

ORIGINAL PAPER  
ΕΡΕΥΝΗΤΙΚΗ ΕΡΓΑΣΙΑ

## 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.<sup>1–4</sup> 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.<sup>5–8</sup> Atrophic gastritis is one of the important causes of vitamin B12 deficiency, particularly, in elderly people.<sup>9</sup>

It has been reported that *Helicobacter pylori* infection, resulting in chronic gastritis, plays a role in the develop-

ment 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.<sup>10</sup>

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. The

ARCHIVES OF HELLENIC MEDICINE 2012, 29(1):85–90  
ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2012, 29(1):85–90

E. Korkut,<sup>1</sup>  
H. Kandis,<sup>2</sup>  
S. Korkut,<sup>2</sup>  
D. Baltaci,<sup>3</sup>  
I.H. Kara,<sup>3</sup>  
A. Saritas<sup>2</sup>

<sup>1</sup>Gastroenterology Clinic, Duzce Public Hospital, Duzce

<sup>2</sup>Department of Emergency Medicine, Duzce University Medical Faculty, Duzce

<sup>3</sup>Department of Family Medicine, Duzce University Medical Faculty, Duzce, Turkey

Συσχέτιση του *H. pylori* με τα επίπεδα της βιταμίνης B12 και τα ευρήματα από γαστροσκόπηση ενηλίκων σε εξωνοσοκομειακή γαστρεντερολογική κλινική

Περίληψη στο τέλος του άρθρου

#### Key words

Dyspepsia  
Elderly  
*Helicobacter pylori*  
Vitamin B12 deficiency

Submitted 20.7.2011

Accepted 1.8.2011

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  $-20^{\circ}\text{C}$  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

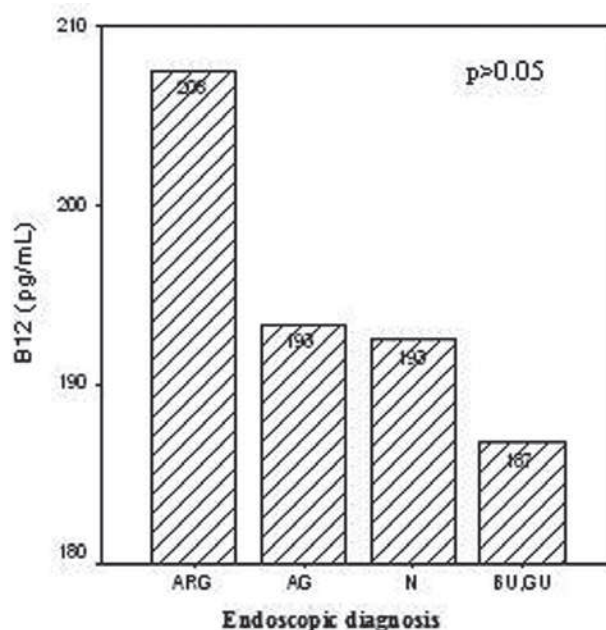
After biochemical analysis and encoding into PC, the Statistical Package for Social Sciences (SPSS), version 11.5 was used (SPSS, Chicago, IL, USA) for statistical analysis. Results were stated as mean  $\pm$  standard deviation for variables with scale, but as median

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

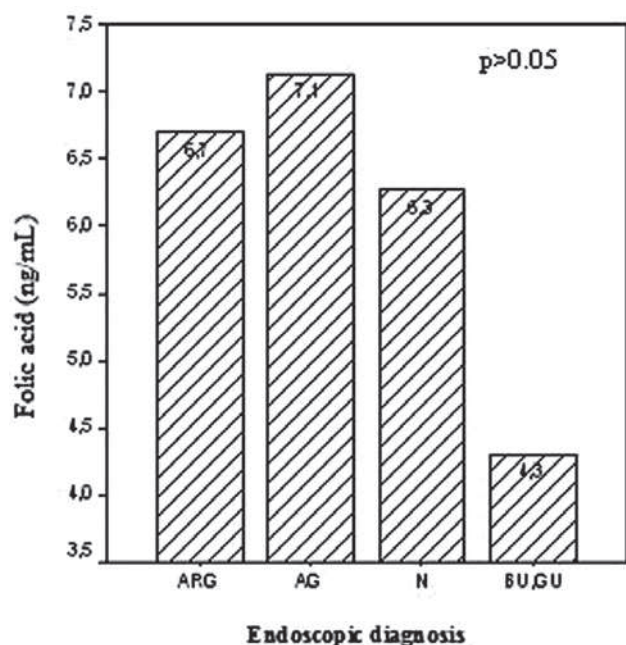
Only patients with dyspepsia and known levels of vitamin B12, along with documented endoscopic findings were enrolled in the study. During the 1-month study period a total of 76 patients fulfilled the study criteria (27 males and 49 females), with a mean age of  $47.3 \pm 16.5$  years. The most common 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 ( $n=76$ ).

N: Normal, AG: Antral gastritis, AEG: Antral erosive gastritis, GU: Gastric ulcers, BU: Bulbar ulcers.



**Figure 2.** Serum levels of folic acid according to gastroendoscopic diagnosis (n=76).

N: Normal, AG: Antral gastritis, AEG: Antral erosive gastritis, GU: Gastric ulcers, BU: Bulbar ulcers.

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  $175.32\pm64.24$  pg/mL,  $242.31\pm181.21$  pg/mL and  $187.12\pm89.32$  pg/mL for 20–49, 50–64 and >65 years, respectively ( $p=0.04$ ), whereas, the mean folic acid levels were  $6.3\pm2.3$  ng/mL,  $7.1\pm8.1$  ng/mL and  $6.7\pm4.8$  ng/mL in the age groups 20–49, 50–64 and >65 years old, respectively ( $p>0.05$ ), although

**Table 2.** Levels of B12 vitamin, folic acid and hemoglobin according to sex.

Parameters	Male n=27	Female n=49	p
Age (years)	49.1±16.7	46.4±16.5	>0.05
Hp (+) n (%)	9 (33.3)	12 (24.5)	>0.05
B12 level (pg/mL)	199.21±129.12	194.13±110.22	>0.05
Folic acid level (ng/mL)	5.8±3.4	7.1±7.0	>0.05
Hb (g/dL)	13.7±2.3	12.8±1.6	0.03
MCV (fL)	83.9±6.9	81.5±7.7	>0.05

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

\*Significant, if  $p<0.05$

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 [+]:  $185.21\pm82.32$  pg/mL versus Hp [-]:  $205.23\pm135.11$  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

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

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

Hp: *Helicobacter pylori*, Hb: Hemoglobin, MCV: Mean corpuscular volume, AG: Antral gastritis, PU: Peptic ulcer, AEG: Antral erosive gastritis

\*Significant, if  $p<0.05$

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

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

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

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

Age	B12 vitamin level		<i>H. pylori</i> infection	
	r	p*	R	p*
Age	0.31	0.01	0.24	0.04

\*Significant, if p<0.05

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

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

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

\*Significant, if p<0.05

megaloblastic anemia and it also may cause neurological problems.<sup>11</sup> 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.<sup>12</sup> Vitamin B12 deficiency is a common but overlooked medical problem.<sup>13–15</sup> It is reported at frequencies ranging from 3% to 40% in the adult population.<sup>16,17</sup> 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.<sup>18</sup>

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.<sup>19</sup> 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.<sup>20</sup> In a study conducted by Kaptan et al,<sup>21</sup> *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<sup>22</sup> 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 of *H. pylori* were markedly elevated compared with those in patients in whom the eradication was unsuccessful.

Sudai et al found that the prevalence of *H. pylori* seropositivity 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.<sup>23</sup>

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.<sup>24,25</sup> The relationship between vitamin B12 deficiencies, particularly in elderly people, and gross pathological findings have not been

not clearly demonstrated, which is why we evaluated gastroscopic findings in this series of patients with vitamin B12 deficiency.<sup>26–28</sup> Serum levels of vitamin B12 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.

## ΠΕΡΙΛΗΨΗ

### Συσχέτιση του *H. pylori* με τα επίπεδα της βιταμίνης B12 και τα ευρήματα από γαστροσκόπηση ενηλίκων σε εξωνοσοκομειακή γαστρεντερολογική κλινική

E. KORKUT,<sup>1</sup> H. KANDIS,<sup>2</sup> S. KORKUT,<sup>2</sup> D. BALTACI,<sup>2</sup> I.H. KARA,<sup>3</sup> A. SARITAS<sup>2</sup>

<sup>1</sup>Γαστρεντερολογική Κλινική, Δημόσιο Νοσοκομείο Duzce, Duzce, <sup>2</sup>Τμήμα Επείγουσας Ιατρικής, Τμήμα Ιατρικής, Πανεπιστήμιο Duzce, <sup>3</sup>Τμήμα Οικογενειακής Ιατρικής, Τμήμα Ιατρικής, Πανεπιστήμιο Duzce, Duzce, Τουρκία

Αρχεία Ελληνικής Ιατρικής 2012, 29(1):85–90

**ΣΚΟΠΟΣ** Αξιολόγηση της συσχέτισης του *H. pylori* με τα επίπεδα της βιταμίνης B12 σε ασθενείς που υποβλήθηκαν σε ενδοσκόπηση του πεπτικού. **ΥΛΙΚΟ-ΜΕΘΟΔΟΣ** Στη μελέτη συμπεριελήφθησαν ασθενείς που υποβλήθηκαν σε γαστροσκόπηση. Διεξήχθη αιματολογικός έλεγχος, καθώς και μέτρηση των επιπέδων φυλλικού οξέος και βιταμίνης B12 στο αίμα. Τα ευρήματα της ενδοσκόπησης συγκρίθηκαν με την κατάσταση του *H. pylori*, σε διάφορες ηλικίες (20–49, 50–64 και >65 ετών) και ανά φύλο των ασθενών. **ΑΠΟΤΕΛΕΣΜΑΤΑ** Στη μελέτη συμμετείχαν 76 ασθενείς, 27 άνδρες και 49 γυναίκες, ηλικίας 47,3±16,5 ετών. Τα μέσα επίπεδα της βιταμίνης B12 σύμφωνα με την ομάδα ηλικίας ήταν 175±64 pg/mL, 242±181 pg/mL και 187±89 pg/mL για τις ηλικίες των 20–49, 50–64 και >65 ετών, αντίστοιχα (p=0,04). Ανεπάρκεια βιταμίνης B12 παρατηρήθηκε στο 81,5% των ανδρών (n=22), αλλά και στο 77,6% των γυναικών (n=38). Τα επίπεδα της βιταμίνης B12 ήταν χαμηλότερα στους ασθενείς με θετικό *H. pylori* σε σχέση με εκείνους που ήταν αρνητικοί σε *H. pylori* (185±82 pg/mL έναντι 205±135 pg/mL, p=0,04). Τα μέσα επίπεδα φυλλικού οξέος ανέρχονταν σε 6,3±2,3 ng/mL, 7,1±8,1 ng/mL και 6,7±4,8 ng/mL στις ομάδες ηλικιών των 20–49, 50–64 και >65 ετών, αντίστοιχα (p>0,05). Βρέθηκε θετική συσχέτιση μεταξύ ηλικίας και επιπέδων της βιταμίνης B12, καθώς και μεταξύ ηλικίας και *H. pylori* [+] (r=0,31, p=0,01 και r=0,24, p=0,04, αντίστοιχα). **ΣΥΜΠΕΡΑΣΜΑΤΑ** Γενικά, τα επίπεδα της βιταμίνης B12 ήταν χαμηλά και στα δύο φύλα, σε ασθενείς με δυσπεψία. Τα χαμηλά επίπεδα βιταμίνης B12, ακόμη και σε άτομα με φυσιολογικά ενδοσκοπικά ευρήματα, έδειξαν ότι η ανεπάρκεια της βιταμίνης B12 μπορεί να οφείλεται σε μη επαρκή διατροφή.

**Λέξεις ευρητηρίου:** Ανεπάρκεια βιταμίνης B12, Δυσπεψία, Ηλικιωμένοι, *H. pylori*

## References

1. DIERKES J, EBERT M, MALFERTHEINER P, LULEY C. *Helicobacter pylori* infection, vitamin B12 and homocysteine. A review. *Dig Dis* 2003, 21:237–244
2. LAHNER E, ANNIBALE B. Pernicious anemia: New insights from a gastroenterological point of view. *World J Gastroenterol* 2009, 15:5121–5128
3. KAPTAN K, BEYAN C, IFRAN A. *Helicobacter pylori* and vitamin B12 deficiency. *Haematologica* 2006, 91(Suppl 12):ELT10
4. HERBERT V. Vitamin E supplementation of elderly people. *Am J Clin Nutr* 1991, 53:976–977
5. DHARMARAJANTS, UGALINO JT, KANAGALA M, PITCHUMONI S, NORKUS EP. Vitamin B12 status in hospitalised elderly from nursing homes and the community. *J Am Med Dir Assoc* 2000, 1:21–24
6. RAJAN S, WALLACE JI, BERESFORD SA, BRODKIN KI, ALLEN RA, STABLER SP. Screening for cobalamin deficiency in geriatric outpatients: Prevalence and influence of synthetic cobalamin intake. *J Am Geriatr Soc* 2002, 50:624–630
7. NILSSON-EHLE H, JAGENBURG R, LANDAHL S, LINDSTEDT S, SVANBORG A, WESTIN J. Serum cobalamins in the elderly: A longitudinal study of representative population sample from age 70 to 81. *Eur J Haematol* 1991, 47:10–16
8. YAO Y, YAO SL, YAO SS, YAO GY, LOU W. Prevalence of vitamin B12 deficiency among geriatric outpatients. *J Fam Pract* 1992, 35:524–528
9. VAN ASSELT DZ, DE GROOT LC, VAN STAVEREN WA, BLOM HJ, WEVERS RA, BIEMOND I ET AL. Role of cobalamin intake and atro-

- phic gastritis in mild cobalamin deficiency in older Dutch subjects. *Am J Clin Nutr* 1998, 68:328–334
10. TOPAL D, GÖRAL V, YILMAZ F, KARA IH. The relation of *Helicobacter pylori* with intestinal metaplasia, gastric atrophy and BCL-2. *Turk J Gastroenterol* 2004, 15:149–155
  11. BAIK HW, RUSSELL RM. Vitamin B12 deficiency in the elderly. *Annu Rev Nutr* 1999, 19:357–377
  12. VOGIATZOGLOU A, SMITH AD, NURK E, BERSTAD P, DREVON CA, UELAND PM ET AL. Dietary sources of vitamin B-12 and their association with plasma vitamin B-12 concentrations in the general population: The Hordaland Homocysteine Study. *Am J Clin Nutr* 2009, 89:1078–1087
  13. WEIR DG, SCOTT JM. The biochemical basis of the neuropathy in cobalamin deficiency. *Baillieres Clin Haematol* 1995, 8:479–497
  14. NILSSON-EHLE H, LANDAHL S, LINDSTEDT G, NETTERBLAD L, STÖCHBRUEGGER R, WESTIN J ET AL. Low serum cobalamin levels in a population study of 70- and 75-year-old subjects. Gastrointestinal causes and hematological effects. *Dig Dis Sci* 1989, 34:716–723
  15. LINDENBAUM J, HEALTON EB, SAVAGE DG, BRUST JC, GARRETT TJ, PODELLER ET AL. Neuropsychiatric disorders caused by cobalamin deficiency in the absence of anemia or macrocytosis. *N Engl J Med* 1988, 318:1720–1728
  16. TEFFERI A, PRUTHI RK. The biochemical basis of cobalamin deficiency. *Mayo Clin Proc* 1994, 69:181–186
  17. DHARMARAJANTS, ADIGA GU, NORKUS EP. Vitamin B12 deficiency. Recognizing subtle symptoms in older adults. *Geriatrics* 2003, 58:30–34, 37–38
  18. TUCKER KL, RICH S, ROSENBERG I, JACQUES P, DALLAL G, WILSON PW ET AL. Plasma vitamin B-12 concentrations relate to intake source in the Framingham Offspring study. *Am J Clin Nutr* 2000, 7:514–522
  19. STOPECK A. Links between *Helicobacter pylori* infection, cobalamin deficiency, and pernicious anemia. *Arch Intern Med* 2000, 160:1229–1230
  20. VAN OIJEN MG, SIPPONEN P, LAHEIJ RJ, VERHEUGT FW, JANSEN JB. Gastric status and vitamin B12 levels in cardiovascular patients. *Dig Dis Sci* 2007, 52:2186–2189
  21. 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, 160:1349–1353
  22. 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, 7:337–341
  23. SHUVAL-SUDAI O, GRANOT E. An association between *Helicobacter pylori* infection and serum vitamin B12 levels in healthy adults. *J Clin Gastroenterol* 2003, 36:130–133
  24. MARINO MC, DE OLIVEIRA CA, ROCHA AM, ROCHA GA, CLEMENTINO NC, ANTONES LF ET AL. Long-term effect of *Helicobacter pylori* eradication on plasma homocysteine in elderly patients with cobalamin deficiency. *Gut* 2007, 56:469–474
  25. SARARI AS, FARRAJ MA, HAMOUDI W, ESSAWITA. *Helicobacter pylori*, a causative agent of vitamin B12 deficiency. *J Infect Dev Ctries* 2008, 2:346–349
  26. ALLEN LH. Causes of vitamin B12 and folate deficiency. *Food Nutr Bull* 2008, 29:20–34
  27. AKCAM M. *Helicobacter pylori* and micronutrients. *Indian Pediatr* 2010, 47:119–126
  28. KOUNTOURAS J, GAVALAS E, BOZIKI M, ZAVOS C. *Helicobacter pylori* may be involved in cognitive impairment and dementia development through induction of atrophic gastritis, vitamin B-12 folate deficiency, and hyperhomocysteinemia sequence. *Am J Clin Nutr* 2007, 86:805–806

*Corresponding author:*

D. Baltacı, Department of Family Medicine, Duzce University Medical Faculty, Duzce, Turkey  
e-mail: davutbaltaci@hotmail.com