The Prevalence of Helicobacter Pylori Infection in Patients with Liver Cirrhosis with Peptic Ulcer Disease with and without Symptoms in a Rural Tertiary Care Centre in South India

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Abstract

Introduction: Liver cirrhosis is a major health problem world-wide and peptic ulcer is a condition that is commonly seen in patients with liver cirrhosis. Helicobacter pylori infection remains one of the most common conditions in Liver cirrhosis patients. This study was done to ascertain the presence of H. pylori in patients with liver cirrhosis being treated a tertiary care hospital in rural part of South India, in both symptomatic and asymptomatic peptic ulcer disease patients.

Methodology: All consecutive patients with liver cirrhosis with or without obvious symptoms of peptic ulcer disease (PUD), attending the gastroenterology department of a rural tertiary care center in Southern India was serially recruited after taking written informed consent to join the study. Liver cirrhosis was diagnosed by history, clinical examination, deranged liver function tests (LFT), prolonged prothrombin time (PT), Ultrasound abdomen and upper GI endoscopy showing varices and/or portal gastropathy. The severity of liver disease was classified as per Child -Pugh criteria. The etiology of liver disease was documented. Duodenal ulcer was diagnosed by endoscopy (well defined defect in the first or second part of the duodenum). Gastric ulcer was diagnosed by endoscopy (well-defined defect in the antrum, pylorus or body of the stomach).

Results: Primary end point of our study, prevalence of Helicobacter pylori in patients with liver cirrhosis attending to the gastroenterology department in a rural tertiary care centre in South India with peptic ulcer disease both in symptomatic and asymptomatic patients was 53.6 % (52). Our secondary end point, prevalence of endoscopy proved peptic ulcer in patients with liver cirrhosis, was found to be 10.3% . Surprisingly all the 10 patients with ulcers were asymptomatic.

Conclusion: Significant prevalence of asymptomatic peptic ulcer disease and also the prevalence of H.Pylori in patients with liver disease. Bleeding peptic ulcer can cause significant mortality and morbidity in these patients and efforts must be made to treat peptic ulcer disease before complications occur.

I. Introduction

Liver cirrhosis is a major health problem world-wide and peptic ulcer is a condition that is commonly seen in patients with liver cirrhosis. Helicobacter pylori infection remains one of the most common chronic bacterial infections in humans. H. pylori are ideally suited to live in the acidic environment of the human stomach. They are spiral in shape and have multiple uni-polar flagella, which allows them to move freely through the gastric mucous layer, where they remain protected from low gastric pH. These organisms produce large amounts of urease, an enzyme that hydrolyzes urea to alkaline ammonia and CO₂. It allows the bacteria to further control the pH of their microenvironment. Urease based clinical diagnostic tests (urea breath test and rapid urea biopsy tests) are in wide use. H. pylori remain difficult to culture because they grow slowly and require specialized culture media and a controlled microaerophilic environment. The various clinical manifestations of H. pylori infection include gastric and duodenal ulcer, gastric mucosa-associated lymphoid tissue (MALT) lymphoma, and adenocarcinoma; but most of the infected patients remain asymptomatic for life despite developing chronic histologic gastritis.

The term peptic ulcer disease (PUD) is used broadly to include ulcerations and erosions in the stomach and duodenum due to a number of causes. Pepsin, which is proteolytic in acidic solution, plays a significant role in causing the mucosal breaks regardless of the cause of the inciting agent (e.g., Helicobacter pylori, aspirin, or a non-steroidal anti-inflammatory drug [NSAID]). Peptic ulcer related complications are a major cause of morbidity and mortality in cirrhotic patients. Peptic ulcer bleeding accounts for 30% of gastro-intestinal (GI) bleeding in patients with cirrhosis. Point prevalence of peptic ulcer disease in cirrhosis was 11.7%, period
prevalence was 15.1% and life time prevalence was 24.2%, nearly 70% of the ulcers were asymptomatic which puts the patient at higher risk for bleeding since absence of symptoms may delay visits to the health care facility(6).

Helicobacter pylori infection is being correlated to various other human diseases, among which liver diseases also include. From a clinical point of view, 3 "areas of interest" for the suggested correlation can be identified: a) Helicobacter pylori and portal hypertension-related congestive gastropathy in cirrhotics(7). b) Helicobacter pylori and duodenal ulcer in cirrhotic patients.

In a study conducted by B. R Devrajani et al, there was a strong association of Helicobacter pylori with peptic ulcer disease in cirrhotic (8). Another study by Kirchner GI et al showed lack of firm association between H. pylori prevalence and ulcer frequency in liver cirrhosis. In the same study it was found that asymptomatic ulcers are more common in cirrhotic with advanced disease(9).

c) Helicobacter pylori, ammonia production and hepatic encephalopathy.

A study by Venkatesh PG et al showed that mortality from the bleeding is high in peptic ulcer associated with cirrhosis(10).

Bleeding ulcers are managed by medical therapy in combination with endoscopic therapy. In patients with advanced liver cirrhosis wound healing is poor as the tissues are oedematous. This combined with lowered immunity puts the patient at increased risk of developing infections after admission to the intensive care units (ICU).

The prevalence of H. pylori in patients with hepatic cirrhosis was found to be 76.2% in a study conducted by Tsai CJ et al. It also showed no difference in H. pylori prevalence between patients with and without peptic ulcer. The prevalence of H. Pylori or peptic ulcer was independent of the severity of liver disease(11). Studies from South India done by V. Kate et al showed that the prevalence of H. Pylori in duodenal ulcer is 66-91% and in gastric ulcer it is 76-100%(12). A recently published study by Chang SS et al reports that early eradication of H. Pylori will reduce the risk of peptic ulcer related complications (13). Our study was done to ascertain the presence of H. pylori in patients with liver cirrhosis being treated a tertiary care hospital in rural part of South India, in both symptomatic and asymptomatic peptic ulcer disease patients.

II. Methods

It is a Cross-sectional study conducted between, April 2015 – April 2016. All consecutive patients with liver cirrhosis with or without obvious symptoms of peptic ulcer disease (PUD), attending the gastroenterology department at MOSC Medical College Hospital which is a rural tertiary care center located in Ernakulam district in Kerala India was serially recruited after taking written informed consent to join the study.

Liver cirrhosis was diagnosed by history, clinical examination, deranged liver function tests (LFT), prolonged prothrombin time (PT), Ultrasound abdomen and upper GI endoscopy showing varices and/or portal gastropathy. The severity of liver disease was classified as per Child -Pugh criteria. The etiology of liver disease was documented. Duodenal ulcer was diagnosed by endoscopy (well defined defect in the first or second part of the duodenum). Gastric ulcer was diagnosed by endoscopy (well-defined defect in the antrum, pylorus or body of the stomach). The presence of esophageal varices was also noted.

Gastric Biopsy was taken from the gastric antrum, body and incisura angularis, one bite each with standard biopsy forceps. Biopsy specimens were sent for histo-pathological examination and for Gram staining to identify H. pylori and inflammatory infiltrate with lymphocytes, neutrophils and mast cells. RUT test was done by placing one sample from the antrum in the well of the kit and the result was read after 3 minutes.

Assessment

End points

The primary end point was to know the prevalence of Helicobacter pylori in patients with liver cirrhosis attending to the gastroenterology department in a rural tertiary care centre in South India with peptic ulcer disease both in symptomatic and asymptomatic patients. Secondary end point was to assess the prevalence of endoscopy proved peptic ulcer in patients with hepatic cirrhosis.

Ethical Considerations

Institutional review board and Ethics committee approval was obtained. All the patients included in the study were given a participant information sheet and a written informed consent was obtained. All procedures followed were routine and there was no additional cost to the patient.

Statistical analysis

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Sample size was calculated by n-Master sample size software for single proportion. In the study by Mario Miglioli et al the prevalence of IgG to Helicobacter pylori in cirrhotics was significantly higher than in the controls (76.5% vs 41.8%; P < 0.0005). Using the prevalence of 76.5% the Sample size for single proportion, calculated for a confidence interval of 95% and precision of 9% was found to be 86 patients with cirrhosis.

### III. Results

Of the 97 patients who participated in the study, 87 were male and 10 were females, all the patients were above the age of 18.

**Age distribution of participants (n = 97)**

21 (21.6%) patients were having Type 2 Diabetes Mellitus, 33 (34%) had systemic hypertension and 2 (2%) were having hypothyroidism. 13 (13.4%) were complaining of dyspepsia and rest 84 (86.5%) were asymptomatic. 12 (12.3%) were using NSAIDs. Of the total study group 3 (3%) were underweight, 35 (36%) were overweight and 5 (5%) were obese according to BMI.

**Proportion of participants with dyspepsia (n = 97)**

78 patients of the study group had chronic liver disease (CLD) due to ethanol intake, 14 patients had non alcoholic fatty liver disease (NAFLD) related CLD, 4 were cryptogenic and 1 was autoimmune related CLD.
Primary end point of our study, prevalence of Helicobacter pylori in patients with liver cirrhosis attending to the gastroenterology department in a rural tertiary care centre in South India with peptic ulcer disease both in symptomatic and asymptomatic patients was 53.6 % (52). Our secondary end point was prevalence of endoscopy proved peptic ulcer in patients with liver cirrhosis, was found to be 10.3%(10). Surprisingly all the 10 patients with ulcers were asymptomatic.

IV. Discussion

Chronic liver disease is growing in incidence in India. In this southern state of India, there is a vast majority of patients, and contribute a significant burden to the health care sector. Upper gastrointestinal bleeding is a significant cause of morbidity and mortality in these patients. The study by Al-Mofleh et al and Schlichting et al shows that peptic ulcer is both more common and causes more morbidity in these patients(14, 15). The study by Al-Mofleh et al and Schlichting et al shows that peptic ulcer is both more common and causes more morbidity in these patients.(14, 15)

The pathogenesis of high peptic ulcer rate in cirrhotic patients is complex and multifactorial. Theoretically, portal hypertension is involved and causes splanchnic congestion, altered normal reparative processes of the gastro-duodenal mucosa, impaired gastric mucosal secretion and gastric microvascular abnormalities. These lead to increased susceptibility to acid and pepsin. It has also been demonstrated that people with cirrhotic condition have impaired gastric mucosal defence mechanisms, including impaired bicarbonate and mucus secretion, reduced gastric mucosal blood flow and impaired mucosal oxygenation(25,26). Chen's study showed that the prevalence of gastric ulcer in 245 cirrhotic patients was significantly higher than in age- and sex-matched healthy subjects (20.8% vs. 4%) (16) Siringo's study showed that cirrhotic patients had high PUD prevalence (point prevalence: 11.7%, period prevalence: 15.1%) with an annual incidence rate of 4.3% and total ulcer bleeding rate of 20%.

In Lo's study, there was high ulcer recurrence rate (48%) in 50 cirrhotic patients even after successful Helicobacter pylori (H. pylori) eradication. In general, use of NSAIDs/ASA, H. pylori infection, history of ulcer/ulcer bleeding and chronic renal disease are all important risk factors for PUB (18,19,20,21) Our study showed that that 53.6% of patients attending the gastroenterology clinic had H.Pylori positive by the RUT test. 10.3% had endoscopic proved peptic ulcer disease. Only 13.4% patients had complaints of dyspepsia. Majority of patients were asymptomatic. In our study majority patients has liver disease due to alcohol. Alcohol can directly damage the gastric mucosa. Bienia et al studied the effects of alcohol on the gastric and duodenal mucosa in patients who consume alcohol regularly. The HCL level in gastric juice was very high. Gastritis was noted on endoscopy and confirmed by biopsy. Atrophy was also noted. These changes would also predispose to peptic ulcer disease.

In conclusion, we would like to highlight the prevalence of asymptomatic peptic ulcer disease and also the prevalence of H.Pylori in patients with liver disease. Bleeding peptic ulcer can cause significant mortality and morbidity in these patients and efforts must be made to treat peptic ulcer disease before complications occur.

References


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