) من الفتيات (46/3% ، $p= 0.03$). ومع ذلك، لم يلاحظ أي اختلاف كبير في العمر والجنس بين المجموعتين ($p> 0.05$). كان قرابة الوالدين [OR (95%):4.1(2.15_7.8), $p=0.0001$] ومشاركة الكلى الثنائية [OR (95%):2.38(1.25_4.53), $p=0.01$] أكثر تواترا بين الأطفال المصابين ببول سيستيني. كان عدد وحجم حصوات السيستين أعلى بكثير من حصوات غير السيستين [$p=0.0001$]. كان فرط كالسيوم البول (60/72٪) وفرط حمض اليوريك (40/1٪) من الاضطرابات الأيضية الأكثر شيوعًا، والتي كانت أكثر شيوعًا في المرضى الذين يعانون من حصوات غير السيستين($p <0.01$). كان معدل الشفاء التام في مرضى البول السيستين أقل بكثير من المرضى الذين يعانون من حصوات غير السيستين (51٪ مقابل 83/2٪، $p=0.0001$).

الاستنتاجات : قد يزيد قرابة الوالدين من خطر تطور بيلة السيستينية .أيضًا ، يبرز الانتشار الملحوظ لداء السيستينية المصحوب بأعراض في الأعمار الأصغر أهمية تقييم التمثيل الغذائي في مرحلة الطفولة المبكرة .قد يؤدي التورط الكلوي الثنائي، والعدد / الحجم الكبير من حصوات السيستين وطبيعتها المتكررة إلى جعل مرضى البيلة السيستينية أكثر عرضة للتلف الكلوي المنتي وأكثر مقاومة للعلاجات.

الكلمات الدالة: طب الأطفال، أمراض الكلى، بيلة سيستينية، تكرار، قرابة.