FREQUENCY OF H. PYLORI SEROPOSITIVITY IN PATIENTS WITH HEPATIC ENCEPHALOPATHY

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Abstract

Objective: To determine the frequency of Helicobacter Pylori seropositivity in patients with hepatic encephalopathy.

Study Design: Descriptive cross sectional study.

Place & Duration of the Study: This study was conducted at the Department of Medicine of Khyber Teaching Hospital Peshawar from February 2014 till September 2014.

Methodology: This study included 137 cirrhotic patients and data was collected on a structured questionnaire. An informed written consent was taken from patients or their attendants, who fulfilled the inclusion criteria. Both male and female Patients (age 15 and above) were assessed in the OPD and admitted to Medical Unit for work up. All patients were investigated for H. Pylori Serology by sending 5ml of venous blood to the same laboratory. Data was analyzed using SPSS version16.

Results: The mean age of all the 137 patients was 41.36 years ± 10.48SD. Out of total patients of 137, 75 (54.75%) were males and 62(45.55%) were females. H. pylori serology was positive in 94 (68.61%) of the patients while 43 (31.39%) had negative antibody results for H. pylori. West-Haven classification of the grades of Hepatic Encephalopathy showed that 25 (18.25%) patients had grade 1, 33 patients (24.09%) had grade 2, 40 patients (29.2%) had grade 3 and 39 participants (28.47%) were in grade 4 Encephalopathy respectively.

Conclusion: Cirrhotic patients are more commonly infected with H. Pylori and the vast majority of them (68.61%) have positive antibody against the causative pathogen.

Key Words: H. Pylori, Cirrhosis, hepatic encephalopathy, liver disease.

Introduction

Cirrhosis represents a major cause of morbidity and mortality in the world. In
United States in 2005 cirrhosis was the first diagnosis upon discharge in 1120, 00 patients. Liver diseases and cirrhosis are also a major cause of hospital admissions in our country. Among the causes viral infection is the leading cause of cirrhosis in our country while in Europe both alcohol abuse and chronic viral hepatitis are important etiological agents.

Cirrhosis is an indolent disease most patients remain asymptomatic until the occurrence of decompensation, characterized clinically by Ascites, Spontaneous bacterial peritonitis, Hepatic Encephalopathy or variceal bleeding from portal hypertension.

The syndrome of hepatic encephalopathy (HE) describes all neuropsychiatric symptoms occurring in patients with acute or chronic liver diseases (CLD) in the absence of other neurological disorders. About 30% of patients with Cirrhosis die in hepatic coma. Hepatic Encephalopathy is among the major complications of liver cirrhosis and its appearance is associated with adverse prognosis.

Patients with Cirrhosis liver may have a chronic neuropsychiatric state due to Porto-systemic shunting. Survival in patient with chronic Porto-systemic shunting is better than those who develop Hepatic Encephalopathy acutely (100% vs. 70%); however survival in latter group can be improved with rapid identification of precipitating factors and their treatment.

Ammonia is fundamental to the pathogenesis of hepatic encephalopathy. Some of the proven events involved in precipitating Hepatic encephalopathy are G.I bleed, large protein meal, Constipation, Electrolyte disturbance, Diuretics, Acute hepatitis, Infections, Sedatives, Narcotics, and Surgery.

Recently role of H. Pylori as a precipitating factor for Hepatic Encephalopathy has been under extensive debate. Colonic bacteria are considered the main source of ammonia and stomach is believed to be an alternative site in H. pylori infected subjects. The relationship between H. pylori and hepatic encephalopathy has been reported in many studies in which hyperammonemia were significantly reduced after eradication of H. pylori with remission of hepatic encephalopathy. The ammonia produced in the stomach by H. pylori is not absorbed normally except in cases of severe atrophic gastritis, renal failure and liver dysfunction. As studies on the presence of H. Pylori in cirrhotic patients and its role as potential trigger to hepatic coma are rare and controversial, we decided to document this study to establish its role and rule out any controversy.

In the management of patients with liver cirrhosis and hepatic encephalopathy it is prudent to stage the overt encephalopathy into grades that range from grade I to IV and then try to identify and treat the precipitating factors. In the presence of the latter the neurological deficits are usually completely reversible upon their correction and the prognosis is better if the precipitant can be treated.

Methodology
This descriptive cross-sectional study was conducted after taking both approval from the ethics committee of the hospital and informed consents from 137 cirrhotic male and female patients admitted to the Medical B Unit of Khyber Teaching Hospital Peshawar between February and September 2014. The patients were selected into the study through non-probability consecutive sampling technique and patients included had age 15 and above. Patients excluded from the study were those who had either received eradication therapy for H. Pylori in the previous two weeks or had hypoglycemic or uremic encephalopathy or acute febrile illness and/or were on any sedating drugs like benzodiazepines, antidepressants, opiates etc.
A 5ml venous blood sample was taken on admission from all the patients and was analyzed by the same laboratory for the antibodies against H. Pylori. All information was recorded onto a structured questionnaire especially designed for this purpose. Strictly exclusion criteria were followed to control confounder and bias in the study results. The data was analyzed using SPSS version 16. Chi-square test and t-test were applied for analyzing the qualitative (categorical) and quantitative variables respectively.

**Results**

The study group comprised of 137 patients who were already diagnosed with liver cirrhosis on the basis of clinical assessment, liver function test and ultrasound features. The mean age of the patients was 41.36 years ± 10.48SD. Minimum age was 28 years and maximum age was 73 years. Of all the patients, 75 (54.75%) were male and 62 (45.55%) were female. Serology for H. Pylori was positive in 94 patients (68.61%) while 43 participants (31.39%) were seronegative for H. Pylori. It was observed that older patients were more likely to have H. pylori positive as compared to those in the younger age group. Amongst the H. pylori positive patients, 48 (51.06%) were in the age range of 41-50 years followed by 17 patients (18.09%) in the range of 31-40 years. Hepatic Encephalopathy grade wise distribution of the patients showed that 25 (18.25%) patients had grade 1, 33 (24.09%) were in grade 2, 40 (29.2%) were in grade 3 and 39 (28.47%) had grade-4 encephalopathy. It is also noteworthy that amongst 94 patients who were seropositive for H. Pylori, 60 were in high grade (grade 3 or 4) while the remainder in low grade (grade 1 or 2) hepatic coma. Those patients who were positive for H. Pylori had mean recovery time of 4.5 days while those without serological evidence for the gram negative H. Pylori had mean recovery time of 3 days.

**Discussion**

An increasingly large number of diseases have been ascribed to infection with H pylon. Some are well documented, others less well so. Prevalently accepted are roles for H pylori in duodenal ulcer, gastric ulcer, gastric adenocarcinoma, and gastric lymphoma. Less well accepted are its role in non-ulcer dyspepsia and its more indirect influences on coronary artery disease, rosacea, diarrheal diseases in children in the developing countries, and hepatic encephalopathy. Colonic bacteria are considered the main source of ammonia and its clearance is impaired in patients with cirrhosis due to decreased urea-cycle function, increased Porto-systemic shunting and decreased uptake by muscle cells peripherally. It is responsible for the neurotoxic manifestations of hepatic encephalopathy. H. pylori mainly infect the stomach and are known to produce copious amount of ammonia due to its strong urease activity many times greater than that of urease positive Enterobacter.

The role of H. pylori in the pathogenesis of hepatic encephalopathy has been a subject of an ongoing debate. Previous studies have reported that ammonia levels of gastric juice and serum ammonia levels in cirrhotic patients were significantly higher in H. pylori positive patients as compared to those with negative status. This study on patients with hepatic encephalopathy was conducted to explore the significance of H. pylori infection in hepatic encephalopathy. The results of the study have shown that the prevalence of Helicobacter pylori infection was high (68%) in patients presenting with porto-systemic encephalopathy. The results of this study (76.5%) are comparable to study conducted in Italy, by Siringo et al. and 76% as reported by Tsai et al. in Taiwanese population with cirrhosis. In Pakistan, the frequency of H. pylori...
antibodies has been reported to be 74% in cirrhotic patients. Xu reported the frequency of H. pylori antibodies to be 71.4% in Chinese patients with Porto-Systemic Encephalopathy (PSE) and 67% in American population with PSE as reported by Dasani et al. There are other studies which have reported a lower frequency (20.3% to 60%) of H. pylori associated with PSE in patients with cirrhosis.

Several extra-intestinal diseases have been associated with Helicobacter pylori infection. Hepatic encephalopathy has been linked to H. pylori infection because of the ammonia produced by the organism in the stomach. H. pylori infection is commoner in cirrhotic patients with hepatic encephalopathy than in those without. Though the amount of ammonia produced by H. pylori may be too small to contribute to hepatic encephalopathy, eradication of H. pylori has been shown to improve the blood ammonia levels and hepatic encephalopathy.

In our study prevalence of H. pylori was significantly high in patients of chronic liver disease with hepatic encephalopathy. Prevalence and titres of H. pylori were found significantly increasing with the severity of hepatic encephalopathy, which suggests H. pylori may have a role in the pathogenesis of hepatic encephalopathy. However, a large number of cases should be studied for further confirmation as these findings do not correlate with the findings of Guillermo et al. In their study they found H. pylori seropositivity in hepatic encephalopathy grade I as (77.63%), grade II (78.13%), grade-III (100.00%) and grade as IV (75.00%).

**Conclusion**

From our study we concluded that H. Pylori was more frequently positive in patients with cirrhosis and the antibody titer rises proportionately with the severity of hepatic encephalopathy. Most of the cirrhotic patients who were positive for H. Pylori were middle aged and the mean recovery time from hepatic coma for seropositive patients was more in comparison to those who didn’t have the serological evidence for recent or past infection with H. Pylori.

**References:**

1. National Hospital Discharge Survey: 2005 Annual Summary with Detailed Diagnosis and Procedure Data, table 45 (see ICD9-CM code 571).
8. Shawcross DL, Shabbir SS, Taylor NJ, Hughes RD. Ammonia and the


Table No 1: Age wise distribution of H.Pylori in Cirrhotic Patients
(n=137)

<table>
<thead>
<tr>
<th>AGE</th>
<th>H. Pylori</th>
<th>PERCENTAGE</th>
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<tbody>
<tr>
<td></td>
<td>Yes. (%)</td>
<td>No (%)</td>
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<tr>
<td>20-30</td>
<td>2(2.13%)</td>
<td>5(11.6%)</td>
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<tr>
<td>31-40</td>
<td>17(18.09%)</td>
<td>6(13.9%)</td>
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<td>41-50</td>
<td>48(51.06%)</td>
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<td>51-60</td>
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<td>&gt;60</td>
<td>6(6.38%)</td>
<td>4(9.3%)</td>
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<tr>
<td>Total</td>
<td>94(100%)</td>
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