Investigation of Some Extrinsic Factors Predisposing to Helicobacter Pylori-Associated Vitamin B12 Deficiency Anemia and Diagnosis and Treatment

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Abstract

In the world, including in Uzbekistan, gastrointestinal diseases and anemia are common diseases among the population. In recent years, it has been shown that *H. Pylori*, which causes gastroduodenal diseases, is also important in the development of anemia. It is emphasized that *H. pylori* is not spread uniformly in different countries of the world, ethnic, geographical factors, genetic tendency, sanitary-hygienic condition in the region and family, diet are important for it. In this article, the level of *H. pylori* antibodies in the blood of patients who were monitored based on a number of external factors, in particular, harmful habits (cigarettes and smoking), eating habits, the presence of central water supply and sewage at the place of residence, was analyzed, and negative conditions increased the indicators of bacterial antibodies in the blood B12 It is confirmed that its deficiency causes the development of anemia.

Keywords: Helicobacter Pylori, Vitamin B12 Deficiency Anemia.

DOI: 10.47750/pnr.2022.13.S03.237

INTRODUCTION

In the world, including in Uzbekistan, gastrointestinal diseases and anemia are common diseases among the population. In recent years, there are reports that *H. Pylori*, which causes gastroduodenal (chronic gastritis, gastric and duodenal ulcer disease, etc.) diseases, also causes extragastroduodenal diseases. They mention the occurrence of hematological, metabolic, cardiovascular, neurodegenerative and allergic diseases under the influence of *H. Pylori* [3, 6,9].

Among the diseases caused by extragastroduodenal effects of *H. Pylori*, anemia has a special place. Because anemia is common among the population in our country as well as in the whole world.

The relationship between vitamin B_{12} deficiency and *H. Pylori* infection was determined in 1984 by O. Connor and co-authors. They found Campylobacter-like organisms in type A gastritis and in patients with pernicious anemia. A number of other observations have also shown a link between *H. Pylori* and anemia.

Sarari and co-authors observed that 67.4% of patients with *H. Pylori* had symptoms of vitamin B_{12} deficiency [13].

Helicobacter pylori is one of the most common infections in the world, found in about 50% of citizens in developed countries and 90% in developing countries [2,5,8].

In Uzbekistan, *H. pylori* is widespread, and 80% of patients with gastrointestinal diseases are diagnosed with its Cag positive strains [2,3].

Available information in the literature confirms that *H. pylori* is not only spread uniformly in different countries of the world, but also that ethnic, geographical factors, genetic predisposition, sanitary-hygienic condition in the region and family (taking into account fecal-oral transmission of infection), and the composition of the food eaten are important. [12].

Some authors believe that the difference in the population of gastroduodenal diseases with *H. pylori* among people living in different regions is related to the different distribution of its highly pathogenic strains [1,4].

In recent years, Helicobacter pylori has been considered as one of the leading factors in the initial processes of the development of idiopathic anemia [10, 7, 11]. G. Vitale and co-authors stated that the eradication of Helicobacter pylori led to an increase in vitamin B_{12} in the blood [14].

Analysis of the mentioned literature confirms that there is an organic relationship between *H. Pylori* infection and anemia. Although the spread of *H.pylori* strains and its genetic characteristics have been studied in Uzbekistan, the external factors (socio-economic-sanitary hygienic condition, harmful habits, etc.) have not been paid enough attention. Their study is important for practical medicine.

The Aim of the Research

Diagnosis and treatment of Helicobacter pylori-associated vitamin B_{12} deficiency anemia and study of some extrinsic predisposing factors.

Research Material and Methods

As a source of research, 90 patients with vitamin B_{12} anemia treated in the multidisciplinary medical center of Samarkand region, who complained of stomach and duodenal diseases, and who had higher than normal levels of Helicobacter pylori antibodies in their blood by the immunoenzyme method, were selected and divided into two groups. The first group consisted of 60 patients with vitamin B12 deficiency anemia. Based on the level of vitamin B12 in the blood and other hematological indicators, as well as the symptoms detected in the gastrointestinal and nervous system, patients in this group are mild (vitamin B12 in the blood -127.8 pg/ml), medium severe (vitamin B12 in the blood - 94.3 pg/ml) and heavy (blood vitamin B12 -73.03 pg/ml) groups. Patients of the main group were initially given complex treatment against Helicobacter pylori (amoxiclav + clarithromycin + ezemeprozole) and then vitamin B12 depending on the severity of the disease (mild 1000 mcg 3 times a week intramuscularly for 2 weeks, then 1000 mcg once every 3 months, moderate In severe cases, 1000 μg every other day intramuscularly for 3 weeks, then once a month for 2 months, and in severe cases 1000 μg every other day intramuscularly for 3 weeks, then 1000 μg once a week for 2 months. The control group consisted of a total of 30 patients with 10 each of mild, moderate and severe disease. This group of patients received only vitamin B12.

The mean age of the first subgroup of patients diagnosed with mild vitamin B12 deficiency anemia was 37.4 ± 2.33 years, 5 (25%) were men and 15 (75%) were women. The age of the control group was 48.3±4.1, 2 (20%) were men, 8 (80%) were women. The average age of patients in the second subgroup diagnosed with moderate vitamin B12 deficiency anemia was 43.6 ± 3.3 years, 3 (15%) were men and 17 (85%) were women. The age of the control group was 53.2±3.05, 2 (20%) were men, 8 (80%) were women. The average age of patients in the third subgroup diagnosed with severe vitamin B12 deficiency anemia was 47.4 ± 2.5 years, 5 (25%) were men and 15 (75%) were women. The age of the control group was 42.9±3.71 years, 2 (20%) were men, 8 (80%) were women.

In addition to antihelicobacter and antianemic treatments, their complaints were determined in all groups of patients. A careful anamnesis was collected in order to study the relationship of certain external factors (smoking-cigarettes, nose, alcohol, diet, centralized water supply and sewage availability) to *H. pylori*. Spasmolytics, gastroprotectors and other drug groups were prescribed based on the results of the objective examination, laboratory and instrumental tests.

Clinical, functional, serum Helicobacter pylori antibodies and vitamin B12 immunoenzyme, biochemical (serum iron, ferritin, transferrin, soluble transferrin receptors, interleukin-6 (IL-6), α- tumor necrosis factor (α-O'NO)) and statistical methods were used.

"VESTER-BEST" immunoenzymatic analysis kit consisting of 96 tests was used for detection of *Helicobacter pylori* antibodies in blood serum. The test range is 0-20Ed/ml.

Vitamin B12 in blood serum was determined using the "ELABSCIENCE B12, Germany" kit. This kit is based on the quantitative determination of Vitamin B12 in human serum using IFA. The detection range is 0.781-50ng/ml. Sensitivity: 0.469ng/ml.

Analysis of Research Results

In the patients under our observation, based on their complaints and sideropenic symptoms, the severity of the disease was determined and studied.

The presence of sideropenic symptoms of anemia in the main and control groups of patients with mild vitamin B12 deficiency anemia was compared before and after treatment (Table 1). As indicated, the values between the main and control groups were not significantly different ($r>0.05$) when compared before the treatments.

A complex (anti *Helicobacter pylori* followed by vitamin B12) treatment in the main group showed that changes in anemia symptoms before and after treatment were highly reliable in all cases.

Table 1: Comparative changes in the dynamics of anemia symptoms before and after treatment in the main and control groups with mild vitamin VB12 deficiency anemia

Indicators	Main group		Control group		R
Anemic and sideropenic symptoms	Before treatment	After treatment	Before treatment	After treatment	
Muscle weakness and extreme fatigue	9 (45%)	1 (5%)***	5 (50%)	3 (30%)**	R>0.05
Feeling of lack of air during physical exertion	10 (50%)	0***	4(40%)	3 (30%)	R>0.05
Dizziness	12 (60%)	0***	5 (50%)	2 (20%)***	R>0.05
Neurological symptoms (paresthesia, ataxia, hyperreflexia)	8 (40%)	0***	4(40%)	2 (20%)***	R>0.05
Sleep disturbance and memory loss	9 (45%)	0***	5 (50%)	4(40%)	R>0.05
Dysphagia	8 (40%)	0***	3 (30%)	2 (20%)	R>0.05
Impaired sense of smell	6 (30%)	0***	2 (20%)	1 (10%)	R>0.05
Complete cognitive impairment	7 (35%)	0***	3 (30%)	2 (20%)	R>0.05
Pallor of the skin and mucous membranes	11 (55%)	1 (5%)***	5 (50%)	4 (40%)	R>0.05
Tachycardia, systolic murmur at the apex of the heart	15 (75%)	2(10%)***	8 (80%)	5 (50%)***	R>0.05
Dry skin	11 (55%)	1 (5%)***	6 (60%)	5 (50%)	R>0.05
Brittleness of nails	8 (40%)	2(100%)***	3 (30%)	2 (20%)	R>0.05
Koylonychia	5 (25%)	1 (5%)***	2 (20%)	1 (10%)	R>0.05
Hair dryness and shedding	14 (70%)	3 (15%)***	7 (70%)	6 (60%)	R>0.05
Stomatitis, glossitis	11 (55%)	0***	6 (60%)	4 (40%)***	R>0.05

Note: R is the difference between baseline and control group scores before treatment. *- difference of indicators before and after treatment: *-r<0.05; **-r<0.01; ***-r<0.001.

In the control group, i.e., in the group receiving only vitamin B12, as shown in the table, muscle weakness and high fatigue decreased from 50% to 30% (r<0.01), dizziness from 50% to 20% (r<0.001), neurological signs (paresthesia, ataxia, hyperreflexia) reliably decreased from 40% to 20% (r<0.01), tachycardia from 80% to 50% (r<0.001), stomatitis and glossitis from 60% to 40% (r<0.01), positive changes in other complaints even if detected, the difference between them was not reliable (Table 1).

Antibodies to *Helicobacter pylori* were detected in the blood serum of patients with mild vitamin B12 deficiency anemia.

In the main group, the indicators decreased reliably (r<0.001) from 35.2±0.4 Ed/ml to 18.5±0.4 Ed/ml before and after treatment, respectively. In the control group, this indicator decreased from 30.9±2.15 Ed/ml to 30.63±2.15 Ed/ml, and no reliable change was observed (r>0.05). The obtained results confirm that treatment with vitamin B12 after eradication therapy with anti *Helicobacter pylori* in the main group was highly effective.

Laboratory parameters used to confirm mild vitamin B12 deficiency in the main and control groups are presented in Table 2.

Table 2: Dynamics of ferrokinetic parameters in blood serum of patients in the main and control groups with mild vitamin B12 deficiency anemia before and after treatment

Indicators	Main group		Control group		R
Laboratory test results	Before treatment	After treatment	Before treatment	After treatment	
Hemoglobin g/l	90,15±1,5	124,25±1,6***	93,1 ± 1,9	112,7 ± 1,9***	r>0.05
Erythrocytes x10	2,95±0,05	3,92±0,05***	3,03±0,08	3,6± 0,09***	r>0.05
Color indicator	0,9±0,004	0,89±0,01	0,9±0,001	0,9± 0,02	r>0.05
Serum vitamin B12 pg/ml	127,9±7,3	279,9±9,4***	122,28±6,99	153,6±12,3*	r>0.05
Serum iron µmol/l	18,02±0,05	22,2±7,1	16,35±0,96	15,22 ±0,99	r>0.05
Ferritin µg/l	124,3±17,03	129,8±11,5	102,3±13,09	100,2±10,28	r>0.05
Transferrin saturation level	27,1%	28,1 %	23,2%	24,2 %	r>0.05

Note: R is the difference between baseline and control group scores before treatment.

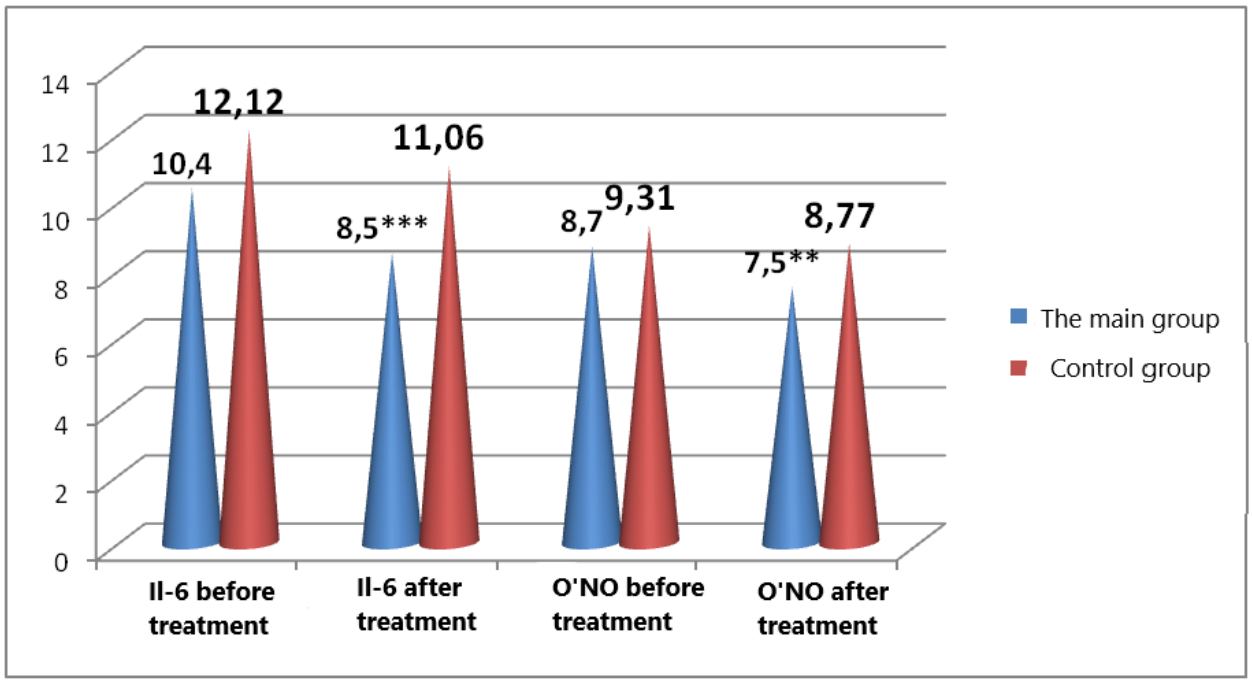
*- difference of indicators before and after treatment: *-r<0.05; **-r<0.01; ***-r<0.001.

According to it, in the main and control groups, iron, ferritin, and transferrin saturation levels in the blood were normal and it was found that vitamin B12 in the blood serum was below the normal level. A hyperchromic state was also noted. These findings confirm that the changes in the patient's blood not only matched the two groups, but also confirmed that they had vitamin B12 deficiency anemia.

After complex treatments (first anti-*Helicobacter pylori*, then vitamin B12), as shown in the table, vitamin B12 levels in the blood increased reliably (r<0.001) and hemoglobin levels increased by 1.4 times.

In the control group, there were reliable positive changes in hemoglobin (r<0.001), erythrocytes (r<0.001) and vitamin B12 levels (r<0.05), although the latter indicator did not reach the standard level.

Serum levels of inflammatory cytokines such as IL-6 and α-O'NO were 10.4±0.2 and 12.1±1.01 ng/ml and 8.7±0.3 ng/ml and 9.31±0.37 ng/ml in the main and control group patients with mild vitamin V12 deficiency anemia, respectively ml, the difference between them was not reliable (r>0.05) (Fig. 1).



Note: *-the difference between pre-treatment and post-treatment indicators: *-r<0.05; **-r<0.01; ***-r<0.001.

Figure 1: Changes in pre- and post-treatment dynamics of inflammatory cytokines in the blood serum of patients with mild vitamin B12 deficiency anemia in the main and control groups

After the complex (anti Helicobacter pylori and then vitamin B12) treatments in the main group, IL-6 levels increased from 10.4±0.2 ng/ml to 8.5±0.2 ng/ml (r<0.001), α-O'NO from 8.7±0.3 ng/ml. It reliably decreased to 7.5±0.2 ng/ml (r<0.01).

In the control group, IL-6 levels increased from 12.1±1.01 ng/ml to 11.06±0.7 ng/ml (r>0.05), α-O'NO from 9.31±0.37 ng/ml to 8.77±0.26 ng/ml (r>0.05r) decreased. Unreliable positive dynamics observed in pro-inflammatory cytokines in this group is related to the lack of Helicobacter pylori eradication therapy.

The presence of symptoms of anemia in the main and control groups of patients with moderate vitamin B12 deficiency anemia was also compared before and after treatment (Table 3). When the analysis compared the values between the main and control groups before the treatments, they were not significantly different from each other (r>0.05) in all cases except for the sign of dryness of the skin layers (r<0.05).

After the complex (anti *Helicobacter pylori* followed by vitamin B12) treatment in the main group, the changes in the symptoms of anemia before and after the treatment were highly reliable in all cases (Table 3).

Table 3: Comparative changes in the dynamics of anemia symptoms before and after treatment in the main and control groups with moderate vitamin B12 deficiency anemia

Indicators	Main group		Control group		R
Anemic and sideropenic symptoms	Before treatment	After treatment	Before treatment	After treatment	
Muscle weakness and extreme fatigue	12 (60%)	2 (10%)***	6(60%)	4(40%)*	r>0.05
Feeling of lack of air during physical exertion	14 (70%	0***	6(60%)	5 (50%)	r>0.05
Dizziness	15 (75%)	0***	7(70%)	6 (60%)	r>0.05
Neurological symptoms (paresthesia, ataxia, hyperreflexia)	10 (50%)	0***	4(40%)	2 (20%)*	r>0.05
Sleep disturbance and memory loss	11 (55%)	0***	6(60%)	5(50%)	r>0.05
Dysphagia	12 (60%)	1 (5%)***	5(50%)	4 (40%)	r>0.05
Impaired sense of smell	7 (35%)	1 (5%)***	3(30%)	2 (20%)	r>0.05
Complete cognitive impairment	10 (50%)	2 (10%)***	4 (40%)	3 (30%)	r>0.05
Pallor of the skin and mucous membranes	9 (45%)	3 (15%)	4(40%)	3 (30%)	r>0.05
Tachycardia, systolic murmur at the apex of the heart	16 (80%)	0***	7 (70%)	6(60%)	r>0.05
Dry skin	3 (15%)	0 (0%)***	4 (40%)	5(50%)	r<0.05
Brittleness of nails	11 (55%)	1 (5%)***	6 (60%)	6(60%)	r>0.05
Koylonychia	9 (45%)	2 (10%)***	4 (40%)	3(30%)	r>0.05
Hair dryness and shedding	13 (65%)	3 (15%)***	6(60%)	5(50%)	r>0.05
Stomatitis, glossitis	9 (45%)	3 (15%)***	5 (50%)	6(60%)	r>0.05

Note: r is the difference between baseline and control group scores before treatment. *- difference of indicators before and after treatment: *-r<0.05; **-r<0.01; ***-r<0.001.

As shown in the table, in the control group, that is, in the group receiving vitamin B12, muscle weakness and fatigue decreased from 60% to 40% (r<0.01), neurological symptoms (paresthesia, ataxia, hyperreflexia) from 40% to 20% (r<0.01) although there was a reliable decrease and positive changes were detected in the remaining complaints, the difference between them was not reliable (Table 3).

Antibodies of Helicobacter pylori were detected in the blood serum of patients with moderate vitamin B12 deficiency anemia. In the main group, values decreased reliably from 39.1±1.2 Ed/ml to 13.1±0.4 Ed/ml before and after treatment (r<0.001). In the control group, this indicator increased from 40.0±0.6 Ed/ml to 41.9±0.7 Ed/ml, respectively. The obtained results confirm that treatment with vitamin B12 after eradication therapy with anti *Helicobacter pylori* was highly effective in the main group.

The laboratory parameters used to confirm the diagnosis in the main and control groups with a moderate level of vitamin V12 deficiency are presented in Table 4.

Table 4: Dynamics of serum ferrokinetic indicators before and after treatment in the main and control groups of patients with moderate vitamin B12 deficiency anemia.

Indicators	Main group		Control group		R
Laboratory test results	Before treatment	After treatment	Before treatment	After treatment	
Hemoglobin g/l	76,25±1,05	125±2,8***	79,2 ± 1,55	101,2 ± 2,99***	r>0.05
Erythrocytes x10	2,4±0,05	3,34±0,08***	2,51± 0,05	3,1±0,08***	r>0.05
Color indicator	0,92±0,01	0,97±0,01**	0,9 ±0,008	0,92± 0,02	r>0.05
Serum iron µmol/l	21,9±1,5	18,8±1,03	20,78 ±1,3	18,99±1,06	r>0.05
Ferritin µg/l	142,5±16,9	164,9±12,8	145,1±15,8	133,2±18,85	r>0.05
Transferrin saturation level	24,1 %	29,3 %	24 %	21 %	r>0.05
Serum vitamin B12 pg/ml	94,3±0,4	202,5±0,2***	117,62±12,1	182,33±11,25**	r>0.05

Note: Note: R is the difference between baseline and control group scores before treatment.

*- difference of indicators before and after treatment: *-r<0.05; **-r<0.01; ***-r<0.001.

As shown in it, iron, ferritin, and transferrin saturation levels in the blood of the main and control groups were normal, and vitamin B12 in the blood serum was found to be below the normal level. Signs of hyperchromic anemia were also observed. Laboratory changes in the blood of the patients confirm that both groups have been selected mutually and that they have vitamin B12 deficiency anemia.

After complex treatments (first anti-Helicobacter pylori, then vitamin B12), as shown in the table, vitamin B12 levels in the blood increased reliably ($r<0.001$) and hemoglobin levels increased by 1.6 times.

In the control group, positive and reliable changes were observed in the level of hemoglobin, erythrocytes and vitamin B12. However, it should be noted that in the main and control groups, vitamin B12 increased by 2.1 and 1.5 times, respectively. Such a high positive change in the main group can be attributed to the fact that patients were prescribed eradication therapy before treatment with vitamin B12.

Serum levels of inflammatory cytokines such as IL-6 and α-O'NO were 10.9±0.4 and 12.16±0.71 ng/ml and 11.9±0.4 ng/ml and 11.46±0.61 ng in the main and control group patients with moderate vitamin B12 deficiency anemia, respectively. /ml, the difference between them was not reliable ($r>0.05$) (Fig. 2).

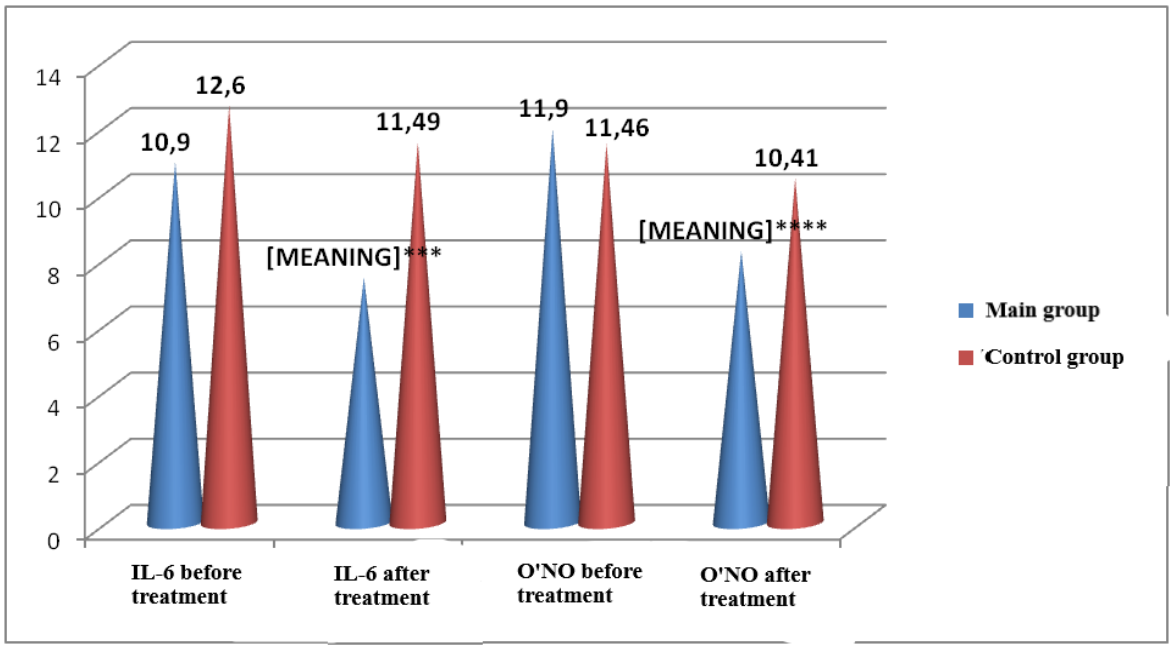


Figure 2. Changes in the dynamics of serum inflammatory cytokines before and after treatment in the main and control groups of patients with moderate vitamin B12 deficiency anemia

After the complex (anti Helicobacter pylori and then vitamin B12) treatments in the main group, IL-6 levels decreased from 10.9±0.4 ng/ml to 7.4±0.2 ng/ml ($r<0.001$), α-O'NO from 11.9±0.4 ng/ml. It reliably decreased to 8.2±0.4 ng/ml ($r<0.001$).

In the control group, IL-6 levels increased from 12.16±0.71 ng/ml to 11.49±0.7 ng/ml ($r>0.05$), α-O'NO from 11.46±0.61 ng/ml to 10.41±0.73 ng/ml ($r>0.05$) decrease was noted. Unreliable positive dynamics observed in pro-inflammatory cytokines in this group is associated with failure of Helicobacter pylori eradication therapy.

In the next stage, the indicators studied in the severe level of vitamin B12 deficiency anemia and its mild and moderate levels were compared.

The presence of symptoms of anemia in the main and control groups of patients with severe vitamin B12 deficiency anemia was compared before and after treatment. Comparative analysis did not significantly differ from each other ($r>0.05$) in all cases when the values between the main and control groups were compared before the treatments.

After complex treatment (anti Helicobacter pylori followed by vitamin B12) in the main group, it was noted that the changes in the anemia symptoms before and after the treatment were highly reliably positive (Table 5).

Table 5: Comparative changes in the dynamics of anemia symptoms before and after treatment in the main and control groups with severe vitamin B12 deficiency anemia

Indicators	Main group		Control group		r
Anemic and sideropenic symptoms	Before treatment	After treatment	Before treatment	After treatment	
Muscle weakness and extreme fatigue	15 (75%)	0***	7(70%)	5(50%)**	r>0.05
Feeling of lack of air during physical exertion	16 (80%)	2 (10%)***	7(70%)	3(30%)***	r>0.05
Dizziness	17 (85%)	0***	8(80%)	7(70%)	r>0.05
Neurological symptoms (paresthesia, ataxia, hyperreflexia)	11 (55%)	1 (5%)***	6(60%)	5(50%)	r>0.05
Sleep disturbance and memory loss	12 (60%)	2 (10%)***	7(70%)	5(50%)**	r>0.05
Dysphagia	13 (65%)	3 (15%)***	6(60%)	5(50%)	r>0.05
Impaired sense of smell	9 (45%)	3 (15%)***	4(40%)	3(30%)	r>0.05
Complete cognitive impairment	11 (55%)	0***	5 (50%)	6(60%)	r>0.05
Pallor of the skin and mucous membranes	17 (85%0	4 (20%)***	9(90%)	8(80%)	r>0.05
Tachycardia, systolic murmur at the apex of the heart	18 (90%)	2 (10%)***	8 (80%)	7(70%)	r>0.05
Dry skin	16 (80%)	6 (30%)***	7(70%)	6(60%)	r<0.05
Brittleness of nails	14 (70%)	3 (15%)***	6(60%)	5(50%)	r>0.05
Koylonychia	9 (45%)	2 (10%)***	4(40%)	4(40%)	r>0.05
Hair dryness and shedding	11 (55%)	4 (20%)***	6(60%)	5 (50%)	r>0.05
Stomatitis, glossitis	14(70%)	0***	7 (70%)	6(60%)	r>0.05

Note: R is the difference between baseline and control group scores before treatment. *- difference of indicators before and after treatment: *-r<0.05; **-r<0.01; ***-r<0.001.

As shown in the table, in the control group, i.e., vitamin B12, muscle weakness and high fatigue decreased from 70% to 50% (r<0.01), shortness of breath during physical exertion from 70% to 30% (r<0.001), and sleep disorders and although memory decline reliably decreased from 70% to 50% (r<0.01), and positive changes were detected in the remaining complaints, the difference between them was not reliable (Table 5).

Antibodies of Helicobacter pylori were detected in the blood serum of patients with severe vitamin B12 deficiency anemia. In the main group, the indicators decreased reliably (r<0.001) from 49.9±2.4 Ed/ml to 17.1±0.4 Ed/ml before and after treatment, respectively. In the control group, this indicator changed from 43.15±2.82 Ed/ml to 44.5±3.5 Ed/ml (r>0.05). The obtained results confirm that treatment with vitamin B12 after eradication therapy with anti Helicobacter pylori was highly effective in the main group.

The laboratory parameters used to confirm the diagnosis in the main and control groups with a severe level of vitamin B12 deficiency are presented in Table 6.

Table 6: The dynamics of serum ferrokinetic parameters in the main and control groups of patients with severe vitamin B12 deficiency anemia before and after treatment

Indicators	Main group		Control group		r
Laboratory test results	Before treatment	After treatment	Before treatment	After treatment	
Hemoglobin g/l	69,1±1,1	117,8±2,4***	65,8± 1,53	82.0 ± 3.17***	r>0.05
Erythrocytes x10	2,1±0,1	3,71±0,08***	1,84± 0,1	2,45± 0,11**	r>0.05
Color indicator	1,02±0,02	0,98±0,01	1,08± 0,043	1,01 ±0,02	r>0.05
Serum vitamin B12 pg/ml	73,0±4,7	148,9±8,05***	65,3 ±2,82	113,51 ± 9,36***	r>0.05
Serum iron µmol/l	27,5±1,5	26,3±1,06	26,77±0,85	24,12± 0,8	r>0.05
Ferritin µg/l	193,8±19,6	205,06±21,3	162,44 ±11,25	141,44 ± 5,85	r>0.05
Transferrin saturation level	24 %	28 %	24%	21%	r>0.05

Note: R is the difference between baseline and control group scores before treatment.

*- difference of indicators before and after treatment: *-r<0.05; **-r<0.01; ***-r<0.001.

As shown in it, in the main and control groups, iron, ferritin, and transferrin saturation levels in the blood were normal, and vitamin B12 in the blood serum was found to be below the normal level. The laboratory changes in the patient's blood confirmed that both groups were matched and that they had vitamin B12 deficiency anemia.

After complex treatments (first anti-Helicobacter pylori, then vitamin B12), as shown in the table, it was found that vitamin B12 levels in the blood increased reliably (r<0.001) and hemoglobin levels increased by 1.7 times.

In the control group, positive and reliable changes were observed in all laboratory parameters, including hemoglobin, erythrocytes and vitamin B12 levels, but they did not reach the standard level.

Serum levels of inflammatory cytokines such as IL-6 and α-O'NO were 18.6±1.1 and 23.49±2.33 ng/ml and 13.1±0.7 ng/ml and 15.62±1.33 ng/ml in the main and control group patients with severe vitamin V12 deficiency anemia, respectively ml, the difference between them was not reliable (r>0.05) (Fig. 3).

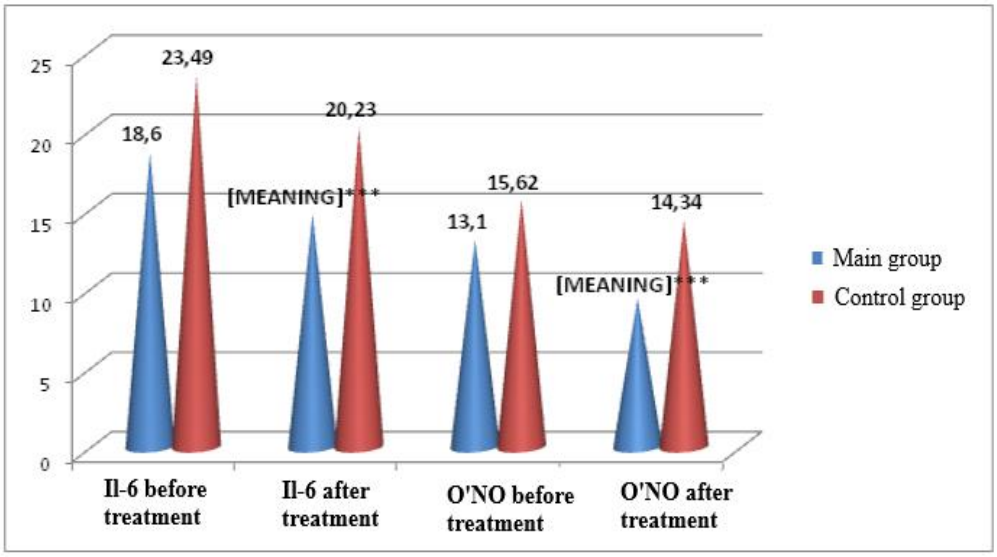


Figure 3: Changes in the dynamics of inflammatory cytokines in the blood serum of patients in the main and control groups with severe vitamin B12 deficiency anemia before and after treatment (**-r<0.01; ***-r<0.001.)

After the complex (anti Helicobacter pylori + vitamin B12) treatment in the main group, IL-6 levels decreased from 18.6±1.1 ng/ml to 14.7±0.4 ng/ml (r<0.01), α-O'NO from 13.1±0.7 ng/ml to 9.4± It was reliably reduced to 0.5 ng/ml (r<0.001).

In the control group, IL-6 levels increased from 23.49±2.33 ng/ml to 20.23±2.18 ng/ml (r>0.05), α-O'NO from 15.62±1.33 ng/ml to 14.37±1.21 ng/ml (r>0.05) was noted to have changed. Unreliable positive dynamics observed in pro-inflammatory cytokines in this group is associated with failure of Helicobacter pylori eradication therapy.

We also analyzed the level of *H. pylori* eradication with some external factors in patients diagnosed with vitamin B12 deficiency anemia based on its severity.

23.3% of patients with mild vitamin B12 deficiency anemia smoked cigarettes or tobacco, 20% drank alcohol, 76.7% did not follow the diet, 73.3% did not have centralized water supply and 76.7% sewage in their places of residence. Accordingly, 76.7% of them had no harmful habits, 80% did not consume alcohol, 23.3% followed the diet, 26.7% had centralized water supply and 23.3% had sewerage. H.pylori antibodies in the blood of patients who smoked cigarettes or snuff, consumed alcoholic beverages, did not follow the diet, and did not have centralized water supply and sewage in their places of residence were 34.2±1.2 Ed/ml, 34.4±0.6 Ed/ml, 33.4±0.6 Ed, respectively. /ml was 34.3±0.6 Ed/ml and 35.2±0.6 Ed/ml.

The number of *H.pylori* antibodies in the blood of the group of patients who do not smoke or smoke, do not drink alcohol, follow the diet, and have centralized water and sewerage at their place of residence was as follows: 26.8±3.2 Ud/ml, 27.1±3.1 Ud/ml, 31.4±0.4 Ed/ml, 32.3±0.4 Ed/ml and 33.7±0.4 Ed/ml. When the differences between the two groups were compared for all indicators, the *H.pylori* antibody response was reliably different from each other. Figure 4 below presents these identified data.

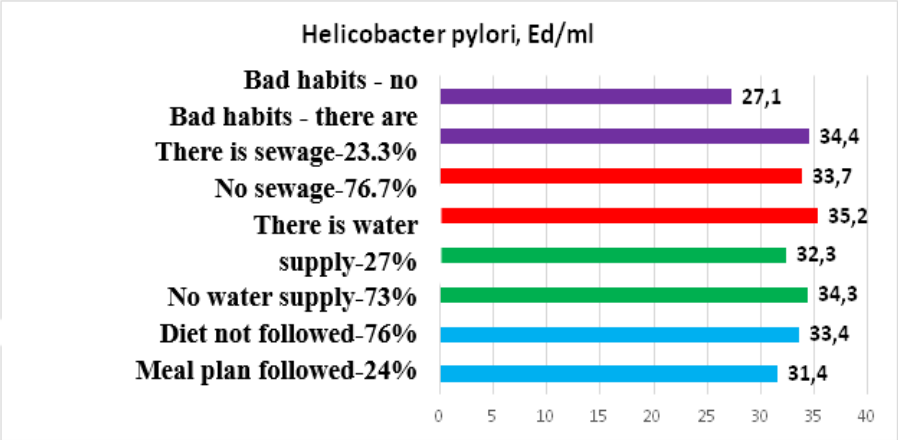


Figure 4. Indicators of detection of Helicobacter pylori antibodies in blood in relation to external factors in patients with a mild degree of vitamin V12 deficiency anemia

13.3% of patients with moderate vitamin B12 deficiency anemia smoked cigarettes or tobacco, 16.6% drank alcohol, 76.7% did not follow the diet, 56.6% had no centralized water supply and 90% had no sewage system. Accordingly, 76.7% of them had no harmful habits, 83.4% did not consume alcohol, 23.3% followed the diet, 43.4% had centralized water supply and 10% had sewerage. *H.pylori* antibodies in the blood of patients who smoked or smoked cigarettes, consumed alcoholic beverages, did not follow the diet, and did not have centralized water supply and sewage in their places of residence were 37.2±1.2 Ed/ml, 37.4±0.6 Ed/ml, 38.4±0.6 Ed, respectively. /ml, 39.3±0.6 Ed/ml and 40.2±0.6 Ed/ml.

The level of H.pylori antibodies in the blood of the group of patients who do not smoke, do not drink alcohol, follow the diet, and have centralized water and sewerage at the place of residence was as follows: 33.7±0.4 Ud/ml, 34.7±0.4 Ud/ml, 35.1±0.6 Ed/ml, 36.3±1.2 Ed/ml and 37.6±0.6 Ed/ml. When the differences between the two groups were compared for all indicators, the H.pylori antibody response was reliably different from each other. Figure 5 below shows these indicators.

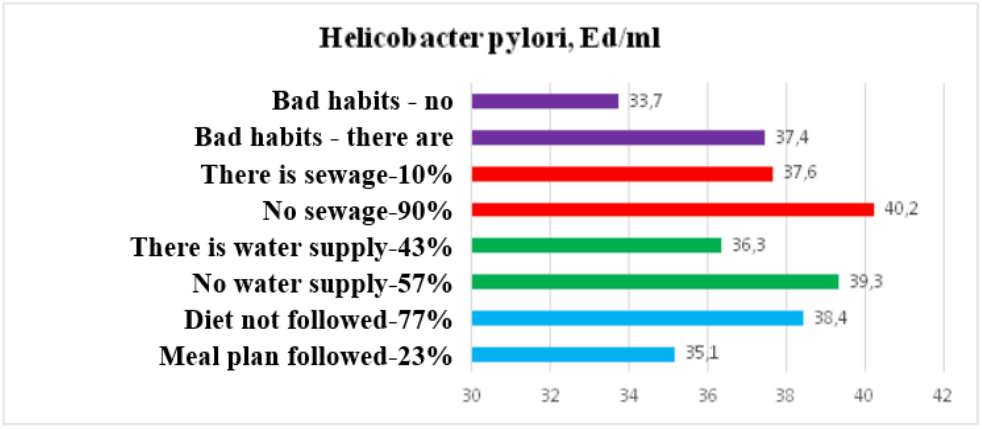


Figure 5. Indicators of detection of Helicobacter pylori antibodies in blood in relation to external factors in patients with moderate vitamin B12 deficiency anemia

20% of patients diagnosed with severe vitamin B12 deficiency anemia in our follow-up smoked cigarettes or tobacco, 16.6% drank alcohol, 76.7% did not follow the diet, 80% did not have centralized water supply and 90% sewage in their places of residence. It was found that 80% of them had no harmful habits, 83.4% did not consume alcohol, 23.3% followed the diet, 20% had centralized water supply and 10% had sewerage. *H. pylori* antibodies in the blood of patients who smoked cigarettes or snuff, consumed alcoholic beverages, did not follow the diet, and did not have centralized water supply and sewage in their places of residence were 46.5±2.6 Ed/ml, 47.4±2.6 Ed/ml, 47.6±2.6

Ed, respectively. /ml was equal to 49.3±2.4 Ed/ml and 49.7±2.4 Ed/ml.

The level of *H.pylori* antibodies in the blood of the group of patients who do not smoke or smoke, do not drink alcohol, follow the diet, and have centralized water and sewerage at the place of residence was as follows: 39.2±2.2 Ud/ml, 39.6±2.2 Ud/ml, 40.1±2.3 Ed/ml, 41.2±2.3 Ed/ml and 41.6±2.3 Ed/ml. When the differences between the two groups were compared for all indicators, the H.pylori antibody response was reliably different from each other. Figure 6 below shows these indicators.

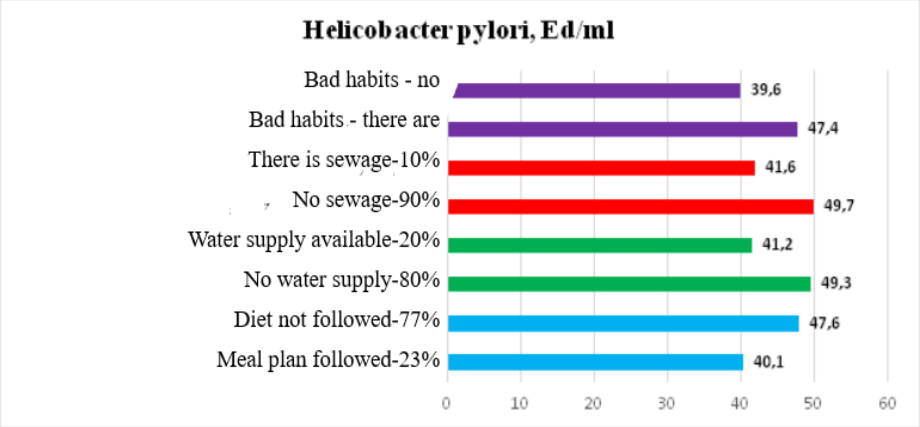


Figure 6: Indicators of detection of Helicobacter pylori antibodies in blood in relation to external factors in patients with severe vitamin V12 deficiency anemia

The study of the effect of external factors in vitamin B12 deficiency anemia showed that there is a relationship between them and the severity of the disease, and accordingly, *H.pylori* antibodies in the blood serum increase. This, in turn, confirms that there is an organic connection between the factors listed with this bacterium (cigarettes, secondhand smoke, poor diet, lack of centralized water supply and sewage) and vitamin B12 deficiency anemia.

Based on our analysis, we can come to the following conclusions:

1. Cigarettes, nose and alcohol increase the acidic environment in the stomach and create alternative conditions for the growth of *H. pylori* and the occurrence of anemia. Active advocacy among the population against harmful habits is important in preventing *H. pylori* infection and related anemia.
2. In residential areas where there is no centralized water supply and sewerage, it is necessary to strictly follow the rules of personal hygiene, taking into account the fecal-oral transmission of *H.pylori*.

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