

Original Article

Hypercalciuria is an important cause of urinary tract infection in children

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Abstract

Urinary tract infection is a common disease in paediatric practice and an important cause of morbidity. Recurrence is frequent and occurs in approximately 40% in female and 32% in male. The association of hypercalciuria and UTI has been pointed out by several authors from different countries during the last 7-10 years. This prospective case control study was designed to evaluate the association between hypercalciuria and UTI in children in the department of Biochemistry, DMC and National Institute of Kidney Diseases and Urology (NIKDU) from July 2007- June 2008 on 30 cases of diagnosed UTI and 40 age-sex matched apparently healthy control. Blood samples of all study subjects were analyzed for serum total calcium concentration to exclude hyper or hypocalcaemia. Random urine samples were analyzed for urinary calcium creatinine ratio to screen hypercalciuria. In this study, urinary calcium creatinine ratio ≥ 0.20 was considered as hypercalciuria. Hypercalciuria were reported in 46.7% cases whereas only in 20.0% controls which was significantly higher in cases ($p < 0.05$). Among the cases, 76.7% had recurrent UTI and 23.3% had first time UTI. Hypercalciuria were reported in 52.2% cases with recurrent UTI and only in 28.6% cases with first time UTI. Hypercalciuria in cases with recurrent UTI were also found significantly higher compared to controls ($p < 0.05$). It was therefore concluded that hypercalciuria is associated with UTI and is an important cause of UTI in children.

Key words : Hypercalciuria, UTI, children

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Introduction

Urinary tract infection (UTI) is a common disease in paediatric practice and an important cause of morbidity,¹ accounting for 4.6%-5.9% of febrile episodes.² UTI may be recurrent. Recurrence is frequent and occurs in approximately 40% in female and 32% in male which may cause renal scar formation leading to hypertension and renal failure.^{3,4,5} There are some known predisposing factors such as urinary stone, voiding dysfunction, neurogenic bladder, vesicourethral reflux and urinary obstruction causing UTI. There are also some undetermined predisposing factors causing UTI. Hypercalciuria (urinary calcium creatinine ratio ≥ 0.20) is suspected as one important undetermined predisposing factor in recurrent UTI patients because hypercalciuria may play an important role in these patients by promoting the formation of microcrystals which damage the uroepithelium.^{6,7}

The association of hypercalciuria and UTI has been pointed out by several authors from different countries during the last 7-10 years. They found hypercalciuria as an important contributing factor in UTI⁸ and suggested to investigate urinary calcium excretion in children with recurrent UTI and a normal urinary tract to evaluate hypercalciuria in these patients.⁷ UTI in children is very common in our country and in many instances, recurrence occur after treatment with an appropriate antibiotic. This prospective case control study was designed to evaluate the association between hypercalciuria and UTI in children with a goal to reduce the incidence of UTI by taking dietary or therapeutic measures.

Methods

This case-control study was conducted in Paediatric Nephrology unit of National Institute of Kidney Diseases and Urology (NIKDU), Dhaka. The study period was from July 2007-June 2008. A total number of 70 children were included in the present study. Among them, 30 diagnosed UTI patients were selected as case and 40 age-sex matched apparently healthy children without UTI were selected as control. The age range of the study subjects were between 1 and 12 years. Blood samples of all the study subjects were collected and analyzed for serum total calcium concentration to exclude hyper or hypocalcaemia (by calcium-cresolphthalein complexone spectrophotometric method). Random mid stream urine

samples were collected and urinary calcium concentration were analyzed by the same method as serum calcium and urinary creatinine concentration were analyzed by kinetic jaffe reaction method. Urinary calcium creatinine ratio was used to screen hypercalciuria. Urine R/M/E and urine culture were done to exclude UTI in control. The data were analyzed by computer using SPSS (version 12 for Windows). Numerical variables were analyzed by the Student's unpaired 't' test and categorical variables were analyzed by the chi-square test to see the difference between two groups. For all tests, p-values less than 0.05 (p<0.05) were considered statistically significant.

Results

Mean age of the cases was 6.87±2.94 years and of controls was 7.73±1.41 years. Mean serum total calcium concentration of cases and controls were 8.87±.70 mg/dl and 9.27±.39 mg/dl respectively. In this study, Uca/Ucr ≥ 0.20 was considered as hypercalciuria. Hypercalciuria was present in 14 out of 30 cases (46.7%) and only in 8 out of 40 controls (20.0%) which was significantly higher in cases compared to control (p<0.05). (Table-I & Figure-I)

Table-I: Comparison of hypercalciuria among case and control

Subjects	Hypercalciuria		Total	x ² value	p value
	present	absent			
Case	14(46.7%)	16	30		
Control	8(20.0%)	32	40	4.48	0.03 (p<0.05)
Total	22	48	70		

Among the cases, 76.7% had recurrent UTI and 23.3% had first time UTI (Table-II).

Table-IV: Comparison of hypercalciuria between controls and recurrent UTI cases

Study Subjects	Hypercalciuria		Total	x ² value	p value
	Present	Absent			
Controls	8	32	40		
Cases with recurrent UTI	12(52.2%)	11	23	5.571	0.01* (p<0.05)
Total	20	43	63		

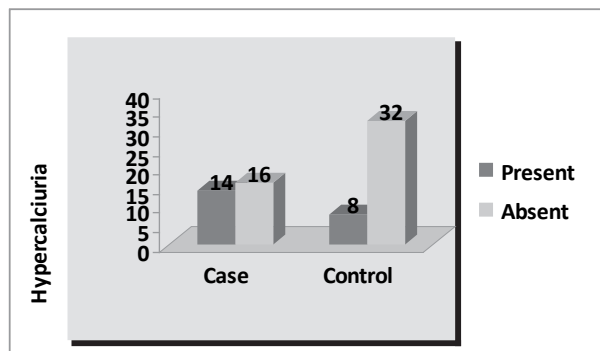


Figure-1: Comparison of hypercalciuria between case and control

Table-II: Frequency and percentage of cases according to first time and recurrent UTI

	Parameter	Frequency	Percent
UTI	First time	7	23.3%
	Recurrent	23	76.6%
	Total	30	100.0%

Hypercalciuria were reported in 52.2% cases with recurrent UTI and in 28.6% cases with first time UTI (Table-III).

Table-III: Comparison of hypercalciuria between first time and recurrent UTI cases

UTI	Hypercalciuria		Total
	present	absent	
First time	2 (28.6%)	5 (71.4%)	7
Recurrent	12 (52.2%)	11 (47.8%)	23
Total	14	16	30

Hypercalciuria in cases with recurrent UTI were also found significantly higher compared to control (p<0.05) (Table-IV).

Discussion

Urinary tract infection (UTI) in childhood is a significant and common problem encountered by primary, secondary and tertiary healthcare professionals and is important cause of acute illness. UTI may be recurrent that causes considerable distress, anxiety and inconvenience to children and their families.⁵ UTI occurs in approximately 1% of boys and up to 3% of girls in school age.⁹ Early recognition and prompt treatment of UTIs are important to prevent progression of infection to pyelonephritis or urosepsis and to avoid late sequelae such as renal scarring or renal failure.¹⁰

Hypercalciuria has been increasingly recognized as a cause of urinary tract infection in clinical paediatrics. The association of hypercalciuria with UTI has been pointed out by several authors during the last 7-10 years. Vesna D et al 2007, Biyikli et al 2005, Maria GM et al 2001, Vachvanichsanong et al 2001 and Lopez M et al 1999 found hypercalciuria as an important contributing factor to recurrent UTI in children.^{4,7,8}

UTI in children is very common in our country. Hypercalciuria may be an important contributing factor associated with UTI in Bangladeshi children. The present study was designed to evaluate the urinary calcium/creatinine ratio in children (aged 1-12 years) with UTI to find out any association between hypercalciuria and UTI.

Total 70 children were included in this study. Among them, 30 diagnosed UTI patients were selected as case and 40 apparently healthy children without UTI were included as control. Mean age of cases was 6.87 years with standard deviation of 2.94 years in comparison with 7.73 ± 1.41 years in control. Among the 30 cases, 14 were male and 16 female; where as, 16 male and 24 female among 40 controls.

In this study, fourteen out of thirty (46.7%) cases had hypercalciuria whereas only eight (20%) among forty control group were found hypercalciuric which was significantly higher ($p < 0.05$) in case compared to control. High incidence of hypercalciuria (46.7%) was observed in this study in comparison to other similar studies conducted in other countries. A Venezuelan study by Lopez et al reported the incidence of hypercalciuria to be 32% among patients with recurrent UTI. They used the ratio of 0.37 for the upper limit of urinary calcium excretion, based on their population studies. An American study by Vachvanichsanong et al choose the ratio 0.3 for the hypercalciuria definition and reported that 31% of hypercalciuria patients had recurrent UTI.¹⁰ Biyikli et al in Turkey found 43% hypercalciuria among children

with recurrent UTI when they set the upper limit of calcium excretion ratio at equal or greater than 0.24.⁴ An explanation for higher incidence of hypercalciuria in this study may be due to higher cutoff level for urinary calcium/creatinine ratio in their series and their mean age of the study population were also different from this study.

One important finding in this study was that hypercalciuria had been found in 20% of the apparently healthy children which may be primary or secondary. These children should be followed-up as they may develop UTI in future. Though secondary cause of hypercalciuria could not be excluded as several other costly investigations were required, we tried to screen them by thorough clinical examination and available previous investigation reports.

Among the thirty children with UTI, twenty three (76.7%) had recurrent UTI and remaining seven children (23.3%) were diagnosed for the first time. In a similar study by Vachvanichsanong et al 2001, recurrent UTI affected 78% of patients where as it was in 33% cases in a study by Vesna et al 2007.⁸

We compared the incidence of hypercalciuria in children with first time and recurrent UTI. Twelve children with recurrent UTI found hypercalciuria (52.2%) whereas only two children with first time UTI (28.6%) had hypercalciuria which was found 44% in recurrent UTI and 10% in first time UTI patients in a study by Vesna et al. in 2007.⁸

We also compared the incidence of hypercalciuria in case with recurrent UTI and control. Twelve children with recurrent UTI (52.2%) had hypercalciuria whereas only eight controls (20.0%) had hypercalciuria which was highly significant in cases compared to controls ($p < 0.05$).

We concluded that hypercalciuria is one of the important predisposing factors for UTI. Though this is very difficult to make any conclusive comment as the sample size was very small, but considering some positive findings it can be said that hypercalciuria can be considered as an important causative factor for the development of UTI, specially recurrent UTI in Bangladeshi children and further population based study with larger sample size should be carried out to find out the incidence of hypercalciuria in our country and its clinical impact.

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