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Original Research Article

Prevalence of duodenal ulcer and associated *Helicobacter pylori* infection in chronic liver disease

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ABSTRACT

Background: Aim was to determine the prevalence of duodenal ulcer (DU) and associated *H.pylori* infection in patients with liver cirrhosis.
Methods: A prospective observational study was conducted at a tertiary care medical college hospital and research center in Suburban Chennai, Southern India, where consecutive patients with cirrhosis of liver undergoing UGI endoscopy were screened for duodenal ulcer and in those with duodenal ulcer *H.pylori* testing was performed with RUT and histology of antral biopsy specimen. Prevalence was compared with age and socioeconomic status matched control population who presented with dyspepsia and underwent UGI endoscopy during the study period.
Results: Total 106 patients with chronic liver disease and 481 matched non cirrhotics with dyspepsia underwent UGI endoscopy during the study.
Duodenal ulcer was diagnosed in 19.08% patients with cirrhosis and in 6.02% non-cirrhotic patients with dyspepsia.16.66% patients with DU in chronic liver disease (CLD) group were diagnosed to have *H.pylori* infection by histology and RUT in comparison to 93.1% *H.pylori* infection in control population with DU.
Conclusions: The incidence of DU in CLD was significantly higher when compared to general population with dyspepsia. However, majority of patients with PUD in cirrhosis of liver did not have associated *H.pylori* infection. Increased incidence of DU in CLD is probably due to several other mechanisms related to portal hypertension. Routine treatment with anti *H.pylori* regime may not be warranted with CLD patients with DU, therefore a test and treat strategy for *H.pylori* will be more optimal in CLD.

Keywords: Cirrhosis liver, Duodenal ulcer, Helicobacter pylori, UGI endoscopy, Rapid urease test, Histology

INTRODUCTION

Peptic ulcer disease is not uncommon in patients with liver cirrhosis and bleeding from peptic ulcer leads to substantial morbidity and mortality in patients with liver cirrhosis.

Although the incidence and prevalence of peptic ulcer disease appear to be higher in chronic liver disease (CLD), the underlying mechanism of peptic ulcer disease in cirrhosis is unclear.[1-3] Unlike in the general population where Helicobacter pylori infection plays an important role in the pathogenesis of peptic ulcer disease, the role of *H.pylori* infection in the pathogenesis of peptic ulcer disease in cirrhotic patients still remains to be elucidated.[4,5] In the setting of acute UGI bleed, diagnosis of duodenal ulcer in patients with CLD may be overlooked and ulcer bleed may be mistaken as variceal bleed as a result of poor visualization during endoscopy due to presence of blood in the lumen and hence appropriate management of duodenal ulcer may be delayed thereby adversely affecting the prognosis. No

data is available regarding frequency of duodenal ulcer among cirrhotics in the geographical location of this study. The aim of this study was to determine the prevalence of duodenal ulcer and associated *H.pylori* infection in patients with liver cirrhosis.

METHODS

A prospective observational study was conducted at Department of Medical Gastroenterology, SRM Medical College Hospital and Research Center, Chengalpet District between June 2020 and October 2020 to determine the prevalence of Duodenal ulcer in CLD and associated *H.pylori* infection among those with duodenal ulcer.

Comparison was also made by selecting age and socioeconomic status matched controls undergoing Upper GI endoscopy for dyspepsia. Informed consent for endoscopy was obtained from all the patients. This study was approved by institutional ethics committee (EC Reg No.1904/IEC/2020).

Sample size was calculated using the following formula

$n = Z^2 \times p\hat{} (1-p\hat{})/E^2$

where n is the sample size of 105, Z is the z score at 80% confidence level, P^ is the population proportion of 20% derived from various studies showing 15-24% prevalence of peptic ulcer in cirrhotics.[1,3,6,34,] E is the margin of error 5%. Consecutive patients of both genders between age group 18-75 years with established diagnosis of chronic liver disease who underwent upper GI endoscopy for various indications between June 2020 – October 2020 were included in the study.

A total of 106 patients with proven Chronic liver disease were enrolled based on inclusion and exclusion criteria. They were studied for endoscopic evidence of Duodenal ulcer and *H.pylori* infection by both slide based rapid urease test and histopathologic examination of antral biopsy specimen. Endoscopic diagnosis of duodenal ulcer was made when a distinct ulcer crater larger than 5 mm was observed.

A total of 481 age matched consecutive patients of both genders who underwent upper GI endoscopy for evaluation of dyspepsia during the same period were used as control population for comparison of prevalence of DU and associated *H.pylori* between the two groups.

Five endoscopic gastric biopsy specimens were taken (4 for HPE and 1 for RUT). 2 biopsy specimens from the antrum, 2 biopsy specimens from the gastric body were used to identify *H.pylori* by Histopathologic examination by pathologist, and one biopsy specimen from antrum was used for performing the rapid urease test. The presence of *H.pylori* infection was determined by positivity of both rapid urease test and histology.

The demographic and clinical characteristics were analyzed statistically using the one-way ANOVA, Chi Square Test and ODDS Ratio as appropriate. A value of $p<0.05$ was considered to be statistically significant.

Inclusion criteria

Inclusion criteria were, patients with chronic liver disease irrespective of etiology and CTP score, uninvestigated dyspepsia between age 18-75 years

Exclusion criteria

Exclusion criteria were UGI malignancy, patients who have received antibiotics in the preceding 2 weeks, patients who are on Aspirin and who had taken NSAIDS in last 1 month.

RESULTS

The demographic profile was comparable between the study group and control group as shown in (Table 1).

Table 1: Demographic profile.

Age (in years)	Number of cases (percentage)			Sex	Number of cases (percentage)			Socioeconomic status	Number of cases (percentage)		
	CLD Group	Dyspepsia Group	ANOVA P value		CLD Group	Dys-pepsia Group	ANOVA p value		CLD Group	Dyspepsia Group	P value
20-30	06	45						I Upper	00	00	
31-40	32	136		Male	92	305		II Upper Middle	18 (16.9%)	89 (18.5%)	
41-50	48	204	0.065				0.137	III Lower Middle	76 (71.6%)	348 (72.3%)	0.292
51-60	18	86		Female	14	176		IV Upper Lower	12 (11.3%)	44 (9.14%)	
61-70	02	10						V Lower	00	00	

In CLD group – 28, 47 and 31 patients had child pugh score A, B, and C respectively. In CLD group - UGI scopy was done for (i) screening of varices in (62) 58.49%, (ii) epigastric pain in (12) 11.32%, (iii) recent hematemesis with or without melena in (22) 20.75%, (iv) recent melena alone in (10) 9.43% (Table 2).

Table 2: Frequency of duodenal ulcer.

Population	Duodenal ulcer present	Duodenal ulcer absent	Total	Chi-Square P value
CLD Group	18(19.08%)	88	106	<0.05
Dyspepsia Group	29 (6.02%)	452	481	

The chi square statistic with Yates correction is 12.69. p=0.0003. The odds of developing duodenal ulcer in patients with CLD was three times that of those patients with dyspepsia. [Odds ratio=3.18 (95%.CI=1.69 to 5.99), p=0.0003].

Table 3: Comparision of *H pylori* frequency by rapid urease test and histology in patients with duodenal ulcer among the 2 study groups.

Groups	RUT/histology positive	RUT/histology negative
Chronic liver disease with DU	3	15
Dyspepsia with DU	27	2

The chi square statistic with Yates correction is 24.89. p=0.0001.

Table 4: Duodenal Ulcer presentation in CLD.

	Number of patients	Percentage
No abdominal pain or GI Bleed	06	33.33%
Epigastric pain alone	09	50%
UGI Bleed±pain	03	16.66%

Table 5: Etiology of UGI bleed in CLD.

Total number -31 patients	Number (%)
Variceal	26 (83.87)
Portal Hypertensive Gastropathy	02 (6.45)
Duodenal Ulcer	03 (9.67)

The frequency of *H.pylori* infection was low and statistically significant in CLD patients with duodenal ulcer when compared to control cohort with duodenal ulcer as evidenced by p<0.05 (Table 3).

Total 1/3 of CLD patients with Duodenal ulcer did not have any symptoms of PUD (Table 4).

Variceal bleed was the cause of UGI bleed in majority (83.8%) of patients with CLD. However, in ~10% cases UGI bleed in CLD was caused by duodenal ulcer (Table 5).

DISCUSSION

The aim of the study was to determine the frequency of duodenal ulcer and associated *H.pylori* infection in patients with liver cirrhosis.

Prevalence of duodenal ulcer in patients with liver cirrhosis in this study was 19.08%, the high prevalence of duodenal ulcer in cirrhotics in our study is consistent with previous reports.[1-3,6-8,34]

The increased rate of peptic ulcer disease in patients with cirrhosis has been explained in some studies, by higher rates of gastric colonization with *H. pylori*.[6,7,9-15] However, other studies have found no relationship between *H.pylori* infection and peptic ulcer disease in cirrhosis.[16-22] In our study, the prevalence of *H.pylori* infection in cirrhotic patients with DU was low at 16.6% in contrast to 93.1% in non cirrhotics with DU.

The low prevalence of *H.pylori* infection in cirrhotic patients in our study can also be explained by the difference in the diagnostic methods used in the setting of *H.pylori* infection. In general, studies that use serologic tests (Serum IgG antibody) report higher prevalence due to past infections than the studies that use the rapid urease test, histology, or urea breath test that reflect current infection (76.2-89% vs. 39~59.7%).[7-9,12,13,19]

It is also shown that eradication of *H.pylori* does not reduce the residual ulcer rate in cirrhotic patients indicating that *H.pylori* might not be a significant risk factor for PUD in chronic liver disease.[23] It has also been suggested that portal hypertensive gastropathy (PHG) does not provide an adequate environment for *H.pylori* colonization.[24,25] Hence routine *H.pylori* eradication might not be warranted in patients with cirrhosis and PUD.

H.pylori infection in the general population correlates with age, social class, overcrowding, bed-sharing, and economic level. Comparison of the prevalence of *H.pylori* infection in patients with cirrhosis and the control group matched by prognostic variables (age and socioeconomic status,) still showed statistically low prevalence of *H Pylori* in CLD group with DU.

In contrast the prevalence of *H.pylori* infection in non cirrhotics with PUD was high in our study. 93.10% non-cirrhotic patients with PUD had *H Pylori* infection. Epidemiologic studies have reported that 50% to 90% of patients with duodenal ulcers (DU) are infected with H pylori.[26,27] Therefore routine testing for *H Pylori* is not needed in non-cirrhotic patients with DU in general population and can be started on anti *H Pylori* regime.

The etiology for increased prevalence of PUD in cirrhosis is a subject of much debate. Therefore besides *H. pylori*, other factors may contribute to the increased risk of duodenal ulcer in cirrhotic patients

Reduced prostaglandins, decreased gastric acid secretion, elevated serum gastrin concentration, impaired mucus secretion, a reduction in potential difference of the gastric mucosa, and portal hypertensive gastropathy may all play a role in the pathogenesis of peptic ulcer disease in cirrhotic patients.[1-3]

Portal hypertension, which causes splanchnic congestion interferes with formal reparative process of gastroduodenal mucosa, leading to increased susceptibility towards acid and pepsin secretion.[28]

In patients with decompensated chronic liver disease, hypercatabolic state independent of portal hypertension may contribute to PUD probably related to impaired reparative process.[29,30]

In our study, DU was the cause of UGI bleed in 3(9.6%) out of 31 patients who had UGI bleed in CLD group. It has been shown in various studies that 5-30% of UGI bleed in cirrhotics is caused by PUD rather than varices.[31-33] There is often tendency to overlook ulcers during endoscopy in the presence of presence of varices due to poor field of vision in the setting of acute GI bleed. Hence in cirrhotic patients with acute UGI bleed, though varices are the most common source of GI bleed it is important to rule out peptic ulcer related GI bleed by thorough inspection. DU bleed can be successfully managed endoscopically which have significant implication in reduction in morbidity and mortality in CLD. Our study showed that even though *H.pylori* infection was low, incidence of DU was high. Based on our observations and those of others, we hypothesize that *H.pylori* may not be a main cause of peptic ulcer disease in cirrhotic patients.[6]

The prevalence of duodenal ulcer was higher and statistically significant with p value<0.05 in patients with cirrhosis when compared to general population presenting with dyspepsia. The child pugh status was effect modifier. It was seen that patients having higher child class were having more incidence of DU. In our study, of the 29 patients with DU, 2 were child A, 15 were child B and 12 were child C. 93.1 percent of DU were seen in child B and C put together.

Another important finding noted was that 33.3% of patients with CLD with DU did not have any symptoms attributable to PUD. Epigastric pain as sole manifestation without bleed was present in 50% and 16.6% of patients who had DU presented with UGI bleed.

CONCLUSION

A significant proportion of patients with cirrhosis develop PUD. Furthermore, H pylori infection is not an important risk factor for DU in cirrhotics. Not all DU in cirrhotics need anti *H.pylori* therapy and only those with positive test for active *H.pylori* infection need to be treated with anti *H.pylori* regime, thereby avoiding unnecessary exposure and side effects of anti *H.pylori* regime in cirrhotics. Also, in the setting of CLD it is imperative to rule out PUD as source of UGI bleed.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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