World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 5.088

CORRELATION OF RANDOM URINARY CALCIUM/CREATININE RATIO WITH 24-HOUR URINE CALCIUM IN 2-16 YEAR OLD IN-PATIENTS OF BANDAR ABBAS PEDIATRIC HOSPITAL IN 2015

Kambiz Ghasemi*, Maryam Esteghamati and Arezoo Masroor

Clinical Research Development Center of Children Hospital, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.

***Corresponding Author: Kambiz Ghasemi**
Clinical Research Development Center of Children Hospital, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.

Article Received on 18/04/2018 **Article Revised on 09/05/2018** **Article Accepted on 30/05/2018**

ABSTRACT

Background: Calcium is the best known ion in the skeletal muscular system of body and kidneys are the key organ for calcium hemostasis. As collecting 24-hour urine samples is hard and time-consuming among young adults and children, measuring non-fasting random urinary calcium/creatinine ratio can be very practical to identify individuals with a high urinary calcium excretion. The present research aims to explore the correlation between 24-hour urine calcium with random urinary calcium/creatinine ratio in terms of patients' age and gender in Bandar Abbas Hospital in 2015. **Methods**: The present cross-sectional research is descriptive and analytical in type. It was conducted on 228 patients between 2 and 16 years of age staying in Bandar Abbas pediatric hospital in 2015. The research sample was selected in a simple randomized convenient sampling method from the target population. Calcium level was measured via Cresolphtalen Complexion Spectrophotometrics while creatinine level was measured through Kinetic Jaffe Reaction via Hitachi autoanalytic device. Finally, UCR/CR was measured manually. **Results:** In this research, 228 patients participated who were between 2 and 16 years of age, whose calcium/creatinine ratio was measured and statistically analyzed. From among them, 127 (55.7%) were male while 101 (44.3%) were female. The highest random urinary calcium/creatinine ratio was 3.55 while the lowest ratio was .21 (mean: .39 SD±.49). The lowest rate of urine calcium excretion was 1.88 mg/Kg/day within 24 hours while the highest rate was 10.91 mg/Kg/day in 24 hours. **Conclusion**: The present research revealed that collecting 24-hour urine samples is a gold standard in diagnosing hypercalciuria and should be used to diagnose patients with this disease.

KEYWORDS: Hypercalciuria, random urinary calcium/creatinine ratio,24-hour urine calcium.

1. INTRODUCTION

Calcium is the most important ion ever recognized in human skeletal muscular system and is in fact the fifth kation in body while kidneys are the main organ for calcium hemostasis in body. The primary function of calcium within body is its role in mineralizing the hard tissue.[1] Urine calcium excretion is increased with such changes as hypocalcemia, high serum phosphate and acidosis. As the most prevalent identifiable metabolic cause of calcemic kidney stone, hypercalciuria.[2,3] entails an over-excretion of calcium through urine. If there is no definite cause identified for this, it is considered as idiopathic hypercalciuria.[4] Hypercalciuria might be without any symptom.[5] It might lack any clinical manifestations such as gross hematuria, stable microscopic hematuria, suprapubic pain, proteinuria, renal colic, enuresis, osteopenia, rickets, sterile pyuria, urinary tract pricking or burning, abdominal pain and so on.[6-10] Calcium is the best known factor involved in the formation of kidney stone. It appears that urine excretion of the stone is correlated with age and gender. The daily excretion of calcium follows a daily pattern which reaches its peak in the midday. Excretion of more than 4 mg/kg within 24 hours is defined as hypercalciuria.[11,12] Due to the fact that collecting urine samples from young adults and children within 24 hours is challenging and time-consuming, measuring non-fasting random urinary calcium/creatinine ratio can be very practical to identify individuals with a high urinary calcium excretion.[5,13,14] A body of research revealed a positive correlation between random urinary calcium/creatinine ratio (UCA/CR) and 24-hour urine calcium.[15,16] According to the reported results in the related literature, the random UCA/CR for hypercalciuric patients was considered to be .21. However, a body of recent research revealed that the mean UCA/CR score varies in accordance with age and geographic area.[17] That is why the urinary excretion of calcium is affected by a variety of factors. Therefore,

in this research so as to minimize the error of urinary calcium measurement, the ratio of this factor to urine creatinine was simultaneously estimated. Creatinine is a substance freely excreted in a constant amount from renal glomeruli without any reabsorption. Thus, it enjoys a constant clearance in those with healthy kidneys.[18] The present research aimed to explore the correlation of the 24-hour urine calcium with the random urinary calcium/creatinine ratio across different genders and age groups among patients in Bandar Abbas in 2015.

2. MATERIALS AND METHODS

The present cross-sectional research was descriptive analytical in type and was conducted on a sample of 228 patients of 2-16 years of age staying in Bandar Abbas pediatric hospital in 2015. The research sample was selected in a simple randomized convenient sampling method from the target population. The data were collected from the test result papers within patients' medical records. Each subject entered according to a randomly selected number. The inclusion criteria were the age of 2-16 years and a ratio of random urinary calcium/creatinine above .21.

The exclusion criteria was a ratio of random urinary calcium/creatinine below .2. Moreover, those test results which supported the secondary causes of hypercalciuria were excluded from the study. Once the informed consent was obtained from the subjects' parents and they were ensured of the confidentiality of the information they provided, a second urine sample was taken from subjects in the morning so as to measure the ratio of random urinary calcium/creatinine. The urine sample was taken to measure the 24-hour urine calcium. Eventually, the correlation of these two factors was explored. In this research, the ratio of random urinary calcium/creatinine above .21 after two years of age was taken as hypercalciuria.[8] To estimate the required sample for this research, a sample size formula was used and as compared to the related literature the confidence interval was taken as 95% and sensitivity as .03. Thus, finally the sample size was decided to be 218. Considering the possibility of attrition, finally 228 subjects were agreed upon. Calcium level was measured via Cresolphtalen Complexion Spectrophotometrics while creatinine level was measured through Kinetic Jaffe Reaction via Hitachi autoanalytic device. Finally, UCR/CR was measured manually. The data were statistically analyzed via SPSS ver19 and the tests used were linear regression analysis and one-way ANOVA, mean and confidence interval of 95%. For the parametric tests, ANOVA and linear regression analysis, the data were required to be normally distributed. The mean and standard deviation of the scores were estimated in the main data. In this research, the level of significance of the data was set at <.05.

3. RESULTS

In this research, a total number of 228 patients entered the gender and age groups (2-16 years). The ratio of random urinary calcium/creatinine of these subjects was estimated and statistically analyzed. From among this number, 127 subjects (55.7%) were male while 101 (44.3%) were female. The oldest subject was 11 years old while the youngest was 3. The highest ratio of random urinary calcium/creatinine was 3.55 while the lowest ratio was .21 (Mean: .39±.49SD). The lowest rate of excreted urine calcium was 1.88 mg/kg a day within 24 hours while the rate of the same variable was 10.91 mg/Kg a day (Table 1).The linear correlation coefficient of these two variables was .188 which was statistically significant (p=.004). However, the correlation coefficient does not point to a strong correlation. As R^2=.0219, the regression model also confirmed this issue (Figure 1).

Table 2 indicates the mean, standard deviation, minimum and maximum scores of the ratio of random urinary calcium/creatinine and the 24-hour urine calcium in the two age groups. In the <7-year age group, the mean ratio of random urinary calcium/creatinine was .46 and the standard deviation was .31. The minimum score of the same variable was .21 while the maximum score was 2. In the ≥7-year group, the mean score of the ratio of random urinary calcium/creatinine was .53 and the standard deviation was .46. The minimum score of this variable was .21 while the maximum score was 3.55. The Mann-Whitney U-test results revealed no statistically significant difference between the two groups in terms of this variable (z=-.381, p=.703). The mean score of calcium excretion through urine within 24 hours in the <7-year age group was 5.47 mg/kg/day with a standard deviation of 1.48. The minimum rate of calcium excretion was 1.88 mg/kg/day while the maximum rate was 10.91 mg/kg/day. The mean rate of calcium excreted through urine in 24 hours in the ≥7-year group was 4.63 mg/kg/day with a standard deviation of 1.03. The minimum rate of excretion was 2.34 mg/kg/day while the maximum rate of excretion was 7.50 mg/kg/day. Mann-Whitney U-test results revealed no statistically significant difference between these two age groups (z=-5.071, p<.001).

In the <7-year age group, as Pearson correlation coefficient showed, the linear correlation between the ratio of random urinary calcium/creatinine and the 24-hour urine calcium was .311 which is a strong correlation and also statistically significant (p<.001). In the ≥7-year group, the Pearson correlation coefficient was estimated as .226 which is lower than the other age group but is still statistically significant (p=.022).

Table 3 includes the mean, standard deviation, minimum and maximum scores of the ratio of random urinary calcium/creatinine and the 24-hour calcium/creatinine across two genders. Among the male, the mean ratio of random urinary calcium/creatinine was .47 (SD=.39). The minimum score of this ratio was .21 while the

maximum ratio was 3.55. Among the female, the mean ratio of random urinary calcium/creatinine was .51 (SD=.39). The minimum ratio was .21 and the maximum ratio was 2.33. Mann-Whitney U-test revealed no statistically significant difference between these two groups (z=-.399, p=.690). The mean rate of 24-hour calcium/creatinine was 5.15 mg/kg/day among the male (SD=1.39). The minimum rate of excreted calcium in urine was 2.34 mg/kg/day while the maximum rate was 10.91 mg/kg/day. The mean rate of excrete calcium over 24 hours among the female was 5.02 mg/kg/day (SD=1.33). The minimum rate of excretion was 1.88 mg/kg/day while the maximum rate of excretion was 9.50 mg/kg/day. Mann-Whitney U-test showed no statistically significant difference between the two groups in terms of this variable (z=-.493, p=.622).

Among the female, Pearson correlation coefficient was .108 for the linear relationship between the two target variables, the ratio of random urinary calcium/creatinine and the 24-hour urine calcium excretion. This value shows a low correlation and is not statistically significant (p=.228). Among the male, as Pearson correlation coefficient showed, the linear correlation between the ratio of random urinary calcium/creatinine and the 24-hour urine calcium excretion was .416 which is a strong correlation and is statistically significant (p<.001).

Table 1: The mean, standard deviation, minimum and maximum scores of the ratio of random urinary calcium/creatinine within 24 hours.

	Mean	SD	Min	Max
Random urine Ca/Cr ratio	.49	.39	.21	3.55
24-h urine ca (mg/kg/day)	5.09	1.36	1.88	10.91

Table 2: The mean, standard deviation, minimum and maximum scores of the ratio of random urinary calcium/creatinine and the 24-hour urine calcium in the two age groups.

Age group		Mean	SD	Min	Max	Pearson correlation coefficient	P-value
<7 years	the ratio of random urinary calcium/creatinine	.46	.31	.21	2	.311	<.001*
	24-hour calcium/creatinine	5.47	1.48	1.88	10.91		
≥7 years	the ratio of random urinary calcium/creatinine	.53	.46	.21	3.55	.226	.022*
	24-hour calcium/creatinine	4.63	1.03	2.34	7.50		

Table 3: The mean, standard deviation, minimum and maximum scores of the ratio of random urinary calcium/creatinine and the 24-hour calcium/creatinine across two genders.

Gender		mean	SD	Min	Max	Pearson correlation coefficient	P-value
Male	The ratio of random urinary calcium/creatinine	.47	.39	.21	3.55	.108	.228
	24-hour calcium/creatinine	5.15	1.39	2.34	10.91		
Female	The ratio of random urinary calcium/creatinine	.51	.39	.21	2.30	.416	<.001*
	24-hour calcium/creatinine	5.02	1.33	1.88	9.50		

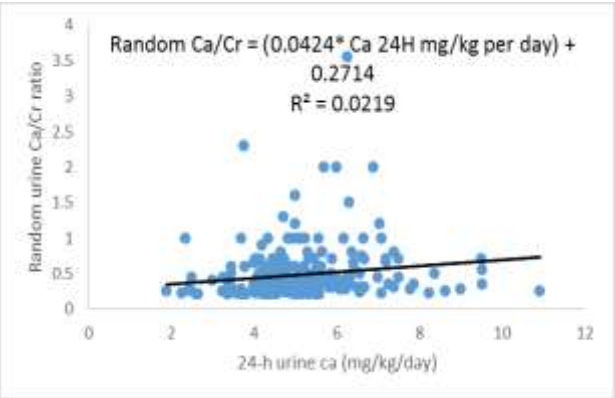

Figure 1: Regression model of the two variables, the ratio of random urinary calcium/creatinine and the 24-hour urine calcium.

4. DISCUSSION

Hypercalciuria is the most prevalent metabolic cause of the calcemic kidney stone formation.[2] Hypercalciuria is in the majority of cases without any symptom. However, a body of recent research indicated the role hypercalciuria plays in producing many symptoms related to the urinary system.[5] The gold standard method of diagnosing hypercalciuria is to measure urine calcium over 24 hours.[19] However, due to the difficulty of collecting 24-hour urine samples from children for the purpose of hypercalciuria screening, we can use the ratio of random urinary calcium/creatinine.[5] Replacing the 24-hour urine calcium with the ratio of random urinary calcium/creatinine is controversial. A number of studies have reported strong correlations while others found no hard evidence.[7] The present findings revealed that a ratio of random urinary calcium/creatinine above .21 in

84.6% of cases is capable of correctly diagnosing patients who excrete more than 4 mg of calcium for each kg of their body mass per day through urine. However, there is no statistically significant correlation between the ratio of random urinary calcium/creatinine and the 24-hour calcium/creatinine.

Koyun et al. investigated 269 patients and concluded that there was a low correlation between the non-fasting random urinary calcium/creatinine ratio and the 24-hour urine calcium. They also found that the mere use of the ratio of random urinary calcium/creatinine is far from adequate to determine hypercalciuria.[20]

In some other research, Alconcher et al. examined 220 patients. They used regression analysis as well as a correlation coefficient and reported a low correlation between the ratio of random urinary calcium/creatinine and the 24-hour calcium/creatinine.

Borkenstein et al. (1997) found a statistically significant correlation between the ratio of random urinary calcium/creatinine and the urine calcium excretion. Their findings showed that estimating the ratio of random urinary calcium/creatinine is a simple reliable method of diagnosing hypercalciuria and needs to be applied for all children afflicted with urinary stones or inexplicable hematuria.[22]

Another study conducted by In so Choi et al. (2013) on 264 patients revealed a positive linear correlation between the ratio of random urinary calcium/creatinine and the 24-hour urine calcium.[7] No such correlation was found in the present research and no positive linear correlation was observed in the regression chart. On the other hand, no correlation was found between the ratio of random urinary calcium/creatinine and the 24-hour urine calcium across age groups or genders.

6. CONCLUSIONS

As maintained in the body of previous literature, the 24-hour urine sample collection is the gold standard method of diagnosing hypercalciuria and should be used to diagnose patients with hypercalciuria.

ACKNOWLEDGEMENTS

This article is part of a thesis entitled as “the correlation of the ratio of random urinary calcium/creatinine with 24-hour urine calcium in 2-16 year old patients in Bandar Abbas in 2015” which received the code 88-94.39. It was supported by the esteemed deputy of research at Hormozgan University of medical sciences.

REFERENCES

1. Spitzer A, Chesney R. Role of the kidney in mineral metabolism. Pediatric kidney disease: Little Brown & Co., Boston, 1992; 147-83.
2. Ahmadzadeh A, Hakimzadeh M, Safa-Abadi A. Idiopathic hypercalciuria in Iranian children. Iranian Journal of Pediatrics, 2008; 18(2): 163-6.
3. Worcester EM, Coe FL, editors. New insights into the pathogenesis of idiopathic hypercalciuria. Seminars in nephrology, 2008: Elsevier.
4. Heiliczer JD, Canonigo BB, Bishof NA, Moore ES. Noncalculi urinary tract disorders secondary to idiopathic hypercalciuria in children. Pediatric Clinics of North America, 1987; 34(3): 711-8.
5. Ajdadi E, Esteghamati M, Ghasemi K, Shahvari SZ. Comparison of urinary sodium and potassium in children older than two with idiopathic hypercalciuria and a healthy control group in Bandar-Abbas, Iran, in 2013. Electronic physician, 2014; 6(3): 872.
6. Weir MR. Atypical idiopathic hypercalciuria in an adolescent. Journal of Adolescent Health Care, 1988; 9(6): 498-500.
7. Choi IS, Jung ES, Choi YE, Cho YK, Yang EM, Kim CJ. Random urinary calcium/creatinine ratio for screening hypercalciuria in children with hematuria. Annals of laboratory medicine, 2013; 33(6): 401-5.
8. Schwaderer A, Srivastava T. Complications of hypercalciuria. Frontiers in bioscience (Elite edition), 2009; 1: 306-15.
9. Langman C, Moore E. Hypercalciuria in clinical pediatrics: a review. Clinical pediatrics, 1984; 23(3): 135-7.
10. Emamghorashi F, Davami MH, Rohi R. Hypercalciuria in Jahrom's school-age children: what is normal calcium-creatinine ratio? Iranian journal of kidney diseases, 2010; 4(2): 112.
11. Moxey-Mims MM, Stapleton FB. Hypercalciuria and nephrocalcinosis in children. Current opinion in pediatrics, 1993; 5(2): 186-90.
12. Stapleton FB, Group SPNS. Idiopathic hypercalciuria: association with isolated hematuria and risk for urolithiasis in children. Kidney Int., 1990; 37(2): 807-11.
13. Ceran O, Akin M, Aktürk Z, Ozkozaci T. Normal urinary calcium/creatinine ratios in Turkish children. Indian pediatrics, 2003; 40(9): 884-7.
14. Sorkhi H, Aahmadi MH. Urinary calcium to creatinin ratio in children. Indian journal of pediatrics, 2005; 72(12): 1055-6.
15. Ghazali S, Barratt T. Urinary excretion of calcium and magnesium in children. Archives of disease in childhood, 1974; 49(2): 97-101.
16. Gökçe Ç, Gökçe Ö, Baydinç C, Īlhan N, Alaşehirli E, Özküçük F, et al. Use of random urine samples to estimate total urinary calcium and phosphate excretion. Archives of internal medicine, 1991; 151(8): 1587-8.
17. Pak CY, Kaplan R, Bone H, Townsend J, Waters O. A simple test for the diagnosis of absorptive, resorptive and renal hypercalciurias. New England Journal of Medicine, 1975; 292(10): 497-500.

18. Nuzzo V, Fittipaldi M, Fonderico F, Esposito DPA, Russo D, Del Puente A, et al. Urinary calcium excretion in a population of children living in southern Italy. Minerva pediatrica, 1999; 51(3): 53-6.
19. Jones A, Shafer M, Keuler N, Crone E, Hansen K. Fasting and postprandial spot urine calcium-to-creatinine ratios do not detect hypercalciuria. Osteoporosis International, 2012; 23(2): 553-62.
20. Koyun M, Güven AG, Filiz S, Akman S, Akbas H, Baysal YE, et al. Screening for hypercalciuria in schoolchildren: what should be the criteria for diagnosis? Pediatric Nephrology, 2007; 22(9): 1297-301.
21. Alconcher LF, Castro C, Quintana D, Abt N, Moran L, Gonzalez L, et al. Urinary calcium excretion in healthy school children. Pediatric Nephrology, 1997; 11(2): 186-8.
22. Ring E, Borkenstein M. Use of the calcium-creatinine ratio in diagnosis and therapy. Padiatrie und Padologie, 1987; 22(3): 245-50.