

**Research Article**

**The Evaluation of Treatment of Helicobacter Pylori Eradication on Platelet Counts in Patients with Immune Thrombocytopenic Purpura Referred to Kashan Shahid Beheshti Hospital**

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**ABSTRACT:**

New drugs for patients with immune thrombocytopenic purpura (ITP), are thrombocytopenicreceptor agonists. This therapy originates from these findings that many patients contrary to previous assumptions, has not increased level of Thrombopoietin in addition, increased platelet destruction is not seen in them. Two products, one oral and another injected subcutaneously were effective in patients with ITP although their role is not clear in the treatment of ITP. British Society of Hematology is currently recommending screening and eradication of H pylori as a treatment for ITP (level of evidence III) until now, there are no reports have been published about the patients, hence in this clinical trial the effect of eradication of helicobacter pylori were investigated in platelet count and adult patients with ITP. Forty of Iranian patients with ITP referred to the Oncology and blood part of ShahidBeheshti hospital were studied in two groups. A group using amoxicillin, clarithromycin and omeprazole were treated. The other group received placebo in the same values. Platelet count before treatment and at the first, second and third month after treatment were analyzed. The findings showed that the mean platelet count before intervention in intervention and control groups, respectively, were 67.85 and 69.4 per cubic ( $p=0.82$ ). This amount in the third month after treatment in the intervention group is 107.15 and in the control group is 71.15 thousand cubic millimeters( $p<0.001$ ). Repeated measures analysis confirmed the positive health eradication of Helicobacter pylori impact on the platelet count ( $p=0.007$ ). In this study it was found that the treatment of Helicobacter pylori eradication in patients with immune thrombocytopenic purpura caused a dramatic increase in the number of platelets.

**Key words:** immune thrombocytopenic purpura, Helicobacter pylori, platelet count, eradication

**INTRODUCTION**

Immune thrombocytopenic purpura (ITP) (its other name idiopathic thrombocytopenic purpura) is acquired disorder that by Immune-mediated platelet destruction and may inhibit the release of platelets from megakaryocytes determined. In children is usually an acute disease that commonly occurs after an infection and is self-limiting process, but takes more

chronic course in adults. The exact nature of immune dysfunction in this disease is unknown. When ITP is related to an underlying medical condition, the secondary term refers to it. Among the most common underlying disorder, particularly immune disorders such as Systemic Lupus Erythematosus (SLE) and infections such as HIV and hepatitis C can be noted. ITP

associated with *Helicobacter pylori* is unknown. *Helicobacter pylori* (*Helicobacter*) is a negative gram microaerophilic that is colonized in more than half of the human population stomach (1 and 2) however, the prevalence of *H. pylori* is not homogeneous across the globe (3 and 4). In Western countries, the incidence of infection has declined during the past few decades (5-7), but the rate of *H. pylori* infection in developing countries like Iran to have been reported approximately 90-80% (8-10). *Helicobacter pylori*, is the main cause active chronic gastritis and gastric ulcer and duodenal ulcer. *Helicobacter pylori* is a contributing factor in the development of stomach cancer and lymphoma associated with mucosa-associated lymphoid tissue (mucosa-associated lymphoid tissue lymphoma) (1 and 2). Immune thrombocytopenic purpura is determined with mucocutaneous bleeding and generally a few number of platelets, while the other cells of peripheral blood and its smear is natural. Patients usually refer presentation with ecchymosis and petechial or their thrombocytopenia, is discovered by accidental in complete blood cells experiment. In these patients, mucocutaneous bleeding, such as bleeding from the lining of the mouth, gastrointestinal tract, or severe bleeding during menstruation may be observed. Rarely life-threatening bleeding may also occur in the central nervous system. Wet purpura (blood blisters in the mouth) and retinal hemorrhages also may indicate life-threatening bleeding. Along with many of the diseases associated with platelet aggregation has been described by *H. pylori* infection. For example, people infected with *H. pylori* tend to develop heart failure, coronary heart disease and stroke (11-16). It has been suggested that *H. pylori* may trigger the Thrombotic Thrombocytopenic purpura (TTP), induced platelet aggregation by interacting with the operating von Willebrand (17). The theory is that *H. pylori* infection may have implications for chronic Idiopathic Thrombocytopenic Purpura (ITP) is associated, which has been shown to eradicate the bacteria from gastric

mucosa is improved in some patients with ITP (18-26). Causal relationship between *H. pylori* infection and the ITP raised showed in studies platelet count improved after eradication in infected patients (27). *H. pylori* infection in patients with ITP are systematically investigated and there has not been found disputes with general healthy population matched for age and geographic area (28). In contrast, a study of Columbia *H. pylori* infection high prevalence in patients with ITP (90.6%), is reported which significantly is different with witness people (43.8%) (18). several studies in adults, have shown positive impact on the eradication of *H. pylori* with triple standard therapy in low platelet count patients (18-21, 24, 28-34) in Cohort studies in Japan and Italy higher response rate compared to other countries has been reported (24, 29, 31 and 33).

The relationship between *H. pylori* infection and ITP was first described in 1998, when an Italian group reported a significant increase in the number of platelets in 8 of 11 patients with ITP, in which the bacteria were eradicated, (32). However, in next reports results are inconsistent. Most studies included patients with mild thrombocytopenia are usually not treated. Therefore, the eradication of *Helicobacter* in the management of patients with ITP need to be investigated further (24, 32, 35 and 36) but there are increasing evidence of an association between *Helicobacter pylori* eradication in patients with ITP and platelet recovery, (23, 26, 39-37). No clear evidence about the association between *H. pylori* eradication and ITP is available and there are many contradictions in the few studies. Previous studies have suggested further investigations in this field (42).

*H. pylori* screening and eradication of infection may be simpler and more secure option to immunosuppression or splenectomy in ITP patients (20 and 40)

British Society of Hematology currently is recommending screening and eradication of *H. pylori* as a treatment for ITP (level of evidence III) (41). Until now, no reports have been published about these patients in Iran. Because

local experiences are important in considering potential regional variations in Helicobacter pylori strains, the aim of this study is to evaluate the effect of treatment of Helicobacter pylori eradication on platelet counts in patients with immune thrombocytopenic purpura.

### Research questions

What is the average number of platelets in patients with immune thrombocytopenic purpura before the treatment?

What is the average number of platelets in patients with immune thrombocytopenic purpura after the treatment?

### The hypothesis

Platelet counts in patients with immune thrombocytopenic purpura before and after the treatment are different.

### The definition of research concepts

Helicobacter pylori: a curved bacterium, Gram-negative, urease-positive, curved or semi-spiral as a pathogen that lives in the human stomach.

**Immune thrombocytopenic purpura (or idiopathic thrombocytopenic purpura):** A type of thrombocytopenia is no exposure to toxins or disease occurs and cause of platelet destruction, immunological or unknown.

**Helicobacter pylori eradication:** eradication of Helicobacter pylori, its main purpose is not only temporary relief of symptoms but also removed H. pylori infection.

Helicobacter pylori Triple Therapy: the eradicate of Helicobacter pylori by the three drugs clarithromycin and amoxicillin, each drug twice a day for two weeks with a PPI for 45 days.

### Research Methodology

The study is quasi-experimental laboratory. The static population included all patients referred to the Hematology and oncology of ShahidBeheshti hospital were diagnosed with immune thrombocytopenic purpura. Patients with confirmed diagnosis of immune thrombocytopenic purpura (ITP) according to the American Society of Hematology (history, physical examination, CBC, peripheral blood smears and bone marrow) and examination of an expert hematologists, who were referred for

treatment to KashanShahidbeheshti hospital. Hematology and the examinations are experienced hematologist, platelet count between 30 to 150 thousand, non-wet purpura, lack of life-threatening bleeding stool test positive for H. pylori antigen) and exclusion criteria (allergy to penicillin, irregular use of the drugs are associated with malabsorption diseases) were enrolled.

After providing written informed consent information on how to conduct the study of all patients participating in the trial. Demographic data (age, sex, duration of disease onset) were recorded. Stool samples for the presence of H. pylori antigens were obtained from all patients. Patients who had a negative stool antigen test were excluded. By taking comparing formula 2 the mean and by mean and standard deviation of similar studies and confidence 95% and power 80% to find differences between groupsthe most number of the 20 cases in each group was calculated. Patients using Permuted-block randomization with block 4 and 6 were divided into two groups. The study was double blind and patients are responsible for examining the patient, were from the treatment groups. Helicobacter pylori eradication regimen in the study group consisting of the following medications was prescribed:

N= 28	BD	500 mg	Clarythromycin
N= 28	BD	1 gr	Amoxicilin
N= 90	BD	20 mg	Omeprazol

Control group in similar promises placebo control group in terms of the number and shape of the case groups were similar. After completion of treatment to ensure eradication of Helicobacter pylori stool samples were repeated. During the treatment, platelet count) was controlled in three times (intervals of one, two and three months) and if the number of platelets increasing before completion of treatment the person was excluded and considered as improved and went on their own. The effect of treatment was evaluated according to the number of platelets. In order to analyze the data from tests Chi square, Independent T test and repeated measures at the significant level P less than 0.05 was used by SPSS16 software.

**Table 1.** Variables studied

Scale	Variable properties		Type (role) variable				Variable	ردیف
	Qualitative	Quantities	Dependence	Independence	Confounding	Background		
The number of cells per cubic liter	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Platelet count	1
year	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Age	2
Male or female	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Gender	3
month	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Duration of disease onset	4
Intervention, control	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Group therapy	5

### Research findings

Based on Table 2. In this study, 40 patients with immune thrombocytopenic purpura in both intervention and control groups were treated with eradication of Helicobacter pylori. The average age of patients studied  $34.82 \pm 9.06$  years in the intervention group, the mean of  $35.2 \pm 9.64$  years and in control group  $34.45 \pm 8.68$  years ( $p=0.8$ ). According to Table 2, 50% of patients in the intervention group and 70% of patients in the control group were male. The two groups were similar in terms of gender ( $p = 0.2$ ).

**Table 2.** The frequency of patients by gender

Total	Group		Gender
	Control	Intervention	
24 60.0%	14 70.0%	10 50.0%	male
16 40.0%	6 30.0%	10 50.0%	female
40 100%	20 100%	20 100%	total
	0.2*		P value

Based on Table 3. The mean duration of diabetes immune thrombocytopenic purpura in all patients was equal to  $20.45 \pm 11.14$  months (median 23 months) the rate in the intervention group  $18.45 \pm 12.45$  months in the control group  $22.45 \pm 9.54$  months, which was not statistically significant between the two groups ( $p=0.26$ ).

**Table 3.** Comparison disease duration in the study groups

P value	Standard deviation	Average	Number	Group
0.26	12.46	18.45	20	Innervation
	9.54	22.45	20	Control

According to Table 4. Comparison of average platelet count before the intervention groups showed that two groups were similar in terms of the number of platelets ( $p=0.82$ ).

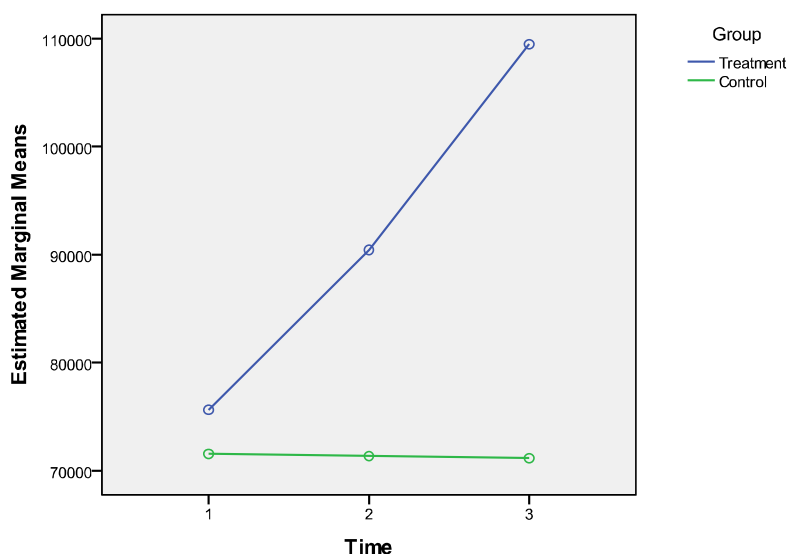
**Table 4** compares the average platelet count before the intervention

P value	Standard deviation	Average	Number	Group
0.82	19770.46	67850.0	20	Innervation
	23685.22	69400.0	20	Control

According to the results presented in Table 5. It was found that the mean platelet counts in the first month after treatment in both groups had the same status while in second and third month after treatment the mean scores in the intervention group was significantly greater than the control group.

Table 5 compares the average platelet count in the first, second and third month after starting treatment

P value	Standard deviation	Average	Group	time
0.7	20255.21	74200.0	Intervention	The first month
	23520.37	71550.0	Control	
0.03	27660.25	88600.0	Intervention	The second month
	21947.96	71350.0	Control	
<0.001	31843.82	107150.0	Intervention	The third month
	20171.04	71150.0	Control	



**Figure 1-** comparing the mean depression scores during treatment in both treatment groups Repeated measures analysis of platelet count at different times showed that the two groups were different changes in platelet count ( $p=0.007$ ) the intervention group than the control group have been better in all phases of the study.

## DISCUSSION AND CONCLUSION

The results showed that treatment of H. pylori eradication in patients with immune thrombocytopenic purpura significantly increased platelet counts in these patients. Several studies conducted in the field in different areas had different results. According to the results of research Kohda and colleagues found that 62.5% of patients with ITP were infected with Helicobacter pylori by eradication treatment with platelet count within 15 months after treatment has increased more than 63.2% of patients (21). Hino et al also reported that 85.7% of patients with ITP were infected with H. pylori eradication that therapy was successful in more than 55% of patients. Study patients showed that the with eradication platelet count

increased significantly during the next few months (19). Similar results with this study and studies mentioned in other studies have also been reported (20, 29, 33, 34 and 43-47). In contrast to the above studies some of incompetent treatment of Helicobacter pylori eradication studies have noted an increase in platelet count. Jarque and colleagues with the effect of Helicobacter pylori eradication on platelet count in patients with chronic ITP have observed that only 5% of these patients following treatment platelet count had increased (48). In a study by Payande and his colleagues has been performed on 92 patients with ITP in Iran it was found that eradication of H. pylori infection triple therapy using amoxicillin, clarithromycin and omeprazole clear

improvement in platelet count in patients with slight ITP while in ITP patients with a severe form of this treatment has no significant effect on platelet count (49). The contradiction noted in other studies have also been reported (2, 24 and 50). Although the number and quality of studies on the positive role of Helicobacter pylori eradication in the treatment of ITP has been pointed out are more, but the paradox observed in some extent justified. Different pathogenicity between the different strains of H. pylori may be one of the most important factors in creating a paradox. Studies have shown that Helicobacter pylori genotypes were significant differences in gastrointestinal symptoms (51 and 52). However, it is unclear that differences gastrointestinal bacteria to what extent involved in causing external genotypic problems, but the geographical distribution of positive results probable these differences impact studies. Most studies previously mentioned, the positive effect have confirmed of H. pylori eradication on platelet count which have been conducted in the Asian region, especially in its eastern part and more studies with negative results related to the European and American regions (2, 24 and 48). However, in a review study regional differences and response to treatment of Helicobacter pylori eradication in patients with ITP have been debated, but because the lack of sufficient information about the strains infecting the patient with ITP conclusion in this regard is difficult (53).

Another possible risk factor in the development of different responses to treatment of H. pylori infection in patients with ITP is a disease duration. In a limited number of studies in this field duration of ITP patients are listed. Comparing the mean change in platelet count after Helicobacter pylori eradication reflects the fact that the platelet count in patients with a shorter duration is more than chronic ITP patients (26, 34, 35, 43, 44, 50 and 54). Further studies in this area and meta-analysis of the results will help to better understand this relationship. The duration of exposure and Helicobacter pylori infection in patients is

another possible factor that could affect the response to eradication treatment. Several mechanisms and intensify the role of H. pylori in ITP such as the production of antibodies, interfering with Von Willebrandfactor, activation of lymphocytes B, increased phagocytic activity of monocytes and so on are noted (35 and 58-55). It seems that eradication therapy given prior to the consolidation of immunological processes decreased platelet increases control success. Evaluation this factor is difficult to existing facilities. Although the etiologic role of H. pylori in the pathogenesis of ITP has been established but it should be borne in mind the fact that other factors such as viral infections (HIV, CMV and VZV) and immune system disorders have also been implicated in the pathogenesis of this disease (59-61) The interaction of these factors can affect, in response to any treatment, including therapy for Helicobacter pylori eradication.

#### **Research limitations**

One limitation of this study is the small sample size because finding people with the right conditions is difficult and this issue existed in previous studies. Unable to perform prognosis endoscopic and tissue direct study are the limitations of the study due to patients' conditions which is impossible to use a highly sensitive and specific method to check for the eradication of Helicobacter pylori.

#### **Research proposals**

The evaluation frequency of various strains relationship of H. pylori in patients with ITP

The evaluation of relationship between duration of ITP and platelet improve the treatment of Helicobacter pylori eradication

#### **RESOURCES**

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