Research Paper

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Determine The Amount of Oxalate, Citrate and Urinary Uric Acid in Primary School Children in Zahedan

Medical Science

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ABSTRACT

Introduction Urolithiasis in children, about 40% -50% of cases are associated with metabolic disorders. The most important metabolic disorders included: Hypercalciuria, hyperoxaluria, hypocitraturia, cysitinuria and hyperuricosuria. The aim of this study was to evaluate the prevalence of hyperoxaluria, hypocitraturia, and hyperuricosuria and the associated factors in Schoolchildren age group population in Zahedan, A southeast city in Iran. Methods Considering that the collection of 24-hour urine in young adults and in children are consuming time and difficult, non-fasting measures of ratios for oxalate, citrate and uric acid, to creatinin to find people with urinary excretion of this mineral is very applicable and useful. Therefore, non-fasting urine samples from healthy schoolchildren in Zahedan were taken. An equal number of boys and girls were randomly selected. Then the ratios of uric acid, citrate, and oxalate to creatinine were measured. Results were expressed as mean and rates and statistical tests applied for the analysis were: Student's t_ test and ANOVA. Results In this study 1157 schoolchildren, 433 male (37.4%) and 724 females (62.6%) aged 7-13, were studied with a mean age of 9 yeas. The mean of Oxalate, citrate and uric acid to creatinine were estimated as 0.02 ± 0.01,2.98 ± 2.39 and 3.22 ±0.59 respectively. The Prevalence's of Hpeyroxaluria,Hpocitraturia and hypruricosuria were 25.3%, 20.3% and 34.6% in the given order. Conclusion Levels of uric acid, citrate and oxalate in urine vary with age, sex and race. Therefore, to obtain the average values and the variation in the different geographical area are noteworthy.

Background

One of the common problems in pediatric is Urolithiasis. Its prevalence is increasing because of changing in life style such as, industrial life, poor nutrition, decreased fluid intake, inappropriate use of drugs. The prevalence of Urolithiasis in boys is more than girls approximately 1.5- 2 times. About 40 % -50 % of kidney stones are associated with metabolic disorders. The most important metabolic disorders are hypercalciuria, hyperoxaluria, hypocitraturia, cysitinuria and hyperuricosuria (2, 6). Hypercalciuria or hypocitraturia has been reported as major findings in children. (1, 2, 7- 8). When children are not yet trained in using toilet, the evaluation may be performed by measuring the ratio of calcium, uric acid, citrate, and oxalate to creatinine in random urine sample. In the biochemistry view urine containing: calcium, oxalate, uric acid, magnesium, citrate and cystein. Oxalate is the end product of the glayoxylate and ascorbic acid metabolic pathway which is primarily excreted by the kidneys. Near 80 % to 85 % of daily urinary excretion of oxalate is produced by normal metabolic homeostasis and the remainder, 10% to 15% is from oxalate oral intake. Daily urinary oxalate excretion is less than 50 mg/ d/1.73 m2 of body surface and when it is exceeded from this amount called hyperoxaluria so that it is a predisposing factor in urolithiasis disorders (3).Uric acid excretion fraction in infants and children is more than adults (30% -50% versus 8% -12%). When urinary excretion is more than 815 mg / d/1.37 m2 of body surface is defined as hyperuricosuria. Among children less than 2 years of age, estimation of uric acid excretion can be resulted from the ratio of random urine uric acid to creatinine, if it is more than 0.56 mg / dL GFR called hyperuricosuria. Hyperuricosuria with significant hyperuricemia is observed in inherited disorders of purine metabolism, lymphoproliferative disorders, and polycythemia. Other causes of Hyperuricosuria are: increasing absorption of purines, hemolysis, uricosuric drugs, and congenital heart patients with cyanotic and idiopathic (3, 4). Citrate is normally distributed in the urine and regulated through a process of both absorption and metabolism at the level of the proximal tubule. Hypocitraturia is defined as a citrate to creatinine is less than 180 mg/gm and in 24-hours urine is less than 300 mg/ gm. The aim of this study was to evaluate the prevalence of Hyperoxaluria, Hypocitraturia,Hyperuricusuria in schoolchildren in Zahedan city in the southeast area of Iran.

Methodology

A cross-sectional study (descriptive and analytical) carried out on 1157 healthy children aged 7-13 years during 2011-2012 in the Zahedan. Multi-stage sampling method applied. Schoolchildren's Parents were invited and a questionnaire completed by the researcher after a deep interview. If a sample had a history of chronic kidney disease, metabolic disease, kidney stones, or taking medications that affect the excretion of urinary solutes were excluded. Demographic information such as age, sex, weight, height, and ethnicity were recorded on the form. Mostly, the collection of 24-hour urine partices in children is difficult and sometimes with time consuming, measuring the ratio of these minerals to creatinine in non-fasting randomized urine to find children with high urinary excretion is extremely applicable and useful.

Morning urine samples of children were taken between 8-11 am and were sent to laboratory. About 6 hours after collection, urine samples frigid at a temperature of - 70 º C and all the samples together were analyzed. Urine creatinein was measured by colorimetric device without removing proteins with BT3000 and Photometer analyzer based on JAFFE method and oxalate , uric acid, citrate were measured using Pars test kits with photometric method and oxalate, citrate and uric acid to creatinine for each child were calculated. If the random urine being more than 0.06 mg / g for oxalate to creatinine, being more than 0.9 g / g for uric acid to creatinine and being less than 0.25 mg / mg for citrate to creatinine called hyperoxaluria,hyperuricusuria and hypocitraturia respectively. Results were expressed in mean and standard deviation for the quantities measures and in proportion and percentage for the qualities measures. Statistical tests applied for the analysis were Student's t_ test and ANOVA by using SPSS 17.

Results

In this study, 1157 school children, 37.4% boys and 62.6% girls entered with age ranged of 7-13 with mean of 9.4±1.56 years.

They were investigated on urinary solutes. The mean of oxalate, citrate and uric acid to urinary creatinine were 0.01± 0.02, 2.98±2.39and 0.59± 0.59 in the given order with ranges of 0.01 to 0.17 mg/mg, 0.1-17.64 mg/mg and 0.1-3.22 mg/mg as well (Table 1). The prevalence of hyperoxaluria, hypocitraturia and hypruricosuria were 25.3%, 20.3% and 34.6% respectively (table 2).

Table1: Descriptive statistics for oxalate/creatinin, citrate/ creatinin and uric acid /creatinin

Parameter	Mean(S.D)	Max	Min
Oxalate/cr (mg/mg)	0.01(0.02)	0.17	0.01
Citrate/cr (mg/mg)	2.98(2.39)	17.64	0.1
Uric acid/cr (g/mg)	0.59(0.59)	3.22	0.1

Table2: Disorders of urinary solutes

urinary solute excretion		
	Normal	Abnormal
oxalate/Cr (<0.003)	866(74.8%)	291(25.3%)
Citrate/Cr (>0.25)	922(79.7%)	235(20.3%)
Uric acid/Cr (<0.9)	757(65.4%)	400(34.6%)

The mean of oxalate, citrate and uric acid to creatinine is varying in different regions, groups, gender and age groups. Therefore after using cut points for each ratio table 3 shows the prevalence values of belonging to the normal and abnormal groups .Clearly is observed that there is a significant association between gender groups (p=0.001).

The mean of ratios of solutes in urine in terms of oxalate, citrate and uric acid to creatinine by age groups were also investigated and depending on the values in Table 3, a significant relationship was found. The highest percent of children in hyperoxaluria , hypocitraturia and hyperuricosuria were belonged to 9-12 years age group.

Table 3: Frequency distribution of children in urinary solutes problems in specific age

Age band	oxalate/Cr		Citrate/Cr		Uric acid/Cr	
	Normal (<0.003)	Abnormal	Normal (>0.25)	Abnormal	Normal (<0.9)	Abnormal
7	108	56	114	50	86	78
8	140	49	152	37	123	66
9	173	56	184	40	154	75
10	174	49	186	37	155	68
11	172	43	180	30	147	68
12	83	17	88	12	76	24
13	6	3	7	2	7	2
Level of sig.	P=0.022		P=0.007		P=0.002	

Table4: Percentile distribution of U solute/Cr ratio in different age

Age	Percentiles	cit/cr	oxa/cr	Uric acid/cr
7	25	1.172	0.007	0.215
	50	2.438	0.013	0.455
	75	3.787	0.019	0.860
	90	7.680	0.038	1.483
	95	9.500	0.057	2.021
8	25	1.225	0.006	0.231
	50	2.178	0.011	0.489
	75	4.025	0.023	0.776
	90	6.664	0.052	1.427
	95	8.520	0.074	1.949
9	25	1.560	0.006	0.209
	50	2.526	0.013	0.407
	75	4.511	0.027	0.757
	90	6.860	0.049	1.376
	95	7.549	0.072	2.006
10	25	1.078	0.006	0.182
	50	2.136	0.011	0.321
	75	3.947	0.027	0.700
	90	6.076	0.052	1.478
	95	8.137	0.072	2.340
11	25	1.272	0.006	0.190
	50	2.194	0.011	0.383
	75	4.108	0.022	0.765
	90	6.780	0.041	1.439
	95	8.411	0.051	2.174
12	25	1.242	0.005	0.193
	50	1.931	0.009	0.315
	75	3.627	0.021	0.631
	90	6.348	0.041	0.893
	95	8.041	0.071	1.282
13	25	0.960	0.005	0.189
	50	1.979	0.021	0.447
	75	3.783	0.031	0.755
	90	5.760	0.089	3.000
	95	5.760	0.089	3.000

Ninety fifth percentile of the ratio for oxalate, citrate and uric acid to creatinine were determined based on age for population in the study (Table4). The 95th percentile value of the U solutes/ Cr was different so that, in oxalate/creatinine is 0.57 for the age of 7 years and the decreases to 0.089 for the age of 13 years. It show arising pattern by age and similar pattern for cit/cr ratio in which valued of 9.5 for the age 7 and decreased to 5.76 for the age of 13 years. In the uric acid ratio we observe non stable trend in which get valued of 2.021 and 3 for the ages of 7 and 13 years. it shows an increase but before reaching to the age of 13 we observed another declining trends we have The dietary intake of proteins, calcium, and other nutrients in these children was less than recommended and explained the reduced urinary

excretion observed.

The prevalence of mineral tract is varying in different geographic regions and different ethnic groups because, the province is the largest in area and different ethnic groups living in. The study conducted on three major ethnics, Baluch, Sistani and the others in which counted 109 and 77 in Hyperoxaluria respectively and 172 persons for the others (Table 5). Using chi-square test showed a significant difference ($p<0.05$) between the groups. Hypocitraturia noted in 125 Baloch-children, 88 in Sistani-children and 157 in the other-children and observed a significant difference ($p<0.001$) in rates. Hyperuricosuria noted in 51 Baloch-children, in 50 Sistani-children and 122 in other-children and not observed a significant difference ($p>0.05$).

Table 5 shows the relationship of ethnic groups and the levels of BMI with U solute/Cr in children. Ethnic groups as a factor considered its relationship on U solutes. The table 5 shows that in the normal situation for Cit/Cr, Oxa/Cr and Uric acid/Cr, Sistani population has the highest percentage in compared to Baluch and the other groups. The situations of Oxa/Cr and Uric acid/Cr affected by Ethnic groups significantly in the level of $p=0.05$ and $p=0.001$ respectively. Cit/Cr , Oxa/Cr and Uric acid/Cr decrease when the level of BMI increases in both normal and abnormal U solutes. Amongst all ratios Uric acid/Cr only shows that has a significant dependency.

Table 5: Frequency and the percentage distribution of children with urinary solutes problems in ethnic groups and body mass index levels

Variables		Oxalate/Cr		Citrate/Cr		Uric/Cr	
		Normal n (%) (<0.003)	Abnormal	Normal n (%) (>0.25)	Abnormal	Normal n (%) (<0.9)	Abnormal
Ethnic groups	Baluch	390 (78.16)	109	327 (72.35)	125	136 (72.73)	51
	Sistani	422 (84.57)	77	350 (79.91)	88	137 (73.26)	50
	Others	372 (68.38)	172	295 (65.27)	157	187 (60.52)	122
	Total	1184 (76.78)	358	972 (72.43)	370	460 (67.35)	223
Level of sig.		P=0.05		P=0.001		P=0.61	
BMI levels	Underweight	183 (26.37)	511	145 (20.8)	552	271 (38.89)	426
	Normal	87 (22.37)	302	74 (19.02)	315	106 (27.25)	283
	Overweight and obese	7 (22.58)	24	7(22.58)	24	10 (32.26)	21
	Total	277 (24.87)	837	226(20.23)	891	387	730
Level of sig.		0.274		0.741		0.001	

Discussion

With the increasing incidence of Urolithiasis in the past decades, epidemiological studies were common in recent decades. The prevalence of Urolithiasis varies in different countries which have been reported in the range of 1 % -15 % (9, 10). With the development of western cultures, the prevalence of Urolithiasis has increased in Iran similar to other countries. Early detection is essential to reduce morbidity due to this disorder. This study is an epidemiological study of 1157 primary schoolchildren which was done in the city of Zahedan in the southeast area of Iran. In the 25.3 % of schoolchildren observed the hyperoxaluria, in 20.3 % of the students observed the hypocitratoria , and in the 34.6 %, hyperuricosuria were observed. A study in British by Coward has reported that, the most common causes for Urolithiasis were metabolic problems and infection in order (10). In another study that was done in Germany in 2011 by Habib, metabolic disorders such as hypercalciuria ,Hyeroxaluria and hypocitraturia determined as risk factors in nephrocalcinosis of children. (11). In a study conducted by Moorani, urinary citrate was measured in 86 children aged 1 to13 years. Hypocitraturia in children with urolithiasis (68.8%) was higher in comparison with healthy children (27.9 %) in which are same with our result (16). Hani A. Sweid and the colleagues in New Delhi in 1997 performed a study to measure uric acid, oxalate, creatinin, and other minerals including calcium, magnesium in 203 children aged 8-15 years old. The mean of 4.4 mg/kg and 1.5mg/kg respectively for uric acid and oxalate in daily excretion and 0.06 mg/mg for random urinary oxalate to creatininn were detected. Therefore, the results of this study related to urinary excretion of solute are less than most studies and suggest that nutritional and special dietary habits in these children existed (12). In our study, the mean of oxalate, citrate and uric acid to urine creatinin measured of 0.01± 0.02, 2.98 ± 2.39 and3.22± 0.59, in the given order in which less than values obtained in the study by Hani A. Sweid. In another study by Ratan in Delhi in 2002, the most common causes of stone were hypercalcuria and hypocitraturia (14). In the Stitchantrakul study in 2007, the most common causes of kidney stones in Thai children were citrate and hypercalciuria deficiency and low urine volume (15). In a study conducted by Naseri in 2011, anatomical disorder especially in less than 5 years old was along with metabolic disorders, and infection of urolithiasis. In this study 42.7% of children had metabolic disorders (13). In a relative study on 125 healthy children, calcium, uric acid and citrate were evaluated. The rates of 24-hour urine calcium and random were 3.75 mg/kg and 0.1 in the given order. The maximum values of uric acid excretion in 24-hour urine were 600, 450, and 320 mg and 13, 15 and 18 mg/kg for adolescents, school and preschool children, respectively; in mg/dl of glomerular filtration rate, in the fasting urine sample, it was 0.47. Positive correlation was observed for the uric acid excretion in 24-hour urine and fasting urine samples. The mean values for the citrate excretion in 24-hour urine were 1.6, 1.1 and 0.5 mmol for adolescents, school and preschool children, respectively; for citrate/creatinine ratio, in the fasting urine sample the mean value was 0.3 (17). In another relative study 128 healthy children aged 4 to 17 years compared with 137 children with 24-hour urinary calcium stones. Oxalate excretion were compared so that, excretion rate per square meter of body surface area was 0.3 ± 0.1 in patients with stones oxalate excretion significantly higher than those of healthy subjects (20). In a relative study 60 children with urinary stones were compared with 35 healthy children aged 4-18 years, Hypercalciuria and mild hyperoxaluria respectively in 23 and 16 children were found. Hypocitraturia was seen in 9 children with calcium stones, but no difference with healthy children. Normal group had mean of 144 ± 385 mg / g citrate to creatinin and therefore

hpocitraturia can being considered as the prevention of urinary tract stones (21).

The mean of oxalate, citrate and uric acid to creatinine in urine in different regions, age groups and sex are different which is in this study the frequency of urinary values of these minerals were carried out based on sex. The results showed a significant difference between the two gender groups. In our study the abnormal values of oxalate, citrate and uric acid to creatinin, were higher in girls in compared boys. May be the reason is the higher proportion of girls. Same assessment was done for age groups and observed a significant correlation between the values . Most people with hyperoxaluria, hypocitraturia and hyperuricosuria were belonged to 9-12 age group. In Safarinejad study the highest level of uric acid to creatinine was for age less than 7 years (0.06 ± 0.07) in children younger than 7 years, 0.041±0.033 in the 11– to 14-year group (2). In 169 children 6 to 13 years randomly performed urinalysis and the association with age and body surface area were determined. This study conducted by Von Schnakenburg C. The greatest amount of oxalate (57 ± 131 mmol / mol) was seen in infants. This finding suggests that muscle mass and creatinine increased with age and proposed that random urine screening fo hyperoxaluria in children with nephrocalcinosis and nephrolithiasis is necessary (18). In a study conducted in the Switzerland, the oxalate excretion rate was the highest (72 mmol/mol) in 7-24 months infants and the lowest in teens (22 mmol/mol) (19). In a study of 1306 children from one month to 15 years old were examined urine for uric acid to creatinine. The results showed that in age group of 7-11 years was 0.14 to 0.9. Girls had the most excretion of uric acid in age group of 12-15 years. Association between dietary protein intake and urinary excretion of uric acid was not observed (22). In our study the highest rate of uric acid excretion was belonged to the age group of 9-12 years. The analysis was done in the term of ethnicity and, hyperoxaluria, hypocitraturia and hyperuricosuria were investigated in our study. All the measures were higher for the other ethnic compared to Baluch and sistani. It showed the importance of ethnicitical factors. We did a study on 100 children with urinary stone disease in the year of 2012 and we observed urine metabolic abnormalities, including hypercalciuria (56%), hypocitraturia (64%), hyperoxaluria (36%), hyperuricosuria (13%), hypocitraturia plus hypercalciuria (40%), hyperoxaluria plus hypercalciuria (23%) and hyperuricosuria plus hypercalciuria (12%). Two children had cystinuria. No metabolic abnormalities were observed in 14 patients. In short, we tried to assess non-fasting random urine excretion of minerals in the children of Zahedan to find the prevalence by age - gender - and ethnic. In other hand we tried to find the mean of urinary salt excretion in terms of race and geographical region and we observed statistical differences. In some countries long-term urinary screening programs are running for early detection of renal diseases (5). As a recommendation, more comprehensive study is needed in this area according to geographic regions and different conditions of health in a specific place of residency.

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Competing Interests:

None of the authors has any conflict of financial or other interest

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