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Original Research Article

Association between hypercalciuria and urinary tract infection in children

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ABSTRACT

Background: Urinary tract infection (UTI) is a common bacterial infection in children and a significant cause of morbidity, particularly in infants and young children. Hypercalciuria, a metabolic abnormality characterized by excessive urinary calcium excretion, may predispose children to UTIs by facilitating uroepithelial irritation and bacterial colonization. Understanding the association between hypercalciuria and pediatric UTI can improve diagnosis and management. This study aimed to evaluate the association between hypercalciuria and urinary tract infection in children.

Methods: This case-control study was conducted at the Department of Paediatric Nephrology, National Institute of Kidney Diseases and Urology (NIKDU), Dhaka, over 18 months from December 2020 to May 2022. Ninety children aged 1-12 years were enrolled, including 45 cases with confirmed UTI and 45 age- and sex-matched healthy controls. Demographic data, urinary biochemical parameters (urinary calcium, creatinine, spot Ca/Cr ratio), and pyuria were assessed. Hypercalciuria was defined by elevated spot urinary calcium-to-creatinine ratio. Statistical analysis was performed using chi-square and independent t-tests, with $p<0.05$ considered significant.

Results: The mean age of cases and controls was 5.23±3.32 and 5.83±3.32 years, respectively, with a female predominance among cases (60%). Urinary calcium levels (1.35±2.01 mg/dl vs. 0.28±0.17 mg/dl, p=0.001) and spot Ca/Cr ratios (0.068±0.106 vs. 0.015±0.012, p=0.002) were significantly higher in UTI cases compared to controls. Hypercalciuria was present in 44.4% of cases versus 15.6% of controls (p=0.003). Pyuria was markedly elevated in cases, with 75.6% showing >10 pus cells/HPF, compared to 57.8% of controls having nil pus cells ($p<0.001$). No significant association was observed between hypercalciuria and UTI recurrence (p=0.420).

Conclusions: Pediatric UTIs predominantly affect younger children, especially females and those from rural areas. Hypercalciuria is significantly associated with UTI, independent of recurrence, highlighting the importance of metabolic evaluation in children presenting with UTI. Early detection and management of hypercalciuria may reduce susceptibility to infection and improve long-term outcomes.

Keywords: Children, Hypercalciuria, Pyuria, Spot calcium-to-creatinine ratio, Urinary calcium, Urinary tract infection

INTRODUCTION

Urinary tract infection (UTI) is one of the most common bacterial infections in children and represents a significant cause of morbidity, particularly in infants and young children. Recurrent UTIs may lead to renal scarring, hypertension, and long-term impairment of renal function if not identified and managed appropriately.

While structural abnormalities of the urinary tract and vesicoureteral reflux are well-recognized risk factors, metabolic contributors to pediatric UTI have gained increasing attention in recent years.[1-3]

Hypercalciuria, defined as excessive urinary calcium excretion in the absence of hypercalcemia, is one of the most frequent metabolic abnormalities encountered in children. It may be idiopathic or secondary to dietary factors, genetic predisposition, or underlying systemic conditions.[4] Pediatric hypercalciuria is commonly associated with hematuria, dysuria, abdominal pain, and nephrolithiasis; however, its role in predisposing children to UTIs remains underrecognized in routine clinical practice. [5]

Several pathophysiological mechanisms have been proposed to explain the association between hypercalciuria and UTI. Excess urinary calcium can lead to the formation of calcium microcrystals, which may cause irritation and microtrauma to the uroepithelium. This epithelial damage may facilitate bacterial adherence and colonization, thereby increasing susceptibility to infection. Additionally, calcium crystals may act as a nidus for bacterial biofilm formation, further contributing to recurrent infections.[6]

Clinical studies have demonstrated a higher prevalence of hypercalciuria among children with recurrent UTIs compared to healthy controls. In many cases, children with hypercalciuria present with UTI-like symptoms even in the absence of detectable bacterial infection, complicating diagnosis and management.[7-8] Failure to identify underlying hypercalciuria may result in repeated antibiotic use without addressing the primary metabolic abnormality.

Early detection of hypercalciuria in children with recurrent or unexplained UTIs is therefore of clinical importance. Timely dietary modification, increased fluid intake, and pharmacological intervention, when necessary, may reduce urinary calcium excretion and lower the risk of infection recurrence. Recognizing hypercalciuria as a modifiable risk factor can improve long-term outcomes and reduce the burden of recurrent UTIs in paediatric populations.

In this context, the present study aimed to evaluate the association between hypercalciuria and urinary tract infection in children, emphasizing the need for routine metabolic evaluation in pediatric patients presenting with recurrent UTIs.

METHODS

The study was designed as a case-control study and was conducted at the Department of Paediatric Nephrology, National Institute of Kidney Diseases & Urology (NIKDU), Dhaka. The study duration was 18 months, spanning from December 2020 to May 2022. The study population consisted of children aged 1 to 12 years of both sexes. Cases included children diagnosed with urinary tract infection who attended both inpatient and outpatient services of the paediatric nephrology department at NIKDU, while controls were age- and sex-matched apparently healthy children. Purposive sampling technique was applied for participant selection.

The sample size was calculated using a standard formula based on previously reported frequencies of hypercalciuria among children with UTI (46.7%) and controls (20.0%) as described by Abdullah et al (2014). A 95% confidence interval ($Z\alpha$=1.96) and 80% study power ($Z\beta$=0.85) were considered. Based on these parameters, the estimated sample size was 45 participants in each group, resulting in a total of 90 study subjects.

Children aged 1-12 years of both genders who met the diagnostic criteria were included in the study. Cases were children with confirmed urinary tract infection attending the paediatric nephrology department of NIKDU, and controls were age- and sex-matched apparently healthy children. Parents or guardians who declined to provide consent were excluded from the study.

The study variables included both demographic and laboratory parameters. Demographic variables comprised age, gender, place of residence, occupational and educational status of parents, socioeconomic status, and type of UTI (first episode or recurrent). Laboratory investigations included routine and microscopic examination of urine, urine culture and sensitivity, spot urinary calcium-creatinine ratio, serum electrolytes, serum creatinine, and serum calcium levels.

A total of 90 children were enrolled, including 45 cases and 45 controls, in accordance with the inclusion and exclusion criteria. Written informed consent was obtained from parents or guardians prior to data collection. A structured questionnaire was used to record sociodemographic information, medical history, clinical findings, and laboratory results. Clean-catch midstream urine samples were collected after proper perineal cleansing, and approximately 30 ml of urine was obtained in sterile containers. Samples were sent for routine microscopic examination and culture sensitivity within one hour of collection, and antibiotic sensitivity was determined using an antibiogram. Hypercalciuria was screened using the spot urinary calcium–creatinine ratio, analyzed with automated chemistry analyzers including Vitro 350 (J&J), Dimension Xpand Plus, and Beckman Coulter AU 480. Approximately 5 ml of venous blood was collected aseptically from each participant for biochemical analysis. Serum electrolytes were measured using the ion-selective electrode method, serum creatinine by the kinetic Jaffe method, and serum total calcium by the calcium-cresolphthalein complexone spectrophotometric method to exclude hypercalcemia or hypocalcemia.

Data collection tools included a checklist prepared for each child and a pretested interview schedule in Bengali, which contained questions relevant to the study objectives. The questionnaire was pretested among patients of similar categories prior to final data collection.

After data collection, all data were checked for completeness and consistency and entered into SPSS version 24 for analysis. Descriptive statistics were used to summarize the study population. Categorical variables were expressed as frequencies and percentages, while continuous variables were presented as means and standard deviations. The chi-square test was applied to assess associations between categorical variables, and the independent sample t-test was used to compare continuous variables between groups. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of the random urinary calcium-creatinine ratio for detecting hypercalciuria. A p-value of less than 0.05 was considered statistically significant at a 95% confidence level.

RESULTS

Table 1 presents the age and socio-demographic characteristics of the study participants. The mean age of children in the case group was 5.23±3.32 years, while that of the control group was 5.83±3.32 years, showing no notable difference between the two groups. The highest proportion of children in both groups belonged to the 1-4-year age group, accounting for 53.3% of cases and 42.2% of controls. Children aged 5-8 years constituted 28.9% of cases and 35.6% of controls, whereas those aged 9-12 years comprised 17.8% and 22.2%, respectively. Regarding gender distribution, females predominated in the case group (60.0%), whereas males were slightly more common in the control group (53.3%); overall, females accounted for 53.3% of the total study population. In terms of residence, the majority of children in both groups were from rural areas, representing 55.6% of cases and 68.9% of controls, while urban residents constituted 44.4% and 31.1%, respectively.

The urinary biochemical profile of children is summarized in Table 2. Children with UTI had significantly higher mean urinary calcium levels (1.35±2.01 mg/dl) compared to controls (0.28±0.17 mg/dl, p=0.001), and the spot urinary calcium-to-creatinine ratio was also significantly elevated in cases (0.068±0.106) versus controls (0.015±0.012, p=0.002). Urinary creatinine levels did not differ significantly between the two groups (30.83±24.82 mg/dl in cases vs. 26.06±18.30 mg/dl in controls, p=0.303). Examination of urinary pus cells revealed that the majority of children with UTI (75.6%) had >10/HPF or plenty of pus cells, while most controls (57.8%) had nil pus cells; this difference was highly significant (p<0.001). These findings indicate that children with UTI exhibit notable biochemical changes in urine, particularly hypercalciuria and pyuria, compared to healthy controls.

Table 1: Age and socio-demographic distribution of children (n=90).

Variables	Case (n=45), N (%)	Control (n=45), N (%)	Total (n=90), N (%)
Age (years)			
Mean±SD	5.23±3.32	5.83±3.32	5.53±3.32
Age group (years)			
1-4	24 (53.3)	19 (42.2)	43 (47.8)
5-8	13 (28.9)	16 (35.6)	29 (32.2)
9-12	8 (17.8)	10 (22.2)	18 (20.0)
Gender			
Male	18 (40.0)	24 (53.3)	42 (46.7)
Female	27 (60.0)	21 (46.7)	48 (53.3)
Residence			
Rural	25 (55.6)	31 (68.9)	56 (62.2)
Urban	20 (44.4)	14 (31.1)	34 (37.8)

Table 2: Association of urinary biochemical profile of children (n=90).

Urinary biochemical variable	Case (n=45) (%) Mean±SD	Control (n=45) (%) Mean±SD	Total (n=90) (%)	P value
Urinary calcium (mg/dl)	1.35±2.01	0.28±0.17		0.001**
Urinary Creatinine (mg/dl)	30.83±24.82	26.06±18.30		0.303**
Spot Ca/Cr	0.068±0.106	0.015±0.012		0.002**
Urinary pus cell				
Nil	1 (2.2)	26 (57.8)	27 (30)	<0.001*
1-5/HPF	4 (8.9)	15 (33.3)	19 (21.1)	
5-10/HPF	6 (13.3)	4 (8.9)	10 (11.1)	
>10/HPF or plenty	34 (75.6)	0	34 (37.8)	

Values are expressed as Mean±SD and as frequency with percentage over column in total; *Chi-squared Test ($\chi 2$); **Student t-test were performed to determine p value

The study assessed the presence of hypercalciuria among children with urinary tract infection and healthy controls. Among the 45 children with UTI, 20 (44.4%) were found to have hypercalciuria, whereas only 7 (15.6%) of the 45

healthy controls exhibited hypercalciuria, resulting in a total prevalence of 30% in the study population. The difference between the case and control groups was statistically significant (p=0.003), indicating that hypercalciuria was more common in children with UTI compared to apparently healthy children (Table 3).

Table 3: Association of hypercalciuria among case and control (n=90).

Hypercalciuria	Case (n=45), N (%)	Control (n=45), N (%)	Total (n=90), N (%)	P value*
Present	20 (44.4)	7 (15.6)	27 (30)	0.003
Absent	25 (55.6)	38 (84.4)	63 (70)	
Total	45 (100)	45 (100)	90 (100)	

Values are expressed as frequency with percentage within parenthesis (%) over column in total; *Chi-squared Test ($\chi 2$) was performed to determine p value

Table 4: Comparison of hypercalciuria between first time and recurrent UTI cases (n=90).

Hypercalciuria	UTI type, N (%)		Total (n=90), N (%)	P value*
	1st onset	Recurrent		
Present	13 (56.5)	10 (43.5)	23 (100)	
Absent	15 (68.2)	7 (31.8)	22 (100)	0.420
Total	28 (62.2)	17 (37.8)	45 (100)	

Values are expressed within parenthesis percentage (%) over row in total; *Chi-squared Test ($\chi 2$) was performed to determine p value

There were no significant association between hypercalciuria and UTI type among cases. Hypercalciuria were reported in 43.5% among cases with recurrent UTI and in 56.5% cases with first time UTI (Table 4).

DISCUSSION

The present study evaluated the age, socio-demographic characteristics, urinary biochemical profile, and prevalence of hypercalciuria among children with urinary tract infection (UTI) compared to healthy controls. The mean age of children in the case group was 5.23±3.32 years, with the highest proportion (53.3%) in the 1-4 year age group. This finding is consistent with previous studies, which have reported that younger children, particularly under five years of age, are more susceptible to UTIs due to anatomical immaturity, shorter urethral length, and immature immune responses.[8] The control group showed a similar age distribution, reflecting appropriate age-matching in the study design.

Regarding gender distribution, females comprised 60% of UTI cases, while males were slightly predominant in controls. This female predominance aligns with existing literature, as multiple studies have reported a higher incidence of UTI among girls beyond infancy. The anatomical proximity of the urethra to the perianal region in females facilitates ascending bacterial infection, which likely explains the observed gender disparity. Studies and other regional research have also highlighted female predominance in pediatric UTI populations, supporting our findings.[9]

Socio-demographically, the majority of children in both groups resided in rural areas (55.6% of cases and 68.9% of controls). Previous studies have similarly demonstrated a higher burden of pediatric UTIs in rural populations, often attributed to limited access to healthcare, inadequate sanitation, and lower awareness of hygiene practices.[10] This rural predominance emphasizes the need for public health interventions targeting hygiene education and early healthcare access in these areas.

Biochemical analysis of urine revealed that children with UTI had significantly higher urinary calcium levels (1.35±2.01 mg/dl) and spot calcium-to-creatinine ratios (0.068±0.106) compared to controls (0.28±0.17 mg/dl and 0.015±0.012, respectively), suggesting an association between hypercalciuria and UTI. The prevalence of hypercalciuria was 44.4% in UTI cases versus 15.6% in controls (p=0.003). These results are in line with studies and others, which reported an increased risk of UTI in children with hypercalciuria.[11-12] However, unlike some prior studies suggesting recurrent UTIs are strongly linked to hypercalciuria, our analysis showed no significant association between hypercalciuria and UTI type; it was observed in 43.5% of recurrent cases and 56.5% of first-time infections (p=0.420). This indicates that hypercalciuria may contribute to susceptibility to UTI regardless of recurrence status.

Pyuria was significantly more pronounced in children with UTI, with 75.6% showing >10 pus cells/HPF, while most controls (57.8%) had nil pus cells (p<0.001). This finding confirms the utility of urinary microscopy as a rapid screening tool for UTI, consistent with earlier studies highlighting pyuria as a hallmark of urinary tract infection.[12-13] Urinary creatinine levels did not differ significantly between groups, suggesting that renal excretory function remained largely intact in uncomplicated UTI cases.

CONCLUSION

The present study demonstrated that urinary tract infection in children predominantly affects younger age

groups, especially those aged 1-4 years, with a higher prevalence among females and children from rural areas. Children with UTI exhibited significantly higher urinary calcium levels and spot calcium-to-creatinine ratios, indicating a strong association between hypercalciuria and UTI, although hypercalciuria was not significantly related to recurrence. Pyuria was markedly elevated in UTI cases, while urinary creatinine and other renal biochemical parameters remained comparable to healthy controls. These findings emphasize the importance of early clinical and biochemical evaluation, including screening for hypercalciuria, to identify children at risk and implement timely management to prevent potential complications.

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