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ORIGINAL ARTICLE

Is Vitamin D Deficiency a Risk Factor for Helicobacter Pylori Eradication Failure?

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SUMMARY

Background: **Host factors related to failure of eradication of *Helicobacter pylori (H. pylori)* are increasingly studied. This work aimed to study the influence of 25-hydroxy-vitamin D [25(OH)-vitD] status on the rate of *H. pylori* eradication.**

Methods: **One hundred and fifty patients infected with *H. pylori* were tested for serum 25(OH)-vitD level prior to 14 days clarithromycin-based triple eradication therapy. Accordingly, patients were divided into: group I (*eradication successful*) and group II (*eradication failure*). Both groups were compared regarding mean level of serum 25(OH)-vitD and number and percentage of patients with deficient 25 (OH)-vitD.**

Results: **Overall rate of eradication was 72%. Mean serum level of 25(OH)-vitD was higher in the *eradication successful* group compared to the group of *eradication failure* (28.12 ± 8.10 vs. 13.54 ± 6.37; p < 0.001). The percentage of patients with 25(OH)-vitD deficiency was higher in the group of *eradication failure* compared to the group of *successful eradication* [30 (71.5%) vs. 19 (17.5%); p < 0.001]. Patients with *sufficient* 25(OH)-vitD had a higher rate of eradication compared to patients with *deficient* 25(OH)-vitD (88% vs. 38.5%).**

Conclusions: **This study suggested that *deficiency* of 25(OH)-vitD could be a risk factor for *H. pylori* eradication failure, and it recommends to investigate the effect of vitamin D supplementation on *H. pylori* eradication.**

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KEY WORDS

vitamin D, deficiency, *Helicobacter pylori*, eradication, failure

INTRODUCTION

Infection with *Helicobacter pylori (H. pylori)* is considered the furthest spread infection all over the world, affecting on average half the world population with infection rates ranging from 25% in developed countries [1] to 90% in the developing countries [2].

It colonizes the human stomach and is an important contributing factor in the pathogenesis of many gastric diseases including gastritis, peptic ulcer, mucosa-associated lymphoid tissue lymphoma (MALT) and gastric

carcinoma [3,4], as well as colorectal polyps and cancer [5].

A recent meta-analysis concluded that *H. pylori* eradication could decrease gastric cancer risk, suggesting that persistence of *H. pylori* infection constitutes a relative risk of 65% for gastric cancers and an increased absolute risk from 1.1% to 1.7% [6]. Therefore, it is clearly important to successfully eradicate *H pylori infection* and its host contributing risk factors [7].

The standard triple therapy with clarithromycin, proton pump inhibitor (PPI), and amoxicillin or metronidazole is the first-line therapy for *H. pylori* eradication. A cure rate of 70 - 85% has been reported by the American College of Gastroenterology in 2007 [8]. A recent systematic review estimated a cure rate of 75.1% for the triple therapy, and 84.1% for the sequential therapy [9]. Apart from antibiotic resistance which has been suggested as the most important host factor affecting *H. pylori* eradication, the host immune system together with virulence factors and host-related genetic disorders (CYP2C19, IL-1B, and multidrug-resistant transporter-1) are important factors in *H. pylori* eradication [10]. Beyond the well-known role of vitamin D in calcium and phosphorous metabolism, both are needed for bone formation. Vitamin D also has an immune-modulator role in targeting different immune cells, including macrophages as well as T-lymphocytes and B-lymphocytes [11]. It enhances immunity by modulating the production of endogenous antimicrobial peptides (AMPs) inside immune cells including macrophages, [12] and through cytokine response, as well as it boosts the activity of macrophages and monocytes [13].

Therefore, vitamin D deficiency appears to be incorporated in immune system disorders; hence, it has been suggested as an important risk factor for *H. pylori* infection and failure of eradication [14].

MATERIALS AND METHODS

This study included patients presented to the family medicine and internal medicine clinic of Umm Alqura University Medical Center, Makkah, Saudi Arabia, during the period from March 2018 to October 2019.

In this study, 150 patients of both genders, aged 18 to 65 years old, and complaining of symptoms of dyspepsia for two or more months were included. Full medical history was obtained, and complete physical examination was performed for every patient. A ^{14}C-urea breath test (UBT) was performed, and those who tested positive were included in the study.

Exclusion criteria involves patients who received previous *H. Pylori* eradication treatment, are currently using vitamin D supplement, have used PPI or antibiotics any time in the prior two months, have known hypersensitivity to PPI or antibiotics, and/or have a history of autoimmune disorder, systemic inflammatory disease, gastric surgery, liver cirrhosis, renal failure, malignancies or are on oral corticosteroid therapy.

Informed consent was obtained from patients after explanation of the objectives and the process of the study, and being assured of keeping their information confidential.

Eradication therapy

All patients were prescribed a 14-day course of clarithromycin-based triple therapy for *H. pylori* eradication (twice daily doses of clarithromycin 500 mg, amoxicillin 1,000 mg, and omeprazole 20 mg).

Laboratory measurements

Diagnosis of *H. pylori* infection via ^{14}C-urea breath test (UBT)

Patients were asked to fast overnight and then ingested urea labeled with 37 kBq of ^{14}C-urea/citric acid composition dissolved in 25 mL of water (1 mCi) (Helicap, Noster System AB, Stockholm, Sweden). Patient's breath samples were obtained before ingestion and 15 minutes thereafter. The liquid β-scintillation counter was used to measure ^{14}C content in breath samples in a Bq mode. A 3.33 Bq was set as a value below which the test result is negative for ^{14}C in breath (successful eradication) and at or above which indicates the test result is positive (failure of eradication).

Evaluation of vitamin D status by measurement of serum 25(OH)-vitD using a quantitative chemiluminescent immunoassay (CLIA) method

The 25 OH Vitamin D TOTAL Assay (DiaSorin Inc. LIAISON 510(K), Italy; DiaSorin LIAISON ® 25 OH Vitamin D TOTAL Assay) is an automated immunoassay that is a solid-phase competitive binding test. Sera were collected in separate tubes, mixed with denaturation buffer to extract the analyte as most circulating 25(OH)-vitD is bound to vitamin D-binding protein (VDBP) *in vivo*. Following neutralization, the enzyme conjugate biotinylated 25(OH)-vitD and the enzyme complex peroxidase-labeled streptavidin are mixed together and the solution is transmitted to the microtiter plate. Endogenous 25(OH)-vitD of the patient sample competes with a 25(OH)-vitD-biotin conjugate to bind to the VDBG. Binding of 25(OH)-vitD-biotin is identified by peroxidase-labeled streptavidin. Unbound components are eliminated by washing. In the next step, the reagents are added to initiate the chemiluminescent reaction. The light signal is detected by a photomultiplier as relative light units. An inverse relationship exists between the intensity of the light and the concentration of 25(OH)-vitD in the study sample [15].

This method measures total 25(OH)-vitD including 25(OH)-vitD2 and 25(OH)-vitD3 and other hydroxylated vitamin D metabolites in human serum [15].

A comparative study of the automated immunoassay DiaSorin LIASON (LSN) with liquid chromatography-tandem mass spectrometry (LC-MS/MS) demonstrated that LSN had comparable correlation coefficient [r] values to LC-MS/MS (0.936 and 0.933), and the LSN assay results were statistically equivalent to those given

Table 1. Demographics and laboratory findings of group I (*eradication successful*) and group II (*eradication failure*).

Variables	Group I (n = 108)	Group II (n = 42)	p-value
Age [years]	36.0 ± 10.30	35.16 ± 9.38	0.649
Gender	male: 62 (57.5%) female: 46 (42.5%)	male: 24 (57 %) female: 18 (3%)	0.977
BMI	24.91 ± 2.037	25.35 ± 2.139	0.243
Smoking	36 (33.3%)	17 (40.4%)	0.411
DM	24 (22.2%)	8 (19%)	0.670
Hb	13.21 ± 1.059	12.89 ± 1.27	0.125
WBCs	6.13 ± 0.878	5.89 ± 0.75	0.126
ALT	22.14 ± 3.67	21.07 ± 4.27	0.126
AST	25.91 ± 5.71	27.50 ± 6.24	0.140
Creatinine	0.841 ± 0.12	0.81 ± 0.12	0.331

There were no significant statistical differences between both groups with regard to demographic characteristics and laboratory findings. BMI - body mass index, DM - diabetes mellitus, Hb - hemoglobin, WBCs - white blood cells, ALT - alanine aminotransferase, AST - aspartate aminotransferase.

Table 2. Differences in vitamin 25(OH)-vitD levels in the *eradication successful* and *eradication failure* groups.

	Group I (*eradication successful*)	Group II (*eradication failure*)	p-value
25(OH)-vitD level (ng/mL) (mean ± SD)	28.12 ± 8.10	13.54 ± 6.37	0.001
Patients with deficient 25(OH)-vitD [n (%)]	19 (17.5%)	30 (71.5%)	0.001

Mean serum level of 25(OH)-vitD was higher in the *eradication successful* group compared to the group of *eradication failure*. Moreover, the percentage of patients with 25(OH)-vitD deficiency was higher in the group of *eradication failure* compared to the group of *successful eradication.*

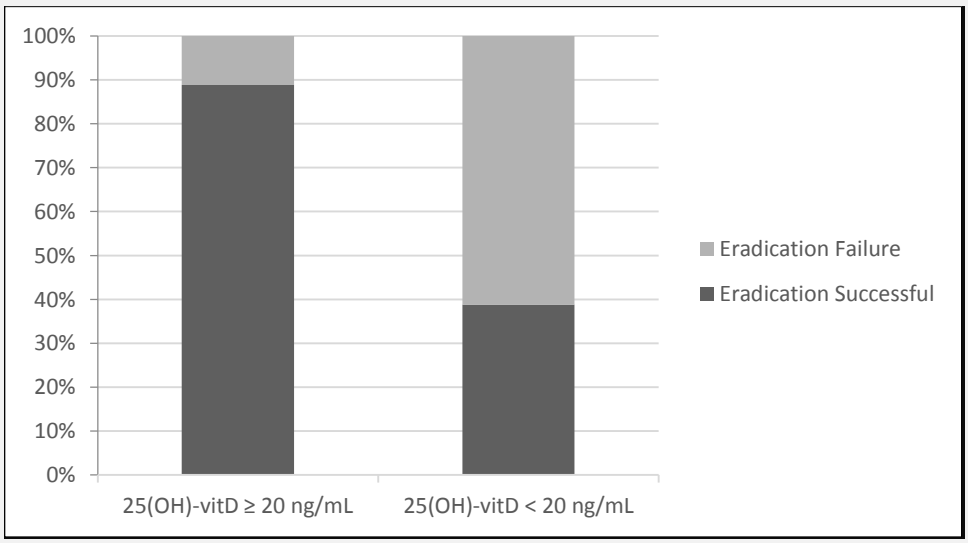

Figure 1. 25(OH)-vitD status in relation to the rate of *H. pylori* eradication.

The rate of eradication in patients with *sufficient* vitamin D (25(OH)-vitD ≥ 20 ng/mL) was 88%, while the rate of eradication in patients with *deficient* vitamin D (25(OH)-vitD < 20 ng/mL) was 38.5%.

by LC-MS/MS (slope 0.93, intercept -2.5). For specificity, based on 25(OH)-vitD2 and 25(OH)-vitD3 levels assessed by LC-MS/MS, LSN showed minor differences in slope (0.9 in groups with detectable 25(OH)-vitD2 and 0.96 in groups with no detectible 25(OH)-vitD2. LSN demonstrated good precision (total coefficient of variation range 5.5 - 10.0%), and functional sensitivity was 2.15 ng/mL by LSN [16]. Similar findings were reported by the American College of Pathologists [17]. In general, the precision levels of LSN and LC-MS/MS are comparable; both have the required sensitivity to identify severe vitamin D deficiency [18].
The test was performed by a laboratory technician who was blind to the aim of the study.
Vitamin-D level was considered *sufficient* if serum 25(OH)-vitD ≥ 20 ng/mL and *deficient* if serum 25(OH)-vitD < 20 ng/mL [15].

Confirmation of *H. pylori* eradication via ^{14}C-UBT
This test was performed at least 4 weeks after treatment completion. Patients were advised not to use antibiotics nor PPIs in the 4 weeks prior to the test.
According to the result of eradiation, patients were divided into two groups as follows: group I *(eradication successful)* and group II *(eradication failure).*

Statistical analysis
Data collected through history, physical examination, and laboratory investigations were analyzed statistically by the SPSS software program, Version 20. Quantitative variables were presented as mean and standard deviation (SD), while qualitative variables were presented as numbers and percentages. To evaluate the variances on quantitative variables, unpaired *t*-test was used, while qualitative variables were compared with Pearson's chi-square test. Statistical significance was set at $p < 0.05$.

RESULTS

The study included 150 patients diagnosed with *H. pylori* infection. Vitamin D status was determined for every patient before commencing eradication therapy. Overall, 101 (68.5%) of patients had serum 25(OH)-vitD ≥ 20 ng/mL (*sufficient*), while 49 (32.5%) had serum 25(OH)-vitD < 20 ng/mL (*deficient*). Overall rate of *H. pylori* eradication was 72%. There was no significant statistical difference between the *eradication successful* and *eradication failure* groups with regard to age, gender, BMI, smoking status, anemia, liver disease, kidney disease, and diabetes mellitus (Table 1, $p > 0.05$). The prevalence of 25(OH)-vitD deficiency was 32.6%. The group with *eradication successful* had a higher mean value of 25(OH)-vitD compared to the group with *eradication failure* (28.12 ± 8.1 vs. 13.54 ± 6.37; $p < 0.001$, Table 2). Furthermore, the percentage of patients with *deficient* 25(OH)-vitD was significantly higher in the group of *eradication failure* in comparison with the group of *eradication successful* [30 (71.5%) vs. 19 (17.5%); $p < 0.001$, Table 2]. Patients with *sufficient* 25(OH)-vitD had a higher rate of eradication compared to patients with *deficient* 25(OH)-vitD (88% vs. 38.5%, Figure 1).

DISCUSSION

In this study, the potential relationship between the rate of *H. pylori* eradication and levels of 25(OH)-vitD was examined.
Diagnosis and post-treatment eradication of *H. pylori* was confirmed via the ^{14}C-UBT. When compared with serology or stool antigen tests, this non-invasive and easy to perform test possesses the highest accuracy to detect *H. pylori* infection in patients without a recent use of antibiotics or PPIs [19]. In a recent systematic review, with specificity estimated at 90%, the sensitivity of these tests were 92% (95% CI; 89% to 94%) for^{14}C-UBT, 84% (95% CI; 74% to 91%) for serology, and 83% (95% CI; 73% to 90%) for stool antigen test [20]. Therefore, ^{14}C-UBT is the most accurate test to diagnose and follow up eradication of *H. pylori* infection [19].
Overall, 72% eradication rate was achieved in the present study using the standard clarithromycin-based triple therapy. In comparison to the current study, a rate of 70 - 85% was reported by the American College of Gastroenterology in 2007 [8], and a rate of 75% was revealed by Feng et al. in their recent systematic review in 2016 with the same triple therapy [9].
A significantly lower rate of *H. pylori* eradication in patients with lower 25(OH)-vitD levels was demonstrated by the current study. Moreover, the eradication failure group had a higher percentage of patients with *deficient* 25(OH)-vitD. A likely explanation of the observed association between the status of 25(OH)-vitD and rates of *H. pylori* eradication is the inadequate immune response due to the impairment of 25(OH)-vitD immune function [21,22]. Vitamin D has been recognized as an effective immune modulator of the immune system, stimulating the immune response to infection [23].
Vitamin D deficiency status has been proposed as a potential factor for the susceptibility to various infections with the first observation of nutritional deficiency in children with rickets who experienced an increased risk for respiratory infections [24]. Recent epidemiologic studies have revealed an association between seasonal variations in vitamin D status and the increased rates of numerous infections including sepsis [25].
More recently, researchers have recognized the relationship between vitamin D deficiency and infectious diseases [26,27]. A large meta-analysis has demonstrated the relationship between low levels of serum 25(OH)-vitD and the increased risk to active tuberculosis [28]. Besides its long tradition on regulating calcium, phosphorus, and bone metabolism, vitamin D may decrease inflammatory markers such as C-reactive protein

(CRP), tumor necrosis factor (TNF-α), interleukine-6 (IL-6), and interleukine-8 (IL-18), while it may increase the level of anti-inflammatory cytokine (IL-10) [29]. A bactericidal effect of vitamin D has been demonstrated through increasing production of cathelicidin and β-defensin by macrophages which possess bactericidal effect against both gram positive and gram-negative bacteria [30].

There is shortage of data indicating a direct relationship between vitamin D and *H. pylori* infection. Hosoda et al. in their *in vitro* study have demonstrated a selective bactericidal effect of vitamin D3 decomposition product (VDP1) against *H. pylori* [31]. Interestingly, a recent study by Guo et al. demonstrated a very specific antimicrobial effect of vitamin D to protect against *H. pylori* infection through its important role in gastric mucosa homeostasis [33]. Moreover, the impaired gastric mucosal immune response may contribute to the eradication failure in *H. pylori* infection. The bactericidal effect of peptides cathelicidin and β-defensin, secreted in the gastric mucosa after infection by *H. pylori*, creates an immune defense against *H. pylori* at the mucosal surface. In the vitamin D deficient state, this action is hindered as the infected macrophages are incapable of producing adequate 25-(OH)-vitD to upregulate formation of both β-defensin and cathelicidin, thus leaving them incapable of eradication *H. pylori* [34].

CONCLUSION

This study has demonstrated a lower rate of *H. pylori* eradication in patients with vitamin D deficiency. Thus, vitamin D deficiency could serve as a risk factor for *H. pylori* eradication failure; thus, vitamin D supplementation to correct its status might be needed prior to *H. pylori* eradication. Clinical trials are needed to test the difference in success of *H. pylori* eradication in patients with vitamin D deficiency both before and after vitamin D supplementation.

Declaration of Interest:

The authors declare no conflict of interest for publication of this work.

Adherence to Ethical Recommendations:

The authors declare adherence to ethical recommendations. Patients' information was kept confidential throughout the work and will not be breached.

References:

1. Pounder RE, Ng D. The prevalence of Helicobacter pylori infection in different countries. Aliment Pharmacol Ther. 1995;9(2): 33-9 (PMID: 8547526).
2. Dunn BE, Cohen H, Blaser MJ. Helicobacter pylori. Clin Microbiol Rev. 1997;10(4):720-4 (PMID: 9336670).
3. Chang AH, Parsonnet J. Role of Bacteria in Oncogenesis. Clinical Microbiology Reviews 2010;23(4):837–57 DOI: 10.1128/CMR.00012-10.
4. Kusters JG, van Vliet AH, Kuipers EJ. Pathogenesis of Helicobacter pylori Infection. Clin Microbiol Rev 2006;19(3):449-90 (PMID: 16847081).
5. Wu Q, Yang ZP, Xu P, Gao LC, Fan DM. Association between Helicobacter pylori infection and the risk of colorectal neoplasia: a systematic review and meta-analysis. Colorectal Dis. 2013; 15(7):e352-64 (PMID: 23672575).
6. Fuccio L, Zagari RM, Eusebi LH, et al. Meta-analysis: can Helicobacter pylori eradication treatment reduce the risk for gastric cancer? Ann Intern Med. 2009;151(2):121-8 (PMID: 19620164).
7. Take S, Mizuno M, Ishiki K, et al. The effect of eradicating Helicobacter pylori on the development of gastric cancer in patients with peptic ulcer disease. Am J Gastroenterol. 2005;100:1037-42 (PMID: 15842576).
8. Chey WD, Wong BC, Practice Parameters Committee of the American College of Gastroenterology. American College of Gastroenterology guideline on the management of Helicobacter pylori infection. Am J Gastroenterol. 2007;102:1808-25 (PMID: 17608775).
9. Feng L, Wen MY, Zhu YJ, Men RT, Yang L. Sequential therapy or standard triple therapy for Helicobacter pylori infection: an updated systematic review. Am J Ther. 2016;23(3):e880-93 (PMID: 25569598).
10. Uotani T, Miftahussurur M, Yamaoka Y. Effect of bacterial and host factors on Helicobacter pylori eradication therapy. Expert Opin Ther Targets. 2015;19(12):1637-50 (PMID: 26245678).
11. Baeke F, Takiishi T, Korf H, Gysemans C, Mathieu C. Vitamin D: Modulator of the immune system. Curr Opin Pharmacol. 2010; 10(4):482-96 (PMID: 20427238).
12. Liu PT, Stenger S, Li H, et al. Toll-like receptor triggering of a vitamin D-mediated human antimicrobial response. Science. 2006;311:1770-3 (PMID: 16497887).
13. Youssef DA, WT Miller C, El-Abbassi AM, et al. Antimicrobial implications of vitamin D. Dermatoendocrinol. 2011;3(4):220-9 (PMID: 22259647).
14. Hong JY, Kim SY, Chung KS, et al. Association between vitamin D deficiency and tuberculosis in a Korean population. Int J Tuberc Lung Dis. 2014;18(1):73-8 (PMID: 24365556).
15. DiaSorin Inc. LIASON 510(K) FDA submission. http://www. accessdata.fda.gov/cdrh_docs/reviews/K071480.pdf. Accessed on February 23, 2020.
16. Hsu SA, Soldo J, Gupta M. Evaluation of two automated immunoassays for 25-OH vitamin D: comparison against LC-MS/MS. J Steroid Biochem Mol Biol. 2013;136:139-45 (PMID: 23202147).
17. Horowitz G and Killeen AA. College of American Pathologists letter, 2012 letter. http://www.cap.org/apps/docs/committees/chemistry/abvd.pdf. Accessed February 24, 2020.
18. Wallace AM, Gibson S, de la Hunty A, Lamberg-Allart C, Ashwell M. Measurement of 25-hydroxyvitamin D in the clinical laboratory: Current procedures, performance characteristics and limitations. Steroids. 2010;75:477-88 (PMID: 20188118).

19. Dumitrescu G, Mihai C, Dranga M, Prelipcean CC. Serum 25-hydroxyvitamin D concentration and inflammatory bowel disease characteristics in Romania. World J Gastroenterol. 2014;20: 2392-6 (PMID: 24605037).

20. Mounsey A, Leonard EA. Noninvasive Diagnostic Tests for Helicobacter pylori Infection. Am Fam Physician 2019 Jul 1;100(1): 16-7 (PMID: 31259496).

21. Best LM, Takwoingi Y, Siddique S, et al. Non-invasive diagnostic tests for Helicobacter pylori infection. Cochrane Database Syst Rev. 2018 Mar 15;3:CD012080 (PMID: 29543326).

22. Borody T, Ren Z, Pang G, Clancy R. Impaired host immunity contributes to Helicobacter pylori eradication failure. Am J Gastroenterol. 2002;97:3032-7 (PMID: 12492186).

23. Clancy R, Borody T, Ren Z, Pang G. Can the response to eradication therapy in Helicobacter pylori infection be predicted? Can J Gastroenterol. 2003 Jun;17 Suppl B:58B-61B (PMID: 128453 54).

24. Penna G, Roncari A, Amuchastegui S, et al. Expression of the inhibitory receptor ITL3 on dendritic cells is dispensable for induction of CD4þFoxp3þ regulatory T cells by 1, 25-dihy-droxyvitamin D3. Blood. 2005;106:3490-7 (PMID: 16030186).

25. Khajavi A, Amirhakimi GH. The rachitic lung: pulmonary findings in 30 infants and children with malnutritional rickets. Clin Pediatr (Phila). 1977;16:36-8 (PMID: 137094).

26. Danai PA, Sinha S, Moss M, Haber MJ, Martin GS. Seasonal variation in the epidemiology of sepsis. Crit Care Med. 2007;35: 410-5 (PMID: 17167351).

27. Sahay T, Ananthakrishnan AN. Vitamin D deficiency is associated with community-acquired clostridium difficile infection: A case control study. BMC Infect Dis. 2014;14:661 (PMID: 254719 26).

28. Grant WB. Variations in vitamin D production could possibly explain the seasonality of childhood respiratory infections in Hawaii. Pediatr Infect Dis J. 2008;27:853 (PMID: 18645543).

29. Nnoaham KE, Clarke A. Low serum vitamin D levels and tuberculosis: A systematic review and meta-analysis. Int J Epidemiol. 2008;37(1):113-9 (PMID: 18245055).

30. Izquierdo MJ, Cavia M, Muñiz P et al. Paricalcitol reduces oxidative stress and inflammation in hemodialysis patients. BMC Nephrol. 2012;13:159 (PMID: 23186077).

31. Wang TT, Nestel FP, Bourdeau V, et al. Cutting edge: 1, 25-dihydroxyvitamin D3 is a direct inducer of antimicrobial peptide gene expression. J Immunol. 2004;173:2909-12 (PMID: 15322146).

32. Hosoda K, Shimomura H, Wanibuchi K, et al. Identification and characterization of a vitamin D_3 decomposition product bactericidal against Helicobacter pylori. Sci Rep. 2015;5:8860 (PMID: 25749128).

33. Guo L, Chen W, Zhu H, et al. Helicobacter pylori induces increased expression of the vitamin d receptor in immune responses. Helicobacter. 2014;19(1):37-47 (PMID: 24188043).

34. Wehkamp J, Schauber J, Stange EF. Defensins and cathelicidins in gastrointestinal infections. Curr Opin Gastroenterol. 2007;23: 32-8 (PMID: 17133082).