ORIGINAL ARTICLE

Frequency of Portal Hypertensive Gastropathy and its Relationship with Biochemical, Haematological and Endoscopic Features in Cirrhosis

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ABSTRACT

Objective: To determine the frequency of portal hypertensive gastropathy (PHG) and its relation with biochemical, haematological and endoscopic findings in cirrhotic patients.

Study Design: Cross-sectional analytical study.

Place and Duration of Study: Jinnah Postgraduate Medical Centre, Karachi, Medical Unit-III, Ward-7, from June 2009 to December 2010.

Methodology: Patients with diagnosis of cirrhosis and either undergoing screening upper gastrointestinal (GI) endoscopy or presented with acute upper GI bleeding were included in the study. Portal hypertensive gastropathy and oesophageal varices were classified using Baveno scoring system. The severity of cirrhosis was classified according to the Child-Pugh criteria. Hypersplenism was assessed by the reduction of haemoglobin, leucocytes and platelets.

Results: Out of 217 patients, 148 were males (68.2%) and 69 were females (31.8%) with ages ranging from 15-85 years, (mean 48.06 years). There were 144 HCV +ve patients (66.4%), 36 HBV +ve patients (16.6%), 15 HCV/HBV co-infected patients (6.9%) and only 1 (0.5%) had co-infection of HBV/HDV. Twenty-one patients (9.7%) were classified as having cryptogenic cirrhosis. Out of 172 patients (79.27%), 56 patients (25.8%) had mild and 116 patients (53.5%) were suffering from severe PHG. Significant positive correlation was found between esophageal variceal grade and PHG ($r=0.46$, $p < 0.001$) but not with etiology ($r=0.05$, $p=0.41$) or hypersplenism ($r=0.08$, $p=0.22$).

Conclusion: The frequency of PHG was 79.27% in the studied group. The grade of oesophageal varices had significant relation with PHG that is the severity of PHG increased with the grade of oesophageal varices, suggesting common pathophysiology of both entities.

Key words: *Portal hypertensive gastropathy. Esophageal varices. Cirrhosis. Child-Pugh score.*

INTRODUCTION

Portal hypertensive gastropathy (PHG) is a rather common finding in patients with liver cirrhosis and portal hypertension, which in recent years has been recognized as a cause of acute or insidious gastro-intestinal bleeding in these subjects.[1] In the last two decades, portal hypertensive gastropathy (PHG) has emerged as a new entity in various devastating complications of chronic liver disease. By definition, it is an endoscopic appearance of gastric mucosa, with a characteristic snake-skin mosaic-like pattern with or without red spots, seen in patients with both cirrhotic and non-cirrhotic portal hypertension. Mainly fundus and body of stomach are involved, but gastric antrum can also be affected. The prevalence of PHG in cirrhotic patients has been reported to be variable, ranging between 11% and 98%, while the incidence varies from 25% to 50%.[1,2] This variation has often been due to the absence of a common classification system, with a subsequent intra and inter-observer variation.[3]

Several controversies exist concerning the incidence of PHG, its relevance as a cause of upper gastrointestinal bleeding, the evolution of the disease after endoscopic sclerotherapy of oesophageal varices and the mortality rates of patients bleeding from PHG.

The pathophysiology of this condition is not clearly understood. The correlation between PHG and the severity of liver disease seems to be fairly weak.[1] Conflicting results exist regarding the alterations of gastric mucosal hemodynamics and permeability.[4-6] It has been suggested that PHG is a dynamic condition, which may not only worsen from mild to severe, but also improve and even disappear completely.[1] This finding suggests that although portal hypertension remains the crucial factor for the development of PHG, other factors should be considered in the development and progression of this condition like hepatic function, oesophageal varices, type of hepatitis virus and hyper-splenism as evidenced by haematological variables (anemia, leucopenia and thrombocytopenia).

The aim of this study was to determine the frequency of PHG and its relationship with the above mentioned factors in cirrhotic patients.

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METHODOLOGY

This cross-sectional descriptive study was conducted at Hepatology Unit of Ward-7, Jinnah Postgraduate Medical Centre, Karachi, from June 2009 to December 2010. Patients with diagnosis of cirrhosis and either undergoing screening upper GI endoscopy or presented with acute upper gastrointestinal (GI) bleeding were included in the study. The diagnosis of cirrhosis was established in all patients with the help of clinical, biochemical, endoscopic, histologic or sonographic criteria. The medical record of all patients were reviewed and advised for assessment of haematological and biochemical workup including complete blood picture, liver function tests, total protein, prothrombin time and albumin estimation. For etiology of cirrhosis, anti-HCV antibody and HBsAg were tested while in suspected cases other causes of cirrhosis were ruled out with the help of serum Ceruloplasmin and slit lamp examination for Wilson's disease, autoantibodies for autoimmune liver disease and iron studies for haemochromatosis.

Patients on treatment with beta-blockers or nitrates, with previous endoscopic treatment of varices (sclerotherapy or endoscopic band ligation), multifocal hepatocellular carcinoma (HCC), severe clotting defects, and hepatic encephalopathy grade-III and IV, non-cirrhotic portal hypertension were excluded from the study.

A verbal and written consent for extended examination was taken from patients and/or their attendants after explaining the intention of procedure. All patients underwent upper gastrointestinal endoscopy after consent. All patients were kept fasting overnight prior to the procedure at our institution. All the endoscopies were performed by first author. Upper gastrointestinal endoscopy was done on Olympus EVIS 180 series endoscopes. Portal hypertensive gastropathy was classified using Baveno scoring system as given in Table I. The oesophageal varices were divided into small or large grade (larger than 5 mm in size) according to Baveno-III consensus statement.[7]

The severity of cirrhosis was classified according to the Child-Pugh criteria.[8] Hypersplenism was assessed by the reduction of haemoglobin (Hb), leucocytes (WBC) and platelets (PLT, Table II). Three to 4 scores were defined for mild hypersplenism, 5-6 scores for moderate and 7-9 scores for severe.

Descriptive analysis was performed for demographic, clinical and radiographic features and results were presented as mean ± standard deviation for quantitative variables and number (percentages) for qualitative variables. Spearman's correlation test was used for correlation analysis while chi-square test was used for relationship between categorical variables. A p-value of less than 0.05 was considered significant.

Table I: Baveno scoring system for portal hypertensive gastropathy.

Endoscopic appearance	Baveno score
Mucosal mosaic pattern	
Mild	1
Severe	2
Red marking	
Isolated	1
Confluent	2
Gastric antral ectasia	
Absent	0
Present	2
Baveno - score	
3 or less = Mild PHG	6 (maximum score)
4 or more =Severe PHG	

Table II: Scores of hypersplenism.

Parameters	1	2	3
WBC (x 10^9/L)	≥ 4.0	2-4	≤ 2
Hb (g/L)	≥ 12	8-12	≤ 8
PLT (x 10/L)	≥ 100	50-100	≤ 50
Score			
3-4 Mild hypersplenism			
5-6 Moderate hypersplenism	9 (maximum score)		
7-9 Severe hypersplenism			

RESULTS

Out of 217 patients included, 148 were males (68.2%) and 69 were females (31.8%) with ages ranging from 15-85 years (mean = 48.06±12.92 years). The number of HCV +ve patients was 144 (66.4%), HBV +ve 36 patients (16.6%), 15 HCV/HBV co-infected patients (6.9%) and only one had co-infection of HBV/HDV (0.5%). Twenty-one patients (9.7%) did not have seropositivity for HCV, HBV /HDV and were classified as having cryptogenic cirrhosis. One hundred and one patients (46.5%) were in Child-Pugh class-A, 105 (48.4%) were in class-B and 11 patients (5.1%) had Child-Pugh class-C. Overall 172 patients (79.27%) had portal hypertensive gastropathy among whom 56 patients (25.8%) had mild and 116 patients (53.5%) had severe PHG. Small grade oesophageal varices were present in 47 patients (21.7%) and 170 (78.3%) had large grade varices. Thirty-seven patients (17.1%) presented with mild hypersplenism, 124 (57.1%) had moderate and 56 patients (25.81%) presented with severe hypersplenism. The relationship of PHG with different variables is given in Table III.

No significant relationship was observed between the Child-Pugh classification grading and the severity of PHG (r=-0.002, p=0.974). Significant positive correlation was observed between grading of oesophageal varices and severity of PHG (r=0.464, p < 0.0001). No relationship of PHG was found with the etiology of cirrhosis (r=0.056, p=0.414) or the severity of hypersplenism and PHG (r=0.081, p=0.223).

Table III: Relationship of PHG with different variables.

Variables		Portal hypertensive gastropathy			p-value
		No (n%)	Mild (n%)	Severe (n%)	
Sex					
Male	148 (68.2%)	26 (12.0%)	85 (39.2%)	37 (17.1%)	p 0.153
Female	69 (31.8%)	19 (8.8%)	31 (14.3%)	19 (8.8%)	Chi-square = 0.749
Virus					
HBV	36 (16.6%)	8 (3.7%)	19 (8.8%)	9 (4.1%)	
HCV	144 (66.4%)	32 (14.7%)	76 (35.0%)	36 (16.6%)	p 0.779
HBV + HCV	15 (6.9%)	3 (1.4%)	6 (2.8%)	6 (2.8%)	Chi-square =4.797
HBV + HDV	1 (0.5%)	0	1 (0.5%)	0	
Others	21 (9.7%)	2 (0.9%)	14 (6.5%)	5 (2.3%)	
Child-Pugh class					
A	101 (46.5%)	21 (9.7%)	54 (24.9%)	26 (12.0%)	p 0.982
B	105 (48.4%)	21 (9.7%)	57 (26.3%)	27 (12.4%)	Chi-square = 0.409
C	11 (5.1%)	3 (1.4%)	5 (2.3%)	3 (1.4%)	
Esophageal varices					
No	26 (12%)	11 (5.1%)	14 (6.5%)	1 (0.5%)	
Small	112 (51.6%)	27 (12.4%)	73 (33.6%)	12 (5.5%)	p < 0.0001
Large	79 (36.4%)	7 (3.2%)	29 (13.4%)	43 (19.8%)	Chi-square = 58.671
Hypersplenism					
Mild	37 (17.1%)	7 (3.1%)	14 (6.5%)	16 (7.4%)	p 0.101
Moderate	124 (57.1%)	26 (12.0%)	72 (33.2%)	26 (12.0%)	Chi-square = 7.755
Severe	56 (25.8%)	12 (5.5%)	30 (13.8%)	14 (6.5%)	

DISCUSSION

PHG has been recently recognized as an important complication of cirrhosis with portal hypertension. It is more frequently observed in patients with more severe liver disease and in patients with cirrhosis who have had previous endoscopic treatment with sclerotherapy or endoscopic variceal ligation.[1,2,9-11] The frequency of PHG in the study was found to be 79.27% with 53.5% patients having severe portal hypertensive gastropathy according to Baveno-III consensus statement. The presently reported high frequency is also consistent with the observation by other studies.[3,12-13]

The relation of hepatic functional status to the development of PHG have been debated and there is no consensus on the relationship between liver function and PHG.[14] Some authors reported higher prevalence and severity of PHG in patients with child class B and C than in class A,[15,16] although others did not observe any relationship.[17] In this series, consisting of patients with various viral aetiology of disease, hepatic function, as assessed by the Child-Pugh class, did not show significant correlation with presence of severity of PHG.

The observation by Primignani *et al.* that frequently observed changes in severity of PHG had no relationship to changes in severity of liver dysfunction as assessed by Child-Pugh score, is also consistent with a lack of influence of hepatic function on the severity of PHG.[1]

PHG severity was also associated with oesophageal varix grade. Our results regarding this relationship were in agreement with other researchers,[13,18] who also found this significant relationship between oesophageal varices and PHG. Furthermore the prevalence of severe PHG was higher in patients with large esophageal varices than in those with small-sized varices. This might be due to sharing of a common mechanism for etiopathogenesis of those two conditions; that is portal hypertension, the more severe result in both severe PHG and large oesophageal varices. Thus, the mechanism for development of PHG may have a similarity with that of oesophageal varix i.e. passive congestion resulted from raised portal pressure initiated the PHG. Furthermore increased portal pressures result in gastric mucosal hyperemia as part of the hyper-dynamic splanchnic circulation in portal hyper-tension and liver cirrhosis.

Hypersplenism also exactly reflects the portal hyper-tension. There is sufficient clinical research regarding relationship between severity of hypersplenism and PHG. Pan *et al.* found a significant correlation between severity of PHG and hypersplenism,[19] but in the present study we observed that there is no significant relation between the severity of PHG and hypersplenism. This disagreement between the two studies might be due to different classifications of PHG used in both studies. In 30-60% of cases, PHG remains stable, but fluctuation suggests that it is a dynamic entity. The reported progression rate from mild to severe in upto 30% of the cases and it regress or disappear in upto 20% of cases.[1,2,9] Therapeutic endoscopic interventions specially oesophageal varices (EV) ligation is associated with faster progression of PHG.[11,20] However, this worsening is usually transient

and PHG can regress in upto 44% of patients after EVL.[11] Patients with PHG are at an increased risk of acute as well as chronic gastrointestinal bleeding.[9] Although the portal hypertensive gastropathy is not the most common cause of significant upper GI bleeding in patients with portal hypertension, but bleeding is the most important complication of this disease. The incidence of acute upper GI bleeding from PHG varies widely (2-12%).[1,2,9] This is likely because of difficulty to make a definitive diagnosis of GI bleeding in terms of PHG, due to inaccuracy in the classification of severe PHG.[21] Most cases (90-95%) of acute bleeding from PHG appear to occur in patients with severe PHG. Regarding chronic GI bleeding, again due to lack of appropriate definition, it is difficult to estimate actual incidence rate of chronic GI bleeding from PHG. The incidence of suspected chronic bleeding from PHG reported in literature ranges from 3 to 26% and appears to occur with equal frequency in patients with mild or severe PHG.[1,2,9]

CONCLUSION

The frequency of PHG was 79.27% in the studied group of cirrhotic patients. The severity of PHG positively correlated with the grading of oesophageal varices suggesting a common pathophysiological pathway of both entities, while the prevalence and severity of PHG are not influenced by gender, type of etiological virus, severity of underlying hepatic dysfunction (assessed by Child-Pugh) and hypersplenism.

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