

Hypercalciuria in Jahrom's School-Age Children What is Normal Calcium-Creatinine Ratio?

Fatemeh Emamghorashi,¹ Mohammad Hassan Davami,²
Reyhaneh Rohi²

¹Jahrom University of Medical Sciences, Jahrom and Shiraz Nephro-Urology Research Center, Shiraz, Iran

²Jahrom Medical School, Jahrom University of Medical Sciences, Jahrom, Iran

Keywords. child, urine calcium, urine creatinine, hypercalciuria

Introduction. The purpose of this study was to determine normal reference values for urine calcium-creatinine (Ca/C) ratio in Iranian children of Jahrom, in south-east of Iran.

Materials and Methods. A total of 1068 school-age children were included by stratified clustered random sampling from primary schools of Jahrom, Iran, between March 2008 and May 2008. Nonfasting random urine specimens from each subject were analyzed for calcium and creatinine concentrations.

Results. The mean ratio of urine Ca/C in all children was 0.123 ± 0.106 (range, 0.01 to 2.25), and the 95th percentile value was 0.25. Nonfasting Ca/C ratios were not significantly different between the boys and the girls. The Ca/C ratio was highest in 9-year-old children (mean, 0.132 ± 0.11). Based on the 95 percentile value of urine Ca/C (> 0.25) in the present study, 5.1% of the children in Jahrom were hypercalciuric. The prevalence of hypercalciuria differed with age ($P = .06$), and the most prevalent rate was observed in 9-year-old group (9.3%).

Conclusions. We provided a reference value for urine Ca/C ratio in south-east Iranian children. A child's age and ethnicity should be taken into consideration when assessing the urinary solute-creatinine ratios.

IJKD 2010;4:112-5
www.ijkd.org

INTRODUCTION

Idiopathic hypercalciuria is a common disorder in children and can present with a range of clinical presentations such as hematuria, voiding dysfunction, flank pain, abdominal pain, nephrolithiasis, urinary tract infection, and decreased bone mineral density.¹ Calcium excretion more than 4 mg/kg measured in 24-hour urine has been defined as hypercalciuria.^{2,3} It is difficult to take the accurate 24-hour urine in young and non-toilet-trained children; therefore, hypercalciuria can be screened by random urine calcium-creatinine ratio (Ca/C).⁴⁻⁶ A random urine Ca/C is of practical use in screening for hypercalciuria. However, due to worldwide variations, reference values for the

pediatric population are not yet well established. Many authors have reported that urine Ca/C and prevalence of hypercalciuria varies with age, diet habit, genetic characteristics, and geographic areas, being low in Japan (0.6), for instance, and high in Aral Sea level.⁵⁻⁷ Similar studies in various parts of Iran showed different results, ranged from 0.11 in Urmia to 0.53 in Kashan.^{8,9} The objective of this study was to determine urine Ca/C in healthy children in Jahrom, Iran.

MATERIALS AND METHODS

A total of 1068 children were selected by stratified clustered random sampling from primary schools of Jahrom, Iran, between March 2008 and May

2008. All of them were told not to change their eating habits and physical activities. Collected data included age, gender, height, weight, urine levels of calcium and creatinine, blood pressure, and history of kidney disease, frequency, dysuria, and nocturnal enuresis. Data on enuresis were obtained from school health records. Children with conditions that would influence urinary calcium excretion such as being on medical treatment or suffering from chronic kidney disease were excluded.

The children's height was measured in the standing position and their weight was measured with the least clothing. Blood pressures were measured in the sitting position from right arm. Early morning nonfasting urine samples were used to determine calcium and creatinine levels. Urine calcium and creatinine were measured by the calorimetric method (BT30000+, Rome, Italy). Urine Ca/C (mg/mg) was calculated. Also, complete urinalysis was done for detection of hematuria (more than 5 erythrocytes per microliter of urine) bacteriuria, and crystals. Based on pediatrics text books, a urine Ca/C higher than 0.2 was considered suggestive of hypercalciuria.¹⁰ Calcium and creatinine in 24-hour urine were measured in cases with a urine Ca/C higher than 0.2.

Statistical analysis was performed using the SPSS software (Statistical Package for the Social Sciences, version 11.5, SPSS Inc, Chicago, Ill, USA). Values of continuous variables were expressed as mean \pm standard deviation. Comparisons of variables between groups were done with the Student *t* test, 1-way analysis of variance, and chi-square test. The Pearson correlation test was used for univariable analysis. *P* values less than .05 were considered significant.

RESULTS

The eligible children were 583 girls (54.6%) and 485 boys (44.6%). Their mean age was 9.17 ± 2.13

years. The mean urine Ca/C was 0.123 ± 0.106 (range, 0.01 to 2.25), and the 95th percentile value for urine Ca/C was 0.25. The mean ratio did not show a significant difference between girls and boys, (0.11 ± 0.07 versus 0.12 ± 0.08 , respectively). The children were grouped to 5 age classes. Analysis of variance showed a relation between age and urine Ca/C ($P = .04$; $f = 2.4$). The mean values for urine Ca/C decreased by age except in the 9-year-old group (Table).

Based on the reference value, urine Ca/C (> 0.2) for diagnosis of hypercalciuria, 10.7% of the school-age children in Jahrom had hypercalciuria, but based on the 95th percentile value urine Ca/C (> 0.25) in the present study, 5.1% were hypercalciuric. The prevalence of hypercalciuria differed with age ($P = .06$); the most prevalent rate was observed in the 9-year-old group (9.3%; Table).

Of the children, 11.8%, 10.5%, and 4.9% had a history of dysuria, frequency, and enuresis, respectively. Urinalysis showed 3.3% hematuria and 1.9% moderate to severe bacteriuria. There were no correlations between the presence of dysuria, frequency, hematuria, and hypercalciuria. The prevalence of enuresis was slightly higher in children with hypercalciuria than the others (9.4% versus 5.5%, $P = .11$). The prevalence of hypercalciuria was higher in the children who showed moderate to severe bacteriuria (25% versus 10.4%; $P = .08$). The mean weight of the children with hypercalciuria was less than nonhypercalciuric ones (26.3 ± 6.7 kg versus 28.0 ± 8.3 kg; $P = .02$). No differences in the mean systolic and diastolic blood pressure were observed between the two groups.

In children with a urine Ca/C more than 0.2, the 24-hour urine calcium excretion was measured. The mean 24-hour urine calcium concentration was 77.31 ± 50.26 mg. A 24-hour urine calcium level higher than 4 mg/kg was considered as hypercalciuria. The 24-hour urine calcium excretion

Urine Calcium-Creatinine (Ca/C) Ratios and Frequency of Hypercalciuria In Relation to Age Groups

Age Group, y	Children	Mean Ca/C	Ca/C Percentiles				Hypercalciuria, %
			25th	50th	75th	95th	
7	193	0.123 ± 0.060	0.077	0.113	0.151	0.239	4.7
8	206	0.122 ± 0.060	0.074	0.108	0.154	0.239	3.8
9	181	0.132 ± 0.110	0.073	0.107	0.160	0.286	9.3
10	156	0.109 ± 0.060	0.064	0.090	0.135	0.233	3.8
11	307	0.115 ± 0.070	0.068	0.099	0.139	0.241	4.6

correlated significantly with a urine Ca/C higher than 0.25 ($P = .04$), but no correlation with urine Ca/C higher than 0.2 was found ($P = .24$).

DISCUSSION

The 95th percentile for urine Ca/C in the present study was 0.25. The reference value for urine Ca/C is 0.2,¹⁰ but many studies showed that reference values for urine Ca/C should be independently established for children in each country and also in each geographic region.^{5,11-14} Our results are similar to the results of Nikibakhsh and colleagues' study, in which the 95th percentile for urine Ca/C was 0.24,⁸ but less than the results from North West of Iran, which was reported to be 0.53.⁹ The 95th percentiles of urine Ca/C values of the American children aged 7 to 14 years was 0.20.¹⁵

In children, urinary solute-creatinine ratio is a useful and reliable method for determining hypercalciuria and also is a noninvasive and relatively inexpensive method. There is a relationship between the morning spot urine and 24-hour urine Ca/C ratio.^{16,17} For determination of correlation between urine Ca/C ratio and 24-hour urine calcium excretion, we measured 24-hour urine calcium concentration in children with a urine Ca/C ratio higher than 0.2. We found that the 24-hour urine calcium excretion more significantly correlated with a urine Ca/C ratio higher than 0.25; thus, screening of hypercalciuria in our region should be based on a urine Ca/C ratio higher than that proposed so far.

Based on our extracted threshold for urine Ca/C ratio, the prevalence of hypercalciuria was 5.1% in our sample. The reported prevalence of hypercalciuria differs based on the upper limit of urine Ca/C ratio considered in each study population. In Japan, hypercalciuria was noted only in 0.6% of the children, based on a urine Ca/C higher than 0.17 as the cutoff.⁶ The mean urine Ca/C was significantly higher in Kazalinsk, Kazakhstan. Hypercalciuria, regarded as a urine Ca/C higher than 0.703 was observed in 38.6% of Kazalinsk children.⁷ Also, in children in the north of Iran, the 95th percentile for urine Ca/C was higher than the reference value (0.36).¹⁸ Hence, it is recommended to determine this ratio in every geographic area.

Urine Ca/C ratio changes with age. In the present study, the highest level was observed in

children aged 9 years old. Previous studies showed a correlation between urine calcium excretion and age. Safarinejad showed the highest ratio between 6 months and 3 years, which was 0.047 ± 0.041 mg/mg.⁵ In Thailand, the 95th percentiles for urine Ca/C in children younger 6 months was 0.75 that decreased with age.¹²

The 95th percentile for urine Ca/C of 0.25 found in our study population is higher than the traditional normal urine Ca/C value of 0.21. Variations in urine Ca/C among different pediatric studies emphasize the role of geographic location. This, as well as other extrinsic factors, such as nutritional habits, source of drinking water, season and climate, and exposure to sunlight may influence normal values of urine Ca/C. A child's age and ethnicity should be taken into consideration when assessing the urinary Ca/C ratios.

CONCLUSIONS

With regard to variations in urine Ca/C among different studies, it is recommended to determine this ratio in every geographic area.

FINANCIAL SUPPORT

This study was supported financially by Jahrom University of Medical Sciences.

CONFLICT OF INTEREST

None declared.

REFERENCES

- Schwaderer A, Srivastava T. Complications of hypercalciuria. *Front Biosci.* 2009;1:306-15.
- Moxey-Mims MM, Stapleton FB. Hypercalciuria and nephrocalcinosis in children. *Curr Opin Pediatr.* 1993;5:186-90.
- Stapleton FB. Idiopathic hypercalciuria: association with isolated hematuria and risk for urolithiasis in children. The Southwest Pediatric Nephrology Study Group. *Kidney Int.* 1990;37:807-11.
- Sargent JD, Stukel TA, Kresel J. Normal values for random urinary calcium to creatinine ratios in infancy. *J Pediatr.* 1993;123:393-7.
- Safarinejad MR. Urinary mineral excretion in healthy Iranian children. *Pediatr Nephrol.* 2003;18:140-4.
- Kaneko K, Tsuchiya K, Kawamura R, et al. Low prevalence of hypercalciuria in Japanese children. *Nephron.* 2002;91:439-43.
- Kaneko K, Chiba M, Hashizume M, et al. Extremely high prevalence of hypercalciuria in children living in the Aral Sea region. *Acta Paediatr.* 2002;91:1116-20.

8. Nikibakhsh A, Seyedzadeh A, Mahmoodzadeh H. Normal values for random urinary calcium to creatinine ratio in Iranian children. *Iran J Pediatr.* 2008;18:263-6.
9. Honarpisheh A, Hooman N, Taghavi A. Urinary calcium excretion in healthy children living in Kashan/Iran. *Iran J Pediatr.* 2009;19:154-8.
10. Davis ID, Avner ED. Upper urinary tract causes of hematuria. In: Kliegman RM, Behrman RE, Jenson HE, Stanton BMD, editors. *Nelson textbook of pediatrics.* 18th ed. Philadelphia: WB Saunders; 2007. p. 2184.
11. Sonmez F, Akcanal B, Altincik A, et al. Urinary calcium excretion in healthy Turkish children. *Int Urol Nephrol.* 2007;39:917-22.
12. Vachvanichsanong P, Lebel L, Moore ES. Urinary calcium excretion in healthy Thai children. *Pediatr Nephrol.* 2000;14:847-50.
13. Esbjorner E, Jones IL. Urinary calcium excretion in Swedish children. *Acta Paediatr.* 1995;84:156-9.
14. Kruse K, Kracht U, Kruse U. Reference values for urinary calcium excretion and screening for hypercalciuria in children and adolescents. *Eur J Pediatr.* 1984;143:25-31.
15. So NP, Osorio AV, Simon SD, et al. Normal urinary calcium/creatinine ratios in African-American and Caucasian children. *Pediatr Nephrol.* 2001;16:133-9.
16. Reusz GS, Dobos M, Byrd D, et al. Urinary calcium and oxalate excretion in children. *Pediatr Nephrol.* 1995;9:39-44.
17. Ring E, Borkenstein M. Use of the calcium-creatinine ratio in diagnosis and therapy. *Pediatr Padol.* 1987;22:245-50.
18. Sorkhi H, Haji Aahmadi M. Urinary calcium to creatinine ratio in children. *Indian J Pediatr.* 2005;72:1055-6.

Correspondence to:

Fatemeh Emamghorashi, MD
 Shiraz Nephro-Urology Research Center, Shiraz University of
 Medical Sciences,
 PO Box: 71348-14336, Shiraz-Iran
 Tel: +98 791 234 1505
 Fax: +98 791 234 1505
 E-mail: ghorashy@yahoo.com

Received May 2009

Revised October 2009

Accepted October 2009