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ORIGINAL ARTICLE

Role of Pernicious Anemia in Patients Admitted to Internal Medicine with Vitamin B12 Deficiency and Oral Replacement Therapy as a Treatment Option

Ferda A. Harmandar [1], Süleyman Dolu [2], Ayhan H. Çekin [1]

[1] *Health Sciences University, Antalya Training and Research Hospital, Internal Medicine /Gastroenterology Department, Antalya, Turkey*
[2] *Eylul University Medical Faculty Hospital, Internal Medicine/Gastroenterology Department, Izmır, Turkey*

SUMMARY

Background: **To determine the role of vitamin B12 deficiency in pernicious anemia and the efficacy of oral vitamin B12 replacement therapy given regardless of the etiology, and to compare the endoscopic and pathological findings in patients diagnosed with vitamin B12 deficiency.**

Methods: **The study included 216 patients, aged 18 - 65 years, diagnosed with vitamin B12 level < 200 pg/mL between May 2015 and May 2016. Evaluation was made of the demographic characteristics of the patients, diseases, drugs used, dietary habits, previous use of vitamin B12 replacement therapy, family history of vitamin B12 deficiency, laboratory test values, and neurological symptoms present at the time of presentation. Endoscopy was applied to all the patients included in the study. Anti-parietal cell antibody (APCA) and anti-intrinsic factor antibody (AIFA) analyses were applied to all patients.**

Results: **Evaluation was made of a total of 216 patients diagnosed with vitamin B12 deficiency, comprising 145 (67.1%) females and 71 (32.9%) males. The mean vitamin B12 level of the patients was determined as 127 pg/mL at the time of presentation and 334 pg/mL after treatment. APCA positivity was determined in 40 (18.5%) patients, and AIFA positivity in 5 (2.3%) patients. Atrophy was determined endoscopically in 53 (24.5%) patients and pathologically in 90 (41.7%). Helicobacter pylori positivity was determined in 196 (90.7%) patients. A diagnosis of pernicious anemia (PA) was made in 4 (1.9%) patients (patients with AIFA positivity or APCA accompanied by corpus atrophy). APCA positivity was determined but not corpus atrophy in 36 (16.7%) patients and these cases were accepted as suspected pernicious anemia.**

In this study of 216 patients with vitamin B12 deficiency, stomach pathologies which could cause vitamin B12 deficiency (atrophic gastritis, HP, PA) and the responses to oral replacement therapy were investigated. As vitamin B12 absorption plays a role in the pathogenesis. Vitamin B12 deficiency can lead to atrophic gastritis, and this was determined with biopsy in 41.7% of the patients. APCA positivity was determined in 18.5% of the patients investigated with respect to autoimmune atrophic gastritis (pernicious anemia) and AIFA positivity in 2.3%. A diagnosis of PA was made in 4 (1.9%) patients from autoimmune marker positivity and the presence of corpus atrophic gastritis. HP was determined in 90.7% of the patients with vitamin B12 deficiency, and although no correlation was determined between HP and atrophy, HP positivity was determined in 84 (93.3%) of the patients with pathological atrophy.

From the time of diagnosis, the patients in the study were prescribed 1,000 µg/day vitamin B12. At the 40-day follow-up examination, a significant increase was observed in the vitamin B12 levels of 92.5% of the patients. At the end of the study, as oral replacement therapy was seen to be effective to a great extent, even in patients with PA, it was concluded that for patients not responding to oral replacement therapy, it would be appropriate to apply parenteral vitamin B12 treatment.

Conclusions: **In developing countries such as Turkey, the role of HP infection in vitamin B12 deficiency must be kept in mind. The incidence of atrophic gastritis and pernicious anemia is higher than expected in vitamin B12 deficiency. Thus, it can be concluded that it is appropriate to investigate patients with vitamin B12 deficiency with respect to atrophic gastritis and PA, and oral replacement therapy should be the first stage in the treatment of vitamin B12 deficiency.**

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Correspondence:
Dr. Ferda Akbay Harmandar
Health Sciences University
Antalya Training and Research Hospital
Internal Medicine/Gastroenterology Department
Antalya
Turkey
Phone: +90 05334141229
Email: harmandarferda@gmail.com

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INTRODUCTION

Vitamin B12 is a fundamental vitamin which must be ingested in the diet [1]. The absorption mechanism of vitamin B12 is complex, involving the stomach, small intestine, and pancreas. In healthy adults, half of the Vitamin B12 ingested is absorbed [2]. However, function impairment in any of these organs impairs absorption, thereby leading to Vitamin B12 deficiency. The main reason that vitamin B12 deficiency leads to severe results is that vitamin B12 has a key role in the catabolism of monoamines and has a function in the production of ribonucleic acid (RNA) and DNA, which are among the most important activities for the continuation of life [3]. The neurological changes that are seen in vitamin B12 deficiency can occur with this mechanism.

When the prevalence of vitamin B12 deficiency is examined, although there are variations depending on age, diet, and country of residence, it is generally estimated to be approximately 20% [4]. In healthy adults, mild-moderate vitamin B12 deficiency may be seen for several reasons such as insufficient red meat consumption, a vegetarian diet, advanced age, drug use, and absorption impairments (atrophic gastritis, a history of stomach or intestine surgery) [5]. As vitamin B12 has important roles in DNA synthesis and neurological functions, hematological and neuropsychiatric diseases are seen when it is deficient. Vitamin B12 deficiency affects the gastrointestinal system. Patients may present with gastrointestinal system complaints such as lack of appetite, pain and redness in the tongue associated with atrophic glossitis, abdominal pain, nausea, vomiting, dyspepsia, mucocutaneous ulcers, jaundice, and diarrhea [6]. Vitamin B12 deficiency requires long-term treatment, which may be administered as a high dose such as 1 mg/day orally or intramuscularly. High-dose oral vitamin B12 can be absorbed with passive diffusion without the need for carrier proteins [1].

In this study, evaluation was made of patients who presented at the Internal Diseases Polyclinic of our hospital for various reasons, were diagnosed with vitamin B12 deficiency, were administered oral treatment, and then attended follow-up examinations. The anamnesis, physical examination, biochemical, endoscopic, and pathology data of these patients were reviewed with respect to the etiology of the vitamin B12 deficiency. Informed consent forms were provided by the patients for whom etiological investigation was completed, then the anti-parietal cell antibody and anti-intrinsic factor levels were examined, which are used in the diagnosis of pernicious anemia.

The aim of the study was to determine the etiological factors in patients determined with vitamin B12 deficiency in the polyclinic and the efficacy of oral replacement therapy. In the treatment of insufficient oral intake, the use of oral B12 is sufficient. However, for reasons such as atrophic gastritis, absorption cannot be achieved even if oral replacement is administered and the vitamin B12 reserves cannot be replenished and, therefore, the etiological reason for vitamin B12 deficiency determines the treatment form. The aim in the current study was to determine the frequency of pernicious anemia in vitamin B12 deficiency and to determine how vitamin B12 treatment should be administered.

MATERIALS AND METHODS

The study included a total of 216 patients, aged 18 - 65 years, who presented at the Internal Diseases Polyclinic of Antalya Training and Research Hospital between May 2015 and May 2016 and were diagnosed with vitamin B12 level < 200 pg/mL. Patients were excluded if they had stomach cancer, a history of stomach surgery, previous vitamin B12 treatment, or chronic renal or heart failure. Endoscopy was applied to all the patients by a single gastroenterology specialist, and to determine the etiology of the Vitamin B12 deficiency, stomach pathologies were investigated, primarily atrophic gastritis and helicobacter pylori (HP). From each patient, 2 biopsies were taken from the antrum, corpus, and incisure of the stomach.

The biopsies were evaluated by a specialist pathologist with respect to atrophy, metaplasia and HP. Anti-parietal cell antibody (APCA) and anti-intrinsic factor antibody (AIFA) analyses were applied to all patients. The diagnoses stated in the esophagogastroduodenoscopy report by a gastroenterology specialist were recorded: normal, antral gastritis, corpus gastritis, pangastritis, erythematosus, gastropathy, gastric ulcer, duodenal ulcer, gastroesophageal reflux disease, atrophic gastritis, alkaline reflux gastropathy, bulbitis. Patients with an endoscopic appearance of atrophy in the stomach were classified separately. The diagnoses stated in the report of the recorded stomach pathologies were separated into 6 categories: chronic non-specific gastritis, HP gastritis, normal stomach mucosa, low-grade dysplasia, high-grade dysplasia, stomach cancer.

The biopsies taken from the antrum, corpus, and incisure were evaluated with respect to the presence or absence of HP and atrophy. Patients with HP positivity in any region were accepted as HP positive, and patients determined with atrophy were accepted as pathological atrophy. APCA and AIFA were evaluated with the immunofluorescent method and the results were stated as positive or negative. Evaluation was made of the demographic characteristics of the patients, diseases, drugs used, dietary habits (frequency of eating red meat and liver), previous vitamin B12 replacement therapy, family history of vitamin B12 deficiency, laboratory test values (hemoglobin, MCV, ferritin, vitamin B12), and neurological symptoms present at the time of presentation (psychiatric problems, pains in the arms and legs).

Patients were questioned in detail about red meat and offal (liver) consumption. Those who responded "yes" to the question, "Do you eat red meat or liver at least once a week?" were included in the group, "patients with red meat and liver in the diet". Patients with anemia (hemogram value < 13 g/dL for males, < 12 g/dL for females) and ferritin value < 30 ng/mL and those with ferritin value < 12 ng/mL were evaluated as iron deficiency anemia. Patients with MCV value > 100 fL were determined and were classified as "patients with elevated MCV". Pernicious anemia diagnosis was classified as definite, suspicious or negative according to the vitamin B12 levels of < 100 pg/mL, 100 - 150 pg/mL, and > 150 pg/mL, respectively.

A definite pernicious anemia diagnosis was made for patients with APCA and/or AIFA positivity together with atrophic corpus gastritis, and a suspicious pernicious anemia diagnosis was made for those with APCA and/or AIFA positivity not accompanied by atrophic corpus gastritis. Patients not determined with APCA and/or AIFA positivity were classified as "no diagnosis of pernicious anemia". Treatment of 1,000 mg/day oral vitamin B12 replacement therapy was started for all patients. Response to treatment was evaluated with measurements of serum vitamin B12 levels taken at a minimum of 30 days and a maximum of 50 days. Response to treatment was accepted as the measurement of vitamin B12 > 200 pg/mL during follow-up or an increase of 25% of the pre-treatment level.

Approval for the study was granted by the Ethics Committee of Antalya Training and Research Hospital (decision no: 59/6, dated: 30.04.2015). Informed consent was obtained from all study participants.

Statistical analysis

Data obtained in the study were analysed statistically using SPSS 22.0 software. Descriptive statistics were stated as number (n), percentage (%) mean ± standard deviation (SD), median, minimum, and maximum values. In the analysis of the relationships between categorical variables, Fisher's exact test or Pearson's Chi-square test was used. In the normality tests, when the number of samples in a group was < 50, the Shapiro-Wilk test was applied and when > 50, the Kolmogorov-Smirnov test. When the difference between the measured values of two groups did not conform to normal distribution, the Mann Whitney *U*-test was used, and when normality assumptions were met, Student's *t*-test was applied. In the comparison of more than two non-parametric groups, the Kruskal-Wallis test was applied, and the Bonferroni Dunn test as a post-hoc test when a significant difference was determined. In the comparison of more than two groups that conformed to normal distribution, the ANOVA test was used, and in paired comparisons, the Tukey test. Relationships between ordinal or continuous variables not conforming to normal distribution were assessed with Spearman's correlation test, and for variables conforming to normal distribution, Pearson's correlation test was applied. In the determination of the factors with the most effect on the B12 variable, multiple regression analysis was performed. In all analyses a value of $p < 0.05$ was accepted as statistically significant.

RESULTS

Evaluation was made of a total of 216 patients diagnosed with vitamin B12 deficiency, comprising 145 (67.1%) females and 71 (32.9%) males. The mean vitamin B12 level of the patients was determined as 127 pg/mL (median: 127, range: 50 - 192) at the time of presentation and 334 pg/mL (median: 292, range: 65 - 1,338) after treatment. A family history of vitamin B12 deficiency was determined in 55 (25.5%) patients. The complaints on presentation at the polyclinic were neurological symptoms in 72 (33.3%) patients.

Drugs which prevent vitamin B12 absorption (proton pump inhibitors and/or metformin) were used by 51 (23.6%) patients. Red meat and/or liver was reported to be in the diet of 47 (21.8%) patients. APCA positivity was determined in 40 (18.5%) patients and AIFA positivity in 5 (2.3%) patients. Atrophy was determined endoscopically in 53 (24.5%) patients and pathologically in 90 (41.7%), and helicobacter pylori positivity was determined in 196 (90.7%) patients (Table 1). A diagnosis of pernicious anemia was made in 4 (1.9%) patients, PA diagnosis could not be discounted in 36 (16.7%), and PA was not determined in 176 (81.5%) patients. Vitamin B12 levels were separated into 3 categories as < 100 pg/mL, 100 - 150 pg/mL and > 150 pg/mL. A total of 41 (19%) patients were determined with vitamin B12 < 100 pg/mL, 118 (54.6%) patients at 100 - 150 pg/mL and 57 (26.4%) patients with > 150 pg/mL (Table 2).

Of the 4 patients with a definite PA diagnosis, 2 had vitamin B12 level of 100 - 150 pg/mL and 2 had a level > 150 pg/mL. Of the patients with a diagnosis of suspected PA, vitamin B12 level was < 100 pg/mL in 7 (19.4%), 100 - 150 pg/mL in 23 (63.9%), and > 150 pg/mL in 6 (16.7%). No statistical analysis of the correlation between PA and vitamin B12 could be made due to the low number (4 patients) with a definite diagnosis of

Table 1. Characteristics of patients with vitamin B12 deficiency.

Age (years) (SD)	**41.4 (12.4)**
Patients using drugs affecting vitamin B12 absorption *, n (%)	**51 (23.6)**
Patients with family history of vitamin B12 deficiency, n (%)	**55 (25.5)**
Patients with neurological complaints, n (%)	**72 (33.3)**
Patients with red meat and liver in the diet, n (%)	**47 (21.8)**
MCV elevation (> 100 fL), n (%)	**2 (0.9)**
Concomitant DEA, n (%)	**120 (56.1)**
Vitamin B12 level (pg/mL), mean (SD)	**127 (33)**
Vitamin B12 level after treatment (pg/mL), mean (SD)	**334 (183)**
APCA positivity, n (%)	**40 (18.5)**
AIFA positivity, n (%)	**5 (2.3)**
(Definite diagnosis)	**4 (1.9)**
Pernicious anemia (Suspected diagnosis)	**36 (16.7)**
(Absent)	**176 (81.5)**
Atrophy visualised endoscopically, n (%)	**53 (24.5)**
Atrophy determined pathologically, n (%)	**90 (41.7)**
HP positivity, n (%)	**196 (90.7)**

*** - Patients using proton pump inhibitors and/or metformin, MCV - mean corpuscular volume, IDA - iron deficiency anemia, APCA - anti-parietal cell antibody, AIFA - anti-intrinsic factor antibody, HP - Helicobacter pylori.**

Table 2. Factors affecting the vitamin B 12 level.

	Vitamin B12 level (pg/mL)			**p**
	< 100	**100 - 150**	**> 150**	
Gender				
-male, n (%)	**16 (22.5)**	**43 (60.6)**	**12 (16.9)**	**0.082**
-female, n (%)	**25 (17.2)**	**75 (51.7)**	**45 (31.0)**	
PPI use, n (%)	**5 (13.2)**	**23 (60.5)**	**10 (26.3)**	**0.572**
Metformin use, n (%)	**3 (18.8)**	**9 (56.3)**	**4 (25.0)**	*
APCA positivity, n (%)	**7 (17.5)**	**25 (62.5)**	**8 (20.0)**	**0.503**
AIFA positivity, n (%)	**1 (20.0)**	**4 (80.0)**	**0 (0.0)**	*
Pernicious Anemaia				
-definitive diagnosis, n (%)	**0 (0.0)**	**2 (50.0)**	**2 (50.0)**	*
-absent, n (%)	**34 (19.3)**	**93 (52.8)**	**49 (27.8)**	
-suspected diagnosis, n (%)	**7 (19.4)**	**23 (63.9)**	**6 (16.7)**	
Endoscopic atrophy, n (%)	**9 (17.0)**	**22 (41.5)**	**22 (41.5)**	**0.15**
Pathological atrophy, n (%)	**17 (18.9)**	**44 (48.9)**	**29 (32.2)**	**0.232**
HP positivity, n (%)	**38 (19.4)**	**109 (55.6)**	**49 (25.0)**	**0.349**

*** - p-value cannot be interpreted, PPI - proton pump inhibitor, APCA - anti-parietal cell antibody, AIFA - anti-intrinsic factor antibody, HP - Helicobacter pylori.**

PA (Table 2).

Of the patients with atrophy determined endoscopically, vitamin B12 level was < 100 pg/mL in 9 (17%), 100 - 150 pg/mL in 22 (41.5%), and > 150 pg/mL in 22 (41.5%).

Table 3. Relationships between autoimmune serology and other parameters.

	APCA			AIFA		
	Pos.	Neg.	p	Pos.	Neg.	p
Pathological atrophy, n(%)	8 (8.9)	82 (91.1)	0.02	1 (1.1)	89 (98.9)	0.404
HP positivity, n (%)	36 (18.4)	160 (81.6)	0.770	5 (2.6)	191 (97.4)	0.999
Family history of vitamin						
- B12 deficiency, n (%)	11 (20.0)	44 (80.0)	0.743	0 (0.0)	55 (100.0)	0.332
- Income level (IL)						
< 1,000, n (%)	4 (12.5)	28 (87.5)		0 (0.0)	32 (100.0)	
1,000 - 2,000, n (%)	23 (21.5)	84 (78.5)	0.509	4 (3.7)	103 (96.3)	*
2,000 - 3,000, n (%)	7 (14.0)	43 (86.0)		0 (0.0)	50 (100.0)	
> 3,000, n (%)	6 (22.2)	21 (77.8)		1 (3.7)	26 (96.3)	

*** - p-value cannot be interpreted, APCA - Anti-parietal cell antibody, AIFA - Anti-intrinsic factor antibody, HP - Helicobacter pylori.**

Table 4. The relationship between Helicobacter pylori distribution and other parameters.

	HP presence				
	Antrum only (+)	Corpus only (+)	Antrum and corpus (+)	Absent (-)	p
n	16	7	173	20	
%	7.4	3.2	80.1	9.3	
Vitamin B12 Level (pg/mL)					
< 100, n (%)	2 (4.9)	(0.0)	36 (87.8)	3 (7.3)	
100 - 150, n (%)	11 (9.3)	5 (4.2)	93 (78.8)	9 (7.6)	
> 150, n (%)	3 (5.3)	2 (3.5)	44 (77.2)	8 (14.0)	
Pernicious anemia					
Definitive diagnosis, n (%)	0 (0.0)	0 (0.0)	3 (75.0)	1 (25.0)	
Absent, n (%)	13 (7.4)	6 (3.4)	141 (80.1)	16 (9.1)	*
Suspected diagnosis, n (%)	3 (8.3)	1 (2.8)	29 (80.6)	3 (8.3)	
Pathological atrophy distribution					
Antrum, n (%)	4 (13.3)	0 (0.0)	24 (80.0)	2 (6.7)	
Corpus, n (%)	2 (9.5)	1 (4.8)	15 (71.4)	3 (14.3)	
Pangastritis, n (%)	1 (4.8)	0 (0.0)	19 (90.5)	1 (4.8)	
No atrophy, n (%)	9 (6.3)	6 (4.2)	115 (79.9)	14 (9.7)	
Response to treatment, n (%)	15 (7.5)	7 (3.5)	160 (80.0)	18 (9.0)	

*** - p-value cannot be interpreted.**

No statistically significant relationship was determined between endoscopic determination of atrophy and the severity of vitamin B12 deficiency (p = 0.15). Of the patients with atrophy determined pathologically, vitamin B12 level was < 100 pg/mL in 17 (18.9%), 100 - 150 pg/mL in 44 (48.9%), and > 150 pg/mL in 29 (32.2%). No statistically significant relationship was determined between pathological determination of atrophy and the severity of vitamin B12 deficiency (p = 0.232) (Table 2).

Of the patients determined with HP positivity, vitamin B12 level was < 100 pg/mL in 38 (19.4%), 100 - 150 pg/mL in 109 (55.6%) and > 150 pg/mL in 49 (25%). No statistically significant relationship was determined between HP positivity and the severity of vitamin B12 deficiency (p = 0.349). In the 40 patients determined

with APCA positivity, no statistically significant relationship was determined with the severity of vitamin B12 deficiency ($p = 0.503$). AIFA positivity was determined in 5 patients, which was not a sufficient number to perform a statistical analysis of the correlation with vitamin B12 level (Table 2).

APCA positivity was determined in 40 patients and AIFA positivity in 5 patients. Of the 90 patients with atrophy determined pathologically, ACPA positivity was determined in 8 (8.9%). In the APCA negative patients, the rate of atrophy was statistically significantly high ($p = 0.02$). Of the patients with atrophy determined pathologically, 1 (1.1%) was AIFA positive, and no statistically significant relationship was determined between pathological atrophy and AIFA positivity ($p = 0.404$) (Table 3).

Of the 196 HP-positive patients, APCA positivity was determined in 36 (18.4%). No statistically significant relationship was determined between APCA positivity and HP ($p = 0.770$). HP positivity was determined in all 5 of the AIFA-positive patients. No statistically significant relationship was determined between AIFA positivity and HP ($p = 0.999$) (Table 3). AIFA positivity was not determined in any of the 55 patients with a family history of vitamin B12 deficiency (Table 3). A definite PA diagnosis was made for 4 patients of the 216 included in the study. Iron deficiency anemia was present in 2 (50%) of the patients diagnosed with PA. Atrophy was determined endoscopically in 3 (75%) of the patients with PA diagnosis, and atrophy was determined pathologically in all 4 (100%).

Of the patients determined with antral gastritis, vitamin B12 level was < 100 pg/mL in 13 (20%), 100 - 150 pg/mL in 31 (47.7%), and > 150 pg/mL in 21 (32.3%). Of the patients determined with corpus gastritis, vitamin B12 level was < 100 pg/mL in 6 (54.5%), and 100 - 150 pg/mL in 5 (44.5%). Of the patients determined with pangastritis, vitamin B12 level was < 100 pg/mL in 2 (15.4%) and 100 - 150 pg/mL in 11 (84.6%). In all the patients with corpus gastritis and pangastritis, the vitamin B12 level was determined to be < 150 pg/mL. No statistically significant relationship was determined between antral gastritis determined endoscopically and the severity of vitamin B12 deficiency ($p = 0.349$). As vitamin B12 deficiency increased, there was an increase in the rate of corpus gastritis determined endoscopically ($p = 0.04$).

In the 4 patients diagnosed with PA, antral gastritis was determined in 2 (50%). Corpus gastritis was not determined in any of these patients. Atrophic gastritis was determined in 3 (75%) patients. Of the 36 patients diagnosed with suspected PA, antral gastritis was determined in 11 (30%), corpus gastritis in 3 (8%), and atrophic gastritis in 9 (25%). No statistical analysis could be made of the relationship between PA and endoscopic antrum and corpus involvement.

A response to oral vitamin B12 treatment was determined in 60 (92.3%) of the 65 patients with antral gastritis, in all 11 (100%) of those determined with corpus gastritis, in 46 (86.6%) of 53 patients determined with atrophic gastritis, in 1 (7.69%) of 13 with pangastritis, and in 19 (95%) of 20 patients with gastric ulcer. A response to oral vitamin B12 replacement therapy was obtained in all the patients with duodenal ulcer, findings of gastroesophageal reflux, hiatal hernia, and alkaline reflux gastropathy. No correlation was determined between the response to vitamin B12 treatment and these parameters ($p > 0.05$).

HP positivity was determined in 196 (90.7%) of the total 216 patients, in 16 (7.4%) patients in the antrum only, in 7 (3.2%) in the corpus only and in 173 (80.1%) patients in both the antrum and corpus (Table 4.). Of the patients determined with HP positivity in the antrum only, vitamin B12 level was < 100 pg/mL in 2 patients, 100 - 150 pg/mL in 11 and > 150 pg/mL in 3. Of the patients determined with HP positivity in the corpus only, vitamin B12 level was < 100 pg/mL in no patients, 100 - 150 pg/mL in 5 and > 150 pg/mL in 2. Of the patients determined with HP positivity in the antrum and corpus together, vitamin B12 level was < 100 pg/mL in 36 patients, 100 - 150 pg/mL in 93 and > 150 pg/mL in 44. No statistically significant interpretation could be made with respect to HP distribution and vitamin B12 deficiency (Table 4).

None of the patients with HP involvement in the antrum or corpus only were diagnosed with PA. The definitive diagnosis of PA was made in 3 patients with antrum and corpus involvement together and in 1 patient with no HP involvement. No statistically significant correlation was made between HP distribution and PA. In 4 patients with HP determined in the antrum only, atrophy was determined pathologically in the antrum, in the corpus only in 2 patients, and in both the antrum and the corpus in 1 patient. In cases with HP determined in the corpus only, atrophy was determined pathologically in the corpus in 1 patient and antrum atrophy was not determined in any of these patients. In 24 patients with HP determined in both the antrum and the corpus, atrophy was determined pathologically in the antrum only, in the corpus only in 15 patients, and in both the antrum and the corpus in 19 patients. No statistically significant interpretation could be made with respect to HP distribution and pathological atrophy distribution (Table 4).

According to the serum vitamin B12 measurements taken 1 - 1.5 months after starting oral replacement therapy, a response to treatment was determined in 200 (92.5%) patients, and 16 (7.5%) patients remained unresponsive to treatment.

DISCUSSION

HP infection is widespread throughout the world. HP has an important role in the pathogenesis of gastritis, peptic ulcer, lymphoma, and stomach cancer and is known to cause vitamin B12 deficiency [7]. In a study by Kaptan et al., the incidence of HP in vitamin B12 deficiency was found to be 56% [8]. In other studies, this

rate was found to be 60% in Italy [9], 11% in the USA [10], and 21.4% in the UK [11]. In a meta-analysis that examined 17 studies including 2,454 patients, it was emphasised that patients infected with HP had lower vitamin B12 levels than patients with no HP infection [12].

Abass et al. also emphasised that vitamin B12 levels were affected by HP [13]. In the current study, HP was determined at the rate of 90.7% in patients with vitamin B12 deficiency. There are authors who have stated that HP eradication increases the vitamin B12 level [14]. Kaptan et al. reported that following eradication treatment in patients with HP positivity and vitamin B12 deficiency, both the vitamin B12 level and megaloblastic anemia improved [7]. As HP eradication treatment was not applied in the current study, no comment can be made on this subject. APCA positivity was determined in 40 (18.5%) of the current study patients and a diagnosis of PA was made in 4 (1.9%) patients with autoimmune marker positivity and the presence of corpus atrophic gastritis.

APCA, which is used as a screening test, is not sufficient alone for a diagnosis of PA but PA diagnosis may be made in these patients in the future. In the current study, the reason that the incidence of PA in vitamin B12 deficiency was lower than expected was that APCA-positivity, which was a parameter used in the PA diagnosis, was not taken as a definitive diagnostic criterion in patients in this study. These patients should be evaluated with respect to PA with close follow-up. Part of vitamin B12 absorption occurs through passive diffusion independently of IF [15]. Replacement therapy for patients diagnosed with vitamin B12 deficiency can be applied through oral or parenteral routes [16]. In guidelines published in 2012 by the British Columbia Medical Association, a daily oral dose of 1,000 µg was recommended [17]. High-dose oral vitamin B12 has been shown to be non-toxic [18]. Recent studies have shown the efficacy of PO and IM treatments to be similar [19]. In the current study, patients were prescribed 1,000 µg/day vitamin B12, and a significant increase was observed in the vitamin B12 levels.

HP positivity was determined in 182 (91%) patients who showed a response to treatment. No statistically significant relationship was found between response to treatment and HP positivity. In 46 (23%) patients with response to treatment, atrophy was determined endoscopically, and in 83 (41.5%) patients, atrophy was determined pathologically. No statistically significant relationship was found between response to treatment and the determination of atrophy endoscopically or pathologically.

CONCLUSION

Oral vitamin B12 treatment has been reported to be of benefit in cases of dietary deficiency and pernicious anemia [20]. In the current study, response to oral replacement therapy was determined in 3 patients with a definite diagnosis of PA and 33 patients with suspected PA. In 1 patient with a definite diagnosis of PA and 3 patients with suspected PA, vitamin B12 levels did not increase with oral replacement therapy. These results were found to be significant with respect to showing the efficacy of Vitamin B12 oral replacement therapy in patients with pernicious anemia.

Declaration of Interest:
We have no conflicts of interest.

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