Original Article

Association Of Vitamin D Deficiency And Urinary Tract Infection At A Tertiary Care Hospital In Karachi

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Abstract

Objective: To determine the association between vitamin D deficiency and urinary tract infections within the local population.

Methods: In this cross-sectional study, urine and blood samples of 174 participants (87 healthy controls and 87 UTI patients) were collected by standard operating procedures. Urine samples were processed for the physical, chemical, microscopic examination and culture & sensitivity. The disinfectant susceptibility examination was skilled by using the Kirby-Bauer disc diffusion test by CLSI recommendations. Vitamin D levels of the participants were determined in blood samples by the ELISA technique.

Results: Out of 87 urine samples of UTI patients, 84 (96.5%) were growth positive; out of these positive cases, Gram-negative bacteria were 75(89.3%) in comparison to Gram-positive bacteria, which were 8(9.5%), and 1(1.2%) was *Candida albicans*. In all of these isolates, *Escherichia coli* was the predominant 49(56.3%) uropathogens and a higher frequency was observed in young females. The majority of the UTI patients, 68(78.2%), revealed a vitamin D deficiency, compared to 5(5.7%) in the control group participants. There was a statistically significant difference (p-value .001).

Conclusion: This study highlights the strong correlation between vitamin D deficiency and UTI.

Keywords: Urinary tract infections, Uropathogenic *Escherichia coli*, Vitamin D deficiency.

Contributions:
WH, SSA, SK, MA, FZ - Conception, Design
WH, SSA, FU, SK, MA - Acquisition, Analysis, Interpretation
WH - Drafting
SSA, FU, SK, MA, FZ - Critical Review

All authors approved the final version to be published & agreed to be accountable for all aspects of the work.

Conflicts of Interest: None
Financial Support: None to report
Potential Competing Interests: None to report

Institutional Review Board Approval
No. F.2-81/2018-GENL/7062/JPMC
22-11-2018
Jinnah Postgraduate Medical Centre

Review began 22/03/2025
Review ended 08/07/2025
Published 29/09/2025

How to cite this article: Hussain W, Ahmed SS, Uddin F, Kashif S, Adnan M, Zeeshan F. Association Of Vitamin D Deficiency And Urinary Tract Infection At A Tertiary Care Hospital In Karachi. JRMC. 2025 Sep. 29;29(3).

https://doi.org/10.37939/jrmc.v29i3.2870

Introduction

Vitamin D deficiency is a predominant health problem around the world due to inadequate nutrition and limited exposure to sunlight.[1] In the Asian continent, above 80% of the community is at high risk for to develop vitamin D deficiency.[2] The majority of the population needs a vitamin D supplement to avoid deficiency. The primary source of vitamin D is cholecalciferol, which is produced in the skin when exposed to sunlight, and about 10% of the body's requirement is fulfilled by dietary sources.[3]

Vitamin D plays a vital role in different metabolic mechanisms and diseases, including infectious diseases, one of which is the protective role in UTIs. It additionally sustains innate immunity via a variety of mechanisms, amongst them is activation of antimicrobial peptides like cathelicidin, which reduces the risk of UTI.[4] Urinary tract infection (UTI) may lead to severe complications and increase the financial burden in case of multidrug-resistant bacteria.[5] More than 50% UTI cases are caused by *Escherichia coli* and followed by the other members of Enterobacterales.[6] It is a common trend that UTI is treated with antibiotics and probiotics. Antibiotics are mostly used without conducting culture and sensitivity; this careless and inappropriate practice has led to antibiotic resistance. Natural remedies are also used to control UTIs, using cranberry capsules for up to 7 days.[7] Hence, it is necessary to circumvent non-judicious use of antibiotics. Recurrent UTIs, which are defined as at least two episodes within six months, are regrettably common in women.[8] Considering the above facts, as the vitamin D deficiency is common in Pakistan,[2] this study was designed.

Materials And Methods

The cross-sectional research was accomplished at the department of Microbiology Basic Medical Sciences Institute (BMSI), Jinnah Postgraduate Medical Centre (JPMC) Karachi Sindh.

The patients included in this study were from the National Institute of Child Health (NICH) and department of Nephrology, JPMC, Karachi, Pakistan.

A total of 174 participants were included in the present study, and the sample size was calculated by Open EPI, an online software, using the prevalence of vitamin D deficiency in Pakistan. The subjects were divided into two groups: Group A (Control Group) consisted of eighty-seven (87) participants, who were healthy, without current or recent history of UTI, and Group B (Patients) consisted of eighty-seven (87) participants, with symptoms of UTI. The participants' age range was 4-60 years, which was further categorised into groups and without gender discrimination, participants were included. The patients with comorbidities including diabetes, pregnancy, receiving vitamin D supplementation, on antibiotics and kidney malfunctioning were excluded. The study was conducted within six months (20th November 2020 to 22nd May 2021) after the approval of ethical considerations.

The research proposal was submitted to the –removed for blind review---, and this was approved by the IRB committee (NO.F.2-81/2018-GEN/7062/JPMC). The written consensus was taken from all the participants/parents, or guardians. Data was protected from unauthorised personnel**.**

Both groups (A and B) participants' blood and urine samples were taken using the aseptic technique. Mid-stream urine samples were collected in universal containers from instructed adults and 4-to 12-year-old children.[9] After being delivered to the Microbiology Department at BMSI, JPMC, Karachi, the urine samples were processed for a detailed report within 2 hours after collection of samples and culture.[10] The urine samples were analysed for culture, physical, chemical and microscopic examination. The chemical analysis of urine was performed by dipstick (Lab strip U11 Plus, USA) results were read visually through colour boxes. The microscopic examination of the urine deposit was determined by the wet preparation technique.

Urine samples were plated on cysteine lactose electrolyte deficient (CLED; Oxoid Ltd., Basingstoke, Hampshire, England) and incubated aerobically at 35-37°C for 24-48 hours. A urine culture is counted as positive if it has 10^5 CFU/mL (Cheesebrough, 2009). The isolates were identified on Gram's staining, cultural characteristics and the manual biochemical tests, including indole, urease, triple sugar iron, citrate and motility test. The antimicrobial susceptibility testing (AST) was determined by the disc diffusion method on Muller Hinton agar (Oxoid Ltd., Basingstoke, Hampshire, England) according to the standard protocol recommended by CLSI (2020).

Serum vitamin 25(OH) D3 was determined using the competitive ELISA technique kit contains a monoclonal antibody against 25(OH) ("25OH Vitamin D Total ELISA 90" kit; DIA S.A- Rue du Bosquet, Belgium). Vitamin D levels and their interpretation are according to the Institute of Medicine (IOM) and the World Health Organisation.[11] The serum/plasma level of Vitamin D3 ≤20 ng/mL, 20–29 ng/mL and ≥30 ng/mL are interpreted, deficiency, insufficiency and sufficient, respectively.

Initially, data was collected on an Excel sheet and exported to SPSS (Statistical Package for Social Science) version 21, for analysis using appropriate statistical tests in relation to variables. The chi-square test was adapted to measure the association of categorical variables. *P*-value at ≤.05 was set for consideration of its significance.

Results

In the present study, the prevalence of UTI was higher, 15(29.4%), in females of the age group 21-30 years. UTI patients revealed different sign and symptoms, in majority (63; 72.4%) of patients were with micturition followed by lumber pain, whereas, retention of urine was the lowest clinical feature (Fig. 1). Group B subjects urine appearance (42; 48.3%) and (41; 47.1%) was yellow and turbid respectively. Whereas in group A, the colour of urine was pale yellow and clear in appearance. The statistical analysis showed a significant difference between the two groups in urine parameters (P=.001) at the ≤.05 level. In chemical analysis of urine, leucocyte esterase and nitrite were determined in both groups (Fig. 2). All the subjects of the control group were negative for both parameters, whereas in majority of patients showed significant pyuria, 81(93.1%), and similar results 93% were obtained by the wet mount. Nitrite were positive in 40(45.97%), and these samples were also culture positive. The entire control group (A) was negative for culture 87(100%). Out of 87 patients of group B, 84(96.5%) were culture positive for uropathogens. The most frequent bacterial uropathogen was E. coli 49(56.3%), followed by E. cloacae complex and Pseudomonas aeruginosa at the frequency of 6(6.9%). The Klebsiella pneumoniae was at the rate of 5.7%. The infrequent uropathogens were P. mirabilis 5(5.7%), S. agalactiae 4(4.6%), Providencia species 3(3.4%) and S. saprophyticus 2(2.3%). The Diphtheroid and Candida albicans 1 (1.2%) of each isolate (Figure 3). Out of 87 patients, 40(46%) and 28 (32.2%) had deficiency and inadequate vitamin D levels, respectively, while, sufficient in 19 (21.8%) in group B subjects (Figure 4). In Group A participants, deficiency in 5 (5.7%), insufficiency in 28 (32.2%), and 53 participants (60.9%) had with sufficient level of Vitamin D3 and intoxication in 1 (1.1%).

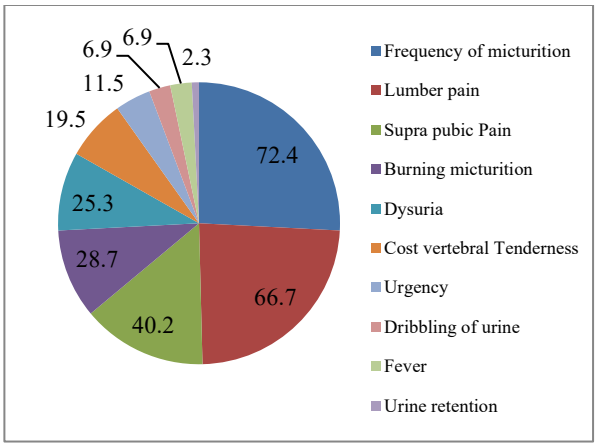

Figure 1: Clinical features of patients with UTI, Group B (n=87)

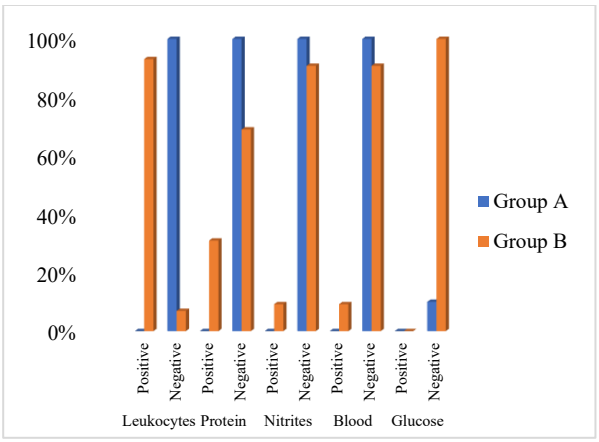

Figure 2: Chemical analysis of the urine of patients and control participants

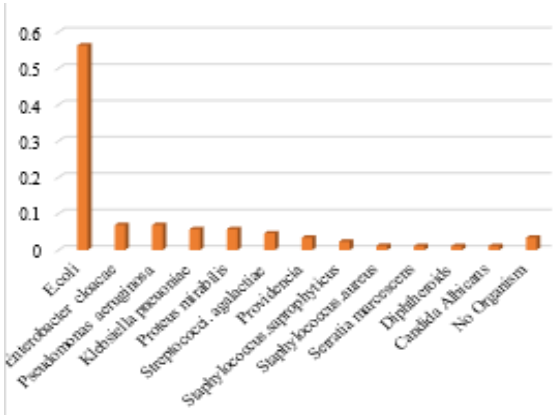

Figure 3: Frequency of different uropathogens in patients' urine samples

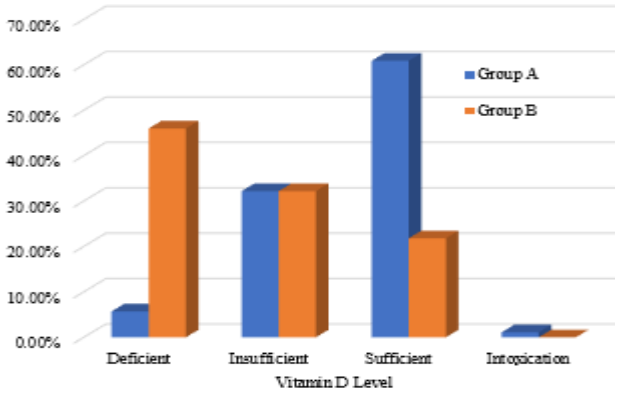

Figure 4: Vitamin D levels in the control group (Group A) and UTI Patients (Group B)

Discussion

Urinary tract infection is a frequent bacterial infection that affects people of all ages, including men, women, and children. The prevalence of UTI was found to be higher in women (29.9%) of the age group 21-30 years, which may be due to physiological and anatomical differences and/or may be of higher sexual activity. Near to similar results (32.6%) have been endorsed by previous studies (Odoki et al., 2019).[12] Urine appearance and turbidity have a major role in the diagnosis of UTI. The colour of urine was yellow and turbid in the most (48.3%) of UTI patients' cases, while, pale yellow and clear in appearance in the control group. These findings are similar to those previously reported by Arienzo et al. (2020).[10] In the present study, the WBCs and proteins were higher in urine from UTI patients. Therefore, urine analysis may be an alternate preliminary diagnostic tool in low-income countries, including Pakistan. It is a rapid and cost-effective dipstick test, and superior in the context of detecting lysed WBCs, reported earlier by Prah et al. (2019).[13] The results of the present work revealed that leucocyte esterase and nitrite were significantly higher (p.001) in the UTI patients' urine compared to the control group's urine.

Urinary tract infections are presumptively diagnosed with microscopic examination. It is dependent on the individual's abilities, approach, and standards for assigning grades to their values.[14] The quantity of urine produced and urinated, as well as the migration of WBCs (inflammation) to the urinary tract, all affect the number of WBCs. The majority of UTI patients in the current study had pyuria, while the control group had less than three pus cells per high-power field (PHF). According to this study, there is a direct correlation between urinary tract infections and pus cells. Similar findings are previously documented.[13]

The diagnosis of UTI on the basis of signs, symptoms and urine examination revealed an error of 33%.[15] The urine culture and sensitivity are the gold standard for the diagnosis, and their correlation with signs and symptoms. Clinically diagnosed patients'

urine was significantly positive for bacterial uropathogens (96.6%). Of these uropathogens, Gram-negative rod bacteria were the most frequent (89.28%) isolates in the present study. These results were similar to those of Carlotta et al. (2024).[16] *E. coli* was the most frequently (56.3%) encountered uropathogens among all the isolates and in Gram-negative bacilli. The higher frequency of *E. coli* from urine is attributed to its adherence mechanism to the epithelial cells, resistance to the flushing action of urine flow, production of exotoxins and presence in the colon, which facilitates the contamination of the urethra. Zhou et al. (2023) have noted similar results, except that the percentage was higher (75%) than in the present study.[17]

In a previous study, Muntean et al. (2021) reported a strong association of vitamin D deficiency with recurrent UTI. [18] Vitamin D is an essential component for the synthesis of antimicrobial peptides (AMPs) by epithelial cells and WBCs. These AMPs are the main components of the defence line at the local level. In this study, out of 87 UTI patients, 40(46%) were with vitamin D deficiency, 28 (32.2%) and 19 (21.8%) were with insufficiency and sufficiency levels. In the control group (group-A), the majority of participants (54;62.06%) had with sufficient level of Vitamin D3, whereas 13.8% and 24.14% participants had insufficiency and deficiency levels, respectively. The statistical analysis revealed that there was a significant difference in the vitamin D3 levels of healthy group A and UTI patients in this research (p.001). These findings revealed that there is a strong association between Vitamin D3 deficiency and UTI. Similar findings have been reported by an earlier study (Chidambaram et al., 2022).[19]

Conclusions

This study revealed a strong association between vitamin D deficiency, insufficiency and UTI. Therefore, vitamin D may play a protective role against UTIs.

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