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RESEARCH ARTICLE

Does the Trace Element Deficiency (Vit A, D & Zinc) Have Any Role in Vulnerability to Urinary Tract Infection in Children: A Case-Control Study: Tehran, Iran

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Abstract:

Background and Objective:

Urinary Tract Infection (UTI) is one of the most common causes of hospital admission in our young population. This prospective cohort study was carried out to assess the relation of serum levels of zinc, vitamins A and D with UTI in children with proven UTI.

Methods:

The serum levels of Zinc, vitamins A and D were compared between 25 proven UTI cases (admitted in 2 educational hospitals in Tehran) and 40 controls without infection (children who had undergone for elective surgery). The average age of children was 2.17 years. Atomic absorption Spectrophotometry, Radioimmunoassay, and HPLC methods were used for measuring the Zinc, Vit D and A, respectively.

Results:

Although the serum levels of zinc were significantly lower in UTI cases (P=0.05), no significant differences had observed between cases and controls for vitamins A and D in sera (P=0.4 and P=0.9).

Conclusion:

Due to established lower zinc level in UTI cases (p-value = 0.05), zinc deficiency might have a role in susceptibility to UTI in studied children. Administration of zinc could be helpful in preventing UTI. To establish the role of Vitamins A and D in vulnerability to UTI, further extensive research with larger samples is needed.

Keywords: Urinary Tract Infection , Pyelonephritis , Children , Vitamin A , Vitamin D , Zinc .

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1. INTRODUCTION

Urinary Tract Infection (UTI) is considered as one of the most common causes of hospital admission with estimated incidences of 1.28 per 1000 in girls and 0.18 per 1000 in boys younger than 14 years and a prevalence of 5.3% in febrile infants [1]. Symptoms of UTI include fever, anorexia, and vomiting, dysuria, frequent and flank pain. These patients are more susceptible to renal scars and other possible complications (growth retardation, hypertension, proteinuria, and chronic renal failure) [2]. The recurrence of APN is independently associated with increased risk of renal scarring

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[1]. Nutritional deprivations in children might have some role in recurrent infections [3, 4]. In addition to the studied factors; bacterial virulence, immunodeficiency and anatomic or functional abnormalities make children with UTI vulnerable to renal scarring [3, 4]. Other factors such as the route of antibiotics administration, the time elapsed before the onset of symptoms and initiation of therapy are important factors [5, 6]. Trace elements like vitamins and minerals are essential for efficient metabolism and proper functioning of various body systems, namely immune system [7 - 9] Youssef *et al.,* (2011) reported antimicrobial implications of vitamin D [9]. Aslan *et al.,* (2012) presented vitamin D receptor gene polymorphism in children with urinary tract infection [10]. The study of Hertting *et al.,* showed that Vitamin D induced antimicrobial Peptide cathelicidin in the urinary bladder [11].

UTI is considered as one of the most common causes of hospital admission in Iranian young children [12 - 18]. According to a trial on UTI, a good correlation between Vitamin A level and progression of UTI in children had found in our country [19].The effect of vitamin A in the prevention of renal damage following APN in Iranian children was reported by Ayazi *et al.,* [20]. Nutritional status of Iranian population might have some role in recurrent infections among Iranian children [21 - 25].

This prospective cohort study was carried out to assess the relation of serum level of zinc, and Vitamins A and D with UTI in children with proven UTI.

2. MATERIALS AND METHODS

This prospective cohort study. was carried out on 25 children (< 5 years old) with hospitalized in 2 referral educational hospitals (Rasul Akraml and Bahrami hospital; 2011-2013) and 40 children without infection (controls). The trial was performed after being credited by the Ethics Committee of Pediatric Infectious Diseases Research Center of Iran University of Medical Sciences to be compatible with Helsinki Regulations. An informed consent was obtained from every patient. A questionnaire on personal information, patients` medical history and imaging results was filled out.

2.1. Subjects

The cases included 25 proven upper UTI cases admitted in 2 referral educational hospitals. Upper UTI was established in cases and documented, based on clinical and laboratory examinations (positive urine culture), and confirmed with imaging studies (ultrasonography with or without DMSA scan).

Exclusion criteria: excluded all cases with Failure To Thrive (FTT) growth problems (*i.e.* weight for age, height for age or weight for height <-2 z-score in WHO Multicenter Growth Reference Study growth curves), underlying diseases, immunodeficient cases known malignancies or malabsorption states.

2.2. Controls

The control group included 40 age-matched children who were admitted for elective general surgery in the surgery department (*i.e.* appendicitis, hernia, orthopedic *etc*.). They were visited by a pediatrician before surgery to be assessed free of infectious status, FTT or malnourishment. Only if they had no manifestation of the disease after appropriate physical exams, they were considered as controls. We used their extra blood (which was taken for their routine blood tests before their respective surgery) for lab tests.

2.3. Lab Tests

Five ml of blood was collected from all children .Blood was centrifuged and sera were separated by centrifugation at 3,000 rpm for 10 minutes and stored in -20°C. The zinc, vitamin A and 25-hydroxyvitamin D (25(OH) D) levels were measured in all samples. Doping was done from the kits' information sheets. The amount for Zinc, vitamins A and D in sera was measured and reported according to the normal cut off points indicated on laboratory kits.

We used the atomic absorption spectrophotometer AVANTA (GBC Scientific Equipment Pty Ltd, Melbourne, Australia). Serum levels of zinc equal or higher than 65µg/dL were considered normal.

Vitamin A levels were measured by High Performance Liquid Chromatography (HPLC) (Craft technologies, Inc). The normal levels were expressed according to the age. In our study, vitamin A levels between 0.2 and 0.49 mg/mL were considered normal.

We measured 25(OH) D levels by a radioimmunoassay kit (Diasorin, Stillwater, MN, USA) and considered a 25(OH) D level ≤ 20 ng/mL (50 nmol/L) as deficient and a higher level of 25(OH) D up to 30 ng/mL (75 nmol/L) as insufficient.

Collected data and lab results were statistically analyzed by SPSS version 13.5. The data was presented using descriptive statistics. We used Chi square and student's t-tests to compare the mean between two groups. All p values were calculated using a two-sided test and values lower than 0.05 were considered significant.

3. RESULTS

Subjects were between 6 months and 5 years old (Mean age=2.7 years); 72% of them were male and 28% female. The Male/female ratio was not different(p=1) between cases and controls(1.7 *vs.* 1.5) ; The BMI (kg/m2) was not different between 2 groups (1.7 *vs.* 1.5;*p*=0.1) ;

The results of serum levels of Vit A, Vit D and Zinc of both the groups are shown in Table **1**.

Zinc levels were significantly lower in patients than in controls (*P* value = 0.05).

Vitamin A levels did not show any significant difference (*P* value = 0.4) between 2 groups. The same results were reported for vitamin D (*P* value = 0.9).

4. DISCUSSION

Here, we found lower serum levels for zinc (normal > 65 µg/dl) in UTI cases as compared to normal children (95.43 *vs.* 106.9 µg/dl; *P*=0.05); but vitamin A level (normal range=0.2 to 0.49 mg/ml) did not have any difference between cases and

Table 1. Comparison of the micronutrient levels in UTI cases and controls.

Micronutrients Urinary Tract Infection (UTI)	Vit A mg/ml		Vit D ng/ml	
	Patient	**Control**	**Patient**	**Control**
Mean	0.41	0.45	45.7	45.9
Standard deviation	0.202	0.211	21.05	24.8
P value	0.4		0.9	

controls (mean =0.4 mg/ml in both groups; P=0.4). Similarly, Vitamin D levels (normal range=7.3 to 59.2 ng/ml) did have any difference between cases and controls (mean =45 ng/ml, *P*=0.9).

In some previous studies, the relationship between trace elements and vitamins serum levels was studied. Cuevas *et al.,* reviewed the relation between the Zinc level and infection [4]. Studies by Castellani *et al.,* indicated an interrelationship between vitamins and cytokines in immunity [5 - 10] Youssef *et al.,* (2011) reported the antimicrobial implications of vitamin D [9]. Aslan *et al.,* presented the vitamin D receptor gene polymorphism in children with urinary tract infection [10]. Munday *et al.,* showed increased Cystitis, pyelonephritis, and urolithiasis in rats accidentally fed a vitamin A deficient diet [7].

Nutritional deprivations especially vitamins and micronutrients such as zinc, vitamin A and vitamin D in our country are common, it might due to inappropriate diet and nutrient loss, as compared to other parts of middle east [22 - 25]. According to our results, Zinc levels were significantly lower in UTI patients than in controls (*P* value = 0.05).Low zinc level might have a role in susceptibility to UTI in studied children. Similar to Youssef *et al.,* (2010) reported the therapeutic effects of zinc supplementation in children with UTI [21]. Abbaspour *et al.,* compared the zinc and iron status in a case study in the Isfahan Province, central part of Iran [23] concluing that lower Iron level than Zinc level could be due to frequent consumption of tea and dairy products [23] while Kashian *et al.,* reported daily intake of Fe, Cu, Ca and Zn through common cereals in Tehran, Iran (2015) [22]. Ghasemi *et al.,* reported the prevalence of serum zinc deficiency and dietary zinc inadequacy to be lower in Iranians, compared to other populations [24].

The effect of vitamin A on renal damage following Acute Pyelonephritis in Iranian children was studied by Ayazi *et al.,* [20] In contrast to some Iranian studies, vitamins A was not different in UTI cases as compared to normal children [19, 20].

5. LIMITATION THE STUDY

The trace elements level, especially of Vitamins A and D are different among patients of various age groups. Due to small sample size, exact matching had not been done. Further extensive research with larger samples is needed.

CONCLUSION

Due to established lower Zinc level in UTI cases (*p*-value = 0.05), zinc deficiency might have a role in susceptibility to UTI in studied children. Administration of zinc could be helpful for preventing UTI. For establishing the role of Vitamins A and D in vulnerability to UTI, further extensive research with larger samples is needed.

LIST OF ABBREVIATIONS

UTI	=	Urinary Tract Infection
HPLC	=	High Performance Liquid Chromatography
Vit	=	Vitamin
Zn	=	Zinc
Ca	=	Calcium
Fe	=	Iron
Cu	=	Copper
APN	=	Acute Pyelonephritis
DMSA	=	Dimercaptosuccinic Acid
RDA	=	Recommended Dietary Allowance

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The trial was performed after being credited by Ethics Committee of Pediatric Infectious Diseases Research Center of Iran University of Medical Sciences.

HUMAN AND ANIMAL RIGHTS

No Animals were used in this research. All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

An informed consent was obtained from every patient.

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AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHORS' CONTRIBUTIONS

The authors' responsibilities were as follows: data acquisition (SA), conception (SA, SN), statistical analysis (SJ), and drafting of manuscript (SJ, SA), critical review, editing, and interpretation of results (ZM). All authors read and approved the final manuscript.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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