

## Eradication of *H. Pylori* in HCV-Related Liver Cirrhosis Does Not Improve Thrombocytopenia

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### ABSTRACT

**Background:** In patients with chronic liver disease, thrombocytopenia is the most prevalent hematological abnormality. Immunological thrombocytopenic purpura (ITP) has been attributed to infection with *Helicobacter pylori* (*H. pylori*). In individuals with persistent ITP, eradication of *H. pylori* causes an increase in platelet counts and is therefore recommended. However, it is uncertain if eradication will influence platelet counts in HCV-related liver cirrhosis in the same way.

**Objective:** The purpose of this study was to determine the prevalence of active *Helicobacter pylori* in patients with HCV-related liver cirrhosis and to evaluate the effectiveness of *H. pylori* eradication on platelet count in HCV-related liver cirrhosis patients.

**Patients and Methods:** A total of 100 individuals were included in the study, and those who were tested positive for *H. pylori* were treated. *H. pylori* eradication was determined by detecting *H. pylori* antigen in the stool four weeks after the end of the therapy. Complete blood count, prothrombin time (PT), and liver function tests were all tested (ALT, total bilirubin, Alfa fetoprotein, serum creatinine and albumin). Platelet counts were assessed following the final eradication medication at 1, 3, and 6 months.

**Results:** *H. pylori* positivity was identified in 66 of the 100 individuals with HCV-related liver cirrhosis. In all of the patients, the oral treatment regimen was successful in eradicating *H. pylori*. All of the patients had a Child-Pugh classification of A. The platelet counts of patients with *H. pylori* eradication did not significantly increase following treatment.

**Conclusion:** In HCV-related liver cirrhosis, eradication of *H. pylori* does not ameliorate thrombocytopenia.

**Keywords:** HCV, *Helicobacter Pylori*, Thrombocytopenia.

### INTRODUCTION

The most prevalent hematological abnormality seen in patients with chronic liver disease (CLD) is thrombocytopenia <sup>(1)</sup>. It frequently hinders important procedures, in addition to being an indicator of severe disease and a dismal prognosis. Historically, hypersplenism has been associated with thrombocytopenia <sup>(2)</sup>. Understanding of thrombopoiesis has improved over the last decade, leading to a better understanding of thrombocytopenia in cirrhosis. Thrombocytopenia is caused by a number of causes, which can be grouped into three categories: decreased production, splenic sequestration, and accelerated destruction <sup>(3)</sup>.

Platelet generation is impaired in CLD patients due to low thrombopoietin levels and direct bone marrow suppression. Platelet production and maturation are both regulated by thrombopoietin, which is impaired in CLD. HCV can lead to bone marrow suppression. Splenic sequestration results from hypersplenism. Increased shear stress, enhanced fibrinolysis, bacterial translocation, and infection result in an increased rate of platelet aggregation, while autoimmune illness and higher antiplatelet immunoglobulin titers result in platelet immunologic destruction <sup>(3)</sup>.

The prevalence of thrombocytopenia varies between non-cirrhotic people and patients with liver cirrhosis, ranging from 6% to 70%. It's also been discovered that the severity of liver disease is correlated to the prevalence and severity of thrombocytopenia <sup>(4)</sup>.

*Helicobacter pylori* (*H. pylori*) infection has been linked to a wide range of nondigestive system disorders, in addition to its well-known function in gastroduodenal diseases. Immune thrombocytopenic purpura (ITP) is one of two extraintestinal diseases for which *H. pylori* infection diagnosis and eradication is recommended (the other being unexplained iron deficiency anemia), according to the Maastricht III consensus conference <sup>(5)</sup>.

In patients with persistent ITP, eradication of *H. pylori* increases platelet counts and is therefore advised <sup>(6)</sup>. Treatment of thrombocytopenia in chronic hepatitis C virus-infected patients is safe even if steroids are used. Treatment of thrombocytopenia in HCV-related liver cirrhosis is difficult, because before the FDA approved eltrombopag in 2008, and the European Medicines Agency (EMA) approved it in 2009, the only options for clinically relevant thrombocytopenia were platelet transfusion, splenic artery embolization, splenectomy, and transjugular intrahepatic portosystemic stent shunting. While these treatments were often helpful in raising platelet counts, the price and hazards were significant. Due to human leukocyte antigen alloimmunization, platelet transfusion, the most successful approach, can become refractory after several transfusions <sup>(7)</sup>.

Because eltrombopag administration has been linked to an increased risk of thromboembolic events in these patients, the goal of this study was to determine the prevalence of active *Helicobacter pylori* in patients

with HCV-related liver cirrhosis and to evaluate the effectiveness of *H. pylori* eradication on platelet count in these patients.

## PATIENTS AND METHODS

### Study population:

This study was conducted in Minya University Hospital between October 2021 and October 2021. Males and females over the age of 18 with liver cirrhosis caused by chronic hepatitis C infection were eligible to participate in the study. HCV infection as confirmed by positive HCV antibodies and HCV RNA. Patients with substantial fibrosis (F4) were identified by liver biopsy (Metavir F4 or Ishak 5) at any time prior to screening or by FibroScan (>14.6 kPa) within one year of baseline.

Receiving immunosuppressive therapy, co-infection with hepatitis B virus, and a history of *H. pylori* eradication therapy, history of proton pump inhibitors, H2 receptor antagonists, or antibiotics in the previous 4 weeks, thrombocytopenia related to autoimmune disorders, drugs, a family history consistent with inherited thrombocytopenia, and human immunodeficiency virus infection were all excluded from the study.

### Detection of *H. pylori* and eradication therapy:

The presence of *H. pylori* antigen in the stool of all individuals was tested. Qualitative detection of helicobacter stool antigen was done using a one-step lateral flow immunoassay (DRG International Inc., USA). The patient was diagnosed with *H. pylori* infection if the test result was positive. Patients with *H. pylori* were treated for two weeks with standard triple therapy (omeprazole 20 mg twice a day, amoxicillin 1,000 mg twice a day, and clarithromycin 500 mg twice a day).

The results of the eradication therapy were assessed by *H. pylori* antigen in stool test 4 weeks after eradication therapy. The patients who did not achieve *H. pylori* eradication with the first therapy were subjected to a second sequential therapy (20 mg b.i.d. esomeprazole, 1000 mg b.i.d. amoxicillin for 5 days, and followed by 20 mg b.i.d. esomeprazole, 250 mg b.i.d. levofloxacin, and 600 mg b.i.d. tinidazole for 7 days), provided they agreed.

### Laboratory investigations:

Platelet counts, prothrombin time (PT), liver function markers (AST, ALT, total bilirubin, and albumin), serum creatinine, and other basic laboratory variables of HCV-infected patients were routinely assessed. A platelet count of fewer than 150,000/l was considered thrombocytopenia.

### Abdominal Ultrasonography:

This was done using a Philips machine with a 3.5 MHz linear transducer (Denmark). The examination included comment on liver, spleen, portal vein diameter and kidneys.

### Assessment of platelet count:

The platelet counts were measured at 1, 3, and 6 months after the final eradication therapy.

### Ethical consent:

An approval of the study was obtained from Minya University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

### Statistical analysis

Statistical analysis was performed by using the Statistical Package for the Social Sciences (SPSS) software, version 16 (Inc, Chicago, III) on a personal computer. Quantitative data were presented as mean±standard deviation (SD) and were compared by independent sample t-test. Qualitative data were presented as frequency and percentage and were compared by  $\chi^2$  test. Differences were considered statistically significant when the P-value was less than 0.05.

## RESULTS

Prevalence of active helicobacter infection in the study patients is shown in figure 1.

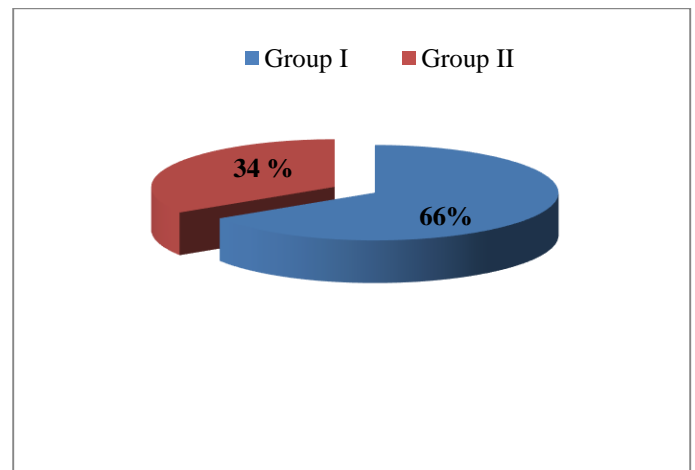


Figure (1): Prevalence of active Helicobacter infection in the study patients

### Patient characteristics:

The patients' baseline characteristics are shown in table 1. There were no statistical differences between the two groups.

**Table (1):** Demographic and laboratory characteristics of the study patients

	H. pylori-positive group n= 66	H. pylori-negative group n= 34	p-value
Age, years	53.7±4	55.2±4	>0.05
Gender			???
-Male	41/66	24/34	
-Female	15/66	10/34	
Baseline platelets, ×10 <sup>3</sup> /μL	78.1±18.33	77.3±17.64	>0.05
WBC, ×10 <sup>3</sup> /μL	5.6±1.31	5.7±1.32	>0.05
Hb, g/dL	11.5±1.4	11.6±2.1	>0.05
INR	1.8 ± 0.8	1.7±0.8	>0.05
Albumin (g/dl)	2.9 ± 0.45	2.9±0.51	1
T. bilirubin (mg/dl)	1.8 ± 0.51	1.8±0.43	1
ALT (IU/L)	61 ± 4	67±1	>0.05
AFP (ug/l)	16.6 ± 3	18.1±3.81	>0.05
Creatinine (mg/dl)	1.1 ± 0.3	1.3±0.4	>0.05
RNA, ×10 <sup>3</sup> /IU	738±54.2	803±64.32	>0.05

Data are presented as mean±SD or number (%). WBC, white blood cell; Hb, hemoglobin;

**Changes in the platelet counts in patients with Helicobacter pylori eradication:**

The platelet counts of the 66 individuals with H. pylori eradication tended to rise after therapy; however the difference between before and after treatment was not statistically significant.

**Comparison of platelet counts between the H. pylori-positive group and the H. pylori-negative group:**

The platelet count at the start of the study did not differ substantially between the two groups (H. pylori-positive group and H. pylori-negative group). Platelet count was measured at 1, 2 and 6 months follow up. A comparison between the eradicated group and the H. pylori-negative group revealed no statistical differences (Table 2).

**Table (2):** Comparison of platelet counts at 1, 2 and 6 months follow-up between the H. pylori-positive group and the H. pylori-negative group

Platelets, ×10 <sup>3</sup> /μL	H. pylori-positive group (After eradication) n= 66	H. pylori-negative group n= 34	p-value
Baseline	78.1±18.21	77.3±18.11	>0.05
At 1 months	81±18.21	77±15.32	>0.05
At 2 months	81±16.52	81±16.21	1
At 6 months	81±17.23	79±13.54	>0.05

Data are presented as mean ±SD.

**DISCUSSION**

Patients with liver cirrhosis have a 70% chance of developing thrombocytopenia. It's also been discovered that the severity of liver illness is linked to the prevalence and severity of thrombocytopenia (4).

Helicobacter pylori (H. pylori) infection is associated with a low platelet count in patients with immune thrombocytopenic purpura (ITP) (9). While H. pylori eradication is a well-established therapy for increasing platelet counts in ITP patients, it is unknown whether eradication will have the same effect in CLD patients.

Many studies have been conducted on the effect of H. pylori eradication on platelet count in HCV patients; Takashima *et al.* (10) conducted a study on individuals with both liver cirrhosis and chronic hepatitis C. (80 percent VS 20 percent ). Hanafy *et al.* study's (11) did not specify which types of patients were included or how they determined the stage of fibrosis. To our knowledge, this is the first study based on either a liver biopsy or a fibroscan that focused solely on HCV-related liver fibrosis.

The purpose of this study was to determine the prevalence of active helicobacter pylori in patients with HCV-related liver cirrhosis and to evaluate the effectiveness of H. pylori eradication on platelet count in HCV-related liver cirrhosis patients alone.

The prevalence of H. pylori was 66 percent in this study. The high prevalence of H. pylori in patients with chronic HCV could be explained by associated T cell dysfunction (10).

All patients with proved active H. pylori infection were given standard triple therapy; patients who did not achieve H. pylori eradication with the first therapy were subjected to a second sequential therapy.

Platelet counts in H. pylori-eradicated group did not differ significantly before and after treatment. Also, a comparison between the eradicated group and the H. pylori-negative group revealed no statistical differences in platelet count within 6 month follow up. Our findings differ from those of Takashima *et al.* (10) and Hanafy *et al.* (11), because these studies included individuals with both chronic hepatitis C and liver cirrhosis.

Reduced production, splenic sequestration, and accelerated destruction are all factors in thrombocytopenia in HCV-related liver cirrhosis (11). As a result, treating thrombocytopenia in these patients is difficult (7).

**CONCLUSION**

In HCV-related liver cirrhosis, eradication of H. pylori does not ameliorate thrombocytopenia.

**Conflict of interest:** The authors declare no conflict of interest.

**Sources of funding:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Author contribution:** Authors contributed equally in the study.

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