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Serum Vitamin D and Zinc Levels in Children with Urinary Tract Infection without Confounding Factors: A Case-Control Study

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Abstract

Background: Urinary tract infections (UTIs) are extremely prevalent bacterial infections among children. They have numerous potential causes. Without proper diagnosis and treatment, UTIs can lead to serious complications in children, including impaired growth, high blood pressure, protein in urine, and eventual chronic kidney disease. Zinc and vitamin D in sufficient concentrations help to maintain the health of the immune system. Therefore, their deficiency can cause various infections. Several factors can contribute to the development of UTIs. This article deals with the role of zinc and vitamin D as immune markers in UTI in children without other risk factors.

Methods: In this case-control study, serum zinc and vitamin D levels without any other risk factors were examined in 40 healthy children and 40 children with UTIs. Data analysis was done through SPSS 26 using the chi-square, the Fisher's exact, and independent t tests.

Results: The study findings demonstrated a statistically significant distinction between the 2 groups regarding serum vitamin D and zinc levels ($P < 0.001$); 80% of children with UTIs and 17.5% in the healthy group had vitamin D deficiency. Also, 60% of the urinary infection group had zinc deficiency, whereas 17.5% of the healthy group had it.

Conclusion: Low serum zinc and vitamin D levels may increase susceptibility to pediatric UTI. Given the data, supplementation with zinc and vitamin D could play a significant role in treating active infections and preventing recurrence in susceptible children.

Keywords: Zinc, Vitamin D, Children, Pediatric, Urinary Tract Infection

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Introduction

Urinary tract infection (UTI), defined as a positive urine culture, represents one of the most common pediatric bacterial infections. The reported incidence is 0.7% in infant girls, 2.7% in uncircumcised infant boys, and 10% in children aged 4 to 7 years (1-4). Early diagnosis and proper treatment are essential to prevent disease complications, including early complications such as sepsis and bacteremia, and late complications such as chronic kidney failure that leads to high blood pressure and failure to try (5).

After any injury, the inflammatory cascade starts, but there are factors that play a role in preventing this cascade, including special genes and minerals such as vitamin D

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↑What is "already known" in this topic:
Zinc and vitamin D in sufficient concentrations help maintain the immune system's health. Therefore, their deficiency can cause various infections such as urinary tract infections (UTIs).

→What this article adds:
Multiple factors potentially contribute to pediatric UTI development. This study examined associations between serum zinc and vitamin D as immune biomarkers and UTI while controlling for other known risk factors. This helps us determine whether optimizing levels of these immune-supportive micronutrients through diet and supplements could lower UTI risk.

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and zinc (6). As the second most abundant bodily mineral, zinc plays critical roles in protein/nucleic acid synthesis, metabolism, and cell membrane integrity (7).

In general, zinc relates to physiological functions—such as growth, cell division, maturation, reproduction, and regulation of the host immune system. Even modest zinc deficiency impairs immune system function. The zinc system function is one of the body's protective mechanisms against rare diseases. This mineral is necessary for the activity of T lymphocytes. Consequently, zinc deficiency degrades cellular immunity, including the production of key immune messengers interferon-γ, interleukin-2, and tumor necrosis factor-α (8).

Zinc is necessary to activate vitamin D to exert its function in immunity (7). Vitamin D has a systemic effect on pathogens and is essential for regulating the immune system. Hypocalcemia caused by vitamin D deficiency can reduce the function of neutrophils and the activity of lymphocytes. Vitamin D has many functions, the most important one being to suppress cytokines (IL6, IL 8). It is also involved in decreasing the inflammatory cascade activated after the pathogen's attachment to the uroepithelium (9).

As a result, the severity of infection, such as the urinary tract, is reduced by zinc and vitamin D. The risk factors for UTI vary (2, 10). Significantly few studies have addressed zinc and vitamin D effects on pediatric UTIs while excluding confounding factors. Given the condition’s significance, high prevalence, long-term financial costs, and risk for engendering antibiotic-resistant uropathogens, preventing or efficiently treating UTIs could provide significant benefits. This study aimed to illuminate associations between the immunomodulators vitamin D and zinc and pediatric UTI risk while controlling other known risk factors. Elucidating the precise contributions of these micronutrients to UTI susceptibility could ultimately inform preventative and therapeutic practices.

Methods

This case-control study was conducted in Kashan's Shahid Beheshti Hospital, Iran. After obtaining parental consent, 80 children aged 1 month to 14 years were included in the study. Based on the previous study (11), the mean (standard deviation) serum vitamin D levels in children with UTIs was 16.72 (8.39) ng/mL, while it was 23.59 (12.37) ng/mL in the healthy control children. Sample size calculations were performed to determine the minimum number of participants needed in each group (UTI vs control) to obtain statistically valid results. It was found that every study arm needed at least 37 children to participate in order to achieve the required confidence level of 95% and 80% power to identify real differences between the groups. To account for potential dropouts, 40 children were ultimately recruited for each group.

The case group included 40 children who were admitted due to UTI and had a positive urine culture using a sterile method. Toilet-trained patients were asked to provide a clean catch midstream urine sample, while those who were not trained were given urinary catheters to collect urine samples. Based on clinical and laboratory criteria, patients are divided into cystitis and pyelonephritis.

Patients with a history of taking zinc and vitamin D supplements, as well as the presence of an underlying disease and known factors of infection, such as a history of diabetes, immunodeficiency, and organ transplants that require immunosuppressive drugs, malnutrition, and severe sepsis, were excluded from the study. Other exclusion criteria were as follows: constipation; uncircumcised boys; genital anatomical problems, such as labia adhesions; congenital anomalies of the genitourinary system, such as genital ambiguity and imperforated anus; abnormal ultrasound of the kidney and the urinary system, such as moderate and severe hydronephrosis; dilated and trabeculated bladder; anatomical problems of the urinary system, such as vesicoureteral reflux and obstruction based on the findings of the VCUG and DTPA scan.

Patients with functional neurogenic bladder who had an abnormal urodynamic test and had a history of filling and voiding dysfunction, such as urinary incontinence, hesitancy, straining, retention, dribbling, intermittency, or low- or high-frequency urination (<4 or >7 times per day), were also excluded from the study. Due to neurologic neurogenic bladder, patients with mental retardation, cerebral palsy, meningocele, spinal cord injuries, and brain structural issues were also excluded from the study.

The control group was selected from the general pediatric population for routine examinations in the same hospital (Beheshti Hospital, Kashan), where potential participants with UTI were selected. This was done to control for potential population-level differences in zinc/vitamin D status among study sites. Only children with no history or signs/symptoms of UTI, vitamin D, and zinc supplementation, or underlying diseases affecting zinc/vitamin D absorption/metabolism and negative urine cultures were eligible for inclusion as controls. After sampling, 3 cc of each child's plasma was centrifuged for up to 2 hours and stored in special free element trace tubes that contain EDTA as an anticoagulant. The normal serum levels of zinc and vitamin D were considered 63.8-110 µg/dL and 30-60 ng/mL. The collected data were analyzed through SPSS 26. The analysis incorporated descriptive statistics, including frequency distributions, means, and standard deviations, and inferential statistics comprised of the chi-square, Fisher’s exact, and independent sample t tests. Also, $P < 0.05$ was considered statistically significant.

Results

The study included 80 children, comprising 52 girls (65%) and 28 boys (35%), divided into the case (UTI) and healthy control groups. Statistical analysis found no significant differences between the 2 groups in terms of age ($P = 0.112$), biological sex ($P = 1$), or underweight status ($P = 0.257$) (Table 1).

The findings demonstrated a significant difference between the 2 groups regarding serum vitamin D and zinc levels ($P < 0.001$). Vitamin D deficiency was found in 80% of UTI cases compared with only 17.5% of healthy controls. Similarly, 60% of UTI cases showed zinc deficiency versus 17.5% in the control group (Table 2).

When the UTI group was divided into pyelonephritis

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Table 1. Comparison of Demographic Parameters Between the 2 Groups

Variable	UTI (Case) (n: 40, 50%)	Healthy (Control) (n: 40, 50%)	*P*-Value
Gender, number (%)			
Male	14 (35)	14 (35)	1 *
Female	26 (65)	26 (65)	
Age, year (mean± SD)	3.55±4.70	3.09±3.85	0.257 **
Under weight, number (%)	20 (50)	13 (32.5)	0.112 *

* Chi-squared test / ** Independent t-test

Table 2. Comparison of Vitamin D & Zinc Between the 2 Groups

Variable	UTI (n: 40, 50%)	Healthy (n: 40, 50%)	*P*-Value
Vitamin D			
Serum level, ng/ml (mean± SD)	12.46±21.18	21.84±42.39	<0.001 *
Deficiency, number (%)	32 (80)	7 (17.5)	<0.001 **
Zinc			
Serum level, µg/dl (mean± SD)	75.02±56.00	71.40±141.72	<0.001 *
Deficiency, number (%)	24 (60)	7 (17.5)	<0.001 **

* Chi-squared test / ** Independent t-test

Table 3. Comparison of Vitamin D & Zinc Between the 2 Groups Based on UTI Type (Pyelonephritis & Cystitis)

Variable	Pyelonephritis (n: 29)	Cystitis (n: 11)	*P*-Value
Vitamin D			
Serum level, ng/ml (mean± SD)	21.28±12.33	20.92±13.41	0.936**
Deficiency, number (%)	23 (79.3)	9 (81.8)	0.859*
Zinc			
Serum level, µg/dl (mean± SD)	65.52±54.79	53.57±100.09	0.081**
Deficiency, number (%)	21 (72.4)	3 (27.3)	0.009*

* Chi-squared test / ** Independent t-test

and cystitis subtypes, a significant between-group difference emerged for zinc deficiency rates ($P = 0.009$). Zinc deficiency occurred in 72.4% of pyelonephritis cases compared with 27.3% of cystitis cases (Table 3).

Discussion

This study aimed to investigate the serum level of vitamin D and zinc in children with UTI without other risk factors and compare it with healthy children. Very few studies have been done in this field, especially in the children population, and no study has investigated and eliminated other risk factors with these details. Plasma or zinc levels in serum are under strict homeostatic control and are highly sensitive to inflammation, cytokines, and hormones (12, 13). According to experimental research, hypozincemia occurs quickly after infection, probably due to internal zinc redistribution (13, 14).

An important strength of the present study was excluding patients with chronic inflammatory diseases, infections, or underlying renal disorders. The status of patients was determined at least 4 weeks after UTI. Vitamins and cytokines are related to the immune system, according to studies by Castellani et al (15). McCarthy et al (2011) investigated vitamin D's antibacterial properties (16).

In this study, serum vitamin D and zinc levels were lower in pediatric UTI patients than healthy controls. These findings align with a study by Zabihi et al, showing significantly decreased serum zinc in children with UTI regardless of age or sex versus controls (17). Similarly, Noorbakhsh et al reported lower serum zinc levels in pediatric cases but found no difference in vitamins A and D (12). However, Amoori et al conversely identified no association between serum zinc and recurrent febrile UTI (18).

This difference can be due to the difference in the sample size, the age of the studied patients, the geographical area, failure to exclude other risk factors, and differences in the urine sampling method. Therefore, we investigated this study according to the existing differences and the importance of this issue.

Conclusion

This study demonstrated significantly lower serum zinc and vitamin D levels among pediatric urinary tract infection cases compared with healthy controls. Given these findings, zinc and vitamin D deficiency may contribute to increased susceptibility to urinary tract infections in children. Supplementation with these micronutrients could aid in preventing recurrent infections. However, larger studies are warranted to conclusively determine the impact of zinc and vitamin D status on urinary tract infection risk. Future investigations should also track infection rates after vitamin D and zinc repletion to directly ascertain the utility of supplementation for reducing infection incidence among deficient children. While the current findings are encouraging, further investigation is required to determine the causal roles of zinc and vitamin D in the pathogenesis of urinary tract infections. This will allow for the development of evidence-based recommendations for micronutrient testing and treatment, which will help prevent this

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common pediatric condition.

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Ethical Considerations

The present study was approved by the Ethics Committee of Kashan University of Medical Sciences (Code: IR.KAUMS.MEDNT.REC.1400.035). The researcher obtained the necessary permission from the university officials to conduct the study. The study objectives were explained to the participants, and their informed consent was obtained. The participants' independence was maintained by assuring them about their voluntary participation, nonparticipation, and withdrawal. The researcher maintained the confidentiality of the data and only utilized it for the intended study. Copyrights were strictly adhered to with regard to translation and the usage of scientific references.

Conflict of Interests

The authors declare that they have no competing interests.

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