Original Article

Association of *Helicobacter Pylori* and Portal Hypertensive Gastropathy in Patients with Cirrhosis of Liver

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Abstract

Portal hypertensive gastropathy (PHG) is a common endoscopic finding in patients of cirrhosis of liver. The cause and pathogenesis of PHG in cirrhotic patients is poorly understood. Some studies showed, association of Helicobacter pylori (H. Pylori) with portal hypertensive gastropathy in cirrhosis of liver, but the evidence is not robust. The aim of this study was to assess the association of H. pylori infection and PHG in patients with cirrhosis of liver. This case control study was conducted in the Department of Gastroenterology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, from April 2016 to August 2018. A total of 230 patients with cirrhosis of liver were included in this study. There were 115 cirrhotic patients with PHG as cases and 115 cirrhotic patients without PHG as controls. Upper gastrointestinal Endoscopy and 13C Urea Breath Test (UBT) was done in both cases and controls. In this study, out of 230 cases, 147 (63.91%) found to have H. pylori infection. Among cirrhotic patients with PHG case, 77 (66.95%) was positive in UBT. Out of these 77 UBT positive cases, 55 had mild PHG whereas 22 cases had severe form of PHG. Among 38 cases of cirrhosis with PHG who had negative UBT, 23 had mild PHG and 15 cases had severe form of PHG. The risk of positive urea breath test was not statistically significant in cirrhotic patients with PHG in comparison with cirrhotic patients without PHG (P=0.337, OR 1.303, 95% CI 0.759-2.235). In this study, statistically significant association was not found between H. Pylori and PHG in cirrhotic patients.

Keywords: Cirrhosis of liver, *helicobacter pylori (H. Pylori),* portal hypertensive gastropathy (PHG)

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INTRODUCTION

Portal hypertension is a common condition in cirrhosis of liver. When hepatic venous pressure gradient (HVPG) >5mmHg is called portal hypertension.[1] Cirrhosis of liver, non-cirrhotic portal fibrosis and extra hepatic portal vein obstruction are common causes of portal hypertension. Gastrointestinal haemorrhage, hepatic encephalopathy, hepato-renal syndrome, ascites are common complications of portal hypertension.[2] Liver cirrhosis and portal hypertensive gastropathy patients are very prone to develop acute or chronic GI bleeding.[3,4] Prevalance of portal hypertensive gastropathy in cirrhotic patients is approximately 9-80%.[5,6,7,8] Portal hypertensive gastropathy causes change in the mucosa of the stomach in patients with portal hypertention. The most common cause of this is cirrhosis of liver. Mucosal changes occur in PHG including friability of mucosa and the presence of erratic blood vessels.[9]

PHG is common both in cirrhotic and non-cirrhotic portal hypertension. The endoscopic findings of PHG is mosaic-like pattern of gastric mucosa.[10] Whole of the stomach can be involved in portal hypertensive gastropathy (PHG). Not only mucosal changes but also the severity mosaic pattern and red spots increase bleeding risk.[11,12]

Numerous mechanisms are involved in the development of PHG. High gastrin level causes huge amount of acid secretion and altered blood flow, reduced prostaglandin secretion and the presence of *H. pylori* infection.[13,14,15,16] In PHG gastric mucosal ability to regenerate has lost.[17] Another study showed increased susceptibility of portal

hypertensive gastropathy by bile acid and *H. pylori* infection [18].

H. pylori is a gram negative organism is found in gastric mucosa or between the epithelial and mucous layer of stomach. In developing country the prevalence of *H.pylori* is higher than the developed countries[17].The prevalence and association of *H.pylori* in cirrhosis of liver is under debate[18,19,20]. *H. pylori* infection is one of the most common cause of peptic ulcer disease. In cirrhosis of liver *H.pylori* may have a role in developing PHG[21,22].

Sensitivity and specificity of serological test to diagnose *H.pylori* is very low. Other than *H.pylori* , no bacteria is found to be involved in the development of PHG[24].

PHG does not provide a favorable environment for colonization by *H. pylori*, suggesting no contribution of the bacteria in the pathogenesis of PHG[25].

Urea breath test (UBT) which is widely used to diagnose *H.pylori* infection.UBT relies on bacterial hydrolysis of orally administered urea tagged with a carbon isotope ^{13}C. Hydrolysis of urea generates ammonia and tagged CO2 which can be detected in breath samples. The specificity of UBT is 95% and sensivity is about 80-95%[26] .Association of *H. pylori* with PHG is still now a debating issue. The mucosal lesion of stomach and several extra-gastric conditions are associated with *H.pylori* infection. Unexplained vitamin B12 deficiency, Idiopathic thrombocytopenic purpura (ITP) and Iron deficiency anaemia (IDA) is associated with *H.pylori* infection[28]. If *H. pylori* is associated with portal hyperensive gastropathy eradication of *H. pylori* may be beneficial in the management of PHG, if *H. p.* To the best of our knowledge, in Bangladesh no such study has been carried out. So this study was carried out to find out the association of *H. pylori* infection with PHG in patients with cirrhosis of liver.

MATERIAL AND METHODS

This case control study was conducted in the Department of Gastroenterology, BSMMU, Dhaka, Bangladesh during the period of April 2016 to August 2018. A total of 230 patients with cirrhosis of were included in this study. There were 115 cirrhotic patients with PHG as cases and 115 cirrhotic patients without PHG as controls. Patients with age < 18 years, peptic ulcer disease found in upper gastrointestinal endoscopy, patients with intake of proton pump inhibitors, bismuth compounds, antibiotics (within 2 weeks), *H. pylori* eradication within past 2 month, patients on NSAIDs or history of gastric surgery were excluded from the study.

DATA COLLECTION

At first, stable cirrhotic patients were selected for study as per inclusion and exclusion criteria. After proper counseling an informed written consent was taken from every participant. Information about demographic and clinical profile and laboratory parameters was collected on the predesigned data sheet. Detailed clinical history including history of jaundice, drug abuse, alcohol intake, blood transfusion, haematemesis, melaena etc was elicited from the participants. General physical and systemic examination was done for presence of ascites, splenomegaly and other peripheral signs of liver cirrhosis such as jaundice, palmar erythema, spider naevi, alopecia, gynaecomastia, testicular atrophy etc. Complete blood count, liver function tests including serum bilirubin, aminotransferase (ALT, AST) enzymes level ANA, 24 hours' urinary copper, prothrombin time, serum albumin, viral markers (HBsAg, Anti-HCV), renal function test and imaging by abdominal ultrasound was done.

Endoscopy of upper gastrointestinal tract was performed in a single endoscopy unit using a video endoscope (OLYMPUS GIF-H190) at gastroenterology department of BSMMU to identify the presence of portal hypertensive gastropathy, assess its severity and also oesophageal or fundal varices. Upper GI endoscopy was done by single endoscopist to avoid interovserber variability. The severity of PHG was graded according to McCormack's classification and the severity of liver cirrhosis was assessed by using Child-pugh classification.

^{13}C UBT was performed to identify *H. pylori* infection at gastroenterology department of BSMMU in accordance with the manufacturer's recommendations (HCBT-01, Headway ^{13}C Urea Breath Analyzer, China). UBT was done after an abstinence of proton pump inhibitor, antibiotics, bismuth compounds for two weeks and fasting for 6 hours on the day of procedure.

STATISTICAL ANALYSIS

After collection of data, all data were checked and cleaned. After cleaning, the data were entered into computer and statistical analysis of the results being obtained using Statistical Packages for Social Sciences (SPSS). Numerical variables were expressed as mean and standard deviation, whereas categorical variables were expressed in percentage. Numerical variables were compared using student's t test

and categorical variables were analyzed by Chi-square test. The risk was expressed in odd's ratio with 95% confidence interval (CI). P value of less than 0.05 was considered statistically significant.

ETHICAL CONSIDERATION

Before starting this study, the research protocol was submitted to the institutional review board of BSMMU, Dhaka and IRB clearance was taken. All participants were informed about the objectives, methodology and purpose of the study in easily understandable way. Informed written consents were obtained from all participants without any influences prior to sample collection.

RESULTS

This case control study was conducted in the Department of Gastroenterology, BSMMU, Dhaka, Bangladesh during the period of April 2016 to August 2018. A total of 230 patients with cirrhosis were included in this study. There were 115 cirrhotic patients with PHG as cases and 115 cirrhotic patients without PHG as controls.

Table I shows the age distribution of the study patients according age-group in patients of cirrhosis with or without PHG. Most of the patients were of age more than 40 years in both groups. The mean age was 54.37 years for cases and 52.03 years for controls. The age difference among the cases and controls was not significant.

Table I: Distribution of the patients according to age in two groups

Age (years)	Cases (n=115) n (%)	Controls (n=115) n (%)	p value
21 – 30	2 (1.7)	4 (3.5)	0.109ns
31 – 40	12 (10.4)	20 (17.4)	
41 – 50	31 (27.0)	31 (27.0)	
51 – 60	37 (32.2)	32 (27.8)	
>60	33 (28.7)	28 (24.3)	
Mean±SD	54.37 ± 10.97	52.03 ± 11.05	

Ns=not significant

Unpaired t test was done to measure the level of significance

Table II shows the gender distribution of cases ad controls. There were 88 (76.5%) male and 27 (23.5%) female patients of cirrhosis with PHG and 83(72.2%) of male and 32 (27.8%) of female cirrhotic patients of cirrhosis without PHG. There was no significant gender difference in cases and controls.

Table II: Distribution of the patients according to gender in two groups

Gender	Cases (n=115) n (%)	Controls (n=115) n (%)	p value
Male	88 (76.5)	83 (72.2)	0.450ns
Female	27 (23.5)	32 (27.8)	

ns= not significant

Chi-square test was done for the level of significance.

Table III shows the distribution of study patients according to clinical features. The cases and controls show no significant differences in presentation of clinical features.

Table III: Distribution of the patients according to clinical features in two groups

Clinical feature	Cases (n=115) n (%)	Controls (n=115) n (%)	p value
Jaundice	30 (26.1)	19 (16.5)	0.096ns
Ascites	94 (81.7)	83 (72.2)	0.085ns
Leg oedema	73 (63.5)	61 (53.0)	0.109ns
Anaemia	73 (63.5)	63 (54.8)	0.180ns
Leukonychia	10 (8.7)	7 (6.1)	0.450ns
Spider	18 (15.7)	17 (14.8)	1.000ns
Splenomegaly	62 (53.9)	51 (44.3)	0.147ns

ns= not significant

Chi-square test was done to measure the level of significance

Table IV shows the laboratory parameters in cases and controls. The patients of cases and controls had no significant difference in the laboratory finding.

Table IV: Investigation findings of the patients in two groups

Investigations	Cases (n=115) [mean±SD]	Controls (n=115) [mean±SD]	p value
Hb (g/dl)	10.77 ± 1.40	11.08 ± 1.14	0.066ns
ESR (mm in 1st hour)	49.64 ± 16.75	45.89 ± 17.55	0.098ns
TC (No/mm3)	6196.35 ± 2164.04	6648.69 ± 1819.77	0.088ns
Platelet count (per mm3)	131426.09 ± 95576.63	151464.91 ± 56544.94	0.055ns
Serum creatinine (mg/dl)	1.05 ± 0.27	1.00 ± 0.27	0.225ns
Na+ (meq/L)	132.62 ± 4.30	133.56 ± 4.61	0.109ns
K+ (meq/L)	3.91 ± 0.44	4.02 ± 0.40	0.057ns
ALT (U/L)	38.98 ± 21.28	36.74 ± 12.48	0.331ns
AST (U/L)	49.96 ± 26.33	48.28 ± 21.77	0.600ns
S. Bilirubin (mg/dl)	1.75 ± 1.08	1.48 ± 1.10	0.063ns
S. Albumin (g/L)	25.11 ± 5.07	26.13 ± 3.46	0.075ns
Prothrombin time			
Control	11.90 ± 0.16	11.88 ± 0.12	0.252ns
Patient	17.32 ± 3.31	16.71 ± 2.61	0.119ns
INR	1.46 ± 0.29	1.41 ± 0.25	0.189ns

ns=not significant

Unpaired t test was done to measure the level of significance

Table V shows the case and control patients of cirrhosis with different etiology. There were 63 (54.7%) patients in cases and 60 (52.1%) patients in controls with CHBV infection. Chronic hepatitis C virus infection was found in 11 (9.6%) of patients in cases and 14 (12.2%) of patients in controls as a cause of cirrhosis. There was no etiological difference among the cases and controls.

Table V: Distribution of the patients according to etiology in two groups (n=230)

Etiology	Cases (n=115) n (%)	Controls (n=115) n (%)	p value
HBsAg	48 (41.7)	43 (37.4)	0.500ns
HbsAg-Anti-HBc	15 (13.0)	17 (14.7)	0.849ns
Anti HCV	11 (9.6)	14 (12.2)	0.525ns

ns=not significant

Chi-square test was done to measure the level of significance

Table VI shows the distribution of cases and controls according to Child-Pugh score. Most of the patients of cases and controls were of Child-Pugh class B and Child-Pugh class C. There were no significant difference in the Child-Pugh class of cases and controls.

Table VI: Distribution of the patients according to Child pugh score in two groups

Child Pugh Class	Cases (n=115) n (%)	Controls (n=115) n (%)	p value
A	12 (10.4)	20 (17.5)	0.074ns
B	48 (41.7)	55 (48.2)	
C	55 (47.8)	39 (34.2)	

ns= not significant

Chi-square test was done to measure the level of significance

Table VII shows the distribution of cases according to grade of PHG. There were78(67.8%) of patients with mild PHG whereas 37(32.2%) of patients had severe PHG.

Table VII: Distribution of cases according to grade of PHG (n=115)

PHG	Frequency (n)	Percentage (%)
Mild	78	67.8
Severe	37	32.2

Table VIII shows distribution of patients according to the test result of UBT. There were 77 (67.0%) patients of case and 70 (60.9%) patients of control with positive UBT. There were 38 (33.0%) patients of case and 45 (39.1%) patients of control had negative UBT. There was no statistically significant difference in test result among the cases and controls with OR 1.303 at 95% CI, 0.759-2.235. Patients with PHG did not have significant increase risk of H.pylori infection.

Table VIII: Distribution of the patients according to ^{13}C Urea Breath Test in two groups

^{13}C Urea Breath Test	Cases (n=115) n (%)	Controls (n=115) n (%)	p value	OR (95% CI)
Positive	77 (67.0)	70 (60.9)	0.337ns	1.303 (0.759-2.235)
Negative	38 (33.0)	45 (39.1)		

ns= not significant

Chi-square test was done to measure the level of significance

Table IX shows the distribution and association of *H. pylori* with severity of PHG. Out of 77 *H. pylori* positive patients with PHG, 55 patients had mild PHG whereas 22 patients had severe form of PHG. There were 38 patients with PHG had negative UBT out of which 23 had mild PHG and 15 patients had severe form of PHG. There was no significant association among the patients of *H. pylori* infection and severity of PHG (p= 0.290).

Table IX: Association of *H. pylori* with severity of PHG (n=115)

PHG	H. pylori		p value
	Positive (n=77) n (%)	Negative (n=38) n (%)	
Mild(78)	55 (70.5)	23 (29.5)	0.290ns
Severe(37)	22 (59.5)	15 (40.5)	

ns= not significant

Chi-square test was done to measure the level of significance

DISCUSSION

This case control observational study was conducted in the Department of Gastroenterology, BSMMU. The objective of the study was to find out the association of *H. Pylori* infection with PHG in the patients of cirrhosis of liver. We included 115 patients as cases (cirrhosis of liver with PHG) and 115 patients as controls (cirrhosis of liver without PHG) for this study who attended inpatient and outpatient department of Gastroenterology, BSMMU during the study period.

In the present study, the mean age of patients was 54.37 ± 10.97 years in cases and 52.03 ± 11.05 years in controls with majority of patients were from fourth to sixth decade of life with no significant difference of age (p=0.109). A study was conducted in India in 2014 to see the association of H. pylori with PHG and the mean age of cases was 54.80±10 years and mean age of controls was 52.09 ± 10.3 years which was almost similar to this study[24]. The gender distribution of the cases and controls in our study were well-matched with no significant difference (p=0.450).

Regarding clinical feature, jaundice was present in 26.1% cases and in 16.5% controls. 81.7% patients in case group had ascites whereas 72.2% patients in control group presented with ascites. Aforementioned study showed ascites in 71.4% cases and in 58.6% controls[24]. Anaemia was more common in cases (63.5%) than controls (54.8%) which may reflect bleeding from PHG in case group but not reached statistical significance (p=0.180). Splenomegaly, a cardinal feature of portal hypertension, was present in 53.9% cases and in 44.3% controls.

In our study we found that chronic HBV was the most common etiology of cirrhosis of liver (41.7% in case group and 37.4% in control group) followed by chronic HCV (9.6% in case group and 12.2% in control group). Whereas HBV in 21.4% cases and in 25% controls, alcohol in 48.6% cases and in 52% controls were in previous study. HBV was the most common cause of cirrhosis in our study which may be due to higher prevalence of HBV in our country.

We quantified the severity of liver disease using the Child Pugh classification. In case group twelve patients (10.04%) had liver cirrhosis with Child class A, 48 (41.7%) Child class B and 55 (47.8%) Child class C whereas the frequency in control group was 20%, 55% and 39% respectively. Our study showed no significant difference between cases and controls regarding Child-Pugh classes, with most of the patients from Child-Pugh B and Child-Pugh C (p=0.074).

In our study, out of 230 patients with cirrhosis, 147 patients were *H. pylori* positive with overall proportion of *H. pylori* infection was 63.91%, which was comparable to another study done by Abbas *et al.*[29] who found a prevalence of *H. pylori* was 62.1% and Safwat *et al*[30]. who found prevalence of *H. pylori* was 60%.

The concern of our study was to find out the association of H. pylori with portal hypertensive gastropathy in cirrhosis of liver. In our study, we had positive UBT in 77 (67.0%) patients of cirrhosis with PHG and 70 (60.9%) patients of cirrhosis without PHG. Thirty-eight patients with PHG had negative UBT out of which 23 had mild PHG and 15 patients had severe form of PHG. There was no significant association of *H. pylori* with presence of PHG in cirrhotic patients (p= 0.337 with OR 1.303 at 95% CI: 0.759-2.235). Hammad *et al.*[31] conducted a similar study in Egypt and reported *H. pylori* infection among 70% cases and 63.3% controls and insignificant association of *H. pylori* with PHG.

The severity of PHG was mild in 55 *H. pylori* positive patients and 23 *H. Pylori* negative patients whereas severe PHG was present in 22 *H. pylori* positive and 15 *H. Pylori* negative patients. The severity of PHG and *H. Pylori* infection had no significant association in cirrhotic patients. These findings were similar as studied by Bahnacy *et al* [32]. *H. pylori* positivity decreased when the severity of PHG increased. As there is severe hemorrhagic congestion and oedema of the gastric mucosa in PHG, so it may not provide a favourable environment for the colonization of *H. pylori*. In contrast Sathar *et al.*[24] and Safwat *et al.* [30] had noticed a significant association between *H. pylori* and severity of PHG ($p< 0.001$). They had suggested that *H. pylori* colonization of the stomach of cirrhotic patients likely to be contributory to the pathogenesis of PHG.

CONCLUSIONS

No significant association was found between *H. pylori* infection and PHG in cirrhotic patients in this study. The data also showed that, severity of PHG was not associated with *H. pylori* infection. Further prospective studies with a large number of samples are required to see the association of *H. pylori* with PHG.

REFERENCES

1. Bacon BR. Cirrhosis and its Complications. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J (editors). Harrison's Principle of Internal medicine. USA: Mc Graw-Hill Companies Inc; 2012: 308.
2. Nusrat S, Khan MS, Fazili J, Madhoun MF. Cirrhosis and Its Complications: Evidence Based Treatment. World Journal of Gastroenterology 2014; 20(18):5442-5460.
3. Rabinovitz M, Yoo Y, Schade RR, Dindzans VJ, Thiel DH, Gavaler JS. Prevalence of endoscopic findings in 510 consecutive individuals with cirrhosis evaluated prospectively. Dig Dis Sci 1990; 35:705-710.
4. de Franchis R and Primignani M. Natural history of portal hypertension in patients with cirrhosis. ClinLiver Dis 2001; 5: 645-663. Primignani M, Carpinelli L, Preatoni P, Battaglia G, Carta A, Prada A et al. Natural history of portal hypertensive gastropathy in patients with liver cirrhosis. The New Italian Endoscopic Club for the study and treatment of esophageal varices (NIEC). Gastroenterology 2000; 119:181-187.
5. Primignani M, Carpinelli L, Preatoni P, Battaglia G, Carta A, Prada A et al. Natural history of portal hypertensive gastropathy in patients with liver cirrhosis. The New Italian Endoscopic Club for the study and treatment of esophageal varices (NIEC). Gastroenterology 2000; 119:181-187.
6. Iwao T, Toyonaga A, Sumino M, Takagi K, Oho K, Nishizono M et al. Portal hypertensive gastropathy in patients with cirrhosis. Gastroenterology 1992; 102:2060-2065.
7. Sarin SK, Shahi HM, Jain M, Jain AK, Issar SK, Murthy NS. The natural history of portal hypertensive gastropathy: influence of variceal eradication. Am J Gastroenterol 2000; 95: 2888-2893.
8. Zaman A, Hapke R, Flora K, Rosen HR, Benner K.Factors predicting the presence of esophageal or gastric varices in patients with advanced liver disease. Am J Gastroenterol 1999; 94: 3292-3296.
9. Garcia-Tsao G and Ripoll C. Management of Gastropathy and Gastric Vascular Ectasia in Portal Hypertension. Clin Liver Dis. 2010; 14(2): 281-295.
10. Cubillas R and Rockey C. Portal hypertensive gastropathy: a review. Liver International. 2010; 1094-1102.

11. Primignani, M. et al. 'Natural history of portal hypertensive gastropathy in patients with liver cirrhosis. The New Italian Endoscopic Club for the study and treatment of esophageal varices (NIEC).' Gastroenterology, 2000:119, pp. 181–187.
12. Ferraz, J.G and Wallace J.L.'Underlying mechanisms of portal hypertensive gastropathy.' J Clin Gastroenterol, 25 (Suppl 1), pp. S73–S78.
13. Sarfeh, I.J., Tarnawski, A., Mason, G.R., Mach, T., Ivey, R.J. 'Portal hypertension and gastric mucosal injury in rats.'Gastroenterology, 1983:84, pp.987-993.
14. Sarfeh, I.J., Tarnawski, A., Maeda, R., Raymont, K., Mason, G.R., Ivey, K.J. 'The gastric mucosa in portal hypertension: effects of topical bile acid.' Scand J Gastroenterol, 1984:9(Suppl 92), pp.189-194.
15. Hopkins, R.J., Girardi, L.S., Turney, E.A.'Relationship between Helicobacter pylori eradication and gastric ulcer and duodenal ulcer reduced recurrence: a review.' Gastroenterology, 1996:110, pp.1244-1252.
16. Akatsu, T. et al. 'Consequences of living-donor liver transplantation for upper gastrointestinal lesions: High incidence of reflux esophagitis.' Dig Dis Sci, 2006:51, pp. 2018–2022.
17. Sarfeh, I.J., Soliman, H., Waxman, K., Coccia, M., Rypins, E.B., Bui, H.X., Tarnawski A.'Impaired oxygenation of gastric mucosa in portal hypertension. The basis for increased susceptibility to injury.' Dig Dis Sci, 1989:34, pp. 225-228.
18. Edward, Lew. 'Peptic Ulcer Disease'. Current Diagnosis &Treatment, Gastroenterology, Hepatology,& Endoscopy. 3rd edition, McGraw-Hill Education, 2016:15:197-208.
19. Pellicano, R., Leone, N., Berrutti, M., Cutufia, M.A., Fiorentino, M., Rizzetto, M. 'Helicobacter pylori seroprevalence in hepatitis C virus positive patients with cirrhosis.' J Hepatol,2000: 33, pp.648-650.
20. Tsai, C.J. 'Helicobacter pylori infection and peptic ulcer disease in cirrhosis.' Dig Dis Sci, 1998:43, pp.1219-1225.
21. Yeh, J.L., Peng, Y.C., Tung, C.F. et al. 'Role of Helicobacter pyloriin cirrhotic patients with dyspepsia: a 13C-urea breath test study.' Adv Ther, 2001:18, pp.140-150.
22. Kamalaporn, P. et al. 'Factors predisposing to peptic ulcer disease in asymptomatic cirrhotic patients.' Aliment Pharmacol Ther, 2005:21, pp. 1459–1465.
23. Urso, G. et al. 'Role of Helicobacter pylori in patients with portal hypertensive gastropathy by liver cirrhosis hepatitis C virus-related.' Minerva Gastroenterol Dietol, 2006:52, pp.303–308.
24. Sathar, S.A., Kunnathuparambil, S.G., Sreesh, S., Narayanan, P., Vinayakumar, K.R. 'Helicobacter pylori infection in patients with liver cirrhosis: prevalence and association with portal hypertensive gastropathy.' Ann Gastroenterol, 2014:27, pp. 48-52.
25. Batmanabane, V., Kate, V., Ananthakrishnan, N. 'Prevalence of Helicobacter pylori in patients with portal hypertensive gastropathy - a study from South India.' Med Sci Monit, 2004:10, pp.133-136.
26. Douglas, R. Morgan & Sheila E. Crowe. CHelicobacter pylori infection'. Sleisenger and Fordtran's Gastrointestinal and Liver disease. 10th edition, Philadelphia, Elsevier, Saunders, 2016:51, pp.856-867.
27. Merli M et al. 'The natural history of portal hypertensive gastropathy in patients with liver cirrhosis and mild portal hypertension.' Am J Gastroenterol, 2004:99, pp. 1959–1965.
28. El-omar E, McLean MH. 'Davidson's Principles and Practice of Medicine'.23rd edition, Philadelphia, Elsevier,2018,pp.764-842.
29. Abbas, Z., Yakoob, j., WM, u., T, S., Hamid, S., Jafri, W.Effect of Helicobacter pylori and its virulence factors on portal hypertensive gastropathy and interleukin (IL)-8, IL-10, and tumor necrosis factor-alpha levels. Saudi Journal of Gastroenterology., 2014:20(2), 120-127.
30. Safwat E, Hussein HA and Hakim SA. 'Helicobacter pylori in Egyptian patients with HCVrelated liver cirrhosis and portal hypertensive gastropathy': Prevalence and relation to disease severity. Life Sci J 2015;12(3):168-173.
31. Hammad OM.'correlation of Portal hypertensive gastropathy with Helicobacter pylori infection, liver dysfuntion, hypersplenism and oesophageal varices.Medical J Cario Univ;77:597-601.
32. Bahnacy, A., Kupcsulik, P., Eles, Z., et al. 'Helico-bacter pylori and congestive gastropathy.' Z. Gastroenterol., 1997:35, pp.109-12.