Hypovitaminosis D leading cause of UTI during the reproductive age of women

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Abstract

Urinary tract infections (UTIs) are extremely common, particularly among reproductive women. While these infections source symptoms, pain, burning through peeing, and an urgent necessity to use the bathroom. UTIs can also come from the urinary bladder to the kidneys and the blood, causing severe complications when they remain untreated. Once women have experienced a single UTI, they are further expected to develop another. Some cases may be developed into chronic urinary tract infections. Many factors may lead to triggers UTIs and make them difficult to treat such as factors related to nutrition particularly well vitamin D deficiency is a wide range problematic. Vitamin D insufficiency leads to numerous health difficulties such as autoimmune diseases, diabetes Mellitus, inflammatory issues, such as increased blood pressure, and tumors. Such vitamin shortage has been predictable by way of a determined deficiency among people, kids, and older individuals in maximum nations. This study highest on the theory that vitamin D deficiency amongst females correlated with the emerging regular UTIs. As females in the generative period have precise anatomical modifications in their urinary tract, category them riskier for the bacterial attack, an existing data was approved to determine positive links bind serum D levels with the urinary tract of females while anticipating the significance of meaningful reasons related to UTI also correspondingly achieved techniques to avoid severe consequences. Numerous females with (patient team) UTIs were distinguished from other healthy (control team). ELISA technic was used to measure Serum 25-hydroxyvitamin D levels. The investigation, as well as evaluation of the data, have occurred of compared groups. Vitamin D average levels in the patient's group remained noticeably lower when compared to the healthy group.

Keywords: Urinary tract infections, Vitamin D, Women, Bacterial attacks

الخلاصة

التهابات المسالك البولية شائعة للغاية ، لا سيما بين النساء الخصبة. في حين أن هذه الالتهابات مصدر الأعراض ، والألم ، والحرقان من خلال التبول ، وضرورة ملحة لاستخدام الحمام. يمكن أن تأتي عدوى المسالك البولية أيضًا من المثانة البولية إلى الكلى والدم ، مما يتسبب في حدوث مضاعفات خطيرة عند عدم علاجها. بمجرد أن تعاني النساء من عدوى المسالك البولية واحدة ، فمن المتوقع أن يصبن بأخرى. قد تتشكل بعض الحالات إلى التهابات المسالك البولية المزمنة. قد تؤدي العديد من العوامل إلى تحفيز عدوى المسالك البولية وتجعل من الصعب علاجها مثل العوامل المتعلقة بالتغذية وخاصة نقص فيتامين (د) الذي يمثل مشكلة واسعة النطاق. يؤدي نقص فيتامين د إلى العديد من الصعوبات الصحية مثل أمراض المناعة الذاتية وداء السكري والعوارض الالتهابية مثل ارتفاع ضغط الدم والأورام. كان نقص الفيتامينات هذا متوقعًا عن طريق نقص محدد بين الناس والأطفال وكبار السن في كثير من الدول. هذه الدراسة هي تاكيد على النظرية القائلة بأن نقص فيتامين (د) بين الإناث مرتبط بالتهاب المسالك البولية المنتظم. نظرًا لأن الإناث في فترة التوليد لديهن تعديلات تشريحية دقيقة في المسالك البولية ، وصنفهن على أنه أكثر خطورة بالنسبة للهجوم البكتيري. وكانت نتائج الدراسة بما يلي تميزت العديد من الإناث المصابات بالتهابات المسالك البولية (فريق المريض) عن غيرهن من الأصحاء (فريق المراقبة). لقياس مستويات مصل 25-هيدروكسي فيتامين د ، وكذلك تقييم البيانات ، لمجموعات مقارنة. فقد وجد نسبة فيتامين (د) في مجموعة المريض أقل بشكل ملحوظ عند مقارنته بالمجموعة السليمة.

Introduction

Insufficiency of vitamin D is a common issue. A wide range of people has vitamin D deficiency because of poor exposure to sunlight [1]. The lack of sunlight and its implication with the overwhelming several diseases due to seasonal variation is noticed in the main circulating profile of vitamin D [2]. Individuals generally at threat of vitamin D shortage include those with lowly sun exposure, inadequate oral consumption, or deteriorated intestinal absorption, Vitamin D competence is superlatively detected by calculation of the 25-hydroxyvitamin D level in the blood [3]. By determining the plasma concentration of vitamin D, the scarcity of this vitamin was identified (Insufficiency is fewer than 10 ng/ml, Satisfactory: 30–70, and possible harmful higher than 70)[4]. Healthy consequences related to 25-hydroxyvitamin D scarcity such as osteoporosis [5], autoimmunity problems, and infections[6]. The latest research demonstrates that the implications of low levels of vitamin D consist of various bacterial infections in the respiratory tract [7] and urinary bladder [8]. Other studies highlight the non-classical roles of vitamin D, additional its impact on bone metabolism, which includes implementing the immune system like cell proliferation, variation as well as immunologic roles [9]. The innate immune is improved via vitamin D, prompting peptide entitled cathelicidin that contributes to bacteriological inhibition. Furthermore, cytokines released from both B and T Cells, and via controlling the infection, vitamin D modifies the immune system [10]. The relationship between vitamin D and infection is unlikely to be limited. The urinary tract is regularly unprotected from possible pathogens and swift defense processes are therefore required. Cathelicidin is activated and released by epithelial cells of the bladder and prevention the urinary system from toxicities [11]. UTIs are a critical health problem that has extraordinary complications since such infections are connected to antimicrobial conflict and threaten life during a lifetime [12].

Aim of the study:

Considering these perspectives, this study aims to highlight the relationship links serum vitamin D3 insufficiency and infections in females' urinary tract during reproductive periods.

Statement of consent

Included random populations of women were submitted both printed and oral information. The informed authorization was achieved from decision-capable individuals.

Case report procedure

There was a prearranged date for the collecting of blood and urine samples from candidates. These samples were gathered on the same day. Moreover, at the same time, nurses recorded age, gender, vitamin D supplementation, temperature, and any new beginning urinary tract signs. Medical inspection, laboratory tests.

Materials and Methods

1. Laboratory tests

1.1Concentrations of vitamin D

At each appointment, blood samples were got from the vein and transferred to a particular tube containing heparin. In three hours of obtaining, blood was centrifuged at 1400 g for a quarter of an hour at 38°C. Sequestered plasma was kept at − 70°C till use. Vitamin D grade will calculate by calculating plasma 25(OH)D, by OCTEIA 25(OH)D ELISA (Immunodiagnostic Systems Ltd, Boldon, Tyne & Wear, UK).

1.2Urine culture

The technical method is defined in detail in earlier published research on bacteriuria linked with interleukin-6 concentrations [13]

Statistical analysis:

Baseline data will be expressed as mean±s.d. For analysis of all hypotheses, tests should be two-tailed and a P value of 0.05 will be considered statistically significant.

3. The outcome

3.1 Urine analysis

For inspection markers of infection, whereas assessing urine exploration, there are numerous elements to anticipate. The hug existence of bacteria in the arena is the maximum shared indicator of microbial contagion. While few bacteria in urine might be normal for the patient have clinical signs, conferring to the description, 5+ is measured to be normal for bacteriuria. Occasionally 2+ is similarly measured positive in people who are required catheterization [14]. The bacterial attack detected by common urine inspection and culturing showed that out of 80 urine samples obtained from the patient group suffering from clinical signs of UTIs, 52 specimens (59.33%) showed bacterial attacks while (25.66%) did not, and pure culture (15%). For positive cultures group showed diverse bacterial sorts were isolated, maximum cases were because of Escherichia coli (Figs. 1,5).

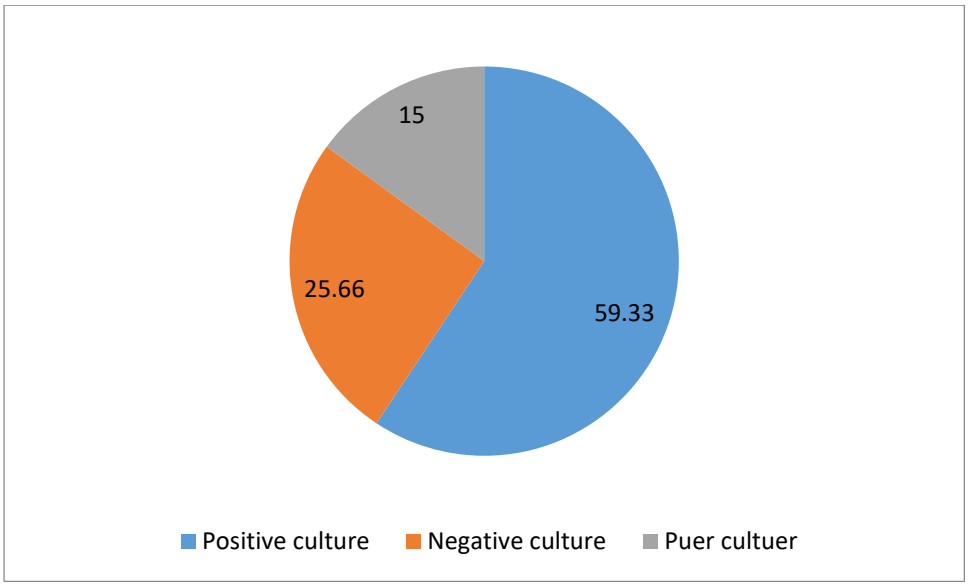


Figure 1 Showed the percentage of positive, and negative cultures and purity of bacterial cultures including the type of bacteria related to gram stain remote from the patient group.

3.2 Measure Vitamin D concentration

Next Renal function examinations and blood tests, the amount of Vitamin D have been measured from blood specimens of the case group, the core emphasis of the current research was Serum 25(OH) range was measured for the case group corresponding to the standard sample. A Vitamin D analysis Kit was chosen to determine the quantity of 25(OH) D in the serum of both compared groups. A serum sample was measured from 80 women, there was a significant decrease amount of Vitamin D ($p < 0.001$) in the serum of the case group in contrast to the standard group (Figure. 3)

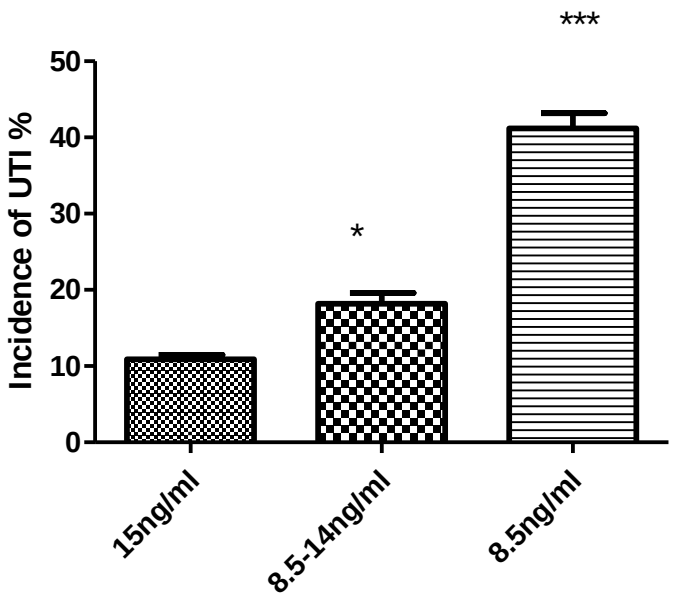


Figure 3. Illustration showed the analysis of vitamin D presented a significantly low level of the vitamins in the patient's serum suffering from UTI.

3.3. Blood parameters and Kidney function measurement

Hemodynamic examination of the blood samples from the groups and calculation comparison of blood parameters such as the whole hemoglobin (HB) and white blood cell count of the groups. According to the graph in (Figure. 4), there is no significant difference between compared groups regards to HB or WBC count. The renal function was also examined the blood urea and creatinine levels were in the standard value for both groups.

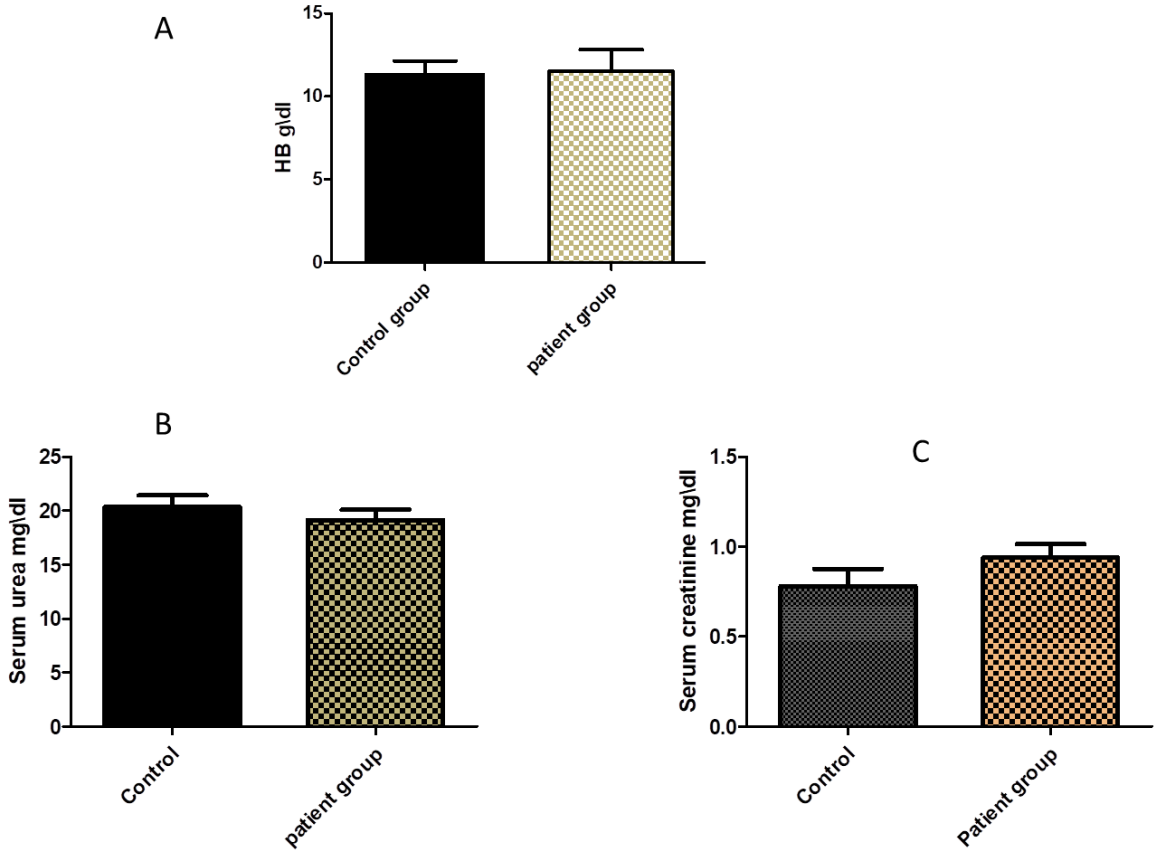
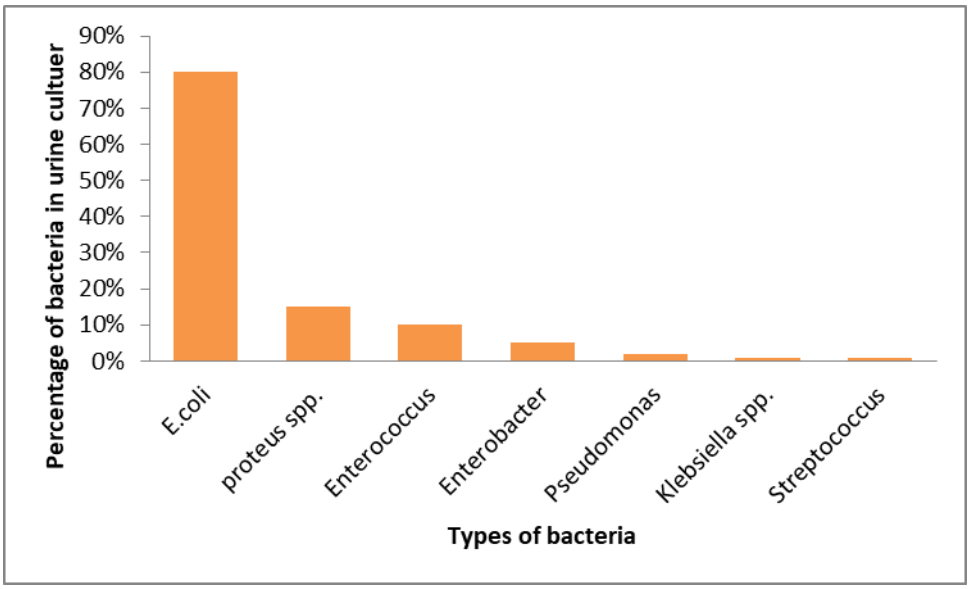


Figure 4 . Expressed blood parameters (A &B), including measurements of Haemoglobin level and WBC between control and patient groups suffering from UIT. Similarly, liver function was measured by calculations of serums creatine and serum urea(C)there were no significant differences between participants groups.

3.4 Bacterial discoveries among populations with vitamin D shortage.

A clean urine specimen is traditionally a procedure for a urine culture. This method targets to avoid bacteria from the vagina contaminating the urine sampling. It's essential to track the clean catch procedure to obtain accurate outcomes from clean samples. Provide a clean catch kit containing a plastic vessel with a lid, a sticker for the patient to write his details on, and a separately enfolded, moist towel or soapy water instead of it. Collect a urine specimen midstream. This suggests that patients must start urinating, then break their flow.

The supreme reason to use a clean catch urine sample is to examine for the urinary tract infection (UTI). Indicators of a UTI contain pain and a continual need to urinate. Urine culture is a step toward a complete diagnosis. This study finds different types of bacteria in cultured urine (Figure 5).



(Figure 5) shows from positive cultures diverse bacterial sort isolated, peak cases were related to Escherichia coli.

Discussion

The outcomes of the present investigation displayed that vitamin D insufficiency in women was connected with UTIs. During the earlier years, numerous studies have provided an augmented suggestion of the role of vitamin D deficiency in deteriorating results and accumulative the vulnerability to infections [10]. Many studies, showed reliable evidence that linked vitamin D deficiencies with UIT[15] . To initiate the immunity system required vitamin D for its heightened role and reaction to contamination or inflammation [16]. As mentioned before the immune system requires vitamin D in the stimulation of WBC and intensification of the septic cells uptake via cytokines, similar cathelicidin is also motivated by vitamin D[16]. This disagreed with our finding (Figure 4) showed no significant difference between patients groups and control regarding WBC and Hb levels. Based on current cultural outcomes, there is a strong relationship linked the power of insufficiency of such vitamins and the culture of urine that contains bacteria, as deficient the patient in vitamin D levels increased the existence of bacterial UTI(Figure1,2), Demonstrating lack of vitamin D as a risk cause for UTI. This agreed with this study's finding, which appeared Escherichia coli was the highest-rated dominant bacteria isolated with a percentage of 80% of UTIs. It is described to be the important cause of UTIs (Figure 5). Numerous barriers alongside immune cells hold different kinds of receptors, including membrane and intracellular receptors, which distinguish diverse microbial antigens. Stimulation of these receptors persuades the production of 1α-hydroxylase, which triggers 25 hydroxyvitamin D to produce intracellular calcitriol. This stimulates its receptor and improves the production of essential human antibiotics comparable to cathelicidin and β2-defensin whereas deterring hepcidin. Latest peptides have the main impact on innate immunity, and peptides control is irregular in hypovitaminosis D. This is confirmed when supplements patients with vitamin D lead to easily recover from UTI(Figure 6). This finding agreed with research by White JH,2022, explaining that calcitriol signaling prompts releasing of antibacterial agents in *vitro* and in *vivo*, and decreased levels flowing of calcifediol are related to varied signs categorized via weakened antibacterial immunity in UTI[17]. Separate cases in Japanese [18] and Mongolian kids displayed a reduced occurrence of UTIs in children supplemented with vitamin D [19]. A trial of this supplementation in young men presented a marginal protective consequence on UTIs [20].

These results disagreed with other researchers showed experimental vitamin D supplementation in the United States in adults [21] and New Zealand[22] failed to demonstrate any therapeutic properties of vitamin D on UTIs. However, a previous study predicted the health-beneficial properties of vitamins in general [23]. Among these, vitamin D supplements showed to lessen numerous diseases, including bacterial infections caused by Mycobacterium tuberculosis [24]. Moreover, 1,25(OH)2-vitamin D expressed to modify cathelicidin antimicrobial peptide in different cells like vascular cells. This peptide can be exciting in most vascular cells. Therefore, additionally to performing as chemo-attractants of further immune cells(25) 1,25(OH)2-vitamin D doing as the key dynamic hormonal formula of vitamin D applies essential elements in innate immunity with comprehensive antimicrobial properties [26].

Conclusion

In assumption, preserving satisfactory vitamin D levels is unique of the most essential fundamentals of women's Healthcare. Consequently, vitamin D is necessary to be supplemented for women with vitamin D inadequacy or shortage throughout pregnancy (27). In this study, similar to our primary supposition, vitamin D deficiency and the presence of UTIs were correlated to each other, confirming vitamin D satisfactory levels act as antibiotics and protection from infections. Further study is required to confirm this outcome on larger sample size.

Conflicts of Interest

The Auther declares no conflicts of interest.

References:

1. Adams JS, Liu PT, Chun R, Modlin RL, Hewison M. Vitamin D in defense of the human immune response. Ann N Y Acad Sci. 2007;1117(1):94–105.
2. Brot C, Vestergaard P, Kolthoff N, Gram J, Hermann AP, Sørensen OH. Vitamin D status and its adequacy in healthy Danish perimenopausal women: relationships to dietary intake, sun exposure and serum parathyroid hormone. Br J Nutr. 2001;86(S1):S97–103.
3. Kennel KA, Drake MT, Hurley DL. Vitamin D deficiency in adults: when to test and how to treat. In: mayo clinic proceedings. Elsevier; 2010. p. 752–8.
4. Hewison M. An update on vitamin D and human immunity. Clin Endocrinol (Oxf). 2012;76(3):315–25.
5. Winzenberg T, Jones G. Vitamin D and bone health in childhood and adolescence. Calcif Tissue Int. 2013;92(2):140–50.
6. Hertting O, Holm Å, Lüthje P, Brauner H, Dyrdak R, Jonasson AF, et al. Vitamin D induction of the human antimicrobial Peptide cathelicidin in the urinary bladder. PLoS One. 2010;5(12):e15580.
7. Laaksi I, Ruohola J-P, Tuohimaa P, Auvinen A, Haataja R, Pihlajamäki H, et al. An association of serum vitamin D concentrations< 40 nmol/L with acute respiratory tract infection in young Finnish men. Am J Clin Nutr. 2007;86(3):714–7.
8. Crescioli C, Morelli A, Adorini L, Ferruzzi P, Luconi M, Vannelli GB, et al. Human bladder as a novel target for vitamin D receptor ligands. J Clin Endocrinol Metab. 2005;90(2):962–72.
9. Keflie TS, Nölle N, Lambert C, Nohr D, Biesalski HK. Impact of the natural resource of UVB on the content of vitamin D2 in oyster mushroom (Pleurotus ostreatus) under subtropical settings. Saudi J Biol Sci. 2019;26(7):1724–30.
10. Holick MF. Vitamin D deficiency. N Engl J Med. 2007;357(3):266–81.
11. Wang T-T, Nestel FP, Bourdeau V, Nagai Y, Wang Q, Liao J, et al. Cutting edge: 1, 25-dihydroxyvitamin D3 is a direct inducer of antimicrobial peptide gene expression. J Immunol. 2004;173(5):2909–12.
12. LeFevre M. Urinary tract infections during pregnancy. Am Fam Physician. 2000;61(3):713–20.
13. Sundvall P-D, Elm M, Ulleryd P, Mölstad S, Rodhe N, Jonsson L, et al. Interleukin-6 concentrations in the urine and dipstick analyses were related to bacteriuria but not symptoms in the elderly: a cross sectional study of 421 nursing home residents. BMC Geriatr. 2014;14(1):1–9.

14. Alqasim A, Jaffal AA, Alyousef AA. Prevalence and molecular characteristics of sequence type 131 clone among clinical uropathogenic Escherichia coli isolates in Riyadh, Saudi Arabia. Saudi J Biol Sci. 2020;27(1):296–302.

15. Lane DR, Takhar SS. Diagnosis and management of urinary tract infection and pyelonephritis. Emerg Med Clin. 2011;29(3):539–52.

16. van Etten E, Mathieu C. Immunoregulation by 1, 25-dihydroxyvitamin D3: basic concepts. J Steroid Biochem Mol Biol. 2005;97(1–2):93–101.

17. White JH. Emerging Roles of Vitamin D-Induced Antimicrobial Peptides in Antiviral Innate Immunity. Nutrients. 2022;14(2):284.

18. Urashima M, Segawa T, Okazaki M, Kurihara M, Wada Y, Ida H. Randomized trial of vitamin D supplementation to prevent seasonal influenza A in schoolchildren. Am J Clin Nutr. 2010;91(5):1255–60.

19. Camargo CA, Ganmaa D, Frazier AL, Kirchberg FF, Stuart JJ, Kleinman K, et al. Randomized trial of vitamin D supplementation and risk of acute respiratory infection in Mongolia. Pediatrics. 2012;130(3):e561–7.

20. Laaksi I, Ruohola J-P, Mattila V, Auvinen A, Ylikomi T, Pihlajamäki H. Vitamin D supplementation for the prevention of acute respiratory tract infection: a randomized, double-blinded trial among young Finnish men. J Infect Dis. 2010;202(5):809–14.

21. Li-Ng M, Aloia JF, Pollack S, Cunha BA, Mikhail M, Yeh J, et al. A randomized controlled trial of vitamin D3 supplementation for the prevention of symptomatic upper respiratory tract infections. Epidemiol Infect. 2009;137(10):1396–404.

22. Murdoch DR, Slow S, Chambers ST, Jennings LC, Stewart AW, Priest PC, et al. Effect of vitamin D3 supplementation on upper respiratory tract infections in healthy adults: the VIDARIS randomized controlled trial. Jama. 2012;308(13):1333–9.

23. Blaszczak W, Barczak W, Masternak J, Kopczyński P, Zhitkovich A, Rubiś B. Vitamin C as a Modulator of the Response to Cancer Therapy. Molecules. 2019;24(3):453.

24. Tukvadze N, Sanikidze E, Kipiani M, Hebbar G, Easley KA, Shenvi N, et al. High-dose vitamin D3 in adults with pulmonary tuberculosis: a double-blind randomized controlled trial. Am J Clin Nutr. 2015;102(5):1059–69.

25. DeLuca HF. Vitamin D: the vitamin and the hormone. In: Federation proceedings. 1974. p. 2211–9.

26. Bah SY, Dickinson P, Forster T, Kampmann B, Ghazal P. Immune oxysterols: Role in mycobacterial infection and inflammation. J Steroid Biochem Mol Biol. 2017;169:152–63.

27. Owens NJ. Vitamin D supplementation for women during pregnancy: Summary of a Cochrane review. Explor (New York, NY). 2019;16(1):73–4.