

The prognostic value of Helicobacter Pylori infection in HCV cirrhotic patients

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Abstract: Background: Helicobacter pylori colonizes the stomach of more than half of the world's population and the infection continues to play a key role in the pathogenesis of a number of gastroduodenal diseases. Chronic hepatitis due to hepatitis C virus is the principal cause of end stage liver disease worldwide. Bacterial co-infection with *H.pylori* in hepatitis C is another important factor in the development of cirrhosis and its decompensation. Aim of work: Is to study the sero-prevalence of *H.pylori* in HCV cirrhotic patients, and the role of *H.pylori* infection and its role of deterioration of the liver functions in such patients. Patients and Methods: Forty patients had been enrolled in the study, patients divided into four groups: ten patients with liver cirrhosis without ascites (group A), ten patients with liver cirrhosis with ascites (group B), ten patients with liver cirrhosis and hepatic encephalopathy (group C), ten healthy volunteers (group D), all groups are subjected to full history taking, clinical examination, Laboratory investigation, Abdominal ultrasonography, Viral markers (HCV Ab, HBs Ag) by enzyme linked immunosorbent assay (ELISA), Detection of *H. pylori* serum IgM antibodies (One step *H.pylori* test device). Results: patients with HCV antibodies have higher percentage of positive cases of serum *H.pylori* IgM antibodies than in HCV antibodies negative control, patients with Child-pugh C have higher number of positive cases of serum *H.pylori* IgM antibodies than patients with Child-pugh A and B. Higher percentage of positive cases of serum *H.pylori* IgM antibodies in ascitic cases than non ascitic cases. higher percentage of positive cases of *H.pylori* IgM antibodies among patients with hepatic encephalopathy than patients without hepatic encephalopathy. Higher number and percentage of positive cases of serum *H.pylori* IgM antibodies in group C in comparison to in group A and B and also in all cirrhotic patients in comparison to control group. In conclusion: our study presented that *H.pylori* infection is considered as a negative predictive factor for HCV cirrhotic patients, further work is needed on a larger scale of patients for more confirmation of these results.

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Introduction

Helicobacter pylori colonizes the stomach of more than half of the world's population and the infection continues to play a key role in the pathogenesis of a number of gastroduodenal diseases and their complications. Also Helicobacter pylori infection is involved in some extragastrointestinal diseases [1].

Chronic hepatitis due to hepatitis C virus is the principal cause of end stage liver disease worldwide [2]. Progression of the disease is variable and is governed by multiple factors [2]. Though there are many factors known, still many remains to be identified. Incidence rate of progression of the disease, its decompensation and risk of carcinoma vary worldwide [3].

Bacterial co-infection with *H.pylori* in hepatitis C is another important factor in the development of cirrhosis and its decompensation [3]. One-third of patients with liver cirrhosis suffers from acute peptic ulcer, a disease strongly correlated with *H. pylori* infection [4].

Helicobacter, a well recognized cause of duodenal and gastric carcinoma, induces a persistent

infection and is thought to be a type-I carcinogen because of its role in the development of gastric carcinoma and gastric mucosal associated lymphoid tissue lymphoma [5]. *Helicobacter* has been detected in bile and gallbladder tissue from patients with chronic cholecystitis [6-7], and in liver tissue from patient with HCC [8-9]. So, it is possible that *H. pylori* may also be risk factor for liver cancer [2].

However, at the present stage of knowledge, the participation of *Helicobacter* bacteria in the pathology of the liver and the bile tract in humans has not been univocally documented. However, apparent are the premises so as to go on performing the examination under discussion since the said participation cannot be excluded. If the more direct evidence of the etiological role of *Helicobacter* in the pathology of liver was available, it would create the chances for the more effective treatment of patients than the case has been so far [10].

Aim of work:

Is to study the sero-prevalence of *H.pylori* in HCV cirrhotic patients, and the role of *H.pylori* infection and its role of deterioration of the liver functions in such patients.

Patients and methods:

Forty patients had been enrolled in the study, they were recruited from internal medicine inpatient and outpatient departments in Ain Shams University Hospital. The patients divided into four groups: ten patients with liver cirrhosis without ascites (group A), ten patients with liver cirrhosis with ascites (group B), ten patients with liver cirrhosis and hepatic encephalopathy (group C), ten healthy volunteers (group D). After obtaining a written informed consent in accordance with the recommendations of the institutional ethics committee all groups are subjected to full history taking, clinical examination (body mass index, hepatomegally,...etc), Laboratory investigation (AST, ALT, ALP, Gamma GT, Albumin, Total protein, Prothrombin time, afetoprotien, CBC), Abdominal ultrasonography (cirrhotic changes, ascites, focal lesions....etc), Viral markers(HCV Ab, HBs Ag) by enzyme linked immunosorbent assay (ELISA), Detection of *H. pylori* serum IgM antibodies (One step *H.pylori* test device)[11] (Alem et al.,2002):

Serum specimen is allowed to reach room temperature (15-30°C) prior to testing.

Bring the pouch to room temperature before opening it

Remove the test device from the sealed pouch and use it as soon as possible.

Place the test device on a clean and level surface. Hold the dropper vertically and transfer 3 drops of serum to the specimen well (s) of the test device, and start the timer. Avoid trapping air bubbles in the specimen well (s).

Wait for the colored line (s) to appear. Read results at 10 minutes. Do not interpret the result after 20 minutes.

Interpretation of Results

Positive: Two distinct colored lines appear.

Negative: One coloured line appears in the control line region.

Invalid: Control line fail to appear. Review the procedure and repeat with a new test.

Statistical analysis:

Statistical presentation and analysis of the present study was conducted, using the mean, standard error, Chi-square, Linear and Analysis of variance [ANOVA] tests by SPSS V17.

Results:

Table (1) shows that patients with HCV antibodies have higher percentage of positive cases of serum *H.pylori* IgM antibodies than in HCV antibodies negative control, however, it is non-significant.

Table (1): the relation between *H. pylori* and HCV infection.

HCV Antibody		<i>H.pylori</i> IgM		
		Positive	Negative	Total
Negative	N	5	5	10
	%	50.00	50.00	25.00
positive	N	19	11	30
	%	63.33	36.33	75.00
Total	N	24	16	40
	%	60.00	40.00	100.00
Chi square	X ²	0.139		
	p- value	0.709		

According to Child- pugh classification, table (2) shows that patients with Child-pugh C have higher number of positive cases of serum *H.pylori* IgM antibodies than patients with Child-pugh A and B. The difference is statistically non- significant.

Table (2): Shows the relation between *H. pylori* and child pugh classification.

HCV Antibody		<i>H.pylori</i> IgM		
		Positive	Negative	total
Class A	N	6	4	10
	%	60.00	40.00	100.00
Class B	N	6	4	10
	%	60.00	40.00	100.00
Class C	N	7	3	10
	%	70.00	30.00	100.00
Chi square	X ²	0.287		
	p- value	0.866		

Table (3) shows that higher percentage of positive cases of seum *H.pylori* IgM antibodies in ascitic cases than non ascitic cases, statistically non-significant difference.

Table (3): Shows the relation between *H.pylori* and ascites in groups A, B and C

Ascites		<i>H.pylori</i> IgM		
		Positive	Negative	total
+	N	11	6	17
	%	64.70	35.30	56.67
-	N	7	6	13
	%	53.85	46.15	43.33
Chi square	X ²	0.051		
	p- value	0.821		

Table (4) shows higher percentage of positive cases of *H.pylori* IgM antibodies among patients with hepatic encephalopathy than patients without hepatic encephalopathy, non significant.

Table(4): Shows the relation between *H. pylori* and hepatic encephalopathy

Hepatic encephalopathy		<i>H.pylori</i>		
		Positive	Negative	total
+	N	12	8	20
	%	60.00	40.00	100.00
-	N	7	3	10
	%	70.00	30.00	100.00
Chi square	X ²	0.018		
	p- value	0.893		

Table (5) shows a higher number and percentage of positive cases of serum *H.pylori* IgM antibodies in group C in comparison to in group A and B and also in all cirrhotic patients in comparison to control group.

Table (5): Shows distribution of positive and negative cases of serum *H.pylori* IgM antibodies in all studied groups (A, B, C and D).

HCV Antibody		<i>H.pylori</i> IgM		
		Positive	Negative	Total
Group A	N	6	4	10
	%	60.00	40.00	100.00
Group B	N	6	4	10
	%	60.00	40.00	100.00
Group C	N	7	3	10
	%	70.00	30.00	100.00
Group D	N	5	5	10
	%	50.00	50.00	100.00
total	N	24	16	40
	%	60.00	40.00	100.00
Chi square	X ²	0.833		
	p- value	0.841		

Discussion:

Since the discovery of presence of *Helicobacter* species DNA in liver material from patients with liver disease, several studies were conducted to determine the role of these bacteria in the evolution of hepatic lesions to cirrhosis and HCC.

Determinants of this evolution are not yet fully understood, including those occurring in HCV positive patients[12].

The present study shows a higher sero-prevalence of anti *H.pylori* IgM antibodies among HCV positive patients than control group (negative HCV antibodies).

These results in agreement with the results conducted by Ponzetto *et al.*, 2003[3] who stated that the seroprevalance of *Helicobacter pylori* antibodies among cirrhotic patients was 79,5% while the seroprevalance of *H.Pylori* antibodies was 47% of controls.

Although statistically insignificant, our study revealed the higher number of cirrhotic patients with ascites harbor *H.pylori* IgM (65.7% ascitic patients with positive *H.pylori* and 35.3% are non-ascitic patients with negative *H.pylori*), Ehab Abdel-atti *et al.*, 2011[13] stated that there is no significant difference between *H.pylori* infected and non- infected cirrhotic patients regarding the presence of ascites (29% in *H. pylori* positive, and 28% in *H.pylori* negative patients).

In the present study revealed the percentage of *H.pylori* infection increases among patients with hepatic encephalopathy (60% of patients with hepatic encephalopathy infected with *H.pylori*). this in agreement with Agrawal *A et al.*, (2011)[14] who found that *H. pylori* infection was more common in patients with liver cirrhosis and MHE (minimal hepatic encephalopathy) than in those with liver cirrhosis but no MHE. Patients with evidence of MHE on psychometric tests had significantly higher ammonia levels than those without MHE. Moreover, the blood ammonia levels in patients with MHE and *H.pylori* infection were significantly higher than in those with MHE but no *H. pylori* infection. These finding support a possible role for infection with these bacteria in the causation of MHE. Also, Suto *H et al.*, (2001)[15] stated that *H.pylori* infection induces hyperammonaemia in gerbils with liver cirrhosis.

Ammonia has been one of the most widely studied etiological factors in the pathogenesis of hepatic encephalopathy[16]. About half of the ammonia produced in the intestine is synthesized by luminal bacteria, with the remainder coming from dietary protein and glutamine. *H. pylori* are rich in urease and can produce ammonia from urea. Previous studies have shown that ammonia levels in gastric juice were higher in patients with liver cirrhosis who had *H. pylori* infection than in those who did not have such infection [17].

The study also showed that the more worsen the liver status the more percent of *H.pylori* infection. Cirrhotic patients with Child Pugh classification grade C with 70% incidence of *H.pylori* infection, however it statistically insignificant.

Ponzetto *et al*[3],proposed that *H. pylori* is implicated in the pathogenesis and progression of cirrhosis, particularly in HCV-infected individuals.

Helicobacters are strong inducers of the inflammatory cascade; infection with *H. pylori* could lead to the accumulation of extraordinary number of lymphocytes and polymorphonuclear cells in the infected tissue [18]. It has been shown that several

Helicobacter species could also secrete a liver-specific toxin that causes hepatocyte necrosis in cell culture and might therefore be involved in damaging liver parenchyma *in vivo* [19] Kim *et al.*,(2008) [20] noted that the prevalence of *H.pylori* infection was related inversely to Child-Pugh classification.

In conclusion: our study presented that *H.pylori* infection is considered as a negative predictive factor for HCV cirrhotic patients, further work is needed on a larger scale of patients for more confirmation of these results

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