cjhr.gums.ac.ir
Caspian J Health Res. 2018;3(1):24-27 doi:10.29252/cjhr.3.1.24

Caspian Journal of Health Research

Original article

Urinary Oxalate, Citrate and Uric Acid in Healthy Primary School Children in Zahedan

Simin Sadeghi Bojd[1], Noor Mohammad Noori[1], Alireza Teimouri[1*]

[1]*Children and Adolescents Health Research Center, Zahedan University of Medical Sciences, Zahedan, Iran*

[*]*Corresponding author: Alireza Teimouri*
Email: alirezateimouri260@gmail.com

ABSTRACT

Background: Urolithiasis in children is associated with metabolic disorders. The most important metabolic disorders are hypercalciuria, hyperoxaluria, hypocitraturia, cysitinuria and hyperuricosuria. This study aimed to evaluate the level of urinary solutes in healthy primary school children in Zahedan, Iran.
Methods: This study was carried out on primary school-aged children. A total of 1800 samples were randomly selected using multistage random sampling method. Morning urine samples of children were taken and sent to the laboratory. Urine creatinine was measured by colorimetric device without removing proteins with BT3000 and photometer analyzer based on Jaffe method. Oxalate, uric acid, and citrate were measured using Pars test kits with photometric method. Weight and height were measured using standard protocols. Body mass index (BMI) was calculated as the ratio of weight in kg to height in square of meter. The ratio of oxalate, citrate, and uric acid to creatinine were then measured based on age, sex, and BMI categories.
Results: Of total, 1157 schoolchildren were participated in the study. The mean age of participants was 9 years (Range: 7-13 years) including 433 males (37.4%) and 724 females (62.6%).The mean level of Oxalate, citrate and uric acid to creatinine were estimated to be 0.02 ± 0.01, 2.98 ± 2.39 and 3.22 ±0.59, respectively. The prevalence of hpeyroxaluria, hypocitraturia and hyperuricosuria was 25.3%, 20.3% and 34.6%, respectively. There was significant relationship between age and ethnicity with urinary metabolic disorder.
Conclusion: In this study, a high prevalence of urinary metabolic disorders were identified in school-aged children. The screening program of urinary solute for early detection of urinary metabolic disorder and kidney stones is recommended.
Keywords: Citrates, Oxalates, Schools, Uric Acid
Citation: Sadeghi Bojd S, Noori NM, Teymouri A. Urinary oxalate, citrate and uric acid in healthy primary school Children in Zahedan. Caspian J Health Res. 2018;3(1):24-27. doi:10.29252/cjhr.3.1.24

ARTICLEINFO

Received: February 25, 2017
Accepted: December 17, 2017
ePublished: March 04, 2018

Introduction

Urolithiasis or kidney stones is one of the most common disorders in pediatrics, and its prevalence has been increasing worldwide (1, 2). About 40 to 50% of kidney stones are associated with urinary metabolic disorders including hypercalciuria, hyperoxaluria, hypocitraturia, cysitinuria and hyperuricosuria (3-8). These metabolic disorders have been reported as major findings of kidney stones (2, 4, 9). The evaluation can be performed by measuring the level of calcium, uric acid, citrate, and oxalate to creatinine in random urine samples of children (4, 9). In the biochemistry view, urine contains calcium, oxalate, uric acid, magnesium, citrate and cysteine, among them oxalate is the final product of the glayoxylate and ascorbic acid metabolic pathway excreted by the kidneys (10, 11). Nearly 85 % of daily urinary excretion of oxalate is produced by normal metabolic homeostasis, and

the remaining 15% is generated from oxalate oral intake. Daily urinary oxalate excretion is less than 50 mg per 1.73 m^2 of body surface, and its higher amount is called hyperoxaluria, which is a predisposing factor in urolithiasis disorders (6). In infants and children, uric acid excretion fraction is more than that in adults, and the values above 815 mg per 1.37 m^2 of body surface is defined as hyperuricosuria (6). Hyperuricosuria with significant hyperuricemia is observed in inherited disorders of purine metabolism, lymphoproliferative disorders, and polycythemia (3). Other causes of Hyperuricosuria are increased absorption of purines, hemolysis, uricosuric drugs, and congenital heart patients with cyanotic and idiopathic (3, 12). Citrate is normally distributed in the urine and regulated through both absorption and metabolism processes at the level of the proximal tubule. Hypocitraturia defined as the ratio of citrate to creatinine lower than 180 mg/mg, and in 24-hour urine is less than 300 mg/ mg.

The prevalence of pediatric urolithiasis in Zahedan, located at south-east of Iran, is reported to be increasing in recent years (13). The urinary composition of pediatrics in a population-based school-aged children can help to identify the crystallization status as a predisposing factor for urinary stone. Therefore, the aim of this study was to evaluate the prevalence of hyperoxaluria, hypocitraturia, hyperuricusuria in school children in Zahedan city, Iran.

Methods

Study population

This cross-sectional study was carried out on primary school-aged children in Zahedan, south-east of Iran. Based on a pilot estimate of 0.25, with confidence interval of 95% and acceptable margin of error being 2%, a total of 1800 sample size were estimated. Multi-stage random sampling method was carried out among all schools in the city of Zahedan. Initially, fifty schools were selected randomly from north, south, west, east and center of the city including ten schools from each area, five for boys and five for girls. The sample size in each school were allocated proportionate to school size. Finally, the students were selected in each class using systematic random sampling method on classroom record list. Out of 1800 families receiving invitation letters, 1500 cases sent their written consent to participate in the study. Students with history of chronic kidney disease, metabolic disease, kidney stones, abnormal urine analysis or taking medications affecting the excretion of urinary solutes were excluded from the study. These symptoms and diseases were diagnosed through interviewing with parents or clinical examination by a nephrologist. Based on exclusion criteria, 643 individuals were excluded from the study, and 1157 samples were entered. The data collection process was performed between December 2015 and February 2016 by permission of the Research and Ethics Committee of the Zahedan University of Medical Sciences.

Measurement

Demographic information including age, sex, weight, height, and ethnicity were recorded on collection form. Morning urine samples of children were taken between 8-11 am and sent to the laboratory. About 6 hours after collection, urine samples were refrigerated at a temperature of -80º C, and all of the samples were analyzed. Urine creatinine was measured by colorimetric device without removing proteins with BT3000 and Photometer analyzer based on Jaffe method. Oxalate, uric acid, and citrate were measured using Pars test kits (made in Iran) with photometric method. The ratio of oxalate, citrate and uric acid to creatinine were calculated for each student. Hyperoxaluria was defined as the ratio of oxalate to creatinine more than 0.06 mg/g. Hyperuricusuriais considered as the ratio of uric acid to creatinine more than 0.9mg/mg and hypocitraturia as the ratio of citrate to creatinine less than 0.25 mg/mg (2).

Weight and height were measured by trained nurses with digital scales and nonexpanding tapes after urine sampling. Weight was measured without shoes and light clothing. Height was measured in standing position with bare feet against the wall as the buttocks, back, shoulders and heels touching the wall with head forward. Body mass index (BMI) was calculated as the ratio of weight in kilogram to height in square of meter. The BMI was classified using age and sex specific percentile according to center for disease control and prevention. BMI less than the 5th percentile considered as underweight, the 5th to less than 85th percentile as normal weight, and equal to or greater than the 85th percentile considered as obese and overweight (14).

Statistical Analysis

Data described as mean and standard deviation expressed in mean and standard deviation for the quantitative and proportion and percentage for qualitative variables. The normal distribution was assessed using Kolmogorov Smirnov test. In case of normal distribution, t-test and ANOVA statistical tests were applied. Otherwise, peer non-parametric tests and chi-squares were used. The analysis was performed using SPSS 18.0 software. P value < 0.05 was considered as a statistically significant level.

Results

In this study, 1157 primary schoolchildren (boys=37.4% and girls=62.6%) participated with mean age of 9.4 years (standard deviation=1.56, Min=6 and Max=13 years). The prevalence of hyperoxaluria, hypocitraturia and hyperuricosuria by age group, ethnicity and BMI categories are shown in tables 1 to 3, respectively.

Table 1. Frequency of Urinary Hyperoxaluria According to Age, Gender, and Ethnic Group and BMI categories in Children

Variables	Normal	Abnormal	Total	P-value
	Number (%)	Number (%)		
Age groups (years)				
7-8	248 (70.3)	105 (29.7)	353	0.006
9-10	347(76.8)	105(23.2)	452	
11-13	261(80.6)	63(19.4)	324	
Ethnic groups				
Baluch	370(77.2)	109(22.8)	479	<0.001
Sistani	412(84.3)	77(15.7)	489	
Others	117(68.4)	54(31.6	171	
BMI categories				
Underweight	511(73.6)	183(26.4)	694	
Normal	302(77.6)	87(22.4)	389	0.328
Overweight & obese	24(77.4)	7(22.6)	31	

The prevalence of hyperoxaluria was 25.3%, and there was significant relationship between hyperoxaluria with age and ethnicity. The highest percentage of abnormality was among children aged 7 to 8 years old. Children with Sistani ethnicity had lowest percentage of abnormality (16%) compared to Baluch (23%) and other ethnicities (32%) (Table 1). The prevalence of hypocitraturia and hyperuricosuria was 20.3% and 34.6%, respectively. Both metabolic abnormalities were significantly associated with age and ethnicity. The prevalence of hypocitraturia and hyperuricosuria in children aged 7 to 8 years was significantly higher than that in older age groups (table 2 and 3). Sistani ethnicity had lowest prevalence of both urinary metabolic disorders compared to other ethnicities.

Table 2. Frequency of Urinary Hyperuricusuria According to Age, Gender, and Ethnic Group and BMI categories in Children

Variables	Normal	Abnormal	Total	P-value
	Number (%)	Number (%)		
Age groups (years)				
7-8	209(59.2)	144(40.8)	353	0.002
9-10	309(68.4)	143(31.6)	452	
11-13	230(71.0)	94(29.0)	324	
Ethnic groups				
Baluch	136(72.7)	51(27.3)	187	<0.001
Sistani	137(73.3)	50(26.7)	187	
Others	187(60.5)	122(39.5)	309	
BMI categories				
Underweight	426(61.10)	271(38.90)	697	0.001
Normal	283(72.80)	106(27.20)	359	
Overweight & obese	21(67.70)	10(32.30)	31	

Table 3. Frequency of Urinary Hypocitraturia According to Age, Gender, and Ethnic Group and BMI categories in Children

Variables	Normal	Abnormal	Total	P-value
	Number (%)	Number (%)		
Age group (years)				
7-8	266(75.4)	87(24.6)	353	0.001
9-10	370(82.8)	77(17.2)	447	
11-13	275(86.2)	44(13.8)	319	
Ethnic group				
Baluch	327(72.3)	125(27.7)	452	0.01
Sistani	350(79.2)	88(20.1)	438	
Others	175(71.1)	71(28.9)	246	
BMI categories				
Underweight	552(79.2)	145(20.8)	697	
Normal	315(81.0)	74(19.0)	389	0.741
Overweight & obese	24(77.4)	7(22.6)	31	

Discussion

The results of current study revealed a high prevalence of urinary metabolic disorders among school aged children. This finding is consistent with previous studies by Naseri et al. who found urinary metabolic disorder among half of children in Mashhad (15). Coward and colleagues reported that the most common causes for urolithiasis were metabolic problems and infection (16). Habbig et al. found that metabolic disorders such as hypercalciuria, hyeroxaluria and hypocitraturia were as main risk factors in nephrocalcinosis of children (17). Moorani et al. revealed that hypocitraturia in children with urolithiasis was higher compared to healthy children (18). In another study conducted by Ratan et al., the most common causes of kidney stones were hyper Cal curia and hypocitraturia (19). Stitchantrakul et al. reported that the most common causes of kidney stones were citrate and hypercalciuria deficiency and low urine volume in Thai children (20). Acoording to previous report by Sikora the oxalate excretion rate per square meter of body surface area in children with calcium urolithiasis was significantly higher than those of healthy subjects (21). In current study, age was associated with all three urinary metabolic disorders and younger children had higher prevalence of abnormality than older students. This finding is in accordance with Safarinejad's study results suggesting that the highest level of uric acid to creatinine was observed in children younger than 7 years old (7). In another study, the highest oxalate excretion rate was observed in 7-24 month infants and the lowest in teens (22). Von Schnakenburg also found an inverse relationship between the oxalate/creatinine ratio and age (23). Regarding to ethnicity, Sistani had the lowest prevalence of urinary metabolic disorders compared to Baluch and other ethnicities. The association between ethnicity and kidney stone has been reported by previous studies. The underlying reason might be due to different dietary pattern and environmental factor rather than heredity (24, 25). In this study, only hyperurocosuria was significantly associated with BMI categories. Normal weight students had lower abnormal urinary uric acid compared to underweight and overweight children. In previous study by Yılmaz, children with lower BMI had higher urinary uric acid in 24 hour urine sample compared to students with higher BMI (26). This may be due to different consumption pattern of underweight and overweight children that might influence the excretion of uric acid.

In this study, the evaluation process of kidney diseases for exclusion criteria was based on interview with parents rather than subclinical examination. This may cause some misclassification bias and result in overestimation of the prevalence of urinary metabolic disorders. We were also limited for a variety of important variables such as food intake, metabolic syndrome, physical activity and some other variables that could estimate the variability of urinary metabolic disorders more accurately.

Conclusion

This study concluded that the prevalence of urinary metabolic disorders including hyperoxaluria, hypocitraturia, cysitinuria, and hyperuricosuria were high among school-aged children. Regarding to the importance and contribution of metabolic disorders on generation of urolithiasis, the early diagnosis, detailed metabolic evaluation, appropriate treatment and follow-up protocols are recommended for school-aged children. It is recommended to conduct more comprehensive study in this area according to geographic regions and different health conditions.

Acknowledgements

Hereby, the cooperation of our participants and their parents is highly appreciated.

Ethical consideration

This study has been approved by Research and Ethics Committee of the Zahedan University of Medical Sciences. The study approval ethical code provided as number 2040.

Conflict of interests
The authors declared no conflict of interest.

Funding
This research funded by the Children and Adolescent Health Research Center, Resistant Tuberculosis Institute, Zahedan, Iran.

References

1. Cameron MA, Sakhaee K, Moe OW. Nephrolithiasis in children. Pediatr Nephrol. 2005;20(11):1587-1592.
2. Saez-Torres C, Grases F, Rodrigo D, Garcia-Raja AM, Gomez C, Frontera G. Risk factors for urinary stones in healthy schoolchildren with and without a family history of nephrolithiasis. Pediatr Nephrol. 2013;28(4):639-645.
3. Copelovitch L. Urolithiasis in children: medical approach. Pediatr Clin North Am. 2012;59(4): 881-896.
4. Daudon M, Bounxouei B, Santa Cruz F, Leite da Silva S, Diouf B, Angwafoo FF, et al. Composition of renal stones currently observed in non-industrialized countries [in French]. Prog Urol. 2004;14(6):1151-1161.
5. Ertan P, Tekin G, Oger N, Alkan S, Horasan GD. Metabolic and demographic characteristics of children with urolithiasis in Western Turkey. Urol Res. 2011;39(2):105-110.
6. Penido MG, Diniz JS, Guimaraes MM, Cardoso RB, Souto MF, Penido MG. Urinary excretion of calcium, uric acid and citrate in healthy children and adolescents [in Portuguese]. J Pediatr (Rio J). 2002;78(2):153-160.
7. Safarinejad MR. Urinary mineral excretion in healthy Iranian children. Pediatr Nephrol. 2003;18(2):140-144.
8. Zhai YH, Xu H, Zhu GH, Wei MJ, Hua BC, Shen Q, et al. Efficacy of urine screening at school: experience in Shanghai, China. Pediatr Nephrol. 2007;22(12):2073-2079.
9. Areses Trapote R, Urbieta Garagorri MA, Ubetagoyena Arrieta M, Mingo Monge T, Arruebarrena Lizarraga D. Evaluation of renal stone disease: metabolic study [in Spanish]. An Pediatr (Barc). 2004;61(5):418-427.
10. Lopez M, Hoppe B. History, epidemiology and regional diversities of urolithiasis. Pediatr Nephrol. 2010; 25(1): 49-59.
11. Spivacow FR, Negri AL, del Valle EE, Calvino I, Fradinger E, Zanchetta JR. Metabolic risk factors in children with kidney stone disease. Pediatr Nephrol. 2008;23(7):1129-1133.
12. Penido MG, Diniz JS, Guimaraes MM, Cardoso RB, Souto MF, Penido MG. Urinary excretion of calcium, uric acid and citrate in healthy children and adolescents [in Portuguese]. J Pediatr (Rio J). 2002;78(2):153-160.
13. Sadeghi BS, Fazeli F, Zarifi E. Clinical characteristics and metabolic abnormalities in pediatric urolithiasis in south east Iran. Iran J Pediatr. 2015;3(4):149-54.
14. Barlow SE. Expert committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report. Pediatrics. 2007;120(Suppl4):S164-192.
15. Naseri M, Varasteh AR, Alamdaran SA. Metabolic factors associated with urinary calculi in children. Iran J Kidney Dis. 2010;4(1):32-38.
16. Coward RJ, Peters CJ, Duffy PG, Corry D, Kellett MJ, Choong S, et al. Epidemiology of paediatric renal stone disease in the UK. Arch Dis Child. 2003;88(11):962-965.
17. Habbig S, Beck BB, Hoppe B. Nephrocalcinosis and urolithiasis in children. Kidney Int. 2011;80(12):1278-1291.
18. Moorani kN, Kumari v, Sherali AR. Urinary citrate level In urinary stone formers versus controls. Journal of Surgery Pakistan. 2011;16(3):98-102.
19. Ratan SK, Bhatnagar V, Mitra DK, Basu N, Malhotra LK. Urinary citrate excretion in idiopathic nephrolithiasis. Indian Pediatr. 2002;39(9):819-825.
20. 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.
21. Sikora P, Bienias B, Wawrzyszuk M, Zajaczkowska M. 24- hour urinary oxalate excretion in healthy children and in children with calcium urolithiasis [in Polish]. Pol Merkur Lekarski. 2008;24(Suppl4):76-79.
22. Sikora P, Bienias B, Majewski M, Borzecka H, Wawrzyszuk M, Zajaczkowska M. Urinary citrate excretion in children with calcium urolithiasis [in Polish]. Przegl Lek. 2006;63(Suppl3):134-136.
23. Von Schnakenburg C, Byrd DJ, Latta K, Reusz GS, Graf D, Brodehl J. Determination of oxalate excretion in spot urines of healthy children by ion chromatography. Eur J Clin Chem Clin Biochem. 1994;32(1):27-29.
24. Michaels EK, Nakagawa Y, Miura N, Pursell S, Ito H. Racial variation in gender frequency of calcium urolithiasis. J Urol. 1994;152(6):2228-2231.
25. Sharma AP, Filler G. Epidemiology of pediatric urolithiasis. Indian J Urol. 2010;26(4):516-522.
26. Yılmaz A, Buyokkarago B, U O. Influence of body mass index on pediatric urolithiasis. J Pediatr Urol. 2015;11(6):350:e1-6.