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Helicobacter pylori: A Cause of Vitamin B12 Deficiency (A Hospital Based Multidisciplinary Study)

[1]*Bikha Ram Devrajani,* [2]*Shaikh Muhammad Zaman,* [1]*Syed Zulfiquar Ali Shah,*
[1]*Tarachand Devrajani,* [1]*Raj Kumar Lohana and* [1]*Thanwar Das*

[1]Department of Medicine, Liaquat University of Medical and Health Sciences Jamshoro, Hyderabad (LUMHS), Pakistan
[2]National Institute of Diabetes and Endocrinology, Ojha Campus, Dow University of Health Sciences, Karachi, Pakistan

Abstract: The present work was carried out to determine the frequency of vitamin B12 deficiency in *Helicobacter pylori* infected patients.This cross sectional study was conducted at Liaquat University Hospital and Dow University of Health Sciences, Pakistan. All patients above 12 years of age, of either gender with *Helicobacter pylori* infection and had raised MCV (>96 fl) were further evaluated for serum vitamin B12 level. The data was analyzed in statistical software (SPSS) and the P-value =0.05 was considered as statistically significant. One hundred and fifty (150) *Helicobacter pylori* infected patients with means age 44.3176±15.9114 (males) and 49.6308±15.1612 (females) were enrolled and evaluated. The Vitamin B12 deficiency was observed in 72(48.0%) subjects. The mean ± SD of serum vitamin B 12 level in overall subjects (male and female) was 308.717±223.447 and 257.342±31.919 (P=0.001), respectively. The mean vitamin B12 level in *Helicobacter pylori* infected subjects (male and female) with low serum vitamin B12 level was 136.250±21.423 and 142.625±19.969 (P=0.22) where as it was is 532.459±157.448 and 618.170±141.931 (P=0.01) in *Helicobacter pylori* infected subjects (male and female) with normal serum vitamin B12 level. In conclusion, Vitamin B12 deficiency is more pronounced in *Helicobacter pylori* infection.

Key words: *Helicobacter pylori* · Vitamin B12 · Megaloblastic anemia

INTRODUCTION

Helicobacter pylori (*H. pylori*) is a type of bacteria responsible for widespread infection with more than 50% of the world's population infected, even though 80% of those infected have no symptoms. Infection with *H. pylori* has been recognized as a public health problem worldwide and more prevalent in developing than the developed countries [1]. The prevalence appears to be higher in African-American and Hispanic populations, although this is likely related to socioeconomic rather than racial factors [2]. The lower rate of infection in the West is largely attributed to higher hygiene standards and widespread use of antibiotics.

Vitamin B12 deficiency is also frequently seen in clinical practice in Pakistan and Despite high rates of infection in certain areas of the world, the overall frequency of *H. pylori* infection is declining, but has a strong association with peptic ulcer disease and adenocarcinoma of stomach [3,4]. It is a common but under recognized disorder with a prevalence ranging from 3% to 40% in the adult population [5]. Vitamin B12 deficiency often goes undetected, with manifestations that range from asymptomatic to a wide spectrum of hematologic and/or neuropsychiatric features. It is worth stating that the stomach plays a major role both in the absorption of B12 and the pathogenesis of cobalamin deficiency [6].Among the etiologies of cobalamin deficiency, pernicious anemia (PA), once believed to be the most common cause [7].

H. Pylori can cause an individual to have a vitamin B12 deficiency. It is also a known contributor to gastritis, ulcers and it can prevent to the stomach from being able to absorb the vitamin B12 you consume and leads to a deficiency of vitamin B12. It has been proposed that pernicious anemia may represent the final phase of a

Corresponding Author: Dr. Bikha Ram Devrajani, Department of Medicine, Liaquat University of Medical and Health Sciences Jamshoro / Hyderabad, Pakistan, Cell: 0346-3912123, E-mail: devrajani62@msn.com.

process that begins with *H. pylori*-associated gastritis and evolves through progressive levels of atrophy until the parietal cell mass is entirely lost. The colonization of gastric mucosa with *H pylori* involves chronic local and systemic immune response. The reported prevalence of vitamin B12 deficiency in *Helicobacter pylori* infected patient was 56% [8].

Therefore by keeping such theme in mind the present study was conducted at a 1500 bedded tertiary care teaching hospital of Hyderabad City. The primary goal of study was to observe whether *H pylori* infection in the gastric mucosa is responsible for vitamin B12 deficiency because as early detection and eradication of *Helicobacter pylori* can prevent to development of complications as gastritis, gastric, duodenal ulcer and megaloblastic anemia.

MATERIAL AND METHODS

This cross sectional study was conducted in the department of Medicine at Liaquat University Hospital and Dow University of Health Sciences (tertiary care teaching hospitals) from September 2009 to August 2010. All patients above 12 years of age, of either gender with history of nausea, vomiting, recurrent abdominal pain, dyspepsia or abdominal discomfort, heartburn, bloating and halitosis through outdoor patient department (OPD), casualty outdoor department (COD) or admitted in medical unit were enrolled in the study. The detailed history of all such patients was taken and complete physical and relevant clinical examination was performed. In first step, for detection of *Helicobacter pylori* infection we advised the participants for collection of stool sample and send to laboratory for *Helicobacter pylori* stool antigen (HpSA) by Enzyme immunoassay (EIA). In second step, The HpSA negative (-) patients were excluded while HpSA positive (+) patients were further evaluated for complete blood picture (CBC) by taking 3cc venous blood sample and send it to the laboratory for the assessment of the mean corpuscular volume (MCV). In third step, the patients who had MCV >96fl were further evaluated for serum vitamin B 12 level. Vitamin B12 deficiency was considered when serum B12 level was $\leq$200 ρg/ml [9].The informed consent was taken from every patient or from attendants of patients after full explanation of procedure regarding the study and all such maneuvers was performed under medical ethics and through the cooperation of whole research team. Sample size was calculated by assessing the prevalence of vitamin B12 deficiency in *Helicobacter pylori* infection (56%) with 8% margin of error.

The exclusion criteria of the study were; (1) Non-cooperative patients who refused to give consent or participate in the study (2) Patients already on steroid or *H. pylori* eradication therapy. (3) Anaemic patients with the primary disease, such as hepatic disease, haemolytic anaemia, cancer, aplastic anaemia, myeloproliferative disease, red cell aplasia, multiple myeloma, leukaemia, chronic lung disease, chronic kidney disease and those using immunosuppressive or chemotherapeutic drugs. (4). Pregnant females and alcoholics. 5. Patients with history of resection of stomach or small bowl surgery, (6). Vegetarian population. (7). Patients with malabsorption syndrome and folic acid deficiency. Where as, to control confounders of the study all patients were also interviewed to exclude known medical problems that could affect vitamin B12 status and to determine that they had not received cyanocobalamin treatment parenterally.

The collected data was analyzed in SPSS version 10.00. The frequency and percentage of gender and serum B12 deficiency in *Helicobacter pylori* patients was calculated. The mean and standard deviation (SD) was calculated for age. The independent-samples t-test was applied between categorical variables, chi-square was applied to determine the statistical difference in gender and the p-value =0.005 was considered as statistically significant. The mentioned statistical tests were applied at 95% confidence interval (CI).

RESULTS

During one year study period, 150 patients with *H. pylori* infection were studied for vitamin B12 deficiency, of which 85 (57%) were males and 65(43%) were females. The observed symptoms included nausea in 20 (13%) patients, vomiting in 25(17%), recurrent abdominal pain in 22(15%), dyspepsia or abdominal discomfort in 24(16%), heartburn in 30(20%), bloating in 08(5%), halitosis in 04(3%) and combined / mixed symptoms in 17(11%) patients. Of one hundred fifty patients, 72 (48%) had raised MCV with vitamin B12 deficiency. The mean age ± SD of overall subjects with statistical difference is shown in Table: 01 whereas the mean age ± SD of vitamin B12 deficient male as well as female subjects was 46.187±16.965 and 47.000±14.068 (P=0.840). Seventy eight (52%) *H. pylori* infected patients had normal vitamin B12 level and the mean age ± SD of such category's male and female was 47.486±15.154 and 48.365±14.277 (P=0.793). The mean ± SD of serum vitamin B 12 level in overall subjects (male and female) was 308.717±223.447 and 257.342±31.919 (P=0.001) respectively. The mean vitamin B12 level in *Helicobacter pylori* infected subjects with

Table 01: Mean age of H. pylori infected patients in relation to gender

	Gender	*n* = 150(%)	Mean	Std. Deviation	P-value
Mean age	Male	85(57)	44.3176	15.9114	0.04*
	Female	65(43)	49.6308	15.1612	

*P value is statistically significant

Table 02: Frequency of vitamin B12 deficiency in *Helicobacter pylori* infected patients

	Gender		Total	P-value
Vitamin B12	Male	Female	Total	
Deficient	48(67%)	24(33%)	72(48.0%)	
Normal	37(47%)	41(53%)	78(52.0%)	0.01*
Total	85(57%)	65 (43%)	150(100.0%)	

*P value is statistically significant

X^2 value = 5.639; df = 1

low vitamin B12 (male and female) was 136.250±21.423 and 142.625±19.969 (P=0.22) where as it was 532.459±157.448 and 618.170±141.931 (P=0.01) in *Helicobacter pylori* infected subjects (male and female) with normal serum vitamin B12 level. Ninety eight (65%) patients belonged to urban area whereas fifty two (35%) were from rural / peripheral areas of the Sindh province. The frequency of vitamin B12 deficiency observed in *H. pylori* infected patients is shown in Table: 02.

DISCUSSION

The present study screened the *Helicobacter pylori* infected subjects for their vitamin B12 status by concentrating on the increasing prevalence of vitamin B12 deficiency in our country that can be predicted from a small study on a hospital based population of patients with megaloblastic anaemia at the Pakistan Institute of Medical Sciences, Islamabad in which the contribution of B12 deficiencies was found to be 76% [10]. In our study, the majority of vitamin B12 deficient *Helicobacter pylori* infected patients were from urban areas (65%) and this is surprisingly a high figure considering that most of the Pakistani population is non-vegetarian.

Helicobacter pylori have been determined as an etiologic factor in vitamin B 12 deficiency [11].In populations with a high prevalence of *H.pylori* infection, the frequency of vitamin B12 deficiency and its clinical consequences can be expected to be high. In this study, the most commonly accepted cutoff value for low vitamin B12 status (<200 pg/ml) was used and a markedly high frequency (48%) of vitamin B12 deficiency was found which is higher than that observed by Gümürdülü *et al.,* and Tucker *et al.* [12, 13]. The present study used serum vitamin B12 level to assess vitamin B12 level because determination of serum vitamin B12 levels is the standard test used for the diagnosis of vitamin B12 deficiency and it is necessary to establish the cause of this deficiency [14].

Helicobacter pylori infection leads to immediate development of persistent gastritis, colonization of the stomach by *H. pylori* is almost always accompanied by clinical and histological signs of chronic gastritis associated with both local and systemic immune response. The resolution of gastritis, mucosal immune response to *H. pylori* and normal appearance of gastric epithelium is demonstrated following eradication of the infection with antibiotic therapy [8].The current study confirmed the strong correlation between vitamin B-12 deficiency and MCV that has been already noted in the literature [15].

A study by Carmel *et al.,* who investigated the association between *H.pylori* infection and megaloblastic anemia, by examining patients with food-cobalamin malabsorption and the investigators found that patients with low levels of serum cobalamin had a higher seroprevalence of *H. pylori* infection [15].The majority of *Helicobacter pylori* infected patients with low serum vitamin B12 level were more than 40 years old and it has been postulated previously that etiological factor for low serum vitamin B12 are dietary deficiency and malabsorption from atrophic gastritis induced by *Helicobacter pylori* infection.

Regarding gender distribution of our study, the vitamin B12 deficiency was more marked in males (67%) with statistically significant difference (P=0.01) whereas the female gender is predominant in the study by Gümürdülü *et al.* [12].

Therefore, we observed that prevalence of megaloblastic anaemia due to vitamin B12 deficiency is

high in Pakistani population and the present study was specific and limited to evaluate vitamin B12 level in *Helicobacter pylori* infected subjects at a limited setup; hence several other multidisciplinary and more in-depth studies are required to screen *Helicobacter pylori* infected patients for their vitamin B12 status from every aspect i.e. diagnostic to treatment effects because the preliminary results of a prospective study by Kaptan *et al*. [8] indicates that improvement of anemia with *H. pylori* eradication therapy and emphasizing the role of *H. pylori* as a novel causative agent.

CONCLUSION

Vitamin B12 deficiency or insufficiency appears to be quite common among population in our country implicating *H. pylori* as an etiological factor for B12 deficiency. Therefore the medical community should seriously consider the merit of early screening (for vitamin B12) of patients with *Helicobacter pylori* infection and precautions against the clinical consequences of vitamin B12 deficiency should be taken.

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