The association of vitamin B12 levels with gastroscopy findings and H. pylori status in adults attending an out-patient gastroenterology clinic

OBJECTIVE To evaluate the correlation of Helicobacter pylori status with the blood levels of vitamin B12 in patients undergoing gastroendoscopic investigation. METHOD Patients who underwent gastroendoscopic investigation of dyspepsia were enrolled in the study. Their blood levels of folic acid and vitamin B12 were measured along with a complete blood count. The gastroendoscopic findings analysed according to the H. pylori status, age group (20−49, 50−64 and >65 years) and sex of the patients. RESULTS The study included 76 patients, 27 males and 49 females with an average age of 47.3±16.5 years. The mean level of vitamin B12 according to age group was 175±64 pg/mL, 242±181 pg/mL and 187±89 pg/mL for 20−49, 50−64 and >65 years, respectively (p=0.04). Vitamin B12 deficiency was observed in 81.5% of the men (n=22) and 77.6% of the women (n=38). The vitamin B12 level was lower in patients with H. pylori positive status (Hp [+] ) than in those with Hp [−] (185±82 pg/mL versus 205±135 pg/mL, p=0.04). The mean folic acid level was 6.3±2.3 ng/mL, 7.1±8.1 ng/mL and 6.7±4.8 ng/mL in the age groups 20−49, 50−64 and >65 years, respectively (p>0.05). A positive correlation was observed between age and vitamin B12 level (r=0.31, p=0.01), and between age and Hp [+] status (r=0.24, p=0.04). CONCLUSIONS In general, vitamin B12 levels were low in patients with dyspepsia of both sexes. Low vitamin B12 levels observed even in patients with normal endoscopic findings indicated that vitamin B12 deficiency was due to inadequate nutrition.

Vitamin B12 deficiency is a common (3−40%), but often overlooked medical problem in the adult population. Vitamin B12 deficiency is observed mostly in the elderly, and its frequency increases to up to 10−15% in the population aged over 60 years. Although vitamin B12 deficiency is usually asymptomatic, it may present with hematological and neuropsychiatric symptoms. Absorption of vitamin B12 is complex, and the stomach plays an important role. Gastric dysfunction, such as gastritis and gastric atrophy, may lead to an increase in intrinsic factor secretion and malabsorption, eventually resulting in vitamin B12 deficiency. Atrophic gastritis is one of the important causes of vitamin B12 deficiency, particularly, in elderly people.

It has been reported that Helicobacter pylori infection, resulting in chronic gastritis, plays a role in the development of gastric atrophy and intestinal metaplasia, and that H. pylori infection is significantly related with neutrophilic activation. The greater the intensity of infection, the greater the degree of chronic gastritis and gastric atrophy.

In view of the important role of the stomach in absorption of vitamin B12, this study aimed to investigate the association of vitamin B12 levels with gastroendoscopic findings in adult patients presenting with dyspepsia at the out-patient clinic of the gastroenterology division.

MATERIAL AND METHOD

Study population and design

The study was designed as retrospective and descriptive.
hospital records were retrieved of all the patients presenting with dyspepsia and undergoing endoscopic investigation in the gastroenterology clinic of Duzce Public Hospital during the month of July 2009. Sociodemographic data (age, sex) and clinical features (character, duration of symptoms, etc.) were recorded. Serum levels of folic acid and vitamin B12 and the complete blood count, including hemoglobin (Hb) and mean corpuscular volume (MCV) were recorded along with the findings on the gastroendoscopic investigation. For definition of folic acid deficiency values of <3 ng/mL, and for vitamin B12 deficiency <250 ng/mL, respectively, were used. For anemia, Hb <13.0 g/dL in men and <12.0 g/dL in women were accepted as the cut-off values.

Biochemical measurements

Venous blood samples for measurement of vitamin B12 and folic acid were collected in the morning, drawn into a standard biochemical tube and stored at -20 °C until the day of biochemical analysis using DXI 800 Beckman Coulter (CA, USA) equipment. Blood samples for complete blood count were drawn into tubes with EDTA.

Gastroendoscopic investigation

Oral and written informed consent from all patients was obtained before the endoscopic procedure. The gastroscopy procedures were performed by a single gastroenterologist and his team, using the Pentax EPK 100P endoscopy instrument. All patients were subjected to local anesthetic with topical pharyngeal 10% xylocaine spray. Intravenous midazolam (2–5 mg) was given to some patients, if light sedation was needed. Tissue biopsy samples from the antrum and corpus of the stomach were taken from all patients.

Histopathological examination

The histopathological biopsy samples of stomach tissue obtained via endoscopy were evaluated by a pathologist, and classified into four categories: normal, antral gastritis (AG), antral erosive gastritis (AEG), and peptic ulcer (PU), which was subdivided into gastric and bulbar ulcers (GU and BU, respectively).

Data analysis

For purposes of analysis, the patients were classified in 3 age groups, 20–49, 50–64 and >65 years. Biochemical analysis and biopsy results in the various age groups and sexes were compared.

Statistical analysis

After biochemical analysis and encoding into PC, the Statistical Package for Social Sciences (SPSS), version 11.5 was used (SPSS, Chicago, IL, USA) for statistical analysis. Results were stated as mean±standard deviation for variables with scale, but as median for variables with nominal and ordinal. Student t test and one way ANOVA (post-hoc Benferroni) was used in analysis of mean differences for two groups and more than two groups, respectively. Fisher’s exact test (chi-square) was used in analysis of categorical variables. Correlation between measurements was investigated with Pearson correlation analysis. For statistical significances, p value <0.05 was accepted as significant.

RESULTS

Only patients with dyspepsia and known levels of vitamin B12, along with documented endoscopic findings were enrolled in the study. During the 1-month study period a total of 76 patients fulfilled the study criteria (27 males and 49 females), with a mean age of 47.3±16.5 years. The most common endoscopic diagnoses in these patients were antral gastritis (AG; n=35, 46.1%) and antral erosive gastritis (AEG; n=18, 13.7%), respectively. According to the endoscopic diagnosis, the mean level of vitamin B12 in all groups was under the determined cut-off level (250 pg/mL), but the mean level of folic acid was above the cut-off level (3 ng/mL). The lowest levels of vitamin B12 (fig. 1) and folic acid (fig. 2) were observed in patients suffering from gastric ulcer (GU) and bulbar ulcer (BU), but the differences were not statistically significant (tab. 1).

Vitamin B12 deficiency was observed in 77.6% of the women (n=38) and 81.5% of the men (n=22). Differences

Figure 1. Serum levels of vitamin B12 according to gastroendoscopic diagnosis (n=76).

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folic acid deficiency was not observed in any subject (tab. 3). Hp [+ ] status increased with aging, and the highest rate of Hp [+ ] was observed in the >65 years group (p=0.02). Positive correlation was detected between age and vitamin B12 level (r=0.31, p=0.01), and between age and Hp [+ ] status (r=0.24, p=0.04) (tab. 4). The levels of vitamin B12 and folic acid were lower in subjects with Hp [+ ] than in those with Hp [−]. Moreover, the mean level of vitamin B12 was found significantly lower: Hp [+]: 185.21±82.32 pg/mL versus Hp [−]: 205.23±135.11 pg/mL, p=0.04 (tab. 4).

DISCUSSION

Although the sample size of this study was small, it was important in displaying that H. pylori gastritis was associated with B vitamin deficiency. The patients with both low level of vitamin B12 and documented endoscopic findings were enrolled over a period of 1 month, which was why the sample was small, in spite of the large numbers of the patients undergoing endoscopic investigations during the course of a year.

Vitamin B12 deficiency is the most common form of folic acid deficiency was not observed in any subject (tab. 3). Hp [+ ] status increased with aging, and the highest rate of Hp [+ ] was observed in the >65 years group (p=0.02). Positive correlation was detected between age and vitamin B12 level (r=0.31, p=0.01), and between age and Hp [+ ] status (r=0.24, p=0.04) (tab. 4). The levels of vitamin B12 and folic acid were lower in subjects with Hp [+ ] than in those with Hp [−]. Moreover, the mean level of vitamin B12 was found significantly lower: Hp [+]: 185.21±82.32 pg/mL versus Hp [−]: 205.23±135.11 pg/mL, p=0.04 (tab. 4).

between the sexes in vitamin B12 and folic acid levels according to age group and evidence of H. pylori infection: H. pylori positive (Hp [+]) or H. pylori negative (Hp [−]) were not statistically significant (tab. 2). The Hb level was significantly higher in males (p=0.03), although MCV level was not significantly different (tab. 2). The mean levels of vitamin B12 according to age group were 175.32±64.24 pg/mL, 242.31±181.21 pg/mL and 187.12±89.32 pg/mL for 20−49, 50−64 and >65 years, respectively (p=0.04), whereas, the mean folic acid levels were 6.3±2.3 ng/mL, 7.1±8.1 ng/mL and 6.7±4.8 ng/mL in the age groups 20−49, 50−64 and >65 years old, respectively (p>0.05), although

Table 1. Levels of vitamin B12, folic acid and hemoglobin according to gastroendoscopic diagnosis (n=76).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Normal n=16</th>
<th>AG n=35</th>
<th>PU n=7</th>
<th>AEG n=18</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>43.6±18.2</td>
<td>46.7±14.9</td>
<td>49.1±21.2</td>
<td>51.3±16.6</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Hp (+) n (%)</td>
<td>5 (31.2)</td>
<td>9 (30.0)</td>
<td>3 (42.9)</td>
<td>4 (25.0)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Vitamin B12 level (pg/mL)</td>
<td>193.21±112.41</td>
<td>193±122</td>
<td>187±98</td>
<td>208±122</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Folic acid level (ng/mL)</td>
<td>6.3±2.3</td>
<td>7.1±8.1</td>
<td>4.3±0.8</td>
<td>6.7±4.8</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td>13.1±1.7</td>
<td>13.2±1.7</td>
<td>13.6±1.3</td>
<td>12.8±1.9</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>82±7</td>
<td>82±8</td>
<td>84±5</td>
<td>84±9</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Hp: Helicobacter pylori, Hb: Hemoglobin, MCV: Mean corpuscular volume, AG: Antral gastritis, PU: Peptic ulcer, AEG: Antral erosive gastritis
*Significant, if p<0.05
megaloblastic anemia and it also may cause neurological problems. Deficiency of vitamin B12 can be seen in conditions of inadequate dietary intake, disorders related to secretion of gastric pepsin, disorders of pancreatic secretion and intrinsic factor secretion from gastric parietal cells, and ileum disease in which absorption is disrupted. Vitamin B12 deficiency is a common but overlooked medical problem. It is reported at frequencies ranging from 3% to 40% in the adult population. In this study of patients with gastric symptoms, a cut-off value which is commonly accepted for vitamin B12 deficiency (i.e., <250 pg/mL) was used, and frequency of vitamin B12 deficiency was observed to be very high (81.5% in males, 77.6% in females). This was markedly higher than the percentages found in the Framingham study, which included 2,999 subjects.

A positive correlation was observed between age and vitamin B12 level, but no sex difference was found. It has been reported that the frequency of vitamin B12 deficiency increases with aging and that it is most commonly seen in those aged over 60 years. The prevalence of pernicious anemia and dietary cobalamin malabsorption increases with age and is generally considered to be associated with atrophic gastritis. In the present study, no appreciable degree of gastric atrophy was found to explain the lower vitamin B12 levels in the older age group. The levels of vitamin B12 and folic acid were significantly lower in cases with Hp [+], consistent with literature reports. In a study conducted by Kaptan et al, H. pylori was detected in 56% of 138 patients with vitamin B12 deficiency, and it was reported that when the serum level vitamin B12 recovered the anemia improved. A study conducted by Serin et al showed that the vitamin B12 level significantly increased, and inflammation in the antrum and corpus, along with neutrophil activation scores, significantly decreased after H. pylori eradication treatment. When the patients were grouped according to eradication status, serum vitamin B12 levels in patients who underwent successful eradication were markedly elevated compared with those in patients in whom the eradication was unsuccessful.

Sudai et al found that the prevalence of H. pylori sero-positivity was higher in patients with a vitamin B12 level >250 pg/mL than in those with levels 145–180 pg/mL or 180–250 pg/mL (51%, 89% and 92%, respectively), and thus reported that H. pylori infection was related with B12 vitamin deficiency.

Recent studies have demonstrated a relationship between H. pylori and vitamin B12 deficiency, and suggested that vitamin B12 deficiency, and even megaloblastic anemia, improve after H. pylori eradication. The relationship between vitamin B12 deficiencies, particularly in elderly people, and gross pathological findings have not been

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**Table 3.** Levels of B12 vitamin, folic acid and hemoglobin according to age group.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>20–49 (n=42)</th>
<th>50–64 (n=22)</th>
<th>≥65 (n=12)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hp (+) n (%)</td>
<td>8 (19.1)</td>
<td>7 (31.8)</td>
<td>6 (50.0)</td>
<td>0.02</td>
</tr>
<tr>
<td>B12 level (pg/mL)</td>
<td>175.32±64.24</td>
<td>242.31±181.21</td>
<td>187.12±88.32</td>
<td>0.04*</td>
</tr>
<tr>
<td>Folic acid level (ng/mL)</td>
<td>6.3±7.3</td>
<td>7.1±4.4</td>
<td>6.7±2.2</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td>13.6±1.7</td>
<td>12.6±1.5</td>
<td>12.6±2.8</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>83.2±5.1</td>
<td>83.4±5.2</td>
<td>80.3±11.1</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Hp: Helicobacter pylori, Hb: Hemoglobin, MCV: Mean corpuscular volume

*Vitamin B12 level was significantly different in patients between 50–64 years-old from 20–49 years-old and ≥65 years-old

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**Table 4.** Correlation of age with B12 vitamin level and H. pylori infection.

<table>
<thead>
<tr>
<th>B12 vitamin level</th>
<th>H. pylori infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>r</td>
<td>p*</td>
</tr>
<tr>
<td>Age</td>
<td>0.31</td>
</tr>
</tbody>
</table>

*pSignificant, if p<0.05

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**Table 5.** Levels of B12 vitamin, folic acid and hemoglobin according to positivity for H. pylori.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Hp (−) n=55</th>
<th>Hp (+) n=21</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>45.1±17.0</td>
<td>53.1±16.1</td>
<td>0.04</td>
</tr>
<tr>
<td>B12 level (pg/mL)</td>
<td>205.23±135.11</td>
<td>185.21±82.32</td>
<td>0.04</td>
</tr>
<tr>
<td>Folic acid level (ng/mL)</td>
<td>7.2±7.2</td>
<td>5.7±2.2</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Hb (g/dL)</td>
<td>13.1±2.0</td>
<td>13.2±1.7</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>82.8±8.1</td>
<td>81.6±5.6</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Hp: Helicobacter pylori, Hb: Hemoglobin, MCV: Mean corpuscular volume

*pSignificant, if p<0.05
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not clearly demonstrated, which is why we evaluated gastroscopic findings in this series of patients with vitamin B12 deficiency. Serum levels of vitamin B12 vitamin and folic acid were lower in the patients with GU and BU than in patients without ulcers, but not to a statistically significant degree. In generally, we did not observe any significant relationship between gastroscopic findings and vitamin B12 deficiency.

In conclusion, we considered that vitamin B12 deficiency is commonly seen in our region, which might be due to insufficient dietary contents of vitamin B12.

References

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