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Original Research Article

Vitamin D and Diarrhea in Childhood: An Observational Study in a Teaching Hospital of Bihar

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Abstract:

Objective: To determine the prevalence of vitamin D deficiency in Indian children hospitalized with diarrhea and evaluates the association between vitamin D status and severity of diarrhea.

Methods: A hospital-based cross-sectional study was conducted from June 2023 to March 2024 in Nalanda Medical College and Hospital in the state of Bihar, India. Infants and young children aged 6–60 months hospitalized with diarrhea were recruited. Serum blood samples were collected on admission and analyzed for total serum 25-hydroxyvitamin D3 and 25-hydroxyvitamin D2 concentrations using liquid chromatography-tandem mass spectrometry. Vitamin D deficiency was defined as a level of serum vitamin D <50 nmol/L. The association between vitamin D deficiency and severity of hospitalized diarrhea patients according to WHO criteria, including the presence of danger signs, signs of severe dehydration, shock, duration of hospitalization, and admission to Intensive Care Unit (ICU), was analyzed using logistic regression.

Results: 133 children with WHO-defined diarrhea were enrolled in the study and 127 (96%) had their vitamin D status determined. The mean vitamin D concentration was 56 (± 18 SD) nmol/L and 30.7% of participants were vitamin D deficient. Age younger than 12 months was associated with prolonged hospitalization (> 5 days) and low birth weight and poor nutritional status on admission were risk factors for severe dehydration. However, vitamin D status was not associated with the presence of danger signs, duration of hospitalization, or severe dehydration.

Conclusions: One in every three children hospitalized with diarrhea was vitamin D deficient. Vitamin D status was not associated with the severity of diarrhea.

Keywords: Vitamin D3, Severe Diarrhea, Dehydration, Sunken Eyes, Immunity, Inflammatory Cascade.

Introduction

Vitamin D, crucial for bone health, immune system regulation, and inflammation modulation, is synthesized in the skin through sunlight exposure. Its deficiency is linked to several diseases, including autoimmune disorders and cardiovascular diseases. Recently, vitamin D's potential role in preventing and treating respiratory infections has garnered attention [1]. Studies suggest that vitamin D has immunomodulatory and anti-inflammatory effects, impacting susceptibility to and severity of respiratory infections [2,3].

Diarrhea remains a pervasive health issue worldwide, particularly affecting developing countries where it accounts for approximately 10% of deaths in children under five, resulting in about 500,000 deaths annually. While viral agents like rotavirus predominantly cause acute diarrhea, bacterial agents, notably Shigella and enteropathogenic Escherichia coli, are prevalent in developing regions, contributing to 34.5% - 60.7% of cases. Factors such as inadequate access to clean water, poor personal hygiene, and insufficient breastfeeding heighten the risk of bacterial diarrhea.

Given the high prevalence of vitamin D deficiency in children, there's growing interest in its potential role in acute bacterial diarrhea. Vitamin D, a fat-soluble secosteroid, not only plays a crucial role in bone metabolism but also exhibits anti-bacterial and immunological effects. While various studies link vitamin D deficiency to infectious diseases like pneumonia, its association with childhood diarrhea

remains debated [4]. In a study investigating micronutrient status, specifically vitamin D and zinc, in children aged 6–24 months in urban slums, no significant association was found between vitamin D status and diarrhea incidence or severity. However, zinc demonstrated a protective effect against diarrhea in normal-weight children living in polluted, hygiene-constrained environments. This suggests that while vitamin D may not play a significant role in these settings, zinc remains vital for managing and preventing acute diarrheal diseases in children.

The study highlighted challenges in resource-constrained urban slums, including poor hygiene practices, inadequate facilities, and exposure to pathogenic microorganisms, which may mask vitamin D's potential protective role against diarrhea. Despite these challenges, the beneficial effects of zinc supplementation were evident, emphasizing its importance in diarrhea prevention.

The findings challenge the adapted framework suggesting vitamin D's immunomodulatory functions in preventing diarrhea. The study suggests that the lack of basic hygiene and environmental factors prevalent in urban slums could influence the protective role of vitamin D against diarrhea.

Overall, while the relationship between vitamin D status and childhood diarrhea remains inconclusive, zinc's protective role in managing acute diarrheal diseases, especially in resource-constrained settings, is evident. Further research is needed to explore vitamin D's role in specific diarrheogenic diseases caused by E.coli and other pathogens.

Materials and Methods

We conducted a hospital-based cross-sectional study in a teaching hospital of Bihar which caters a large number of people from different adjoining districts. All infants and children aged 6–60 months who were firstly admitted with diarrhea during the study period, were eligible for recruitment to the study. Following written informed consent from the parent, on admission we documented the clinical characteristics of the child, symptoms and signs of diarrhea including the presence of danger signs, nutritional status, and mental status. Standard case definitions were used for diarrhea, which included passage of three or more loose/watery stools in the last 24 hours. A new diarrheal episode was defined as three or more loose/watery stools in 24 hours followed by two consecutive days with fewer than three loose/watery stools passed by the child. Rate of diarrhea was calculated by dividing the number of days with diarrhea by total number of days of observation [7]. The diarrheal episodes were categorised as diarrhea with no dehydration, with some dehydration and with severe dehydration according to the method described in WHO protocol. Only the patients with some and severe dehydration were selected for the study. The exposure of interest, vitamin D status at enrolment, was categorised as deficient (<50 nmol/L), insufficient (≥50 and <75 nmol/L) and sufficient (≥75 nmol/L) [22]. Under nutrition was defined by WHO definition: underweight for weight-for-age -3 SD to < -2 SD, stunted for height(or length)-for-age -3 SD to < -2 SD, and wasted for weight-for-height (or length) - 3 SD to < -2 SD. Severe under nutrition was defined as: severely underweight for weight-for-age < -3SD, severely stunted for height(or length)-for-age < -3SD, and severely wasted for weight-for-height (or length) <-3SD [23]. Vitamin D estimation was done on serum using liquid chromatography and tandem mass spectroscopy.

Statistical Analysis: Continuous variables were presented as mean ±SD for normal distribution or median and interquartile range for skewed variables. Categorical variables were presented as proportions (%). Vitamin D levels were summarized as continuous and categorical variables. Data was analysed using SPSS version 20. Binomial categorization of vitamin D was used in the univariate and multivariate logistic regression analysis for exploring the association between vitamin D status and the indicators of severity of diarrhea as binary variables. Results were presented as Odds ratios (ORs) with 95% CIs. A p-value of < 0.05 was considered statistically significant.

Results

During the study period total of 133 patients were enrolled who were admitted in the hospital. Out of these, 127 (96%) had vitamin D results available for analysis. No mortality was reported but two ICU admissions were documented due to severe dehydration with shock at presentation. The median age of participants was 12 months old with the majority of participants from the rural area (83%) and of male sex (59%). Seventy four (56%) of participants were exclusively breastfed until six months and rest were formula fed or cow's milk fed along with mother's milk in initial 6 months of life. The mean age of mothers was 32 (SD± 6.4) years and participants were predominantly from low-income families and (Table 1). Thirty participants (23%) were underweight or severely underweight (based on weight for age < -2 SD), and of the 70 participants with weight-for length recorded, 14 (20%) were wasted or severely wasted. The vitamin D level was normally distributed (mean (± SD): 56 ± 18 nmol/L) with 30.7% (39/127) of participants having serum vitamin D less than 50 nmol/L. Of these vitamin D deficient participants, 36% (14/39) had serum vitamin D level less than 30 nmol/L. Vitamin D deficiency was not associated with the presence of

danger signs, the duration of stay in the hospital and severe dehydration (Table 3). A sensitivity analysis using a higher and a lower vitamin D cut off (< 75 nmol/L and <25 nmol/L) did not alter the findings (Table 3). Participants younger than 12 months were twice as likely to have prolonged hospitalization compared to older participants (AOR 2.91, 95% CI: 1.23–6.92, (Table 3). Low birth weight and poor nutritional status on admission were significant independent risk factors for dehydration and shock on admission in the hospital.

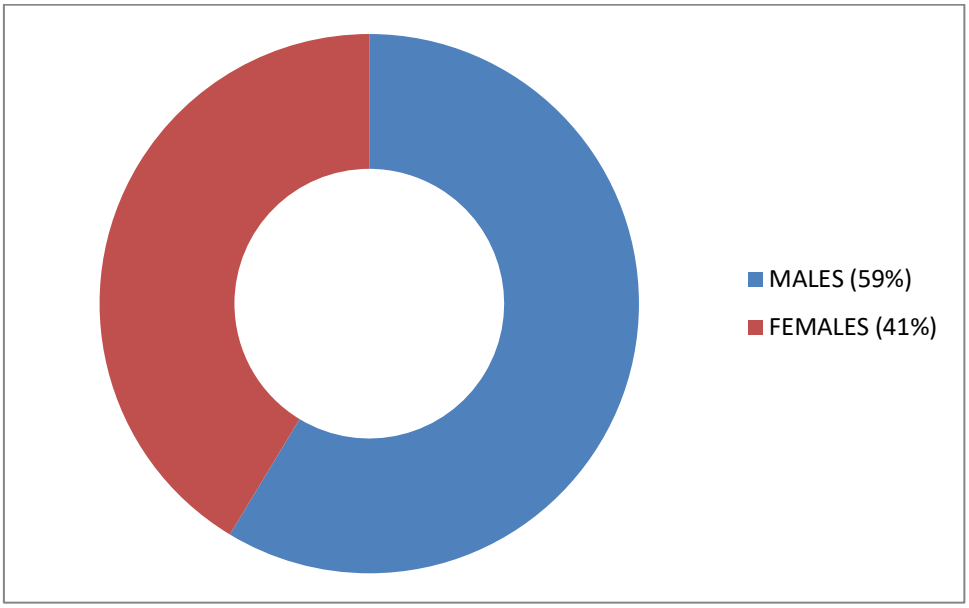

Figure 1: Demographics of the study population

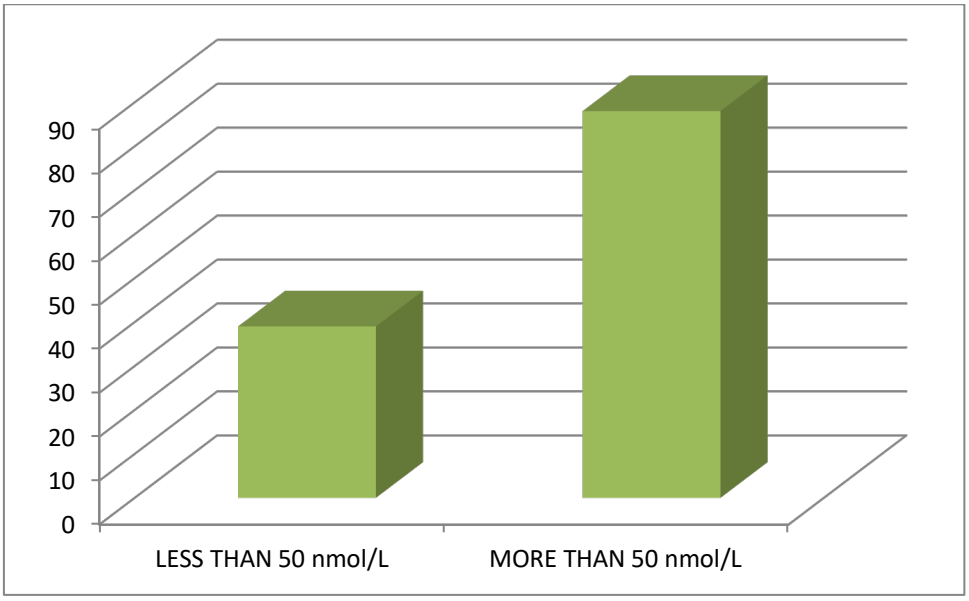

Figure 2: Vitamin D3 level of study population

Table 1: Baseline demographics of participants (N= 133)

Variables	**N (%)**
Characteristics of participants	
Gender (male)—n (%)	79(59%)
Location-n (%)	
Rural	110 (83%)
Urban	23(17%)
Age (in months)—n (%),N= 133	
6–11	58(44%)
12–23	31(23%)

24–60	44(33%)
Birth weight (in grams),median(IQR),N=124	3000(2775–3300)
Normal (2500–4200g)	112 (90%)
Low (1500–<2500g)	10(8%)
Very low<1500g	2(2%)
Exclusive breast feeding (EBF)—n (%),N=133	
No	59(44%)
EBF until 6 months of age, now completed	74(56%)
Socio-environmental characteristics	
Mother's age-n (%),N=123	
<25 years old	16(13%)
25–29 years old	35(29%)
30–34 years old	27(22%)
35–39 years old	32(26%)
> 40 years old	13(11%)
Mother's educational level—n (%),n=126	
Completed middle school or less	47(37%)
Completed high school	63(50%)
Attended University	16(13%)

Discussion

We found that one in every 3 children aged 6–60 months admitted to hospital with diarrhea was vitamin D deficient (<50 nmol/L), but vitamin D status was not associated with the severity of diarrhea as indicated by the presence of danger signs, shock or prolonged hospitalization. A

study by Thornton et al. on 475 school-aged children showed that 10% of the children suffered from vitamin D deficiency and 47% were vitamin D insufficient. The one-year follow-up showed that the incidence of diarrhea is higher in children with vitamin D deficiency [8]. Bener et al showed a significantly higher incidence of diarrhea in vitamin D deficient children. Differing with this was the result of Urashima et al. This concluded that the diarrhea incidence risk did not decrease with vitamin D supplementation [12]. Ahmed et al. also indicated no correlation between vitamin D deficiency and diarrhea caused by Enteropathogenic E. coli (EPEC), Enterotoxigenic E. coli (ETEC), and Enteroaggregative E. coli (EAEC). They asserted that this result might be specific to enterotoxin-producing bacteria. Different sample sizes, exposure to the sunlight, climatic conditions, nutritional status, age, and race of patients can justify these contradictions [19]. Besides the main role in regulating calcium metabolism, vitamin D also has other functions, such as anti-inflammatory, antibacterial, and immunomodulatory effects [20]. For example, it can affect the synthesis of bactericidal peptides [21] and regulate the adaptive immune system through IgA up regulation [22]. In our study, the higher prevalence of vitamin D insufficiency and deficiency in the acute diarrhea group possibly shows a more significant role of vitamin D against viral diarrheagenic pathogens.

Vitamin D is mainly synthesized by the action of ultra violet spectrum of sunlight on the skin. A minority of Vitamin D is obtained from foods like fatty fish, liver, cheese and egg [25]. Both the ingested and UVB-synthesized forms of vitamin D are biologically inactive; activation requires Hydroxylation in the liver and kidney [27]. Calcitriol, which is the active form of vitamin D acts as a hormone performing a myriad of functions in the body. Its level in the body depends on number of nephrons, level of FGF-23 and some inflammatory cytokines. Vitamin D functions through a cytoplasmic receptor called VDR which is present in the body ubiquitously. Vitamin D facilitates the synthesis of various functional proteins through gene expression [28].

An important function is its modulating property of the innate and adaptive immune systems through the inflammatory cascade. The mechanism by which vitamin D regulates inflammation and immunity is multi-faceted. It controls macrophage and dendritic cell activities and various Toll-like receptor mediated events in neutrophils [29], and it decreases the function of dendritic cells by delaying maturation, antigen presentation and the production of cytokines such as interleukin (IL)-12 and IL-23 [27,28]. Moreover, treating macrophages with 1,25(OH)D results in the expression of various cytokines and chemokines, including CXCL8, IL-6, and IL-12, and tumor necrosis factor (TNF)-α [29,30]. Various studies have been conducted relating to vitamin D deficiency and different infections of the body. Vitamin D deficient children have been shown to be more susceptible to pneumonia, otitis media, bronchiolitis, and tonsillopharyngitis. We found that young age (<12 months) and low birth weight and poor nutritional status on admission were risk factors for severe diarrhea. Under nutrition is well known to be

associated with the frequency, severity, and mortality of diarrhea due to the weakened host defense mechanisms against infections. Even immunogenicity post-vaccination is affected in malnutrition.

Table 2: Clinical and laboratory profiles of participants (n=133)

Sunken eyes	104 (78%)
Decreased skin turgor	133 (100%)
Drowsiness	83(62%)
Acidotic breathing	
Length of stay (in days),median (IQR)	5(4–6)
Prolonged stay (>5days)—n (%)	49(37%)
Weight for age—n (%)	
Normal (-2SDto2SD)	100 (75%)
Underweight (-3SD to<-2SD)	18(14%)
Severely underweight (<-3SD)	12(9%)
>2SD	2(2%)
Length for age—n (%),N=69	
Normal (-2SDto2SD)	42(61%)
Stunted (-3 SD to <-2 SD)	17(25%)
Severely stunted(<-3SD)	8(12%)
Tall>2SD	2(3%)
Weight for length—n (%),N=70	
Normal (-2SDto2SD)	51(73%)
Wasted(-3SDto <-2SD)	9(13%)
Severely Wasted (<-3 SD)	5(7%)
Overweight >2SD	5(7%)
Anemia—n (%)	57(43%)
Leukocytosis—n (%)	105 (79%)
Neutrophilia—n (%),N=132	25(19%)
Lymphocytosis—n (%)	63(47%)

Table 3: Risk factors for severe diarrhea (danger signs, prolonged stay)

	With danger signs		**Prolonged stay**	
Characteristics	**Adjusted OR**	**p-value**	**Adjusted OR**	**p-value**
Vitamin D level				
<75 nmol/L^2	1.04 (0.37–2.84)	0.94	0.62 (0.25–1.52)	0.29
<50 nmol/L^2	0.80 (0.25–2.56)	0.71	0.72 (0.25–2.08)	0.57
<25 nmol/L^2	1.10 (0.20–5.95)	0.92	1.10 (0.20–5.95)	0.92
Younger age (6 month to 1 yr)	1.53 (0.61–3.85)	0.36	**2.92 (1.23–6.93)**	**0.02**
Younger Gestational age (in weeks)	1.11 (0.93–1.31)	0.26	0.99 (0.84–1.16)	0.88
LBW (<2500g)	1.28 (0.35–4.67)	0.71	1.09 (0.33–3.68)	0.89
Increased maternal age	0.99 (0.92–1.06)	0.69	0.97 (0.91–1.03)	0.30
Weight for age				
-2SD to2 SD	Ref		Ref	
<-2SD (underweight)	0.94 (0.27–3.25)	0.92	1.55 (0.52–4.62)	0.43
<-3SD (severely underweight)	0.93 (0.21–4.16)	0.92	**8.55 (1.89–36.48)**	**0.007**
Length for age				
>2SD	3.14 (0.35–28.56)	0.31	1.88 (0.22–16.49)	0.57
-2SD to2 SD	Ref		Ref	
<-2SD (wasted)	1.81 (0.35–9.42)	0.48	1.38 (0.27–6.94)	0.70
<-3SD (severely wasted)	2.36 (0.29–18.86)	0.42	2.89 (0.40–20.75)	0.29
Anemia	1.00 (0.37–2.72)	0.99	0.93 (0.38–2.23)	0.86

Talachian et al. study on 25 children with acute diarrhea and 25 healthy children showed that serum 25 (OH) Vit. D concentrations are significantly lower in children affected with diarrhea [12]. The study by Bucak et al. on 70 patients with rotavirus diarrhea and 60 healthy children as control group revealed that serum levels of vitamin D are significantly lower in children with diarrhea compared with healthy children (14.6 _ 8.7 ng/mL vs. 29.06 _ 6.51 ng/mL). These mentioned studies

confirmed that vitamin D deficiency is a predisposing factor for rotavirus diarrhea [13].

Previous studies have presented frameworks for understanding the mechanisms through which vitamin D plays a role in the activation of innate and adaptive immunity for infectious diseases including diarrhea [14, 19-22]. Vitamin D has been shown to give a protective effect against infection through the up-regulation of genes involved in strengthening the barrier function of the epithelial membrane including gastrointestinal tract. A strengthened barrier function would inhibit the attachment of entry of microorganisms to the epithelial and subsequent infection [23]. It also induces production of the antimicrobial peptides, cathelicidin, that have a broad spectrum of antimicrobial activity against viruses, bacteria and fungi [29,30]. Production of antimicrobial peptides (cathelicidin) is the key pathway to preventing diarrhea since these peptides appear to play a role in the regulation of innate and adaptive immunity in gastrointestinal infection [33, 34]. We assume that similar protective mechanisms would be induced in our study participants with better vitamin D status. In a longitudinal study among school-going children (mean age 8.9 years) in Colombia, researchers found vitamin D deficient children were at greater risk of gastrointestinal illness [7]. Our study consisted of children aged 6–60 months living mostly in rural areas where the burden of disease is highest due to poor sanitation and low socio-economic status. They reside in an environment where hygiene is not up to the mark. These conditions may result in constant exposure to pathogenic organisms and subsequently infections by multiple enteric pathogens and increased diarrheal disease incidence [32, 33]. Continuous and overwhelming infections by enteric pathogens could be masking the role of vitamin D in this population. Poor caregiving could be another potential explanation for no association of vitamin D for reducing incidence and severity of diarrhea in our children. Probably for this reason, our study findings were concordant with the finding of an RCT with vitamin D supplementation conducted in a similar setting in Afghanistan [3].

Limitation of the study was small sample size which may have diminished the power to detect an association between vitamin D deficiency and diarrhea severity. Further studies are needed to correlate vitamin D deficiency with incidence and severity of diarrhea. Strengths of the study included a recruitment period of over 12 months enabling us to include all seasons.

Conclusion

Vitamin D deficiency was found to be common in under-five children hospitalized with diarrhea but was not related to diarrhea severity and hospitalization outcomes.

Data from ongoing clinical trials are needed for better elucidation of the effects of vitamin D supplementation on the severity of diarrhea.

References

1. Bui L., Zhu Z., Hawkins S., Cortez-Resendiz, A., Bellon A. Vitamin D regulation of the immune system and its implications for COVID-19: A mini review. SAGE Open Med. 2021; 9: 20503121211014073.
2. Adams JS, Hewison M. Extrarenal expression of the 25-hydroxyvitamin D-1-hydroxylase. Arch Biochem Biophys. 2012; 523:95-102.
3. Aluisio AR, Maroof Z, Chandramohan D, et al. Vitamin D(3) supplementation and childhood diarrhea: a randomized controlled trial. Pediatrics. 2013; 132: e832-840.
4. Hewison M. An update on vitamin D and human immunity. Clin Endocrinol (Oxf). 2012; 76:315-325.
5. Liu PT, Stenger S, Li H, et al. Toll-like receptor triggering of a vitamin D-mediated human antimicrobial response. Science. 2006; 311:1770-1773.
6. Engelsen, O. The relationship between ultraviolet radiation exposure and vitamin D status. Nutrients. 2010; 2: 482–495.
7. Athanassiou, L.; Mavragani, C.P.; Koutsilieris, M. The Immunomodulatory Properties of Vitamin D. Mediterr. J. Rheumatol. 2022; 33: 7–13.
8. Thornton KA, Marin C, Mora-Plazas M, et al. Vitamin D deficiency Associated with Increased Incidence of Gastrointestinal and Ear Infections in School-Age Children. Pediatr Infect Dis J. 2013; 32:585-593.
9. Yamshchikov AV, Desai NS, Blumberg HM, et al. Vitamin D for treatment and prevention of infectious diseases: a systematic review of randomized controlled trials. Endocr Pract. 2009; 15:438-449.
10. Youssef DA, Miller CW, El-Abbassi AM, et al. Antimicrobial implications of vitamin D. Dermatoendocrinol. 2011; 3:220-229.
11. Walker CL, Rudan I, Liu L, et al. Global burden of childhood pneumonia and diarrhoea. Lancet. 2013; 381:1405-1416.
12. 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.
13. Mayo-Wilson E, Junior JA, Imdad A, et al. Zinc supplementation for preventing mortality, morbidity, and growth failure in children aged 6 months to 12 years of age. Cochrane Database Syst Rev. 2014; 5:Cd009384.

14. Adams JS, Hewison M. Unexpected actions of vitamin D: new perspectives on the regulation of innate and adaptive immunity. Nat Clin Pract Endocrinol Metab. 2008; 4:80- 90.
15. Paxton GA, Teale GR, Nowson CA, Mason RS, McGrath JJ, Thompson MJ, et al. Vitamin D and health in pregnancy, infants, children and adolescents in Australia and New Zealand: a position statement. Med J Aust. 2013; 198(3):142–3.
16. Craig TA, Benson LM, Naylor S, et al. Modulation effects of zinc on the formation of vitamin D receptor and retinoid X receptor alpha-DNA transcription complexes: analysis by microelectrospray mass spectrometry. Rapid Commun Mass Spectrom. 2001: 15: 1011-1016.
17. Gudmundsson GH, Bergman P, Andersson J, et al. Battle and balance at mucosal surfaces--the story of Shigella and antimicrobial peptides. Biochem Biophys Res Commun. 2010; 396:116-119.
18. Wehkamp J, Schauber J, Stange EF. Defensins and cathelicidins in gastrointestinal infections. Curr Opin Gastroenterol. 2007; 23:32-38.
19. Ahmed AM, Soares Magalhaes RJ, Long KZ, Ahmed T, Alam MA, Hossain MI, et al. Association of vitamin D status with incidence of enterotoxigenic, enteropathogenic and enteroaggregative Escherichia coli diarrhoea in children of urban Bangladesh. Trop Med Int Health. 2016; 21(8):973–84.
20. Abdelfatah M, Nayfe R, Moftakhar B, Nijim A, El Zoghbi M, Donskey CJ, et al. Low vitamin D level and impact on severity and recurrence of Clostridium difficile infections. J Investig Med. 2015; 63(1):17–21.
21. Talachian E, Bidari A, Noorbakhsh S, Tabatabaei A, Salari F. Serum levels of vitamins A and D, and zinc in children with acute diarrhea: Abcross-sectional study. Med J Islam Repub Iran. 2015; 29:207.
22. Bucak IH, Ozturk AB, Almis H, Cevik MO, Tekin M, Konca C, et al. Is there a relationship between low vitamin D and rotaviral diarrhea? Pediatr Int. 2016; 58(4):270–3.
23. Lind C, Chen J, Byrjalsen I. Enzyme immunoassay for measuring 25-hydroxy vitamin D3 in serum. Clin Chem. 1997: 43:943-949.
24. Lee G, Penataro Yori P, Paredes Olortegui M, et al. An instrument for the assessment of diarrhoeal severity based on a longitudinal community-based study. BMJ Open. 2014; 4:e004816.
25. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011: 96:1911-1930.
26. World health organization. Nutrition Landscape Information System (NLIS) country profile indicators: interpretation guide. Geneva, Switzerland: WHO Document Production Services; 2010.
27. White JH. Vitamin D signaling, infectious diseases and regulation of innate immunity. Infect Immun. 2008; 76:3837-3843.
28. Schwalfenberg GK. A review of the critical role of vitamin D in the functioning of the immune system and the clinical implications of vitamin D deficiency. Mol Nutr Food Res. 2011; 55:96-108.
29. Liu PT, Stenger S, Tang DH, et al. Cutting edge: vitamin D-mediated human antimicrobial activity against Mycobacterium tuberculosis is dependent on the induction of cathelicidin. J Immunol. 2007; 179:2060-2063.
30. Rook GA, Steele J, Fraher L, et al. Vitamin D3, gamma interferon, and control of proliferation of Mycobacterium tuberculosis by human monocytes. Immunology. 1986; 57:159-163.
31. Klotman ME, Chang TL. Defensins in innate antiviral immunity. Nat Rev Immunol. 2006; 6:447-456.
32. Komatsuzawa H, Ouhara K, Yamada S, et al. Innate defences against methicillin-resistant Staphylococcus aureus (MRSA) infection. J Pathol. 2006: 208:249-260.
33. Lopez-Garcia B, Lee PH, Yamasaki K, et al. Anti-fungal activity of cathelicidins and their potential role in Candida albicans skin infection. J Invest Dermatol. 2005; 125:108-115.
34. Bartley J. Vitamin D: emerging roles in infection and immunity. Expert Rev Anti Infect Ther. 2010; 8:1359-1369.