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Original Research Paper

The Role of Vitamin D Deficiency in Predicting Peptic Ulcer Risk

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Abstract: Peptic ulcer continues to be a significant global health issue, largely due to Helicobacter pylori infection and vitamin D deficiency. H. pylori acts on mucosal damage through inflammation and increased gastric acid secretion, while vitamin D deficiency compromises immune defenses and hinders mucosal healing. The study aimed to assess the impact of vitamin D levels and H. pylori infection as predictive risk factors for peptic ulcer development. A total of 110 patients (aged 20–65) from the Gastroenterology Clinic in Babylon Province, Iraq, between March and October of 2024 were chosen for this cross-sectional study; they were categorized based on upper gastrointestinal endoscopic for peptic ulcer diagnosis and H. pylori status. A strong correlation was observed between H. pylori infection and PU ($p = 0.001$). Remarkably, vitamin D deficiency (<20 ng/mL) was highly significant ($p < 0.001$) and more distributed in patients with H. pylori Ve+ (84.3%) and displayed lower vitamin D levels (12.65 ng/mL) compared to H. pylori Ve- patients (39.0%) with levels of 17.37 ($p = 0.017$). Logistic regression analysis identified vitamin D deficiency as a strong independent risk factor for both H. pylori infection (OR = 8.41, 95% CI: 3.36–21.07) and progressive peptic ulcer (OR = 4.54, 95% CI: 1.92–10.72), $p < 0.001$. Conclusions: the crucial association of vitamin D deficiency with increased vulnerability to H. pylori infection as predicted factors in the progression of peptic ulcer risk. vitamin D screening in high-risk groups may well be an effective strategy for preventing peptic ulcer.

Keywords: Vitamin D, H. pylori, Peptic Ulcer, and Gastrointestinal infections

1. Introduction

Peptic ulcers are open lesions that develop on the upper part of the small intestine and the stomach's inner lining. Long-term use of nonsteroidal anti-inflammatory medicines (NSAIDs) or Helicobacter pylori (H. pylori) infections are the most common causes of them. Recent research has investigated the connection between H. pylori infection and vitamin D levels [1] For gastrointestinal (GI) health, vitamin D is essential. As a way to safeguard the GI tract from harmful microbes, it serves as vital to support the immune system. Vitamin D deficiency can impair immunity, leaving the gastrointestinal system more vulnerable to inflammation and infections. Additionally, vitamin D contributes to the preservation of the gut's mucosal barrier. Essential nutrients can flow past this barrier, which serves as a shield to keep dangerous invaders at away. Sufficient vitamin D levels promote the stomach lining's healing process and lower the risk of GI illnesses, including inflammatory bowel disease and leaky gut syndrome. These problems are more likely to occur when the mucosal barrier is compromised due to low vitamin D levels. [2,3].

H. pylori is a key factor in peptic ulcer development, this is a gram-negative bacterium that colonizes the human gastric mucosa. Many studies have demonstrated that H. pylori infection and as an inflammatory response

disrupts the protective mucosa and, along with an increase in gastric acid secretion, creates the ideal conditions for ulcers to form causes chronic inflammation of the stomach lining, leading to tissue damage, mucosa-associated lymphoid tissue lymphoma, and formation peptic ulcer and gastric cancer [4-6]. H. pylori is highly prevalent around the world, especially in developing regions. Studies have also pointed to an inverse relationship between vitamin D levels and H. pylori infection, suggesting that low vitamin D might be a risk factor for both acquiring the infection and facing challenges in eliminating it [7]. This study aims to highlight the association between vitamin D deficiency and the prevalence of H. pylori infection, as predictive risk factors for the development of complications linked to peptic ulcers. Further research is needed to understand whether vitamin D supplementation could serve as a beneficial addition to traditional treatments.

2. Methodology

Subject and Data Collection

A total of 110 participants (aged 20–65) who visited the Gastroenterology Center in the Morgan Teaching Hospitals and the external Gastroenterology Clinic in Babylon province, Iraq, between March and October of 2024 were chosen for this cross-sectional study. Iraq.

Every participant had an upper gastrointestinal endoscopy. Endoscopy is used to diagnose and assess peptic ulcers based on the results of the examination. In order to examine the ulcer samples, the endoscope—a flexible tube equipped with a camera—is sent via the mouth into the stomach and duodenum (Figure 1). Participants were divided into two groups: 40 who without have PU and 70 with PU. All demographic including BMI, age, smoking status, and sex, were recorded through structured questionnaires and medical records. Exclusion criteria encompassed individuals with chronic liver and kidney disease, autoimmune disorders, metabolic disorders, cancers, prior gastric surgery, or those who had taken vitamin D supplementation within the past three months

Methods and Biochemical Analysis

H. pylori infection was diagnosed using a combination of the urea breath test and stool antigen test, both of which provide high sensitivity and specificity. A five mL venous blood sample taken from all participant. Centrifugation at 3,000 rpm for 10 minutes was used to extract the serum, which was then kept at -20°C for further quantification of serum parameters screening testing. Serum vitamin D levels were quantified using enzyme-linked immunosorbent assay (ELISA), ensuring precise measurement of 25-hydroxyvitamin D concentrations kits provided by Bioassay Technology Laboratory. Simultaneously, the lipid profile, which includes total cholesterol (CHO), high-density lipoprotein (HDL), and triglycerides (TG), along with liver and pancreatic enzymes amylase and lipase, were analyzed using automated biochemical analyzers following standardized laboratory protocols (Linear, Spain).

For these biochemical analyses, the absorbance of the samples was measured at 450 nm using an Agilent 8453 spectrophotometer (Agilent Technologies, Inc., USA). The concentrations of CHO, TG, and HDL were then calculated using the specified formula.

Serum concentration (mg/dl) = (Ab sample/Ab of standard) × concentration of the standard (mg/dl)

Serum very-low-density lipoprotein-cholesterol (VLDL) and low-density lipoprotein-cholesterol (LDL) were calculated according to the equation of Friedewald [9], respectively.

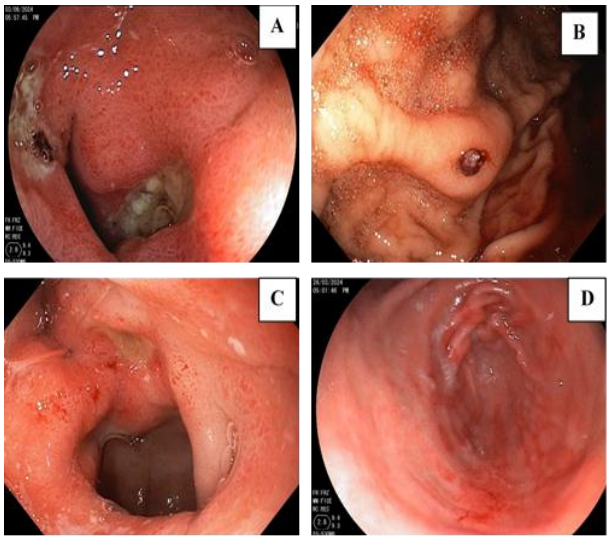
Serum LDL concentration (mg/dl) = CHO- (TG/5)- HDL

Serum VLDL-C concentration (mg/dl) = (TG/5)

Statistical analysis

The analysis was performed using IBM SPSS 28 (IBM Corp., Chicago, Illinois, USA). Continuous data were tested for normality with the Kolmogorov-Smirnov test and expressed as mean ± standard deviation (SD), while nominal data were summarized as frequencies and percentages, with chi-square tests used for comparisons. Group differences were evaluated using independent t-tests or univariate ANOVA, supplemented by Tukey's post hoc tests for multiple comparisons. Logistic regression with Log Likelihood of Reduced Model was performed to determine independent risk factors for H. pylori infection and Peptic Ulcer. A p-value below 0.05 was considered statistically significant.

Fig.1 Peptic Ulcer in stomach and duodenum under Endoscope.



The provided endoscopic photographs show areas of the stomach lining (gastric mucosa) that appear reddened and inflamed, with some visible depressions or craters that could be consistent with ulcerative lesions. In several images, A, B, and C there seem to be shallow to moderately deep defects in the mucosa, some with whitish or yellowish exudates, The surrounding tissue looks erythematous (red) and inflamed, but D was normal gastric without Peptic Ulcer.

3. Results and discussion

Clinical and Demographic Factors According H. Pylori Infection status

The statistical results in the table 1. Indicated that peptic ulcers, 80.4% of individuals with peptic ulcers (PU) are H. pylori Ve+, while only 19.6% without peptic ulcers are H. pylori Ve+, (p-value = 0.001). A significant difference (p-value = 0.013) among males, 37.3% are H. pylori Ve+, while 62.7% of females are H. pylori Ve+. A non-significant in the mean (SD) age of H. pylori Ve+ patients compared to patients have H. pylori Ve- were 40.12 (16.22) Vs. 38.71 (13.51), p= 0.621 years. For patients aged ≤40 years, 64.7% are H. pylori Ve+, while 35.3% of patients aged >40 years are H. pylori Ve+ (p-value = 0.690, non-significant). There was a significant decrease (p=0.001) in the mean BMI for H. pylori Ve+ patients, which averaged 22.13 (3.50) kg/m², compared to 24.83 (4.44) kg/m² for H. pylori Ve- groups. Additionally, 72.5% of H. pylori Ve+ individuals had a BMI of less than 25, whereas only 27.5% had a BMI greater than 25 (p=0.003). Not significantly impact of smoking with H. pylori infection rates, with 43.1% of smokers and 56.9% of non-smokers being H. pylori Ve+ (p-value = 0.419). For vitamin D levels, 84.3% of H. pylori Ve+ individuals have levels below 20 ng/mL, compared to 15.7% with levels at or above 20 ng/mL, with high significant (p=0.0001). There are significant differences in ulceration locations. Among H. pylori Ve+ patients, 21.6% have duodenal ulcers, 41.2% have gastric ulcers, and 17.6% have both duodenal and gastric ulcers. In contrast, for H. pylori Ve-patients, the respective percentages are 11.9%, 16.9%, and 20.3% with p-value 0.002.

The logistic regression analysis in the same Table 1. observed of several factors significantly affect the likelihood of H. pylori infection. Patients with PU were 4.54 times more likely to be H. pylori Ve+ compared to those without peptic ulcers, indicating a strong association (p-value = 0.001). Age don`t have a significant impact on the likelihood of H. pylori infection (OR = 1.12, p-value = 0.796). Although not statistically significant, females have lower odds of H. pylori infection compared to males (OR = 0.42, p-value = 0.084). Patients with a BMI < 25 are 2.85 times more likely to be H. pylori Ve+ compared to those with a BMI > 25 (p= 0.013). No significant impact of Smoking status on the likelihood of H. pylori infection (OR = 1.22, p= 0.695). Vitamin D status is a highly significant predictor, with patients Vt. D deficiency < 20 ng/mL being 8.41 times more likely to be H. pylori Ve+ compared to patients have sufficient Vit. D ≥ 20 ng/mL (p< 0.001). The location of ulceration (duodenal or gastric) not statistically significant impact on the likelihood of H. pylori infection.

Biochemical Markers Associated with PU and H. Pylori Status

The results of lipid profile in Table 2. Show no significant difference in the mean (SD) cholesterol (CHO) level for H. pylori Ve+ patients were 177.74 (43.44), as compared with 166.82 (40.83) mg/dL for H. pylori Ve- patients, with p-value = 0.177. Also, no significant in HDL level when compared between H. pylori Ve+ and Ve- were (33.8 (8.3) Vs. 34.24 (9.26), p-value of 0.794). Furthermore, TG and VLDL were indicted to significant increase in H. pylori Ve+ at 187.49 (69.89) and 37.5 (13.98) mg/dL compared to 157.41 (61.4) and 31.48 (12.28) in H. pylori Ve- individuals, with a p-value of 0.018 and 0.019 respectively. The mean LDL levels are 106.44 mg/dL (SD: 37.53) for H. pylori Ve+ group and 101.09 mg/dL (SD: 37.35) for H. pylori Ve- patients, with a non-significant p-value of 0.457. no significant differences in means of pancreatic enzymes between both patients H. pylori Ve+ and H. pylori Ve- Amylase were (89.23 (21.53) Vs. 89.74 (20.64) U/L), p=0.900, and Lipase were 41.73 (13.02) Vs. 41.49 (15.57) with p=0.930, respectively.

Relationship Between Vitamin D levels and H. pylori Infection Status

The relationship between Vitamin D levels and H. pylori infection status in two groups: all patients (Part A) and those with PU (Part B) Figure 2, which was described through pie charts and population pyramids. It shows that H. pylori Ve+ patients have a higher percentage of Vit D deficiency (< 20 ng/mL) when compared to H. pylori Ve-. Conversely, H. pylori Ve- groups were more likely to have higher Vit. D levels (≥ 20 ng/mL). With statistically significant association in Part A (X^2 = 23.42, P < 0.001), all patients. And in Part B (X^2 = 7.87, P = 0.005), patients with PU, respectively.

Multivariate compares the Vit. D levels in H. pylori Ve+ and H. pylori Ve- patients, associated of both groups with and without PU, Table 3, and Figure 3. For patients without PU, the mean Vit. D in H. pylori Ve+ patients were 21.37 (SD: 7.86), but in H. pylori Ve-, it was 26.17 (SD: 6.45). The median (IQR) values for these groups are 18.08 ng/mL (16.15–28.61) and 26.48 ng/mL (22.19–29.76), respectively, and indicating a non-significant difference p=0.080. For patients with PU, the mean Vit. D level in H. pylori Ve+ group is significantly lower at 12.65 (SD: 5.65) compared to 17.37 (SD: 2.26) in H. pylori Ve- patients, with a p-value of 0.017. The median (IQR) values for these groups are 10.80 ng/mL (8.86–14.25) and 19.24 (8.77–21.59), respectively. Overall, the total mean Vit. D in H. pylori Ve+ group was 14.34 (SD: 6.99), while in H. pylori Ve-, it was 21.85 (SD: 8.12) ng/mL, with a highly significant p-value of 0.001. The total median (IQR) values for these groups are 13.12 ng/mL (9.29–17.59) and 21.88 (16.57–27.74), respectively.

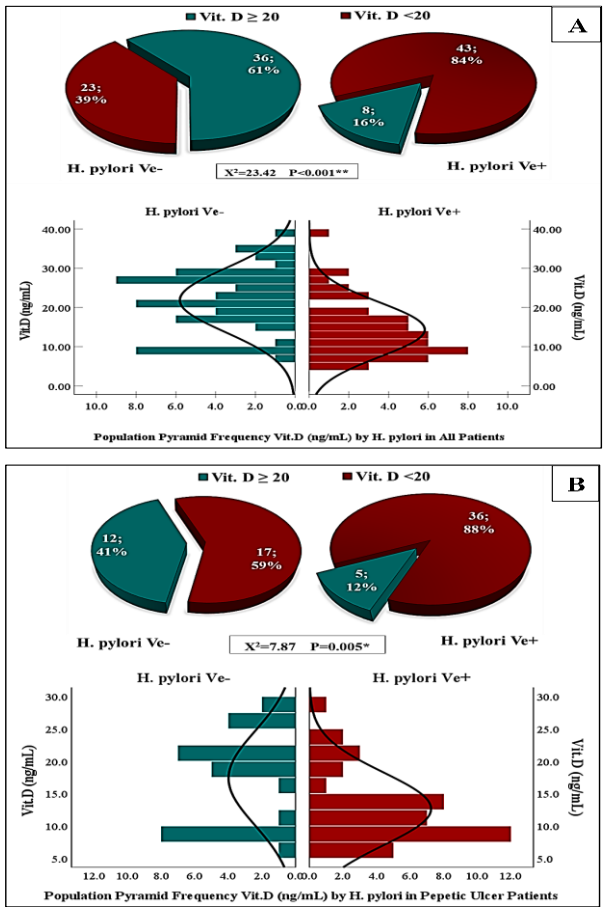


Fig 2. Prevalence and population pyramid Frequency among Vit. D and H. pylori status, A in all patients, B. in PU patients only

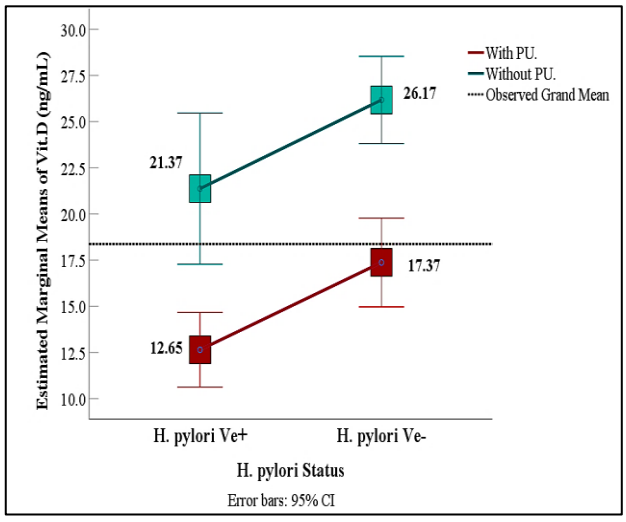


Fig 3. Multivariate Analysis of Estimated Marginal Mean of Vit. D level levels based on H. pylori Status in with and without PU Patients.

Table 1: Association of H. pylori Infection and Various Clinical and Demographic Factors

Clinical and Demographic characteristics		H. pylori Status						p-value	OR (95%CI)	p-value
		H. pylori Ve+		H. pylori Ve-		Total				
		N	%	N	%	N	%			
Peptic Ulcer	With PU.	41	80.4%	29	49.2%	70	63.6%	X^2=11.54	4.54(1.92–10.72)	0.001
	Without PU.	10	19.6%	30	50.8%	40	36.4%	0.001*	**Ref.**	
Sex	Male	19	37.3%	36	61.0%	55	50.0%	X^2=6.18	0.42(0.16–1.13)	0.796
	Female	32	62.7%	23	39.0%	55	50.0%	0.013*	**Ref.**	
Age (year)	**Mean (SD)**	**40.12 (16.22)**		**38.71 (13.51)**				**0.621¥: NS**		
	≤ 40 years	33	64.7%	36	61.0%	69	62.7%	X^2=0.16	1.12(0.48–2.58)	0.084
	> 40 years	18	35.3%	23	39.0%	41	37.3%	0.690 NS	**Ref.**	
BMI (kg/m^2)	**Mean (SD)**	**22.13 (3.50)**		**24.83 (4.44)**				**0.001*¥**		
BMI Status	BMI < 25	37	72.5%	26	44.1%	63	57.3%	X^2=9.07	2.85(1.24–6.54)	0.013
	BMI >25	14	27.5%	33	55.9%	47	42.7%	0.003*	**Ref.**	
Smoking	Yes	22	43.1%	30	50.8%	52	47.3%	X2=0.65	1.22(0.46–3.26)	0.695
	No	29	56.9%	29	49.2%	58	52.7%	0.419 NS	**Ref.**	
Vit. D (ng/mL) Status	Vit. D <20	43	84.3%	23	39.0%	66	60.0%	X^2=23.42	8.41(3.36–21.07)	0.0001
	Vit. D ≥ 20	8	15.7%	36	61.0%	44	40.0%	0.0001**	**Ref.**	
Ulceration Locate	Non	10	19.6%	30	50.8%	40	36.4%	X^2=14.72	**Ref.**	
	Duodenal ulcer	11	21.6%	7	11.9%	18	16.4%	0.002*	2.02(0.38–10.84)	0.412
	Gastric ulcer	21	41.2%	10	16.9%	31	28.2%		3.13(0.75–13.10)	0.118
	Duodenal+ Gastric ulcer	9	17.6%	12	20.3%	21	19.1%		0.88(0.19–4.11)	0.876

Significant differences at *p-value ≤0.05, **<0.01. SD: Standard Division. NS: Non- significant. X2: Chi-square test. ¥: P-value for independent t-test. a. The reference category is: H. pylori Ve-. 95%CI: 95% Confidence Interval for Odds Ratio (OR).

Table. 2: Comparison of Biochemical Markers in Patients Based on H. Pylori Status

Biochemicals Lab.		Mean (SD)	p-value	Effect Sizes
CHO (mg/dL)	H. pylori Ve+	177.74(43.44)	0.177 NS	0.260
	H. pylori Ve-	166.82(40.83)		
TG (mg/dL)	H. pylori Ve+	187.49(69.89)	0.018*	0.459
	H. pylori Ve-	157.41(61.4)		
HDL (mg/dL)	H. pylori Ve+	33.8(8.3)	0.794 NS	-0.050
	H. pylori Ve-	34.24(9.26)		
VLDL (mg/dL)	H. pylori Ve+	37.5(13.98)	0.019*	0.459
	H. pylori Ve-	31.48(12.28)		
LDL (mg/dL)	H. pylori Ve+	106.44(37.53)	0.457 NS	0.143
	H. pylori Ve-	101.09(37.35)		
AMY (U/L)	H. pylori Ve+	89.23(21.53)	0.900 NS	-0.024
	H. pylori Ve-	89.74(20.64)		
LIP (U/L)	H. pylori Ve+	41.73(13.02)	0.930 NS	0.017
	H. pylori Ve-	41.49(15.57)		

Significant differences at *p-value ≤0.05. SD: Standard Division. NS: Non- significant. Effect Sizes: Cohen's d for independent two samples.

Table 3. Comparative Analysis of Vitamin D Levels in Relation to H. pylori Status and Peptic Ulcer Occurrence

Groups	Vit. D	H. pylori		Z	p-value
		H. pylori Ve+	H. pylori Ve-		
Without PU.	Mean (SD)	21.37 (7.86)	26.17 (6.45)	-1.75	0.080 NS
	Median (IQR)	18.08 (16.15–28.61)	26.48 (22.19–29.76)		
With PU.	Mean (SD)	12.65 (5.65)	17.37 (2.26)	-2.40	0.017*
	Median (IQR)	10.80 (8.86–14.25)	19.24 (8.77–21.59)		
Total	Mean (SD)	14.34(6.99)	21.85(8.12)		0.001*
	Median (IQR)	13.12(9.29–17.59)	21.88(16.57–27.74)		

Significant differences at *p-value ≤0.05. SD: Standard Division. NS: Non- significant. IQR: Inter Quartile Range. Z: Standardized distribution.

According to the study, there is a significant correlation between H. pylori infection and peptic ulcers. Approximately 80.4% of patients with PU tested positive for H. pylori Ve+, compared to 19.6% of patients without PU (p=0.001). This supports the results of recent research showing that H. pylori is a primary cause of peptic ulcer disease. [10] However, the fact that 19.6% of cases have H. pylori-negative peptic ulcers points to other causes, like the use of NSAIDs or stress-related variables, which are also covered in the most recent evaluations. [6,11].

The prevalence of H. pylori varied significantly by sex, with 37.3% of male and 62.7% of female H. pylori Ve+, p=0.013. A recent study suggested that higher prevalence rates in females might be caused by immunological or hormonal differences, principally the modulatory effect of estrogen on immune responses [12, 13], even though previous studies found no sex-related differences [14]. These hormonal variables may influence H. pylori vulnerability. There was no noticeable effect of age on H. pylori infection rates. These results are consistent with studies viewing that H. pylori infections are primarily acquired during childhood and can continue untreated [15]. However, other studies show that age-related variables and cumulative exposure lead to greater infection rates in elderly groups [16].

The results indicate a significant association between lower BMI and H. pylori Ve+. Moreover, only 27.5% of people with H. pylori Ve+ had a BMI ≥25 (H. pylori = 0.003), whereas 72.5% of them had a BMI <25. The outcome of the current study indicates that an H. pylori infection may change metabolic pathways, resulting in a reduced BMI. [17,18] They are consistent with this finding. However, there are conflicting results; according to some research, there is no direct link between H. pylori infection and BMI [11]. The complex link between H. pylori, metabolic syndrome, and nutritional status will require more investigation. Smoking and H. pylori infection rates did not significantly correlate (p = 0.419). This finding is consistent with recent research that found no connection between smoking and the prevalence of H. pylori, but according to some studies, smoking makes H. pylori-induced stomach inflammation worse, raising the possibility of problems. [19] This study's lack of significance could be explained by sample size restrictions or confounding variables like smoking intensity and duration.

A highly significant association was observed between vitamin D deficiency (<20 ng/mL) and H. pylori infection, with 84.3% of H. pylori Ve+ patients having low Vit. D levels (p<0.001). In addition to the logistic regression analysis, it was identified that patients with PU were 4.54 times more likely to be H. pylori Ve+ (p = 0.001), and Vit. D deficiency (<20 ng/mL) increased the OR by 8.41 times (p < 0.001). This finding is supported by recent studies suggesting that Vit D deficiency may impair immune responses, increasing susceptibility to H. pylori infection, and the relationship between Vit D deficiency and H. pylori infection in the context of peptic ulcer risk is a complex and multifaceted issue. Several studies have highlighted the significant association between low Vit D levels and the prevalence of H. pylori infection, which is a known risk factor for peptic ulcers [6].

Vitamin D plays a crucial role in modulating the immune system and keeping the integrity of the gastric mucosa. Deficiency in Vit. D can impair the body's ability to mount an effective immune response, making individuals more susceptible to infections, including H. pylori. A study found that serum vitamin D levels were significantly lower in individuals with H. pylori infection compared to those without the infection. These suggest that Vit. D deficiency may increase the risk of acquiring H. pylori infection, which in turn can lead to the development of peptic ulcers [20].

One of the most intriguing studies on vitamin D was recently published by Guo et al., which revealed that vitamin D possesses antibacterial properties against H. pylori. Vitamin D is crucial for maintaining the homeostasis of the stomach mucosa and protecting the host from H. pylori infection [21]. Together with its impact on bone metabolism, vitamin D may also raise levels of the anti-inflammatory cytokine IL-10 and

decrease inflammatory markers like CRP, TNF-α, IL-6, and IL-18 [22].

Additionally, vitamin D is known to control the expression of AMPs that kill bacteria, such as cathelicidin and β-defensin. Although cathelicidin's effect has only been shown in macrophages infected with Mycobacterium TB, it has also been shown to have antibacterial activity against both Gram-positive and Gram-negative bacteria [23]. When the infected macrophage is vitamin D deficient, it cannot make enough 1,25-(OH) D2 to increase the production of cathelicidin and β-defensin, which prevents them from killing the H. pylori strains.

Conclusion

The finding concluded that vitamin D deficiency is a significant risk factor for prevalence of H. pylori infection and the subsequent as important predictors for development peptic ulcer risk. And treatment vitamin D deficiency through supplementation and dietary interventions may help reduce the risk of H. pylori infection and improve the outcomes of peptic ulcer treatment.

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Author's Contributions

The author, Intisar Razzaq Sharba, were responsible for planning, supervising the work, drafting the manuscript, and designing the figures. Zahraa Majid Abd-Alameer conducted the measurements and processed the experimental data. Both authors collaboratively contributed to the research's design and implementation, analyzed the results, and participated in writing the manuscript.

Ethics

This study was conducted under approval by the medical ethics committee at the University of Kufa (2024). Verbal and written consent was provided by all participates and agreement for publication was obtained from both participants and researchers.

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