

*Research Article***“Helicobacter pylori infection in HCV related liver cirrhotic patients; prevalence and association with upper gastrointestinal bleeding.”****Ahmed A. Mohamed, Mahmoud R. Mohamed, Hanan M. Kamel and Wessam E. Naguib Aziz**

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Abstract

Introduction: Hepatitis C virus (HCV) infection is one of the most serious global health problems. The incidence of HCV infection is increasing, with over 185 million people infected worldwide. **Aim of the work:** The aim of the study was to evaluate the serological rate of Helicobacter pylori (H. pylori) infection in HCV related liver cirrhotic patients, determine its role in upper gastrointestinal bleeding whether variceal or not and demonstrate its role in progression of liver disease. **Subjects And Methods:** The current study is a Prospective cross sectional study conducted on: **Group I:** 100 patients of post hepatitis C liver cirrhosis presented with upper gastrointestinal bleeding. Age ranges between 40 to 83 years old; 56 male and 44 females, recruited from internal medicine department at Minia university hospital from march 2018 to december 2018. **Results:** Demographic data of the patients: The present study was conducted in Minia University hospital at endoscopic unit from march 2018 to December 2018. On 100 patients of post hepatitis C liver cirrhosis. Age ranges between 40 to 83 years old; (56 male and 44 females) Also, this study included 50 patients (28 male and 22 females) healthy subjects as a control group. **Summary:** The aim of the study was to evaluate the serological rate of Helicobacter pylori (H. pylori) infection in HCV related liver cirrhotic patients ,determine its role in upper gastrointestinal bleeding whether variceal or not, and demonastrate its role in progression of liver disease.

Keywords: Hepatitis C virus, Helicobacter pylori, Age**Introduction**

Hepatitis C virus (HCV) infection is one of the most serious global health problems. The incidence of HCV infection is increasing, with over 185 million people infected worldwide⁽¹⁾. Moreover, approximately 370000 HCV-infected individuals die of liver-related causes each year, HCV-related liver disease can progress in an insidious manner over several decades⁽²⁾. The advanced forms of the disease are liver cirrhosis (LC) and hepatocellular carcinoma (HCC). Approximately 20%-30% of subjects chronically infected with HCV are estimated to develop LC 15-25 years later. A recent systematic review found that, in HCV-infected patients with compensated LC, 2.8%,11.7% develop hepatic decompensation, 1.8%-8.3% develop HCC, and 2.7%-6.7% die or undergo liver transplantation each year⁽³⁾.

Upper G.I bleed is a common and serious complication of liver cirrhosis which is

associated with high mortality. The mortality in cirrhotic patients during the first episode of upper G.I bleed is found to be 20% despite the advancements in management. Hence it is one of the important objectives in current gastroenterology practice to reduce the incidence of upper G.I bleed in cirrhotic patients. There are many factors implemented in upper G.I bleeding in cirrhotic patients such as esophageal varices, gastric varices, portal hypertensive gastropathy, gastric ulcer and duodenal ulcer, gastritis and duodenitis.⁽⁴⁾

Most of cirrhotic patients are immunodeficient and all host systems are comprimised.e.g the acute phase response, macrophage, neutrophils, and lymphocyte function⁽⁵⁾, so these patients are more prone to infections (e.g H.Pylori) and it is seen that there is association between infections and the cirrhosis related complications such as hepatic encephalopathy, variceal bleeding, peptic ulcer and portal hypertensive gastropathy⁽⁶⁾.

H. pylori infection is a common infection in our population. Prevalence is thought to be as high as 80% in developing countries and 30-50% in developed countries⁽⁷⁾. *H. pylori* is a gram-negative bacterium that colonizes the gastrointestinal tract and is an established cause of peptic ulcer. It also causes gastritis, duodenitis, oesophagitis that contributes to upper gastrointestinal bleeding. It is seen that these complications are markedly decreased after the eradication of *H. pylori* infection in normal population. However, in cirrhotic patients it is still unclear, whether they should be treated for *H. pylori* infection or not.⁽⁸⁾

Liver cirrhosis and *H. Pylori* infection are two common diseases in our population and reducing the incidence of complications in cirrhotic subjects is an important step in current gastroenterology practice, early diagnosis and effective prevention of complications and its contributing factors will help in reducing mortality and morbidity in these patients, so considering the role of *H. Pylori* infection in cirrhosis related complications⁽⁹⁾

Esophageogastric variceal bleeding still remains a major problem in patients with liver cirrhosis and portal hypertension, however, the role of *H. Pylori* infection is not well understood in variceal bleeding, It is thought to be due to mucosal damage caused by *H. Pylori* infection⁽⁹⁾

The term portal hypertensive gastropathy (PHG) refers to the mosaic pattern, congestion and edema of the mucosa with or without red spots seen endoscopically in patients with portal hypertension⁽¹⁰⁾. It is a common endoscopic finding in patients with portal hypertension and is the cause of one out of five bleeding episodes in these patients The pathophysiology of this condition is not clearly understood. It has been suggested that PHG is a dynamic condition, which may not only worsen from mild to severe, but also improve and even disappears completely⁽¹¹⁾. This finding suggests that although portal hypertension remains the trigger for the development of PHG, other factors should be considered in the progression of this condition (e.g *H. Pylori*)⁽¹²⁾

Peptic ulcer disease (PUD) is a break in the lining of the stomach, first part of the small intestine or occasionally the lower

esophagus⁽¹³⁾. A major causative factor (60% of gastric and up to 50–75% of duodenal ulcers) is chronic inflammation due to *Helicobacter pylori* that colonizes the antral mucosa. (The immune system is unable to clear the infection, despite the appearance of antibodies. Thus, the bacterium can cause a chronic active gastritis (type B gastritis). Gastrin stimulates the production of gastric acid by parietal cells. In *H. pylori* colonization responses to increased gastrin, the increase in acid can contribute to the erosion of the mucosa and therefore ulcer formation⁽¹⁴⁾.

Aim of the work

The aim of the study was to evaluate the serological rate of *Helicobacter pylori* (*H. pylori*) infection in HCV related liver cirrhotic patients, determine its role in upper gastrointestinal bleeding whether variceal or not and demonstrate its role in progression of liver disease.

Subjects And Methods

The current study is a **Prospective cross sectional** study conducted on:-

Group I: 100 patients of post hepatitis C liver cirrhosis presented with upper gastrointestinal bleeding. Age ranges between 40 to 83 years old; 56 male and 44 females, recruited from internal medicine department at Minia university hospital from march 2018 to december 2018.

Liver cirrhosis diagnosis is based upon; detailed history, general examination based on liver disease stigmata (jaundice, spidernevia, foeter hepaticus, gynecomastia, caput medusa, splenomegaly, ascitis, peripheral oedema...etc), investigations which include (CBC, liver function, viral markers, abdominal ultrasound). Severity of liver disease assessed through Child-Pugh score system.

All patients underwent upper endoscopy to detect cause of upper GIT bleeding. *Helicobacter pylori* infection will be diagnosed based on level of *H. Pylori* specific IgG measure using a commercially available enzyme linked immunosorbent assay kit

Group II: included 50 healthy subjects (28male and 22 females) as a control group matched for age and sex.

All patients will be subjected to following ;

Full history: age ,smoking status, alcohol consumption, presence of liver disease and its duration, presence of chronic renal disease, history of current medication or previous medication for H.Pylori. Clinical examination: liver disease stigmata Investigations

- Laboratory (CBC, liver function, renal function, viral markers ,measure of H–Pylori specific Ig G)
- Radiology abdominal ultrasound
- Upper endoscopy : to detect source of upper GIT bleeding

Exclusion criteria

1. Patients who had received specific pylori eradication therapy in the past.
2. Patients who had previous history of endoscopic evidence of old acid peptic disease.
3. Patients with advanced renal impairment
4. Non hepatitis C positive cirrhotic patients
5. Non co-operative patients who refuse to participate in study.

Clinical Study

Whole patient group was classified according to severity of liver disease based on score into to **Child-Turcotte-Pugh (CTP) Scoring system** three groups:

***Group A:** child score 5-6

***Group B:** child score 7-9

***Group C:** child score 10-15

Calculation:

The CTP scoring system incorporates five parameters: serum bilirubin, serum albumin, prothrombin time, ascites, and grade of encephalopathy. Based on the sum of the points from these five parameters, the patient is categorized into one of three CTP classes: A, B, or C.

Results**Demographic data of the patients:**

The present study was conducted in Minia University hospital at endoscopic unit from march 2018 to December 2018. On 100 patients of post hepatitis C liver cirrhosis. Age ranges between 40 to 83 years old; (56 male and 44 females) Also, this study included 50 patients (28 male and 22 females) healthy subjects as a control group.

After applying the exclusion criteria, a total of 150 participants (84 men) were enrolled in the study. Of these, 82 were HP seropositive, and 68 were HP were seronegative.

Table (1): Comparison between groups according to demographic characteristics

Demographic characteristics	Cases N = 100	Controls N = 50	P – value
Age			
Range	40 - 80	41 - 85	0.145
Mean ± SD	58.44 ± 8.8	60.9 ± 11.9	NS
Sex			
Male	56 (56%)	28 (56%)	1
Female	44 (44%)	22 (44%)	NS
Smoking			
Yes	36 (36%)	16 (32%)	0.627
No	64 (64%)	34 (68%)	NS
DM			
Yes	36 (36%)	24 (48%)	0.157
No	64 (64%)	26 (52%)	NS
HTN			
Yes	42 (42%)	26 (52%)	0.246
No	58 (58%)	24 (48%)	NS

No significant statistical difference between patient and control in sociodemographic data as regard terms of : age, sex, smoking , diabetes and hypertension.

Table (2): Comparison between groups according to some laboratory data

Laboratory data	Cases N = 100	Controls N = 50	P – value
Platelet			
Range	87 - 135	162 - 380	0.001*
Mean ± SD	109.4 ± 11.1	243.1 ± 69.4	
Median	107	222	
Creatinine			
Range	0.5 – 1.3	0.5 – 1.3	0.090 NS
Mean ± SD	0.97 ± 0.24	0.90 ± 0.24	
Median	1	0.9	
ALT			
Range	32 - 83	10 - 26	0.001*
Mean ± SD	52.6 ± 11.9	18 ± 4.7	
Median	50.5	18	
AST			
Range	38 - 90	9 - 24	0.001*
Mean ± SD	61.2 ± 12.7	15.7 ± 3.9	
Median	59	16	
Albumin			
> 3.5	34 (34%)	50 (100%)	0.001*
2.8 – 3.5	52 (52%)	0 (0%)	
< 2.8	14 (14%)	0 (0%)	
Bilirubin			
< 2	52 (52%)	50 (100%)	0.001*
2 – 3	44 (44%)	0 (0%)	
> 3	4 (4%)	0 (0%)	

There is Significant statistical difference in between patient and control as regard terms: Platelet count and serum albumin which are significantly higher in control with (p value of 0.001). ALT, AST and bilirubin are significantly higher in cirrhotic patients with (p value of 0.001).

Conclusion, Recommendations & Limitations

Helicobacter pylori is a microaerophile, a Gram-negative bacillus, resistant to the activity of gastric juice. The bacteria may take the vegetative form (spiral shape) or sporulation form. *H. pylori* lives mainly on the surface of epithelial cells of mucous membranes of the prepyloric part of the stomach. The cilia present on the bacteria allow it to move into intercellular spaces and adhere to the surface of cell. Infection with these bacteria is one of the most common in the world

Chronic hepatitis C constitutes a major public health problem, affecting around 200 million

people worldwide and predisposes to liver fibrosis and end-stage liver complications.

Upper gastrointestinal tract hemorrhages are one of the main complications of liver cirrhosis. the most common lesions responsible for gastrointestinal hemorrhage in patients with cirrhosis are thought to be esophageal and cardiac varices, peptic ulcers, and congestive gastropathy.

Liver cirrhosis and *H. Pylori* infection are two common diseases in our population and reducing the incidence of complications in cirrhotic subjects is an important step in current gastroenterology practice, early diagnosis and effective prevention of complications and its contributing factors will help in reducing mortality and morbidity in these patients, so considering the role of *H. Pylori* infection in cirrhosis related complications.

Our study, demonstrates an association between *H. pylori* infection and cirrhosis in patients with

hepatitis C virus, it also confirms the role of *Helicobacter pylori* as risk factor for peptic ulcer in patients with liver cirrhosis.

Our study also reveals a correlation between H Pylori and severity of liver cirrhosis

This study has some limitations:-

First, this was a single-center, cross-sectional study. Therefore, we could not detect a causal relationship, and the generalization of our results should be with caution.

Second, the sample size used in the present study was smaller than that of the studies that showed significant relationship between liver cirrhosis and HP infection and also smaller than the studies that revealed the relationship between upper gastroduodenal bleeding and HP infection

Third, diagnosis of H.pylori infection based on the levels of HP-specific IgG measured using a commercially available enzyme-linked immunosorbent assay kit which is inexpensive and noninvasive. However, serologic tests require validation at the local level, which is impractical in routine practice. In addition, concerns over its accuracy have limited its use. Guidelines recommend that serologic testing should not be used in low prevalence populations as the low accuracy of serology would result in inappropriate treatment in significant numbers of patients.

Fourth, need to follow up patients after eradication of H.pylori infection.

We recommend

First, larger cohort studies and comparative studies & follow up the cases to better assess.

Second, further research is needed to reveal the precise mechanism involved in the relationship between liver cirrhosis and HP, also Additional in-depth studies are required to confirm the actual involvement of *H.pylori* in the progression of liver fibrosis

Third, presence of *H. pylori* infection should be searched for in all patients with chronic hepatitis and liver cirrhosis as well as its cure would at least reduce the risk of bleeding due to peptic ulcer.

Fourth, further research is needed to reveal the role of HP as a risk factor for development of peptic ulcer in patients with liver cirrhosis as well as its protective role in both PHG and variceal bleeding

Fifth, further research is needed to reveal role of HP as risk factor for thrombocytopenia and hepatic encephalopathy in liver cirrhotic patients.

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