

## The Relationship Between Helicobacter Pylori Infection And Childhood Idiopathic Thrombocytopenic Purpura

Sawsan S.Abbas\* Ph.D  
Tariq M.Hadi\*\*Ph.D

### Summary:

**Background:** Idiopathic thrombocytopenic purpura , a disorder characterized by autoantibody mediated platelets destruction causing decreased number of circulating platelets manifest as bleeding tendency. Since the discovery of *Helicobacter pylori* (*H. pylori* ) several studies have been published concerning a hypothetical role of this bacteria in idiopathic thrombocytopenic purpura.

**Aim of the study:** Evaluate the pathogenic correlation between *H.pylori* infection and idiopathic thrombocytopenic purpura.

**Patients and Method:** A cross sectional study was done on 30 cases of idiopathic thrombocytopenic purpura admitted to the Pediatric Hemato-Oncology unit in ALKadhimiya Teaching Hospital and 20 cases of sex and age matched healthy children as a control to determine the relation between *H. pylori* infection and idiopathic thrombocytopenic purpura. The peak age for idiopathic thrombocytopenic purpura was between ( 6-10 years) of age, (43.33%) . Male :female ratio equal to 2:1 . ELIZA test was used to measure the serum IgG antibody titer against *H. pylori* , 5 cases of idiopathic thrombocytopenic purpura was found to be positive for *H.pylori* (16.67%)while the test was negative in all of the control group (100%) ,

**Results:** a result which is statistically highly significant,  $p$  - value<0.05. Of the positive cases 3 (60%) was chronic idiopathic thrombocytopenic purpura and two cases (40%) was acute idiopathic thrombocytopenic purpura. Patients with positive test were older than those with negative test. The mean platelet count was less in the positive than those with negative test. A weak inverse correlation was found between platelet count and *H.pylori* serum antibody titer(  $r$  - value equal to - 0.13437). The test was sensitive in (20%) and specific in (100%) of cases.

**Conclusion:** *H. pylori* infection may play a role in the initiation of idiopathic thrombocytopenic purpura and eradication of *H.pylori* infection can cure idiopathic thrombocytopenic purpura specially in chronic and resistant cases. The ELIZA test can be used as a screening test to detect *H.pylori* infection in children with idiopathic thrombocytopenic purpura.

**Key word:** *Helicobacter pylori* infection, idiopathic thrombocytopenic Purpura

*J Fac Med Baghdad*  
2007; Vol. 49, No.2  
Received July 2006  
Accepted Dec. 2006

### Introduction:

Idiopathic thrombocytopenic purpura (ITP), a disorder characterized by auto- antibody mediated platelets destruction <sup>(1),(2)</sup> causing decreased number of circulating platelets manifest as bleeding tendency, easy bruising (purpura) or extravasations of blood from capillaries into skin and mucous membrane (petechiae) <sup>(3)</sup> . Since the discovery of *Helicobacter pylori* ( *H. pylori*), several studies have been published concerning a hypothetical role of this bacteria in different extra gastric diseases , such as ischemic heart disease, idiopathic thrombocytopenic purpura , iron deficiency anemia <sup>(4)</sup> with a high prevalence of *H. pylori* in adult patients with chronic idiopathic thrombocytopenic purpura <sup>(5)</sup>, but the role of *H. pylori* infection in relation to the development and / or persistence of ITP in

infected patients still controversial with few paediatric studies have been undertaken <sup>(6)</sup>. Eradication of *H. pylori* was reported to increase the platelet counts in some *H. pylori* positive patients<sup>(7)</sup> for this reason treatment guidelines for patients with idiopathic thrombocytopenic purpura have been changed due to clinical application of *H. pylori* eradication <sup>(8)</sup> .

### **Aim of the study:**

Evaluate the pathogenic correlation between *Hpylori* infection and idiopathic thrombocytopenic purpura.

### **Patients and Method:**

A cross sectional study was done on cases of idiopathic thrombocytopenic purpura admitted to the pediatric Hemato-oncology unit /AL-Kadhimiya Teaching Hospital. Acute idiopathic thrombocytopenic Purpura are cases with typical presentation of bleeding episodes lasting for few days or weeks but no longer than 6 months. <sup>(9)</sup> Chronic idiopathic thrombocytopenic Purpura is defined as platelet count of < 150 x

\* Department of Pediatric College of Medicine AL-Nahrain University

\*\* Department of Pediatric AL-Kadhimiya Teaching Hospital

10<sup>9</sup>/L persisting for more than 6 months from the onset of illness (10<sup>11</sup>). Thirty cases were collected randomly, history was taken, physical examination was done, complete blood picture was aspirated using K3-EDTA anticoagulant to calculate the platelet count, definite diagnosis was established depending on clinical manifestation with normal blood element in the peripheral blood, film apart from low platelet count. Bone marrow aspirate was done in few cases. Another 3 cc of blood was collected in a plane tube to determine the serum IgG antibody titer against Helicobacter pylori using ELIZA test (Biohit Plc, Laipatie, Finland) (12), a value > 38EIU is considered to be positive. Another 20 samples were aspirated from normal age and sex matched healthy children as a control. Mean and standard deviation was estimated, statistical analysis was done using the chi-square test through Microsoft Excel Program, p-value < 0.05 is considered as statistically significant. Pearson correlation was done between the platelet count and H. pylori antibody titer. Both sensitivity and specificity were estimated.

**Results:**

Total number of patients was thirty cases the mean age of the patients was (6.67 + 3.46) years while the mean age of the control group was (6.25 ± 3.30) years. Peak age of patients with disease was between (6 -10) years, 13 cases (43.33%) as it is shown in (Table -1-). Twenty cases were males and 10 cases females with male: female ratio of 2:1 as it is shown in (Table-1). Most of the patients were from Baghdad Governorate, 22 cases (73.34%) as it is shown in (Table-2-). Of the studied patients 18 cases (60%) had acute idiopathic thrombocytopenic purpura while 12 cases (40%) had chronic idiopathic thrombocytopenic purpura as it is shown in (Table -3-) Patients with acute idiopathic thrombocytopenic purpura were younger than those with chronic idiopathic thrombocytopenic purpura with a mean age of (4.64 ± 2.72 and 9.58 + 2.19) years respectively. Complete blood picture shows normal blood elements apart from low platelet counts with a range of (3000 -88000 x 10<sup>9</sup>/L) as it is shown in (Table-4). H.pylori infection was found to be positive in (5) patients of idiopathic thrombocytopenic purpura (16.67%), and negative in all of the control group, 20 cases (100%) Using the Chi square test the result was statistically highly significant (X' equal to 2.73921E-07, P-value < 0.05) as it is shown in (Table -5-). Of the positive cases 2 cases (40%) was with acute idiopathic thrombocytopenic purpura and 3 cases (60%) was with chronic idiopathic thrombocytopenic purpura, 3 cases

(60%) were males while 2 cases (40%) were females. The serum IgG antibody titer for H.pylori was higher in positive than negative group of patients with a mean and standard deviation of (64.80 ± 21.44 and 11.87 + 9.81EIU) respectively while in the control group the mean serum antibody titer for H. pylori is (9.75 ± 11.58) as it is shown in (Table -6-). Using the Pearson correlation analysis a weak inverse correlation was found between H.pylori antibody titer and platelet counts (r-value equal to -0.13437 i.e.) with 0.99 confidence of (0.053729) as it is shown in (Figure -1). In this study the ELIZA test for detecting serum IgG antibody titer was found to be sensitive in (20%) of cases and specific in (100%) of cases as it is shown in (Table -7).

**Table -1- shows the age of the patients at the onset of the diseases 20 cases (66.67%) males 10 cases (33.33 %) female M: F ratio = 2:1**

Age /year	No.	
< 1	1	3.33
1-5	12	40
6-10	13	43.33
>10	4	13.34

**Table 2 shows the residence of the patients**

Residence	No.	%
Baghdad	22	73.34
Other governorates	8	26.66

**Table 3 shows the duration of the disease**

Duration /monthes	No.	%
<6	18	60
>6	12	40

**Table 4 shows peripheral blood indices in the patients studied**

Blood indices	Mean ± standard deviation
PCV%	33.2± 7.4
WBCs count x10 <sup>9</sup> /L	6120± 2752.47
Platelets count x10 <sup>9</sup> /L	35566.66± 27378.17

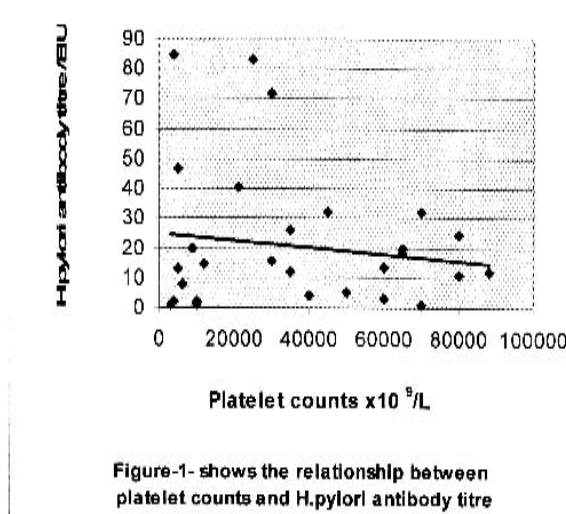
**Table 5 shows the result of ELIZA test in the studied groups**

ELIZA test	patients		control	
	No.	%	No.	%
Positive	5	16.67	0	0
Negative	25	83.33	20	100

*Chi square (X<sup>2</sup>) = 2.73921 E-07*  
*Degree of Freedom = 1*  
*P.value = <0.05 highly sign*

**Table 6 shows the mean level of serum IgG antibody titer**

Serum antibody titer (EIU)	Mean ± standard deviation
Patients-positive	64.8 ± 21.44
Patients – negative	11.87 ± 9.81
Control group	9.75 ± 11.58



*r - value = - 0.13437*

**Table -7- shows sensitivity ,specificity, positive and negative predictive value of ELIZA test in the patients**

	Sensitivity %	Specificity %	PPV %	NPP%
Patients	20	100	100	50

**Discussion:**

In this study the peak age for idiopathic thrombocytopenic Purpura was between (6-10) years of age which is in agreement of previous studies<sup>(13,14)</sup>. Male . female ratio equal to 2:1 which is against previous studies which showed that female are involved more the males<sup>(13, 14)</sup>, this may be due to random collection of cases . Most of the patients were from Baghdad which is the main pool for the Hospital.H. pylori was found to be positive in 5 cases only(16.67%) , in comparison with studies done elsewhere H. pylori was positive in (81.8%)<sup>(16)</sup> , (83%)<sup>(17)</sup> of cases of idiopathic thrombocytopenic purpura in Japan and in (58%) in Italy<sup>(18)</sup> and in (29%) of cases in France<sup>(19)</sup>. This low prevalence of H.pylori can be attributed to the possibility of lower prevalence of H. pylori infection in our country as the prevalence of this organism was reported to be high in Japan, China, Peru and Ethiopia<sup>(20)</sup>, Of those patients positive for H.pylori 3 cases (60%) were chronic and 2 cases was acute( 40%) ,In Japan H.pylori was positive in (85%) of cases with chronic idiopathic thrombocytopenic purpura<sup>(1)</sup> while in Taiwan it positive in (40.99%) of cases with chronic idiopathic thrombocytopenic purpura<sup>(6)</sup>. H. pylori positive patients were older than H. pylori negative patients which is in agreement

of previous studies (17, 22), this can be explained by the fact that the rate of infection with H.pylori increase with age as does gastritis<sup>(20)</sup>. The platelet count was lower in H.pylori - positive patients than H.pylori - a negative patient which indicates that the destruction is more i. e. the disease is more severe. An inverse correlation was found between the platelets count the serum IgG antibody titer against H.pylori which indicates that the higher the titer the more the platelets destruction. In this study the ELIZA test was found to be sensitive in (20%) and specific in (100%) of cases which indicate that this test can be used as a screening test for detection of H. pylori infection among children with newly diagnosed idiopathic thrombocytopenic purpura, as it was proved that eradication of H. pylori infection in idiopathic thrombocytopenic purpura can improve the outcome in term of raising the platelet count specially in chronic and resistant cases of idiopathic thrombocytopenic purpura (23)

**References:**

1-Franchini M, Veneri D, Helicobacter pylori associated immune thrombocytopenic purpura: Platelets . 2006Mar, 17(2): 71-7.  
 2-Gasbarrini A, Franceschi F, Does H. pylori infection play a role in idiopathic thrombocytopenic Purpura and other

- autoimmune diseases? *Am J. Gastroenterol.* 2005 June, 100(6), 1271 - 3.
- 3- Sandler SG, Katherine I. Schexneider, et al, *Immune thrombocytopenic Purpura. J. emedicine*, 6, 2004, 1-22.
- 4- Franceschi F, Roccarina D, Gasbarrini A *Extra gastric manifestations of Helicobacter pylori infection, Minerva Med.* 2006 Feb, 97(1), 39-45.
- 5-Hayashi H, Okuda M, Aoyagi H, Yashiyama M, Miyashiro E, Kounami S, Yoshikawa N, *Helicobacter pylori infection in children with chronic idiopathic thrombocytopenic Purpura pediatric Int.* 2005 June, 47(3), 292 -5.
- 6- Jaing TH, Yang CP, Hung JJ, Chiu H, Chang KW, *Efficacy of Helicobacter pylori eradication on platelet recovery in children with chronic idiopathic thrombocytopenic purpura: Acta Paediatr.* 2003 Oct, 92(10):1153 -7.
- 7- Suzuki T, Matsushima M, Masui A, Watanabe K, Takagi A, Ogawa Y, Shirai T, Mine T, *Effect of Helicobacter pylori eradication in patients with chronic idiopathic thrombocytopenic Purpura - a randomized controlled trial, Am J. Gastroenterol* 2005 June 100 (6), 1265 - 70.
- 8-Hashino S, Ota S, Kobayashi S, Tanako J, Musashi M et al, *Current status of treatment for patients with idiopathic thrombocytopenic Purpura in the Hokkaido area (evaluation of Helicobacter pylori eradication) . Rinsho Ketsueki*, 2004 Jul, 45(7): 539 - 45.
- 9-Novi S, *idiopathic thrombocytopenic Purpura in children, Med - Pregl*, 1998, 51 (3 - 4), 127- 34.
- 10- Blanchette VS, Price V, *childhood chronic immune thrombocytopenic Purpura: unresolved issue, J. Pediatr Hematol Oncol*, 2003, 25 suppl 1. S28 - 33.
- 11-Amendola G, Danise P, D Arco A, *Longterm follow up of chronic immune thrombocytopenic Purpura in children, Pediatr-Med-Chir*, 2000, 22(1):39-41.
- 12-ELIZA Kit for measurement of human IgG class antibodies to Helicobacter pylori in serum and EDTA or heparin plasma, *Biohit Plc, Laippatie I, Finland.*
- 13- AL - Nadawi MN, AL -Hadad SA, Umran SK, *idiopathic thrombocytopenic Purpura, clinical manifestation and treatment, J. Fac. Med.*, 2002, 44, 1, 71 - 76.
- 14-Nugent DJ, *Childhood immune thrombocytopenic Purpura, Blood - Rev.* 2002, 16(1):27- 9.
- 15- Mantadakis E, George RB, *Splenectomy in children with chronic idiopathic thrombocytopenic Purpura, 40<sup>h</sup> annual meeting of the American society of hematology, 1998.*
- 16-Sato K, Nagai T, Muroi K, Komatsu N, Ozawa K, *Helicobacter pylori in patients with idiopathic thrombocytopenic purpura - the association between the activity of Helicobacter pylori and platelet recovery, Rinsho Ketsueki.* 2004 Dec, 45 (12) :1252 -4.
- 17- Ando K, Shimamoto T, Tauchi T, Ito Y, Kuriyama Y, et al, *Can eradication therapy for Helicobacter pylori really improve the thrombocytopenia in idiopathic thrombocytopenic purpura? our experience and literature review Int. J. Hematol*, 2003 Apr, 77(3).-239-44.
- 18-Franchini M, Veneri D, *Helicobacter pylori infection and idiopathic thrombocytopenic Purpura: an update, Helicobacter* 2004 Aug, 9(4) :342 -6.
- 19- Michel M, Khellaf M, Desforges L, Lee K, et al *Autoimmune thrombocytopenic purpura and Helicobacter pylori infection, Arc. Int. Med.* 2002 May 13, 162(9).-1033 -6.
- 20-Ralph D. Feigin, Ameeta B. Martin, *Helicobacter pylori (Campylobacter pylori), Nelson text book of pediatrics ch. 12.42, P. 758 -759, 14<sup>th</sup> ed. 1992, WB Saunders Company.*
- 21-Ando K, Tsuzuki T, Mizuno T, Minami M, et al *Characteristics of Helicobacter pylori- induced gastritis and the effect of Hpylori eradication in patients with chronic idiopathic thrombocytopenic purpura, Helicobacter*, 2004 Oct, 9(5), 443 -52.
- 22- Michel M, Cooper N, Jean C, Frissora C, Bussel JB *Does Helicobacter pylori initiate or perpetuate immune thrombocytopenic purpura, Blood*, 2004 Feb 1, 103(3) :890 6.
- 23- Fujimura K, *Helicobacter pylori infection and idiopathic thrombocytopenic purpura, Int. J. Haematol*, 2005 Feb, 81(2): 113 -8.