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Helicobacter Pylori have positive association in developing peptic ulcers in patients with chronic liver diseases-an experience from Eastern India.

Dr. Kalidas Biswas[1], Dr.Arup Chakraborty[2]
1Associate Professor, Medical gastroenterology, Medical College, Kolkata,
2Assistant Professor, Community Medicine Medical College, Kolkata

Corresponding Author: Dr. Kalidas Biswas

Abstract : *H .pylori infection is commonly associated with Peptic Ulcer Disease (PUD). Role of H. pylori in the development of peptic ulcers with Chronic Liver Disease (CLD) is still not clear. The aim of this study is to find out the prevalence of H. pylori infection among the CLD patients and to identify its relationship in development of peptic ulcer among CLD patients. 60 patients were enrolled from Out Patient Department (OPD) of Medical Gastroenterology in a tertiary care hospital, Kolkata. All patients underwent blood tests to evaluate the liver chemistry. To establish the etiology of chronic liver disease, various biochemical parameters were examined. To find presence of peptic ulcer upper gastrointestinal endoscopy, ultrasonography was conducted. For H.pylori infection, Rapid Urease Test (RUT) and serum IgG for H. pylori were conducted. Active peptic ulcers were detected in 15% among study subjects. Among them, 55.5% tested positive for H. pylori where as among non peptic ulcer subjects, 3.9% tested positive for Helicobacter pylori and the difference was statistically significant (p<.001).The prevalence of peptic ulcer according to UGI endoscope was 15% among patients with CLD, found higher than previous studies. The higher statistically significant prevalence of H. pylori infection among CLD patients with peptic ulcer than without peptic ulcer was also supported by different previous studies done in different settings. This study revealed that there was more prevalence of H. pylori infection in peptic ulcers cases among the CLD patients which is statistically significant.*

Keywords - *Peptic ulcer, chronic liver disease, H. pylori*

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I. INTRODUCTION

Helicobacter *pylori* (H. *pylori*) infection is more common in third world countries. It is known to cause gastritis, peptic ulceration, gastric carcinoma and mucosa associated lymphoid tissue tumor (MALT). Chronic liver disease (CLD) is also prevalent in our country. Spectrums of changes in esophageal, gastric, intestinal, colonic and rectal mucosa are noted in this disease. It is well known that peptic ulcer disease (PUD) is encountered more frequently in patients with CLD (1). H .*pylori* infection is commonly associated with PUD. Role of H. *pylori* in the development of this alteration in terms of prevalence of infection in patients with CLD is still not clear (2-4). Portal hypertensive gastropathy (PHG) defines a pathological endoscopic finding characterized by the presence of alterations of the gastric mucosa found in patients of CLD. Mild form of PHG characterized by diffuse congestion, petechiae of gastric mucosa (scarlatina type rash) and by the presence of typical hyperemic and edematous polygonal areas, delimited by a thin snake skin reticulation.In severe form PHG, together with such changes, mucosal erosion, red spots or a diffused hemorrhagic gastropathy noted. The reason for the occurrence of PHG only in a subset of patients with CLD is not known (5). H .*pylori* is established as an important etiologic factor for chronic gastritis and peptic ulcer disease (6). Eradication of H .*pylori* gastric infection markedly decreases peptic ulcer recurrence in patients (7). It also decreases the risk of recurrence in patients with bleeding peptic ulcer (8). Factors related to peptic ulcer development and the causes of increased prevalence of the disease in patients with CLD are poorly understood. Patients with CLD are frequently subjected to a number of disorders of the gastric mucosa. Peptic lesions in the gastro duodenal mucosa have been found to be more frequent in CLD than control. Many studies have suggested a role for H .*pylori* infection in the pathogenesis of peptic ulcer disease in cirrhotic patients, but several studies have found no relationship (9-13). A previous report shows that H .*pylori* infection increases the risk of peptic ulcer in cirrhotic patients by 2.7 folds(16). However, subsequent study does not confirm this finding (13). Studies have shown that the prognosis of CLD due to hepatitis B may benefit from early eradication of H.*pylori* (17). An increased anti -H.*pylor*i IgG levels in cirrhosis was reported (18). Another study of 153 cirrhotic patients,

anti-H.*pylori* IgG levels had been significantly higher than controls (76.5% vs 41.8%) and was not influenced by etiology of cirrhosis, Child class, portal hypertensive gastropathy or gender (19). Moreover, there is a debate concerning the relationship between H.*pylori* infection and the etiology or severity of cirrhosis. The aim of this study was to find out the prevalence of H. *pylori* infection among the CLD patients and to identify any significant relationship with different causes of CLD, if any.

II. MATERIALS AND METHODS

After the patients were enrolled, detailed history and clinical examination were recorded on the proforma maintained for the purpose. The procedures to be employed were explained to the patients and after obtaining informed written consent, they were included in the study. All patients underwent blood tests to evaluate the liver chemistry (liver function tests, prothrombin time) and to establish the etiology of chronic liver disease (viral markers, anti-nuclear factor, serum ceruloplasmin, anti- smooth muscle antibody, anti-mitochondrial antibody) were done. To find esophageal varices and features of portal hypertension (upper gastrointestinal endoscopy, ultrasonography with or without doppler study), liver biopsy (as and when necessary), for Helicobacter *pylori* infection, Rapid Urease Test (RUT) and serum IgG for H. *pylori* were conducted. All patients underwent investigations to rule out intrinsic cardio-pulmonary disease (chest x-ray, echocaiography). Routine investigations (complete hemogram, urea, creatinine, random sugar, electrolytes) were done for each subject.

An auto-analyzer (ERBA XL 300, Tranasia) was used for liver function test (LFT). Prothrombin time was estimated with fully automated coagulation analyzer (Sysmex CA 550/560). ERBA LISA SEN HBsAg kit (Tranasia Biomedicals Ltd.) for HBsAg and ELISCAN HCV kit (Microwell ELISA, RFCL Ltd.) along with Micro ELISA plate washer and reader (TECAN, Australia) for anti-HCV was used. USG of whole abdomen was done with 3.5 to 5 Hz probe in *hp* Agilant Machine (Netherlands). For upper GI endoscopy, Fujinon EG 265 WR flexible Scope was used. Fully automated five part differential cell counter (Sysmex SS 300) was used for complete blood count. Serum urea was estimated by Urease Berthelot method (Caltek Diagnostic Pvt. Ltd., India). For serum creatinine, alkaline picrate Jaffe's reaction method was used. Rapid Urease Tests was done by (urease enzyme test to detect H. *pylori* observe color change. HP test kit Mfg. and Mkt. by Allied Marketing Corporation, Kolkata).

Sixty patients with CLD between May 2008 and April 2009 were enrolled in the study. A diagnosis of CLD was made on the basis of clinical findings, abdominal sonogram, endoscopic procedure done by the fellows in gastroenterology besides laboratory parameters and or liver biopsy. At the time of inclusion a questionnaire was completed and patient's serum was obtained and stored at – 70 degree *C* until analyzed. All the enrolled patients underwent upper gastrointestinal endoscopy with biopsy taken from the antrum and gastric body. Endoscopy was performed by using Biopsy specimens from the antrum and gastric body were used to identify H. *pylori* using RUT (Rapid urease test) to detect H.*pylori* by observing color change .This study was approved by the Institutional Ethics Committee and informed consent for endoscopy was obtained from all the patients. At the end of study, the data were compiled, tabulated and analyzed with appropriate statistical tests using medical statistical software (EP_Iinfo version 3.5). All results of continuous variables were expressed as mean ± SD. Results were considered statistically significant at p-value<0.05.

III. RESULTS

The mean age of study subjects was 42.6 years (range was 18 to 72 years). Decade-wise analysis of the age of the patients showed that the largest number of patients belonged to the 4th Decade (30%). The lowest incidence was in the 1st and 2nd decade (1.6%). (Figure1). Out of the 60 patients, 49 patients (81.67%) were males and 11 (18.33%) were females. (Figure2)

Table 1 shows the distribution of the participants as per the history obtained. Majority of the patients (52/60 , i.e. 86.67 %) had GI bleeding during presentation. When patients were enquired about alcohol intake 36 patients (60%) had positive history and remaining 24 patients (40%) had negative history.

In this study etiologically most of the patient had alcoholic cirrhosis (63.3%), least prevalent were Wilson and Chronic autoimmune liver disease (both 3.33 %). (Figure 3)

The findings on clinical examination are presented in table 2. 61.67% patients (37/60) had reduce liver span which was an important positive findings for CLD patients, 19/60 patients (31.67 %) had enlarge liver span and remaining 04/60 patients (6.66 %) were normal liver size. 40 patients presented with ascites. Splenomegaly, an important feature of portal hypertension was found in 95% of the patients.

Varices represents the presence of portal hypertension and here maximum patients with esophageal varices was in grade 3 (23.33 %) and 18.33 % of patients did not have any varices. Active peptic ulcer was detected in 9 patients by means endoscope. Among the 9 patients with peptic ulcer, 5(55.5%) tested positive for Helicobacter *pylori* (RUT positive) where as among non peptic ulcer 51 subjects,

2(3.9%) tested positive for Helicobacter *pylori*. The difference in the prevalence of H. *pylori* infection among CLD patients with peptic ulcer (55.5%) and without peptic ulcer (3.9%) found statistically significant (p=<.001). Peptic ulcer was detected in antrum, fundus and duodenal area. (Table.5)

Among the observed biochemical parameters of the patients, mean bilirubin, albumin, globulin levels were 2.7 (SD .053), 3.2 (SD .358), 4.09 (SD .449) mg/dl respectively. (Table 4) Normal Albumin Globulin (A/G) ration was found reversed in all the CLD patients.

Most of the patient with chronic liver disease was alcoholic (63.33%). Next common was chronic liver disease due to hepatitis B. But there was no statistical significance of prevalence of H. *pylori* infection in different etiology of CLD (p value = 0.8512). (Table 5)

IV. DISCUSSION

There are many factors that could have induced peptic ulcer. As regards gastric acidity in CLD, there was marked hypoacidity over the entire circadian cycle which was evaluated from 24-hour gastric acidity. Nevertheless, the actual mechanism of hypoacidity was poorly understood. The degree of acidity and modulators of gastric mucosal response needed further investigation to confirm its association with the pathogenesis of peptic ulcer in CLD. The most important etiology of peptic ulcer was H. *pylori* infection. But the etiology of CLD was not related to the prevalence of Helicobacter pylori infection and on the other hand Helicobacter *pylori* infection was not related to sex, age and etiology of CLD.

Peptic ulcer was a major problem in patients with CLD and the risk of the peptic ulcer was greater in these patients. In a study by Chen et al. had shown that *H .pylori* infection increased the risk of peptic ulcer in cirrhotic patients by 2.7 folds (16). In coherence with these observations the inference was similar to that of a study (17) that the prognosis of CLD due to hepatitis B may benefit from early eradication of *H. pylori*. Prospective endoscopic surveys (18) have shown the incidence of peptic ulcer of 4.3% in patients with CLD which was between 20 and 47 times greater than in the general population.

It had been demonstrated that patients with CLD were frequently subjected to a number of disorders of the gastric mucosa which had been observed more often in CLD patients than in controls. Helicobacter *pylori* infection was also an important factor in the pathogenesis of peptic ulcer but H. *pylori* eradication did not protect all cirrhotics from ulcer recurrence.

The prevalence of peptic ulcer according to UGI endoscope was 15% among patients with CLD, which was more than previous studies. Our results demonstrate that, H. *pylori* infection was an independent factor associated with CLD and peptic ulcer. The difference in the prevalence of H. *pylori* infection between CLD patients with peptic ulcer (55.5%) and without peptic ulcer (3.9%) found statistically significant (p=<.001). Etiological distribution of H. *pylori* in patients with CLD did not reveal any statistical significance (p value= 0.8512).

V. CONCLUSION

In conclusion**,** the difference in the prevalence of H. *pylori* infection between CLD patients with peptic ulcer (55.5%) and without peptic ulcer (3.9%) found statistically significant (p=<.001). So, the etiology of the peptic ulcer in patients with CLD could be related to Helicobacter *pylori* infection was confirmed by the study. Larger multicentric studies might require for further exploration of the effect of *H. pylori* on causation of PUD in CLD patients.

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Figures And Tables

Figure 1. Distribution of the participants as per age groups. (n=60)

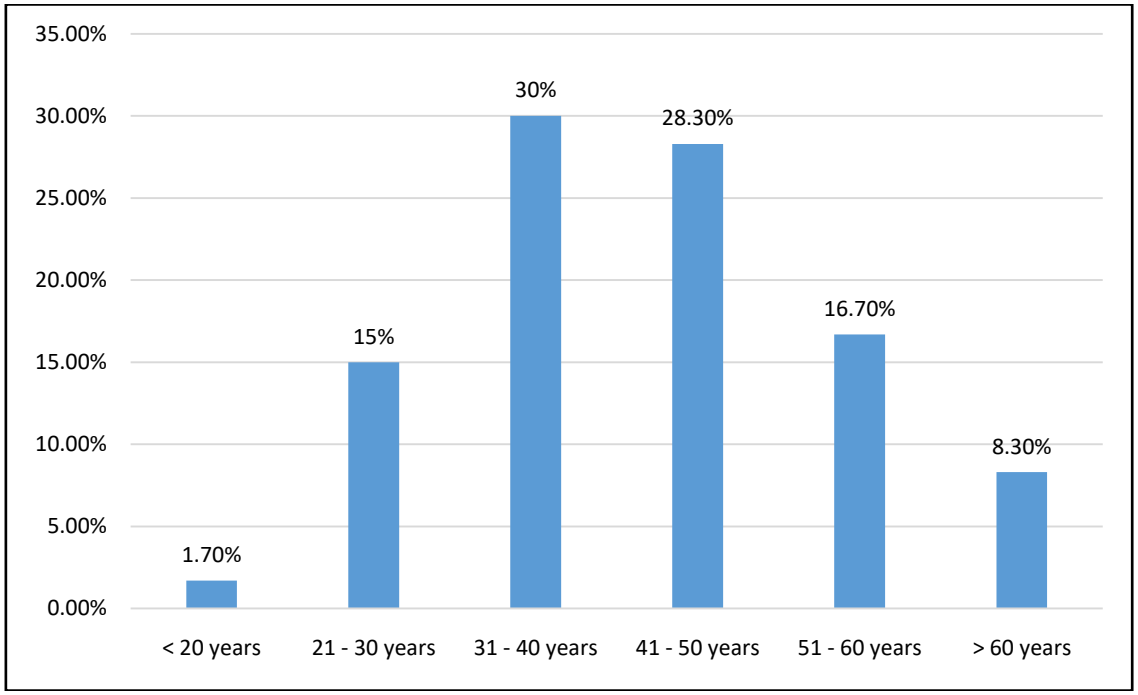

Figure 2. Distribution of the study participants as per gender. (n=60)

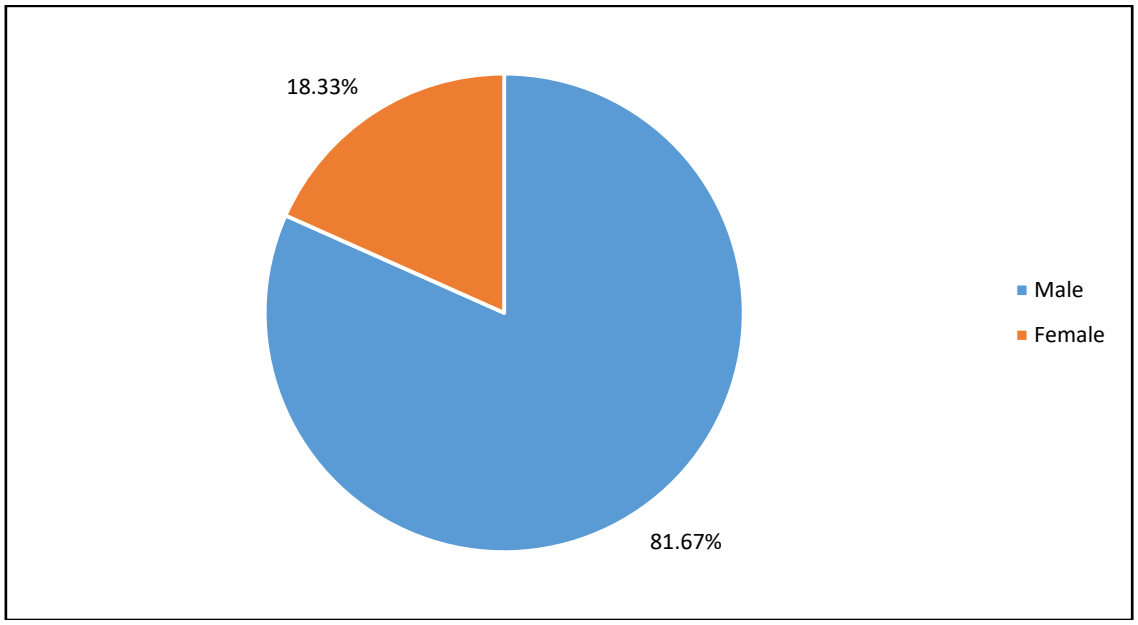

Figure 3. Distribution of the participants according to etiology of CLD. (n=60)

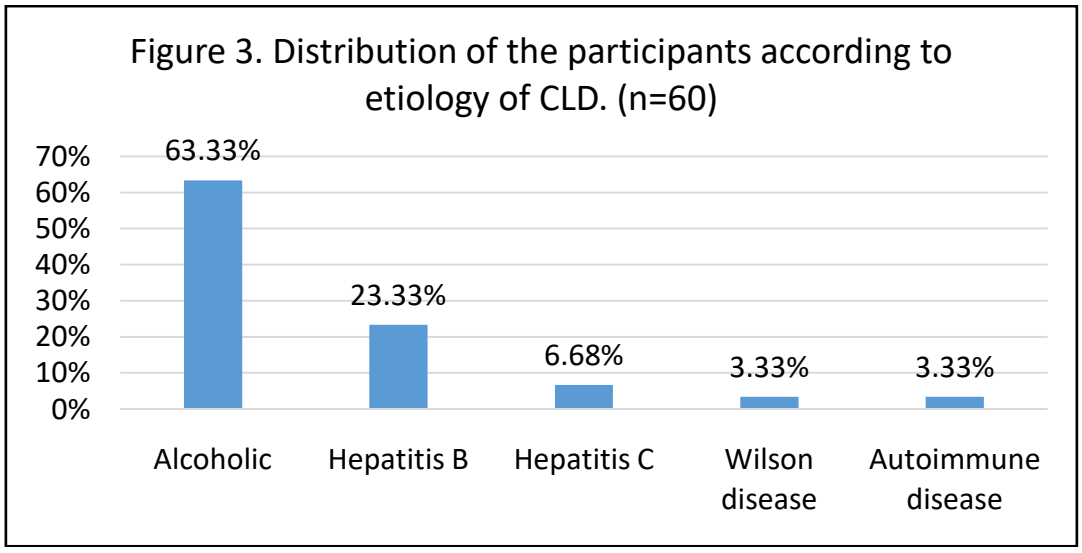

Table 1. Distribution of the study participants according to history obtained. (n=60)

History of	Findings	Frequency	Percentage
GI bleeding	Presence	52	86.67
	Absence	08	13.33
Alcohol intake	Positive	36	60
	Negative	24	40

Table 2. Distribution of the patients according to findings on clinical examination. (n=60)

Clinical examination – points noted	Findings	Frequency	Percentage
Size of liver	Normal	04	6.66
	Enlarge	19	31.67
	Reduce	37	61.67
Ascites	Presence	40	66.67
	Absence	20	33.33
Size of spleen	Enlarge	57	95
	Normal	03	5

Table 3. Distribution of study participants according to endoscopic findings. (n=60)

Endoscopy - observations	Findings	Frequency	Percentage
Grading of varices	No varices	11	18.33
	Grade I	10	16.67
	Grade II	13	21.67
	Grade III	14	23.33
	Grade IV	12	20
Peptic ulcer disease	Positive	9	15%
	Negative	51	85%
Rapid urease test (RUT)	Positive	07	11.67
	Negative	53	88.33

Table 4. Distribution of the study subjects as per the observed biochemical parameters (n = 60)

Biochemical parameters	Mean (mg/dl)	Median (mg/dl)	Standard deviation (mg/dl)	Range (mg/dl)
Bilirubin	2.7	3.5	0.5260	0.8 - 21.0
Albumin	3.2	2.25	0.3584	1.3 - 3.2
Globulin	4.09	4.0	0.4493	3.2 - 5.2
Hemoglobin	8.82	8.95	1.4755	5.4 - 12.4
Urea	25	34	13.920	17 - 72
Creatinine	1.2	0.9	0.6554	0.5 - 3.2
SAAG	1.25	1.8	0.4780	1.1 - 3.0
ALP	205.35	191.5	62.9137	112 - 334

Table 5. Relationship of RUT status with peptic ulcer disease and etiology of CLD. (n=60)

Factor considered	**Category**	**Rapid Urease Test**		**p-value**
		Positive	**Negative**	
Peptic Ulcer Disease	Present	5	4	<0.001
	Absent	2	49	
Etiology of CLD	Alcohol	4	34	0.8512
	Hep B	2	12	
	Hep C	1	3	
	Autoimmune	0	2	
	Wilson's Disease	0	2	

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