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Normal Urinary Calcium/Creatinine Ratios in Turkish Children

Omer Ceran, Mehmet Akin, Zekeriya Aktürk*, and Tamay Ozkozaci

From the Departments of Pediatrics, Haydarpasa Numune Training and Research Hospital, Uskudar, Istanbul, and Family Medicine, University of Trakya, Turkey.*

Correspondence to: Mehmet Akin, Baraj yolu Cad, Kiptas Unalan Bloklari 1. Block Kat: 6 Daire: 26 Unalan 81190 Uskudar, Istanbul. Turkey. E-mail: drmakin80@hotmail.com.

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Abstract:

A random urine calcium/creatinine ratio (UCa/Cr) is of practical use in screening for hypercalciuria. However, due to worldwide variations, reference values for the pediatric population are not yet well established. Furthermore, no study has been conducted to establish normal UCa/Cr values in Turkish children. The objectives of the present study were to set normal values of random UCa/Cr by age in the pediatric population of Istanbul City. A total of 324 healthy children of both genders were enrolled in the study. They were divided into four age groups as follows: (1) *<7 months,* (2) *8-18 months,* (3) *19 months to 6 years, and* (4) *7-14 years. A non-fasting random urine specimen from each subject was analyzed for calcium and creatinine. The median UCa/Cr values were 0.19, 0.20, 0.14 and 0.10 respectively. The data showed a strong inverse relationship with age. The age-dependent 95th percentiles of UCa/Cr values were 0.76, 0.60, 0.69 and 0.24 respectively. The child's age and geographic location should be taken into consideration when interpreting UCa/Cr ratio.*

Keywords: *Creatinine, Urinary calcium.*

Hypercalciuria is implicated in the frequency-dysuria syndrome, enuresis, abdominal pain, hematuria and urolithiasis. Hypercalciuria is defined as urinary calcium excretion of >4 mg/kg/day(3). Due to the difficulty of obtaining 24-h urine collection in children, a random urine calcium to creatinine ratio (UCa/Cr) is routinely used in clinical practice to screen for hypercalciuria, as it is found to have a good correlation with the 24 h calcium excretion(4-5). Traditionally, a UCa/Cr of 0.21 has been regarded as abnormal and suggestive of hypercalciuria(6). However, recent studies have shown that UCa/Cr varies with age and geographic area (*Table I*). The objective of this study was to establish the age-related reference values for UCa/Cr in our metropolitan area.

Table I

95th Percentile Values for Random UCa/Cr Ratio (mg/mg)

Age	n	95th percentile	Country (Reference)
<7 months	103	0.86	New Hampshire, (USA)(7)
8-18 months	40	0.60	
19 months-6 years	41	0.42	
Adults	31	0.22	
<7 months	30	0.70	Metropolitan Kansas City, (USA)(11)
8-18 months	35	0.50	
19 months-6 years	67	0.28	
7-16 years	42	0.2	
1 month-1 year	79	0.81	Switzerland(9)
1-2 years	48	0.56	
2-3 years	41	0.5	
3-5 years	54	0.41	
5-7 years	40	0.30	
7-10 years	50	0.25	
10-14 years	51	0.24	
2-6 years	32	0.63	Sweden(8)
7-10 years	79	0.42	
11-18 years	42	0.35	
6-17.9 years	564	0.22	Germany(13)
6-13 years	220	0.26	Argentina(14)
8-15 years	208	0.15	Northern India(15)
7-10 years	345	0.14	Taiwan(16)
11-14 years	340	0.10	

Subjects and Methods

Children, between the ages of 1 month-14 years, who presented to the outpatient clinic of Haydarpasa Numune Training and Research Hospital between March 2001 and January 2002 were included in the study. These children were healthy except that they had simple viral illness such as viral upper airway infection. Children chronically on medica-tions, those with chronic illness, kidney disease, malnutrition and who born preterm were excluded from the study. Permissions were taken from the families. The children were randomly selected and non-fasting urine specimen were taken between 9.30 a.m. and 12.00 noon. Urine calcium was measured by the cresolphthalein complexone spectro-photometric method and creatinine by the Jaffle reaction. Both measurements were performed on COMAS-Mira automated analyzer (Roche Diagnostics, Mannheim, Germany). Urine Ca/Cr (mg/mg) values were calculated and the results assigned to four age groups (group 1, n = 114) <7 months, (group 2, n = 62) 8-18 months, (group 3, n = 58) 19 month-6 years old, (group 4, n = 90) above 7 years old. The mean, median and 25th, 50th, 75th and 90th percentiles were calculated. For showing the relationship between the UCa/Cr, ANOVA, linear regression analysis and for the differences, univariate analysis was done. Statistical analysis was performed on SPSS 7.5.

Results

Of 324 children, 163 (50.3%) were girls. The geometric means of UCa/Cr ratios declined with age (*Table II*): group 1 = 0.26 (95% CI 0.22-0.31), group 2 = 0.21 (0.15-0.27), group 3 = 0.16 (0.09 - 0.22), group 4 = 0.12 (0.09-0.14) (*Table II*). Similar relationship between UCa/Cr and age were observed for the median, 25th, 50th, 75th and 50th percentiles. ANOVA followed by the Tukey's multiple comparison showed that the geometric mean of group 1 was significantly different from the rest of the groups. The interquartile range, adapted to determine the interindividual variations in the different age groups for UCa/Cr, showed a narrowing of the interquartile ranges as age progressed at 0.23, 0.25, 0.07 and 0.07 for groups 1,2,3 and 4, respectively.

Table II

Urinary Ca/Cr Ratios (mg/mg) Based on Age Groups

	Geometric mean (mg/mg)	25th centile	50th centile	75th centile	95th centile
Group 1 (n = 114)	0.26	0.10	0.19	0.33	0.76
Group 2 (n = 62)	0.21	0.07	0.20	0.31	0.60
Group 3 (n = 58)	0.16	0.08	0.14	0.15	0.69
Group 4 (n = 90)	0.12	0.07	0.10	0.14	0.24

There was a clear relationship of the logistic regression model which included the gender, nutrition, weight and age. Also, there was a negative correlation between the age and UCa/Cr (r = 0.261, P = 0.000). Similarly, there was a negative correlation between the body weight and UCa/Cr (r = –0.282, p = 0.000). The mean UCa/Cr for the infants who were breast-fed was 0.26 ± 0.26 and 0.25 ± 0.21 for those not breast-fed. The UCa/Cr ratio was similar in infants consuming milk and those who did not (0 = 0.846). There were no difference in UCa/Cr ratio between the girls and the boys (P = 0.363). The mean UCa/Cr ratio was 0.22 ± 0.24 and 0.20 ± 0.17 for girls and boys respectively.

Discussion

The 95th percentile values for UCa/Cr in the Turkish children was found to have an inverse relationship with age (*Table II*), an observation that is in agreement with previous reports (7-9). Specifically, the 95th percentile values for UCa/Cr ratio was 3 times higher in group 1 than in group 4 (*Table II*). Further-more, the interquartile range, a reflection of interindividual variability, was widest among group 1 infants and declined with advancing age. The wider variability in infants and young children has been observed also in previous studies. It thus seems that an elevated UCa/Cr in infants and high interindividual variations in this group is usual. Sargent, *et al.*(7) proposed that the elevated UCa/Cr in infants may be secondary to the diminished creatinine excretion per unit body mass. However, timed urinary calcium excretion has also been reported to exceed the upper limit of normal of 4 mg/kg/day. Manz, *et al.*(10) found the cutoff value of 4 mg/kg/24 h would result in significantly more infants and pre-school children being defined as having hyper-calciuria. Matos, *et al.*(9) suggested that a difference in diet may contribute to the higher values of UCa/Cr, especially in European and North American children. Among infants in group 1, there were no significant differences between those breast-fed and those fed by mixed food (commercial formula, fruit juice and rice flour) in terms of the mean UCa/Cr as has also been previously described(11).

The 95th percentile for UCa/Cr of 0.24 found in our study population group 4 (*Table II*) is similar to the traditional normal adult UCa/Cr value of <0.21, reported by other worker(6,7,9). UCa/Cr is reported to achieve adult values by 4-7 years of age(9,11,12).

The variations in UCa/Cr among different pediatric studies emphasize the role of geographic location (*Table I*). 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 UCa/Cr.

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Competing interests: None stated.

Key Messages

• A random urine calcium/creatinine ratio (Uca/cr) is of practical use in screening for hypercalciurea.

• The 95th percentile values for Uoa/cr in children was found to have an inverse relationship with age.

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