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Relationship Between Vitamin D and Recurrent Urinary Tract Infections in Premenopausal Women

Premenopozal Kadınlarda Tekrarlayan İdrar Yolu İnfeksiyonları ve Vitamin D Düzeyi Arasındaki İlişki

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ABSTRACT

Objective: This study aimed to determine the effect of vitamin D deficiency on recurrent urinary tract infections (UTIs) in premenopausal women.

Materials and Methods: We conducted this study with the case group consisting of premenopausal women with recurrent UTIs (n=59) and the control group consisting of age-matched premenopausal women without recurrent UTIs (n=59). Vitamin D deficiency was diagnosed when 25-hydroxyvitamin D (25(OH)D) level was less than 20 ng/mL, and a serum 25(OH)D level of above or equal to 20 ng/mL was accepted as normal.

Results: The mean age of patients in the case group and the control group was 32.22 ± 5.26 years and 31.78 ± 5.60 years, respectively (p=0.661). The mean value of 25(OH)D level was 18.97 ± 6.91 ng/mL in the case group and 22.27 ± 5.21 ng/mL in the control group. A statistically significant difference was found in terms of marital status (p=0.015) and serum 25(OH) D levels (p=0.004) between the two groups. Independent risk factors for recurrent UTIs were analyzed by a logistic regression analysis. Marital status (p=0.028) and vitamin D deficiency (p=0.015) were independently associated with recurrent UTIs in premenopausal women.

Conclusion: We found a significant relationship between recurrent UTIs and vitamin D deficiency in premenopausal women.

Keywords: Recurrent urinary tract infections, vitamin D, premenopausal women

ÖZ

Amaç: Bu çalışmamızda vitamin D eksikliğinin premenopozal kadınlarda tekrarlayan idrar yolu enfeksiyonları (İYE) üzerindeki etkisini incelemeyi amaçladık.

Gereç ve Yöntemler: Çalışmada vaka grubu (tekrarlayan İYE olan 59 premenopozal kadın) ve control grubu (yaş uyumlu tekrarlayan İYE olmayan 59 premenopozal kadın) çeşitli faktörler açısından karşılaştırıldı. Serum 25-hidroksivitamin D düzeyi (25(OH)D) <20 ng/mL olması vitamin D eksikliği olarak değerlendirildi. Serum 25(OH)D düzeyi ≥ 20 ng/mL olması yeterli vitamin D düzeyi olarak değerlendirildi.

Bulgular: Vaka grubu ve kontrol grubunun yaş ortalaması sırasıyla 32.22 ±5.26 ve 31.78 ±5.60 olarak bulundu (p=0.661). Vaka grubunda ortalama 25(OH)D seviyesi 18.97±6.91 ng/mL olarak bulundu. Kontrol grubunda ise ortalama 25(OH)D seviyesi 22.27±5.21 ng/mL olarak tespit edildi. İki grup arasında medeni durum ve serum 25(OH)D seviyeleri açısından istatiksel olarak anlamlı fark bulundu (p=0.015 ve p=0.004). Tekrarlayan İYE için bağımsız risk faktörlerin tespit edilmesinde lojistik regresyon analizi kullanıldı. Medeni durum (p=0.028) ve vitamin D eksikliğinin (p=0.015) premenopozal kadınlarda tekrarlayan İYE ilişkili olduğu gösterildi.

Sonuç: Premenopozal kadınlarda tekrarlayan İYE ile vitamin D eksikliği arasında istatiksel olarak anlamlı bir ilişki olduğunu gösterdik.

Anahtar Kelimeler: Tekrarlayan idrar yolu enfeksiyonu, premenopozal kadın, vitamin D

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INTRODUCTION

Urinary tract infections (UTIs) are one of the most common infectious diseases throughout the world. The annual incidence of people diagnosed with UTIs in the world is approximately 200 million, and this situation causes a significant clinical and economic burden for countries (1). Although it is a significant health problem for all age groups and both sexes, its frequency changes according to sex and age groups (2). UTIs are more commonly seen in women than men, and nearly half of the women will be diagnosed with UTI until the postmenopausal age. This higher incidence can be attributed to the anatomical differences in the urogenital organs of the women and men (3). The other main risk factors for UTIs are sexual intercourse, renal tract anomalies, and use of spermicides (4).

The definition of recurrent UTI can be widely accepted as three UTIs in the last 12 months or two UTIs in the last 6 months (5). The recurrence rate is high after an initial UTI. In a study involving female students aged between 17 and 39 years, the recurrence after a single UTI event in the first 6 months was 27% (6). Evidence from the literature shows that the majority of women with recurrent UTIs have no anatomical abnormalities, and these patients are otherwise healthy individuals (7). Studies showed that recurrent UTIs negatively affect the quality of life and also cause an economic burden due to health care costs of outpatient visits, diagnostic tests, and prescriptions (8, 9). In premenopausal women, risk factors for recurrent UTIs and sporadic UTIs are the same. The frequency of sexual activity and contraceptive usage associated with acute UTIs were also associated with recurrent UTIs. A prior history of UTI is also one of the mostly associated risk factors (10). There are also risk factors that are not well defined in the literature such as body mass index, certain behavioral patterns, and genetic factors (11).

Vitamin D deficiency is a widespread disorder across the world. It affects nearly all age groups, and it is commonly seen in the women at reproductive age, especially in developing countries (12, 13). A meta-analysis from Turkey also revealed a high rate of vitamin D deficiency in the population. In this study, pregnant women and premenopausal women have a higher risk of vitamin D deficiency (14). Vitamin D deficiency is related to a number of inflammatory disorders such as infections, cardiovascular disease, and autoimmune disease (15). There are increasing number of studies that showed the association of vitamin D deficiency with respiratory tract infections, but very few studies investigated the relationship between vitamin D deficiency and recurrent UTIs (16).

In the light of above knowledge, we want to show the effect of vitamin D deficiency on recurrent UTIs in premenopausal women. We want to provide useful information to the current literature on this rarely studied topic.

MATERIALS AND METHODS

Study design

We examined the association between vitamin D and recurrent UTIs in our study. The study was conducted with the case group consisting of premenopausal women with recurrent UTIs and the control group consisting of age-matched premenopausal women without recurrent UTIs. Premenopausal women aged between 18 years or above and 50 years or below with no history of antibiotic prophylaxis for recurrent UTIs were included in the study. Ultrasonography was performed in both the groups to rule out abnormalities of the urinary system. The exclusion criteria were unwillingness to participate in the study, immunosuppression and immunosuppressive drug usage, history of chronic kidney disease (defined as glomerular filtration rate <60 mL/min/1.73 m^2), history of chronic liver disease, history of autoimmune disease, pregnancy, history of malignancy, history of urinary catheter and/or urinary tract stent, urinary incontinence, kidney malformations, history of kidney stones, history of organ transplant, active gynecological problems, history of vitamin D supplementation in the last 1 year. A total of 59 premenopausal patients with recurrent UTIs were recruited in a 1-year period. Age-matched control cases (±5 years) without UTIs were randomly taken into study from internal medicine clinic. We recruited one control patient for each patient with recurrent UTI. We obtained written consent from all the participants. The study approval was taken from the local ethics committee of Erzincan University (December 2018; 35-3).

Data collection

Age, marital status, oral contraceptive usage, history of diabetes mellitus, cigarette smoking, maternal history of recurrent UTIs, routine laboratory analyses, and serum 25(OH)D levels were assessed for all study population. The results of laboratory analyses (urine culture and urine analysis) were evaluated. Liquid chromatography tandem mass spectroscopy was used for detecting 25(OH)D levels (LC–MS, Agilent Technologies).

Definitions

Premenopausal woman was defined as a woman still having either regular or irregular menstrual cycles. UTIs can be presented with clinical signs of cystitis such as dysuria, urgency, and/or frequency of urination; clinical signs of pyelonephritis such as fever, chills, and loan pain; and clinical signs of urosepsis (17). Recurrent UTIs (including relapses and reinfection) are symptomatic UTIs following recovery of a UTI (usually needing treatment) and defined as three UTIs in the last 12 months or two UTIs in the last 6 months (5). All patients in the case group had one or more culture-confirmed UTI to

Table 1. Comparison between two groups in terms of clinical and laboratory parameters

	Premenapasual women with recurrent UTIs (n=59)	Age-matched control group (n=59)	p
Age (years)	32.22±5.26	31.78±5.60	0.661
Diabetes mellitus	10 (16.9%)	9 (15.3%)	0.804
Marital status			0.015
Married	48 (81.4%)	36 (61.0%)	
Single	11 (18.6%)	23 (39.0%)	
Cigarette smoking			0.601
Smoking	11 (18.6%)	13 (22.0%)	
Nonsmoking	48 (81.4%)	46 (78.0%)	
Maternal history of recurrent UTIs	10 (16.9%)	6 (10.2%)	0.286
Oral contraceptive usage	5 (8.5%)	7 (11.9%)	0.546
25(OH)D (ng/mL)	18.97±6.91	22.27±5.21	0.004

25(OH)D: 25-hydroxyvitamin D; UTIs: urinary tract infections.

Table 2. Factors associated with recurrent UTIs in premenopausal women according to logistic regression analysis

		95% confidence interval		
	Odds ratio	Lower	Upper	p
Age (years)	0.994	0.925	1.069	0.881
Marital status (married)	2.668	1.111	6.411	0.028
Vitamin D deficiency	2.581	1.202	5.542	0.015

UTIs: urinary tract infections.

meet this criterion. There is no consensus about the optimal serum 25(OH)D levels. Serum 25(OH)D level <20 ng/mL is accepted as vitamin D deficiency according to most of the experts in this specific area (18, 19). For this reason, patients with a serum 25(OH)D level of <20 ng/mL were defined as patients with vitamin D deficiency, and patients with a serum level of ≥20 ng/mL were identified as patients with normal serum vitamin D levels.

RESULTS

A total of 118 premenopausal women were included in the study according to study criteria. The group with 59 patients with recurrent UTIs was defined as the case group, and the other group of 59 patients with no medical history of UTI was defined as the control group. The mean age of patients was 32.22±5.26 years in the case group and 31.78 ± 5.60 years in the control group (p=0.661). The mean serum 25(OH)D level was 18.97±6.91 ng/mL in the case group and 22.27±5.21 ng/mL in the control group. A statistically significant difference was found between the two groups in terms of marital status (p=0.015) and serum 25(OH)D levels (p=0.004) . Clinical and laboratory parameters of the groups are presented in Table 1.

A logistic regression analysis was used to show independent risk factors for recurrent UTIs. We found that marital status (p=0.028) and vitamin D deficiency (p=0.015) were independent risk factors for recurrent UTIs in premenopausal women. Logistic regression analysis results are shown in Table 2.

DISCUSSION

UTIs are one of the leading causes of bacterial infections, especially in women. Approximately 50%-60% of women will get a UTI at least once during their lifetime. Women in premenopausal age group are more prone to UTIs. In this patient group, recurrence is also common, and half of the patients have had a second infection within a year (21). UTIs are a significant cause of morbidity and can cause a serious sequela such as sepsis and renal damage. They are one of the significant reasons of health care visits and cause a significant economic burden for health care expenses (22). Vitamin D deficiency is also a prevalent disorder across the world, and premenopausal women are one of the mostly affected subgroups for this disorder. Vitamin D promotes the immune system both by increasing immunity against antigens and modulation of

the immune response. Therefore, it also plays a role in the infectious diseases process by potentiating antimicrobial pathways against bacterial, viral, and fungal agents (16). There are studies in the literature showing the relationship between vitamin D deficiency and various infectious disease (23). These studies usually investigated the linkage between vitamin D deficiency and human immunodeficiency virus infection, tuberculosis, sepsis, and upper respiratory tract infections (24). However, when it comes to the linkage between UTIs and vitamin D deficiency, there are very limited number of studies in the literature, and most of these studies were conducted in children (25).

A case-control study (70 children with UTI and 70 healthy children) showed the relationship albetween UTI and serum 25(OH)D levels, and it was concluded that 25(OH) D has a role in the pathogenesis of UTI (26). Another study in children by Shalalby et al. (27) showed that vitamin D deficiency is an independent risk factor for UTI. Tekin et al. (28) also showed the relationship between vitamin D deficiency and UTI in children in a study from Turkey. Also another case-control study comparing 75 healthy children with 75 children with UTI showed that low vitamin D level is a risk factor for UTI (29). In contrast with these studies, a study by Sherkatolabbasieh et al. (30) showed no relationship between vitamin D deficiency and UTI in children. Another study in children investigating the role of vitamin D supplementation on prevention of UTI showed no significant role of vitamin D supplementation (31).

As mentioned above, there are also studies examining the relationship between UTI and vitamin D in other populations other than children, but these are few in number. Kwon et al. (32) founded that vitamin D deficiency was an independent risk factor for UTI after renal transplantation. A study conducted in pregnant women showed that pregnant women with vitamin D deficiency are at increased risk of UTI (33). Ali et al. (34) showed that women at reproductive age with low vitamin D levels are at increased risk for UTI than women with the normal vitamin D levels. Haghighi et al. (35) investigated the relationship between asymptomatic bacteriuria and vitamin D deficiency in premenopausal and postmenopausal women, and they demonstrated that serum vitamin D levels were significantly associated with asymptomatic bacteriuria in both groups of women, but another study in the literature conducted in 385 nursing home residents to evaluate the relationship between bacteriuria and vitamin D deficiency found no association between bacteriuria and serum 25(OH)D levels (36).

In our study, we evaluated one of the mostly affected subgroup for recurrent UTIs. Frequent sexual intercourse is a well-known risk factor for recurrent UTI in women (5). Therefore, we also expected to find a relationship between marital status and recurrent UTIs, and we showed this relationship as consistent with the literature. In the literature, there are also studies that showed that maternal history of recurrent urinary UTIs is also a risk factor for recurrent UTI.[10] However, in our study, we did not find the relationship between maternal history of recurrent UTI and recurrent UTIs in our study population. We also believe that this relationship may be best investigated with the registered data of both mother and daughter by more comprehensive studies. We also found a statistically significant relationship between vitamin D deficiency and recurrent UTIs in premenopausal women. This finding was consistent with the majority of the studies in the literature, although most of them investigated this relationship in children and different groups. A study by Nsei et al. (37), the only study in the literature that specifically investigated the relationship between vitamin D and recurrent UTIs in premenopausal women, found that vitamin D deficiency is associated with recurrent UTIs in premenopausal women, but they did not find a statistically significant relationship between sexual intercourse and recurrent UTIs.

There are several limitations of our study. First, we cannot establish a casual relationship between vitamin D deficiency and recurrent UTIs because of the cross-sectional nature of the study. The relatively small sample size is another limitation of the study, although the sample size is adequate for showing the statistical significance of the relationships. Another limitation of our study may be the using of marital status in spite of a sexual intercourse frequency. Moreover, maternal history of recurrent UTIs is not based on registered laboratory data, and this can cause misinterpretation of the results.

In conclusion, we found a relationship between marital status and recurrent UTIs, as expected. We also found a significant relationship between vitamin D deficiency and recurrent UTIs. However, we believe that this relationship between vitamin D deficiency and recurrent UTIs should be evaluated by more comprehensive studies, especially considering the simplicity of the diagnosis and treatment of vitamin D deficiency.

Ethics Committee Approval: The study approval was taken from the local ethics committee of Erzincan Binali Yıldırım University (December 2018; 35-3).

Informed Consent: Informed consent was obtained for each participant.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.V.K.; Design - A.V.K., A.A.; Supervision - E.K., A.V.K.; Resources - A.V.K., A.A., A.T., Y.S.; Materials - A.A., A.T., Y.S.; Data Collection and/or Processing - A.V.K., A.A., A.T., Y.S.; Analysis and/or Interpretation - E.K., A.V.K.; Literature Search - A.V.K.; Writing Manuscript - A.V.K.; Critical Review - E.K., A.V.K.

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