Original Article

Noninvasive clinical predictors of portal hypertensive gastropathy in patients with liver cirrhosis

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ABSTRACT

Background and Objectives: Portal hypertensive gastropathy (PHG) is described endoscopically as "mosaic-like appearance" of gastric mucosa with or without the red spots. It can only be diagnosed by upper gastrointestinal (GI) endoscopy. The aim of this study was to determine the diagnostic accuracy of platelet count to spleen diameter ratio (PSR) and right liver lobe diameter to albumin ratio (RLAR) in the detection of PHG using upper GI endoscopy as a gold standard in patients with liver cirrhosis. **Material and Methods:** This cross-sectional study was conducted in the Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation, Karachi. All consecutive patients with ages 18–65 years who were screened using esophagogastroduodenoscopy (EGD) to exclude esophageal varices were enrolled. At the same time, findings related to PHG were noted. After informed consent, all the patients had blood tests including platelet count and albumin and abdominal ultrasound determining spleen diameter and right liver lobe diameter. **Results:** Out of 111 patients, 59 (53.15%) were males with a mean age of 44 ± 12.61 years. Rate of PHG was observed in 84.68% (94/111) cases confirmed by EGD. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of PSR were 87.23%, 5.88%, 83.67%, 7.69%, and 74.7%, respectively, and those of RLAR were 28.72%, 70.59%, 84.38%, 15.19%, and 35.14%, respectively. **Conclusion:** PSR is better predictor of PHG than RLAR but at the expense of relatively lower specificities and NPV likely because of underlying pathophysiology (portal hypertension) which is similar for esophageal varices, PHG, and ascites.

Key words: sensitivity, specificity, gastropathy, endoscopy

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INTRODUCTION

Portal hypertensive gastropathy (PHG) is a complication of liver cirrhosis, characterized by changes in the gastric mucosa of variable severity. It appears endoscopically as "snakeskin-like appearance" of gastric mucosa and mainly involves body and fundus of the stomach.[1] According to Baveno III consensus, it is classified as mild and severe. Mild PHG is defined as mosaic-like appearance without redness of the areola, while severe PHG is manifested by red marks. Furthermore, gastric antral vascular ectasia (GAVE), which is characterized by stripes of red mucosa separated by normal mucosa, is considered a particular pattern of severe PHG (watermelon stomach), predominantly affects antrum.[2,3]

The prevalence of PHG in patients with cirrhosis varies from 11% to 98%. According to Ahmed *et al.* and Abbasi *et al.* from Pakistan, its prevalence was around 80%.[4-7] In patients with cirrhosis, PHG is an important cause of either acute or chronic upper gastrointestinal (GI) blood loss.[8] It accounts for 2–12% of acute upper GI bleeding, and up to 95% of cases are related to severe PHG, which can be life threatening, whereas in 3–26% of cases, it leads to chronic GI bleeding resulting in iron-deficiency anemia. The mortality rate related to PHG bleeding is nearly 12.5%.[9] According to the study by Kim *et al.*,[10],severe PHG showed

a significantly high risk of mortality and reduced expected survival time than none or mild PHG.

The gold standard for the diagnosis of PHG is esophagogastroduodenoscopy (EGD). EGD is not only an invasive procedure but it also poses financial and psychological impact on the patient with limited therapeutic options. Thus noninvasive parameters are required to avoid EGD. Ultrasound (US) is widely available imaging modality required in all patients with cirrhosis to identify features of cirrhosis and development of hepatocellular carcinoma. Therefore, the aim of our study was to determine the diagnostic accuracy of platelet count to spleen diameter ratio (PSR) and right liver lobe diameter to albumin ratio (RLAR; noninvasive parameters) in the detection of PHG using upper GI endoscopy as a gold standard in patients with liver cirrhosis.

MATERIAL AND METHODS

This cross-sectional study was conducted in the Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation, Karachi. The diagnosis of cirrhosis was established on the basis of any three of the following radiologic features of cirrhosis: altered echo texture of liver, irregular margins, spleen diameter of >12 cm, portal vein diameter of >12 mm, and ascites.[11,12] Abdominal ultrasonography was performed to measure the maximum spleen bipolar diameter and right liver lobe diameter in millimeters, using US (TOSHIBA-apleo 50Model MCM17545TS), by single senior radiologist to minimize interobserver variability.

All patients with cirrhosis with ages 18–65 years visiting Outpatient Department of Hepatogastroenterology, SIUT (GI-OPD) were enrolled after informed consent. A blood sample was drawn for complete blood count, creatinine, albumin, bilirubin, alkaline phosphatase, gamma glutamyl transferase, alanine and aspartate aminotransferase, international normalized ratio, and hepatitis viral serology. All enrolled patients were subjected to EGD, and findings related to PHG and varices were recorded. EGD was performed with Olympus GIF-XP180 by single senior endoscopist to curtail interobserver variation.

To avoid bias, patients on treatment with beta blockers, with the history of variceal band ligation, bleeding disorders, renal disease, acute illness, and malignancy and those with portal vein thrombosis were excluded from the study. This study was approved by our institutional ethical committee.

Statistical analysis

Statistical analysis was performed by IBM-compatible Statistical Package for Social Sciences (SPSS) version 20.0 (SPSS Inc., Chicago, IL, USA). Frequencies and percentages were computed for categorical variables, while quantitative values were presented as mean ± standard deviation. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy of each of the indices PSR and RLAR for the diagnosis of PHG were calculated by taking EGD as gold standard.

RESULTS

A total of 111 newly diagnosed patients with cirrhosis undergoing screening endoscopy were included in this study. The average age of the patients was 44 ± 12.61 years, and other average clinical parameter were also estimated and shown in Table 1. Regarding grade of ascites, 37.84% were mild, 18.92% were moderate, and 17.12% were severe grades of ascites. Rate of PHG was observed in 84.68% (94/111) of cases confirmed by upper GI endoscopy. Gastric vascular antral ectasia was seen in 17 (15.3%) patients. Hepatitis C virus was the most common cause of underlying liver disease.

The association of PHG with ascites ($P = 0.01$), esophageal varices (p = 0.003), and Child-Turcotte-Pugh (CTP) class ($P = 0.01$) was statistically significant. However, no statistically significant association of PHG was observed with Model for End-Stage Liver Disease (MELD) score ($P = 0.84$).

Diagnostic accuracy of PSR and RLAR in the detection of PHG in patients with liver cirrhosis is presented in Tables 2 and 3, respectively. Sensitivity, specificity, PPV, NPV, and accuracy of PSR were 87.23%, 5.88%, 83.67%, 7.69%, and 74.7%, and those of RLAR were 28.72%, 70.59%, 84.38%, 15.19%, and 35.14%, respectively.

DISCUSSION

About 2–12% of acute upper GI bleeding cases are related to severe PHG, which can sometimes be life threatening. While up to 26% patients present with chronic GI blood loss. According to Cremers *et al.*[9] and Kim *et al.*,[10] severe PHG was significantly associated with higher mortality and reduced expected survival time than none or mild PHG.

This study was aimed to evaluate the diagnostic accuracy of PSR and RLAR to diagnose PHG without endoscopy in patients with liver cirrhosis irrespective of etiology. The frequency of PHG observed in our study was 84.68% (94/111) with 30.6% patients having severe PHG. Ahmed *et al* [6] and Abbasi *et al.*[7] from Pakistan found similar prevalence.

According to Hepatitis Antiviral Long-term Treatment against Cirrhosis (HALT-C) trial, albumin and platelets

Table 1: Baseline clinical and laboratory parameters of patients (*n* = 111, mean ± SD)

Age (years)	**44.00 ± 12.61**
Gender M/F, *n*	59/52
Cause of CLD (HCV/HBV/AIH/Cryptogenic/others)	66/22/5/16/4
Ascites, *n* (absent/mild/moderate/severe)	29/42/21/19
CTP class (A/B/C)	31/55/25
PHG (absent/mild/severe)	17/60/34
GAVE (absent/present)	94/17
Esophageal varices, *n* (grade = absent/I/II/III/IV)	20/31/32/20/08
Fundal varix, *n*	06
Platelet count	113.91 ± 69.02
Serum albumin (g/dL)	2.7688 ± 0.789
Serum creatinine (mg/dL)	1.49 ± 1.86
Spleen diameter (mm)	146.56 ± 31.87
Right liver lobe diameter (mm)	101.63 ± 26.81
Platelet count to spleen diameter ratio	827.17 ± 637.20
Right liver lobe diameter to albumin ratio	41.43 ± 21.29

PHG: portal hypertensive gastropathy; AIH: autoimmune hepatitis; CLD: chronic liver disease; CTP: Child-Turcotte-Pugh; F: female; HBV: hepatitis B virus; HCV: hepatitis C virus; M: male; SD: standard deviation.

Table 2: Diagnostic accuracy of platelet count to spleen diameter ratio in the detection of PHG in patients with liver cirrhosis

Platelet count to spleen diameter ratio	**Upper GI Endoscopy (Gold Standard)**		**Total**
	Positive	**Negative**	
Positive ≤1,326.58	82 (TP)	16(FP)	98(88.3%)
Negative >1,326.58	12(FN)	1(TN)	13(11.7%)
Total	**94(84.7%)**	**17(15.3%)**	**111**
	Estimate	**95% Confidence Interval**	
		Lower	**Upper**
Sensitivity	87.23%	79.0%	92.54%
Specificity	5.88%	1.05%	26.98%
Positive predictive value	83.67%	75.11%	89.69%
Negative predictive value	7.69%	1.37%	33.31%
Diagnostic accuracy	74.77%	65.96%	81.93%

PHG: portal hypertensive gastropathy; FN: false negative; FP: false positive; TN: true negative; TP: true positive.

Table 3: Diagnostic accuracy of right liver lobe diameter to albumin ratio in the detection of PHG in patients with liver cirrhosis

Right liver lobe diameter to albumin ratio	**Upper GI Endoscopy (Gold Standard)**		**Total**
	Positive	**Negative**	
Positive ≥44.22	27 (TP)	5(FP)	**32(28.8%)**
Negative <44.22	67(FN)	12(TN)	**79(71.2%)**
Total	**94(84.7%)**	**17(15.3%)**	**111**
	Estimate	**95% Confidence Interval**	
		Lower	**Upper**
Sensitivity	28.72%	20.55%	38.56%
Specificity	70.59%	46.87%	86.72%
Positive predictive value	84.38%	68.25%	93.14%
Negative predictive value	15.19%	8.91%	24.7%
Diagnostic accuracy	35.14%	26.89%	44.38%

PHG: portal hypertensive gastropathy; FN: false negative; FP: false positive; TN: true negative; TP: true positive.

count are independently associated with the presence of PHG. HALT-C trial also suggested that PHG is associated with the presence of severe portal hypertension, which is related to high morbidity.[13,14] Similarly, our patients had signs of portal hypertension and liver dysfunction such as enlarged spleen, low platelets, and low serum albumin. We used serum albumin level as a marker of hepatic function in combination with right liver lobe size. The RLAR and PSR are noninvasive parameters that can predict the presence and severity of PHG in patients with liver cirrhosis.[15]

Esmat *et al.*[16] investigated on PSR and RLAR for the detection of varices. None of the study was performed previously to assess noninvasive predictors of PHG. As we did not have any pre-defined cut off values, we used 1,326.58 as cut-off value for the PSR for the detection of PHG, at which sensitivity was 87.23%, specificity 5.88%, PPV 83.67%, NPV 7.69%, and accuracy 74.7% to determine the PHG. Esmat *et al.* observed 96.34% sensitivity, 83.33% specificity, and 94% accuracy for detecting the esophageal varices.

Similarly, in this study, cut-off value of 44.25 for RLAR was used to detect PHG. Sensitivity, PPV, NPV, and accuracy of RLAR were 28.72%, 70.59%, 84.38%, 15.19%, and 35.14%, respectively, to detect PHG. Esmat *et al.*[16] found that sensitivity of RLAR was 91.46%, specificity was 77.78%, and accuracy was 89.00% to detect the esophageal varices. Our results showed that the PSR is relatively better predictor of PHG than RLAR. However, our study found that these ratios had relatively lower specificities and NPV likely because of underlying pathophysiology (portal hypertension) which is similar for esophageal varices, PHG, and ascites.

According to the research by Kumar *et al.*,[17] PHG is more often associated with advanced portal hypertension and advanced liver failure. They also found that ascites was significantly associated with PHG. Our study revealed that PSR was found to have diagnostic accuracy of 64.29% and 77.5% in relation to mild and moderate/severe ascites, respectively. In accordance to severity of ascites, diagnostic accuracy of RLAR for the detection of PHG was 38.1% and 42.5% for mild and moderate/severe ascites, respectively. When severity of ascites was considered, PSR was found to be a better predictor than RLAR for PHG. Similar to most studies, our study also has few limitations. It is a single center study with small sample size that would limit to extrapolate the present study findings on general population. The identification of these noninvasive parameters is an important clinical goal, thus reducing the need to perform upper GI endoscopy in all patients with liver cirrhosis. To ensure that, patients with PHG are not missed especially with severe PHG, such predictors must have a high sensitivity, even at the expense of a lower specificity. There is need to perform large multicenter center study and to determine cut-off values specific to PHG and our population.

CONCLUSION

PHG is very common in patients with liver cirrhosis. About one-third of the patients had severe PHG. The presence of ascites, esophageal varices, and CTP class were significantly associated with the presence of PHG. PSR was better predictor of PHG than RLAR but at the expense of relatively lower specificities and NPV likely because of underlying pathophysiology (portal hypertension), which is similar for esophageal varices, PHG, and ascites.

Disclosure

The authors declare that they have no sources of funding for this study and no conflicts of interest to declare.

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