Original Article

Türk Pediatri Arşivi
Turkish Archives of Pediatrics

Prevalence of hypercalciuria and urinary calcium excretion in school-aged children in the province of Tokat

Ali Gül[1], Samet Özer[1], Resul Yılmaz[1], Ergün Sönmezgöz[1], Tuba Kasap[1], Şahin Takçı[1], Erhan Karaaslan[1], Yalçın Önder[2], Rıza Çıtıl[2], İlknur Bütün[3], Osman Demir[4]

[1]Department of Pediatrics, Gaziosmanpaşa University School of Medicine, Tokat, Turkey
[2]Department of Public Health, Gaziosmanpaşa University School of Medicine, Tokat, Turkey
[3]Department of Medical Biology, Gaziosmanpaşa University School of Medicine, Tokat, Turkey
[4]Department of Biostatistics, Gaziosmanpaşa University School of Medicine, Tokat, Turkey

Abstract

Aim: Hypercalciuria is an important cause of urinary tract symptoms, and also frequently results in urolithiasis. Urinary calcium excretion varies for geographic areas. We aimed to assess percentiles of urinary calcium excretion and prevalence of hypercalciuria for school-aged children in Tokat (city located in inner northern region of Turkey).

Material and Methods: One thousand three hundred seventy-five children aged 6 to 18 years were enrolled in the study. Urine samples were obtained randomly. The children's variables as sex, age, length, and weight were recorded. Urinary calcium and creatinine determined from the urine samples and urinary calcium/creatinine ratios (mg/mg) were calculated. Percentiles of urinary calcium/creatinine ratios were also assessed for each age of the children.

Results: Six hundred eighty-three of the 1 375 children were girls and 692 were boys. The mean age of the children was 11.68±3.43 years. Some 23.9% of the children were living in rural regions and 76.1% were were living in urban regions. The mean urinary calcium/creatinine ratio was 0.080±0.24 and the 95th percentile value of the urinary calcium/creatinine ratio was 0.278. The hypercalciuria prevalence for school-aged children was 4.7% when the urinary calcium/creatinine ratio value for hypercalciuria was accepted as ≥0.21. The prevalence of hypercalciuria in rural and urban regions was 7.60% and 3.82%, respectively ($p<0.05$). Hypercalciuria was present in 7 of 141 patients who were obese (4.96%) and 58 of 1 234 patients who were not obese (4.70%) ($p>0.05$).

Conclusion: The prevalence of hypercalciuria and urinary calcium excretion vary for different geographic areas, not only for countries. The percentiles of urinary calcium excretion should be assesed for every geographic region and the prevalance of hypercalciuria should be determined with these values. There is controversy as to whether obesity is a risk factor for hypercalciuria. (Turk Pediatri Ars 2016; 51: 193-7)

Keywords: Calcium creatinine ratio, children, hypercalciuria, urinary calcium excretion, obesity

Introduction

Hypercalciuria is significant in children, because it may lead to many problems including hematuria, urolithiasis, abdominal pain, and urination symptoms (1). In our country, hypercalciuria still predominates among the causes of end-stage renal disease. Therefore, hypercalciuria should be detected, its cause should be elucidated, and follow-up should be pursued (2). Hypercalciuria is one of the important causes of urolithiasis and it is important to detect hypercalciuria, because it may lead to osteopenia and growth retardation in untreated children (3).

Address for Correspondence: Ali Gül E-mail: draligul@yahoo.com
Received: 23.03.2016 **Accepted:** 04.10.2016

DOI: 10.5152/TurkPediatriArs.2016.4162

Hypercalciuria is defined as calcium excretion above 4 mg/kg/day in urine in children (4). The spot urine calcium/creatinine ratio (UCa/Cr) is frequently used in the diagnosis of hypercalciuria because of difficulties in collecting 24-hour urine in children (1, 2, 4-6). In children aged above seven months, a uCa/Cr value of ≥0.21 is considered hypercalciuria (4, 5, 7). However, other studies have considered different UCa/Cr values as limit values (8, 9).

Urinary calcium excretion varies by age, the amount of calcium in diet, geographic area, and ethnic origin (4, 8, 9). Therefore, definitions of hypercalciuria should be made after calcium excretion is specified for different countries and areas considering the 95th percentile values as limit values (5, 9-11).

In this study, calcium and creatinine were measured in urine samples of school-age children aged between 6 and 18 years in the province of Tokat with the aim of specifying the prevalence of hypercalciuria and percentile values by age and sex.

Material and Methods

According to data of the Provincial Directorate of National Education in Tokat, there are a total of 710 schools in the provincial center of Tokat and all its districts and bound villages, and 108 514 students were receiving education in these schools in the academic year of 2013-2014. Sex and age groups of the whole group were recorded. The number of children to be included in the study was calculated using the formula known as the sample size formula:

$$n = \frac{N(t_{1-a})\ 2x(pxq)}{S^2(N-1)+(t_{1-a})^2\ (pxq)}$$

P=prevalence, q = 1-p, S = standard deviation, N = the total number of children aged between 6 and 18 years in Tokat. =degree of freedom in the confidence interval (t value: 1.96 for a confidence interval of 95%). The number of students to be included in the study and the number of groups to be included in the study from each school were specified with the multilayer proportional group sampling method considering the numbers of students in primary, secondary, and high schools in the provincial centers and districts, and the sex and age groups according to the Provincial Directorate of National Education 2013-2014 academic year records.

The age, sex, body mass index, and height values of the subjects were recorded; presence of chronic diseases and drug use was interrogated. Body mass index (BMI) was calculated. The children included in the study were divided into three age groups, as 6-9, 10-13, and 14-18 years. Random urine sample was obtained and UCa/Cr was calculated for these three groups. Percentiles were specified for all ages and for these three groups with the mean value.

A urinary calcium/creatinine ratio of 0.21 (mg/mg) was considered as the limit value and the prevalence of hypercalciuria was calculated. Prevalence, which was calculated by considering the 95th percentile as the limit value in our study, was recorded seperately.

In addition, UCa/Cr was calculated separately for two subgroups, obese and non-obese subjects, as determined using BMI. The relation between BMI and calcium excretion was investigated.

Ethics committee approval for the study was obtained from the Gaziosmanpaşa University Medical Faculty Ethics Committee (number: 16-KAEK-051). The necessary aprroval was obtained from the Tokat Provincial Directorate of National Education. An information leaflet was sent to the guardians (generally parents) of the children included in the study by way of class teachers, and written informed consent was obtained.

Statistical analysis

The mean and standard deviation values were calculated for the data obtained. The independent samples t-test or one-way analysis of variance was used for inter-group comparison. Tukey HSD test was used for multiple comparisons. Chi-square tests were used for categorical data in inter-group comparisons. Categorical variables were obtained as numbers and percentages. A p value of <0.05 was considered statistically significant. Statistical Package for the Social Sciences version 19.0 (SPSS Inc.; IBM Corp., Somers, NY) was used for statistical analyses.

Results

We planned to include 1584 children aged between 6 and 18 years in a cross-sectional design. However, 209 of the

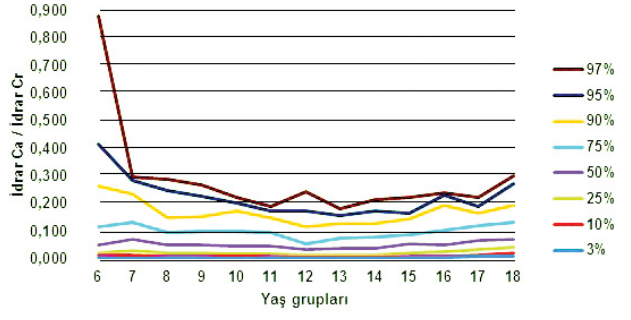

Figure 1. The percentile curves of the UCa/Cr values for children aged between 6 and 18 years

Table 1. The percentiles of the UCa/Cr (mg/mg) values for children aged between 6 and 18 years

Age	n	Mean±SD	3%	10%	25%	50%	75%	90%	95%	97%
6	96	0.166±0.571	0.005	0.013	0.022	0.050	0.118	0.263	0.415	0.879
7	96	0.095±0.085	0.002	0.012	0.029	0.071	0.134	0.236	0.284	0.298
8	103	0.071±0.070	0.004	0.010	0.022	0.050	0.097	0.148	0.247	0.290
9	122	0.122±0.586	0.004	0.010	0.021	0.052	0.100	0.155	0.227	0.270
10	132	0.069±0.067	0.004	0.008	0.019	0.047	0.101	0.176	0.203	0.225
11	122	0.063±0.055	0.006	0.008	0.017	0.046	0.095	0.150	0.175	0.190
12	133	0.050±0.063	0.003	0.006	0.013	0.033	0.056	0.116	0.174	0.246
13	121	0.053±0.051	0.002	0.006	0.014	0.038	0.075	0.128	0.156	0.182
14	118	0.059±0.058	0.003	0.006	0.015	0.041	0.081	0.131	0.172	0.214
15	92	0.065±0.054	0.007	0.011	0.023	0.054	0.086	0.145	0.168	0.225
16	93	0.073±0.064	0.004	0.012	0.027	0.051	0.103	0.195	0.231	0.241
17	102	0.081±0.061	0.010	0.016	0.036	0.068	0.121	0.164	0.190	0.225
18	45	0.095±0.071	0.011	0.020	0.043	0.073	0.132	0.194	0.274	0.301
Total	1375	0.080±0.239	0.004	0.012	0.023	0.055	0.108	0.178	0.278	0.321

children were excluded from the study because of the inability to obtain urine, broken sample tubes, and spillage from tubes during transportation. The remaining 1375 children were included in the study. Five children who were to be included in the study had epilepsy, five had familial mediteranean fever (FMF), one had atypical autism, and one had celiac disease; twelve children from the waiting list were included in the study in place of these children.

Six hundred eighty-three (49.7%) of 1375 children included in the study were girls and 692 (50.3%) were boys. The mean age of the whole study group was 11.68±3.43 years and the mean ages of the girls and boys were similar (11.70±3.46 and 11.66±3.41, respectively). Three hundred twenty-nine (23.9%) were living in rural areas and 1046 (76.1%) were living in the provincial center or in county towns.

The mean UCa/Cr was found as 0.080±0.24. The mean UCa/Cr values of the girls and boys were calculated (0.080±0.22 and 0.079±0.25, respectively) and the difference was not found statistically significant. The mean UCa/Cr value was calculated seperately for all ages (Table 1). With these values, the percentile curves of the UCa/Cr values for children aged betwen 6 and 18 years who lived in the province of Tokat were established (Figure 1). In addition, UCa/Cr values were compared between subjects who lived in provincial centers and rural areas. The mean UCa/Cr value was 0.122±0.472 in subjects who lived in rural areas and 0.066±0.064 among subjects who lived in urban areas; the difference between rural and urban areas was significant (p<0.001). As shown in Table 2, a marked difference was found in the mean UCa/Cr value between the three age groups and calcium excretion was found higher in children aged between 6 and 9 years.

Table 2. Urinary calcium excretion by age groups (mean UCa/Cr)

Age group (years)	n	Mean±SD
6-9	417	0.113±0.422
10-13	508	0.059±0.060
14-18	450	0.072±0.061

A significant difference was found between the 6-9 years age group and the 10-13 years age group (p=0.002) and between the 6-9 years age group and the 14-18 year age group (p=0.029).

When a UCa/Cr value of 0.21 and above was considered hypercalciuria, hypercalciuria was found in 65 of the 1375 children; the prevalence was 4.7%. The UCa/Cr values at the 90th and 95th percentiles were 0.178 and 0.278, respectively (Table 1).

When the 95th percentile was considered as the limit value for UCa/Cr, 30 children were found as hypercalciuric (prevalence=2.2%).

The mean UCa/Cr value was 0.070±0.068 in 141 obese patients who had a BMI at the 95th percentile and above by age and sex and 0.081±0.251 in 1234 non-obese patients. Obesity was not considered a factor in calcium excretion because the difference was not significant (p = 0.602). Hypercalciuria was found in seven (4.96%) of 141 obese patients and in 58 (4.70%) of 1234 non-obese patients. Obesity was not a significant factor in terms of hypercalciuria prevalence (p=0.889).

Discussion

Hypercalciuria is one of the important causes of urolithiasis in children and adults. In a study conducted with 143 children with urolithiasis aged between two and six years, hypercalciuria was found in 21.7% of the patients (12). In the chemical analysis of 54 renal stones obtained from children with urolithiasis, 98% of the stones were found to have calcium content (3).

There are different views for limit values in the definition of hypercalciuria. A daily calcium excretion of 4 mg/kg is considered as the limit value (4). Collecting 24-hour urine for screening is not a very useful method (1, 4). Specifying the UCa/Cr ratio in the definition of hypercalciuria is the preferred method, because it is easy. However, UCa/Cr is affected by factors including age, diet, geographic area, and ethnic origin, and it is recommended that different limit values should be specified according to these factors (4, 8, 9).

However, there are also studies that advocate that the UCa/Cr ratio could not take the place of calcium excretion in 24-hour urine (13). In Antalya, calcium exretion in 24-hour urine was 4 mg/kg/kg and above in only 24.5% of 269 patients with hypercalciuria who were had a UCa/Cr ratio of 0.21 and above among 2143 school-age children (13).

We found the prevalence of hypercalciuria as 4.7% in school-age children aged between 6 and 18 years in the province of Tokat. The prevalence of hypercalciuria was 9.6% in a previous regional study conducted in 2252 children in the Aydın region (11). We think that the prevalence was high because children aged between 0 and 15 years were included in the study and UCa/Cr was considered 0.21 for all children. In previous studies, it has been shown that this limit was high especially in children aged below 2 years (5, 14). Therefore, considering 0.21 as the limit value may lead to increased hypercalciuria prevalence findings, especially in infancy.

In a study conducted with 614 children aged between one month and 16 years in the province of Bursa, the prevalence of hypercalciuria was 4.7%, similar to our study, when the 95% percentile was considered as the limit by age (14). This was a significant finding in terms of showing that a single limit value for UCa/Cr might not be valid for children with different ages. Thus, specifying the limit values for age and regions and establishing the percentiles gain importance. In Antalya, the prevalence of hypercalciuria was as high as 12.5% in school-age children (13). However, the prevalence of hypercalciuria was reduced to 4.5% when the 95th percentile was considered as the upper limit (13).

In the Eastern part of Turkey, the prevalence of hypercalciuria was found as 5.88% (15) in a study conducted in Erzurum in 1647 school-age children, and 2.9% in a study conducted with 592 children aged between 6 months and 16 years in Sivas (16). We think that the low hypercalciuria prevalence found in Sivas arose from the fact that the 97th percentile was considered as the limit value. In a study conducted with 324 healthy children in Istanbul, the UCa/Cr value at the 95th percentile was 0.24, and the mean UCa/Cr was 0.10 for the 7-14 years age group (17). In our study, the limit value of 0.21 corresponds to the 90-95th percentile. When the limit value at the 95th percentile for UCa/Cr was considered as 0.278, the prevalence of hypercalciuria became 2.2%.

In Japan, the prevalence of hypercalciuria was only 0.6% in 529 school-age children, though the limit value for UCa/Cr was considered 0.17 (18). It was thought that this low prevalence of hypercalciuria was related with low calcium and dietary salt intake, and this could be one of the causes of the low incidence of urolithiasis in Japan (18). In a study conducted with children aged between 5 and 12 years in India, the prevalence of hypercalciuria was 6.5% (19). In Iran, the prevalence of hypercalciuria was 5.6% in school-age children (20).

These findings support the use of regional percentiles for specifying hypercalciuria.

Urinary excretion of calcium was higher in subjects who lived in rural areas compared with those who lived in the city center. The fact that the prevalence of hypercalciuria was increased in subjects who lived in rural areas suggests that this might be related with drinking calcium-rich milk and eating calcium-rich dairy products, because excretion of calcium in urine is proportional to the amount of dietary calcium intake (21, 22). However, eating habits were not interrogated, a such we believe this is a limitation of our study; fluid and sodium consumption may also have affected urinary calcium excretion.

The mean UCa/Cr value (0.080±0.24) found in our study was lower compared with previous studies conducted in Turkey (3, 11). This might be related with differences in geographic area and calcium intake through diet and drinking water.

Urinary calcium excretion (mean UCa/Cr) was not found different in obese children compared with non-obese children. In a study conducted in adults (23), urinary cal-

cium excretion was found markedly higher in obese individuals, but urinary calcium was not proportionate to creatinine and BMI. Similarly, urinary calcium excretion and urolithiasis were determined at a higher rate in obese and overweight adult patients with renal stones; only daily calcium excretion was investigated and it was not proportionate to creatinine or body weight (24).

In conclusion, the frequency of hypercalciuria and urinary calcium excretion show regional differences. It has been recommended that regional percentiles should be developed for urinary calcium excretion because of these differences. Urinary calcium excretion is higher in rural areas compared with city centers. This difference may be related both with diet and vitamin D levels. Obesity was not found as a risk factor for hypercalciuria, nor was it an important risk factor for urinary calcium excretion.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Gaziosmanpaşa University School of Medicine (16-KAEK-051).

Informed Consent: Written informed consent was obtained from parents who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - S.Ö., A.G., R.Y.; Design - E.S., S.Ö.; Supervision - A.G., Y.Ö., R.Ç.; Funding - Y.Ö., R.Ç.; Materials - İ.B.; Data Collection and/or Processing - A.G., İ.B., E.K.; Analysis and/or Interpretation - A.G., Ş.T., S.Ö.; Literature Review - R.Y., E.S.; Writing - A.G., S.Ö.; Critical Review - R.Y., S.Ö., Ş.T.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: This study was supported financially by Commission of Scientific Researches in Gaziosmanpasa University.

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