CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187
http://doi.org/10.5281/zenodo.4318854

Avalable online at: http://www.iajps.com *Research Article*

HELICOBACTER PYLORI INFECTION IN PATIENTS WITH HCV-ASSOCIATED LIVER CIRRHOSIS AND ITS ASSOCIATION WITH THE SEVERITY OF PORTAL HYPERTENSIVE GASTROPATHY

[1]Dr Momal Jaleel Khan, [2]Dr Sara Sahar, [3]Dr Nida E Zahra

[1]Sheikh Zayed Hospital, Rahim Yar Khan., [2]Quaid-e-Azam Medical College, Bahawalpur.,
[3]Quaid-e-Azam Medical College, Bahawalpur.

Article Received: October 2020 **Accepted:** November 2020 **Published:** December 2020

Abstract:

Aim of the study: *Helicobacter pylori infection is a serious health problem as approximately 50% of all people in the world are infected with Helicobacter pylori. Portal hypertensive gastropathy (PHG), a term used to describe the endoscopic appearance of the gastric mucosa with a characteristic mosaic-like pattern with or without red spots, is a common symptom in patients with portal hypertension. The role of H. pylori infection in the severity of Portal hypertensive gastropathy is controversial, so we are trying to prove whether there is any role for H. pylori infection and the severity of PHG.*

Place and Duration: *In the Medicine Unit-II of Sheikh Zayed Hospital, Rahim Yar Khan for one-year duration from September 2019 to September 2020.*

Patients and Methods: *Eighty consecutive patients with HCV-associated cirrhosis were enrolled in the study. The diagnosis of H. pylori infection was made by detecting H. pylori Ag in the feces by ELISA. 80 consecutive patients with HCV-related cirrhosis were enrolled in the study. All patients underwent upper gastrointestinal endoscopy and an ELISA test for H. pylori Ag in the stool. The diagnosis and severity of portal hypertensive gastropathy (PHG) was assessed during endoscopy. Child-Pugh and MELD scores were calculated to assess the severity of cirrhosis.*

Results: *H. pylori infection was reported in 46 patients, with the overall frequency of 57.5%. PHG was found in 57 patients (71.25%); Of these, 36 (63.15%) had mild and 21 (36.15%) severe PHG. H. pylori was more common in patients with PHG than without PHG (57.5% vs 42.5%; p <0.001). There was no significant association between H. pylori infection and the severity of cirrhosis according to Child-Pugh (p = 0.383) and MELD (p = 0.666).*

Conclusion: *Our results showed a significant association between H. pylori infection and the incidence and severity of PHG in patients with HCV-associated cirrhosis. However, the severity of cirrhosis in itself did not correlate with H. pylori or the severity of PHG. Thus, eradication of H. pylori may be beneficial for improving PHG.*

Key words: *portal hypertensive gastropathy, Helicobacter pylori, liver cirrhosis.*

Corresponding author:
Dr Momal Jaleel Khan
Sheikh Zayed Hospital, Rahim Yar Khan.

QR code

Please cite this article in press Momal Jaleel Khan et al, ***Helicobacter Pylori Infection In Patients With Hcv-Associated Liver Cirrhosis And Its Association With The Severity Of Portal Hypertensive Gastropathy.,*** *Indo Am. J. P. Sci, 2020; 07(12).*

INTRODUCTION:

Cirrhosis of the liver is a serious health problem with a high incidence and distribution worldwide. It is associated with changes in the gastrointestinal mucosa, with an increased risk of gastric ulcer disease. Portal hypertensive gastropathy (PHG) is one of the clinically important changes in the gastric mucosa as it can cause acute or chronic gastrointestinal blood loss leading to anemia. It is characterized by the endoscopic appearance of the gastric mucosa, which is classically described as a mosaic pattern that resembles a snake's skin, with or without red spots. H. pylori infection is highly prevalent, especially in the weaker socioeconomic strata of developing countries, responsible for lesions such as gastric and duodenal erosions and ulcers. In patients with cirrhosis, their incidence is controversial, as is the association with PHG.

PATIENTS AND METHODS:

This study was conducted in the Medicine Unit-II of Sheikh Zayed Hospital, Rahim Yar Khan for one-year duration from September 2019 to September 2020. Eighty (80) consecutive HCV-related cirrhosis patients were enrolled in this study. Informed consent was obtained from each patient. At least one of the following diseases was excluded from the study: patients with primary or secondary liver cancer, a history of gastric surgery, cirrhosis of the liver of any etiology other than HCV, bleeding from the upper gastrointestinal tract or previous endoscopic treatment for portal hypertension or prophylactic or therapeutic treatment , history of antibiotic use (up to 1 month) or prior therapy for eradication of H. pylori or proton pump inhibitors or H2 blockers within 4 weeks of endoscopy, and patients treated for portal hypertension (e.g. non-selective beta blockers, carvidalol). All patients enrolled in this study underwent a full medical history, full clinical examination, laboratory tests to assess liver health and ensure the diagnosis of HCV infection, abdominal ultrasound performed on all patients using a Toshiba real-time scanner with a 3.5 MHz convex head for assessment of the liver, spleen, portal vein diameter, the presence of collateral protections and the presence or absence of ascites and its degree. The severity of liver disease was assessed using the Child-Pugh classification, including total bilirubin, albumin, international normalized ratio (INR) or prothrombin time, hepatic encephalopathy, and ascites. The End-Stage Liver Disease (MELD) model, which has been calculated from serum bilirubin, the international normalized ratio of prothrombin time and serum creatinine, offers an objective result that accurately predicts the risk of short-term mortality from chronic liver disease. MELD result = 3.8 x log (serum bilirubin) + 11.2 x log (INR) + 9.6 x log (serum creatinine). Fecal helicobacter pylori Ag was performed two days prior to endoscopic examination by ELISA. All patients underwent endoscopy of the upper gastrointestinal tract using the Pentax EG-3440 videoscope in order to: identify esophageal varices and classify using the Paquet scale. The diagnosis and severity of PHG were classified according to criteria established by the McCormack classification.

Statistical analysis of data:

The data was entered into a computer and analyzed using the IBM SPSS 20.0 software package

RESULTS:

80 patients with HCV-related cirrhosis were enrolled in the study. They were 42 men (52.5%) and 38 women (47.5%); and their age ranged from 38 to 66 years (mean age 51.96 ± 7.02 years). Detection of H. pylori infection showed that 46 patients (57.5%) were positive and 34 patients (42.5%) were negative. Endoscopic examination revealed 57 patients with PHG (71.25%) and 23 patients without PHG (28.75%). The patients were divided into two groups. Group with PHG and group without PHG. In the PHG group, 36 patients (63.16%) had mild PHG and 21 patients (36.84%) had severe PHG. Demographic data showed that age was significantly higher in patients with PHG ($p = 0.014$). There was no significant difference between the two groups in terms of sex ($P = 0.333$) (Table 1).

Table 1: comparison between patients with PHG and patients without PHG according to the demographic data.

	Without PHG (n = 23)		With PHG (Mild/Severe) (n = 57)		Total (n = 80)		P
	No.	%	No.	%	No.	%	
Sex							
Male	10	43.5	32	56.1	42	52.5	0.333
Female	13	56.5	25	43.9	38	47.5	
Age (years)							
Min. – Max.	38.0 – 66.0		39.0 – 66.0		38.0 – 66.0		
Mean ± SD.	48.96 ± 7.64		53.18 ± 6.44		51.96 ± 7.02		0.014*
Median	49.0		54.0		53.0		

Compared to radiographs in both groups, all PHG patients had splenomegaly (P> 0.001), ascites severity (P> 0.001), and portal vein dilation (P> 0.001) were significantly higher in patients with PHG. When it comes to comparing endoscopic data between the two groups, the presence of esophageal varices was highly significant and more severe in patients with PHG (P> 0.001) (Table 2).

Table 2: comparison between patients with PHG and patients without PHG according to the esophageal varices

	Without PHG (n = 23)		With PHG (Mild/Severe) (n = 57)		Total (n = 80)		Test of sig.	p
	No.	%	No.	%	No.	%		
Esophageal varices								
0	20	87.0	2	3.5	22	27.5	χ^2=57.667*	<0.001*
1	2	8.7	18	31.6	20	25.0		
2	1	4.3	22	38.6	23	28.8		
3	0	0.0	15	26.3	15	18.8		
4	0	0.0	0	0.0	0	0.0		

The presence of H. pylori infection was significantly higher in the PHG group (79%) compared with patients without PHG (4%) and (P> 0.001) (Table 3).

Table 3: relation between H. pylori infection and PHG

	Without PHG (n = 23)		With PHG (Mild/Severe) (n = 57)		Total (n = 80)		χ^2	P
	No.	%	No.	%	No.	%		
H. Pylori								
Negative	22	95.7	12	21.1	34	42.5	37.319*	<0.001*
Positive	1	4.3	45	78.9	46	57.5		

There was a significant relationship between H. pylori infection and the severity of PHG (P3 = 0.021) (Table 4).

Table 4: comparison between the severity PHG and H. pylori

	Without PHG (n = 23)		With PHG				Total (n = 80)		P
			Mild (n = 36)		Severe (n = 21)				
	No.	%	No.	%	No.	%	No.	%	
H. pylori Negative	22	95.7	11	30.6	1	4.8	34	42.5	<0.001*
Positive	1	4.3	25	69.4	20	95.2	46	57.5	
Sig.bet. Grps	$p_1<0.001^*$, $p_2<0.001^*$, $p_3=0.021^*$								

DISCUSSION:

PHG develops as a result of portal hypertension, which leads to an increase in blood flow in the stomach and congestion of the mucous membranes and submucosal blood vessels, which leads to a decrease in mucus secretion and a decrease in local mucosal defense, and the mucosa becomes susceptible to harmful factors such as non-steroidal anti-inflammatory drugs and H, pylori colonization. In our current study, 80 patients with cirrhosis associated with hepatitis C were enrolled in our study. From a demographic point of view, our study showed that there is no difference between male and female in terms of developing PHG, on the other hand, the older the patient, the greater the possibilities of developing PHG in our study, the age of the patients varied from 38 to 66 years. Safwat et al. in their studies showed a significant relationship between the age of patients with cirrhosis of the liver and the development of PHG, with no relationship between the patients' gender and the development of PHG. Merli et al. Also reported that there is a cumulative incidence of PHG in patients with cirrhosis.

In their study, the incidence of PHG between their patients in the first year was 3%, in the second year it increased to 10%, in the third year the incidence increased to 24%. The conclusion from these studies is that the incidence of PHG is higher in older patients with cirrhosis. The frequency of PHG in our study was 71%. Cormack et al. reported that the incidence of PHG varies considerably from 20% to 75% in patients with portal hypertension and varies significantly from approximately 35% to 80% in patients with cirrhosis. This large variability likely reflects variability in the criteria for classification, interpretation of endoscopic lesions, populations tested, and the natural history of PHG. When examining the association of PHG with laboratory tests, anemia was higher in patients with PHG. In cases with PHG, anemia develops due to blood loss, which is one of the clinical symptoms of PHG. This upper gastrointestinal bleeding may be acute or chronic blood loss is more common with PHG and is manifested by iron deficiency anemia. In addition, other factors such as hypersplenism, liver cirrhosis, and portal hypertension may contribute to anemia which lead to gastric congestion and reduce iron absorption and excessive H. pylori infection. We found a significant drop in platelet counts in PHG patients, and this is consistent with other studies. Kim et al. and Safwat et al. The results of their studies showed that the platelet counts were lower in patients with PHG. This is confirmed by the result of our study. In addition, laboratory studies showed a significant increase in INR in PHG, serum bilirubin was significantly higher in PHG, and serum albumin was significantly lower in PHG. Fontana et al. report that PHG is associated with the histological and biochemical severity of liver disease in HCV patients with advanced fibrosis, and their results showed that serum bilirubin was higher in PHG, INR was prolonged, and serum albumin was lower. Regarding the radiographs (ultrasound), our study found that the size of the spleen was significantly larger in patients with PHG. Anegawa et al. reported that PHG may be associated with splenomegaly and that laparoscopic splenectomy may have a beneficial effect on PHG, at least for a short time. Fontana et al. Also reported that in their study there was a significant association between spleen size and the severity of PHG. Kim et al. showed that spleen size increased with increasing PHG severity. In the present study, the portal vein was significantly dilated in patients with PHG compared to those without PHG. Zardi et al. in their study reported that the mean portal vein diameter was 10.4 ± 1.67 mm in patients with cirrhosis without PHG and 11.6 ± 2.0 mm in patients with cirrhosis and PHG ($P = 0.0002$). The portal vein was more dilated in patients with cirrhosis and PHG. In addition, ascites was more significant in patients with PHG compared to patients

without PHG. Kumar et al. in their study showed a significant association between PHG and ascites, with ascites being more common in patients with cirrhosis and PHG. When it comes to evaluating esophageal varices and PHG by endoscopy in our current study, it has been shown that there is a significant association between PHG and the presence and size of esophageal varices. Esophageal varices were increasing in patients with PHG. As reported by Abbasi et al., 2011, the results of their study showed that the degree of oesophageal varices had a significant relationship with PHG, ie the severity of PHG increased with the degree of oesophageal varices, suggesting a common pathophysiology of both subjects. Primignani et al. Also demonstrated that PHG was significant with the presence and size of esophageal and gastric varices and concluded that PHG is common in patients with cirrhosis of the liver, and its incidence is consistent with the severity of portal hypertension. PHG can go from mild to severe and vice versa, and even disappear completely. On the other hand, Gupta et al. Found no significant association between PHG alone and esophageal varices themselves, but there was an association with esophageal varices and found that PHG is common in patients with cirrhosis, and its incidence increases with the presence of esophageal varices and after sclerotherapy. Also, Bellis et al. found that there was no significant correlation between PHG and the severity of esophageal varices and their size. These discrepancies, because studies with a negative correlation between PHG and the size of esophageal varices concerned a relatively small number of cases, for example, Bellis et al. Studied 59 patients and used different methods of diagnosing and classifying both PHG and esophageal varices in their study. Spleen enlargement, ascites, dilated portal veins, and esophageal varices were part of the clinical and radiological manifestation of portal hypertension. Regarding the relationship between PHG and the severity of liver disease, our current study found a significant correlation between PHG and the severity of monitored liver disease as per ChildPaugh Score. Merli et al. demonstrated the presence of esophageal varices, and Child-Pugh Class B or C was a predictor of the incidence of PHG, while only Child-Pugh Class B or C was correlated with mild to severe PHG progression. In addition, they concluded that the natural course of PHG was significantly influenced by the severity of the liver disease and the severity of PH. Acute PHG bleeding is rare but can be severe.

Also, Sarin et al. reported that the incidence of PHG in Child-Pugh C patients is higher than in Child-Pugh A patients. De Lisi et al. Reported a significantly higher incidence of PHG in the Child-Pugh B or C grades compared to stage A. In a minority of studies, a negative association was found between PHG and the Child Score. Primignani et al. reported that the incidence of severe PHG was lowest at Child-Pugh Stage C. In the NIEC trial, Child-Pugh B patients had a higher incidence of PHG than those with Stage A or C.

Fontana et al. reported in their studies that there is an association between PHG and biochemical markers of liver disease severity (albumin was lower, and bilirubin and PT were higher). Regarding the prognosis of liver disease, as calculated by the MELD scale, our study showed a significant relationship between the PHG and MELD scores. Kim et al. reported that there is a significant association between PHG, MELD score and concluded that PHG is associated with the severity of portal hypertension and the prognosis of patients with cirrhosis. On the other hand, Zardi et al. Reported that there was no significant correlation between PHG and MELD scores. Our present study found a significant association between H. pylori infection and the incidence of PHG, where our results showed that H. pylori infection was positive in 57.5% of PHG patients and H. pylori infection was negative in 95.7% of patients. . without PHG with high significant P ratio (<0.001 (H. pylori infection was significantly higher in patients with severe PHG (95.2%) compared to patients with mild PHG (69.4%)). This is consistent with Safwat and co-workers showed that the frequency of H. pylori infections was higher in patients with PHG compared to patients without PHG (69.2% vs 42.9%; p = 0.022), and H. pylori infection was higher in patients with severe PHG (55.6%) compared to patients with mild PHG (44.4%).

CONCLUSION:

The conclusion of their study was a significant relationship between H. pylori infection and the incidence and severity of PHG in patients with HCV-associated cirrhosis. Moreover, Abdul Sattar et al. Found that the presence of H. pylori infection was observed in 31 (44.3%) patients with cirrhosis and PHG (cases), compared to 19 (27.1%) patients with cirrhosis without PHG (group control). In addition, of 31 patients with PHG and H. pylori infection, 19 had severe PHG and 12 had mild PHG, while 5 patients had severe PHG and 34 had mild PHG in the H. pylori negative patient group. They concluded that there is a significant association between H. pylori infection and PHG in patients with cirrhosis, which is also associated with the severity of PHG. Therefore, H. pylori should be eradicated in patients with cirrhosis and PHG. On the other hand, there have been many

studies that contradict the link between PHG and H. Pylori infection.

Abbas et al. concluded that the presence of H. pylori infection did not affect the severity of PHG. There was a decrease in virulent H. pylori strains and IL levels in patients with advanced PHG.

Batmanabane et al. concluded that hypertensive portal gastropathy does not provide a favorable environment for H. pylori colonization. The decrease in positive H. pylori results with the severity of PHG suggests that this bacterium is unlikely to be involved in the pathogenesis of congestive gastropathy and therefore may not need to be routinely controlled in PHG patients. However, the results of this study are questionable due to the small number of patients enrolled in the study (37 patients).

This discrepancy in results can be explained by a number of reasons, such as the use of different methods in the diagnosis of H. pylori infection, the small number of patients enrolled in this study insufficient to obtain significant statistical results, the use of different scoring systems for the diagnosis and classification of PHG. , different etiology of cirrhosis in patients enrolled in the studies and ultimately inter-observator variability.

REFERENCES:

1. Nishino, Ken, Miwa Kawanaka, Mitsuhiko Suehiro, Naoko Yoshioka, Jun Nakamura, Noriyo Urata, Tomohiro Tanigawa et al. "Gastric Hyperplastic Polyps after Argon Plasma Coagulation for Gastric Antral Vascular Ectasia in Patients with Liver Cirrhosis-A Case Suggesting the" Gastrin Link Theory"." *Internal Medicine* (2020): 5837-20.
2. Habib, Shahid. "Portal Hypertensive Gastropathy." In *Variceal Bleeding in Liver Cirrhosis*, pp. 123-140. Springer, Singapore.
3. Simbrunner, Benedikt, Andrea Beer, Katharina Wöran, Fabian Schmitz, Christian Primas, Marlene Wewalka, Matthias Pinter et al. "Portal hypertensive gastropathy is associated with iron deficiency anemia." *Wiener klinische Wochenschrift* 132, no. 1-2 (2020): 1-11.
4. Abdel-Razik, Ahmed, Nasser Mousa, Rania Elhelaly, Rasha Elzehery, Ahmad S. Hasan, Mostafa Abdelsalam, Ahmed Salah Seif, Ahmed M. Tawfik, Niveen El-Wakeel, and Waleed Eldars. "Helicobacter pylori as an Initiating Factor of Complications in Patients With Cirrhosis: A Single-Center Observational Study." *Frontiers in medicine* 7 (2020): 96.
5. Bharath, H. R., Anupam Dutta, Ajit Kumar Pegu, Balaji Dhanabalan, and Bhabani Sankar Dhal. "Study of Aetiological and Endoscopic Profile of Patients with Upper Gastrointestinal Bleed in North East India--A Hospital Based Cross Sectional Study." *Journal of Evolution of Medical and Dental Sciences* 9, no. 42 (2020): 3112-3117.
6. Shah, Harshil, Tsu Jung Yang, Ivan Wudexi, Shantanu Solanki, Shakumar Patel, Don Rajan, Aaron Rodas et al. "Trends and outcomes of peptic ulcer disease in patients with cirrhosis." *Postgraduate Medicine* (2020): 1-8.
7. Shiekh, Shabir, Showkat Kadla, Bilal Khan, and Nisar Shah. "PORTAL HYPERTENSIVE GASTROPATHY: A COMPREHENSIVE REVIEW." *International Journal of Medical and Biomedical Studies* 4, no. 4 (2020).
8. Chávez Cieza, Lenar Anthony. "Infección por helicobacter pylori y litiasis vesicular." (2020).
9. Smith, Zachary L., and Daniel K. Mullady. "Gastrointestinal Procedures 26." *The Washington Manual Gastroenterology Subspecialty Consult* (2020).
10. Sierra, Enrique Mendoza. *The general practitioner's bible*. Vol. 2020. Enrique Mendoza Sierra, 2020.
11. Kumar, Parveen, Michael L. Clark, and M. D. Frcp, eds. *Kumar & Clark's Cases in Clinical Medicine E-Book*. Elsevier, 2020.
12. Giefer, Matthew J., Erin R. Lane, Nicole Green, Talya L. Miller, and Michelle Pietzak. "GASTROINTESTINAL DISORDERS." *General Pediatrics Board Review* (2020): 392.
13. Alvarez, C., J. P. Regan, and D. Merianos. "Bibliography Current World Literature Vol 21 No 5 September 2005." *Pancreas* 6 (2020): 18.
14. Карпов, И. А., Ю. Л. Горбич, Н. В. Соловей, Д. В. Литвинчук, Д. Е. Данилов, А. И. Василенко, and И. О. Стома. "Инфекционные болезни." (2020).
15. Tiwari, Pratap S., K. C. Sudhamshu, Dilip Sharma, Mukesh S. Paudel, and Amrendra Mandal. "Prevalence of Portal Hypertensive Gastropathy in Chronic Liver Disease and Correlation with the Severity of Liver." (2019).