Ulutas Med J 2019;5(1):84-90
DOI: 10.5455/umj.20190227101537

ORIGINAL ARTICLE OPEN ACCESS

Is There Any Relationship Between Circulating Serum 25-Hydroxyvitamin D Level and Presence of Helicobacter Pylori As Well As Gastric Inflammation Severity?

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Background: Helicobacter Pylori (H. Pylori) and ongoing chronic gastric inflammation are the most crucial factors leading to gastric cancer. The serum 25 Hydroxyvitamin D is the fundamental keys to the proper functioning of the immune system and reduction of inflammation. The primary aim of this study is to evaluate the association between the serum level of 25 Hydroxyvitamin D and the presence of H. Pylori as well as gastric inflammation.

Materials and Methods: A total of 91 (18-85 years old) dyspeptic patients having a standard laboratory parameter (hematologic, liver and kidney) without chronic medical problems and were enrolled in this study. During an upper endoscopy, at least four stomach biopsies were taken and evaluated according to Sydney classification. The serum 25-Hydroxyvitamin D level was also calculated at the same time endoscopy.

Results: In population, 48 (52.7%) were H. Pylori positive, while 41 (47.3%) were H. Pylori negative. The mean age, gender, hemoglobin, mean corpuscular volume, mean platelet volume, CRP, ferritin, red cell distribution width, endoscopic findings, and iron were similar in two groups ($p<0.05$). The mean serum 25-Hydroxyvitamin D level was not different between the two groups ($p=0.375$). The mean serum 25-Hydroxyvitamin D vitamin level was also not different in gastric inflammation sub-groups ($p>0.05$). The serum 25-Hydroxyvitamin D levels were similar in groups of H. Pylori positive and negative.

Conclusion: This is the first study investigating the relationship between the serum 25-Hydroxyvitamin D level and H. Pylori as well as gastric inflammation sub-groups. Consequently, we found no relationship between serum 25 Hydroxyvitamin D level and H. Pylori as well as gastric inflammation severity.

Keywords: 25-Hydroxyvitamin D, helicobacter pylori, gastric inflammation, gastritis

Introduction

Helicobacter pylori (*H.Pylori*) is still a common health problem in all over the world country, especially in developing countries (1, 2). Pylori and its related problems are still not solved even in developed countries. The main reasons are that, first; the sanitation conditions are still not corrected. Consequently, the new contaminations and transmissions cannot be prevented sufficiently. The second is the low eradication rate due to antibiotic resistance caused by the inability to use the drugs given in

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Received: Feb 1, 2019 **Accepted**: February 25, 2019
Published: Mar 21, 2019

sufficient amount and duration and the inadequate use of these drugs due to toxic side effects (2). *H. Pylori* can cause many diseases ranging from a mild problem such as simple ulceration to gastric cancer in some individuals according to genetic predisposition, as well as problems in many organs outside of the stomach in various degrees of tissue (3, 4). According to the World Health Organization, if an individual has an *H. Pylori* virus, it is recommended to be eradicated in high-risk patients, and those with an average risk should be eradicated after the patient is informed (5). Benefits of eradication are mainly that not only the shortening of clinical problems such as ulcers within a short period but also the preventing effect against to development of gastric cancer in a long period (2).

The main transmission of *H. Pylori* is by oral ingestion, and after the ingestion of infected food and water, it is settled in the host. The most important factors in settlement of the host to the natural immunity, as well as the immunity, obtained later in immunity is of great importance (5). Some factors are particularly important in ensuring and adapting this adaptive immunity. One of them is the 25-Hydroxyvitamin D level (6). According to the old information; while it is known that the serum 25-Hydroxyvitamin D level plays a major role in our body's bone and calcium mineral balance circle, it is known that the immune system plays a critical role in sustaining the immune system, preventing chronic infections and even preventing the formation of cancer in recent years (7).

In recent studies, it was found that the serum 25-Hydroxyvitamin D level was significantly lower in cancer patients compared to healthy subjects in many cancer studies (7-9). Similarly, in many chronic inflammatory diseases, a similar 25-Hydroxyvitamin D deficiency has been demonstrated (10-12). The *H. Pylori* induced chronic gastric inflammation is known to decrease the levels of vitamins such as iron, vitamin B-12, and folic acid. However, there is no information in the literature as to any relationship between the presence of *H. Pylori* and serum 25-Hydroxyvitamin D. Moreover, there is no data about whether serum 25-Hydroxyvitamin D levels affect the *H. Pylori* condition or gastric inflammation severity. In this study, we wanted to investigate whether the serum 25-Hydroxyvitamin D levels are different in patients with *H. Pylori* positive and negative as well as whether there is a relationship between the severity of gastric inflammation severity and the serum 25-Hydroxyvitamin D level. This study is the first study investigating the relationship between *H. Pylori* and stomach inflammation as well as serum 25-Hydroxy vitamin D level for the first time in the literature.

Materials and Methods

The current study was carried out in the Gastroenterology Clinic of Bülent Ecevit University Medical Faculty, which was accepted as the reference center in the region, between September 2017 and February 2018. Sample group, which was planned to be studied, consisted of a special patient population that was applied to this clinic and whose medical records had no important chronic disease such as diabetes mellitus, cancer, and inflammatory disease. A total of 750 case files were analyzed retrospectively. The main criteria for inclusion in this study are as follows; first, patients aged between 18-85 years old without any other chronic problem (anemia, iron deficiency, thrombocytopenia, elevation of liver enzyme, height of C-reactive protein), second, those

have dyspeptic complaint that was performed an upper endoscopy (at least four biopsy specimens were taken from the stomach and evaluated according to Sydney classification), third, patients were documented serum 25-Hydroxyvitamin D level, which did not receive vitamin D replacement therapy, at the same time with endoscopic examination. The routine blood examinations and serum 25-Hydroxy vitamin D level was analyzed with a commercial technique during admission. The level of serum 25-Hydroxyvitamin D level was calculated in the standardized laboratory compatible with the literature. Initially, hemoglobin, the mean erythrocyte volume, red cell distribution width, C-reactive protein, platelet count and mean platelet volume values were evaluated, and patients with abnormal values were left out. The endoscopy procedure was performed by a single operator by the recommendations of the guidelines. Pathological examination was performed according to Sydney classification with hematoxylin and eosin dye and other required dyes (4). The study was carried out by the International Helsinki Declaration by the ethical rules, and local ethics committee approval was obtained (2017-06-22;2017-113).

Statistical Analyze

Statistical analysis was performed with SPSS-18. After investigation of the distribution of the values was normal or not with at least three different tests, chi-square, one-way ANOVA, and the correlation tests were performed. A p-value <0.05 was considered significant.

Results

A total of 91 patients were admitted to the study. The study group was first divided into two groups as Hp positive and Hp negative. While 48 (52.7%) patients were Hp positive, 43 (47.3%) patients were Hp negative. There was no significant difference between the two groups (p>0.05). The mean erythrocyte volume, red cell distribution width, C-reactive protein, platelet count, mean platelet volume and ferritin values were not different in both groups (p>0.05). There was also no difference between the two groups in terms of endoscopic findings.

Table-1. Demographics and Laboratory findings between groups of H. Pylori positive and negative

Variables	H. Pylori (+)	H. Pylori (-)	*P*
Patient (n, %)	48 (52.7%)	43 (47.3%)	
Age	55±11.9	51.02±15.2	0.169
Gender (Female/Male)	27/21	20/23	0.353
Serum 25-OH Vitamin D (mg/dl)	19.7±8.95	18.1±8.01	**0.375**
Hemoglobin (mg/dL) (NR:12-16.5)	14.1±1.39	14.1±1.01	0.84
Mean Corpuscular Volume (fL)(NR:80-99)	87±2.81	87.8±3.59	0.21
Mean Platelet Volume (fL)(NR:7-10.5)	8.63±1.02	8.6±0.76	0.909
Serum Iron (υg/dl) (NR:60-180)	74±25.4	74.4±27.04	0.950
C-reactive protein (mg/dl) (NR:0-8)	2.54±1.46	3.06±1.12	0.854
Red Cell Distribution Width (NR:12-16)	13.3 (11.9-17)	13.35 (12-16)	0.275
Ferritin (mg/dl) (NR:10-350)	48.2 (12-253)	37.8 (11-302)	0.718
Endoscopic findings; 1-Superficial gastritis(SG)	20	14	
2-Low esophageal sphincter opening+SG	26	27	0.669
3-Low esophageal esophageal sphincter opening+ Ulcer/ Erosion	2	2	

All parameters were given as mean±standard deviation except Red Cell Distribution Width and Ferritin. NR means normal ranges. There were no significant differences between H. Pylori positive and negative groups regarding the basic characteristics of study patients. Moreover, there was no significant difference between Pylori positive and negative groups regarding 25 Hydroxyvitamin D levels (p=0.375).

Table-2. Levels of 25-OH Vitamin D according to the Sydney Classification

Sydney Classification (n)	25 OH Vitamin D (mg/dl)	*P*
Helicobacter pylori		
None (0) (43)	18.11 ±8.01	0.63
Mild (+) (31)	20.13 ±8.61	
Moderate (++) (12)	20.08 ±11.2	
High (+++) (5)	16.16 ±4.7	
Inflammation		
None (0)	0	-
Exist (91)	19.1 ± 7.8	
Activation		
None (52)	18.7 ±8.1	0.672
Exist (38)	19.5 ±9.03	
Metaplasia		
None (66)	19.4 ±8.83	0.331
Exist (42)	17.5 ±7.59	
Atrophia		
None (77)	18.6 ±8.65	0.431
Exist (14)	20.6 ±7.74	

All parameters were given as mean±standard deviation. The examining was made the relationship between 25 hydroxy vitamin D levels and the subgroup of chronic gastritis according to Sydney classification, and found that 25 hydroxyvitamin D levels were not different between the gastric subgroups.

The serum 25-Hydroxyvitamin D level, which is the main subject of study, was 19.7±8.95 and 18.1±8.01 in *H.Pylori* positive and negative patients, respectively, and no difference was seen between two groups (p=0.375)(Table-1).

Table-3. Serum 25-OH vitamin D according to H. Pylori positive or negative

Variables	Serum 25-OH vitamin D			Total	P
	<10 mg/dl	10-20 mg/dl	>20 mg/dl		
H.pylori negative	6	22	15	43	0.48
H.pylori pozitive	7	19	22	48	
Total	13	41	37	91	

The serum 25 Hydroxyvitamin D levels were stratified at three different levels as <10 mg/dl, 10-20 mg/dl and >20 mg/dl) and there was no difference between Helicobacter positive and negative groups (p=0.48).

When subject of gastritis is examined according to Sydney classification, there is no difference in serum 25-Hydroxyvitamin D levels according to the severity of gastric inflammation. Similarly, the serum 25-Hydroxy vitamin D levels were similar in subgroups of gastric inflammation as activation, intestinal metaplasia, and atrophy (Table-2). When the serum 25-Hydroxyvitamin D investigated as 25-Hydroxyvitamin D<10 mg/dl significantly low, 10-20mg/dl incomplete and >20 mg/dl normal, there is no statistical differences between HP positive and negative (Table-3).

Discussion

In this study, we investigated whether there is a relationship between 25-Hydroxyvitamin D levels and the presence of *H. Pylori* as well as the severity of gastritis according to Sydney Classification. Unfortunately, we found that there was no relationship between the presence of *H. Pylori* and 25-Hydroxyvitamin D levels as well as chronic gastric severity. To our best knowledge, this study is the first study on this subject in the literature.

Many *H. Pylori* related clinical outcomes, including gastric cancer, is still being a significant health problem in the worldwide especially for developing countries (1, 2). The main reason for this is the increasing severity of chronic gastric inflammation due to the long-term presence of *H. Pylori*. Chronic stomach inflammation may get the tissues to lose their natural state and enter a pathway towards cancer (4). In this pathway, some subgroups of *H. Pylori* related inflammation contribute significantly. Therefore, both *H. Pylori* and *H. Pylori* related low-grade chronic gastric inflammation is still the subject of essential articles published important journals (13-15).

The most important factors leading to gastric cancer are *H. Pylori* density, the presence of intestinal metaplasia, atrophy and dysplasia. In these factors, while *H. Pylori* can be eliminated, other factors cannot be removed precisely. Therefore, regular follow-up is recommended at specific time intervals to catch a premature malignant lesion in early stage (2). Although the primary function of vitamin D in the organism is known to be only calcium metabolism in the past, its relationship with cancer and other chronic inflammatory diseases has been increasing in recent years. In recent years, vitamin D is an important key molecule that has been learned in the immune system and many important pathways in the cell (6). The level of serum vitamin D circulating in the blood is best examined as 25 (OH) vitamin D. In many recent studies, serum 25-Hydroxyvitamin D levels are low in many different cancer types and inflammatory patients compared to the control group (5, 16). In this context, the vitamin D level in gastrointestinal tract cancers (such as the stomach, large intestine) was found lower than the control group and were associated with poor prognosis (17). In the same way, it is claimed that there is a low vitamin D level in chronic inflammation and there is a connection between inflammation severities (18). Similarly, it is claimed that vitamin D and vitamin D receptor alteration play important roles in the cell and as a result, it can be claimed that it can facilitate cancer and chronic inflammation diseases (18, 19).

Antico et al. reported that serum 25-Hydroxy vitamin D levels were significantly lower in autoimmune gastritis groups compared to 21 *H. Pylori* gastritis and therefore he was claimed that low vitamin D levels might be a risk factor for autoimmune gastritis (8). Yıldırım et al. found that the rate of vitamin D was lower in those who failed H. pylori eradication (9.13±4.7 vs. 19.03±8.13; p=0.001). It was suggested in the discussion part of this study that vitamin D deficiency may be an important risk factor for *H. Pylori* eradication and it may be necessary to increase the eradication rates of vitamin D supplementation (20).

In a study performed by Archontogeorgis et al, 107 patients with respiratory sleep apnea were divided into two parts according to the presence of metabolic syndrome and vitamin D levels and serum 25-Hydroxyvitamin D level was found significantly lower in patients with metabolic syndrome (21). In a study conducted by Bae et al., 85 type 1 diabetic patients and 518 healthy control groups were compared according to serum 25-Hydroxyvitamin D level and it was found that serum 25-Hydroxyvitamin D levels were significantly lower in type-1 diabetic patients (9). In the study of Costanza et al., it was emphasized that the vitamin D supplementation significantly suppressed the inflammation, indicating that many infectious markers such as Tumor Necrosis Factor-alpha, Interleukin 8, Interleukin 6 and Interleukin 10 decreased after D-vitamin supplementation (22). In the review of D'Aurizio et al., the vitamin D level has been shown to be affected by many inflammatory diseases such as Graves, Hashimoto thyroiditis, multiple sclerosis, type 1 diabetes, and rheumatoid arthritis are the most common ones (11). In the study of Wallbaum et al., it was shown in mouse pancreas that serum 25-Hydroxyvitamin D had an anti-fibrinolytic property (23). A similar molecular effect was demonstrated by Costanzo et al. in their study on the intestinal mucosa. In this study, it was also found that vitamin D supplementation decreased microflora in intestine by decreasing

harmful bacterium and inflammatory cytokines (22). In a study performed by Liop and et al. in patients with 333 uveitis and 329 control groups, he suggested that vitamin D deficiency increases the risk of uveitis 1.92 times and vitamin D deficiency is a risk factor for uveitis formation (24). Jiménez-Sousa et al. reported that there was a link between vitamin D deficiency and immune system weakness, which might predispose to viral infections. In fact, it is emphasized that vitamin D supplementation can be achieved by contributing to the development of the immune system (14). In the study of Wallbaum et al., they have been found to have anti-fibrinolytic properties of vitamin D in their study in mouse pancreas (23).

Consequently, 25-Hydroxyvitamin D and its relationship with cancer and inflammation have been increasing of matter in recent years. We have studied the relationship between serum Hydroxyvitamin D and *H. Pylori* as well as gastric inflammation severity, but no data was found to be an association. In our opinion, this may be due to the fact that inflammation of the stomach caused by Helicobacter pylori is not affected by systemic events.

This study revealed that the Helicobacter pylori did not directly reduce the serum 25-Hydroxyvitamin D or serum 25-Hydroxyvitamin D level had no effect on *H. Pylori* positivity.

Conflict of Interests

The author declared no conflict of interest with the present article.

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How to cite?

Akar T. Is There Any Relationship Between Circulating Serum 25-Hydroxyvitamin D Level and Presence of Helicobacter Pylori As Well As Gastric Inflammation Severity? Ulutas Med J. 2019;5(1):84-90

DOI: 10.5455/umj.20190227101537