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H.PYLORI INFECTION;
FREQUENCY IN CIRRHOTIC PATIENTS WITH UPPER G.I BLEED.

1. Assistant Professor, Medical Unit III, Ward-7, Jinnah Postgraduate Medical Centre Karachi
2. Professor and Head of Department Medical Unit III, Ward-7, Jinnah Postgraduate Medical Centre Karachi
3. Associate Professor, Medical Unit III, Ward-7, Jinnah Postgraduate Medical Centre Karachi
4. Postgraduate Trainee, Medical Unit III, Ward-7, Jinnah Postgraduate Medical Centre Karachi
5. Postgraduate Trainee, Medical Unit III, Ward-7, Jinnah Postgraduate Medical Centre Karachi
6. Postgraduate Trainee, Department of Nephrology, Jinnah Postgraduate Medical Centre Karachi
7. Assistant Professor Medicine United Medical College Karachi.

Correspondence Address:
Dr. Zeeshan Ali
Senior Registrar, Medical Unit III, Ward-7,
Jinnah Postgraduate Medical Centre Karachi
dr.zeeshan.j@gmail.com

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Dr. Shabnam Naveed[1], Prof. Syed Masroor Ahmed[2], Dr. Zeeshan Ali[3], Romana Awan[4], Humaira Zakir[5], Lubna Ghazi[6], Ayesha Nageen[7]

ABSTRACT… Objectives: To study the frequency of H. pylori infection and its association as a cause of upper G.I bleeding in cirrhosis. **Study Design:** Cross Sectional Study. **Setting:** Medical Unit III, JPMC Karachi. **Period:** January 2014 to December 2014. **Methods:** 100 patients of established cirrhosis with upper G.I bleeding were included in this study. These patients were evaluated for viral etiology of cirrhosis. An upper G.I Endoscopy was performed in all patients and antral biopsies were taken. Rapid urease test was performed on biopsy specimen for detection of H.pylori infection. **Results:** Out of 100 patients 71 were males and 29 were females with age ranging between 14 to 70 years. Among them 53% patients turned out to be positive for H.Pylori infection with rapid urease test. H.pylori infection was detected in 68.7% of HBsAg positive patients and in 50% of Anti HCV positive patients. On upper G.I endoscopy 96 patients had PHG and among them 50 (52%) were positive for H.pylori. 4 patients did not have PHG and among them 3 (75%) were positive for H.pylori. Gastric ulcer was present in 17 patients and amongst them H.pylori was detected in 10 (58.8%) cases. Duodenal ulcer was present in 5 patients and among them 2 (40%) were positive for H.pylori. Gastritis was present in 17 cases among them 11 (64%) were positive for H.pylori. Duodenitis was present in 13 cases among them 11 (84.6%) patients were positive for H.pylori infection. **Conclusion:** The frequency of H.pylori infection was low in cirrhotic patients. No association was seen in H.pylori infection and causes of upper G.I bleeding in cirrhosis including PHG, gastric ulcer and duodenal ulcer.

Key words: H.Pylori, Gastrointestinal bleed, Rapid ureaes test, Gastritis

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INTRODUCTION

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. Though esophageal varices are the commonest cause of upper G.I bleed in cirrhotic patients, it is a common observation that the frequency of peptic ulcer is also high in these patients. It is still debated that whether this increased risk is due to the cirrhosis of liver per se or due to some other factors i.e. H.pylori infection. Due to immunodeficient state infections are common in cirrhotic patients and the relationship between H.pylori infection and cirrhosis related complications have been reported in many studies.[1,2,3] The clinical data suggest that PHG is the commonest gastric mucosal injury in cirrhotic patients and it also leads to upper G.I bleed in these patients. Several studies have been carried out in past to assess the role of H.pylori as an aggravating factor for PHG.[5]

H.pylori infection is a common infection in our population and is strongly associated with peptic ulcer disease. Prevalence is thought to be as high as 80% in developing countries and 30-50% in

developed countries.[4] 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 recurrence of both duodenal and gastric ulcers is 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.[6]

Considering the high prevalence of H.pylori infection in our society and the grave consequences of upper G.I bleed in cirrhotic patients, this study was carried out to assess the frequency of H.pylori infection in cirrhotic patients and to evaluate its role in the contribution of upper G.I bleeding.

MATERIAL AND METHODS

This study was carried out in Medical Unit III, JPMC from January 2014 to December 2014.100 patients were included in this study. They were above the age of 13 years, of either gender and with established cirrhosis. These patients were admitted with the complaint of upper G.I bleed. Patients who had received specific H. pylori eradication therapy in the past or had previous history of endoscopic evidence of acid peptic disease were excluded from the study.

A detailed physical examination was carried out and standard emergency treatment was initiated. An informed consent was taken when patients recovered from acute emergency condition. The upper G.I Endoscopies were performed, endoscopic findings were recorded and antral biopsies were taken for histologic evaluation. The samples were tested for the evidence of H. pylori by using CLO test and results were documented on a standard proforma. CLO kits were provided by PMRC JPMC Karachi on subsidized rates for which the investigators paid.

CLO test

This test is based upon the strong urease activity of H. pylori. The medium contains the substrate for the enzyme urease, a Ph indicator, phenol red and a buffering agent. The medium is stored in refrigerator at temperature 2 – 8^{O}C. The medium is warmed to room temperature prior to the test to make sure that its color is yellow. The biopsy specimen is inserted in the bottom of the tube by removing the cap. Then cap is replaced tightly and tube is incubated at room temperature.

The urea present in the specimen is hydrolyzed to ammonia by the urease of H. pylori. It raises the PH of specimen and the colour changes from yellow to pink. Color change is observed every half hour to maximum of 4 hours. In absence of organism there is no change in color.

STATISTICAL ANALYSIS

The data collected for 100 patients were converted into database on SPSS version 10.0 for windows. To compute the frequency of helicobacter pylori positive cases, the proportion of patients with helicobacter pylori was calculated among total patients of cirrhosis and was presented by its percentages. Complications with Helicobacter pylori were ranked and presented by their percentages. For scale measurements such as age and laboratory investigations mean $\pm$ S.D value was computed and nominal measurements such as gender and causes of upper G.I bleed along with the percentages were computed. Variables in this study included age, sex, viral etiology of cirrhosis, PHG, Gastric / Duodenal ulcer, gastritis and Duodenitis .p-value <0.05 was taken as significant.

RESULT

Out of 100 patients 71 were males and 29 were females. Ages of the patients ranged from 14 to 70 years. Among them 53% patients were found out to be positive for H.pylori infection on the basis of rapid urease test (Table-I). It was found that frequency of H.pylori was higher in males 42 (59%) than in females 11 (38%).On the basis of age, 21 patients were below the age of 40 years among them 11(52.4%) patients were positive for H.pylori.66 patients were between the age of 40-60 years and among them 33 (50%) were positive for H.pylori.13 patients were above the age of 60

years and among them 9(69.2%) were positive for H.pylori infection.

CLO – rapid urease test for H. pylori	Number / Percent
Negative	47
Positive	53
Total	**100**

Table-I: Frequency of H. pylori in cirrhotic patients with upper G.I bleed

Portal Hypertensive Gastropathy (PHG)	Total number of patients	H. pylori positive cases (%)
Present	96	50 (52)
Absent	4	3 (75)

Table-II. Relationship between H.pylori infection with portal hypertensive gastropathy (PHG):

Complications	Helicobacter Pylori		P-value
	Positive (n=49)	Negative (n=51)	
Gastric Ulcer	8 (16.3%)	9 (17.6%)	0.860
Duodenal Ulcer	2 (4.1%)	3 (5.9%)	0.680
Gastritis	11 (22.4%)	6 (11.8%)	0.155
Duodenitis	11 (22.4%)	2 (3.9%)	0.006 *

Table-III. Relationship between H.pylori infection and it's complications.
** p<0.05 statistically significant*

Considering viral etiology of cirrhosis, it was found that the frequency of H.pylori was higher among hepatitis B infected patients (68.7%) than hepatitis C infected patients (50%).

On upper G.I endoscopy 96 patients had PHG and among them 50 (52%) were positive for H.pylori. 4 patients were without PHG and among them 3 (75%) were positive for H.pylori. Out of 100 patients, Gastric ulcer was present in 17 cases and among them H.pylori was detected in 10 (58.8%) cases. Duodenal ulcer was present in 5 patients and among them 2 (40%) were positive for H.pylori. Gastritis was present in 17 cases among them 11 (64%) were positive for H.pylori. Duodenitis was present in 13 cases among them 11 (84.6%) patients were positive for H.pylori infection.

DISCUSSION

Liver cirrhosis is a major burden on the health system and upper G.I bleed is one of the most frequent and life threatening complication of cirrhosis.[6] On upper G.I endoscopy of these patients, commonly observed lesions are bleeding esophageal or gastric varices, portal hypertensive gastropathy and peptic ulcers. There are many studies conducted that showed relationship between H.pylori and cirrhosis related complications including upper G.I bleeding.[1,2,3] Reports on frequency of H.pylori and its association with the causes of upper G.I bleeding in cirrhosis are conflicting. The patients with cirrhosis are immunodeficient and are more prone to infections and H.pylori is a common infection in our population.

The results of this study showed that the frequency of H.pylori in cirrhotic patients was only 53% that was quite low compared to the general population.[7] The data regarding frequency of H. pylori in cirrhotic patients is conflicting ranging from 43.4% to 77.6%.[1,2,4,8,9,10,11] These contrasting results from different studies might have arisen due to the selection of different types of the tests for the diagnosis of H. pylori infection. The studies in different socioeconomic groups may be the cause for this difference. Our result was consisted with the study of Lo GH et al. A meta-analysis of 21 European articles also supports our result.[8,11]

In this study it is observed that increase in age, male gender and hepatitis B infection, are associated with higher risk to develop H.pylori infection in the cirrhotic patients.[4] It is a known fact that H.pylori infection is acquired predominately in childhood. Adult cirrhotic patients have alterations in immune response that also increase the chance to acquire the infection. The gender-based difference is noticed in many other studies[3] that may be explained on the basis that the males have a higher gastric acid secretory capacity as compared with the women of the similar age and height. The males might have cigarette smoking as an additional risk factor. Many studies showed

relationship of H. pylori infection with viral etiology of liver cirrhosis.[2,8,12] Our results showed that H. pylori infection was more common in hepatitis B infected patients than those who were infected with hepatitis C infection. A local study reported by Sethar GH et al. was conducted in Pakistan that also showed higher seroprevalence of H. pylori infection among HBV positive patients than the HCV positive patients.[2]

Association between H.pylori infection and peptic ulcer disease in cirrhotic patients is still a controversial topic. It is suggested by many studies that the prevalence of peptic ulcer is higher in cirrhotic patients as compare to general population. Peptic ulcer itself is the second most common cause of bleeding in cirrhotic patients. H.pylori infection has a well-known universal role in the etiology of peptic ulcer disease. It is observed that gastritis duo to H.pylori is a major factor that leads to development of peptic ulcer disease; especially the duodenal ulcer. In this study the higher frequencies of gastric ulcer, gastritis and duodenitis were observed, while the frequency of duodenal ulcer was low. When these patients were tested for H.pylori infection we did not find significant difference in percentages of H.pylori infection positive and H.pylori negative cases except in the cases of Duodenitis.[7] In cases with Duodenitis we found the highest percentage of H.pylori infection. Duodenitis is considered as an initial step in pathology of duodenal ulcer formation. The increased frequency of H.pylori in cases of duodenitis is suggestive that it has some role in the pathogenesis of duodenal ulcer disease in cirrhotic patients. We did not find significant relationship between H.pylori infection and gastric ulcer and gastritis in cirrhotic patients. The results of study have shown that H.pylori is not the risk factor for peptic ulcer disease in the patients with liver cirrhosis.

PHG is also an important cause of upper G.I bleeding in patients of liver cirrhosis.[10] In this study we found inverse relationship between the presence of PHG and the H.pylori infection. The infection rate was highest in the patients without PHG. It has suggested that PHG does not provide a favorable environment for the colonization of H.pylori.

CONCLUSION

In this study the frequency of H.pylori infection was low in cirrhotic patients. Male gender, advanced age and HBsAg seropositivity were the important risk factors for Helicobacter pylori infection. No significant correlation was seen in H.pylori infection and the causes of upper G.I bleed in cirrhosis i.e. PHG, gastric ulcer and duodenal ulcer.

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Unknown

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Dr. Shabnam Naveed	Conceptualized the study and contributed in manuscript writing.	
2	Prof. Syed Masroor Ahmed	Organized & Supervised the study	
3	Dr. Zeeshan Ali	Worked on results and critically reviewed the manuscript.	
4	Romana Awan	Contributed in manuscript writing	
5	Humaira Zakir	Contributed in acquisition, analysis and interpretation of data.	
6	Lubna Ghazi	Review literature and contributed in acquisition, analysis and interpretation of data	
7	Ayesha Nageen	Reviewed literature and contributed in discussion	