





Effect of vitamin D on *Helicobacter pylori* infection and eradication: An updated systematic review and meta-analysis

Ahmed N Albatineh ¹, Rozbeh Sohrabi ², Vajiheh Baghi ³, Reza Ghanei Gheshlagh ^{4*}

¹ Department of Community Medicine and Behavioural Sciences, Faculty of Medicine, Kuwait University, Kuwait

² Student Research Committee, Kurdistan University of Medical Sciences, Sanandaj, Iran

³ Besat Hospital, Kurdistan University of Medical Sciences, Sanandaj, Iran

⁴ Social Determinants of Health Research, Research Institute for Health Development, Kurdistan University of Medical Sciences, Sanandaj, Iran

* **Corresponding author:** Reza Ghanei Gheshlagh, Social Determinants of Health Research, Research Institute for Health Development, Kurdistan University of Medical Sciences, Sanandaj, Iran. **Email:** rezaghanei30@gmail.com

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Abstract

Background: Various studies that have examined the association between *Helicobacter pylori* (*H. pylori*) and vitamin D (25-hydroxyvitamin D [25(OH)D]) have reported different and sometimes controversial results.

Objectives: This systematic review and meta-analysis was performed to investigate the relationship between vitamin D and *H. pylori* infection and its eradication.

Methods: Observational studies published in English were searched in PubMed, Scopus, and ISI databases up to August 1, 2021. The odds ratio of *H. pylori* infection and eradication in the low vitamin D group and the control group was calculated using the standardized mean difference (SMD). The pooled estimate was calculated using a random effects model. Heterogeneity was assessed using Cochran's Q test and the I² index.

Results: Twelve studies were analyzed in this meta-analysis, and the results showed that the level of 25(OH)D in *H. pylori*-positive patients was significantly lower than those without infection (SMD = -0.66 ng/mL, 95% CI: -0.99, -0.33, P<0.001). Also, the level of 25(OH)D in *H. pylori* successful eradication individuals was significantly higher than those with unsuccessful eradication (SMD = 1.53 ng/mL, 95% CI: 1.34–1.71, P<0.001).

Conclusion: There is a significant relationship between vitamin D levels and *H. pylori* infection and its eradication. Therefore, paying attention to vitamin D levels when treating *H. pylori* infection is necessary.

Keywords: *Helicobacter pylori*, Disease eradication, Vitamin D.

Introduction

Helicobacter pylori (*H. pylori*) infection is a known cause of chronic gastritis, affecting 50% of the world's population, and plays an important role in the pathogenesis of gastrointestinal diseases such as peptic ulcer disease, gastric adenocarcinoma, and gastric lymphoma.¹ Approximately 76 to 95% of gastric cancers and more than 90% of duodenal cancers are associated with *Helicobacter pylori* infection.² *Helicobacter pylori* infection spreads through the fecal-oral route and can infect people of all ages globally.³

This infection is more common in developing countries and in populations with low socioeconomic backgrounds.^{4,5} Large differences in the prevalence of *H. pylori* in different ethnic groups indicate a possible genetic susceptibility to this infection.⁵⁻⁸ Furthermore, *H. pylori* is not limited to gastrointestinal diseases. However, it is also associated with several systemic diseases, such as coronary heart disease, Alzheimer's disease, and iron deficiency anemia.⁹⁻¹³ The National Institute of Health Consensus Development Conference (NIHCDC) states that patients with *H. pylori* infection should receive antimicrobial

therapy because the risk of recurrence of peptic ulcers and related complications is not reduced unless the infection is treated.¹⁴ Although triple therapy with proton pump inhibitor (PPI), clarithromycin, and amoxicillin or metronidazole has been used as the first line of treatment for *H. pylori*, the American College of Gastroenterology reports that the treatment rate in 2007 was between 70% and 85%.¹⁵

One of the factors that may be associated with *H. pylori* infection and its treatment is vitamin D levels.¹⁶ It is estimated that approximately one billion people worldwide have moderate-to-severe vitamin D deficiency.^{17,18} A vitamin D deficiency causes osteoporosis, muscle weakness, and an increased risk of fractures. It is also associated with an increased risk of infectious, autoimmune, malignant, and chronic diseases.¹⁹⁻²⁵ The results of the Kawaura et al., study demonstrated that vitamin D could significantly reduce the rate of *H. pylori* infections.²⁶ Different studies in this area have reported different and controversial results.^{3, 27-37}

Objectives

Accordingly, the present systematic review and meta-analysis study was conducted to investigate the association between vitamin D and *Helicobacter pylori* infections and their eradication.

Methods

In this systematic review and meta-analysis study, all articles published in the English language examining the association between vitamin D levels and *H. pylori* infection and its eradication were assessed according to the PRISMA guidelines.³⁸

Data sources and search strategy

The ISI/WoS, Scopus, PubMed, and Embase databases were searched until August 1, 2020, with the following keywords: *Helicobacter pylori*, *H. pylori*, vitamin D, 25(OH)D, 25-hydroxyvitamin D, hydroxycholecalciferols, hypovitaminosis D, cholecalciferol, 25-hydroxycholecalciferols, calcitriol, and 25-hydroxyvitamin D3. To access additional articles, a list of references to selected articles was also reviewed.

Selection criteria

This systematic review and meta-analysis examined observational studies, published in English, that were full-text and reported vitamin D levels in patients infected with *H. pylori* and the control group, or vitamin D levels in patients with successful eradication and unsuccessful eradication, included in the study. Intervention articles, letters to the editor, and reviews were excluded from the analysis. The modified Newcastle-Ottawa Scale (NOS) was used to assess the methodological quality of the articles. NOS evaluates the quality of an item based on three criteria: 1) selection, 2) comparison, and 3) exposure.³⁹

Data analysis

The purpose of this systematic review and meta-analysis was to assess the standardized mean difference (SMD) of vitamin D in *Helicobacter pylori*-infected, *Helicobacter pylori*-eradicated, and control groups. The I^2 index and Cochrane Q test were used to assess heterogeneity between studies.^{40,41} To combine studies and calculate the SMD, if the I^2 index was $>50\%$ or the Cochrane Q test was significant (p -value <0.1), the random effects model was used, and otherwise, the fixed effects model. A forest plot was used to display the SMD for each study and its 95% confidence interval. A leave-one-out sensitivity analysis was used to evaluate the effect of each study on the pooled SMD.⁴² A bar graph was used to visually display the mean vitamin D value and its standard deviation in the *H. pylori*-positive and *H. pylori*-negative groups. Due to the small number of studies, regression-based methods such as Egger's regression test and Begg's rank test were used to examine publication bias and the small study effect.^{43,44} Stata software version 12 was used to analyze the data.

Results

The first search found 508 articles. After reviewing the titles and removing duplicates, 292 articles remained. After screening the titles and abstracts, 280 unrelated articles were removed from the analysis, and 12 final eligible studies were analyzed. The items selected were of good quality. The articles search and screening process in detail is shown in Figure 1.

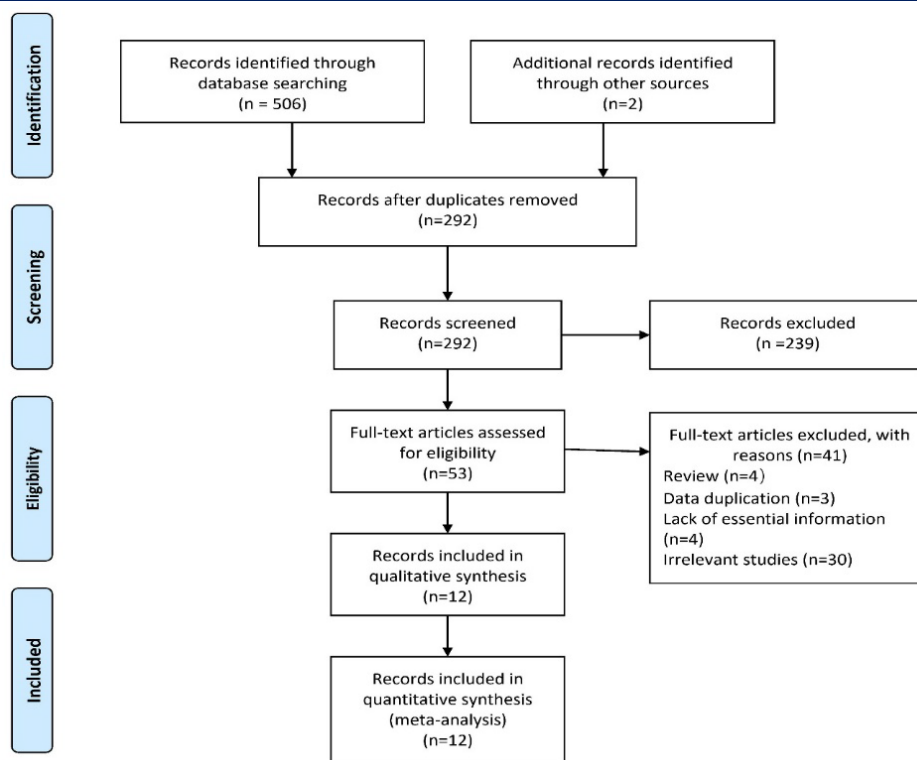


Figure 1. The search and screening process with PRISMA for accessing qualified articles

Six studies examined the effect of vitamin D on the eradication of *H. pylori*,^{29,32,34–37} and six other studies compared vitamin D levels in the *H. pylori*-infected group with those in the control group.^{3,27,28,30,31,33} The Ibrahim et al. study was conducted on two groups of women with and without abortion, and the results were reported separately so that each group was included in the analysis as an

independent study.³³ Eight studies were conducted in Asia, two in Africa, and two in Europe. Of the six studies reporting *H. pylori* eradication, four selected 14-day triple therapy^{29,34–36} and 14-day quadruple therapy.^{32,37} Since $I^2 > 50\%$, the random effects model was used to perform the meta-analysis [Tables 1 and 2].

Table 1. Studies that examined the association between vitamin D and Helicobacter pylori infection

First author	Year	Country	Hp+ (n)	Vitamin D level in Hp+ (ng/mL)	Hp- (n)	Vitamin D level in Hp- (ng/mL)
Ibrahim ³³	2020	Iraq	52	6.91±4.17	48	11.35±7.28
			17	9.91±5.43	83	16.97±5.20
Assaad ²⁸	2019	Lebanon	225	18.04±7.16	235	30.74±15.66
Han ³¹	2019	China	496	17.0±6.9	257	19.2±8.0
Surmeli ³	2019	Turkey	43	9±8.37	211	13.60±11.26
Gerig ³⁰	2013	Switzerland	85	19.60±12.00	315	20.80±11.60
Antico ²⁷	2012	Italy	21	11.10±8.40	212	21.30±12.20

Association between Helicobacter pylori infection and vitamin D

Six studies reported vitamin D levels in *H. pylori*-positive and *H. pylori*-negative individuals. Due to study heterogeneity ($I^2 = 89.8\%$, $Q = 58.79$, p -value 0.0001), a random effects model was employed to evaluate the

difference in mean vitamin D levels between the two groups. The random effects model showed that the average vitamin D content in patients infected with Helicobacter pylori was 0.66 ng/ml (95% CI: -0.99 to -0.33) lower than that in the control group. Because the Gerigi study was excluded and estimates of random effects were used, the

average vitamin D content in the H pylori-positive group was 0.76 ng/ml lower than that in the control group (I²=88.6%, Q=43.96, P value 0.0001) [Figure 2]. It should be highlighted that the deletion of this study had no effect

on the heterogeneity of studies [Figure 3A]. The publication bias of studies using Egger's test (p=0.399) and Begg's test (p=0.100) was not significant [Figure 3B].

Table 2. Studies that examined the association between vitamin D eradication and Helicobacter pylori

First author	Year	Country	Hp+ successful eradication (n)	Vitamin D (ng/mL)	Hp- eradication unsuccessful (n)	Vitamin D (ng/mL)
Magsi ³⁵	2021	Pakistan	88	31.01±7.8	36	18.9±5.6
Shatla ³⁶	2021	Egypt	108	28.12±8.10	42	13.54±6.37
Huang ³²	2019	China	124	19.87±6.35	36	15.09±7.72
El Shahawy ²⁹	2018	Egypt	105	24.71±7.10	45	14.70±4.50
Yildirim ³⁷	2017	Turkey	170	19.00±8.10	50	9.10±4.70
Korkmaz ³⁴	2015	Turkey	29	25.50±10.00	43	14.70±8.50

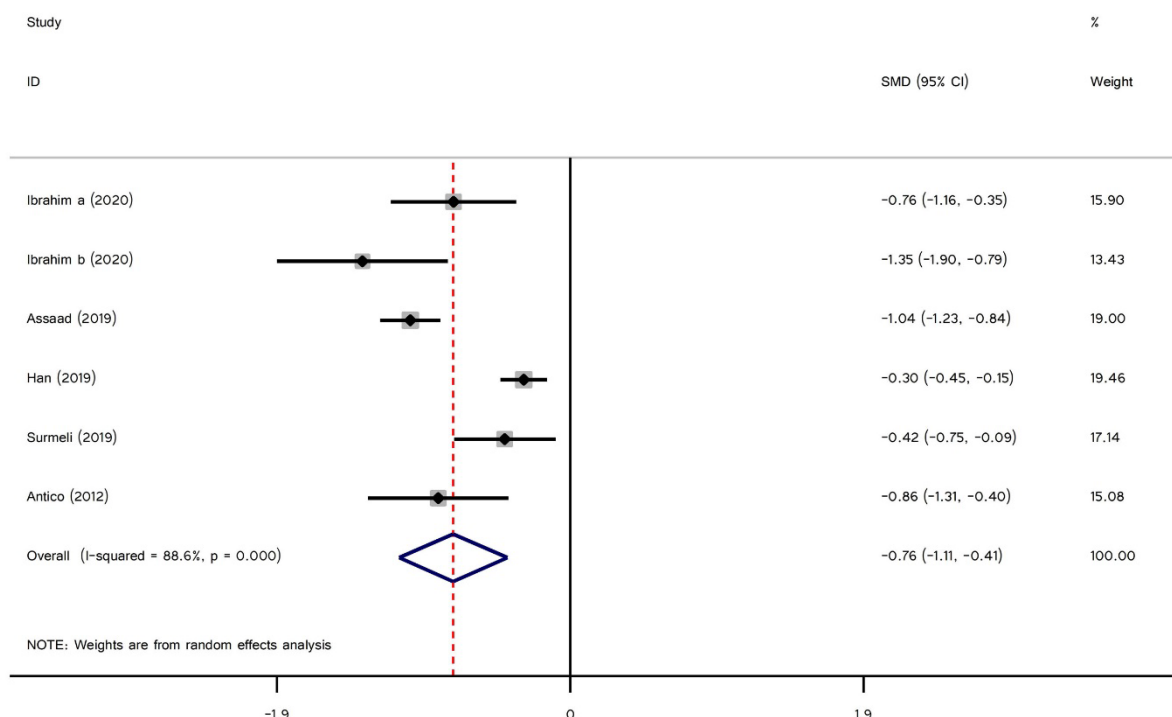


Figure 2. The SMD of vitamin D level in H pylori-positive patients was 0.76 ng/mL lower than that in H pylori-negative patients

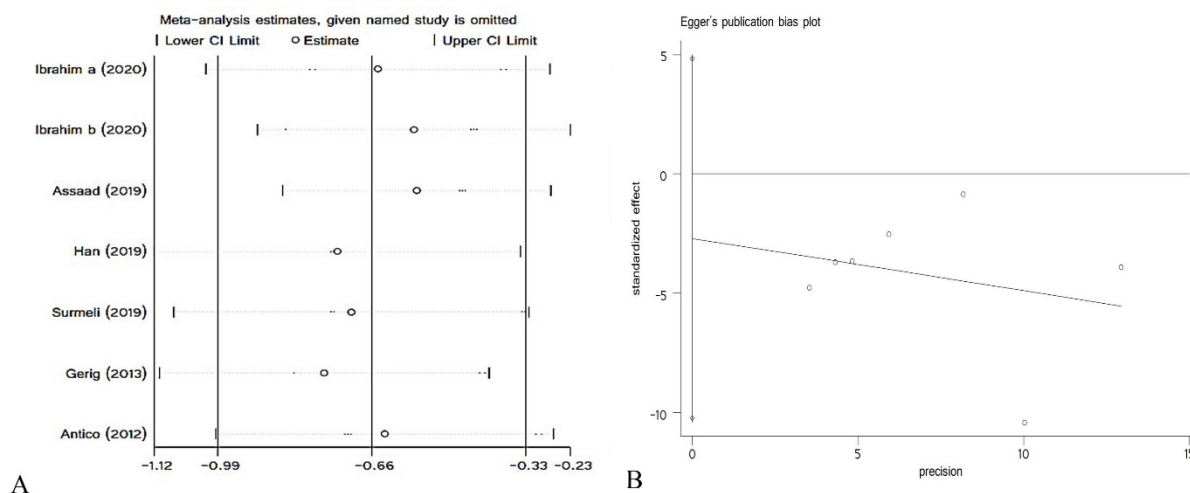


Figure 3. A) Results of sensitivity analysis; B) Publication bias test

The association between Helicobacter pylori eradication and vitamin D

A random effects model was used to determine the standardized mean difference (SMD) between the mean vitamin D values in the two groups due to study heterogeneity ($I^2 = 76.1\%$, $Q = 20.96$, $p\text{-value} = 0.001$). The results showed that the average vitamin D content in patients with successful eradication was 1.39 ng/mL (95% CI: 1.05–1.73) higher than in patients with failed eradication [Figure 4]. According to the sensitivity analysis results [Figure 5A], excluding the Huang study greatly

reduced the heterogeneity of the studies ($I^2=40.1\%$, $Q=6.68$, $P\text{ value}=0.154$). After removing the study and using the fixed effects model, the vitamin D SMD was 1.53 ng/mL (95% CI: 1.34–1.71) higher in the successful eradication group than in the unsuccessful eradication group. Publication bias was tested for all articles describing the association between vitamin D deficiency and H. pylori infection and its eradication. The publication bias of studies using the Egger ($p=0.699$) and Begg ($p=0.573$) test methods was not significant [Figure 5B].

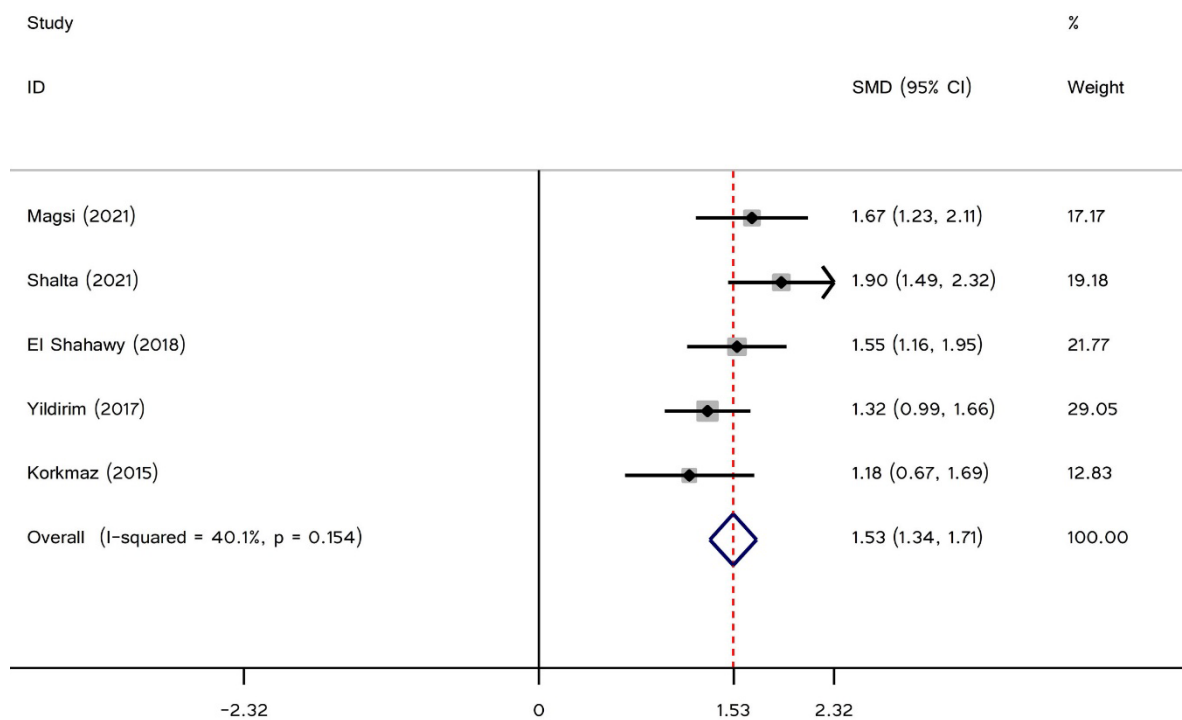


Figure 4. SMD of vitamin D levels in subjects with successful or unsuccessful Helicobacter pylori eradication

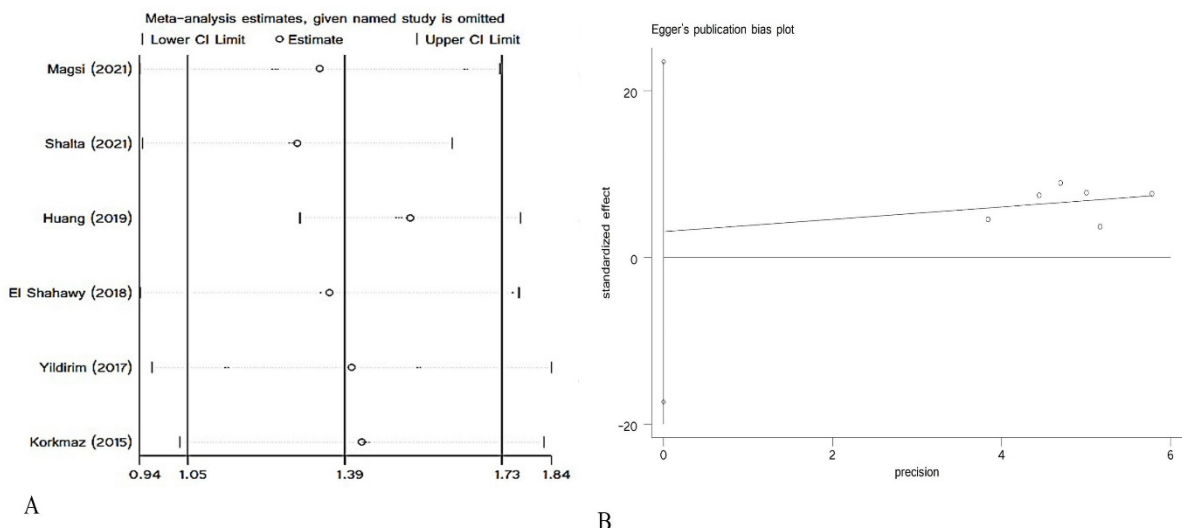


Figure 5. A) Sensitivity analysis results; B) Publication bias test

Discussion

The relationship between vitamin D and *H. pylori* infection, and especially the effect of vitamin D on the eradication of this infection, is still controversial in clinical studies. Therefore, to sufficiently increase the risk of infections through various mechanisms, vitamin D strengthens the innate immune system by up-regulating the expression of antimicrobial peptides and defense in immune cells.²⁹ Therefore, vitamin D deficiency may increase immune system disorders and be a risk factor for the development of infectious diseases.⁴⁵ The results of the present study confirmed that vitamin D levels were higher in subjects who successfully completed eradication than in subjects who failed. *H. pylori* infection was also more likely to be eradicated in people with normal vitamin D levels than in most people with vitamin D deficiency. Results of a study showed that vitamin D3 decomposition product (VDPI) selectively affects *H. pylori*.⁴⁶ When VDPI comes into contact with dimyristoylphosphatidylethanolamine (DMPE), a key component of *H. pylori*, it dissolves.⁴⁷ Vitamin D plays its biological role by associating with VDR in tissues such as the kidney, thyroid, intestine, skin, immune cells, nonparenchymal hepatocytes, and biliary epithelial cells.⁴⁸ Therefore, VDR is involved in a variety of biological responses and is able to reduce infections due to its antibacterial effects against *H. pylori*.⁴⁹ Guo believes that vitamin D may have an antimicrobial effect due to its important role in gastric mucosal homeostasis and in protecting the host against *Helicobacter pylori*.⁵⁰ Infected macrophages are unable to synthesize 1,25(OH)D₂ in vitamin D insufficiency, hence cathelicidin and β -defensin are not formed to kill *H. pylori* strains. Vitamin D deficiency may be a risk factor for *Helicobacter pylori* treatment failure and may require vitamin D supplementation before *Helicobacter pylori* eradication.²⁹

Conclusions

The results of this study showed that there is an association between vitamin D deficiency and *Helicobacter pylori* infection and its failure to eliminate it, and it seems necessary to take vitamin D levels into account in patients with *Helicobacter pylori* infections. Prospective studies are also needed to confirm these findings.

Acknowledgment

None.

Competing interests

The authors declare that they have no competing interests.

Abbreviations

National Institute of Health Consensus Development Conference: NIH/CDC; Proton pump inhibitor: PPI; Newcastle-Ottawa Scale: NOS; Standardized mean difference: SMD.

Authors' contributions

RGG, VB, and RS contributed to designing and performing this systematic review. RGG and ANA checked the data and conduct data analyses. ANA and RGG contributed to writing and editing the paper. All authors read and approved the final manuscript. All authors take responsibility for the integrity of the data and the accuracy of the data analysis.

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Availability of data and materials

The data used in this study are available from the corresponding author on request.

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki. Institutional Review Board approval was obtained.

Consent for publication

By submitting this document, the authors declare their consent for the final accepted version of the manuscript to be considered for publication.

References

1. Sokwala A, Shah MV, Devani S, Yonga G. *Helicobacter pylori* eradication: A randomised comparative trial of 7-day versus 14-day triple therapy. *S Afr Med J*. 2012;102(6). doi:10.7196/SAMJ.5302 PMID:22668909
2. Rana R, Wang SL, Li J, Wang Y, Rao Q, Yang C. *Helicobacter pylori* infection: A recent approach to diagnosis and management.

- J Biomed. 2017; 2(1):45-56. doi:10.7150/jbm.17612
3. Surmeli DM, Surmeli ZG, Bahsi R, Turgut T, Ozturun HS, Atmis V, et al. Vitamin D deficiency and risk of Helicobacter pylori infection in older adults: a cross-sectional study. *Aging Clin Exp Res.* 2019;31(7):985-91. doi:10.1007/s40520-018-1039-1 PMID:30267333
 4. Graham DY, Malaty HM, Evans DG, Evans Jr DJ, Klein PD, Adam E. Epidemiology of Helicobacter pylori in an asymptomatic population in the United States: effect of age, race, and socioeconomic status. *Gastroenterology.* 1991;100(6): 1495-501. doi:10.1016/0016-5085(91)90644-Z PMID:2019355
 5. Khalifa MM, Sharaf RR, Aziz RK. Helicobacter pylori: a poor man's gut pathogen? *Gut Pathog.* 2010;2(1):1-12. doi:10.1186/1757-4749-2-2 PMID:20356368 PMCID:PMC2861632
 6. Brown LM. Helicobacter pylori: epidemiology and routes of transmission. *Epidemiol Rev.* 2000;22(2):283-97. doi:10.1093/oxfordjournals.epirev.a018040 PMID:11218379
 7. Hunt R, Xiao S, Megraud F, Leon-Barua R, Bazzoli F, Van der Merwe S, et al. Helicobacter pylori in developing countries. World gastroenterology organisation global guideline. *J Gastrointest Liver Dis.* 2011;20(3):299-304.
 8. Goh KL, Chan WK, Shiota S, Yamaoka Y. Epidemiology of Helicobacter pylori infection and public health implications. *Helicobacter.* 2011;16:1-9. doi:10.1111/j.1523-5378.2011.00874.x PMID:21896079 PMCID:PMC3719046
 9. DuBois S, Kearney DJ. Iron-deficiency anemia and Helicobacter pylori infection: a review of the evidence. *Clin Transl Gastroenterol.* 2005;100(2):453-9. doi:10.1111/j.1572-0241.2005.30252.x PMID:15667507
 10. Haider AW, Wilson PW, Larson MG, Evans JC, Michelson EL, Wolf PA, et al. The association of seropositivity to Helicobacter pylori, Chlamydia pneumoniae, and cytomegalovirus with risk of cardiovascular disease: a prospective study. *J Am Coll Cardiol.* 2002;40(8):1408-13. doi:10.1016/S0735-1097(02)02272-6 PMID:12392829
 11. Kountouras J, Boziki M, Gavalas E, Zavos C, Grigoriadis N, Deretzi G, et al. Eradication of Helicobacter pylori may be beneficial in the management of Alzheimer's disease. *J Neurol.* 2009;256(5):758-67. doi:10.1007/s00415-009-5011-z PMID:19240960
 12. Kountouras J, Tsolaki M, Gavalas E, Boziki M, Zavos C, Karatzoglou P, et al. Relationship between Helicobacter pylori infection and Alzheimer disease. *Neurology.* 2006;66(6):938-40. doi:10.1212/01.wnl.0000203644.68059.5f PMID:16567719
 13. Rathbone B, Martin D, Stephens J, Thompson JR, Samani NJ. Helicobacter pylori seropositivity in subjects with acute myocardial infarction. *Heart.* 1996;76(4):308-11. doi:10.1136/hrt.76.4.308 PMID:8983674 PMCID:PMC484539
 14. Anonymous. NIH Consensus Conference. Helicobacter pylori in peptic ulcer disease. NIH Consensus development panel on Helicobacter pylori in peptic ulcer disease. *JAMA.* 1994;272:65-9. doi:10.1001/jama.272.1.65 PMID:8007082
 15. Chey WD, Wong BC, Gastroenterology PPCotACo, ACG. American College of Gastroenterology guideline on the management of Helicobacter pylori infection. *J Am Coll Gastroenterol.* 2007;102(8):1808-25. doi:10.1111/j.1572-0241.2007.01393.x PMID:17608775
 16. Lu C, Yu Y, Li L, Yu C, Xu P. Systematic review of the relationship of Helicobacter pylori infection with geographical latitude, average annual temperature and average daily sunshine. *BMC Gastroenterol.* 2018; 18 (1):1-9. doi:10.1186/s12876-018-0779-x PMID:29665777 PMCID:PMC5905136
 17. Holick MF. Vitamin D deficiency. *N Engl J Med.* 2007;357(3):266-81. doi:10.1056/NEJMra070553 PMID:17634462
 18. Sullivan SS, Rosen CJ, Halteman WA, Chen TC, Holick MF. Adolescent girls in Maine are at risk for vitamin D insufficiency. *J Am Diet Assoc.* 2005;105(6):971-4. doi:10.1016/j.jada.2005.03.002 PMID:15942551
 19. Balion C, Griffith LE, Striffler L, Henderson M, Patterson C, Heckman G, et al. Vitamin D, cognition, and dementia: a systematic review and meta-analysis. *Neurology.* 2012;79 (13): 1397-405. doi:10.1212/WNL.0b013e31826c197f PMID:23008220 PMCID:PMC3448747
 20. Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB, Orav JE, Stuck A, Theiler R, et al. Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials. *BMJ.* 2009;339. doi:10.1136/bmj.b3692 PMID:19797342 PMCID:PMC2755728
 21. Bischoff-Ferrari HA, Dietrich T, Orav EJ, Hu FB, Zhang Y, Karlson EW, et al. Higher 25-hydroxyvitamin D concentrations are associated with better lower-extremity function in both active and inactive persons aged ≥ 60 y. *Am J Clin Nutr.* 2004;80(3):752-8. doi:10.1093/ajcn/80.3.752 PMID:15321818
 22. Jenab M, Bueno-de-Mesquita HB, Ferrari P, van Duijnhoven FJ, Norat T, Pischon T, et al. Association between pre-diagnostic circulating vitamin D concentration and risk of colorectal cancer in European populations: a nested case-control study. *BMJ.* 2010; 340.
 23. Lee DM, Tajar A, O'Neill TW, O'Connor DB, Bartfai G, Boonen S, et al. Lower vitamin D levels are associated with depression among community-dwelling European men. *J Psychopharmacol.* 2011; 25(10):1320-8. doi:10.1177/0269881110379287 PMID:20823081
 24. Wang L, Song Y, Manson JE, Pilz S, März W, Michaëlsson K, et al. Circulating 25-hydroxy-vitamin D and risk of cardiovascular disease: a meta-analysis of prospective studies. *Circ Cardiovasc Qual Outcomes.* 2012;5(6):819-29. doi:10.1161/CIRCOUTCOMES.112.967604 PMID:23149428 PMCID:PMC3510675
 25. Basyigit S, Unsal O, Uzman M, Sapmaz F, Dogan OC, Kefeli A, et al. Relationship between Helicobacter pylori infection and celiac disease: a cross-sectional study and a brief review of the literature. *Prz Gastroenterol.* 2017;12(1):49. doi:10.5114/pg.2017.65681 PMID:28337237 PMCID:PMC5360666
 26. Kawaura A, Takeda E, Tanida N, Nakagawa K, Yamamoto H, Sawada K, et al. Inhibitory effect of long term 1 α -hydroxyvitamin D3 administration on Helicobacter pylori infection. *J Clin Biochem Nutr.* 2006; 38(2):103-6. doi:10.3164/jcbn.38.103
 27. Antico A, Tozzoli R, Giavarina D, Tonutti E, Bizzaro N. Hypovitaminosis D as predisposing factor for atrophic type A gastritis: a case-control study and review of the literature on the interaction of vitamin D with the immune system. *Clin Rev Allergy Immunol.* 2012;42(3):355-64. doi:10.1007/s12016-011-8255-1 PMID:21286859
 28. Assaad S, Chaaban R, Tannous F, Costanian C. Dietary habits and Helicobacter pylori infection: a cross sectional study at a Lebanese hospital. *BMC Gastroenterol.* 2018;18(1):1-13.

- doi:10.1186/s12876-018-0775-1 PMid:29661143
PMCID:PMC5902873
29. El Shahawy MS, Hemida MH, El Metwaly I, Shady ZM. The effect of vitamin D deficiency on eradication rates of *Helicobacter pylori* infection. *JGH Open*. 2018;2(6):270-5. doi:10.1002/jgh3.12081 PMid:30619936 PMCID:PMC6308038
 30. Gerig R, Ernst B, Wilms B, Thurnheer M, Schultes B. Preoperative nutritional deficiencies in severely obese bariatric candidates are not linked to gastric *Helicobacter pylori* infection. *Obes Surg*. 2013;23(5):698-702. doi:10.1007/s11695-013-0878-2 PMid:23430478
 31. Han C, Ni Z, Yuan T, Zhang J, Wang C, Wang X, et al. Influence of serum vitamin D level on *Helicobacter pylori* eradication: A multi-center, observational, prospective and cohort study. *J Dig Dis*. 2019;20(8):421-6. doi:10.1111/1751-2980.12793 PMid:31145549 PMCID:PMC6851741
 32. Huang B YS, Chen C, Ye S. Effect of 25-hydroxyvitamin D on *Helicobacter pylori* eradication in patients with type 2 diabetes. *Wien Klin Wochenschr Educ*. 2019;131(3):75-80. doi:10.1007/s00508-018-1416-y PMid:30542778 PMCID:PMC6394653
 33. Ibrahim HA. Relationship Between *Helicobacter pylori* Infection, Serum Vitamin D3 Level and Spontaneous Abortion. *Int J Gen Med*. 2020;13:469. doi:10.2147/IJGM.S251075 PMid:32801841 PMCID:PMC7395681
 34. Korkmaz H, IPEKCI S, Baldane S, Sozen M, Abusoglu S, Kebapcilar L. Examining the relationship between vitamin D levels and *Helicobacter pylori* infection and its effect on the hypothalamic-pituitary-adrenal axis in dyspeptic patients. *J Exp Clin Med*. 2015;32(3).
 35. Magsi I. Response of *Helicobacter Pylori* Eradication Treatment in Patients With Normal and Below-Normal Serum Vitamin D Levels. *Cureus*. 2021;13(4). doi:10.7759/cureus.14777
 36. Shatla MM, Faisal AS, El-Readi MZ. Is Vitamin D Deficiency a Risk Factor for *Helicobacter Pylori* Eradication Failure? *Clin Lab*. 2021;67(2). doi:10.7754/Clin.Lab.2020.200118 PMid:33616339
 37. Yildirim O, Yildirim T, Seckin Y, Osanmaz P, Bilgic Y, Mete R. The influence of vitamin D deficiency on eradication rates of *Helicobacter pylori*. *Adv Clin Exp Med*. 2017;26(9):1377-81. doi:10.17219/acem/65430 PMid:29442458
 38. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6(7):e1000097. doi:10.1371/journal.pmed.1000097 PMid:19621072 PMCID:PMC2707599
 39. Lo CK-L, Mertz D, Loeb M. Newcastle-Ottawa Scale: comparing reviewers' to authors' assessments. *BMC Med Res Methodol*. 2014; 14(1):1-5. doi:10.1186/1471-2288-14-45 PMid:24690082 PMCID:PMC4021422
 40. Higgins J, Altman D. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.0.0 (updated February 2008). The Cochrane Collaboration, 2008. Available from www.cochrane-handbook.org. 2008. doi:10.1002/9780470712184
 41. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327(7414):557-60. doi:10.1136/bmj.327.7414.557 PMid:12958120 PMCID:PMC192859
 42. Patsopoulos NA, Evangelou E, Ioannidis JP. Sensitivity of between-study heterogeneity in meta-analysis: proposed metrics and empirical evaluation. *Int J Epidemiol*. 2008;37(5):1148-57. doi:10.1093/ije/dyn065 PMid:18424475 PMCID:PMC6281381
 43. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997; 315 (7109):629-34. doi:10.1136/bmj.315.7109.629 PMid:9310563 PMCID:PMC2127453
 44. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics*. 1994:1088-101. doi:10.2307/2533446 PMid:7786990
 45. Hong J, Kim S, Chung K, Kim E, Jung J, Park M, et al. Association between vitamin D deficiency and tuberculosis in a Korean population. *Int J Tuberc Lung Dis*. 2014;18(1):73-8. doi:10.5588/ijtld.13.0536 PMid:24365556
 46. Hosoda K, Shimomura H, Wanibuchi K, Masui H, Amgalanbaatar A, Hayashi S, et al. Identification and characterization of a vitamin D 3 decomposition product bactericidal against *Helicobacter pylori*. *Sci Rep*. 2015; 5(1):1-9. doi:10.1038/srep08860 PMid:25749128 PMCID:PMC4352922
 47. Malfertheiner P, Megraud F, O'Morain C, Bazzoli F, El-Omar E, Graham D, et al. Current concepts in the management of *Helicobacter pylori* infection: the Maastricht III Consensus Report. *Gut Pathog*. 2007; 56 (6):772-81. doi:10.1136/gut.2006.101634 PMid:17170018 PMCID:PMC1954853
 48. Lu C, Yang J, Yu W, Li D, Xiang Z, Lin Y, et al. Association between 25 (OH) D level, ultraviolet exposure, geographical location, and inflammatory bowel disease activity: a systematic review and meta-analysis. *PloS one*. 2015;10(7):e0132036. doi:10.1371/journal.pone.0132036 PMid:26172950 PMCID:PMC4501705
 49. Yang L, He X, Li L, Lu C. Effect of vitamin D on *Helicobacter pylori* infection and eradication: A meta-analysis. *Helicobacter*. 2019;24(5):e12655. doi:10.1111/hel.12655 PMCID:PMC6790945
 50. Guo L, Chen W, Zhu H, Chen Y, Wan X, Yang N, et al. *Helicobacter pylori* Induces Increased Expression of the Vitamin D Receptor in Immune Responses. *Helicobacter*. 2014;19(1):37-47. doi:10.1111/hel.12102 PMid:24188043

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