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ORIGINAL ARTICLE

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Urinary calcium excretion in healthy Thai children

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Abstract The objective of this study was to determine age-specific reference values for urinary calcium/creatinine ratios (UCa/Cr) of children in southern Thailand. Non-fasting urine samples were collected from a random population of 488 healthy children (282 males, 206 females) ranging in age from 17 days to 15 years. Samples were divided into six groups by age. Subjects whose calcium levels exceeded the 95th percentile within each age group were classified as having hypercalciuria. Pyuria, hematuria, proteinuria, urinary sodium, and potassium levels in children with normal UCa/Cr were compared with levels in children with high UCa/Cr. The 95th percentiles for UCa/Cr (mg/mg) by age were: <6 months, 0.75; 6 months to <12 months, 0.64; 12 months to <2 years, 0.40; 2 years to <5 years, 0.38; 5 years to <10 years, 0.29; and 10 years to <15 years, 0.26. Pyuria, hematuria, and proteinuria were no more prevalent in the 22 children with hypercalciuria than in children with normal urinary calcium levels. Urinary sodium/creatinine ratios (UNa/Cr) and urinary sodium/potassium ratios (UNa/K) were correlated with UCa/Cr (r=0.41, P<0.0001 and r=0.24, P<0.0001, respectively). Urinary potassium/creatinine ratios (UK/Cr) were not (r=0.05, P>0.1)). Children with high UCa/Cr ratios also had higher UNa/Cr and UNa/K (5.6±7.1 vs. 2.6±1.5, P<0.001 and 5.4±2.3 vs. 2.5±0.23, P<0.05, respectively) The study established reference values for random, non-fasting UCa/Cr for healthy Thai children and indicated that urinalysis is not a good indicator of hypercalciuria.

Key words Pediatric hypercalciuria · Thailand reference values · Urinary calcium/creatinine · Urinary calcium excretion · Urinary sodium excretion · Urinary potassium excretion

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Introduction

Hypercalciuria can be asymptomatic or symptomatic. While it is well known that hypercalciuria can cause numerous urinary symptoms in addition to urolithiasis, defining hypercalciuria in children remains difficult [1]. Age, race, and gender as well as diet (including intake of sodium, potassium, calcium, and vitamin D) influence urinary excretion of calcium [1, 2]. Hypercalciuria in children has been defined by values ranging from greater than 2 mg/kg body weight per day to greater than 8 mg/kg body weight per day [3, 4]. A complete 24-h urine collection is difficult in children and is nearly impossible without bladder catheterization in very young children. Nordin [5] first proposed the use of random urine calcium/creatinine ratios (UCa/Cr) for initial assessment of hypercalciuria in adults. More recently, Reusz et al. [6] showed a strong linear correlation between 24-h urinary calcium excretion and the UCa/Cr of the first-morning urine sample in children ($y=0.73x+0.07$, r=0.84, P<0.01, n=94). Abnormal values of random UCa/Cr in children were reported to range from 0.18 to greater than 0.37 mg/mg [4, 7–9]. The purpose of our study was to determine reference values for UCa/Cr in southern Thai children and also to compare urinalysis and urinary sodium and potassium levels in children with normal UCa/Cr with those with high UCa/Cr.

Materials and methods

This cross-sectional study was performed in Hat-Yai, southern Thailand (930 km south of Bangkok). Children in the study population were from five schools and from the well-baby clinic of Songklanagarind Hospital. All children were apparently healthy; i.e., they were ingesting normal diets, were not receiving medications, and had normal levels of activity. Late-morning or early afternoon samples were collected from volunteers between January 1991 and February 1992. Urinalysis was carried out. Microscopic hematuria and pyuria were defined as red blood cells (RBC) and white blood cells (WBC) in urine greater than 3 RBC/high-power field (HPF) and 3 WBC/HPF, respectively. Proteinuria was defined by urine reagent strips as a reaction greater than it, or if equal to 1^+ then urine specific gravity had to be less than 1.015. Urinary concentrations of creatinine and calcium were measured by Hitachi Method 717. Urinary sodium and potassium were measured by Nova model Nucleus using routine laboratory methods. The 95th percentile value was used for the upper limit of UCa/Cr within each age group. Hematuria, pyuria, proteinuria, sodium, and potassium in urine samples from children with normal UCa/Cr levels were compared with samples from children with high UCa/Cr ratios. Statistical analyses were performed using statistical software STATA 5.0 (Stata , College Station, Texas, USA).

Results

A total of 488 children (282 males and 206 females) were enrolled in the study. Ages ranged from 17 days to 15 years, weight from 2.9 kg to 60.9 kg, and height from 45 cm to 158.5 cm. UCa/Cr ratios ranged from 0.00 to 0.89 mg/mg. The rank correlations of UCa/Cr with age, height, and weight were significant and very similar. (r=0.27, 0.28, and 0.24 respectively, all P<0.0001) The strongest correlation was with height. The linear correlations between log UCa/Cr and the three variables were also very similar, with height again showing the strongest correlation (r=0.27, P<0.0001). To be consistent with other studies, however, we used the relationship between UCa/Cr and age. This correlation is also easier to use in practice. A frequency distribution of the UCa/Cr in each age group is shown in Fig. 1. The 95th percentiles for UCa/Cr (mg/mg) by age were: <6 months, 0.75; 6 months to <12 months, 0.64; 12 months to <2 years, 0.40; 2 years to <5 years, 0.38; 5 years to <10 years, 0.29; and 10 years to <15 years, 0.26 (Table 1).

There were no differences in the UCa/Cr ratios of males and females. There was, however, a decrease with age. Because UCa/Cr ratios change rapidly in very young children then more slowly as children grow older, the age range for young children was more narrow. Of the six groups, for example, the age range for the first two was only 6 months, while the middle two groups spanned 1 and 3 years and the older two groups spanned 5 years.

The 95th percentile within each group was considered the upper limit. There were 22 children whose UCa/Cr exceeded this limit. The prevalence of hypercalciuria was similar in boys (4.6%, n=13) and girls (4.4%, n=9).

Among the children with normal UCa/Cr ratios, the prevalence of pyuria was 8.2% (n=38), hematuria 2.8% (n=13), and proteinuria 0.6% (n=3). For children with high UCa/Cr ratios, the prevalence of pyuria was 5% (n=1) and none of these children had hematuria or proteinuria. The differences were not statistically significant (P>0.2).

Urinary calcium was positively correlated with urinary sodium (r=0.41, P<0.0001), but there was no correlation between urinary calcium and urinary potassium

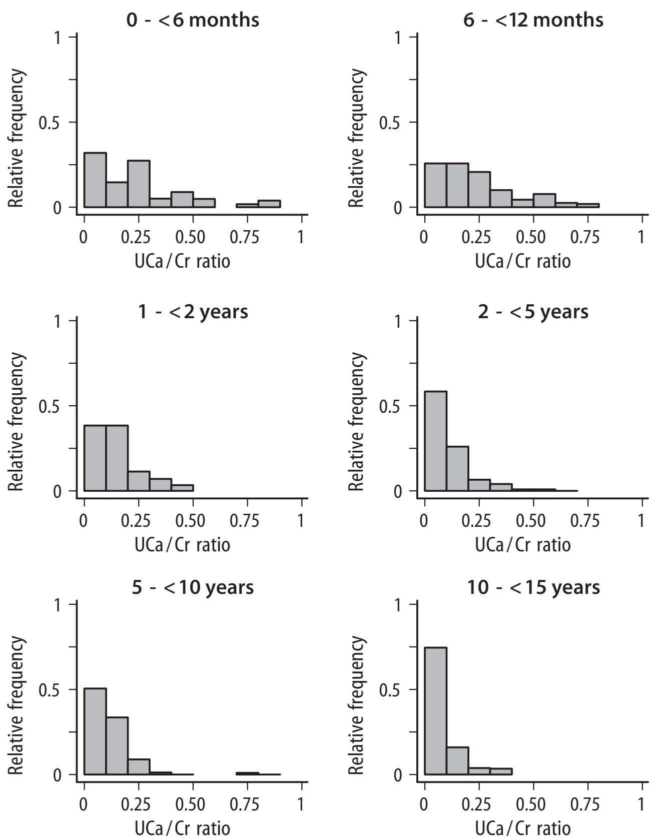

Fig. 1 Distribution of urinary calcium/creatinine ratios (UCa/Cr) according to age

Table 1 Random non-fasting urinary calcium/creatinine (UCa/Cr) ratios (mg/mg) in children in southern Thailand

Age	n	Mean	SD	Percentiles					95th confidence intervals[a]
				25th	50th	75th	90th	95th	
<6 months	54	0.22	0.23	0.08	0.20	0.32	0.51	0.75	0.49–0.89
6 to <12 months	39	0.23	0.18	0.08	0.20	0.34	0.53	0.64	0.46–0.75
1 to <2 years	26	0.16	0.11	0.07	0.13	0.21	0.36	0.40	0.29–0.41
2 to <5 years	129	0.12	0.12	0.04	0.08	0.14	0.25	0.38	0.26–0.54
5 to <10 years	149	0.12	0.12	0.04	0.10	0.16	0.22	0.29	0.24–0.66
10 to <15 years	91	0.08	0.07	0.03	0.06	0.10	0.19	0.26	0.19–0.34

[a] Of 95th percentile

Table 2 UCa/Cr ratio (mg/mg) in different studies

Present study	Sargent et al. [11] (1993)	Stapleton [15] (1994)	Chen et al. [17] (1994)	Esbjorner and Jones [9] (1995)	Alconcher et al. [18] (1997)
Thai	American	American	Taiwanese	Swedish	Argentinian
Non-fasting	Non-fasting	Fasting(or 24-h urine)	Fasting	Non-fasting	Fasting
95th percentile	95th percentile	–	95th percentile	97th percentile	95th percentile
<6 months 0.75	<7 months 0.86	0–6 months <0.8	–	–	–
6 to <12 months 0.64	7–18 months 0.60	7–12 months <0.6	–	–	–
1 to <2 years 0.40	–	>2 years <0.2	–	–	–
2 to <5 years 0.38	19 months to 3 years 0.42	–	–	2–6 years 0.64	–
5 to <10 years 0.29	adult 0.22	–	7–10 years 0.142	7–10 years 0.43	6–9 years 0.264
10 to <15 years 0.26	–	–	11–14 years 0.101	11–18 years 0.36	10–13 years 0.265
–	–	–	15–18 years 0.213	–	–

(r=0.05, P>0.1). Children with high UCa/Cr ratios also had higher urinary sodium/creatinine ratios (UNa/Cr) (5.6±7.1 vs. 2.6±1.5, P<0.001), but the mean urinary potassium/creatinine ratios (UK/Cr) were not significantly different between children who had normal and high UCa/Cr (1.7±1.2 vs. 3.2±5.7, P>0.1). There was also a positive correlation between the urinary sodium/potassium ratio (UNa/K) and UCa/Cr (r=0.24, P<0.0001), and children with high UCa/Cr had higher UNa/K than children with normal UCa/Cr. (5.4±2.3 vs. 2.5±0.23, P<0.05).

Discussion

UCa/Cr is widely used for estimating calcium excretion because it is simple, cost-effective, and reliable [4, 6, 10–13]. We found a strong inverse correlation of UCa/Cr with age, but a positive correlation with body weight and with height. This is in agreement with the study by DeSanto et al. [14] for 24-h urinary calcium.

Infants less than a year old had the highest UCa/Cr. Normal UCa/Cr ratios were up to 0.75 mg/mg during the first 6 months of life, up to 0.64 mg/mg from 6 months to 1 year, and gradually declined with age. These high values in infants are due to the fact that the infant diet is mainly milk, which is richer in calcium than other food. Since the UCa/Cr ratios did not approximate a normal distribution, we used the 95th percentile for the upper limit rather than a multiple of the mean value. The UCa/Cr ratios in our study were comparable to other studies in young age groups (Table 2) [9–12, 14–18]. However, our study showed slightly higher values in children of more than 2 years of age. This may reflect the different statistical values used, the different time of collection of urine specimens, a lower urinary creatinine, a greater calcium or sodium, or less potassium in the diet of Thai children [2, 19]. This has not been confirmed. It should be noted that the cut-off values have rather wide 95% confidence intervals (Table 1), which suggests either doubt about comparability or the need for further study with a larger sample size. Recently, Alconcher et al. [18] reported UCa/Cr ratios in school children using the 95th percentile for the upper limits of normal, which were similar to ours.

The UCa/Cr, UNa/Cr, and UK/Cr in randomly collected urine samples allowed for variations of hydration as well as weight. As reported by Muldowney et al. [20], our data showed that (1) UNa/Cr correlated with UCa/Cr whereas UK/Cr did not and (2) high sodium intake enhanced calciuria and natriuria. Our data also showed that children who had hypercalciuria also had higher UNa/Cr and UNa/K than normal, but similar UK/Cr. A study reported by Rodriguez-Soriano et al. [21] showed that hypercalciuric children had significantly increased levels of sodium excretion, but decreased levels of fractional potassium excretion.

Fasting influences UCa/Cr. The first-morning urine has lower UCa/Cr than non-fasting urine. The dietary calcium intake was not controlled in our children, as we wanted to determine the normal range of urine calcium excretion under the usual conditions of clinical observation. Fasting urine is not a reliable specimen for determining hyperabsorption of hypercalciuria. All UCa/Cr results in this study represent late-morning or afternoon urine samples.

Idiopathic hypercalciuria is thought to be the most-common etiology of hematuria in children [22]. In our study, however, children who had high UCa/Cr ratios did not show significant hematuria compared with the normal group. This may reflect the fact that hypercalciuria and hematuria in asymptomatic children could be intermittent [23]. In addition, neither pyuria nor proteinuria was found. We determined, therefore, that urinalysis was not a good predictor of hypercalciuria.

This study presents the first standard values for UCa/Cr in children in southern Thailand for a series of age groups from under 6 months to 15 years. The suggested reference values in our study should, therefore, be considered preliminary; and the width of the confidence intervals should not be taken as conclusive (see Table 1). The reference UCa/Cr values in each age group are for non-fasting urine in healthy children; i.e., those with regular diets, no medications, and with normal levels of activity.

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