



Thrombocytopenia Association with *H pylori* Infection

Jawad Khan First, Saira Nasr Malik*, Komal Iqbal, Ansa Rehman, Safia Rehma, Neelum Ahmad and Muhammad Imran Yahya

Department of Hematology/Gastroenterology, Pakistan

*Corresponding Author: Saira Nasr Malik, Department of Hematology/Gastroenterology, Pakistan.

Received: September 19, 2022

Published: February 22, 2022

© All rights are reserved by Saira Nasr Malik, et al.

Abstract

Objective: To observe the presence of thrombocytopenia associated with confirmed chronic *H pylori* infection.

Study Design: Descriptive cross-sectional study.

Place and Duration of Study: Khyber Teaching Hospital and Police and Services Hospital Peshawar.

Methodology: Those patients who were diagnosed with confirmed *H pylori* infection were included in this study. Total number of patients were 230. Both outpatients and admitted patients were included. The age range was between 20 to 70 years. Strict exclusion criteria were followed as thrombocytopenia can be caused by multiple other diseases like HCV, HBV, cirrhosis due to other causes like autoimmune hepatitis, primary biliary cholangitis, NASH, primary sclerosing cholangitis, certain drugs, other autoimmune diseases affecting multiple organs like SLE. Also those patients were included who didn't receive any *H pylori* eradication therapy in the past. *H pylori* was diagnosed by stool antigen which is the most sensitive test for *H pylori* diagnosis after confirming that patient was not on PPI and didn't take any antibiotics in the last 2 weeks. Platelet counts were measured by automated hematological analyzer followed by peripheral smear for confirmation. Data was analyzed by SPSS 17 and presented with frequencies and percentages, chi-square was applied and p value < 0.05 was considered as significant.

Results: Out of total 230 patients, 31 patients were found to have thrombocytopenia after following exclusion criteria. 19 out of 31 were above 50 years. Range of platelet counts were between 60,000 to 100,000, P value was 0.001. Number of male and female patients were same so gender difference was insignificant in this study.

Conclusion: Patients presenting with chronic *H pylori* infection did show thrombocytopenia especially in older patients above 50.

Keywords: *Helicobacter pylori*; Platelets; Proton Pump Inhibitors; Thrombocytopenia

Introduction

Helicobacter pylori infection is extremely common all around the world and is present in about 50% of the world population, usually resides in stomach mucosa. It is a gram-negative bacterium usually colonized in human stomach. It can cause multiple diseases in stomach and duodenum like erosive gastritis, peptic ulcer, atrophic gastritis, adenocarcinoma and MALToma [1,2]. It has been clas-

sified as class 1 carcinogen by WHO. Association of *H pylori* with thrombocytopenia has been described in different studies but with some conflicting results as well. Some studies have shown improvement of platelet counts with *H pylori* eradication while others have denied it [3-5]. More recently it has been shown that *H pylori* is also associated with ischemic heart diseases, chronic iron deficiency anemia and other autoimmune diseases like rheumatoid arthritis and

autoimmune thyroiditis [6-9]. Thrombocytopenia due to *H pylori* is called secondary thrombocytopenia [10-12]. Possible mechanism of lower platelets is unknown one possible mechanism is that *H pylori* has CAG A factor which makes and CAG antibodies [13]. These antibodies then work against platelets due to similarity between cag a and platelet [13]. One other possible mechanism is that IGG antibodies are produced then these antibodies and *H pylori* causes platelet activation and move selectin to platelet surface. These aggregation causes platelet aggregation and apoptosis. Then platelet to platelet and platelet granulocytes complexes are formed that cause's thrombocytopenia then [14,15]. While some other studies have shown opposite results in this regard so it is yet to be known what is the exact mechanism pf thrombocytopenia in *H pylori* infection.so more studies are needed in this regard as it will be a great success to treat it as *H pylori* eradication is not that difficult.

Methodology

This is descriptive cross sectional study which was performed in Khyber Teaching Hospital Hematology Department and Police and Services Hospital Gastroenterology Department after approval from concerned ethical committee. duration was from January 22 till July 22.total number of patients included were 230 with confidence interval 95%.patients were diagnosed with *H pylori* infection by performing stool antigen test.it is the most sensitive test ,non-invasive ,cheap and readily available. Blood samples were taken in EDTA tube and analyzed by automated hematology analyzers followed by peripheral smear to confirm it. Whose platelets counts were low below 100000, strict exclusion criteria was applied as thrombocytopenia can be caused by multiple diseases like viral hepatitis, cirrhosis due to other causes like autoimmune hepatitis, other autoimmune diseases involving multiple organs like SLE. Informed consent was taken and data was analyzed SPSS 17 and presented in frequencies and percentages. Chi square test was applied were needed and P valve of less than 0, 05 was considered significant.

Results

Total number if patients enrolled were 230, both, male and female who's stool test comes positive for *H pylori* infection. Age range was between 20 and 70 years. Of 230, 140 were males and 90 were females, thrombocytopenia was found in 31 patients, and patients above 50 years were significantly more involved, of 31 patients having *H pylori* infection 19 very between 50 to 70 years.

Platelets range was between 60000 to 100000, out if 31 patients, 17 were male and 14 were females so gender difference was insignificant. different disease duration groups either less than 6 months or more than 6 months has made no difference regarding positivity of *H pylori* (p < 0.05).

Table 1: Frequency of thrombocytopenia.

Present	31(13.4%)
Absent	199(86.5%)
Total	230

Table 2: Age based stratification of thrombocytopenia.

Age (years)	Thrombocytopenia Present N (%)	Thrombocytopenia Absent N (%)	total	P value
20 to 30	3(6.67)	42(94.3)	45	0.01
30 to 40	3(5.6)	50(95.4)	53	0.01
40 to 50	6(13.6)	38(87.4)	44	0.01
50 to 60	9(21.9))	32(78.1)	41	0.01
60 to 70	10(21)	37(79)	47	0.01

Discussion

Our study was one of very few study in Pakistan that has been done to show association of thrombocytopenia with *H pylori* infection.in our study, 230 patients were enrolled out of which 140 were males and 90 where females. Out of 230, 31(13.7%) patients were confirmed with thrombocytopenia having *H pylori* infection. Gender difference has no significance with thrombocytopenia in our study as 17 were males and 14 were females having confirmed *H pylori* infection. Out of 31 patients with confirmed infection, 19 patients were between 50 and 70 years that shows that thrombocytopenia significantly increases as age increases.

There are multiples studies done on association of thrombocytopenia with *H pylori*. Some studies did shows some association while other denies it. there are different studies done in patients which shows that platelet counts becomes normal after *H pylori* eradication.one study by umet in turkey shows the same results that platelet counts increases to normal after eradication of h *H pylori* [16]. Another two studies by Bilal and raza [17] from Pakistan and from Sudan by ali¹⁸ showed the same results which are con-

sistent with our study. There is another study from Pakistan that shows that platelet counts improves in 40 percent after eradication [19], in another study from Pakistan also shows consistently increased platelet numbers 3 to 6 months after eradication therapy [18]. In contrast there are also some studies done that fail to associate our findings. A study done in netherland [20] fails to demonstrate any association between platelets count and *H pylori*. These variable finding might be due to variation in age, outcome uncertainty, study protocol, inclusion and exclusion criteria ,different other tests used to diagnose *H pylori* infection, differences in distribution of factors regarding platelet count and study design. Also different strains of *H pylori* may be associated with more profound thrombocytopenia like cag A plus H strains [20] which is the predominant strain in the world. We also used EDTA bottles for blood sample collection which is sometime associated with change in morphology and platelets numbers [21], although our samples were usually tested with 2 hours so this effect is very unlikely in our study.

There are different hypotheses regarding thrombocytopenia association *H pylori* infection. Possible mechanism of lower platelets is still unknown one possible mechanism is that *H pylori* has CAG A factor which makes and CAG antibodies [9]. These antibodies then work against platelets due to similarity between CAG A and platelet [10,11]. One other possible mechanism is that IGG antibodies are produced then these antibodies and *H pylori* causes platelet activation and move selectin to platelet surface. These aggregation causes platelet aggregation and apoptosis. Then platelet to platelet or platelet granulocytes complexes are formed that causes thrombocytopenia then. So still there is a lot of work and further studies needed to clear the exact mechanism of thrombocytopenia with *H pylori* infection.

Conclusion

Patients those are infected with *H pylori* infection do have association with thrombocytopenia. It shows strong correlation with age as older patients have higher percentage of thrombocytopenia above 50 as compared to young patients.

Bibliography

1. Suerbaum S and Michetti P. "*Helicobacter pylori* infection". *The New England Journal of Medicine* 347 (2002): 1175-1186.
2. Logan RP and Walker MM. "ABC of the upper gastrointestinal tract: Epidemiology and diagnosis of *Helicobacter pylori* infection". *BMJ* 323 (2001): 920-922.
3. Liebman HA and Stasi R. "Secondary immune thrombocytopenic purpura". (2008): 206-211.
4. Fujimura K, *et al.* "Is eradication therapy useful as the first line of treatment in *Helicobacter pylori*-positive idiopathic thrombocytopenic purpura? Analysis of 207 eradicated chronic ITP cases in Japan". *International Journal of Hematology* 81 (2005): 162-168.
5. Soldinger E, *et al.* "Multi-resistant idiopathic thrombocytopenia successfully treated by eradication of *Helicobacter pylori*". *Digestive and Liver Disease* 33 (2001): 732.
6. Rinaldi CR, *et al.* "Complete remission in a case of severe multi-resistant idiopathic thrombocytopenic purpura after *Helicobacter pylori* eradication". *American Journal of Hematology* 83 (2008): 683-684.
7. de Barbosa AMC, *et al.* "Platelet count response to *Helicobacter pylori* eradication for idiopathic thrombocytopenic purpura in northeastern Brazil". *Hematology, Transfusion and Cell Therapy* 40.1 (2018): 12-17.
8. Rocha AM, *et al.* "Cytokine profile of patients with chronic immune thrombocytopenia affects platelet count recovery after *Helicobacter pylori* eradication". *British Journal of Hematology* 168.3 (2015): 421-428.
9. O'Neill CM, *et al.* "Ethnic and racial difference in *Helicobacter pylori* infection in patients with immune thro".
10. Shaikh KH, *et al.* "Association of *Helicobacter pylori* infection with idiopathic thrombocytopenic purpura". *Journal of Pakistan Medical Association* 59.10 (2009): 660.
11. Gasbarrini A, *et al.* "Regression of autoimmune thrombocytopenia after eradication of *Helicobacter pylori*". *Lancet* 352 (1998): 878.
12. Emilia G, *et al.* "*Helicobacter pylori* eradication can induce platelet recovery in idiopathic thrombocytopenic purpura". *Blood* 97 (2001): 812-814.

13. Takahashi T, *et al.* "Molecular mimicry by *Helicobacter pylori* CagA protein may be involved in the pathogenesis of H. pylori-associated chronic idiopathic thrombocytopenic purpura". *British Journal of Hematology* 124 (2004): 91-96.
14. Kodama M., *et al.* "Immune response to CagA protein is associated with improved platelet count after *Helicobacter pylori* eradication in patients with idiopathic thrombocytopenic purpura". *Helicobacter* 12 (2007): 36-42.
15. Hwang JJ, *et al.* "The effects of *Helicobacter pylori* eradication therapy for chronic idiopathic thrombocytopenic purpura". *Gut Liver* 10.3 (2016): 356-361.
16. Umit H and Umit EG. "*Helicobacter pylori* and mean platelet volume: a relation way before immune thrombocytopenia?" *European Review for Medical and Pharmacological Sciences* 19 (2015): 2818-2823.
17. Raza AB and Bilaal MH. "Comparison of platelet counts between *H. pylori* infected and non-infected individuals". *P J M H S* 10 (2016): 405-408.
18. Ali SA and Gaufri NEAM. "Platelet characterization in *Helicobacter pylori* patients". *OAlib* 04 (2017): 1-6.
19. Sheema K., *et al.* "Role of *Helicobacter pylori* eradication therapy on platelet recovery in chronic immune thrombocytopenic purpura. *Gastroenterol Res Pract* 2017 (2017): 9529752.
20. Samson AD., *et al.* "*Helicobacter pylori* infection is not correlated with subclinical thrombocytopenia: a cross-sectional study". *Platelets* 25 (2014): 221-223.
21. Sibanda N., *et al.* "*Helicobacter pylori* infection and the platelet count". *New Zealand Journal of Medical Laboratory Science* 70 (2016): 96-100.
22. Bath PM. "The routine measurement of platelet size using sodium citrate alone as the anticoagulant". *Thrombosis and Haemostasis* (1993).