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Values of Urinary Mineral Excretion in Healthy Iranian Children

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Introduction: Normal values of urinary mineral excretion differ in different geographic parts. The aim of this study was to determine age-related reference intervals for urinary minerals in healthy children in the south-west of Iran.
Materials and Methods: Midstream non-fasting urine samples were collected and the amount of calcium, oxalate, uric acid, phosphate, magnesium, citrate, and creatinine was measured in all urine samples. The urinary mineral concentrations were reported as mineral to creatinine ratios (mg/mg). Data were analyzed by SPSS software version 16 and independent t-test and T-Hoteling test was used.
Results: The study involved 232 children aged 7 to 10 years. The 5th and 95th percentile values of urinary minerals to creatinine ratios were determined. The mean urinary Ca/Cr ratio was 0.14± 0.18 with a 95th percentile value of 0.295. For oxalate to creatinine ratio, the mean value was 0.068± 0.09 mg/mg with a 95th percentile value of 0.23. The mean uric acid to creatinine ratio was 0.358±0.211 mg/mg with an upper 95th percentile value of 0.69 and the mean Ph/Cr ratio was 0.439 and the 95th percentile was 1.01 mg/mg.
Conclusions: We found out that the normal values of random urinary mineral to creatinine ratio differ in our region from the other countries and even from the other regions in Iran. We concluded that child's age and ethnicity should be taken into consideration when assessing the urinary mineral to creatinine ratio.

Keywords: Urine Specimen Collection; Urine minerals; Child; Iran; Calcium; Oxalate; Citrate; Uric Acid; Phosphate.

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Running Title: Urinary Mineral Excretion in Children

Introduction

In order to study urinary mineral excretion in children it is necessary to compare it with reference standards. It has been well established that normal values of urinary mineral excretion differ in different parts of the world and even of a country [1-9]. So it seems necessary for each region to have their own reference standards.

As 24 hour urine collection is difficult in clinical practice, spot solute to creatinine (cr) ratio is a reasonable and sensitive method to study mineral excretion [5,6,10]. So we performed this study to determine age-related reference intervals for calcium (Ca), oxalate (Ox), uric acid (Ua), magnesium (Mg), phosphorus (Ph), and citrate

(Ci) to creatinine concentration ratios in healthy children in the south-west of Iran.

Materials and Methods

Two hundred and thirty-two healthy children (128 girls, 104 boys) aged 7 to 10 years were selected by stratified random sampling from primary schools in different regions of Ahvaz in 2011 to encompass the different ethnic and socioeconomic groups representative of the whole population.

A questionnaire was completed by the parents to find out about any renal problems and a positive family history of urolithiasis or renal disease. Children with any evidence of acute or chronic renal disease, with prolonged use of antibiotics or other drugs or with a positive family history of renal or metabolic disease were excluded from the study. Midstream non-fasting urine samples were collected between 10 am and 12:00 am. Urine samples were carried by cold box and were sent to the laboratory within less than one hour. The amount of calcium, oxalate, uric acid, phosphate, magnesium, citrate, and creatinine was measured in all urine samples. The urinary mineral concentrations were normalized for creatinine and reported as mineral to creatinine ratios (mg/mg). Urinary oxalate was measured by oxalate oxidase enzymatic assay and urinary citrate by citrate lyase assay. These tests were performed on an Awarness Stat Fax 3300 analyzer. Urine creatinine concentration was measured by kinetic Jaffe reaction, and urinary calcium by Arsenazo reaction. Both tests were performed on a Biotechnical Biochemical Analyzer BT analyzer. Urinary phosphate, magnesium, and uric acid were measured by phosphomolybdate, xildlblue, and uricase assays respectively and all of these tests were performed on a Biotechnical Biochemical Analyzer BT 3000 analyzer.

Data were analyzed by SPSS software version 16 and the mean values and standard deviations were determined. Independent t-test was used to compare the mean values between the sexes and T-Hoteling test was used to compare multiple variables.

Results

The study involved 232 children (128 girls, 104 boys) aged 7 to 10 years. All the values of urinary mineral to creatinine ratios are presented as mean±standard deviation (SD). The 5th and 95th percentile values of urinary mineral to creatinine ratios are also presented (Table 1). A statistically significant difference was not observed between boys and girls ($p>0.05$) for all the minerals studied (Table 2). The mean urinary Ca/Cr ratio was 0.14±0.18 with a 95th percentile value of 0.295.

Table 1. Non fasting urinary mineral to creatinine ratios⇧

Minerals	Mean± SD	5th percentile	95th percentile
Calcium	0.142±0.186	0.053	0.295
Oxalate	0.068±0.09	0.011	0.23
Uric acid	0.358±0.211	0.118	0.69
Magnesium	0.101±0.081	0.041	0.227
Phosphate	0.439±0.426	0.163	1.01
Citrate	0.454±0.591	0.079	1.00

For oxalate to creatinine ratio, the mean value was 0.068±0.09 mg/mg with a 95th percentile value of 0.23. The mean uric acid to creatinine ratio for the whole group was 0.358±0.211 mg/mg with an upper 95th percentile value of 0.69.The number and incidence of outliers for urinary mineral to creatinine ratios are presented in (Table 3). Totally 16 girls (6.86%) and 6 boys (2.46%) had one or more outliers. The mean Ph/Cr ratio was 0.439 and the 95th percentile was 1.01 mg/mg. We considered the 5th percentile values of Mg and Cit due to the fact that they are inhibitors of stone formation and increased levels are protective against the formation of stones. For Mg/Cr ratio, the mean and the 5th percentile values were 0.1 and 0.041 mg/mg respectively. The mean and 5th percentile values for Cit/Cr ratio were 0.454 ±0.591 and 0.079 respectively.

Discussion

Urinary mineral excretion is usually studied by 24 hour urine collection. With regard to difficulty in obtaining 24 hour urine samples, mineral to creatinine ratio in a random urine sample can be very helpful [11]. However, random urine mineral excretion can be affected by age, diurnal status, and prandial state [12,13]. Random urinary excretion of oxalate, uric acid, phosphate, magnesium, and citrate has been studied in a few studies, which show different excretion rates of

these solutes [1,2,3,7,13]. What is clear is that urinary mineral excretion may be affected by differences in genetics, race, age, climatic condition, nutrition and mineral content of drinking water [2,5,6,14,15,16,17].

Table 3. Incidence of urinary mineral/Cr ratios outliers⇧

Minerals	Gender	
	Female (128)	Male(104)
Low Ca/Cr	0	0
High Ca/Cr	1(0.4%)	0
Low Ox/Cr	0	0
High Ox/Cr	3(1.3%)	1(0.4%)
Low Ua/Cr	0	1(0.4%)
High Ua/Cr	3(1.3%)	2(0.86%)
Low Ph/Cr	1(0.4%)	0
High Ph/Cr	3(1.3%)	1(0.4%)
Low Mg/Cr	0	0
High Mg/Cr	2(0.86%)	0
Low Cit/Cr	0	0
High Cit/Cr	3(1.3%)	1(0.4%)
Total	16(6.86%)	6(2.46%)

With regard to Ca/Cr ratio, the 95th percentile in our study was 0.29. When we take a look at different studies in Iran, different results are found. In desert area of Kashan, a study by Honarpishe et al, on 362 children aged 7 to 12 years showed the 95th percentile of Ca/Cr ratio to be 0.53 which is quite higher than our result. It was suggested that children living in desert areas have higher urinary calcium excretion compared to those who live near sea and differences in drinking water, dietary habits, and higher sun exposure have been proposed as etiologic factors [6]. This may explain the lower Ca/Cr ratio in our study, since Ahvaz is at sea level. In studies from the United States, Turkey, Taiwan, and India different ratios are observed [2,3,5,7,9,18]. This may again emphasize the importance of aforementioned conditions in influencing the urinary calcium excretion.

Although urine Ca/Cr was slightly higher in girls than boys but this was not statistically significant (p=0.346) in our study. Oner and Seifert separately found gender differences in Ca excretion but other researchers found no significant difference between genders [2,3,4,7,8,14].

The mean Ox/Cr ratio in our study was 0.068 mg/mg and the 95th percentile was 0.23 mg/mg. We could find no study in Iran about urinary oxalate excretion in healthy children.

In a study by Matos et al, the 95th percentile for Ox/Cr was found to be 0.048 mg/mg which is lower than our result [17]. In another study in India by Sweid et al, on 208 children aged 8 to 15 years, the 95th percentile value was found to be 0.15 [19]. Different levels of Ua/Cr are reported by different studies in Iran, Switzerland, India, and Turkey [1,17,19,20].

Ua/Cr ratios were not significantly different between boys and girls in our study. In the study by Poyrazoglu et al, there were no significant differences in Ua/Cr ratios between boys and girls up to 12-15 years. Girls aged 12-15 years had higher urinary Ua/Cr ratios when compared with boys [20]. For Ph/Cr ratio, our results are different from the other studies which showed a lower ratio than what we obtained [1,7].

We found no sex predilection regarding the phosphorus excretion. Other studies found similar ratios between boys and girls as our study [1,7,21]. The urinary Mg/Cr ratio in our study is comparable to that by Sweid et al, in which the 95th percentile was reported as 0.22 [19]. Other studies have yielded different results [1,21]. Although excretion rate was similar in boys and girls in our study, in other studies different and heterogeneous results are obtained [1,19,21].

When we take a look at different studies about urinary Cit/Cr value in normal children surprisingly few studies are found. The normal urinary Cit in children is expressed with different values ranging from >180 to >408 mg/g of Cr based on Cit lyase assay [1]. According to Miller and Stapelton the value of 2 SD below the mean for Cit/Cr in children was 182 mg/g although the numbers of enrolled children were quiet small [22]. Srivastava and colleagues found the 5th percentile value of Cit/Cr to be 176 mg/g [10]. We found the 5th percentile value of Cit/Cr to be 79 mg/g, much lower than the previous studies. Nutritional and genetic factors may explain this difference [23]. Like the study by Srivastava [10],

there was no statistically significant difference in Cit/Cr ratio in our study (P= 0.52) although females had slightly higher Cit/Cr ratio.

Conclusions

We concluded that child's age and ethnicity should be taken into consideration when assessing the urinary mineral to creatinine ratio.

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Conflict of Interest

None declared

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None declare

Table 2. Normal mineral to creatinine ratios in relation to gender ⇧

Minerals	Mean±SD		5th percentile		95th percentile		P value
	F	M	F	M	F	M	
Calcium	0.151±0.068	0.131±0.067	0.049	0.055	0.30	0.289	0.346
Oxalate	0.100±0.069	0.076±0.067	0.011	0.011	0.235	0.219	0.812
Uric acid	0.358±0.168	0.358±0.207	0.105	0.130	0.708	0.698	0.523
Magnesium	0.102±0.055	0.101±0.056	0.036	0.044	0.216	0.232	0.382
Phosphate	0.444±0.33	0.433±0.265	0.153	0.180	1.08	1.00	0.55
Citrate	0.491±0.449	0.408±0.344	0.086	0.075	1.22	0.966	0.528

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