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RESEARCH ARTICLE

# Risk Factor of Vitamin-D Deficiency for Urinary Tract Infections in Women at Reproductive Age

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## ABSTRACT

**Background:** Urinary tract infections (UTIs) are common health infections in women with high complications. Many of the worldwide population suffer from vitamin D deficiency (VDD) due to insufficient exposure to sunlight. The relationship between VDD and resistance antibiotics isolates on UTI from women of different ages did not study in Basrah city for years.

**Aim:** The present study aim to find the effect of VDD and resistance antibiotic isolates on UTIs in women of reproductive age.

**Methods:** The samples were collected from September 2022 to January 2023 from outpatients of gynecology clinics and private clinics in Basrah city. A total of 70 samples were collected from females and 60 samples from males suffering recurrent UTI of different ages. The concentration of vitamin D is determined by using the Cobas e411 analyzer. In addition, the identification of bacterial isolates and antibiotic sensitivity is determined using a VITEC device.

**Results:** This study included 130 midstream urine samples obtained from 70 females and 60 males. The ages of these patients ranged between 18 and 72 years. These samples were cultured on primary media, and then the identification of these unknown bacteria was done. The current study showed that the infections in females were significantly higher than in males. Infection was found to be significantly higher in the age group of 31 to 50 years than in the other age groups, followed by the age groups of 18 to 30 years. This study showed that *E. coli* is the most prevalent bacteria isolated from UTI patients, followed by *Pseudomonas aeuroginosa*. They occur mainly in females as compared to males, especially in the age group between 31 and 50 years. We sought to identify the prevalence of vitamin D3 deficiency among different ages. The deficiency of vitamin D levels in women was 82%. The levels of deficiency were significantly higher in the age group 25 to 34 years is 71.1%, followed by 15 to 24 years is 63.2%, and 35 to 45 years is 50%, with a mean 24 ± 6.8 years. In addition, we found isolates of *E.coli* have multidrug resistances.



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**Conclusion:** Our current study revealed that there is a clear correlation between women who suffer from VDD and UTIs, whether severe or frequent infection at reproductive age and this affects their fertility and pregnancy. In addition, the study showed that *E. coli* is the most prevalent bacteria isolated from UTI patients, followed by *Pseudomonas aeuroginosa*. There was a significant relationship between a decrease of serum vitamin D levels and the severity of urinary incontinence among reproductive-aged women. Our study demonstrates that a significant frequency of multidrug-resistant *E. coli*. In addition, imipenem was an appropriate drug to treat infections caused by these uropathogens. These findings may aid physicians in the management of UTI infections.

## INTRODUCTION

Urinary tract infections (UTIs) are common health infections in pregnant women with high complications. UTIs are the third infection after respiratory tract and gastrointestinal infections. It occurs as a self-limiting infection but has tended to be recurrent, and its infections threaten health because it is related to antibiotic resistance.[1] In general, urinary tract infections occur at different ages in women of reproductive age and about 11% at the age of 18 to 24 years among women in the United States suffer from a urinary tract infection each year.[2] UTIs are risks for women during pregnancy, which may cause preterm birth, affect the intrauterine growth of the fetus, as well as preeclampsia. UTIs appear in cystitis, acute pyelonephritis, and asymptomatic bacteriuria.[3]

In a study conducted in the US by Ramos *et al*. (2018), it was reported that 39% of women aged 39 to 56 years had slight urinary incontinence, 45% had moderate urinary incontinence, and 17% had severe urinary incontinence.[4] In Germany and Denmark, the prevalence rate of UI was 48.3 and 46.4%, respectively.[5] In a study in Pakistan (2019) and Baghdad (2020), the overall prevalence of UI was 44 and 40%.[6,7]

Vitamin D deficiency is a pandemic. One-third of the worldwide population suffers from vitamin D hypovitaminosis due to inadequate exposure to sunlight. It is estimated that In Africa and Asia, more than 80% of the people are prone to vitamin D deficiency. Serum 25-hydroxy vitamin D deficiency can play a role in increasing the risk of many chronic illnesses, including common cancers, autoimmune diseases, infectious diseases, and cardiovascular diseases.[8]

Some researchers believe that a relationship between vitamin D deficiency (VDD) and urinary tract infection and giving vitamin D supplementation contributes to preventing UTI, but the association between its deficiency and urinary tract infection has not been known.[9] Vitamin D is a group of fat-soluble secosteroids that are produced in the skin after exposure to ultraviolet radiation. Many of the worldwide population suffer from VDD due to insufficient exposure to sunlight. Almost 80% of people in Africa and Asia are vitamin D deficient. Recent studies have indicated that vitamin D has an important role in protecting against autoimmune diseases and other infections.[10] VDD is associated with many diseases, including osteoporosis, preeclampsia, autoimmune diseases, cancers, cardiovascular disease, respiratory and urinary tract infections caused by bacterial infections.[11] The present study aims to find the effect of VDD and antibiotic resistance isolates on UTIs in women in Basrah city.

## MATERIAL AND METHODS

### Design of the Study

The cross-sectional study included 70 participants of, women and 60 men no use any antibiotics. The samples were collected between the period of September 2022 to January 2023 from patients who attended General AL-Basrah Hospital and private clinics.

### Methods

#### *Urine samples*

Urine samples were collected from each participant in sterile containers, and then transported to the laboratory for further analysis. The urine samples were processed routinely then cultured on blood and MacConkey agar. The positive growth samples were further analyzed using the macroscopic characteristics of the colonies and the microscopic examination using gram's stain. Then, the colonies were examined for their biochemical profile using routine biochemical tests (Oxidase, catalase, manitol salt agar, novobiocin tests, IMViC) and identification of isolates were confirmed by the VITEC-2 Compact System.[12]

#### *Detection of vitamin-D concentrations*

A 5 mL of the venous blood samples were obtained to determine the vitamin D3 test in gel tube and separate by centrifugation at 1500 × g at 4°C. Samples were tested by the Cobas e411 analyzer that is an automated analyzer. It is designed for determinations of broad range of applications according to the manufacturer's instructions.[13]

#### *Antibiotics sensitivity test*

Species identification of gram-positive bacteria (GPB), gram-negative bacteria (GNB) and antibiotics susceptibility testing were determined with VITEK® 2 compact system (bioMérieux, France) using GN, GP, AST-P641, AST-N326, and AST-N327 cards. The investigated antibiotics by VITEK® 2 cards were the following: piperacillin, piperacillin/tazobactam, ceftazidime, cefepime, aztreonam, imipenem, meropenem, amikacin, gentamicin, netilmicin, tobramycin, ciprofloxacin, levofloxacin, tetracycline, tigecycline, trimethoprim/sulfamethoxazole, fosfomycin, nitrofurantoin, benzylpenicillin, erythromycin, clindamycin, linezolid, daptomycin, teicoplanin, vancomycin, and fusidic acid. The results were interpreted according to the 2018 Clinical and Laboratory Standards Institute (CLSI) criteria.[14]

### Statistical Aanalysis

All data were analyzed using SPSS software. Calculation of mean values and standard deviation (SD) made for characterization of the study population. We tested the relationship between concentrations of vitamin- D and antibiotics sensitivity with UTIs by Chi-square and the t-test. $p < 0.05$ considered statistically significant.

## RESULTS AND DISCUSSION

### Patients and Clinical Isolates

The current study showed that the infections in females were significantly higher than in males (Figure 1).

This finding is consistent with many studies as well as local research conducted in Baghdad City, which revealed that females were more likely to have UTIs (81.8%) as compared to male (18.2%).[15] Another study by Ibrahim *et al*. also showed that infection of UTI in female was significantly higher than in males.[16]

The higher incidence of UTIs in females may be due to the proximity of the urethra to the anus, the broader and shorter urethra, sexual activity, incontinence, vaginal surface's less acidic pH, and unsanitary living situations.[17]

The present study showed that among males and females, the age group of 31 to 50 years had the highest number of infected females, followed by the age group of 18 to 30 years (Figure 2).

There were very few studies about infections among different age groups. Study showed that 58.4% of patients were in the age range of 21 to 30 years, followed by 26% of patients in the age range of 31 to 40 years.[18] Additionally, Anili *et al*. discovered that the prevalence of bacterial UTIs was greater in the age group of 30 to 39 years (25.40% of the study population).[6]

Figure 3 shows the percentage of all isolates collected from clinical specimnes in the present work. Only (42.5%), (22.5%), (12.5%), (10%) and (5%), (5%) identified as *E. coli*, *P. aeruginosa, P. mirabilis,S. epidermidis, S.aureus*, and *K. pneumoniae*, respectively.

In Iraq, the current findings are in an agreement with Al-naimi *et al*.[19] who have recorded (31.82 %) of UTI cases caused by *E. coli* followed, *K. pneumonia*e (22.2 %) and the remaining percentage caused by different bacterial isolates. Meanwhile, the results of Martin *et al*.[20] supported the present study results, who have explained the most prevalent bacterial uropathogen was *E. coli* (41.9%) followed by *S. aureus* (31.4%). In addition, the results of the current study are agreement with Ibrahim *et. al.,*[16] who have noticed the preidominant isolate in UTI was *E. coli* (55%).

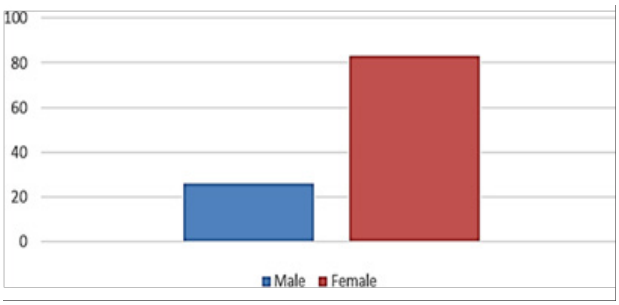


**Figure 1:** Number of infected males and females

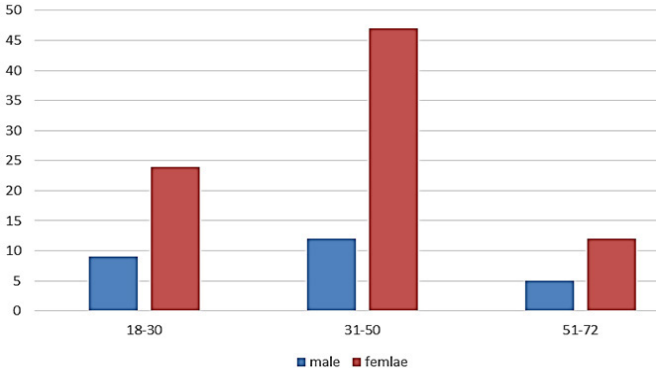


**Figure 2:** Distribution of infected people as per age groups

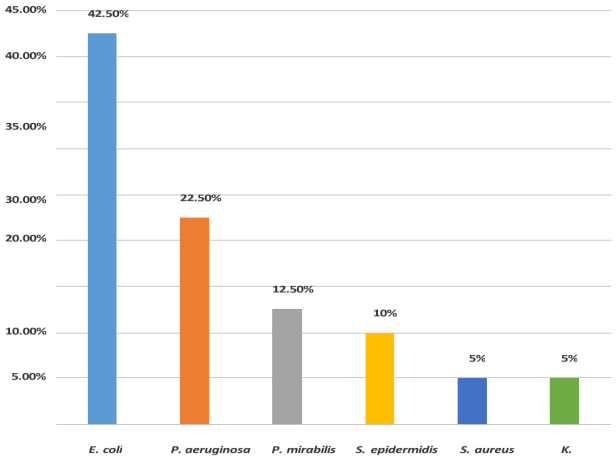


**Figure 3:** The percentage of bacterial isolates collected from specimens of the current study

### Vitamin-D Concentration

The population based on the level of vitamin D in their serum in respective with Roche company reference range for vitamin D level, of 70 females patients. They are vitamin D3 deficiency level (< 20 ng/mL) with a mean of 8.4 ± 4.43, Patients were at Vitamin D3 insufficiency level (20–30 ng/mL) with a mean of 24 ± 2.9, whereas patients were at vitamin D3 sufficient level (30–100 ng/mL) with a mean of 40.3 ± 14.1 and patients were at excess level of vitamin D (100–150 ng/mL) with a mean of 102.5 ± 1.8, no patients were at intoxication level of Vitamin D3 >150 ng/mL (Figure 4).

VDD is a health problem for women that need great attention. VDD is known as deficiency mineralization defect or demineralization of the skeleton that leads to osteomalacia, osteoporosis, and hyperparathyroidism. There are many classifications for the level of vitamin D range in blood, but according to the American College of Cardiology, vitamin D is classified into severe deficiency, deficiency, mild-to-moderate, and sufficient level.[21]

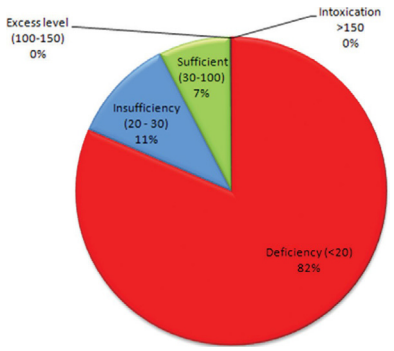


**Figure 4:** Vitamin D3 levels in Basrah city population

The present results indicated that the age groups 15 to 34 years are the most vulnerable to VDD than the older women with age group 35 to 45 years; these explain that age has a role in affecting vitamin D levels and skin production for vitamin D decreases with age and skin thickness.[22]

Vitamin D is a fat-soluble vitamin, which not only plays a role as a vitamin but also as a hormone. Vitamin D is formed in the skin under the influence of sunlight. Further metabolism of vitamin D to its major circulating form (25(OH)D) takes place in the liver and to its hormonal form (1,25(OH)2D) in the kidney, but in other tissues where the 1,25(OH)2D produced serves as a paracrine or autocrine function.[23] Furthermore, this vitamin plays a crucial role in homeostasis of calcium, which is essential for optimal health of the body. A deficiency of this vitamin is also associated with osteoporosis. Vitamin D deficiency is common worldwide, with 78% of adults in the United States and 80% of women of reproductive age having insufficient levels of vitamin D.[24]

## Antibiotic Resistance Phenotype

Analysis of the antimicrobial susceptibility profile of the isolates showed that most of *E. coli* isolates (100%) were susceptible to carbapeneme antibiotics (imipenem) followed by nitroforantion 81.9%. This isolate showed resistance to other tested antibiotics. Of 63 isolates, 95.2% of the isolates were resistant to B-lactam antibiotics (amoxicillin-clavulanic acid) and cephalosporins (cefixime, ceftriaxone, cefotaxim, cefoperazon) which was (90.5, 76.2, 71.4 and 66.7%), respectively, as shown in Table 1. The estimated of *E. coli*, (71.42% ) were found to be multidrug drug- resistant (MDR),

The vast majority of national and international guidelines recommend empirical antibiotic therapy for UTI treatment. However, the effectiveness of such an empirical antibiotic treatment relies upon local antimicrobial resistance patterns. It is worth mentioning that the spectrum of microorganisms isolated from subjects suffering from UTI is almost stable and *E. coli* remains as the most prevalent causative agent. In a study conducted in Basrah city where, it was found that *E. coli* was the most common pathogen especially in women. In another study carried out in Turkey involving 429 women between the age of 18 to 65 years old, *E. coli* was found to be the most common causative agent of UTI.[7] In agreement with this, it was revealed that *E. coli* strains were the most common causative microorganisms of UTI in our locality. It is important to notice that significant changes in bacterial susceptibility profile have been demonstrated over the last decades.[25] For example, the average resistance for ampicillin is more than 50% in some countries. In a study conducted in Turkey, the resistance rates of *E. coli* for ampicillin, amoxicillin/clavulanic acid, ceftriaxone, ciprofloxacin as well as sulfamethoxazole/trimethoprim were 55.1, 32.7, 15.9, 25.2, and 41.1%, respectively[26] In the present study,estimated of *E. coli*, (71.42% ) were found to be multidrug drug- resistant (MDR). It was previously revealed that the high resistance rate to the commonly used antimicrobial medications might also play a role in occurrence of complicated and recurrent UTI. Besides, variations in antibiotic resistance have been demonstrated in different geographical regions.[10] Therefore, it is recommended that antibiotic resistance pattern for any

**Table 1:** Antibiotic susceptibility of *E. coli* strains

| *Antimicrobial drug symbols* | *Resistance pattern (n = 63)* | | | | | | |
|---|---|---|---|---|---|---|---|
| | *Sensitivity* | | *Resistance* | | *Intermediate* | | *p-value* |
| | *No.* | *%* | *No.* | *%* | *No.* | *%* | |
| CRO | 6 | 9.5 | 48 | 76.2 | 9 | 14.3 | 0.0001 ** |
| CFP | 3 | 4.8 | 42 | 66.7 | 18 | 28.6 | 0.0001 ** |
| CFM | 0 | 0 | 57 | 90.5 | 6 | 9.5 | 0.0001 ** |
| CTX | 12 | 19 | 45 | 71.4 | 6 | 9.5 | 0.0001 ** |
| GM | 24 | 38.1 | 21 | 33.2 | 18 | 28.8 | 0.381 NS |
| AK | 21 | 33.3 | 24 | 38.1 | 18 | 28.6 | 0.177 NS |
| IPM | 63 | 100 | 0 | 0 | 0 | 0 | 0.0001 ** |
| NB | 0 | 0 | 42 | 66.7 | 21 | 33.3 | 0.0001 ** |
| F | 51 | 81.9 | 6 | 9.5 | 6 | 9.5 | 0.0001 ** |
| AMC | 3 | 4.8 | 60 | 95.2 | 0 | 0 | 0.0001 ** |
| AZM | 18 | 28.6 | 18 | 28.6 | 27 | 42.9 | 0.0419 * |
| *p-value* | --- | 0.0001 ** | --- | 0.0001 ** | --- | 0.0001 ** | --- |

Notes: * ($p \leq 0.05$): Significant, ** ($p \leq 0.01$): Highly Significant, NS: Non-Significant.

infection be investigated in different countries since this plays a pivotal role for both correct management and antimicrobial resistance prevention.

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