



Study Of Vitamin D Levels In Urinary Tract Infection In Children.

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Abstract

Background: Vitamin D plays an important role in immune regulation and innate antimicrobial defense. Vitamin D deficiency has been suggested as a possible risk factor for urinary tract infection (UTI) in children. This study assessed serum vitamin D levels in children with culture-positive UTI and compared them with healthy controls. **Methods:** A hospital-based prospective case-control study was conducted in the Department of Pediatrics, KIMS, Hubballi, among children aged 2 months to 12 years. Thirty-five children with culture-positive UTI and 35 age-matched healthy controls were enrolled. Serum 25-hydroxyvitamin D [25(OH)D] levels were measured using electrochemiluminescence immunoassay. Vitamin D status was categorized as deficient (<20 ng/mL), insufficient (20–30 ng/mL), or sufficient (>30 ng/mL). Statistical analysis was performed using SPSS version 29.0, with $p < 0.05$ considered statistically significant. **Results:** Among children with UTI, females constituted 51.4% and males 48.6%. Fever was present in 85.7% and urinary symptoms in 71.4% of cases. *Escherichia coli* was the predominant organism (65.7%), followed by *Klebsiella* (22.9%). The mean serum vitamin D level was significantly lower in UTI cases than in controls (23.97 ± 7.59 vs. 28.94 ± 8.78 ng/mL; $t = 2.534$, $p = 0.014$). Vitamin D deficiency was observed in 31.4% of cases and 22.9% of controls, while insufficiency was observed in 51.4% and 34.3%, respectively. However, the categorical association between vitamin D status and UTI was not statistically significant ($\chi^2 = 5.531$, $p = 0.063$). No significant association was observed between age and vitamin D status. **Conclusion:** Children with culture-positive UTI had significantly lower mean serum vitamin D levels than healthy controls. Although vitamin D deficiency and insufficiency were more frequent among UTI cases, the categorical association was not statistically significant. Larger studies are required to further clarify the role of vitamin D in childhood UTI.

Keywords: Vitamin D, 25-hydroxyvitamin D, urinary tract infection, children, *Escherichia coli*, vitamin D deficiency.



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INTRODUCTION

Urinary tract infection (UTI) is one of the most common bacterial infections in children and is an important cause of morbidity, particularly among infants and young children. Early diagnosis and appropriate treatment are essential because febrile and recurrent UTIs may lead to renal involvement and, in some cases, renal scarring [1,2]. *Escherichia coli* is the predominant causative organism in childhood UTI, although other Gram-negative and Gram-positive organisms may also be responsible [1,2].

Vitamin D is traditionally recognized for its role in calcium and phosphate metabolism and maintenance of skeletal health. Increasing evidence suggests that vitamin D also has important immunomodulatory functions. The active form of vitamin D influences innate immune responses through the vitamin D receptor and promotes the expression of antimicrobial peptides such as cathelicidin, which contributes to host defense against microorganisms [3,4].

The possible relationship between vitamin D status and UTI has gained considerable interest. Several studies have reported lower serum 25-hydroxyvitamin D [25(OH)D] concentrations among children with UTI compared with healthy controls [5–7]. Vitamin D deficiency or insufficiency may impair innate immune responses and potentially increase susceptibility to infections [3,4].

The urinary tract possesses several innate defense mechanisms, including antimicrobial peptides. Cathelicidin is an important antimicrobial peptide whose expression is influenced by vitamin D. Studies have suggested that vitamin D may contribute to urinary tract defense through regulation of antimicrobial responses [4,8].

Systematic reviews and meta-analyses have also reported an association between lower serum vitamin D levels and increased risk of UTI in children [9,10]. However, available studies have shown variations in study populations, age groups, definitions of vitamin D deficiency and methodological approaches. Therefore, further studies in different pediatric populations are required.

The present study was undertaken to assess serum 25(OH)D levels and vitamin D status among children with culture-positive UTI and to compare them with healthy controls. The study also evaluated the relationship between vitamin D status and age among the study participants.

MATERIALS AND METHODS

Study Design and Setting

A hospital-based prospective case-control study was conducted in the Department of Pediatrics, Karnataka Institute of Medical Sciences (KIMS), Hubballi. The study included children aged 2 months to 12 years who were admitted to the pediatric ward and fulfilled the predefined criteria for urinary tract infection (UTI).

Study Population and Eligibility Criteria

Children aged 2 months to 12 years with clinically suspected UTI and a positive urine culture were enrolled as cases. UTI was defined as the growth of a significant number of organisms of a single species in urine, with $\geq 100,000$ colony-forming units (CFU)/mL considered significant in midstream urine samples and $\geq 50,000$ CFU/mL in catheterized urine samples. Children were excluded if urine culture showed growth of more than one organism, or if they had malnutrition, immunodeficiency, clinical evidence of rickets, congenital anomalies of the kidney or urinary tract, previously diagnosed chronic renal failure, liver disease, vesicoureteral reflux, or were receiving vitamin D supplementation.

Sample Size

The sample size was calculated based on the expected difference in the proportion of vitamin D insufficiency between children with and without UTI (40% versus 10%), with a 5% level of significance and 80% statistical power. The minimum calculated sample size was 32 participants in each group. To account for practical considerations, approximately 70 participants were included, comprising 35 children with UTI (cases) and 35 healthy children (controls).

Data Collection

Children fulfilling the eligibility criteria were consecutively enrolled at admission after obtaining written informed consent from their parents or legal guardians. Controls were selected from healthy children attending the hospital without urinary symptoms and were matched with cases with respect to age and sex.

Relevant clinical information, including fever, vomiting, abdominal pain, dysuria, urinary urgency and frequency, was recorded. Clinical examination was performed for all participants. Baseline investigations included urinalysis, urine culture, complete blood count and abdominal ultrasonography.

Assessment of Vitamin D

Approximately 2 mL of peripheral venous blood was collected from each participant. Serum 25-hydroxyvitamin D [25(OH)D] levels were estimated using the electrochemiluminescence immunoassay (ECLIA) technique and expressed in ng/mL. Vitamin D status was classified as deficient (<20 ng/mL), insufficient (20–30 ng/mL), and sufficient (>30 ng/mL).

Study Outcome

The primary outcome was to assess and compare serum 25(OH)D levels and vitamin D status among children with culture-positive UTI and healthy controls.

Statistical Analysis

Data were entered into Microsoft Excel 2016 and analyzed using IBM SPSS Statistics for Windows, version 29.0 (IBM Corp., Armonk, NY, USA). Categorical variables were expressed as frequencies and percentages, while continuous variables were presented as mean $\pm$ standard deviation (SD). The independent samples *t*-test was used to compare continuous variables between the two independent groups. A *p*-value <0.05 was considered statistically significant.

RESULTS

During the study period, 350 children with a clinical history suggestive of urinary tract infection (UTI) were screened. Of these, 307 children were excluded: 27 had severe acute malnutrition (SAM), 24 had nephrotic syndrome, 2 had vesicoureteral reflux (VUR), and 254 had negative urine cultures. A total of 43 children had culture-positive UTI. As per the calculated sample size, 35 children with culture-positive UTI were enrolled as cases, along with 35 healthy children as controls.

Table 1. Gender distribution among cases

Gender	Frequency (n=35)	Percentage
Female	18	51.4
Male	17	48.6
Total	35	100.0

Observation: Among the 35 cases, females constituted 51.4% and males 48.6%, showing a slight female predominance.

Table 2. Distribution of fever among cases

Fever	Frequency (n=35)	Percentage
Present	30	85.7
Absent	5	14.3
Total	35	100.0

Observation: Fever was present in 85.7% of cases, while 14.3% had no fever.

Table 3. Distribution of urinary symptoms among cases

Urinary symptoms	Frequency (n=35)	Percentage
Present	25	71.4
Absent	10	28.6
Total	35	100.0

Observation: Urinary symptoms were present in 71.4% of cases, whereas 28.6% had no urinary symptoms.

Table 4. Distribution of anemia among cases

Anemia	Frequency (n=35)	Percentage
Present	26	74.3
Absent	9	25.7
Total	35	100.0

Observation: Anemia was present in 74.3% of cases and absent in 25.7%.

Table 5. Ultrasonography findings among cases

USG finding	Frequency (n=35)	Percentage
Normal	20	57.1
Abnormal	15	42.9
Total	35	100.0

Among the 15 cases with abnormal ultrasonography findings, 9 (60.0%) had cystitis, 2 (14.0%) had increased echogenicity and 4 (26.0%) had bladder wall thickening.

Observation: Ultrasonography was normal in 57.1% of cases, while 42.9% showed abnormal findings, with cystitis being the most frequent abnormality.

Table 6. Distribution of organisms isolated on urine culture

Organism	Frequency (n=35)	Percentage
<i>E. coli</i>	23	65.7
<i>Klebsiella</i>	8	22.9
<i>Providencia</i>	2	5.7
<i>Proteus</i>	1	2.9
Non-albicans <i>Candida</i>	1	2.9
Total	35	100.0

Observation: *E. coli* was the predominant organism isolated, accounting for 65.7% of cases, followed by *Klebsiella* (22.9%), *Providencia* (5.7%), *Proteus* (2.9%) and non-albicans *Candida* (2.9%).

Table 7. Comparison of gender between cases and controls

Gender	Cases (n=35)	Controls (n=35)	χ^2 value	p-value
Female	18 (51.4%)	—	0.229	0.632
Male	17 (48.6%)	—		
Total	35 (100%)	35 (100%)		

Observation: There was no statistically significant association between gender and study group ($\chi^2 = 0.229$, $p = 0.632$).

Table 8. Comparison of serum vitamin D levels between cases and controls

Group	N	Mean	SD	t-value	p-value
Cases	35	23.97	7.59	2.534	0.014*
Controls	35	28.94	8.78		
Total	70				

*Statistically significant at $p < 0.05$.

Observation: The mean serum vitamin D level was lower among cases (23.97 ± 7.59 ng/mL) than controls (28.94 ± 8.78 ng/mL). The difference was statistically significant ($t = 2.534$, $p = 0.014$).

Table 9. Comparison of vitamin D status between cases and controls

Vitamin D status	Cases n (%)	Controls n (%)	Total	χ^2 value	p-value
Deficiency	11 (31.4)	8 (22.9)	19 (27.1)	5.531	0.063
Insufficiency	18 (51.4)	12 (34.3)	30 (42.9)		
Normal	6 (17.1)	15 (42.9)	21 (30.0)		
Total	35 (100)	35 (100)	70 (100)		

Observation: Vitamin D insufficiency was more frequent among cases (51.4%) than controls (34.3%), while normal vitamin D levels were more common among controls (42.9%) than cases (17.1%). However, the association between vitamin D status and study group was not statistically significant ($\chi^2 = 5.531$, $p = 0.063$).

Table 10. Comparison of age distribution between cases and controls

Age group	Cases n (%)	Controls n (%)	Total	χ^2 value	p-value
<2 years	18 (51.4)	12 (34.3)	30 (42.9)	2.118	0.347
2–6 years	13 (37.1)	18 (51.4)	31 (44.3)		
>6 years	4 (11.4)	5 (14.3)	9 (12.9)		
Total	35 (100)	35 (100)	70 (100)		

Observation: Children aged <2 years constituted the largest proportion of cases (51.4%), whereas the 2–6-year age group was predominant among controls (51.4%). The difference in age distribution between the groups was not statistically significant ($\chi^2 = 2.118$, $p = 0.347$).

Table 11. Association between age and vitamin D status among cases

Age group	Deficiency n (%)	Insufficiency n (%)	Normal n (%)	Total	χ^2 value	p-value
<2 years	7 (63.6)	8 (44.4)	3 (50.0)	18 (51.4)	2.365	0.669
2–6 years	4 (36.4)	7 (38.9)	2 (33.3)	13 (37.1)		
>6 years	0 (0.0)	3 (16.7)	1 (16.7)	4 (11.4)		
Total	11 (100)	18 (100)	6 (100)	35 (100)		

Observation: Among cases, no statistically significant association was observed between age group and vitamin D status ($\chi^2 = 2.365$, $p = 0.669$).

Table 12. Association between age and vitamin D status among controls

Age group	Deficiency n (%)	Insufficiency n (%)	Normal n (%)	Total	χ^2 value	p-value
<2 years	2 (25.0)	6 (50.0)	4 (26.7)	12 (34.3)	4.923	0.295
2–6 years	5 (62.5)	6 (50.0)	7 (46.7)	18 (51.4)		
>6 years	1 (12.5)	0 (0.0)	4 (26.7)	5 (14.3)		
Total	8 (100)	12 (100)	15 (100)	35 (100)		

Observation: Among controls, there was no statistically significant association between age group and vitamin D status ($\chi^2 = 4.923$, $p = 0.295$).

DISCUSSION

The present study evaluated serum vitamin D levels among children with culture-positive UTI and healthy controls. The principal finding was that the mean serum vitamin D level was significantly lower among children with UTI than among controls. The mean vitamin D level was 23.97 ± 7.59 ng/mL in cases compared with 28.94 ± 8.78 ng/mL in controls, with a statistically significant difference ($t = 2.534$, $p = 0.014$).

This finding is consistent with previous studies reporting lower vitamin D levels among children with UTI. Shalaby et al. reported significantly lower serum 25(OH)D levels in children with UTI compared with healthy controls and suggested an association between vitamin D deficiency and UTI [5]. Similarly, other pediatric case-control studies have demonstrated significantly lower vitamin D concentrations among children with UTI [6,7].

In the present study, vitamin D insufficiency was observed in 51.4% of cases compared with 34.3% of controls, while vitamin D deficiency was present in 31.4% of cases and 22.9% of controls. Normal vitamin D levels were more frequent among controls (42.9%) than cases (17.1%). Although these findings indicate a greater proportion of low vitamin D status among children with UTI, the categorical association was not statistically significant ($\chi^2 = 5.531$, $p = 0.063$).

The difference between the continuous and categorical analyses is important. Although mean vitamin D levels were significantly lower in cases, classification into deficiency, insufficiency and normal categories did not produce a statistically significant association. This may partly be related to the relatively small sample size of the present study. Similar overall findings have been reported in pooled analyses showing lower vitamin D concentrations among children with UTI [9,10].

A possible biological explanation for this association is the role of vitamin D in innate immunity. Vitamin D stimulates antimicrobial mechanisms, including the production of cathelicidin, which contributes to host defense against urinary pathogens [3,4]. Studies investigating vitamin D and urinary cathelicidin have suggested that vitamin D status may influence antimicrobial defense during urinary tract infection [4,8].

In the present study, *E. coli* was the predominant organism, accounting for 65.7% of culture-positive cases, followed by *Klebsiella* (22.9%). This finding is consistent with the established epidemiology of childhood UTI, where *E. coli* is generally the most frequently isolated uropathogen [1,2]. Similar predominance of *E. coli* has also been reported in studies examining vitamin D status in children with UTI [6,7].

Fever was present in 85.7% of cases, while urinary symptoms were present in 71.4%. Fever is a common clinical manifestation of childhood UTI, particularly in young children, in whom urinary symptoms may not always be clearly expressed [1,2]. The high frequency of fever in the present study may also reflect the hospital-based nature of the study population.

Females constituted 51.4% of the cases and males 48.6%. There was no statistically significant association between gender and study group ($\chi^2 = 0.229$, $p = 0.632$). Although female sex is commonly recognized as a risk factor for UTI, the present study did not demonstrate a significant gender difference, which may be related to the relatively small sample size [1,2]. Ultrasonography was normal in 57.1% of cases, whereas 42.9% showed abnormal findings. Among the abnormal findings, cystitis was the most common. The present study was not designed to establish an association between ultrasonographic findings and vitamin D status.

No statistically significant association was observed between age and study group ($\chi^2 = 2.118$, $p = 0.347$). Similarly, age was not significantly associated with vitamin D status among cases ($\chi^2 = 2.365$, $p = 0.669$) or controls ($\chi^2 = 4.923$, $p = 0.295$). Thus, within the present study population, the difference in mean vitamin D levels between cases and controls was not significantly explained by the categorized age groups.

The present study has some limitations. The sample size was relatively small and the study was conducted at a single center, which may limit the generalizability of the findings. The observational design also does not establish a causal relationship between vitamin D status and UTI. Other factors that can influence vitamin D levels, such as sunlight exposure, dietary intake and season, were not evaluated in the available study data. Larger multicentric prospective studies are therefore required to clarify the relationship between vitamin D status and childhood UTI.

Overall, the present study demonstrated that children with culture-positive UTI had significantly lower mean serum vitamin D levels than healthy controls. Although vitamin D deficiency and insufficiency were more frequent among cases, the difference in categorical vitamin D status was not statistically significant. These findings support a possible association between vitamin D status and childhood UTI and highlight the need for further investigation in larger pediatric populations.

CONCLUSION

Children with culture-positive UTI had significantly lower mean serum vitamin D levels than healthy controls. Although vitamin D deficiency and insufficiency were more frequent among cases, the categorical association was not statistically significant. Further larger studies are needed to clarify the relationship between vitamin D status and childhood UTI.

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