J Ped Nephrol
Journal of Pediatric Nephrology
2024. Volume 12

Research Paper

The Relationship Between Serum Vitamin D3 Levels and Recurrent Urinary Tract Infection in Children Aged 2-15 Years

Elham Emami[1], Atrin Oroojeni[2], Maryam Mansouri[3*]

1. Department of Pediatrics, Faculty of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran.
2. Department of Pediatrics, Faculty of Medicine, Jundishapur University of Medical Sciences, Ahvaz, Iran.
3. Faculty of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran.

Use your device to scan and read the article online

Citation Emami E, Oroojeni A, Mansouri M. The Relationship Between Serum Vitamin D3 Levels and Recurrent Urinary Tract Infection in Children Aged 2-15 Years. Journal of Pediatric Nephrology. 2024; 12:E48523. http://dx.doi.org/10.22037/jpn.v12i1.48523

http://dx.doi.org/10.22037/jpn.v12i1.48523

Article info:
Received: 13 January 2024
Accepted: 10 Mar 2024
Publish: 24 Apr 2024

Corresponding Author:
Maryam Mansouri
Address: Faculty of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran.
E-mail: mansoori888@yahoo.com

ABSTRACT

Background and Aim: Urinary tract infection (UTI) is one of the most common infectious diseases in children, which may cause certain complications, such as growth disorders, hypertension, proteinuria, and chronic kidney failure. In addition to vitamin D's vital role in bone formation, it also contributes to the functioning of the immune system, and its low levels are associated with increased susceptibility to infections. Given the role of vitamin D in regulating the immune system, the present study was conducted to investigate the relationship between serum vitamin D levels and recurrent UTI in children.

Methods: In this cross-sectional study, 90 children aged 2-15 years who were referred to the Pediatrics Department of Hajar Hospital, Shahrekord, in 2022 were included and divided into two groups: Cases (with UTI) and controls (not suffering from UTI). Children's information was recorded and blood samples were collected to measure 25-hydroxyvitamin D3 levels. Data were analyzed using SPSS.

Results: The groups showed no significant difference in age and gender (P>0.05). The groups showed a significant difference in the frequency of serum vitamin D levels (P<0.0001); vitamin D deficiency and insufficiency were more common in children with UTI compared to those without UTI (24.4% and 48.9% vs 8.9% and 15.6%, respectively).

Conclusion: Vitamin D deficiency is correlated with UTI in children, and its supplements are a low-risk treatment of choice to prevent UTI.

Keywords: Urinary Tract Infection (UTI), 25-Hydroxyvitamin D3, Vitamin D deficiency

Copyright © 2024 The Author(s);
This is an open access article distributed under the terms of the Creative Commons Attribution License (CC-By-NC: https://creativecommons.org/licenses/by-nc/4.0/legalcode.en), which permits use, distribution, and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

J Ped Nephrol
Journal of Pediatric Nephrology

Introduction

Urinary tract infection (UTI) is the second leading bacterial disease in children after upper respiratory tract infections, and the most common bacterial infection that affects humans throughout life. UTI refers to the presence of more than 100,000 colony-forming units (CFU)/mL in culture medium; however, recent studies have revealed that clinical urinary system infection can occur with the presence of less than 105 CFU/mL [1, 2]. Children with UTI are predisposed to complications, such as growth disorder, arterial hypertension, proteinuria, and chronic kidney failure. UTI imposes a substantial economic burden on the healthcare system [3-5]. The prevalence of UTI in children varies depending on age, gender, race, circumcision, and the presence of fever. UTIs in children are primarily caused by gram-negative coliform bacteria that originate from fecal flora, which colonize the perineum and ascend into the urinary tract. *Escherichia coli* is the most prevalent uropathogen associated with UTIs in children, accounting for approximately 80% of cases [6-11]. The incidence of UTIs is higher in females and uncircumcised male infants [6-8]. Other common uropathogens include *Klebsiella*, *Proteus*, *Enterobacter*, and *Enterococcus* species. Five percent of the main infections are caused by gram-positive bacteria, including staphylococcus *saprophyticus* and *Enterococcus* species [12, 13].

Probiotics may serve as an alternative therapy for children at risk of developing UTIs. As non-pharmaceutical options, they could be utilized as natural preventive measures against UTIs. However, the existing published evidence does not conclusively demonstrate that probiotics effectively protect against urinary bacterial infections. Therefore, there is a need for large-scale randomized clinical trials to explore the potential prophylactic benefits of probiotics [14].

Vitamin D comprises a group of fat-soluble secosteroids that play a crucial role in the intestinal absorption of calcium, the regulation of serum calcium and phosphate levels, and various other biological functions [15, 16]. It is vital for bone growth and regeneration, and it also contributes to immune system function and neuromuscular activity [17]. There are two physiological forms of vitamin D, commonly referred to as calciferol: Vitamin D2 (ergocalciferol) and vitamin D_3 (cholecalciferol) [18-20]. Following transcription and translation, proteins, such as osteocalcin or calcium-binding protein, are produced, the latter of which causes calcium to be absorbed from the intestine. 1,25-dihydroxyvitamin D_3 [$1,25(OH)_2D$] production is stimulated by parathyroid hormone and decreased by calcium [21].

25-hydroxyvitamin D_3[25(OH)D] levels of less than 30 ng/dL are considered vitamin D insufficiency, which is mostly asymptomatic, and the levels less than 10 ng/dL are considered vitamin D deficiency [17, 22]. Around one billion people worldwide have vitamin D deficiency or insufficiency [23]. Studies conducted in Iran have shown that 70-50% of Iranian adults suffer from vitamin D deficiency in varying degrees [24]. A study of children and adolescents in the United States has shown that 9% of the pediatric population (7.6 million children and adolescents) suffer from vitamin D deficiency, and 61% (50.8 million children and adolescents) have insufficient vitamin D levels [25]. In a meta-analysis, the prevalence of vitamin D deficiency in Iranian boys and girls was found to be 35% and 61%, respectively, and vitamin D insufficiency in them was reported as being 31% [26].

Data from various sources indicate that vitamin D has a wide range of actions against autoimmune diseases and infections, including tuberculosis, respiratory tract infections, asthma, and atopic dermatitis [27, 28]. Vitamin D receptors have known direct effects on innate and adaptive immunity [29, 30]. During a bacterial infection, macrophages convert circulating 25(OH) D into $1,25(OH)_2D$, which induces the expression of the gene encoding the antibacterial peptide, which plays a crucial role in the body's defense against pathogens by enhancing the immune response and clearing bacteria from defense barriers and immune cells [31, 32]. Vitamin D also stimulates the production of endogenous antimicrobial peptides, cathelicidin and beta-defensin-2, which are expressed in the urinary tract and are important for preventing UTIs [33]. In this regard, a study has shown that recurrent UTI is related to vitamin D deficiency in postmenopausal women [34]. Additionally, the vitamin D receptor gene polymorphism has been identified as a significant factor in the predisposition to UTIs in children [35]. However, a study involving children aged 6 months to 5 years with UTIs found that while the vitamin D levels were lower in affected children compared to healthy children, the difference was not statistically significant [36]. Therefore, it is necessary to investigate this subject across different age groups and with larger sample sizes to achieve more definitive evidence.

In the Middle East and Asia, poverty of micronutrients and vitamins, especially vitamin D, is very common due to improper diet and the loss of these substances during recurrent infections. It is estimated that approximately 70% of the Iranian population suffers from vitamin D

deficiency, and it has been reported that the rate of the deficiency is 61% in girls and 35% in boys among children and adolescents. Therefore, we investigated the serum vitamin D levels and their relationship with recurrent UTI in pediatrics. According to a systematic review in 2018, the vitamin D deficiency prevalence in Iranian boys and girls was respectively 35% and 61%. The overall rate of vitamin D insufficiency among Iranian adolescents and children is 31%. Common symptoms include feelings of depression, bone pain, muscle weakness or cramps, and fatigue. Vitamin D deficiency can lead to rickets in children and infants, a condition characterized by weak, thin, and deformed bones.

Materials and Methods

This case-control study was conducted on 90 children aged 2-15 years after obtaining the necessary approvals from the Vice-chancellor for Research and Technology and Ethics Committee of Shahrekord University of Medical Sciences. The sample size was calculated at 45 individuals for each group, taking into account the error level of 0.01, test power of 90%, and vitamin D levels of 24.8±45.9 ng/mL in children with UTI [36], along with a clinically significant change of 15 units for vitamin D. Participants were selected using convenience sampling. To this end, children admitted to the Pediatrics Department of Hajar Hospital, Shahrekord, in 2022 were visited by a pediatrician, and 45 children diagnosed with recurrent UTI were enrolled in the study (case group). Additionally, 45 healthy children without recurrent UTI were also selected as controls.

Because no relationship between the season and vitamin D deficiency has yet been established, no specific season was selected to conduct the present study [37]. First, the purpose and procedure of the study were fully explained to the parents of the patients, and then the patients who met the inclusion criteria and whose parents provided consent were enrolled in the study. The parents of the children were also provided with explanations about the possible results and significance of the study.

The inclusion criteria included an age range of 2 to 15 years and a diagnosis of recurrent UTI. Exclusion criteria encompassed detectable underlying factors for UTI, such as vesicoureteral reflux, kidney stones, hydronephrosis, chronic diseases, and the receipt of vitamin D at a therapeutic dose. Then, the patients' medical files were studied to record their demographic information, medication status, history of imaging, and history of bladder stones and urinary reflux using a checklist. In addition, 1.5 mL of blood was collected from all participants in clot tubes with no anticoagulant. The samples were transferred to the laboratory while maintaining the cold chain, and after centrifugation and serum separation, they were stored in a freezer at -20 ˚C until further testing. Vitamin D levels were measured using an enzyme-linked immunosorbent assay (ELISA) Diaplus kit. Two milliliters of fasting venous blood were also collected from the participants in the Laboratory of the Faculty and after centrifugation, the resulting serum was divided and stored at -25 ˚C until subsequent measurements. Serum 25(OH)D levels were measured using an ELISA kit (EUROIMMUN, Germany) and an ELISA reader (Fax Stat Awareness, USA). The detection limit for 25(OH)D was set at 5.9 ng/mL. According to the manufacturer's instructions, the serum 25(OH)D status was classified as follows: Less than 10 ng/mL=extremely severe deficiency, 10-20 ng/mL=severe deficiency, 20-30 ng/mL=deficiency, and 30-100 ng/mL=optimal level.

The results were analyzed by the chi-square and independent t-test using SPSS software, version 20. Significance level (P) was considered to be <0.05, and the results were expressed as Mean±SEM.

Results

A total of 90 children referred to the Pediatrics Department of Hajar Hospital, Shahrekord, in 2022 were enrolled and divided into two groups of 45 cases (with UTI) and controls (not suffering from UTI). The mean age of the children was 6.60±3.88 years, and 42(46.7%) of them were girls. Serum vitamin D levels were measured as follows: Less than 10 ng/dL in 15(16.7%) individuals, 10-20 ng/dL in 29(32.2%), 25-30 ng/dL in 11(12.2%), and 30-100 ng/dL in 35(38.9%) (Table 1).

The mean age in the case and control groups was 7.09 and 6.11 years, respectively, with no statistically significant difference (P>0.05, Table 2). Also, there was no statistically significant difference in gender between cases and controls (P>0.05, Table 3).

The results of the vitamin D level measurements are presented in Table 4. Children with UTI had a higher prevalence of vitamin D deficiency (>10 ng/dL) compared to controls. Among our participants, 24.4% of those with UTI had vitamin D deficiency, while the rate of vitamin D deficiency in the control group was 8.9%. Vitamin D insufficiency (10-20 ng/dL) was also more prevalent in children with UTI than in controls, with 48.9% of children with UTI exhibiting vitamin D insufficiency, compared to 15.6% in the control group. A statistically significant difference was observed in serum

J Ped Nephrol
Journal of Pediatric Nephrology

Table 1. Frequency distribution of the studied variables in participants

Variables	Level	No. (%)
UTI	No	45(50)
	Yes	45(50)
Gender	Female	42(46.7)
	Male	48(53.3)
Vitamin D (ng/dL)	10>	15(16.7)
	10-20	29(32.2)
	20-30	11(12.2)
	30-100	35(38.9)

Table 2. Comparison of the mean age of cases (with UTI) and controls (without UTI)

Variable	Mean±SEM		P
	UTI		
	No	Yes	
Age (y)	7.09±3.99	6.11±3.75	0.811

vitamin D levels between the two groups (P<0.0001). This indicates that serum vitamin D status was associated with UTI, with vitamin D deficiency and insufficiency being more common in children with UTI than in controls.

Discussion

This study aimed to investigate the relationship between serum vitamin D_3 levels and recurrent UTI in children aged 2-15 years. For this purpose, 90 children referred to the Pediatrics Department of Hajar Hospital in Shahrekord in 2022 were enrolled in the study and subsequently divided into two groups: 45 cases (with UTI) and 45 controls (without UTI). No significant difference was detected in gender and average age between children with and without UTI. There was a significant difference in the frequency of serum vitamin D status between the two groups, indicating that vitamin D deficiency (less than 10 ng/mL) and insufficiency (less than 20 ng/mL) were more prevalent in children with UTI than in healthy children. Similar results have already been reported by Mahmoudzadeh et al.; in their study, vitamin D levels below 20 ng/mL were significantly more frequent in children with UTI than in the control group [38]. Our findings are also in line with another study performed in Egypt by Shalaby et al. In their study involving children aged 2 months to 6 years, Shalaby et al. observed a significant difference in serum vi-

Table 3. Comparison of frequency distribution of gender in cases (with UTI) and controls (without UTI)

Variable	Category	No. (%)		p
		UTI		
		No	Yes	
Gender	Female	17(37.8)	25(55.6)	0.139
	Male	28(62.2)	20(44.4)	
	Total	45(100)	45 (100)	

Table 4. Comparison of frequency distribution of serum vitamin d levels in cases (with UTI) and controls (without UTI)

Variable	Level	No. (%)		p
		UTI		
		No	Yes	
Vitamin D (ng/dL)	10>	4(8.9)	11(24.4)	0.0001
	10-20	7(15.6)	22(48.9)	
	20-30	7(15.6)	4(8.9)	
	30-100	27(60)	8(17.8)	
	Total	45(100)	45(100)	

tamin D levels between children with and without UTI. Their findings also showed that a vitamin D level of ≤25 nmol/l was associated with UTI (OR=1.94) [39]. A study conducted in China by Yang et al. involving 132 infants aged 1-12 months with their first UTI and 106 healthy infants (controls) indicated that serum vitamin D levels were markedly lower in children with UTI than in the controls. In addition, the incidence of UTI was lower in infants who received vitamin D supplementation compared to those who did not [40]. Chidambaram et al. in a study on children with and without UTI, observed that the mean serum vitamin D levels were significantly different between the two groups, and vitamin deficiency was more frequent in children with UTI compared to those without UTI (41.5% vs 2.2%) [41]. Other studies by Becerra-Loaiza et al. on children and adults with and without UTI have also shown a significant association between vitamin D receptor gene polymorphism and UTI [42, 43].

The findings mentioned above have been corroborated by systematic reviews and meta-analyses. A systematic review and meta-analysis by Deng et al. showed a significant relationship between UTI and vitamin D deficiency in children (OR=4.78) [43, 44]. Another systematic review and meta-analysis on six studies (including a total of 339 UTI cases and 306 healthy controls) showed that serum vitamin D levels were significantly lower in children with UTI than in healthy controls [45]. A meta-analysis conducted in 2023, encompassing 13 studies with a total of 839 UTI cases and 929 controls, yielded similar results. It was found that children with UTI had lower levels of vitamin D compared to healthy children, and those with serum vitamin D levels below 20 ng/mL were 5.49 times more likely to acquire UTI than children with sufficient vitamin D levels [46].

Inconsistent with the aforementioned studies, some research has not found a significant relationship between vitamin D deficiency and UTI. For example, in the study by Javadi Nia et al. on children aged 6 months to 5 years with UTI, despite the lower levels of vitamin D in children with UTI compared to the control group, no significant difference was observed [26]. Similarly, in the study by Sherkatolabbasieh et al. which included 44 children with UTI and 214 healthy children, no significant relationship was found between serum vitamin D levels and UTI acquisition [46, 47]. The inconsistency in the findings of these studies and the present study may be attributed to various factors, such as demographic differences, variations in the sample size of the case and control groups, and differing cutoff points for vitamin D deficiency.

It has been suggested that the positive impact of vitamin D in preventing infections, including UTIs, is associated with the production of antibacterial peptides like cathelicidin and beta-defensin, the regulation of cytokine production, and the reduction of inflammation [48]. In the case of vitamin D deficiency, macrophages infected with bacterial pathogens are unable to provide sufficient antibacterial peptides [49]. A study in Turkey on 38 healthy children and 36 children with UTI showed that in patients with vitamin D deficiency, urinary cathelicidin levels decrease during infection, suggesting that vitamin D prevents the occurrence of UTI by enhancing cathelicidin production [48]. In research on infants and children with UTI, Georgieva et al. (2019) found that serum vitamin D levels were directly correlated with cat-

helicidin levels, but not with beta-defensin-2 levels [33]. In the study by Hertting et al., a 3-month vitamin D-enriched diet did not significantly affect the amount of cathelicidin produced by the bladder tissue; however, when bladder biopsy tissue was infected with uropathogenic *E. coli*, the tissue treated with vitamin D produced higher levels of cathelicidin. It was thus suggested that vitamin D enhances antibacterial activity and could serve as a complementary treatment for UTI [29]. In addition to its role in innate immunity (macrophages), vitamin D also modulates adaptive immunity (lymphocytes), which can significantly reduce inflammation and the risk of autoimmune diseases. Specific genes targeting $1,25(OH)_2D$ in mature T helper cells have been identified [31]. Furthermore, hypocalcemia induced by vitamin D deficiency impairs the function of lymphocytes and neutrophils, which is associated with an increased susceptibility to infections [49].

The results of the present study showed that serum vitamin D levels were related to UTI, with vitamin D deficiency and insufficiency being more prevalent in children with UTI than in controls. However, this study had certain limitations, such as a small sample size and a case-control, cross-sectional design, which meant that vitamin D concentrations were measured after the children had acquired UTIs. This makes it difficult to draw causal conclusions, as it has been argued that vitamin D deficiency not only can be a cause of chronic inflammation but can also be a consequence of it [46]. Therefore, prospective studies with larger sample sizes are needed to better elucidate the association between serum vitamin D levels and UTI. Another important point to address is the role of vitamin D supplementation, including dosage and duration of treatment, in preventing and treating UTI. Low levels of vitamin D are associated with a higher risk of recurrent UTIs, particularly in children, due to Vitamin D's anti-inflammatory, immune-protective, and anti-infectious properties [49].

Conclusion

Our results showed that serum vitamin D levels were associated with UTI, with vitamin D deficiency being more prevalent in children with UTI than in controls. Therefore, vitamin D supplementation could be a low-risk option for preventing UTI. Although we did not include complicated UTIs, such as those involving neurogenic bladder, we suggest that vitamin D supplementation may help prevent the recurrence of UTIs in complicated cases. In patients with reflux nephropathy, vitamin D deficiency can also lead to recurrent UTIs. While the evidence suggests that vitamin D deficiency is a risk factor for UTIs, more interventional studies are needed to confirm whether vitamin D supplementation can effectively prevent recurrent UTIs.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Research Ethics Committee of Shahrekord University of Medical Sciences, Shahrekord, Iran (Code: IR.SKUMS.MED.REC.1401.003).

Funding

This study was supported by Shahrekord University of Medical Sciences, Shahrekord, Iran (Grant No.: 315844).

Authors' contributions

All authors contributed equally to the conception and design of the study, data collection and analysis, interpretation of the results, and drafting of the manuscript. Each author approved the final version of the manuscript for submission.

Conflict of interest

The authors declared no conflict of interest.

References

[1] Cheng YW, Wong SN. Diagnosing symptomatic urinary tract infections in infants by catheter urine culture. J Paediatr Child Health. 2005; 41(8):437-40. [DOI:10.1111/j.1440-1754.2005.00662.x] [PMID]

[2] Bonadio M, Meini M, Spitaleri P, Gigli C. Current microbiological and clinical aspects of urinary tract infections. Eur Urol. 2001; 40(4):439-45. [DOI:10.1159/000049813] [PMID]

[3] Chang SL, Shortliffe LD. Pediatric urinary tract infections. Pediatr Clin. 2006; 53(3):379-400. [DOI:10.1016/j.pcl.2006.02.011] [PMID]

[4] Vachvanichsanong P. Urinary tract infection: one lingering effect of childhood kidney diseases--review of the literature. Children. 2007; 9:17. [PMID]

[5] Mattoo TK, Shaikh N, Nelson CP. Contemporary management of urinary tract infection in children. Pediatrics. 2021; 147(2):e2020012138. [DOI:10.1542/peds.2020-012138] [PMID]

[6] Stein R, Dogan HS, Hoebeke P, Kočvara R, Nijman RJ, Radmayr C, et al. Urinary tract infections in children: EAU/ESPU guidelines. 2015; 67(3):546-58. [DOI:10.1016/j.eururo.2014.11.007] [PMID]

[7] Habib S. Highlights for management of a child with a urinary tract infection. Int J Pediatr. 2012; ;2012:943653. [DOI:10.1155/2012/943653] [PMID]

[8] Rushton HG. Urinary tract infections in children: Epidemiology, evaluation, and management. Pediatr Clin North Am. 1997; 44(5):1133-69. [DOI:10.1016/S0031-3955(05)70551-4] [PMID]

[9] Zagaglia C, Ammendolia MG, Maurizi L, Nicoletti M, Longhi C. Urinary tract infections caused by uropathogenic Escherichia coli strains-new strategies for an old pathogen. Microorganisms. 2022; 10(7):1425. [DOI:10.3390/microorganisms10071425] [PMID]

[10] Hilbert DW. Uropathogenic Escherichia coli: The pre-eminent urinary tract infection pathogen. In: ROGERS MC, Peterson ND, editor. E coli infections: causes, treatment and prevention. Hauppauge: Nova Science Publishers; 2011. [Link]

[11] Ejrnæs K. Bacterial characteristics of importance for recurrent urinary tract infections caused by Escherichia coli. Dan Med Bull. 2011; 58(4):B4187. [PMID]

[12] Chon CH, Lai FC, Shortliffe LMD. Pediatric urinary tract infections. Pediatr Clin North Am. 2001; 48(6):1441-59. [DOI:10.1016/S0031-3955(05)70385-0] [PMID]

[13] Dougnon V, Assogba P, Anago E, Déguénon E, Dapuliga C, Agbankpè J, et al. Enterobacteria responsible for urinary infections: A review about pathogenicity, virulence factors and epidemiology. J Appl Biol Biotechy. 2020; 8(1):117-24. [DOI:10.7324/JABB.2020.80118]

[14] Emami E, Mt Sherwin C, Heidari-Soureshjani S. Effect of probiotics on urinary tract infections in children: A systematic review and meta-analysis 2024: 19(1):111-121 [DOI: 10.2174/2772432817666220501114505] [PMID]

[15] Holick MF. Vitamin D deficiency. New England J Med. 2007; 357(3):266-81. [DOI:10.1056/NEJMra070553] [PMID]

[16] Norman AW, Roth J, Orci L. The vitamin D endocrine system: steroid metabolism, hormone receptors, and biological response (calcium binding proteins). Endocr Rev. 1982; 3(4):331-66. [DOI:10.1210/edrv-3-4-331] [PMID]

[17] Cashman KD, Dowling KG, Škrabáková Z, Gonzalez-Gross M, Valtueña J, De Henauw S, et al. Vitamin D deficiency in Europe: Pandemic? Am J Clin Nutr. 2016; 103(4):1033-44. [DOI:10.3945/ajcn.115.120873] [PMID]

[18] Rafeeq H, Ahmad S, Tareen MBK, Shahzad KA, Bashir A, Jabeen R, et al. Biochemistry of fat soluble vitamins, sources, biochemical functions and toxicity. Haya Saudi J Life Sci. 2020; 5(6):188-96. [DOI:10.36348/sjls.2020.v05i09.007]

[19] Wimalawansa S. Biology of vitamin D. J Steroids Horm Sci. 2019; 10(198):2. [Link]

[20] Saponaro F, Saba A, Zucchi R. An update on vitamin D metabolism. Int J Mol Sci. 2020; 21(18):6573. [DOI:10.3390/ijms21186573] [PMID]

[21] Wimalawansa S. Vitamin D: What clinicians need to know. Sri Lanka J Diabetes Endocrin Metab. 2012; 2(2). [DOI:10.4038/sjdem.v2i2.4776]

[22] Bikle DD. Vitamin D and bone. Handbook of nutrition and diet in therapy of bone diseases: Wageningen Academic Publishers; 2016. p. 2063-8. [DOI:10.3920/978-90-8686-823-0_9]

[23] Heshmat R, Mohammad K, Majdzadeh S, Forouzanfar M, Bahrami A, Ranjbar Omrani G. Vitamin D deficiency in Iran: A multi-center study among different urban areas. Iran J Public Health. 2008; 37(1):72-8. [Link]

[24] Kumar J, Muntner P, Kaskel FJ, Hailpern SM, Melamed ML. Prevalence and associations of 25-hydroxyvitamin D deficiency in US children: NHANES 2001-2004. Pediatrics. 2009; 124(3):e362-70. [DOI:10.1542/peds.2009-0051] [PMID]

[25] Jazayeri M, Moradi Y, Rasti A, Nakhjavani M, Kamali M, Baradaran HR. Prevalence of vitamin D deficiency in healthy Iranian children: A systematic review and meta-analysis. Med j Islamic Republic of Iran. 2018; 32(3):83-91. [DOI:10.14196/mjiri.32.83] [PMID]

[26] Chang SW, Lee HC. Vitamin D and health-the missing vitamin in humans. Pediatr Neonatol. 2019; 60(3):237-44. [DOI:10.1016/j.pedneo.2019.04.007] [PMID]

[27] Hosseininejad N, Kalbasi Z, Afshar J. [Vitamin D and childhood pneumonia (Persian)]. Razi J Med Sci. 2016; 22(140):109-16. [Link]

[28] Youssef DA, Miller CW, El-Abbassi AM, Cutchins DC, Cutchins C, Grant WB, et al. Antimicrobial implications of vitamin D. Dermato-endocrinol. 2011; 3(4):220-9. [DOI:10.4161/derm.3.4.15027] [PMID]

[29] Gombart AF. The vitamin D-antimicrobial peptide pathway and its role in protection against infection. Future Microbiol. 2009; 4(9):1151-65. [DOI:10.2217/fmb.09.87] [PMID]

[30] Adams JS, Hewison M. Unexpected actions of vitamin D: New perspectives on the regulation of innate and adaptive immunity. Nat Rev Endocrinol. 2008; 4(2):80-90. [DOI:10.1038/ncpendmet0716] [PMID]

[31] Nelson CD, Reinhardt TA, Beitz DC, Lippolis JD. In vivo activation of the intracrine vitamin D pathway in innate immune cells and mammary tissue during a bacterial infection. PloS One. 2010; 5(11):e15469. [DOI:10.1371/journal.pone.0015469] [PMID]

[32] Georgieva V, Kamolvit W, Herthelius M, Lüthje P, Brauner A, Chromek M. Association between vitamin D, antimicrobial peptides and urinary tract infection in infants and young children. Act Paediatr. 2019; 108(3):551-6. [DOI:10.1111/apa.14499] [PMID]

[33] Nseir W, Taha M, Nemarny H, Mograbi J. The association between serum levels of vitamin D and recurrent urinary tract infections in premenopausal women. Int J Infect Dis. 2013; 17(12):1121-4. [DOI:10.1016/j.ijid.2013.06.007] [PMID]

[34] Aslan S, Akil I, Aslan G, Onay H, Ozyurt BC, Ozkinay F. Vitamin D receptor gene polymorphism in children with urinary tract infection. Pediatr Nephrol. 2012; 27:417-21. [DOI:10.1007/s00467-011-2000-0] [PMID]

[35] Javadi Nia S, Noorbakhsh S, Izadi A, Tabatabaei A, Shokrollahi MR. [Comparison of vitamin A, D & zinc serum levels between children with urinary tract infection and control group in two university hospital (Persian)]. Tehran Uni Med J. 2013; 71(4):22-33. [Link]

[36] Aldrees T, Alohali S, Albosaily A, Almatrafi S, Aldhahri S. Seasonal variations in serum levels of vitamin D and other biochemical markers among KSA patients prior to thyroid surgery. J Taibah Univ Med Sci. 2020; 15(6):522-8. [DOI:10.1016/j.jtumed.2020.08.006] [PMID]

J Ped Nephrol
Journal of Pediatric Nephrology

[37] Mahmoudzadeh H, Nikibakhsh AA, Pashapour S, Ghasemnejad-Berenji M. Relationship between low serum vitamin D status and urinary tract infection in children: A case-control study. Paediatr Child Health. 2020; 40(3):181-5. [DOI:10.1080/20469047.2020.1771244] [PMID]

[38] Shalaby SA, Handoka NM, Amin RE. Vitamin D deficiency is associated with urinary tract infection in children. Arch Med Sci. 2018; 14(1):115-21. [DOI:10.5114/aoms.2016.63262] [PMID]

[39] Yang J, Chen G, Wang D, Chen M, Xing C, Wang B. Low serum 25-hydroxyvitamin D level and risk of urinary tract infection in infants. Medicine (Baltimore). 2016; 95(27). [DOI:10.1097/MD.0000000000004137] [PMID]

[40] Tekin M, Konca C, Celik V, Almis H, Kahramaner Z, Erdemir A, et al. The association between vitamin D levels and urinary tract infection in children. Horm Res Paediatr. 2015; 83(3):198-203. [DOI:10.1159/000370046] [PMID]

[41] Chidambaram S, Pasupathy U, Geminiganesan S, Divya R, Pasupathy Sr U. The association between vitamin D and urinary tract infection in children: A case-control study. Cureus. 2022; 14(5):33-44. [DOI:10.7759/cureus.25291] [PMID]

[42] Becerra-Loaiza DS, Sánchez-Zazueta JG, Ochoa-Ramírez LA, Velarde-Rodríguez I, Rodríguez-Millán J, Velarde-Félix JS. Study on vitamin D receptor gene polymorphisms in patients with urinary tract infections conducted in Northwestern Mexico. Rev Mex de Urol. 2018; 78(6):419-24. [DOI:10.48193/revistamexicanadeurologa.v78i6.100]

[43] Deng QF, Chu H, Wen Z, Cao YS. Vitamin D and urinary tract infection: A systematic review and meta-analysis. Ann Clin Lab Sci. 2019; 49(1):134-42. [PMID]

[44] Li X, Yu Q, Qin F, Zhang B, Lu Y. Serum vitamin D level and the risk of urinary tract infection in children: A systematic review and meta-analysis. Front Public Health. 2021; 9:87-99. [DOI:10.3389/fpubh.2021.637529] [PMID]

[45] Gan Y, You S, Ying J, Mu D. The association between serum vitamin d levels and urinary tract infection risk in children: A systematic review and meta-analysis. Nutrients. 2023; 15(12):2690. [DOI:10.3390/nu15122690] [PMID]

[46] Sherkatolabbasieh H, Firouzi M, Shafizadeh S, Nekohid M. Evaluation of the relationship between vitamin D levels and prevalence of urinary tract infections in children. New Microbes New Infect. 2020; 37:1007-28. [DOI:10.1016/j.nmni.2020.100728] [PMID]

[47] Hacihamdioglu DÖ, Altun D, Hacihamdioglu B, Çekmez F, Aydemir G, Kul M, et al. The association between serum 25-hydroxy vitamin D level and urine cathelicidin in children with a urinary tract infection. J Clin Res Pediatr Endocrinol. 2016; 8(3):66-78. [DOI:10.4274/jcrpe.2563] [PMID]

[48] 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. [DOI:10.1371/journal.pone.0015580] [PMID]

[49] Esteghamati M, Sorkhi H, Mohammadjafari H, Derakhshan A, Sadeghi-Bojd S, Momtaz HE, Mohkam M, Safaeian B, Hooman N, Safaeiasl A, Sepahi MA, Ghasemi K, Bazargani Z, Emami E. Prevalence of reflux nephropathy in Iranian children with solitary kidney: results of a multi-center study. BMC Nephrol. 2022; 23(1):70. [DOI: 10.1186/s12882-022-02703-z] [PMID]