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Research Article

The Frequency of Vitamin B12 Deficiency in Patients with Helicobacter Pylori Infection and the Relationship Between Helicobacter Pylori and Vitamin B12 Deficiency

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Abstract

Objectives: This study aims to investigate the relationship between Helicobacter pylori (H. pylori) and vitamin B12 deficiency, one of the effects of H. pylori outside the gastrointestinal system.

Methods: Between January 1, 2013 and September 1, 2013, the data of 175 patients who required vitamin B12 examination and upper gastrointestinal endoscopy procedure by the attending physician in the internal medicine outpatient clinic of Kartal Dr. Lütfi Kırdar Training and Research Hospital were retrospectively evaluated. Patients with H. pylori infection (n=125) were included in the patient group, while patients without H. pylori infection (n:50) were included in the control group.

Results: Vitamin B12 deficiency was present in 32.57% (n=57) of all patients included in the study. While vitamin B12 deficiency was detected in 37.6% (n=47) of 125 H. pylori positive patients, vitamin B12 deficiency was not detected in 62.4% (n=78) patients. While vitamin B12 deficiency was detected in 20% (n=10) of 50 H. pylori negative patients, vitamin B12 deficiency was not detected in 80% (n=40).

Conclusion: The statistical relationship between H. pylori and vitamin B12 deficiency was significant (p:0.025).

Keywords: Helicobacter pylori, vitamin B12 deficiency, vitamin B12

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Helicobacter pylori (H. pylori) infection is the most common infection worldwide. Approximately half of the world's population carries this microorganism. Although most people infected with this microorganism have an asymptomatic clinical course, H. pylori is recognized to lead to major gastroduodenal pathologies such as acute gastritis, chronic active gastritis, atrophic gastritis, duodenal ulcer, gastric adenocarcinoma, mucosa-associated lymphomas (MALT lymphomas) and gastroesophageal reflux disease. Apart from the gastrointestinal system, many studies have investigated the association of H. pylori with hematological diseases such as inexplicable vitamin B12 deficiency and iron deficiency anemia, idiopathic thrombocytic purpura, neurological diseases such as stroke, Alzheimer's disease, idiopathic Parkinson's disease, cardiovascular diseases such as ischemic heart disease and skin diseases.[1–3]

Vitamin B12 functions as a co-enzyme in chemical reactions involved in DNA synthesis. It is essential for the formation of mature blood cells and for the proper functioning of the

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nervous system. Vitamin B12 deficiency is one of the leading factors in megaloblastic anemia and can result in neuropsychiatric symptoms.[4]

The fact that atrophic gastritis was not detected and H. pylori was observed in most of the biopsy examinations obtained from upper gastric endoscopy procedures of patients with inexplicable vitamin B12 deficiency and anemia indicated the possible effect of H. pylori pathogen in the etiology of vitamin B12 deficiency that cannot be explained by traditional causes and many studies have been conducted on this subject. In the study by Kaptan K. et al.[5] it was suggested that there was a relationship between H. pylori density and vitamin B12 deficiency and that vitamin B12 levels and even megaloblastic anemia improved after H. pylori eradication. It has been suggested that H. pylori stimulates gastric autoimmunity and provokes the production of autoantibodies against intrinsic factor (IF) or parietal cells and these autoantibodies or H. pylori itself inhibits vitamin B12 absorption by directly inhibiting IF production, IF functions, binding of vitamin B12 to IF or by affecting R proteins to which IF connects in the stomach.[6,7]

In this study, serum vitamin B12 levels were considered as the criterion for vitamin B12 deficiency. In order to exclude the causes of traditional vitamin B12 deficiency, a total of 175 patients between the ages of 18-65 years, without a history of atrophic gastritis, pernicious anemia and chronic diseases, without malabsorption findings, a history of vegetarian diet, a history of gastrointestinal system surgery, long-term use of drugs that may lead to vitamin B12 deficiency and without multivitamin use in the last month were included in our study. In this study, we aimed to investigate the relationship between H. pylori and vitamin B12 deficiency, one of the effects of H. pylori outside the gastrointestinal system.

Methods

Between January 1, 2013 and September 1, 2013, data of 175 patients who required vitamin B12 examination and upper gastrointestinal endoscopy by the consulting physician in the internal medicine outpatient clinic of Kartal Dr. Lütfi Kırdar Training and Research Hospital were evaluated retrospectively. Patients with H. pylori infection were included in the patient group, while patients without H. pylori infection were included in the control group. Of the 125 patients with H. pylori infection, 81 (64.8%) were female and 44 (35.2%) were male. In the control group of 50 patients without H. pylori infection, 34% (n=17) were male and 66% (n=33) were female. Vitamin B12 deficiency, which can be explained by traditional causes, was determined as an exclusion criterion in both groups. Serum vitamin B12 levels (<200 pg/ml) were considered as the criterion for vitamin B12 deficiency. In order to exclude the causes of classical vitamin B12 deficiency, we included patients aged 18-65 years with no history of atrophic gastritis, pernicious anemia and chronic diseases, no malabsorption findings, no history of vegetarian diet, no history of gastrointestinal system surgery, no long-term use of drugs that may cause vitamin B12 deficiency and no multivitamin use in the last month. The data obtained were analyzed through SPSS -PASW Statistics-17 package program and evaluated with Chi-Square test.

Results

Of a total of 175 patients aged between 18 and 65 years, 34.86% (n=61) were male and 65.14% (n=114) were female. The mean age of all patients included in the study was 42.58±11.329 years. The mean vitamin B12 value of all patients was 255.91±107 pg/ml, the minimum vitamin B12 value was 79 pg/ml and the maximum vitamin B12 value was 572 pg/ml. Vitamin B12 deficiency was observed in 32.57% (n=57) of all patients included in the study. The mean vitamin B12 value of all male patients included in the study (292.50±112.213 pg/ml) was higher than the mean vitamin B12 value of all female patients (246.50±108.112 pg/ml). The mean vitamin B12 value of male patients with H. pylori infection was 268±106.82 pg/ml and 235.7±116 pg/ml in women. The mean vitamin B12 value of male patients without H. pylori infection was 306±126.12 pg/ml and 274±158 pg/ml in women. In the group of 125 patients with H. pylori infection, 35.2% (n=44) were male and 64.8% (n=81) were female. The mean age of our patient group was 41.17±10.947 years, the minimum age was 18 years and the maximum age was 65 years. The mean value of vitamin B12 was 246.47±101.892 pg/ml, the minimum vitamin B12 value was 79 pg/ml and the maximum vitamin B12 value was 550 pg/ml. In the control group consisting of 50 patients without H. pylori infection, 34% (n=17) were male and 66% (n=33) were female. The mean age of our control group was 46.12±11.602 years, the minimum age was 18 years and the maximum age was 65 years. The mean value of vitamin B12 in our control group was 279.50±118.114, the minimum vitamin B12 value was 83 pg/ml and the maximum vitamin B12 value was 572 pg/ml.

While vitamin B12 deficiency was detected in 37.6% (n=47) of 125 H. pylori positive patients, vitamin B12 deficiency was not detected in 62.4% (n=78). While vitamin B12 deficiency was detected in 20% (n=10) of 50 H. pylori negative patients, vitamin B12 deficiency was not detected in 80% (n=40). The statistical relationship between H. pylori and vitamin B12 was significant (p=0.025).

Discussion

H. Pylori is the most encountered infection in the World. [8] It has been reported that its prevalence varies between countries according to development rates and age and is comparable in men and women. The prevalence of H. pylori antigen in developed countries is reported to be 30-50% in adults. In developing countries including Turkey, this rate is reported to be 85-90%.[9–12] The higher prevalence in some racial and ethnic groups suggests that there may be a genetic predisposition. In both developed and developing countries, infection peaks around the age of 50. The prevalence of infection increases in direct proportion to age.

Although the transmission modes of H. pylori are not defined precisely, living in crowded environments, poor hygiene conditions, low socioeconomic level, malnutrition, iron deficiency anemia, coronary heart disease, being in blood group O, and low maternal education level are considered as risk factors for the transmission of the microorganism into the body.[13] The fact that H. pylori infection is observed more frequently especially in those living in crowded environments and under poor hygiene conditions supports the possibility of transmission via fecal-oral route. Although human-to-human transmission is rarely observed, it has been reported that it can be transmitted from one patient to another patient with poorly sterilized endoscopes.[14]

Although most infected individuals develop an asymptomatic clinical course, H. pylori is capable of leading to major gastroduodenal pathologies such as acute gastritis, chronic active gastritis, atrophic gastritis, duodenal ulcer, gastric adenocarcinoma, mucosa-associated lymphomas (MALT lymphomas) and gastroesophageal reflux disease. Apart from the gastrointestinal system, many studies have investigated the association of H. pylori with hematological diseases such as unexplained vitamin B12 deficiency and iron deficiency anemia, idiopathic thrombocytic purpura, neurological diseases such as stroke, Alzheimer's disease, idiopathic Parkinson's disease, cardiovascular diseases such as ischemic heart disease and skin diseases.[1–3]

Invasive and non-invasive diagnostic methods are implemented in the diagnosis of H. pylori (Table 1). Invasive tests include urease activity, histopathologic examination, culture and PCR of endoscopic biopsy material, while non-invasive tests include urea-breath test, serology and stool test. According to the Maastricht consensus, which defines treatment and diagnostic criteria for H. pylori infections, in developed countries where infections are sporadic, the clinical preliminary diagnosis of patients should be made under endoscopy and the laboratory diagnosis should be supported by biopsy material taken during endoscopy. In these countries, non-invasive tests that do not require endoscopic intervention and biopsy material are also recommended as secondary diagnostic criteria. On the other hand, in developing countries where infections are endemic, endoscopy is not recommended for diagnosis, except in patients under 5 years of age and over 45 years of age and in all age groups with alarm symptoms, because it is expensive and time-consuming, and the diagnosis should be based on clinical findings and supported by non-invasive tests. In patients with alarming symptoms, endoscopic intervention followed by biopsy-based invasive tests is desirable. In recent years, the increase in the development of resistance to first-line antibiotics has made biopsy-based diagnosis without symptoms necessary in endemic countries. Endoscopic evaluation is extremely important in determining the location, clinical prognosis and severity of the lesion.[15]

In the Maastricht III consensus report by the Helicobacter Pylori Study Group EHPSG, indications for H. pylori treatment were specified (Tables 2-3). These diseases include gastric ulcer, duodenal ulcer, endoscopically and histopathologically proven atrophic gastritis, gastric cancer or gastric surgery for other reasons, post gastric cancer surgery, gastric MALT lymphoma, history of gastric cancer in first degree relatives, uninvestigated dyspepsia (H. pylori

Table 1. Non-invasive and invasive methods implemented in the diagnosis of H. pylori

Non-invasive Tests	Invasive Tests
1- serologic tests	1- histologic evaluation
2- urea-breath test	2- culture isolation
3- stool tests looking for antigens	3- rapid urease test
	4- molecular diagnosis methods

Table 2. H. Pylori treatment indications strongly recommended

Duodenal or gastric ulcer (active or uncomplicated)
MALT-lymphoma (in stomach)
Atrophic gastritis
Previous gastric surgery
First-degree relatives with a history of stomach cancer
Treatment of H. Pylori is requested by the patient themself

Table 3. Indications for recommended treatment of H. pylori

Dyspepsia patients
Gastroesophageal reflux disease
Nonsteroidal anti-inflammatory drugs
Idiopathic thrombocytopenia
Unexplained iron deficiency anemia

prevalence >10%), non-ulcer dyspepsia, unexplained iron deficiency anemia, ITP, patient request before starting NSAIDs in NSAID naive patients (after discussion of risks and benefits).

In our study, we investigated the frequency of vitamin B12 deficiency in patients with H. pylori infection and the relationship between H. pylori and vitamin B12 deficiency. As in many studies investigating the relationship between H. pylori and vitamin B12 deficiency, which is a subject of growing interest, a significant relationship was found between vitamin B12 deficiency and H. pylori in the light of statistical data in our study ($p<0.05$). There are also various studies suggesting that vitamin B12 levels and even megaloblastic anemia improved after H. pylori eradication.

As a result of studies investigating the mechanisms by which H. pylori contributes to vitamin B12 deficiency, it has been suggested that H. pylori activates gastric autoimmunity and causes the production of autoantibodies against intrinsic factor or parietal cells, and that these autoantibodies or H. pylori itself inhibits vitamin B12 absorption by directly inhibiting IF production, IF functions, binding of vitamin B12 to IF or by affecting R proteins to which IF connects in the stomach.[6,7] In addition, the possible effects of H. pylori infection on vitamin B12 absorption are believed to be inhibition of vitamin B12 release from foods, inhibition of binding of vitamin B12 and its analogues by cobalophilins in the stomach, impaired digestion of cobalophilins by pancreatic enzymes in the gastrointestinal tract and impaired binding of cobalomins (except analogues) to IF, and H. pylori colonized in the stomach consumes vitamin B12.[16–19] In a study by Carmel et al.[20] H. pylori was detected in 78% of patients with severe cobalomin malabsorption, 45% of patients with mild cobalomin malabsorption and 42% of patients with normal absorption. In another study by Carnel et al.[21] food-cobalamin malabsorption was detected in approximately half of patients with low serum cobalamin levels that could not be explained by traditional causes. In a study by Negrini et al.,[22] it was suggested that H. pylori exhibited antigenic cross-reaction not only in the antral mucosa but also with parietal cells in some diseases and this may be a probable mechanism in the development of food-cobalamin malabsorption.

In the 4th Maastricht consensus report produced by the EHPSG in 2012, iron deficiency anemia and ITP as well as vitamin B12 deficiency were included as extragastrointestinal manifestations of H. pylori and it is recommended that H. pylori should be investigated and eradicated in unexplained iron deficiency anemia, ITP and vitamin B12 deficiency.[23]

Conclusion

In our study, we investigated the frequency of vitamin B12 deficiency in patients with H. pylori infection and the relationship between H. pylori and vitamin B12 deficiency. The statistical relationship between H. pylori and vitamin B12 deficiency was significant ($p=0.025$).

Disclosures

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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References

1. Wedi B, Wagner S, Werfel T, Manns MP, Kapp A. Prevalence of Helicobacter pylori-associated gastritis in chronic urticaria. Int Arch Allergy Immunol 1998;116(4):288–294.
2. Farinati F, De Bona M, Floreani A, Foschia F, Rugge M. Helicobacter pylori and the liver: Any relationship? Ital J Gastroenterol Hepatol 1998;30(1):124–128.
3. Cammarota G, Pasceri V, Gasbarrini A, Gasbarrini G. Helicobacter pylori is an aetiological factor for ischaemic heart disease: the case against. Dig Liver Dis 2000;32(1):65–68.
4. Dharmarajan TS, Norkus EP. Approaches to vitamin B12 deficiency. Early treatment may prevent devastating complications. Postgrad Med 2001;110(1):99–106.
5. Kaptan K, Beyan C, Ural AU, Cetin T, Avcu F, Gülşen M, et al. Helicobacter pylori- Is it a novel causative agent in Vitamin B12 deficiency? Arch Intern Med 2000;160(9):1349–1353.
6. Shuval-Sudai O, Granot E. An association between Helicobacter pylori infection and serum vitamin B12 levels in healthy adults. J Clin Gastroenterol 2003;36(2):130–133.
7. Serin E, Gümürdülü Y, Ozer B, Kayaselçuk F, Yilmaz U, Koçak R. Impact of Helicobacter pylori on the development of vitamin B12 deficiency in the absence of gastric atrophy. Helicobacter 2002;7(6):337–341.
8. Cave DR. Transmission and epidemiology of Helicobacter pylori. Am J Med 1996;100(5A):12S–18S.
9. Tünger Ö. Helicobacter pylori infections. Turk J Infect 2008;22(2):107–115. Turkish.
10. Yucel T, Aygin D, Sen S, Yucel O. The prevalence of Helicobacter pylori and related factors among university students in Turkey. Jpn J Infect Dis 2008;61(3):179–183.
11. Açık Y, Gülbayrak C, Dönder E, Yalnız M. Frequency of helicobacter pylori and relation of etiologic factors who applied to Fırat Medical Center with dispeptic complaints. OMÜ Tıp Fak Derg 2003;20(2):82–88. Turkish.

12. Göral V, Özdal B, Kaplan A, Şit D, Danış R. The prevalence of Helicobacter pylori in the Diyarbakır city. Turk J Acad Gastroenterolog 2006;5(1):47–50. Turkish.
13. Seyda T, Derya C, Füsun A, Meliha K. The relationship of Helicobacter pylori positivity with age, sex, and ABO/Rhesus blood groups in patients with gastrointestinal complaints in Turkey. Helicobacter 2007;12(3):244–250.
14. Tytgat GN. Endoscopic transmission of Helicobacter pylori. Aliment Pharmacol Ther 1995;9(Suppl 2):105–110.
15. Kapoor N, Bassi A, Sturgess R, Bodger K. Predictive value of alarm features in a rapid access upper gastrointestinal cancer service. Gut 2005;54(1):40–45.
16. Kittang E, Schjønsby H. Effect of gastric anacidity on the release of cobalamins from food and their subsequent binding to R-protein. Scand J Gastroenterol 1987;22(9):1031–1037.
17. Lee GR. Nutritional factors in the production and function of erythrocytes. In: Lee GR, Bithell TC, Foerster J, Athens SW, Lukens JN, editors. Wintrobe's Clinical Hematology. Philadelphia: Lea and Febiger; 1993. pp. 158–169.
18. Jacob E, Baker SJ, Herber V. Vitamin B12 binding proteins. Phsiol Rev 1980;60:918.
19. Fairbanks VF, Klee GG. Vitamin B12. In: Tietz W, editor. Textbook of Clinical Chemistry. Philadelphia: W.B. Saunders Company; 1999. pp. 1565–1573.
20. Carmel R, Perez-Perez GI, Blaser MJ. Helicobacter pylori infection and food-cobalamin malabsorption. Dig Dis Sci 1994;39(2):309–314.
21. Carmel R, Sinow RM, Siegel ME, Samloff IM. Food cobalamin malabsorption occurs frequently in patients with unexplained low serum cobalamin levels. Arch Intern Med 1988;148(8):1715–1719.
22. Negrini R, Lisato L, Zanella I, Cavazzini L, Gullini S, Villanacci V, et al. Helicobacter pylori infection induces antibodies cross-reacting with human gastric mucosa. Gastroenterology 1991;101(2):437–445.
23. Malfertheiner P, Megraud F, O'Morain CA, Atherton J, Axon AT, Bazzoli F, et al; European Helicobacter Study Group. Management of helicobacter pylori infection- The Maastricht IV/ Florence Consensus Report. Gut 2012;61(5):646–664.