Helicobacter pylori eradication therapy in patients with immune thrombocytopenic purpura: a single-center experience

Nabila Faiek, Safinaz Hussein, Reham Badr

Department of Internal Medicine, Clinical Hematology Unit, Faculty of Medicine, Assiut University, Assiut, Egypt

Correspondence to Safinaz Hussein, MD, Clinical Hematology, Department of Internal Medicine, Assiut University, Assiut, 71516, Egypt.
Tel: +201007711092;
Fax: +201115758111;
e-mail: dr.safenazh@gmail.com

Received 15 October 2019
Revised 15 October 2019
Accepted 22 October 2019
Published 05 February 2020

Journal of Current Medical Research and Practice
2020, 5:32–35

Objective
The aim was to determine the frequency of *Helicobacter pylori* infection in patients with immune thrombocytopenic purpura (ITP) and to detect the effect of its eradication therapy on platelet count response in *H. pylori*-positive patients.

Patients and methods
H. pylori stool antigen enzyme immunoassay test was done for 54 patients with ITP. *H. pylori*-positive patients received standard triple therapy for 2 weeks. Platelet count response to *H. pylori* eradication therapy was evaluated 2 and 3 months after the treatment.

Results
H. pylori infection was positive in 38 (70.4%) patients with ITP. Eradication of *H. pylori* was achieved in 30 (78.9%) patients (responder group). There were statistically significant increases in platelet count (among the responder group) after *H. pylori* eradication therapy at 2 and 3 months ($P < 0.05$).

Conclusion
Eradication of *H. pylori* infection in patients with ITP is associated with significant increase in platelet counts.

Keywords:
eradication, *Helicobacter pylori*, immune thrombocytopenic purpura

J Curr Med Res Pract 5:32–35

2357-0121

Introduction

Helicobacter pylori is a gram-negative microaerophilic bacterium that colonizes the human stomach of more than 50% of the world population [1]. *H. pylori* is considered as the main agent of gastritis and peptic ulcer, and it has been connected with gastric cancer development [2]. *H. pylori* was considered as a class I carcinogen by the WHO [3].

H. pylori infection is associated with several extragastrointestinal diseases, such as neurological (stroke, Parkinson's disease, and Alzheimer's disease), obesity, cardiovascular (ischemic heart diseases), skin disorders, and hematological diseases [unexplained iron-deficiency anemia (IDA) and immune thrombocytopenic purpura (ITP)] [4].

ITP, an acquired immune condition, is caused by autoantibody-mediated platelet destruction. ITP is diagnosed by a low platelet count ($<100 \times 10^9$/l) after exclusion of secondary causes of thrombocytopenia [5,6], such as lymphoproliferative diseases, autoimmune disorders, drugs, and infectious diseases [7].

Helicobactor pylori is an important infectious agent and can cause persistence of thrombocytopenia [8]).

The association between *H. pylori* and ITP has been explained by several mechanisms. One of them, antibodies against *H. pylori*, against *cytotoxinassociated* gene A (*cagA*) protein have been cross-reacting with platelet antigens, leading to platelet clearance [9]. Variations in platelets response to eradication of *H. pylori* infection can be explained by increasing the frequency of CagA-positive strains of *H. pylori* in Japan than in North America [10].

Following colonization by *H. pylori*, modulation of host immunity leads to overproduction of autoreactive B cells (antiplatelets)[11] and increases the phagocytic capacity of monocytes together with low levels of the inhibitory Fc^{++} receptor IIB [12].

After the results of Gasbarrini *et al.*[13] which have shown improvement in platelet counts in *H. pylori*-positive patients with ITP after successful *H. pylori* eradication therapy, several studies from different geographical areas have evaluated this effect with highly variable results (0–100%) [14].

The aim of this study was to determine the frequency of *H. pylori* infection in patients with ITP and to detect

the effect of its eradication therapy on platelet count response in *H. pylori*-positive patients.

Patients and methods

This prospective, observational, study was done at Clinical Hematology Unit, Internal Medicine Department, Assiut University, during the period between May 2018 and May 2019. Written informed consent was taken from all participants, and this study was approved by the Ethical Committee of Assiut University.

It included 54 patients with persistent ITP (platelet count <100 and >30 × 10^9/l), in the absence of secondary causes of thrombocytopenia, and previous therapy with prednisone.

H. pylori infection was detected among studied group by *H. pylori* stool antigen enzyme immunoassay test.

H. pylori-positive patients were given triple eradication therapy for 2 weeks (amoxicillin 1 g twice daily; clarithromycin 500 mg twice daily; proton pump inhibitor 20 mg twice daily).

Assessment of response, eradication, or persistence of *H. pylori* was done after 8 weeks using the *H. pylori* stool antigen enzyme immunoassay method.

To evaluate platelet count response to *H. pylori* eradication therapy, platelet counting was performed at 2 and 3 months after the treatment.

Statistical analysis

Data entry and data analysis were done using SPSS version 19 (Statistical Package for the Social Sciences, IBM corp., Armonk, NY). Data were presented as number, percentage, mean, and SD. Independent samples *t*-test was used to compare quantitative variables between groups. Paired samples *t*-test was done to compare quantitative data between before and after treatment. *P* value considered statistically significant when less than 0.05.

Results

Between May 2018 and May 2019, 54 patients (34 female, 20 male), with ages ranging from 19 to 55 years (mean: 34.07 ± 8.95 years) were enrolled in the study. Overall, 38 (70.4%) were positive for *H. pylori* and 16 (29.6%) were negative (Fig. 1).

At the beginning of the study, platelets counts at the beginning of the study, platelet counts in *H. pylori*-positive patients ranged from 30.0 to 77.0 × 10^9/l, with a mean of 41.38 ± 12.68, and platelet counts in *H. pylori*-negative patients ranged from 31.0 to 77.0 × 10^9/l, with a mean of 40.44 ± 11.64. There were no statistically significant difference in baseline platelet count between *H. pylori*-positive and *H. pylori*-negative patients (*P* = 0.799) (Table 1).

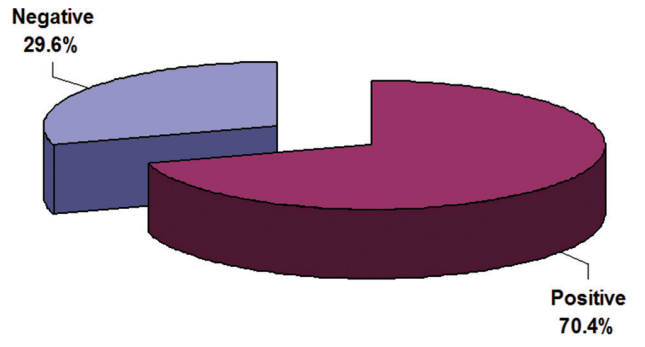
Overall, 30 (78.9%) of the 38 *H. pylori*-positive patients responded to eradication therapy (responder group) and eight (21.1%) did not respond (nonresponder group) (Fig. 2).

Assessment of platelet count in response to the eradication therapy

Among 30 patients (responder group) who responded to *H. pylori* eradication therapy, there were statistically significant increase in platelet count before and after the treatment at 2 and 3 months (*P* < 0.05).

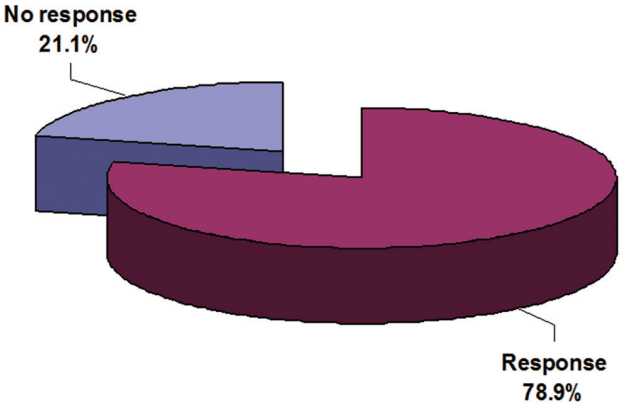
Platelet count before the therapy ranged from 30.0 to 77.0 × 10^9/l, with mean of 42.13 ± 12.98; at 2 months after treatment, ranged from 33.0 to 96.6 × 10^9/l, with mean of 63.87 ± 19.97; and at 3 months after treatment

Figure 1



Helicobacter *pylori* Infection among patients with immune thrombocytopenic purpura.

Figure 2



Percentage of response to *Helicobacter pylori* eradication therapy.

were, ranged 39.0 to 110.0 × 10^9/l, with a mean of 76.38 ± 22.11 (Table 2).

On the contrary, among eight patients (nonresponders) who did not respond to *H. pylori* eradication therapy, there were statistically significant decreases in platelet count before and after the treatment at 2 and 3 months ($P < 0.05$).

Platelet count before the therapy ranged from 30.0 to 60.0 × 10^9/l, with a mean of 38.56 ± 11.84, at 2 months after treatment ranged from 11.0 to 55.0 × 10^9/l, with a mean of 26.54 ± 16.53; and at 3 months after treatment ranged from 10.0 to 50.0 × 10^9/l, with a mean of 24.73 ± 15.57 (Table 3).

Table 1 The platelet count at the beginning of the study

Platelet count	*Helicobacter pylori* Ag in stool		*P*
	Positive (*n*=38) (70.4%)	Negative (*n*=16) (29.6%)	
Mean±SD	41.38±12.68	40.44±11.64	0.799
Range	30.0-77.0×10^9/l	31.0-77.0×10^9/l	

Table 2 Platelet count before and after treatment in responder group

Platelet count	Mean±SD	Range
Before treatment	42.13±12.98	30.0-77.0
8 weeks after treatment	63.87±19.97	33.0-96.6
12 weeks after treatment	76.38±22.11	39.0-110.0
P^a	<0.001*	
P^b	<0.001*	
P^c	<0.001*	

[a]Comparison between before treatment and 8 weeks after treatment. [b]Comparison between before treatment and 12 weeks after treatment. [c]Comparison between 8 weeks after treatment and 12 weeks after treatment. *Statistical significant difference (P<0.05).

Table 3 Platelet count before and after treatment in nonresponder group

Platelet count	Mean±SD	Range
Before treatment	38.56±11.84	30.0-60.0×10^9/l
8 weeks after treatment	26.54±16.53	11.0-55.0×10^9/l
12 weeks after treatment	24.73±15.57	10.0-50.0×10^9/l
P^a	0.001*	
P^b	0.000*	
P^c	0.025*	

[a]Comparison between before treatment and 8 weeks after treatment. [b]Comparison between before treatment and 12 weeks after treatment. [c]Comparison between 8 weeks after treatment and 12 weeks after treatment. *Statistical significant difference (P<0.05).

Discussion

Since its discovery in the 1980s, the relation between *H. pylori* infection and peptic ulcer and gastric cancer has been established by extensive research [15]. In the past few years, various studies have supported the link between *H. pylori* and ITP [16].

In our study, a high frequency of *H. pylori* infection in patients with ITP 38/54 (70.4%) was found. In concordance with our study, Ando *et al.*[17] and some Pakistani studies have also reported 83 and 63%, respectively, of *H Pylori* infection in patients with chronic ITP [18]. However, other studies reported a low frequency of *H. pylori* infection in France[19] and USA [20]. This might be related to the low prevalence of *H. pylori* in local population as the socioeconomic status affected the prevalence of *H. pylori* infection [21].

In our study, the *H. pylori* eradication rate was 78.9% (30/38). In agreement with our results, several studies reported eradication rates above 70% [22,23], except one study from Japan (42.9%)[24].

The link between *H. pylori* and ITP was first studied by Gasbarrini *et al.*[13] by evaluating platelet count improvement in 8 of 11 patients following eradication of *H. pylori*.

In this study, there were statistically significant increase in platelet count after *H. pylori* eradication therapy ($P < 0.001$). In this regard, multiple studies evaluated the effect of eradication therapy on platelet count [25–27]. In concordance with our results, Suzuki *et al.*[28] in Japan and Rostami *et al.*[29] showed a significantly increased platelet count in response to *H. pylori* eradication therapy.

In contrast with our results, the study by Jarque *et al.*[30] and other multicenter trials in Thailand [31] showed lower platelet response to the eradication therapy.

In our opinion, this variability in the results of studies are related to multiple factors that affect the interaction between host (age, duration of thrombocytopenia, and socioeconomic status) and infectious agent (prevalence and bacterial strains), and in particular, prevalence of infection, which varies in different regions and generations.

Conclusion

Regarding our results, *H. pylori* eradication therapy patients with in ITP showed significant improvement of platelet count in most patients. So, it is important to include a screening tests for *H. pylori* in patients with ITP and initiate treatment in the infected cases. However, Further studies are required to understand the mechanism underlying the response to eradication therapy with longer follow-up duration.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

1 Suerbaum S, Michetti P. *Helicobacter pylori* infection. N Engl J Med 2002; 347:1175–1186.

2 Parsonnet J, Friedman GD, Vandersteen DP, Chang Y, Vogelman JH, Orentreich N, *et al. Helicobacter pylori* infection and the risk of gastric carcinoma. N Engl J Med 1991; 325:1127–1131.

3 Roberto S, Drew P. *Helicobacter pylori* and chronic ITP. ASH Education Book 2008; 1:206–211.

4 Huck JT, Khean LG. Extragastrointestinal manifestations of *Helicobacter pylori* infection: Facts or myth? A critical review. J Dig Dis 2012; 13:342–349.

5 Lichtman MA, Beutler E, Seligsohn V, Kaushansky K, Kipps TO. *Williams Hematology*. 7th ed.: New York, NY: McGraw-Hill,2008:2231–2236

6 Liebman HA, Pullarkat V. Diagnosis and management of immune thrombocytopenia in the era of thrombopoietinmimetics. Hematol Am Soc Hematol Educ Program 2011; 2011:384–390.

7 Kühne T, Berchtold W, Michaels LA, Wu R, Donato H, Espina B, *et al.* Intercontinental Cooperative ITP Study Group. Newly diagnosed immune thrombocytopenia in children and adults: a comparative prospective observational registry of the Intercontinental Cooperative Immune Thrombocytopenia Study Group. Haematological. 2011; 96:1831–1837.

8 Cines DB, Liebman H, Stasi R. Pathobiology of secondary immune thrombocytopenia. Semin Hematol 2009; 46 (Suppl 2):S2–S14.

9 Franceschi F, Christodoulides N, Kroll MH, Genta RM. *Helicobacter pylori* and idiopathic thrombocytopenic purpura. Ann Intern Med 2004; 140:766–767.

10 Perez-Perez GI, Bhat N, Gaensbauer J, Fraser A, Taylor DN, Kuipers EJ, *et al.* Country-specific constancy by age in cagA+proportion of *Helicobacter pylori* infections. Int J Cancer 1997; 72:453–456.

11 Yamanishi S, Iizumi T, Watanabe E, Shimizu M, Kamiya S, Nagata K, *et al.* Implications for induction of autoimmunity via activation of B-1 cells by *Helicobacter pylori* urease. Infect Immun 2006; 74:248–256.

12 Asahi A, Nishimoto T, Okazaki Y, Suzuki H, Masaoka T, Kawakami Y, *et al. Helicobacter pylori* eradication shifts monocyte Fc gamma receptor balance toward inhibitory Fc gamma RIIB in immune thrombocytopenic purpura patients. J Clin Invest 2008; 118:2939–2949.

13 Gasbarrini A, Franceschi F, Tartaglione R, Landolfi R, Pola P, Gasbarrini G. Regression of autoimmune thrombocytopenia after eradication of *Helicobacter pylori*. Lancet 1998; 352:878.

14 Frydman GH, Davis N, Beck PL, Fox JG. *Helicobacter pylori* eradication in patients with immune thrombocytopenic purpura: a review and the role of biogeography. Helicobacter 2015; 20:239–251.

15 Kandulski A, Selgrad M, Malfertheiner P. *Helicobacter pylori* infection: a clinical overview. Dig Liver Dis 2008; 40:619–626.

16 Emilia G, Luppi M, Zucchini P, Morselli M, Potenza L, Forghieri F, *et al. Helicobacter pylori* infection and chronic immune thrombocytopenic purpura. Blood 2007; 12:3833–3841.

17 Ando K, Shimamoto T, Tauchi T, Ito Y, Kuriyama Y, Gotoh A, *et al.* Can eradication therapy for *Helicobacter pylori* really improve the thrombocytopenia in idiopathic thrombocytopenic purpura? Our experience and a literature review. Int J Hematol 2003; 77:239–244.

18 Shaikh KH, Ahmed S, Ayyub M, Anwar J. Association of *Helicobacter pylori* infection with idiopathic thrombocytopenic purpura. J Pak Med Assoc 2009; 59:660–663.

19 Michel M, Khellaf M, Desforges L, Lee K, Schaeffer A, Godeau B, *et al.* Autoimmune thrombocytopenic purpura and *Helicobacter pylori* infection. Arch Intern Med 2002; 162:1033–1036.

20 Michel M, Cooper N, Jean C, Frissora C, Bussel JB. Does *Helicobacter pylori* initiate or perpetuate immune thrombocytopenic purpura? Blood 2004; 103:890–896.

21 Webb PM, Knight T, Greaves S, Wilson A, Newell DG, Elder J, *et al.* Relation between infection with *Helicobacter pylori* and living conditions in childhood: evidence for person to person transmission in early life. Br Med J 1994; 308:750–753.

22 Alzira MCB, Rosangela AR, Ccero SMS, Francisco WSC, Orleancio GRA, Maria HSP, *et al.* Platelet count response to *Helicobacter pylori* eradication for idiopathic thrombocytopenic purpura in northeastern. Brazil Hematol Transfus Cell Ther 2018; 40:12–17.

23 Campuzano MG. Proof of an association between *Helicobacter pylori* and idiopathic thrombocytopenic purpura in Latin America. Helicobacter 2007; 12:265–273.

24 Stasi R, Sarpatwari A, Segal JB, Osborn J, Evangelista ML, Cooper N, *et al.* Effects of eradication of *Helicobacter pylori* infection in patients with immune thrombocytopenic purpura: a systematic review. Blood 2009; 113:1231–1240.

25 Emilia G, Longo G, Luppi M, Gandini G, Morselli M, Ferrara L, *et al. Helicobacter pylori* eradication can induce platelet recovery in idiopathic thrombocytopenic purpura. Blood 2001; 97:812–814.

26 Franchini M, Cruciani M, Mengoli C, Pizzolo G, Veneri D. Effect of *Helicobacter pylori* eradication on platelet count in idiopathic thrombocytopenic purpura: a systematic review and meta-analysis. J Antimicrob Chemother 2007; 60:237–246.

27 Stasi R, Rossi Z, Stipa E, Amadori S, Newland AC, Provan D. *Helicobacter pylori* eradication in the management of patients with idiopathic thrombocytopenic purpura. Am J Med 2005; 118:414–419.

28 Suzuki T, Matsushima M, Masui A, Watanabe K, Takagi A, Ogawa Y, *et al.* Effect of *Helicobacter pylori* eradication in patients with chronic idiopathic thrombocytopenic purpura-a randomized controlled trial. Am J Gastroenterol 2005; 100:1265–1270.

29 Rostami N, Keshtkar JM, Rahnavardi M, Keshtkar JM, Esfahani FS. Effect of eradication of *Helicobacter pylori* on platelet recovery in patients with chronic idiopathic thrombocytopenic purpura: a controlled trial. Am J Hematol 2008; 83:376–381.

30 Jarque I, Andreu R, Llopis I, De la Rubia J, Gomis F, Senent L, *et al.* Absence of platelet response after eradication of *Helicobacter pylori* infection in patients with chronic idiopathic thrombocytopenic purpura. Br J Haematol 2001; 115:1002–1003.

31 Treepongkaruna S, Sirachainan N, Kanjanapongkul S, *et al.* Absence of platelet recovery following *Helicobacter pylori* eradication in childhood chronic idiopathic thrombocytopenic purpura: a multi-center randomized controlled trial. Pediatr Blood Cancer 2009; 53:72–77.