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A STUDY OF HELICOBACTER PYLORI INFECTION IN PATIENTS WITH CIRRHOSIS

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ABSTRACT

Introduction: The role of Helicobacter pylori *(*H. pylori*)* in the pathogenesis of portal hypertensive gastropathy (PHG) in cirrhotic patients is poorly defined.

Aims: To determine the incidence of H. Pylori infection among patients with liver cirrhosis, to correlate the presence of H. Pylori infection with the etiology of cirrhosis, severity of the liver disease, Complications of cirrhosis of liver; oesophageal varices and portal hypertensive gastropathy.

Materials and methods: It is Observational cross-sectional study in 100 patients with cirrhosis of liver.

Results: Bilirubin, Albumin, Prothrombin Time RUT Positive And RUT Negative Group Is Statistically Significant Difference Was Found Between The Two Groups. Ascities, High-Grade Encephalopathy, Esophageal Varices And Portal Hypertensive Gastropathy In RUT Positive And RUT Negative Group Is Statistically Significant Difference.

Conclusions: Patients with H. pylori infection had relatively higher prevalence of higher grade of EV, PHG, compared to patients without H. pylori infection.

Keywords: Helicobacter pylori *(*H. pylori*)*, portal hypertensive gastropathy (PHG) , Cirrhotic, Gastric cancer.

INTRODUCTION

Helicobacter pylori is a microaerophile, gram-negative bacillus, resistant to gastric juice. The bacteria live mainly on the surface of epithelial cells of mucous membranes of prepyloric part of the stomach. H. pylori prevalence ranges between 85 -95 % in developing countries and between 30-50 % in developed countries. In India, approximately 80 % of the population may be infected by the age of 20. [1]

H. pylori infection is typically acquired in childhood. The risk of infection is inversely related to the overall sanitary conditions and requires exposure to other infected humans. Contaminated water is often the primary mode of transmission in rural areas without reliable supplies of potable water. However, in regions of higher socio- economic status the risk of infection best correlates with the level of household hygiene.[2,3]

H. pylori is a significant human pathogen responsible for considerable morbidity and mortality and is the major cause of gastric cancer. The majority of investigators in the field believe that whenever the infection is detected, it should be eradicated.

H. pylori infection causes local and systemic inflammatory response. It causes chronic atrophic gastritis, metaplasia and dysplasia leading to development of gastric cancer. According to WHO, the bacteria is a class 1 carcinogenic factor. It may also influence extra gastric organ disturbances, exacerbating cardiovascular diseases, metabolic diseases, disturbances in liver functions, especially in patients with cirrhosis. H. Pylori infection influences disturbances of lipid metabolism, manifesting with hyper triglyceridemia and hypercholesterolemia, with fall in HDL. This is important in metabolism of hepatocytes, their steatosis, and liver fibrosis.[4]

Liver diseases are fast being recognized as public health priorities in India. The burden of liver disease in India is significant because it alone contributed to 18.3% of the two million global liver disease–related deaths in 2015. Cirrhosis is widely prevalent worldwide and can be a consequence of different causes, such as obesity, non-alcoholic fatty liver disease, high alcohol consumption, hepatitis B or C infection, autoimmune diseases, cholestatic diseases, and iron or copper overload. Cirrhosis develops after a long period of inflammation that results in replacement of the healthy liver parenchyma with fibrotic tissue and regenerative nodules, leading to portal hypertension. The disease evolves from an asymptomatic phase (compensated cirrhosis) to a symptomatic phase (decompensated cirrhosis), the complications of which often result in hospitalisation, impaired quality of life, and high mortality. Progressive portal hypertension, systemic inflammation, and liver failure drive disease outcomes.[5]

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The present study aims to determine H. Pylori infection and its correlation with the presence of cirrhosis and its complications. This study can give us insight about cytopathological effects of helicobacter pylori infection on hepatocytes in patients with cirrhosis.

MATERIAL AND METHODS:

It is Observational cross-sectional study done at Malla Reddy Narayana multispecialty hospital, tertiary care hospital attached to Malla Reddy medical college for women. After obtaining institutional ethical committee clearance the study was carried out in department of General medicine and its allied branch of Gastroenterology at Malla Reddy Medical College for Women and Malla Reddy Narayana multispeciality hospital, Hyderabad in 100 patients with cirrhosis of liver from January 2021 – October 2022.

Inclusion Criteria: Age more than 18 years of either sex with cirrhosis both compensated and decompensated. Hepatitis B and hepatitis C cases.

Exclusion Criteria: pregnant females , cases with hepatocellular carcinoma, Patients with comorbid conditions like hypertension, diabetes mellitus, coronary artery disease, renal diseases, respiratory conditions, thyroid disorders, active infection, patients with history of antibiotic use and PPI use in the past one month, patients with active upper gastrointestinal bleed in the past one week.

The data will be collected in the form of an approved proforma (including detailed demographic information, detailed history, clinical examination and investigations).

METHODOLOGY:

Patients who attended op or got admitted in the hospital are screened according to inclusion and exclusion criteria. Informed and written consent was obtained from each patient. Detailed history including present, past, treatment, personal history was taken. Patients with other co morbid conditions like hypertension, diabetes mellitus, coronary artery disease, renal diseases, respiratory conditions, thyroid disorders, active infections, have been excluded, as these conditions can affect the clinical consequences in liver disease. patients with history of antibiotic use and PPI use in the past one month are excluded as they can interfere with the test results for detection of h. pylori. Patients were subjected to clinical examination and followed by relevant investigations to identify presence cirrhosis and its complications, presence or absence of H. pylori infection.

Investigations like complete blood picture, liver function tests, renal function tests, prothrombin time with international standardized ratio, hepatitis B surface antigen, anti-hepatitis C virus antibodies were carried out on all patients

All patients were evaluated with ultrasonography abdomen and pelvis with doppler study to look for liver size and architecture, splenic size and architecture, portal hypertension, ascites and grading of ascites.

Upper gastrointestinal endoscopy was done to look for presence of varices and grading of oesophageal varices and portal hypertensive gastropathy.

After informing about the procedure informed consent was taken. Patients were kept nil by mouth for 4-5 hours. Flexible esophagogastroduodenoscopy was passed through mouth after spraying oral cavity with 50 mg xylocaine local anaesthetic spray with patient lying in left lateral position. Gastric and esophageal mucosa was examined while retracting the scope.

Rapid urease test was done on the biopsy specimen taken from appropriate gastric mucosal site through endoscopy. A small biopsy of normal looking antral mucosa was collected using standard biopsy forceps and subjected to RUT test by putting the collected sample in the specified portion of RUT kit. The RUT test was said to be positive when the colour of the RUT kit changed to pink colour within 24 hours of putting the antral tissue at specified spherical portion of the kit which was originally yellow coloured. Most of the results were positive within few minutes to 2 – 3 hours. Patients are categorized into RUT Positive and RUT negative patients depending on the test results.

Cirrhosis patients were scored based on modified Child-Pugh scoring system.

Table-1: Modified Child-Pugh score

CRITERIA	**POINTS**		
	1	**2**	**3**
Bilirubin (mg/dl)	<2	2-3	>3

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Albumin (g/dl)	>3.5	2.8-3.5	<2.8
Prothrombin time Prolonged in seconds International normalized ratio (INR)	<4 <1.7	4-6 1.7-2.3	>6 >2.3
Ascites	None	Mild to moderate (Diuretic responsive)	Severe (Diuretic resistant)
encephalopathy	None	Mild to moderate (grade 1 or 2)	Mild to moderate (grade 3 or 4)

Child-Turcotte-Pugh Class is obtained by adding score for each parameter Class A - 5 to 6 points (less severe)
Class B - 7 to 9 points (moderate)
Class C – 10 to 15 points (most severe)
Hepatic encephalopathy was graded using west haven criteria.
Oesophageal varices were classified as:[6]
Grade 1 – small, straight varices
Grade 2 – enlarged tortuous varices occupying less than one third of the lumen.
Grade 3 – large coiled varices occupying more than one third of the lumen, blue tone, blue extensions and red colour signs.
Grade 4 – bleeding varices.

Grade 1 and grade 2 were categorized into low grade varices. And grade 3 and grade 4 were categorized into high grade varices.
Portal hypertensive gastropathy was graded according Mc cormack classification Mild PHG – fine pink speckles, superficial redness, mosaic pattern.

Severe PHG – discrete red spots, black brown spots or diffuse hemorrhage. Ethical Considerations: The results of their assessment are shared with them and those needing medical Attention are given treatment according to the current guidelines.

Statistical Analysis: All the data is collected in approved proforma and entered in Excel 2007. All the statistical analysis is performed using Statistical Software SPSS 16.0 windows software. Continuous variables are expressed as titre of mean ± SD. Categoriable variables are expresses as proportions. Chi 2 test is used to study the association between proportions. All tests will be two sided and P value less than 0.05 is considered statistically significant.

RESULTS
Out of 100 patients, 52 tested positive for helicobacter pylori infection, while 48 tested negative.

Table-1: Demographic distribution in present study

	RUT positive	**RUT negative**
Number of patients	52	48
Mean age ± SD	48.55 ± 9.97	49.06 ± 12.52
Male	43 (82.6%)	36 (75%)
Female	9 (17.3%)	12 (25%)
Ethiology		
Alcohol	35	29
Hep B	2	8
Hep B + Alcohol	3	0
Hep C	2	2
Hep C + Alcohol	2	1
NASH	5	3
Others	3	5
All patients	52	48
P – value 0.21		

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The mean age of patients in RUT positive group is 48.5 years, RUT negative group is 49 years. No statistically significant difference was found between two groups.

In RUT positive patients 43 are male and 9 are female. In RUT negative patients 36 are male and 12 are female. No statistically significant difference was found between two groups.

Alcohol was most common cause in both the groups. RUT was negative in 8 out of 13 Hepatitis B cases. All patients with combined alcohol and hepatitis B were RUT positive. Statistically significant difference was not found in etiologies between two groups.

Table-2: Distribution of modified child pugh score

Child Pugh Score	**RUT positive**	**RUT negative**
A	12 (23%)	21 (43.7%)
B	24 (46.1%)	21 (43.7%)
C	16 (30.7%)	6 (12.5%)
	52	48
P – value 0.03		

In RUT positive group, 12 (23%), 24 (46.1%) and 16 (30.7%) patients had Child- Pugh score of A, B, C respectively.

In RUT negative group 21 (43.7%), 21 (43.7%) and 6 (12.5%) patients had Child- Pugh score of A, B, C respectively. With statistically significant difference between the two groups.

Table-3: Modified CHILD PUGH score results

	RUT positive	**RUT negative**	**P- value**
Total bilirubin (mean ± SD)	2.53 ± 1.50	1.82 ± 0.89	0.006
Albumin (mean ± SD)	2.75 ± 0.77	3.31 ± 0.69	0.002
Prothrombin time (mean ± SD)	15.76 ± 2.49	14.59 ± 2.22	0.016
Ascites: (n) None Mild Mod severe	 19 10 12 11	 29 8 7 4	
Encephalopathy: (n) None Low grade High grade	 41 8 3	 41 6 1	

In RUT positive group mean total bilirubin is 2.53 ± 1.50 whereas in RUT negative group is 1.82 ± 0.89. statistically significant difference was found between the two groups.

In RUT positive group mean albumin is 2.75 ± 0.77 whereas in RUT negative group is 3.31 ± 0.69. statistically significant difference was found between the two groups.

In RUT positive group mean prothrombin time is 15.76 ± 2.49 whereas in RUT negative group is 14.59 ± 2.22. statistically significant difference was found between the two groups.

Table-4: Modified CHILD PUGH score distribution

Distribution of Ascites	**RUT positive**	**RUT negative**
None	19 (36.5%)	29 (60.4%)
Mild	10 (19.2%)	8 (16.6%)
Moderate	12 (23%)	7 (14.5%)
severe	11 (21.1%)	4 (8.3%)
Distribution of encephalopathy		
NONE	41 (78.8%)	41 (85.4%)
LOW GRADE G1, G2	8 (15.3%)	6 (12.5%)
HIGH GRADE G3, G4	3 (5.7%)	1 (2%)
P – value 0.569		
Distribution of esophageal varices		
NONE	9 (17.3%)	37 (77%)
LOW GRADE G1, G2	27 (51.9%)	9 (18.7%)
HIGH GRADE G3,G4	16 (30.7%)	2 (4.1%)
P – value <0.005		

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In RUT positive patients 11 (21.1%) patients had severe ascites while 4 (8.3%) patients in RUT negative patients had severe ascites. But statistically significant difference was not found between two groups.

In RUT positive patients 41 (78.8%), 8 (15.3%) and 3 (5.7%) had none, low grade and high-grade encephalopathy respectively. In RUT negative patients 41 (85.4%), 6 (12.5%) and 1(2%) had none, low grade and high-grade encephalopathy respectively. No significant association was found between presence of helicobacter pylori infection and presence of encephalopathy.

In RUT positive patients 9 (17.3%), 27 (51.9%) and 16 (30.7%) had no varices, low grade varices and high-grade varices respectively. In RUT negative patients 37 (77%), 9 (18.7%) and 2 (4.1%) had no varices, low grade and high-grade varices respectively. As p value is <0.005, there is high significance between presence of high-grade varices in helicobacter pylori infected cirrhotics.

Table-5: Distribution of PHG

	RUT positive	**RUT negative**
None	19 (36.5%)	35 (72.9%)
Mild	16 (30.7%)	8 (16.6%)
severe	17 (32.6%)	5 (10.4%)
P – value 0.01		

In RUT positive group 19 (36.5%), 16 (30.7%) and 17 (32.6%) had no PHG, mild and severe PHG respectively. In RUT negative patients 35 (72.9%), 8 (16.6%) and 5 (10.4%) had no PHG, mild and severe PHG respectively. As p value is < 0.01, there is high significance between presence of helicobacter pylori infection and presence of severe PHG.

DISCUSSION

Out of total 100 patients of cirrhosis, 52 patients tested positive for helicobacter pylori infection, while 48 patients tested negative. Mean age of patients with RUT positivity is 48.55 ± 9.97 and mean age of patients with RUT negativity is 49.06 ± 12.52. with no statistically significant difference between two groups. In Girish Kumar et., al. study mean age of presentation of cirrhotic cases with RUT negativity was significantly higher (p – 0.02) compared to cases with H. pylori infection. Other previous studies found no significant difference in age between two age groups. In RUT positive patients 43 are male and 9 are female. In RUT negative patients 36 are male and 12 are female. There is no significant difference in gender between the two groups. This finding correlates with results from prior studies.[7]

Alcoholic etiology is more common in both the groups. Followed by chronic hepatitis B infection. No significant etiological difference was found between the two groups. Pogorzelski *et al*.[8] , reported that alcoholic liver disease was less susceptible to suffer from H. pylori infection compared to cirrhotic cases with post inflammatory (HBV and HCV related) and non-alcoholic background. Whereas Research by Sumida *et al*.[9] clearly points to high significance of H. pylori infection in patients with non-alcoholic fatty liver for the development of non-alcoholic steatohepatitis. Eradication of this bacteria significantly simplifies the therapy of fatty liver. These observations comply with the research by Hanafy *et al*. , who have demonstrated H. pylori infection in 70% (281/400) of patients chronically infected with HCV. A meta-analysis of 20 studies, performed by Wang *et al*.[10], clearly shows higher incidence of H. pylori infection among HCV-positive patients versus people not infected with the virus. In the study by Zhang *et al*.[11] performed in 225 patients chronically infected with HBV and compensated liver cirrhosis with thrombocytopenia, eradication of H. pylori irrespective of the antiviral therapy positively impacted the progression of the disease and increased platelet count. Such varied outcome regarding etiological factor requires further studies to validate its significance.

In our study higher Child Pugh severity score was more common among H. pylori infected patients compared with noninfected patients. With significant difference between two groups. Prior studies have similar findings . Ascites is more prevalent in helicobacter pylori infected patients with significant difference. Hepatic encephalopathy was found to be common among patients with helicobacter pylori infection with no significant difference.

Licinio *et al*[12]. argue for high probability of the influence of H. pylori infection on increase of portal hypertension, which is one of the most important causes of the development of esophageal varices. In our study, among RUT positive patients 9 (17.3%), 27 (51.9%) and 16 (30.7%) had no varices, low grade varices and high-grade varices respectively. In RUT negative patients 37 (77%), 9 (18.7%) and 2 (4.1%) had no varices, low grade and high-grade varices. As p value is <0.005, there is high significance between presence of high-grade varices in helicobacter pylori infected cirrhotic patients. Previous studies suggested that cirrhotic cases with H. pylori infection were not only more susceptible to development of esophageal varices but also are more prone to suffer from higher grade of esophageal varices, compared

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to cases without H. pylori infection, which suggests that possibly H. pylori infection has detrimental effect on liver function. This study results correlate with prior studies.
Sather *et al*.[13] reported that cirrhotic cases with H. pylori infection were not only more susceptible to suffer from PHG, but also more prone to suffer from higher grade of PHG. In this study, among RUT positive group 19 (36.5%), 16 (30.7%) and 17 (32.6%) had no PHG, mild and severe PHG respectively. In RUT negative patients 35 (72.9%), 8 (16.6%) and 5 (10.4%) had no PHG, mild and severe PHG. As p value is < 0.01, there is high significance between presence of helicobacter pylori infection and presence of severe PHG. These results are in correlation with prior studies.

Our study has some limitations, it is a single centre study in a tertiary care centre. The sample size obtained is small and is not adequate to analyse other outcomes. It is not a prospective study and could not evaluate the results of helicobacter pylori treatment.

CONCLUSION

This study has shown the prevalence of 52% helicobacter pylori infection in patients with cirrhosis. There is no correlation of age and gender with helicobacter pylori infection in patients with cirrhosis. Alcohol is the most common etiology in both helicobacter pylori infected and non-infected group. Etiological difference is not significant between both the groups. Prior studies have shown difference in prevalence of helicobacter pylori infection in different etiological groups. Further studies are required to validate this point. Presence of ascites and severity correlates with presence of helicobacter pylori infection. Patients with H. pylori infection had relatively higher prevalence of higher grade of EV, PHG, compared to patients without H. pylori infection.

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