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ORIGINAL RESEARCH

Evaluation of Vit. D3 and Zn levels in patients with urinary tract infections

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ABSTRACT

Background: Vitamin D, known for its immunoregulatory effects and antimicrobial properties, plays a crucial role in regulating inflammation and chemokine production. Zinc is influential for a healthy immune system and human health, influencing cell differentiation, proliferation, and apoptosis, which impact organism growth.

Objectives: Determine the serum zinc and vitamin D3 levels in UTI patients and controls to detect the role of Vit. D3 and Zn in UTIs, and their levels in recurrent and non-recurrent infections.

Methodology: Samples of 60 urinary tract infection patients, distributed between 30 females and 30 males, were collected from Imam Hassan Al-Mujtaba Hospital for the period from December 2022 to April 2023. After collecting venous blood samples from patients and the controls, the serum was separated to measure the concentrations of vitamin D3 and zinc. The concentration of vitamin D3 was measured using the Cobas system, while the concentration of zinc was measured using a Mindray device.

Results: UTI patients have lower serum zinc levels than the controls group, with the patient group having 83.0 mg/dL compared to the control group. Vitamin D3 was also low in the patients group compared to controls (10.50, 12.58 respectively).

Conclusion: Vitamin D3 and zinc levels can influence UTI development, with patients having lower serum vit. D3 and zinc than the controls group, indicating a potential risk of UTI.

Keywords: UTI, Vitamin D, Zinc, Recurrent infection, non-recurrent infections.

INTRODUCTION

Urinary tract infections (UTIs) are considered as one of the common causes of infection in the communities and with a prevalence ranging from 1.8% to 7.5%. UTIs, which include pyelonephritis and cystitis, are a common bacterial illness in adults and children of all ages [1, 2].

The most prevalent bacterial infection in urinary tract infections (UTIs) which impact 150 million individuals annually worldwide is Escherichia coli [3]. It is the primary cause of (70–90%), with other common pathogenic bacteria including Klebsiella, Proteus, Enterococcus, and Enterobacter species all contributing to the illness [4]. Renal scarring and possibly serious renal damage can result from UTIs [5].

UTIs are a major cause of morbidity in older men and women, leading to serious complications like pyelonephritis, renal damage, and antibiotic resistance. Clinically, they can be uncomplicated or complicated [2]. Complicated UTIs involve urinary tract issues due to neurological disease, immunosuppression, renal failure, transplantation, pregnancy, or foreign bodies like calculi or catheters [6]. A number of risk factors, such as sexual activity, vaginal infections, diabetes, obesity, history of UTIs, sex, and genetic vulnerability, are linked to cystitis [7].

Zinc can raise the chance of contracting infectious illnesses [8]. The host immune system is regulated by zinc, and immune system malfunction could be result from even a mild zinc shortage T lymphocyte growth and function depend on zinc, and low zinc levels result in reduced cellular immunity [9].

Vitamin D3 has long been recognized for its antibacterial qualities and plays a significant role in controlling inflammation and the production of chemokines [10]. Vitamin D3 receptors are found in immune cells, affecting immunomodulatory effects and enhancing macrophages' oxidative ability, including cytokine synthesis and hydrogen peroxide production [10]. Additionally, vitamin D3 increases phagocytic activity and neutrophil motility [11, 12].

Urinary tract infections are a severe public health issue with significant economic burden on the individual and on the healthcare communities.

AIMS OF THE STUDY

The current study aimed to determine the correlation between the levels of vit. D3 and zinc in sera of patients and controls and the UTI, and if these levels have role in developing UTI and can have effect on the recurrent infections..

METHODOLOGY

Venous blood samples were collected from 60 patients with the urinary tract infection at Imam Hassan Al-Mujtaba Hospital for the period from December 2022 to March 2023, and control samples which was 20 venous blood samples. The patients were diagnosed with UTI by flowing three main steps, which were the clinical diagnosis by the specialized doctors in the hospital, and the general urine examination and the urine culture was performed in the hospital's laboratory for each patient. The general urine examination and urine culture were also done for the controls group. The venous blood samples for patients were distributed between 30 females and 30 males. The sera of patients and controls were separated to measure the concentrations of vitamin D3 and zinc. All the information related to the patients and controls was collected using a questionnaire prepared for this study, which included age, gender, recurrent and non-recurrent urinary tract infections, and others. The study's protocol followed the declaration of Helsinki and was confirmed by College of Science, University of Kerbala (Approval Code: no. 6/4071 on November 23, 2022).

Zinc evaluation was done using a Mindray device in conditions of wavelength/filter of approximately 570 nm/yellow, temperature at room temperature, and one centimeter of light path. The materials mentioned in the table 1 were placed in dry, clean tubes marked as plank, standard and test Sequentially. 1 ml of the reagent was added to the plank tube and 0.05 ml of distilled water was added to it, then 1 ml of the reagent was added to the standard tube and 0.05 ml of zinc standard was added to it. Finally, 1 ml of the reagent was added to the test tube and 0.05 ml of reagent was added to the test tube. Five ml of sample into it. Incubation was done at room temperature for five minutes after mixing was completely done. Finally, the absorbance was measured within twenty minutes for both the standard absorbance and the test absorbance against the Blanck absorbance to determine the zinc concentration according to the equation below.

Zinc mg/dl = (Abs.T/ Abs S) × 200

Vitamin D evaluation by the Cobas e 411 system was depended on an electrochemiluminescence (ECL)-based completely autonomous autoanalyzer used for immunological analysis. ECL technology makes use of interference suppression techniques, streptavidin-coated magnetic microparticles, and antigen/antibody interactions as its solid phase. The roche rack cup was adapted within the rack, the samples were loaded and also routine was loaded without barcodes, then it was filled up on supplies and was executed experiments, finally outcomes had gotten.

Statical analysis:

The study used SPSS for statistical analysis, presenting results as mean±standard error. Graphs and charts were created using Prism 9. The independent sample T test, ANOVA test, and Square-Chi square were used to examine significant differences.

RESULTS

This study included 80 participants; the gender was distribution to 50% females and 50% males; the ratio of females to males was 1:1. The ages of the participants ranged from 18 to 50 years. Patients were divided into subgroups: 35 (58.3%) of them were diagnosed with recurrent urinary tract infections while 25 (41.6%) were diagnosis with non-recurrent urinary tract infections. It was found that most of the patients had a significant difference in the mean level of Pus Cells, RBCs, Epithelial Cells comparing to healthy controls, p values were <0.001, as presented in Table 2.

Concentrations of Vit. D3 and Zn in patients and controls

The UTI patients in the present study show insufficient levels of Vitamin D3 compared to the healthy controls, and it was below the mean of the group, the differences between two groups were insignificant, p value > 0.05. The mean level of Vit D3 in urinary tract infection patients' group was (10.50±0.81) which lower than in controls group (12.58±1.58) (ng/ml), as presented in table 3 and figure 1.

On the other hand, the mean serum zinc levels were lower in UTIs than in the controls group. The mean level of Zn in patients' group was 83.0 mg/dL while in the controls group was 86.27 mg/dL, the p value > 0.05 as illustrated in table 3 and figure 1.

Concentration of Vit. D3 and Zn in recurrent and non-recurrent infections

Vitamin D3 has emerged as a key factor in innate immunity. Its involvement in the pathogenesis of urinary tract infections (UTIs) has gained a lot of attention recently. In this study, the mean level of both Vit. D3 and Zinc were measured in recurrent and non-recurrent urinary infections groups.

Vitamin D3 presented a non-significantly lower value in the patient subjects than in healthy controls. Patients with non-recurrent UTIs presented non significantly lower levels of vitamin D3 than those with recurrent infections and controls. The mean level of vitamin D3 in the recurrent Infections was 11.50 ng/ml, in non-recurrent infections was 9.085 while in healthy control was 12.58 ng/ml, as presented in Table 4 and figure 2. On the other hand, the mean level of zinc in the recurrent Infections was 83.27 mg/dl, in non-recurrent Infections was 82.63 mg/dl while 88.84 mg/dl in healthy control, for both biomarkers the p value was > 0.05.

DISCUSSION:

The study postulated that low zinc and vitamin D3 levels could serve as a risk factor for urinary tract infections. As a result, the relationship between serum vitamin D3 level, zinc, and UTI patients were examined in this study. The findings showed lower levels of both markers, which may be related to their function as a UTI risk factor. These findings come along with those of earlier investigators who found evidence between the risk of UTI and serum vitamin D3 level. They demonstrated a strong correlation between low serum vitamin D3 levels and the incidence of UTI in both adults and children [13].

Li X et al. [14] have reported their main finding that low serum vitamin D3 levels are negatively correlated with the risk of urinary tract infections. Vitamin D3 ability to regulate both innate and adaptive immune functions through a variety of mechanisms may be the cause of that [15] and control the inflammatory reaction to the harmful substances

[16]. Low vitamin D3 levels reduce inflammatory responses, both systemic and local, by effecting cytokine responses and activating toll-like receptors in immune cells [17]. In addition to reducing immune cell activities through hypocalcemia, vitamin D3 absence additionally decreases the synthesis of b-defensin-2 and cathelicidin [18]. Vitamin D3 receptors on immune cells such T cells, dendritic cells, macrophages, and monocytes control their antimicrobial activity [19]. It was shown by Aslan et al. [20] that the pathophysiology of UTI involves the vitamin D3 receptor. Since the urinary tract epithelium is one of the barrier regions where endogenous antimicrobial peptides (AMPs) are widely produced, they serve as the innate immune system's first line of defense against pathogens. These are multifunctional peptides found on the skin, gastrointestinal, respiratory, and urine tract epithelial surfaces. By damaging the bacterial membrane, AMPs exhibit antibacterial activity. They also prevent the formation of biofilms and alter a number of immunological processes. On the other hand, AMPs activity in the epithelial surfaces is associated with UTI severity [21].

Zinc is among the top listed micronutrient with immunological activity. It plays a crucial role in cellular growth and metabolism [22] Furthermore, it is crucial for immunity and free radical scavenging [23]. Several studies have reported that this trace element also has antibacterial properties and investigated its role in different infectious disorders [24]. Changes in zinc levels seem to have a special effect on the immune system; in fact, zinc levels seem to be directly or indirectly tied to every reaction [25]. As previously said, nutritional immunity has been the primary factor taken into account when it comes to zinc at the host-pathogen interaction. In this case, a bacterial pathogen cannot acquire zinc due to the action of the innate immune system. Zn is transferred to different tissues during this process, which lowers serum Zn levels. The process can be facilitated by the up-regulation of ZIP14, the zinc transporter that accumulates zinc in infected sites, in an IL-6-dependent manner. The mechanism behind the depletion of plasma zinc also seems to involve metallothionein, which is stimulated by inflammatory cytokines like IL-1 and accumulates in the liver in its Zn-bound form. The human protein calprotectin, which sequesters zinc and deprives the bacterial pathogen of these trace metal nutrients, is another example of zinc nutritional immunity. Neutrophil extracellular traps, a crucial mechanism of neutrophil extracellular bactericidal killing, are rich in calprotectin. It should be mentioned that calprotectin likely only starts to work when it is liberated from the neutrophil [26]. The Middle East is known to have a higher rate of vitamin D3 deficiency. In addition, the hot weather limits sunlight exposure, which makes the study more intriguing. The results showed a clear correlation between urinary tract infections and vitamin D3 deficiency, and these findings were consistent with other studies that reported the same finding [27].

A 2-3-fold increase in infections, including urinary tract infections, is observed in previous case-control studies [28] when there is a vitamin D3 shortage. On the other hand, the deficiency of Vit D3 either in recurrent or non-recurrent infections might be due to kidney impairment. Since The body uses vitamin D3 primarily through the kidneys, so vitamin D3 levels in chronic kidney disease are typically below normal, and in some cases, they are extremely low. This is because damage to the kidneys reduces their capacity to convert vitamin D3 into its active form [29]. Vitamin D3 is necessary for the innate and adaptive immune systems to operate properly and respond to inflammation and infection [30]. Vitamin D3 is necessary for the immune system to activate white blood cells and promote the removal of infected cells [31]. The current study findings indicate that there was no statistically significant correlation between the study groups' serum zinc levels. The group with non-recurrent UTIs had lower serum zinc levels than the recurrent UTIs and controls group; this could be because the zinc supplementation for the previous infection may have reduced the duration and limited the complications of UTIs [32]. Therefore, these results were disagreed with Mohsenpour et al., [33] who shown opposite results when reported that serum zinc levels were decreased in recurrent UTIs.

The innate and adaptive immune system function is impaired even in cases of moderate zinc deficiency [33]. Reduced immunoglobulin production, thymic atrophy, lymphocyte depletion, compromised phagocytic function, and decreased interleukin (IL)-2 production are all linked to zinc deficiency [34]. Moreover, individuals with zinc deficiency may be vulnerable to certain infections secondary to damage to the epithelial line of defense and reduction in the antioxidant activity [35]. Furthermore, it was confirmed that zinc low levels have been linked to poor outcomes from sepsis and bacterial infections [36]. It is not possible to express a definite opinion about the effect of zinc deficiency on increasing the risk of UTI.

CONCLUSIONS:

In conclusion, however that the current result was not significant, the low levels of vit. D3 and Zn may have a negative impact on the immune system in general and may have a role in increasing the UTIs and affect the recurrent infections. The correlation between D3 and zinc and UTI still needs much investigation to determine exactly when these two factors can have significant effect on the developing UTI and what other factors can alter the results.

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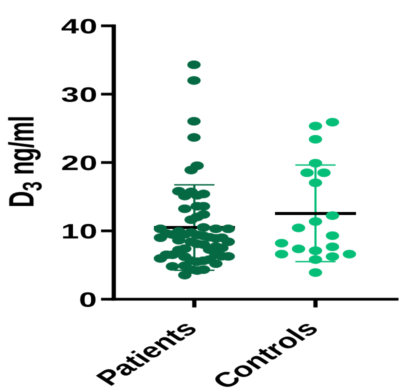
TABLES:

Table (1): Blank (B), Standard (S) and Test (T) concentrations in ml to evaluate zinc levels in serum.

Addition Sequence	B (ml)	S (ml)	T (ml)
Working reagent	1.0	1.0	1.0
Distilled Water	0.05	---	---
Zinc Standard	---	0.05	---
Sample	---	---	0.05

Table (2): Demographics of the subjects (patients and controls) included in the study

Characteristics	Patients		Controls		P- value
	Number, (%)	Mean±SE	Number	Mean±SE	
Number	60	-----	20	-----	-----
Age range	18-50	-----	18-50	-----	X^2= 0.02 P = 0.99
Sex: Females Males	30 (50%) 30 (50%)	-----	6 (30%) 14 (70%)	-----	X^2= 2.42 P = 0.12
Recurrent Non-recurrent	35 (58.3%) 25 (41.6%)	-----	-----	-----	-----
Pus Cells	-----	17.78± 2.163	-----	1.750± 0.09934	<0.0001***
RBCs	-----	5.850±1.223	-----	2.000±0.2052	0.0041**
Epithelial Cells	-----	13.08±1.366	-----	4.500±0.5000	<0.0001***
Specific Gravity	-----	1.040±0.01630	-----	1.025±0.001901	0.6463 (NS)



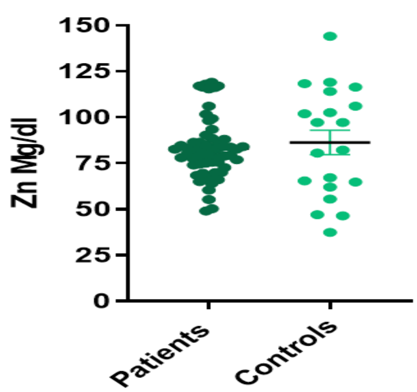


Figure (1): The concentrations of Vit D3 and Zn among patients of urinary tract infection and controls groups

Table (3): The Mean differences of Vit. D3 and Zn level among patients with urinary tract infection and controls group

The Groups	Mean ± SE	
	Vit. D_3 (ng/ml)	Zn (mg/dl)
Patients	10.50±0.81	83.00±2.136
Controls	12.58±1.58	86.27±6.612
P-value	0.28 (NS)	0.77 (NS)
NS: Non-Significant		

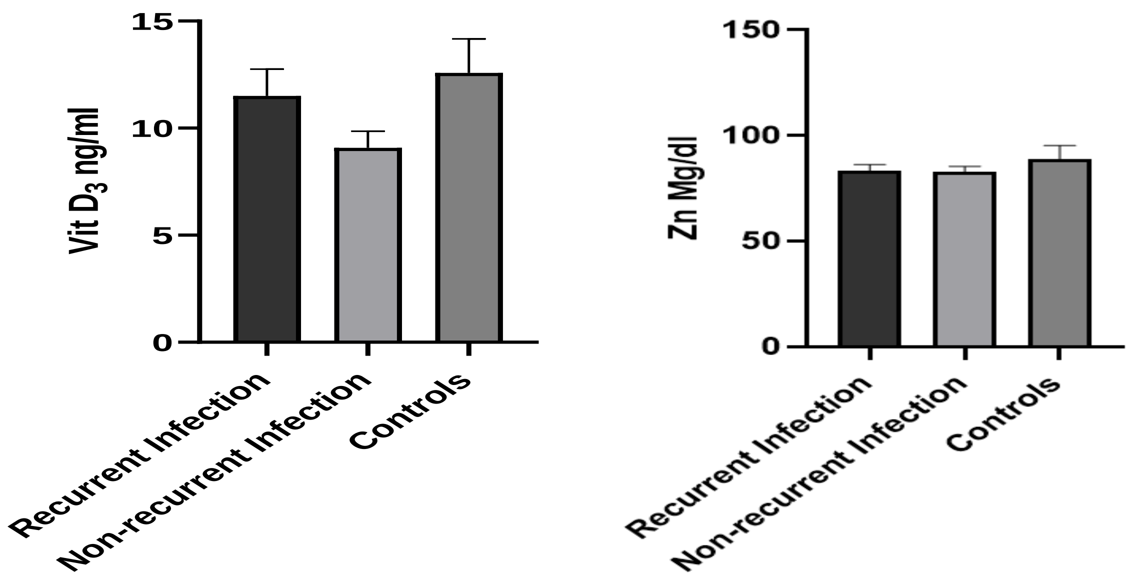


Figure (2): The Mean ± SE of Vit. D3 and Zn levels in recurrent and non-recurrent urinary tract infection groups compared to controls group

Table (4): The Mean differences of Vit D3 and Zn level in recurrent and non-recurrent Urinary tract infection groups compared to control group

The Groups	Mean ± SE	
	Vit. D3 (ng/ml)	Zn (Mg/dl)
Recurrent Infections	11.50±1.26	83.27± 3.076
Non-recurrent Infections	9.085±0.77	82.63± 2.851
Controls	12.58±1.58	88.84± 6.421
P-value	0.32 (NS)	0.5377 (NS)
NS: Non-Significant		