Research Article

A CROSS SECTIONAL ANALYSIS OF VITAMIN B12 DEFICIENCY IN PATIENTS WITH HELICOBACTER PYLORI INFECTION

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Abstract:

Objective: To determine the frequency of vitamin B12 deficiency in patients with Helicobacter pylori infection.

Methodology: This cross sectional descriptive study was conducted from 01-01-2015 to 30-06-2015 at Liaquat University Hospital Jamshoro / Hyderabad. All the patients of 19-60 years of age, of either gender with Helicobacter pylori infection for more than 02 weeks duration 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.

Results: During six months study period, total 340 (225 males and 115 females) Helicobacter pylori infected patients were enrolled and entered in the study. The vitamin B12 deficiency was observed in 236 (69.4%) subjects of which 148 (65.8%) were males and 88 (76.5%) were females. The mean ±SD for age of overall population was 42.94±9.86 years while the mean age ±SD for vitamin B12 deficient and non-deficient was 40.76±8.75 and 41.38±8.97 years respectively. The mean ± SD for duration of infection in overall population was 6.93±1.93 weeks while it was 6.72±2.30 and 6.54±1.75 weeks in vitamin B12 deficient and non-deficient individuals. The mean ± SD of vitamin B12 level in deficient and non-deficient population was 143.63±8.75 and 283.95±10.77 respectively.

Conclusion: The Vitamin B12 deficiency is more pronounced in Helicobacter pylori infection. In present study vitamin B12 deficiency was observed in 236 (69.4%) patients with male predominance 148 (65.8%)

Key Words: Helicobacter pylori, Vitamin B12, Megaloblastic anemia.

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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 leads to chronic gastritis, peptic ulcer disease and gastric malignancies [1,2]. The prevalence of infection is thought to be 80% in developing countries and 30-50% in developed countries [3]. The lower rate of infection in the West is largely attributed to higher hygiene standards and widespread use of antibiotics [4,5]. The reported prevalence of H. pylori in Pakistan, was 49% [4]. The serological tests detect the presence of antibody (IgG) to H. pylori [6]. Vitamin B12 deficiency is seen in clinical practice and observed in patients with Helicobacter pylori infection [7], the reported prevalence for vitamin B12 deficiency in Helicobacter pylori infection was 67% [8]. Vitamin B12 deficiency often goes undetected with manifestations that range from asymptomatic to a wide spectrum of hematologic and/or neuropsychiatric features [9]. It is worth stating that the stomach plays a major role both in the supportive absorption of vitamin B12 and the pathogenesis of cobalamin deficiency [10,11]. Among the etiologies of vitamin B12 deficiency, the pernicious anemia (PA), once believed to be the major cause [12]. In various studies, H. pylori can be seen as a cause of vitamin B-12 deficiency as a result of gastric atrophy with loss of stomach acid production and treatment of H. pylori can relieve the vitamin B-12 deficiency and the Megaloblastic anemia due to B-12 deficiency [13-15].

The present study was designed to investigate the vitamin B12 deficiency in H. pylori infected patients as the prevalence of H. pylori in our setup is larger so it is expected that prevalence of vitamin B12 deficiency in H. pylori infected patient may be larger as compared to western population that’s why such study was considered.

METHODOLOGY:
This cross sectional descriptive study was conducted from 01-01-2015 to 30-06-2015 at Liaquat University Hospital Jamshoro / Hyderabad, on a sample of 340 Helicobacter pylori infected patients with the age between 19-60 years. Patients of either gender, chosen via Non-probability consecutive sampling with Helicobacter pylori infection for more than 02 weeks duration and who gave written consent for participation in the study, were further evaluated for serum vitamin B12 level. Helicobacter pylori infection was detected through serology by quantitative enzyme linked immunosorbent assay (ELISA) method. The anti-Helicobacter pylori antibody (IgG) concentration ≥ 20 U/mL was considered as positive Helicobacter pylori infection. While the benchmark for Vitamin B12 deficiency was considered with level of ≤200 μg/ml. Patients who are on Helicobacter pylori eradication and vitamin B12 therapy, pregnant ladies, alcoholics, those with history of resection of stomach or small bowl surgery, malabsorption syndrome, folic acid deficiency, anemia with the primary disease such as hepatic disease, hemolytic anemia, cancer, a plastic anemia, myeloproliferative disease, red cell aplasia, multiple myeloma, leukemia, chronic kidney disease and those using immunosuppressive or chemotherapeutic drugs were excluded from the disease. The data was analyzed in statistical software (SPSS. V. 16.0) and the p-value ≤0.05 was considered as statistically significant.

RESULTS:
During six month study period, total 340 patients with Helicobacter pylori infection were evaluated for vitamin B 12 deficiency. Out of which 225 (66.2%) were males and 115 (33.8%) were females.

Gender Distribution of Sample

![Gender Distribution of Sample](image-url)
Vitamin B12 deficiency was found in 236 patients i.e. 69.4% with a level of \( \leq 200 \) pg/ml while 104 i.e. 30.6% patients were having normal B12 levels.

The mean ±SD for age of overall population was 42.94±9.86 years while the mean age ±SD for vitamin B12 deficient and non-deficient was 40.76±8.75 and 41.38±8.97 years respectively.

<table>
<thead>
<tr>
<th>AGE (yrs)</th>
<th>VITAMIN B12 DEFICIENCY</th>
<th>P- Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>19-29</td>
<td>38</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>55.1%</td>
<td>44.9%</td>
</tr>
<tr>
<td>30-39</td>
<td>108</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>74.5%</td>
<td>25.5%</td>
</tr>
<tr>
<td>40-49</td>
<td>68</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>72.3%</td>
<td>27.7%</td>
</tr>
<tr>
<td>50-60</td>
<td>22</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>68.8%</td>
<td>31.2%</td>
</tr>
<tr>
<td>Total</td>
<td>236</td>
<td>104</td>
</tr>
<tr>
<td></td>
<td>69.4%</td>
<td>30.6%</td>
</tr>
</tbody>
</table>

*p-value is statistically significant

The vitamin B12 deficiency was observed in 236 (69.4%) subjects of which 148 (65.8%) were males and 88 (76.5%) were females.

The mean ± SD for duration of infection in overall population was 6.93±1.93 weeks while it was 6.72±2.30 and 6.54±1.75 weeks in vitamin B12 deficient and non-deficient individuals.
Table 2: The Distribution of Duration in Relation to Vitamin B12 Deficiency

<table>
<thead>
<tr>
<th>DURATION (weeks)</th>
<th>VITAMIN B12 DEFICIENCY</th>
<th>Total</th>
<th>P- Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>2-4</td>
<td>56</td>
<td>22</td>
<td>78</td>
</tr>
<tr>
<td></td>
<td>71.8%</td>
<td>28.2%</td>
<td>100.0%</td>
</tr>
<tr>
<td>4-6</td>
<td>75</td>
<td>33</td>
<td>108</td>
</tr>
<tr>
<td></td>
<td>69.4%</td>
<td>30.6%</td>
<td>100.0%</td>
</tr>
<tr>
<td>&gt;6</td>
<td>105</td>
<td>49</td>
<td>154</td>
</tr>
<tr>
<td></td>
<td>68.2%</td>
<td>31.8%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Total</td>
<td>236</td>
<td>104</td>
<td>340</td>
</tr>
</tbody>
</table>

*P-value is statistically non-significant

The Distribution of Gender in Relation To Vitamin B12 Deficiency

<table>
<thead>
<tr>
<th>Deficient B12 Levels</th>
<th>Non Deficient B12 Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>65.8%</td>
</tr>
<tr>
<td>Female</td>
<td>76.5%</td>
</tr>
<tr>
<td></td>
<td>34.2%</td>
</tr>
<tr>
<td></td>
<td>23.5%</td>
</tr>
</tbody>
</table>

Fig 3: The Distribution of Gender in Relation to Vitamin B12 Deficiency
DISCUSSION:
Vitamin B12 deficiency is the most common cause of megaloblastic anemia. The determination of serum vitamin B12 levels is the standard test used for the diagnosis of vitamin B12 deficiency. H. pylori infection causing immediate developments 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 the local and systemic immune response [16]. 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. 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. The association between H. pylori and vitamin B12 deficiency remains even more argumentative. Previous studies by Karnes et al [17] and Varis et al [18] had showed that the most patients with atrophic gastritis of the stomach body have been infected with H. pylori and had suggested that H. pylori is involved in initiating an irreversible process leading to vitamin B12 deficiency.

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 anemia at the Pakistan Institute of Medical Sciences, Islamabad in which the contribution of B12 deficiencies was found to be 76% [19]. In present study, the majority of vitamin B12 deficient Helicobacter pylori infected patients were from urban areas (59%) 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 B12 deficiency [20]. 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 (69.4%) of vitamin B12 deficiency was found which is higher than that observed by Gumurdulu, et al and Tucker, et al [21,22]. 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 [23]. 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 [24]. The majority of Helicobacter pylori infected patients with low serum vitamin B12 level were more than 30 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.

It may be speculated that association of vitamin B12 deficiency and H. pylori infection is coincidental, but restoration of anemia and the vitamin B12 deficient state in a significant group of patients via eradication therapy is strongly suggestive of this gram-negative rod's role in the pathogenesis. There is little information available regarding the possible association of H pylori infection with non-pernicious megaloblastic anemias. One study that investigated the association between H pylori infection and megaloblastic anemia, examined patients with food-cobalamin malabsorption. The investigators found that patients with low levels of serum cobalamin had a higher sero-prevalence of H pylori infection. Low serum cobalamin levels were unrelated to pernicious anemia in this case [25], and the association between H pylori infection and food-cobalamin malabsorption suggests that gastritis induced by H pylori infection predisposes to a more severe form of food-cobalamin malabsorption. Moreover, a former study has demonstrated improved protein-bound vitamin B12 absorption in 8 hypochlorhydric-achlorhydric elderly patients following antibiotic therapy [26]. Peoples with H pylori infection may have circulating IgG autoantibodies against epitopes on specialized cells in the gastric mucosa [27]. It has been shown that the lipopolysaccharide of 80% of H pylori strains has an antigenic structure that mimics Lewis x and y blood group antigens of the host [28]. The β-chain of the parietal-proton pump has Lewis y epitopes in common with most H pylori strains. Studies suggest that autoimmunity may play a role in the development of H pylori gastritis [29,30]. There may be a relationship between intrinsic factor produced by the parietal cells of stomach and antibody produced by the host against H pylori. These antibodies or H pylori may affect the parietal cells, production of intrinsic factor, function of intrinsic factor or R proteins that bind cobalamin in the stomach.

Regarding gender distribution of present study, the vitamin B12 deficiency was more marked in males (65.8) with statistically significant difference
Therefore, it has been 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 indicates that improvement of anemia with H. pylori eradication therapy and emphasizing the role of H. pylori as a novel causative agent [31].

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. In present study vitamin B12 deficiency was observed in 236 (69.4%) patients with male predominance 148 (65.8%). Therefore the medical community should seriously consider the merit of early screening (for vitamin B12) of patients with Helicobacter pylori infection and precautions and appropriate measures should be taken against the clinical consequences of vitamin B12 deficiency and its complications.

REFERENCES:


