URINARY CALCIUM CREATININE RATIO AND HYPERCALCIURIA

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ABSTRACT

Random urine samples of 352 children in the age group of 5-12 yrs were studied for urinary calcium-creatinine ratio (Uca/Ucr mg/mg). None had any predisposing factor for secondary hypercalciuria. Calcium and creatinine both were estimated by colorimetric method. We observed that Uca/Ucr in the general pediatric population was skewed, the pattern was similar to that described in western children and it was independent of age and sex. The mean and standard deviation (SD) of Uca/Ucr was 0.10 ± 0.094. Considering mean +2SD as the upper limit of normal, which was 0.29 in this series, the prevalence of hypercalciuria was 6.5%.

Key words: *Idiopathic hypercalciuria, Urinary calcium excretion, Calciuria.*

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The prevalence of idiopathic hypercalciuria (IH) has been reported to vary between 2.9-6.2% in the age group of 3 months to 18 years(l,2). Majority of these cases are asymptomatic. Symptomatic cases have various manifestations such as gross hematuria, dysuria, nocturnal enuresis, urinary frequency—urgency syndrome, suprapubic and abdominal pain, and recurrent urinary tract infections(3). It predisposes to nephrolithiasis that may cause renal damage. These complications are avoidable if appropriate preventive measures are undertaken following early detection of IH. The data about IH available from the developed countries(l,2) may not be applicable to the rest of the world. Teotia(4) has investigated urinary calcium excretion in healthy Indian children aiming to establish norms for calcium excretion. However, her sample size was small and no efforts were made to find out the prevalence of hypercalciuria. This prompted us to undertake this exploratory pilot study which incidentally happens to be the first of this kind from India.

Material and Methods

Three hundred and fifty two children (219 boys, 133 girls, 305 with minor ailments—mostly upper respiratory tract infections and 47 of their accompanying healthy siblings) aged 5-12 years were studied between May 92 to July 92. About 90% were from low socio-economic status and the rest came from middle class. They were on usual family diet and the average dietary calcium content ranged from 400-700 mg/24 h. No one was getting any additional vitamin D supplementation. Random urine samples were obtained in clean calcium free bottles. The children had had their breakfast 2-3 hours earlier. Urinary calcium (Uca) was estimated by modified method of Lorentz(5) and urinary creatinine (Ucr) by

Jaffe's method(6). The children whose Uca/Ucr was <0.18 mg/mg on first screening were interviewed in detail, a detailed history taken (with special emphasis on dietary habits, immobilization, abdominal pain, urinary complaints, hematuria, family history of nephrolithiasis) and physical examination done as per set proforma to exclude the known secondary causes of hypercalciuria. The children were asked to provide four urine samples at weekly intervals. Serum calcium, phosphate, alkaline phosphates were estimated and renal ultrasonography (US) done in the children who provided random urine samples for analysis on four different occasions. Two way analysis of variance with log transformation was employed to test for differences in the mean values of Ca/Cr ratio between different age and sex groups. Normal deviate test was employed to test for difference in percentile values.

Results

No child had any obvious cause to account for secondary hypercalciuria. The values of Uca/Ucr ranged from 0.001-0.644 mg/mg with a mean and SD of 0.10 ± 0.094, respectively (0.10 ± 0.103 for boys ' and 0.09 ± 0.079 for girls). The distribution of Uca/Ucr in the general pediatric population is depicted in *Fig. 1.* The values were positively skewed. The five (1.4%) cases whose values exceeded 0.40 were distributed evenly between 0.40-0.65. All of them were boys. Ninety per cent of the population had values of <0.20. The 97th percentile value was 0.323. After transforming the data to the log scale, the distribution looked somewhat normal though not strictly so *(Fig. 2).* In this scale the mean and +2 SD values were —1.185 and —0.34 corresponding to 0.06 and 0.46 in arithmetic scale, respectively.

Table I shows the mean and SD of Uca/Ucr according to age and sex. There was no significant difference in the mean values for various age groups of either sex ($p > 0.20$).

Considering the mean +2 SD value of 0.29 as the upper limit of normal, there were total 23 children (6.5% of total population) who had hypercalciuria. This included 17 boys (7.7% of boys's population) and 6 girls (4.5% of girls' population). Although hypercalciuria was seen more frequently in boys, the difference was not significant ($p=0.58$).

Figure 3 compares the percentile values obtained from the present series with those of Kruse *et al.(2).* The present values were almost double those of Kruse *et al.* in fasting state, were comparable to their post-absorptive values upto 50th percentile beyond which they were significantly higher ($p<0.05$).

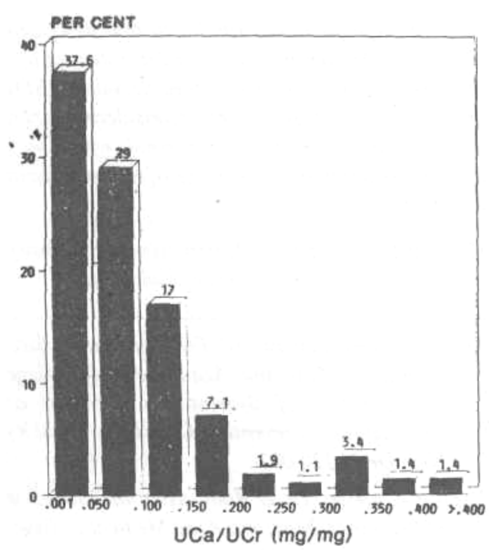

Fig. 1. Frequency distribution of Uca/Ucr in general pediatric population—arithmetic scale.

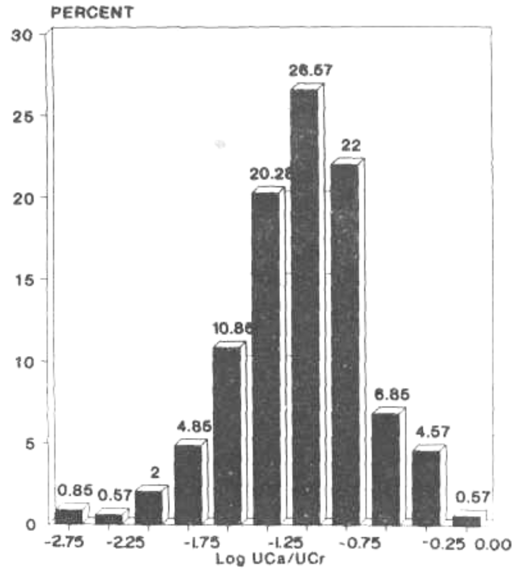

Fig. 2. Frequency distribution of Uca/Ucr in general pediatric population—log scale.

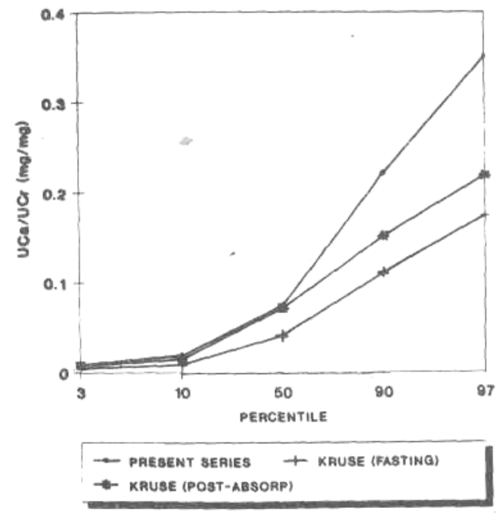

Fig. 3. Comparison of percentile values of present series with those of Kruse et al.(2).

Of the 17 children who reported for revaluation, 12 had hypercalciuria (Uca/Ucr > 0.29) on one or more occasions. Their follow up Uca/Ucr values, other relevant investigations and associated symptoms have been depicted in *Table II*. There were wide fluctuations in Uca/Ucr values tested on different occasions especially in Patients 3 and 6, the higher values being 2-5 times the lower ones. Patients 4, 7 and 12 provided fasting urine samples on the second time which accounts for the fluctuation. None of the six patients whose serum was studied for calcium, phosphorus and alkaline phosphatase had any evidence of hyperparathyroidism. Their renal ultrasounds were normal. Eight children complained of nonspecific abdominal or flank pain either at the time of interview or in the recent past compared to 4/17 children of similar age without hypercalciuria. Seven had nocturnal enuresis and four had history of dysuria and/or turbid urine. Urinary frequency urgency, past history of hematuria and history of urolithiasis in father was present in one case each.

Discussion

The positively skewed distribution of Uca/Ucr value has been observed by Moore *et al/*.(l). Our findings that Uca/Ucr is independent of age and sex is in conformity with the observation of other authors(l,2,7). Our mean value is midway between that of Moore(l) and Kruse *et al.* (2) on one hand and Teotia(4) on the other and very close to the mean value obtained by Stapleton(7) for healthy children in fasting state. It supports Moore's(l) finding that hypercalciuria is more frequently seen in boys than girls.

The observation that Uca/Ucr values could have wide fluctuations in the same individual from normocalciuric to hypercalciuria range on different occasions has also

TABLE *I-Urinary Calcium-Creatinine Ratio According to Age and Sex*

Age (years)	Boys			Girls		
	n	Mean	SD	n	Mean	SD
5 - 6	57	0.11	0.097	41	0.11	0.078
7 - 8	54	0.12	0.124	34	0.09	0.086
9 - 10	52	0.09	0.065	33	0.09	0.065
11 - 12	56	0.08	0.111	25	0.08	0.087
All ages	219	0.10	0.103	133	0.09	0.079

been made by others(l,2,7). Besides dietary intake of calcium(4,7), urinary calcium is also affected by urinary Na(2), phosphate and magnesium(4). The wide fluctuations noticed in patients 3 and 6 could be due to combination of several such factors. They were probably cases of dietary hypercalciuria, as proposed by Kruse(2) whereas cases 4, 7 and 12 satisfy the criteria of absorptive hypercakiuria(2,8). However, the diagnosis remains presumptive in absence of a for mal calcium loading test and urinary Na estimation.

Recently, Gokce *et al.(9)* have demonstrated strong correlation between spot urine Ca/Cr and 24 h urinary calcium estimation in adults and have concluded that quantitative estimation of Ca/Cr in a single voided random urine specimen is a simple cost effective and reliable method for estimating total urinary calcium excretion. A spot urine specimen being easily obtainable, its Ca/Cr ratio is preferred by many for a screening test for hypercalciuria(l,2,7-9). However, patients of absorptive hypercalciuria which constitute 21-62% of children with IH(3) will be missed if only fasting samples are used for screening purposes resulting in underestimation of the prevalence rate. As temporary hypercalciuria may lead to nucleus formation and clinicians would like to play safe, it is important not to miss the "absorptive" ones. Hence, for a screening test we felt it more rational to study random urine samples collected 2-3 hours after food rather than studying fasting samples. We believe that data obtained from random samples will be more useful for comparison as this specimen is easy to obtain. However, it must be remembered that Uca/Ucr is at best a screening test and all suspected cases of IH must be subjected to quantitative analysis of 24 h urinary calcium excretion before putting the label of IH and starting therapeutic measures.

The upper limit of Uca/Ucr to define hypercalciuria is still controversial. Stapleton(7) feels that the upper limit for fasting Uca/Ucr should be 0.21 whereas after oral calcium load values above 0.27 should be considered abnormal. Norman(10) agrees with Stapteton regarding the fasting value. Chantler and Barratt(ll) feel that for children the upper limit should be 0.25. Kruse *et al(2)* have used their own 97th percentile, *i.e.,* 0.219 mg/mg as the cut-off value. Moore *et* al.(l) have used their own +2 SD/ + 3 SD values (corresponding to 0.18/ 0.25, respectively) as cut-off points. Nordin(12) studying random urine of adults

TABLE II–*Follow up Data of Hypercalciuric Children*

Sl. No.	Uca/Ucr values on different samples				Serum biochemistry			Clinical symptoms				
	1st	2nd	3rd	4th	Ca (mg/dl)	P (mg/dl)	Alk. phos-phatase	Abd. pain	Noct. enuresis	Dysuria	Turbid urine	Others
1.	.352	.506							+			
2.	.358	.330										
3.	.184	.278	.320	.160	8.3	4.3	74.4	+	+	+	+	
4.	.308	.085						+	+			
5.	.250	.321	.301	.366	9.0	5.4	71.6	+	+		+	
6.	.182	453	.113	.170	10.0	4.8	96.0	+				Urinary frequency urgency
7.	.644	.144						+		+		Frank hematuria
8.	.505	.329						+	+	+	+	Nephro-lithiasis in father
9.	.327	.448	.675	.540	10.3	5.0	91.2		+			
10.	.400	.308	.518	.305	8.4	3.8	81.6	+				
11.	.400	.286	.300	.355	9.8	5.0	8.16	+		+		
12.	.336	.193							+		+	

advocated that it should be 0.28. Teotia(4) studying 49 healthy Indian children aged 5-12 years on usual unrestricted diet noticed the Uca/Ucr to be 0.2 ± 1 (range 0.1-0.5 for ages 5-10 and 0.1-0.3 for 10-12 years). Our mean +2 SD value of Uca/Ucr is 0.29 which is midway between 0.27 advocated by Stapleton(7) following oral calcium load and the absolute value of 0.28 advocated by Nordin(12) for random urine samples on one side and mean +1 SD value of Teotia(4) on the other. It is not too far from the absolute value of 0.25 suggested by Chantler and Barratt(11). Besides it is derived from our own population from a large sample. We propose that this should be taken as the upper limit of normal for Indian children.

The 97th percentile values in the present study is much higher compared to that of Kruse *et al.* (2) in the post absorptive state and +3 SD values of Moore *et al.(1)*. The prevalence rate of hypercalciuria is 6.5% which is higher compared to western figures(2,7). Whether it is due to dietary or other factors needs further study.

The study concludes that the mean Uca/ Ucr in random urine specimen for Indian children is 0.10 ± 0.094. Uca/Ucr value of 0.29 mg/mg in random urine specimen should be considered as upper limit of . normal and with this criteria the prevalence of IH is 6.5% in Indian children.

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