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Original Research Article

H PYLORI INFECTION AND ASSOCIATED VITAMIN B12 DEFICIENCY

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Abstract: *Helicobacter pylori (H. pylori) infection is one of the most common gastrointestinal infections worldwide, and it has been implicated in the development of vitamin B12 deficiency. Chronic H. pylori infection leads to gastric mucosal inflammation, which may impair the absorption of vitamin B12. Early identification and treatment of H. pylori infection may prevent the clinical consequences of vitamin B12 deficiency, such as anemia and neurological disorders.* ***Objective:*** *To evaluate the incidence and association factors of vitamin B12 deficiency in patients who are suffering from H pylori infection. Study Design: Cross Sectional Study Duration of Study: Department of Internal Medicine, Islamabad Medical Complex from August 2021 to May 2022.* ***Methods:*** *All patients having Helicobacter pylori serology, Urea breath test or H pylori stool antigen positive were included. A detailed history and clinical evaluation of patients was done. All patients were provided standard triple regimen fr H-pylori eradication. Demographic details, symptoms, blood complete picture including the mean corpuscular volume (MCV), hemoglobin and Vitamin B12 level were evaluated. B-12 levels less than 190 pg/ml were considered low and MCV between 80-100 fl was considered normal. Chi-square as applied to see the association.* ***Results:*** *A total of 200 cases participated in the study. There were 102(51%) females and 98 (49%) were male. The mean age of the patients was 41.77+ 12.67 years. Among the participants, most common symptom was dyspepsia present in 61 (30.5%). A total of 149 (74.5%) patients were diagnosed through H pylori serology. Although 54.5% of patient were deficient in B-12 levels yet only 34 (17%) had macrocytosis and 14 (7%) showed microcytosis. Anemia was present in 89 (44.5%) showing mixed picture. So, B-12 deficiency was sub-clinical. Patients with anemia responded better to standard treatment (p value=0.025).****Conclusion:*** *The incidence of vitamin B 12 deficiency is high among H pylori infected cases. Prompt treatment of H pylori gastritis may help prevent clinical manifestation of B 12 deficiency.*

Keywords: Cobalamin, Dyspepsia, Eradication, Helicobacter Pylori, Mean Corpuscular Volume

Introduction

Helicobacter pylori also commonly known as H pylori, is a gram negative spirochete that is responsible for causing a widespread infection in more than half of the world's population, although among them 80% do not show any symptoms. H pylori infection has been considered as a public health problem around the world, being more common in developing countries than developed countries (1). The infection has many associated micronutrients deficiencies (1). Although the majority of individuals that suffer from this infection are asymptomatic, it is a known fact that H. pylori is involved in ulcers of the stomach and duodenum, gastritis, adenocarcinoma of the stomach as well as mucosa-associated lymphoid tissue lymphoma. A number of researches have shown that H pylori infection is associated with atrophic gastritis (2). Research has proved that H. pylori infection is correlated to the deficiency of vitamin B (12). Scientists have isolated the H. pylori bacteria in more than half of patients suffering from pernicious anemia, which is because of the untreated deficiency of vitamin B (2). Megaloblastic anemia is one of the causes of impaired DNA synthesis that results from insufficiencies of either folic acid, vitamin B12 or both ( ). Unusually low values of vitamin B12 or folic acid or a combination is found in 30% to 50% in patients who are hospitalized who also have raised MCV (5). Deficiency of Vitamin B12 occur in most patients who show up in hematology departments. The deficiency of vitamin B (12). Is common yet a very under recognized disorder. It has a wide range of prevalence starting from 3% to around 40% in human adult population (3). Vitamin B (12). Deficiency has a spectrum of manifestation that start from being asymptomatic to neuropsychiatric, hematological and developmental complications (6).Gastric acid and pepsin secreted by gastric mucosa is needed for the release of cobalamin from food. Cobalamin that is released forms a complex with gastric R binder which then gets attached to intrinsic factor to get absorbed(4). A result of H pylori induced gastritis and ulcers, there is destruction of parietal cell responsible for producing intrinsic factor that is needed for the absorption of Vitamin B (12) (4). In Pakistan there is lack of research on association factors of H pylori infection and published data shows conflicting outcomes. An article by Nizami and colleagues showed incidence of B 12 deficiency to be as high as 13% whereas another research shows iron deficiency anemia to be as high as 35% (,). The study was undertaken to evaluate the incidence of vitamin B (12). Deficiency in patients who are suffering from H pylori infection. The correlation was established, as the early detection and eradication of H pylori infection can prevent the development of complications such as gastritis, gastric and duodenal ulcers as well as megaloblastic anemia.

Methodology

It was a descriptive cross sectional study conducted in department of department of internal medicine, Islamabad medical Complex. It was conducted from August 2021 to

May 2022. Prior ethical approval was sought from review board (IERB 212/10/21). Sample size was calculated using WHO calculator. Incidence of B 12 deficiency among Helicobacter pylori infected individuals was 13%, Power of test was 80%.[8] Sample size was 200. Non-probability consecutive sampling was done. All patients having Helicobacter pylori serology, Urea breath test or H pylori stool antigen positive were included. Patients aged 15 years and above. Both genders. Patients who gave consent. Patients who were treatment naïve. Patients with treatment failures Patients with normal prior Foli acid levels. Age less than 15 years. Patients who did not give consent. Pregnant female. Patients with post gastrectomy status. Patients taking metformin. Having any type of organ failure. Immunocompromised individuals.

Celiac disease. After taking approval from the ethical committee, proper written informed consent was taken. Patients were briefed about the study and after taking history and performing detailed clinical evaluation patients demographic details, treatment history, symptoms, blood complete picture including the mean corpuscular volume, hemoglobin and Vitamin B12 level were evaluated having either H. pylori serology, H. pylori stool antigen test or urea breath test positive.

Data was studied and analyzed using SPSS 25. Mean and standard deviation was calculated for quantitative variables that is age and categorical variables such as gender and the correlation of H. pylori infection with Vitamin B12 deficiency were represented as total and percentages. Stratification was done based on mean corposcular volume, presence of anemia and B-12 levels and chi square was applied. P-value < 0.01 was considered significant.

Results

Total 200 patients who were diagnosed to be suffering from H-Pylori infection through either stool antigen test, H pylori serology or urea breath test were enrolled in the study after taking informed consent. Patients of both sex aged between 12-60 years were recruited in the study. All the patients had at least one of the symptoms of H pylori infection. There were 102(51%) females and 98 (49%) were males. The mean age of the patients was 41.77± 12.67 years. Among the participants, most common symptom was dyspepsia present in 61 (30.5%) patients. Rest of symptoms are shown in Figure 1. 149 (74.5%) patients were diagnosed through H pylori serology 23 (11.5%) through the stool antigen test and 28 (14%) turned out to be positive through urea breath test. The mean vitamin B12 levels, Hemoglobin and Mean corpuscular volume are shown in Table I. Vitamin B-12 levels below 190 pg/ml were regarded as low, Hemoglobin less than 12 g/dl was regarded as anemic, whereas, MCV levels Between 80-100 fL were normal, more than 100 showed macrocytosis and less than 80 as microcytosis. Among the patients, Vitamin B-12 deficiency was present in 109 (54.5%) patients and 89 (44.5%) were anemic. Macrocytosis was present in 34 (17%) cases, microcytosis in 14 (7%) whereas 152 (76%) had normocytic red blood cells. All patients were given standard triple regimen for 2 weeks and at the end of treatment urea breath test was repeated which showed 78 (39%) were still positive and it was negative in 122 (61%) cases. Further stratification based on B12 levels, Anemia and MCV is shown in table 2.

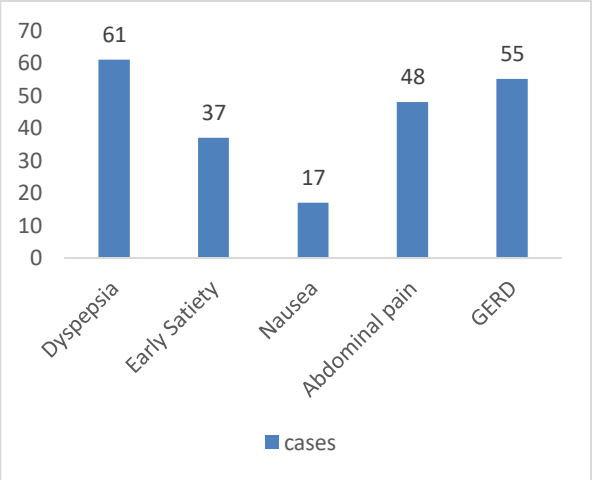

Figure 1: Showing symptoms of H.Pylori positive patients (n=200)

Table 1: Mean B12 Levels, Hemoglobin and Mean carpusular Volume in cases (n=200)

Variable	Mean ± SD	Median (IQR)
B12 (pg/ml)	199.39 ± 117	180.5 (114)
Hemoglobin (g/dl)	12.56 ± 1.99	12.7 (3.0)
Mean Corpuscular Volume (fL)	89.75 ± 9.09	88 (14)

Table 2: Association between treatment outcome and B-12 levels, gender, Anemia and MCV (n=200)

S.no	Variable	Urea Breath Test at end of treatment		
		Positive N=78	Negative N=122	P value
1	B-12 levels • Low • Normal	 40 (51.3%) 38(48.7%)	 69(56.6%) 53(43.4%)	0.471
2	Gender • Male • Female	 39(50%) 39(50%)	 59(48.4%) 63(51.6%)	0.821
3	Mean Corpuscular Volume • Microcytic • Normal • Macrocytic	 11 (14.1%) 63 (80.4%) 4 (5.1%)	 3 (2.5%) 89 (73%) 30 (24.6%)	<0.001
4	Hemoglobin • Low • Normal	 27 (34.6% 51(65.4%)	 62(50.8%) 60(49.2%)	0.025

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Discussion

Vitamin B12 deficiency is a leading cause of megaloblastic anemia and pernicious anemia is the most common cause of its severe deficiency. The megaloblastic anemia caused by the low levels of vitamin B12 is reversible (5). Vitamin B12 (Cobalamin) has a key role in cellular metabolism, specifically in DNA synthesis, methylation and metabolism of the mitochondria. It is usually obtained from dietary sources that includes meat, animal food, egg, milk, fish and selfish. Under physiological conditions intrinsic factor mediated intestinal absorption of vitamin B12 is said to be saturated at 1.5- 2.0ug per meal (5). Vitamin B12 deficiency is a growing health problem worldwide due to the emerging vegetarianism. The outcomes of the vitamin B12 deficiency ranges from lethargy and weight loss to dementia (5). It should be treated at early stages to avoid the complications. Helicobacter pylori is demonstrated as a causative agent in vitamin B12 deficiency by using H pylori diagnostic tests and serum vitamin B12 levels. In our local population where the incidence of H pylori infection is very high the associated frequency of vitamin B12 deficiency is also expected to be high. The H pylori leads to a malabsorption of vitamin B12 due to hypochlorhdria that is in turn associated with atrophic gastritis. A decrease in the gastric acid results in failure of Vitamin B12 splitting from food binders and its transfer to salivary R-binders in stomach (5). In our study patients presented with a wide range on gastric symptoms that included abdominal pain, dyspepsia, early satiety, nausea and GERD symptoms. All patients which were H pylori positive were included in the study and their individual serum vitamin B12 levels were analyzed. The normal value of vitamin B12 was taken as 190 pg/ml and all those who had values less than 190 pg/ml were considered vitamin B12 deficient. Among the 200 individuals enrolled in the study about 109 (54.5%) were vitamin B12 deficient. Majority of the patients i.e. about 149 patients were diagnosed positive on H pylori serology. The most common symptom of presentation was dyspepsia which was experienced by around 61 patients. Our study pointed out that contrary to the previous findings in Pakistan, incidence of B-12 deficiency was high.8 In Israel, Shuval-Sudai and Granot investigated 133 individuals and found that there was a significant association of H pylori infection with low cobalamin levels (5). Similarly, there was another study done by Kapta et al which concluded that in 56% of the 138 participants of the study had an improved vitamin B 12 levels after the H pylori eradication therapy (6). A study conducted in Bangalore by Ravi K at el analyzed 120 patients with proven vitamin B12 deficiency and among them 58% patients had associated H pylori infection (7). It is also pertinent to mention that although 54.5% of patient were deficient in B-12 levels yet only 34 (17%) had macrocytosis and 14 (7%) showed microcytosis. Anemia was present in 89 (44.5%) showing mixed picture. So, B-12 deficiency was sub-clinical. Interestingly, patients with anemia responded better to standard treatment. This association was not seen in International literature. However, this needs to be investigated further owing to high incidence of thalasemia trait in our population which was not assessed at initial screening (7). Limitations this study was conducted in H. pylori prevalent area and we have not assessed the frequency of H. pylori in general population. Likewise, other reasons of vitamin B 12 deficiency were not completely excluded. Study would have been enhanced if improvement of vitamin B 12 levels was evaluated following H. pylori eradication therapy which deserves the need of further follow up visits to analyze the data.

Conclusion

The incidence of vitamin B 12 deficiency is high among H pylori infected cases. Prompt treatment of H pylori gastritis may help prevent clinical manifestation of B 12 deficiency.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department Concerned. (IERB 212/10/21).
Consent for publication
Approved
Funding
Not applicable

Conflict of interest

The authors declared absence of conflict of interest.

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Coordination of collaborative efforts.
Study Design, Review of Literature.
FAZEELAT IFTIKHAR (Post Graduate Resident Medicine)
Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, final approval of manuscript.
Conception of Study, Final approval of manuscript.
AYESHA WAQAR NIAZI (Consultant Medical Specialist)
Manuscript revisions, critical input.
Coordination of collaborative efforts.
MARYUM MEHBOOB (Consultant Medical Specialist)
Manuscript drafting.
ASIF RAZA BHATTI (Rheumatologist)
Data entry and Data analysis, drafting article.
LUBNA NAZ (Medical officer)
Coordination of collaborative efforts.

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