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Urinary excretion of minerals, oxalate, and uric acid in north Indian children

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Abstract. Urinary excretion of calcium, magnesium, phosphate, uric acid, oxalate, and creatinine was measured in 208 children (aged 8–15 years, 124 boys, 84 girls), living in a residential school near New Delhi. Levels were reduced compared with those reported from developed countries. The 95th percentile value of 24-h creatinine excretion was 33.4 mg/kg, calcium 2.2 mg/kg, magnesium 2.9 mg/kg, phosphate 9.4 mg/kg, uric acid 4.4 mg/kg, and oxalate 1.5 mg/kg. The 95th percentile value of the urine calcium/creatinine ratio was 0.15 and oxalate/creatinine 0.06. The dietary intake of proteins, calcium, and other nutrients in these children was less than recommended and explained the reduced urinary excretion observed. Physicians need to be aware of the regional patterns of normal urinary excretion of these constituents.

Key words: Nephrolithiasis – Calcium – Magnesium – Creatinine

Introduction

Idiopathic hypercalciuria and hyperoxaluria are the most common metabolic disturbances causing nephrolithiasis in children [1]. High urinary excretion of calcium and uric acid have also been found in children with microscopic or gross hematuria [2]. Availability of reference standards for normal urinary excretion of these constituents are essential to identify abnormal patterns of excretion. Previous studies indicate that normal values for urinary excretion of different constituents may vary in different regions [3–8]. Some of these variations are probably due to differences in the diets consumed by these children [5, 6, 8].

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The dietary habits of children in India are considerably different from those in the developed world. There are, however, a paucity of data on the normal urinary excretion of calcium, phosphate, magnesium, uric acid, oxalate, and creatinine in Asian, and particularly Indian, children. The aim of this study was to obtain normal values for 24-h urinary excretion of these constituents in healthy school children.

Patients and methods

The study was performed at a residential school, Navodya Vidyalaya, Chhainsa, 50 km south of New Delhi during July to September 1994. Permission was obtained from the school authority. Of 280 children, aged 8–15 years, 258 consented to the study. They received all meals at school; the content of this food was almost constant from day to day. The age of each child was obtained from the school records. The body weight and height were measured using standard methods and the body mass index (kg/m^2) calculated.

Urine collections (24 h) were performed in all cases. On the day preceding the collection, the children were given a large-necked plastic bottle of 5-l capacity, containing 5 ml 0.33 N hydrochloric acid as preservative. Precautions for handling the bottles and the method for accurate collection of specimens were explained. When the bottles were returned the children were asked if all voidings had been collected. Samples considered to be incomplete were discarded. The volume of urine was measured to the nearest milliliter. Urine samples were analyzed for calcium by the *o*-cresolphthalein method [9], magnesium by the xylidyl blue method [10], phosphate by the molybdate method [11], uric acid by the uricase method [12], creatinine by the Jaffe reaction [13], and oxalate by the chromotropic acid reaction [14].

The children were divided into age-groups of 8–10, 11–12, and 13–15 years, corresponding to primary, middle, and high school. A pediatric dietitian obtained the dietary history of 4 children in each age-group, by the method of dietary recall, on the day the urine was returned. The intake of calories, protein, calcium, magnesium, phosphate, and oxalate was estimated and compared with that recommended for Indian children [15].

The 24-h urinary excretions were correlated with age and sex. The excretions of these compounds were also expressed in relation to creatinine. Significance of differences in urinary excretion between boys and girls were evaluated by the Wilcoxon rank sum test and among age-groups by Kruskal-Wallis test; P values < 0.05 were considered significant.

Table 1. Weight, height, and body mass index (BMI) (mean ± SD) of children studied

	8–10 years		11–12 years		13–15 years	
	Girls (n = 19)	Boys (n = 32)	Girls (n = 31)	Boys (n = 24)	Girls (n = 34)	Boys (n = 68)
Weight (kg)	30.1 ±5.4	30.1 ±6.4	37.0 ±5.0	33.9 ±4.2	43.1 ±6.3	42.8 ±7.9
Height (m)	1.35±0.09	1.35±0.13	1.45±0.06	1.41±0.06	1.51±0.06	1.55±0.09
BMI (kg/m^2)	16.2 ±1.1	16.3 ±1.8	17.5 ±1.8	16.9 ±1.4	18.8 ±2.0	17.6 ±1.9

Results

Of 258 children, 50 were excluded since the urine collections were considered incomplete. Table 1 shows the age and sex distribution of 208 children who completed the study.

Dietary intake

Since all children in the school were consuming a similar diet, evaluation of the dietary intake in 12 children was considered representative of the entire group. Their caloric intake ranged from 950- to 1,200 calories (recommended 1,900–2,100 calories). The chief sources of proteins were pulses (legumes, peas, beans) and cereals; animal proteins were lacking. The daily protein intake ranged between 30 and 40 g (recommended 52–60 g), calcium 200–400 mg (recommended 800–1,200 mg), phosphate 500–700 mg (recommended 800–1,200 mg), magnesium 200–300 mg (recommended 200–270 mg), and oxalate 10–12 mg.

Urinary excretion patterns

The 24-h urinary excretions of calcium, magnesium, phosphate, uric acid, oxalate, and creatinine (mg/kg) were not normally distributed but skewed to the left. They were therefore expressed as 50th (median) and 95th percentiles. The 24-h urinary excretion of the constituents in various age-groups is shown in Table 2. Table 3 depicts grouped data, in all subjects, of the excretion of these constituents in relation to creatinine. Grouped data of 24-h excretion in this and other population-based studies are shown in Table 4.

Creatinine. The 24-h creatinine excretion was significantly related to age in boys ($P < 0.05$) and girls ($P < 0.001$); highest levels of excretion were seen at 11–12 years of age. Boys in the 8- to 10- and 11- to 12-year age-groups had significantly higher creatinine excretion than girls ($P < 0.001$ and < 0.05 respectively, Table 2). The median and 95th percentiles of 24-h excretion, for all subjects, were 15.5 and 33.4 mg/kg, respectively (Table 4).

Calcium. The 24-h calcium excretion was similar in boys and girls in all age-groups (Table 2). The median and 95th percentiles of calcium/creatinine ratio, for all children, were 0.04 and 0.15, respectively (Table 3). The median and 95th percentiles of 24-h calcium excretion, for all children, were 0.7 and 2.2 mg/kg, respectively (Table 4).

Magnesium. Magnesium excretion was significantly higher with increasing age in boys ($P < 0.001$) and girls ($P < 0.05$). The excretion was greater in boys than girls in all age-groups ($P < 0.05$, Table 2). The median and 95th percentiles of magnesium/creatinine ratio were 0.07 and

Table 2. Median and 95th percentile values of 24-h urinary excretion (mg/kg) in relation to age and sex[a]

	8–10 years		11–12 years		13–15 years	
	Girls (n = 19)	Boys (n = 32)	Girls (n = 31)	Boys (n = 24)	Girls (n = 34)	Boys (n = 68)
Creatinine*	8.0 (33.1)	18.5** (32.0)	18.0 (30.0)	20.0** (38.0)	13.8 (30.0)	13.9 (32.8)
Calcium	0.7 (2.5)	0.7 (2.5)	0.6 (1.3)	0.7 (2.5)	0.8 (2.5)	0.8 (2.2)
Magnesium*	0.7 (2.7)	1.1** (3.8)	0.9 (2.3)	1.1** (3.0)	1.0 (1.7)	1.7** (3.1)
Phosphate	2.0 (6.9)	3.4** (10.0)	2.6 (5.1)	2.9 (9.1)	2.4 (4.2)	4.2** (9.0)
Uric acid*	1.1 (2.5)	1.6** (6.9)	0.5 (2.2)	1.1** (3.7)	1.2 (2.7)	2.1** (4.7)
Oxalate*	1.1 (2.2)	0.8 (1.3)	0.8 (2.1)	0.7 (1.3)	0.6 (1.2)	0.5 (1.1)

* Excretion significantly related to age in boys and girls; ** significant difference between boys and girls within same age-group
[a] 95th percentiles in parentheses

Table 3. Grouped data on 24-h urinary excretion of constituents in relation to creatinine (n = 208)

	Median	95th percentile
Calcium/creatinine	0.04	0.15
Magnesium/creatinine	0.07	0.22
Phosphate/creatinine	0.20	0.59
Uric acid/creatinine	0.07	0.48
Oxalate/creatinine	0.01	0.06

Table 4. Comparative data on 24-h urinary excretion (mg/kg) of constituents in population-based studies

	De Santo et al. [5][a] (n = 220)	Chen et al. [6][a] (n = 125)	This study[b] (n = 208)
Creatinine	33.2 (57.0)	21.5 (28.0)	15.5 (33.4)
Calcium	2.3 (5.7)	2.1 (4.5)	0.7 (2.2)
Magnesium	2.1 (3.6)	0.5 (0.9)	1.1 (2.9)
Phosphate	22.7 (45.3)	12.5 (21.7)	2.9 (9.4)
Uric acid	10.4 (24.4)	3.2 (6.8)	1.4 (4.4)
Oxalate	1.0 (2.2)	–	0.7 (1.5)

[a] Values are means (mean +2 standard deviations)
[b] Values are medians (95th percentiles)

0.22, respectively (Table 3). The group median and 95th percentiles of 24-h magnesium excretion were 1.1 and 2.9 mg/kg, respectively (Table 4).

Phosphate. Phosphate excretion was similar in children between 8- and 15 years of age. Boys in the 8- to 10- and 13- to 15- year age-groups had significantly higher levels of phosphate excretion than girls ($P < 0.05$ and < 0.001, respectively; Table 2). The median and 95th percentiles of 24-h phosphate excretion, for all children, were 2.9 mg/kg and 9.4 mg/kg, respectively (Table 4).

Uric acid. The group median and 95th percentiles of 24-h uric acid excretion were 1.4 mg/kg and 4.4 mg/kg, respectively (Table 4). Uric acid excretion was related to age both in boys ($P < 0.001$) and girls ($P < 0.05$); lowest values were found at 11–12 years. Boys showed significantly higher excretion of uric acid than girls in all age-groups ($P < 0.05$, Table 2).

Oxalate. Oxalate excretion was similar in boys and girls, but reduced significantly with increasing age ($P < 0.001$, Table 2). The median and 95th percentiles of oxalate/creatinine ratio were 0.01 and 0.06, respectively. The group median and 95th percentile values of 24-h oxalate excretion were 0.7 mg/kg and 1.5 mg/kg, respectively (Table 4).

Discussion

The normal excretion of constituents implicated in the formation of urinary tract stones varies in different regions [5–8]. Factors influencing excretion of these substances include age, sex, and dietary intake [5, 6, 8]. In the present study, conducted in a residential school in north India, their urinary excretion was found to be reduced compared with that reported from developed countries (Table 4). Similar to previous reports [7, 8, 16, 17], the excretions of these substances were not normally distributed but skewed to the left.

The median 24-h creatinine excretion in the present study of 15.5 mg/kg was reduced compared with values ranging from 21.5- to 33.2 mg/kg described previously [5, 6]. The total protein intake in children in this study was low and composed mainly of low biological value proteins. Studies by other workers in north India have also shown that the total protein intake among adolescents may be deficient by 25%–40% compared with recommendations [18–20]. The body mass index of our subjects was lower than in developed countries [5], but similar to that reported in India [19–21]. The low protein intake and body mass index in our subjects probably explains the reduced levels of creatinine excretion.

Urinary calcium excretion of more than 4 mg/kg per day [3–6] or calcium/creatinine ratio of more than 0.2–0.5 [4–8, 17] are generally considered suggestive of hypercalciuria. In the present study the 95th percentiles for 24-h urinary calcium excretion and calcium/creatinine ratio were 2.2 mg/kg and 0.15, respectively. The low levels of urinary calcium excretion were possibly due to its deficient dietary intake, as observed in this and other studies from north India [18, 20].

The median and 95th percentiles of 24-h magnesium excretion in the present study were less than those reported previously [3–5]. Urinary magnesium excretion increased significantly with age, being higher in boys than girls. Other workers, however, have found higher levels of urinary magnesium in younger children [5, 6] and either similar [5] or higher levels in girls [6].

The median 24-h phosphate and uric acid excretion in this study was lower than reported previously (Table 4) [5, 6]. Low levels of urinary phosphate in our children could be ascribed to low intake of animal proteins and a high phytate content of the predominantly cereal-based diet. The median and 95th percentiles of 24-h urinary oxalate excretion and oxalate/creatinine ratio were also lower than those reported by other workers [5, 16, 17]. Our findings confirmed the decline in urinary oxalate excretion with increasing age [5, 16, 17].

To summarize, we found reduced urinary excretion of creatinine, calcium, phosphate, uric acid, oxalate, and magnesium in normal Indian children compared with reports from developed countries. Our subjects were shorter and lighter and had a lower body mass index than their western counterparts. The dietary intake of proteins and other nutrients was less than recommended and explained the reduced urinary excretion observed.

Renal stones generally form when the activity product of their ionic constituents exceeds a critical level. However, the pathogenesis of stone formation is complex and also depends on the urinary volume, pH, and concentration of inhibitory factors, including magnesium, pyrophosphate, and citrate [22]. Epidemiological studies on renal stones in children in India are lacking. It is therefore not clear if the low urinary excretions of calcium, phosphorus, oxalate, and uric acid, as observed in this study, provide Indian children with a degree of protection against nephrolithiasis.

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