ORIGINAL ARTICLE

CORRELATION BETWEEN SEVERITY OF PORTAL HYPERTENSIVE GASTROPATHY AND SIZE OF OESOPHAGEAL VARICES IN CIRRHOTIC HEPATITIS-C PATIENTS

Khurram Saleem, Faisal Amin Baig, Mahwish Nida, Munaza Javed
Department of Medicine, University College of Medicine and Dentistry, Lahore-Pakistan

Background: Portal hypertension can lead to oesophageal varices (EV) and portal hypertensive gastropathy (PHG). The aim of this study is to determine the relationship between severity of Portal hypertensive gastropathy and size of oesophageal varices. **Methods:** One hundred and ninety-five patients of hepatitis C positive chronic liver disease having oesophageal varices were assessed for severity of portal hypertensive gastropathy. **Results:** Mild Portal Hypertensive Gastropathy was observed in 16 (8.2 %), moderate in 54 (27.7 %) and severe in 120 (61.6 %) patients. Grade 1 Oesophageal Varices were present in 79 (40.5%) patients, grade 2 in 44 (21.9%) patients, grade 3 in 62 (31.8%) and grade 4 in 10 (5.2%) patients. No significant correlation was observed between grades of gastropathy and size of varices. **Conclusion:** The frequency of portal hypertensive gastropathy was 97.5% in Hepatitis C positive cirrhotic patients having oesophageal varices. Severity of gastropathy is not related to the grade
or size of oesophageal varices.

Keywords: Portal hypertensive gastropathy; Oesophageal varices; Cirrhosis

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INTRODUCTION

Worldwide prevalence of chronic liver disease is not known exactly but approximately 1% of population is estimated to be suffering from this condition.[1] According to National statistics in the UK, liver diseases have been ranked as the fifth most common cause of death.[2]

Oesophageal varices develop as a result of portal hypertension in patients of chronic liver disease. The incidence of oesophageal varices is around 7% per year. Size of oesophageal varices increases in linear fashion with increasing duration and severity of liver disease.[3] Large sized oesophageal varices and presence of red wale mark predict the greater risk of upper gastrointestinal bleeding from varices[4] which is associated with nearly 20% mortality[5].

Portal hypertensive gastropathy develops in 8–90% of patients of chronic liver disease. Portal hypertension leads to regurgitation of portal blood in the stomach vascular bed resulting in changes in gastric mucosal friability and dilated blood vessels.[6] The mechanism of PHG is not fully understood and involves interplay of various gastric growth factors like epidermal growth factor, and cytokines like tumour necrosis factor, nitric oxide and prostaglandins.[7] The significance of PHG lies mainly as a focus of acute and chronic upper gastrointestinal bleeding which can be very severe and fatal occasionally.[8]

The relationship between oesophageal varices and portal hypertensive gastropathy is not fully clear. While presence of oesophageal varices has been linked to the increasing frequency of portal hypertensive gastropathy[9], endoscopic therapy of grade 3 and 4 oesophageal varices has been found to be associated with increasing severity of portal hypertensive gastropathy[10]. The aim of our study is to determine the relationship between size of oesophageal varices and severity of PHG.

MATERIAL AND METHODS

This cross-sectional study was carried out for the period of six months from January to June 2016 in the department of Medicine of Punjab Employee's Social Security Institute affiliated with University of Lahore. Non-probability target sampling was done. Sample size was calculated by applying formula used for qualitative variables[11] and total 195 patients of hepatitis C positive chronic liver disease having oesophageal varices were recruited. Patients having previously diagnosed varices or PHG, Hepatocellular carcinoma, Portal vein or splenic vein thrombosis, Liver diseases from causes other than hepatitis C and on prophylactic beta blocker therapy were excluded. Demographic variables of all patients like age and gender were recorded. Upper GI endoscopy was performed in every patient after taking informed consent. Paquet's grading system was used for grading of oesophageal varices which is as follows:[12]
Grade 1: Varices, disappearing with insufflation.

Grade 2: Larger, clearly visible, usually straight varices, not disappearing with insufflation.
Grade 3: More prominent varices, locally coil shaped and partly occupying the lumen.
Grade 4: Tortuous, sometimes grape like varices, occupying the oesophageal lumen.
Whereas portal hypertensive gastropathy was classified according to new Italian endoscopic club criteria for the study and therapy of oesophageal varices (NIEC) which is as follows:[13]
Mild: Pink in centre mosaic present
Moderate: Flat red spot mosaic present
Severe: Diffusely red mosaic present
Standardized level of significance (5%) was used for decision making about status of parameters. The data was entered in SPSS version 21 for statistical analysis. The data contained qualitative categorical variables like gender, portal hypertensive gastropathy (mild, moderate and severe) and size of oesophageal varices (grade 1–4) and quantitative variable like age. Mean and standard deviation were calculated for quantitative variables and percentages for qualitative variables. Chi-square test was applied on categorical variables to diagnose the correlation of severity of portal hypertensive gastropathy (PHG) with the size of oesophageal varices.

RESULTS

We performed upper GI endoscopy in total 195 patients (n=195). There were 102 (52.3%) male and 93 (47.7%) female. The mean age of patients was 55.64. All patients had hepatitis C and oesophageal varices. The table-1 shows that grade 1 oesophageal varices were mostly found in male patients (21.5%) followed by grade 3 varices which were more frequently observed in female patients (20.5%). The *p*-value is 0.001 showing that gender bears significant relationship with oesophageal varices. Similarly, gastric varices were more prevalent in female patients (13.8%) with a significant *p*-value (0.025). Portal hypertensive gastropathy was not detected in 5 patients. Mild gastropathy was observed in 16, moderate in 54 and severe in 120 patients. Severe portal hypertensive gastropathy equally affected both male and female patients. The *p*-value (0.074) is insignificant for gastropathy and gender which shows that male and female patients have equal chances to develop any type of gastropathy.

Table-2 shows that 48 patients had severe gastropathy but grade 1 oesophageal varices while 7 patients with severe gastropathy had grade 4 oesophageal varices. Similarly, 2 patients with Moderate type of gastropathy had grade 4 oesophageal varices while in same group grade 1 varices were found in 21 patients. Mild portal hypertensive gastropathy was observed in 16 patients only. The *p*-value is 0.94 and concluded that there is no correlation between variceal grade or size and severity of portal hypertensive gastropathy.

Table-1: Endoscopic findings: Frequencies of oesophageal varices, gastric varices and portal gastropathy

Variable Name	Categories	Gender	Frequency	Percentage	*p*-value
Oesophageal Varices	Grade 1	Male	42	21.5	0.001
		Female	37	19	
	Grade 2	Male	33	16.3	
		Female	11	5.6	
	Grade 3	Male	22	11.3	
		Female	40	20.5	
	Grade 4	Male	5	2.6	
		Female	5	2.6	
Gastric Varices	None	Male	86	44.1	0.025
		Female	66	33.8	
	Yes	Male	16	8.2	
		Female	27	13.8	
Gastropathy	None	Male	5	2.6	0.074
		Female	0	0.0	
	Mild	Male	11	5.6	
		Female	5	2.6	
	Moderate	Male	26	13.3	
		Female	28	14.4	
	Severe	Male	60	30.8	
		Female	60	30.8	

Table-2: PHG severity in relation to various grades of oesophageal varices

		Gastropathy				Total
		None	Mild	Moderate	Severe	
Esophageal Varices Grade	Grade 1	3	7	21	48	79
	Grade 2	0	4	11	29	44
	Grade 3	2	4	20	36	62
	Grade 4	0	1	2	7	10
Total		5	16	54	120	195

DISCUSSION

Upper GI bleeding in the cirrhotic is the most serious complication leading to substantial increase in morbidity and mortality.[14] The risk of first episode of upper GIT bleeding varies from 25–35% in 2 years with the occurrence of first bleed within a year of diagnosis.[15]

A complex relationship between severity of PHG and oesophageal variceal size has been observed in various studies. On one hand, new onset or severe PHG has been found to be associated with new onset or higher grade of EV.[16] On the other hand; endoscopic obliteration of large grade varices and thus reduction in size has been studied as a risk factor to endoscopic and pathologic deterioration of PHG.[10]

In our study, frequency of PHG was 97.5% which is relatively higher than other studies done in Pakistan by Abbasi *et al* (79.27%)[17] and Ahmed S *et al* (83%)[18]. This difference could be due to the fact that all patients in our study had oesophageal varices of varying grades which is supported by another study done by Sarwar *et al* who also conducted their study entirely in patients having different grades of EV and found out a frequency of 98.8 % of portal hypertensive gastropathy in those patients.[19]

The most striking feature that we found in our study was the presence of severe PHG mainly in patients having grade 1 EV (48 out of 79). However, this finding is not statistically significant and there is no significant relationship between oesophageal grade and severity of PHG. Similar results have been found by Dong *et al* who suggested that grading of Esophagogastric varices does not relate to the severity of PHG.[20]

Bellis *et al* also demonstrated that there is no statistically significant relationship between grade of oesophageal varices (F 1, 2, 3 by North Italian Endoscopic Club) and severity of PHG (mild or severe by third Baveno International Consensus Workshop).[21] Another study done by Safwat *et al* also described an insignificant relationship between mild and severe PHG with small, medium and large varices (p value 0.803).[22] Similar results were validated by Gupta *et al* which revealed that the relationship of PHG was not positively correlated with history of upper GI bleed, size of varices, aetiology of liver disease and Child's score.[23]

Our results are in contrast to the study done by Pan et al who observed that large grade (Dagradi grades 4 and 5) EV have a significant relationship with increasing severity (Mc-Cormack grade 3) of PHG.[24] Abbasi *et al* also confirmed that out of 112 patients having small sized varices, severe PHG was present in only 5.5% of patients while severe gastropathy with large varices was found in 19.8% patients. They found a significant relationship between size of EV and severity of PHG and concluded it as a result of similar effects of raised portal pressure on oesophageal and gastric mucosae.[17] Fontana et al also published results of HALT –C trial which showed that 40% of patients with PHG had varices compared to only 17% of subjects without PHG (p<0.0001). Additionally, patients having PHG were more likely to have medium or large varices as compared to those without PHG.[25]

The discrepancy in correlation between variceal size and severity of PHG is difficult to explain. Studies which suggest a positive correlation explain a common pathophysiology behind these two conditions that is portal hypertension and liver dysfunction. (Primignani *et al*[26] and Kumar *et al*[27]). However, Bellis *et al* demonstrated no change in hepatic venous pressure gradient in patients possessing different sizes of varices and severity of PHG.[21] Zardi *et al* also studied portal vein diameter in patients of chronic liver disease and suggested a slight and not significant increase in PV diameter in patients having PHG compared to patients with negative endoscopy, a reduction of diameter was observed in F1 grade of EV patients and then a progressive increase of diameter in larger grade of EV patients.[28]

Another study done by Wu *et al* also demonstrated that there is no significant difference in incidence of oesophageal and gastric varices and PHG in patients having common and uncommon collateral circulation. Uncommon collateral circulation though relieve complications due to raised portal pressure.[29] Moreover, interplay of various gastric mucosal hemodynamic and permeability factors is also known to exert influence on the development and severity of PHG.[8]

These findings are also supported by studies done by Sarin *et al* and Gupta *et al* which have shown that prevalence of PHG is significantly higher in patients having both oesophageal and gastric varices than oesophageal varices alone (69 Vs 55% p<0.05).[30,23] Based on above mentioned data and results of our study, it seems reasonable to consider portal hypertension as one of the trigger to development of PHG rather than assuming its definite role in altering the relationship between size of EV and severity of PHG.

CONCLUSION

The frequency of PHG was 97.5% in HCV cirrhotic patients having oesophageal varices. Severity of PHG is not related to grade or size of oesophageal varices.

AUTHORS' CONTRIBUTION

KS: Conceptualization of study design. KS, FAB: Data collection. MJ: Data Analysis. KS, MN: Data interpretation. MN, FAB: Literature search. MN, KS, MJ: Write-up, proof reading.

REFERENCES

1. Schuppan D, Afdhal NH. Liver Cirrhosis. Lancet 2008;371(9615):838–51.
2. UK national statistics. [Internet]. [cited 2017 Dec 10]. Available from: https://www.gov.uk/government/publications/liver-disease-applying-all-our-health/liver-disease-applying-all-our-health
3. Biecker E. Portal hypertension and gastrointestinal bleeding: diagnosis, prevention and management. World J Gastroenterol 2013;19(31):5035–50.
4. Turon F, Casu S, Hernández-Gea V, Garcia-Pagán JC. Variceal and other portal hypertension related bleeding. Best Pract Res Clin Gastroenterol 2013;27(5):649–64.
5. Triantos C, Kalafateli M. Endoscopic treatment of esophageal varices in patients with liver cirrhosis. World J Gastroenterol 2014;20(36):13015–26.
6. Chung WJ. Management of portal hypertensive gastropathy and other bleeding. Clin Mol Hepatol 2014;20(1):1–5.
7. Urrunaga NH, Rockey DC. Portal Hypertensive Gastropathy and Colopathy. Clin Liver Dis 2014;18(2):389–406.
8. Bang CS, Kim HS, Suk KT, Kim SE, Park JW, Park SH, *et al*. Portal hypertensive gastropathy as a prognostic index in patients with liver cirrhosis. BMC Gastroenterol 2016;16(1):93.
9. Gjeorgjievski M, Cappell MS. Portal hypertensive gastropathy: A systematic review of the pathophysiology, clinical presentation, natural history and therapy. World J Hepatol 2016;8(4):231–62.
10. Elwakil R, Al Breedy AM, Gabal HH. Effect of endoscopic variceal obliteration by band ligation on portal hypertensive gastro-duodenopathy: endoscopic and pathological study. Hepatol Int 2016;10(6):965–73.
11. Charan J, Biswas T. How to Calculate Sample Size for Different Study Designs in Medical Research? Indian J Psychol Med 2013;35(2):121–6.
12. Paquet KJ. Prophylactic endoscopic sclerosing treatment of the esophageal wall in varices-a prospective controlled randomized trial. Endoscopy 1982;14(1):4–5.
13. Eleftheriadis E. Portal hypertensive gastropathy. Ann Gastroenterol 2001;14(3):196–204.
14. Biecker E. Gastrointestinal Bleeding in Cirrhotic Patients with Portal Hypertension. ISRN Hepatol 2013;2013:541836.
15. Northern Italian Endoscopic Club for the Study and Treatment of Esophageal Varices. Prediction of the first variceal hemorrhage in patients with cirrhosis of the liver and esophageal varices: a prospective multi-center study. N Engl J Med 1988;319(15):983–9.
16. Fontana RJ, Sanyal AJ, Ghany MG, Bonkovsky HL, Morgan TR, Litman HJ, *et al*. Development and progression of portal hypertensive gastropathy in patients with chronic hepatitis C. Am J Gastroenterol 2011;106(5):884–93.
17. Abbasi A, Bhutto AR, Butt N, Munir SM, Dhillo AK. Frequency of portal hypertensive gastropathy and its relationship with biochemical, haematological and endoscopic features in cirrhosis. J Coll Physicians Surg Pak 2011;21(12):723–6.
18. Ahmed S, Mumtaz K, Ahmed US, Shah HA, Abid S, Hamid S, *et al*. Frequency and characteristic features of portal hypertensive gastropathy in patients with viral cirrhosis. J Coll Physicians Surg Pak 2010;20(11):714–8.
19. Sarwar S, Khan AA, Alam A, Butt AK, Shafqat F, Malik K, *et al*. Effect of band ligation on portal hypertensive gastropathy and development of fundal varices. J Ayub Med Coll Abbottabad 2006;18(1):32–5.
20. SY. Portal hypertensive gastropathy and its interrelated factors. Hepatobiliary Pancreat Dis Int 2003;2(2):226–9.
21. Bellis L, Nicodemo S, Galossi A, Guarisco R, Spilabotti L, Durola L, *et al*. Hepatic venous pressure gradient does not correlate with the presence and the severity of portal hypertensive gastropathy in patients with liver cirrhosis. J Gastrointestin Liver Dis 2007;16(3):273–7.
22. Safwat E, Hussein HA, Hakim SA. Helicobacter pylori in Egyptian patients with HCV-related liver cirrhosis and portal hypertensive gastropathy: Prevalence and relation to disease severity. Life Sci J 2015;12(3):168–73.
23. Gupta R, Saraswat VA, Kumar M, Naik SR, Pandey R. Frequency and factors influencing portal hypertensive gastropathy and duodenopathy in cirrhotic portal hypertension. J Gastroenterol Hepatol 1996;11(8):728–33.
24. Pan WD, Xun RY, Chen YM. Correlations of portal hypertensive gastropathy of hepatitis B cirrhosis with other factors. Hepatobiliary Pancereat Dis Int 2002;1(4):527–31.
25. Fontana RJ, Sanyal AJ, Mehta S, Doherty MC, Neuschwander-Tetri BA, Everson GT, *et al*. Portal hypertensive gastropathy in chronic hepatitis C patients with bridging fibrosis and compensated cirrhosis: results from the HALT-C trial. Am J Gastroenterol 2006;101(5):983–92.
26. 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 italin endoscopic club for the study and treatment of esophageal varices (NIEC). Gastroenterology 2000;119(1):181–7.
27. Kumar A, Mishra SR, Sharma P, Sharma BC, Sarin SK. Clinical, laboratory, and hemodynamic parameters in portal hypertensive gastropathy: a study of 254 cirrhotics. J Clin Gastroenterol 2010;44(4):294–300.
28. Zardi EM, Uwechie V, Gentilucci UV, Dobrina A, Petitti T, Laghi V, *et al*. Portal diameter in the diagnosis of esophageal varices in 266 cirrhotic patients: which role? Ultrasound Med Biol 2007;33(4):506–11.
29. Wu Q, Shen L, Chu J, Ma X, Jin B, Meng F, *et al*. Characterization of uncommon portosystemic collateral circulations in patients with hepatic cirrhosis. Oncol Lett 2015;9(1):347–50.
30. Sarin SK, Sreenivas DV, Lahoti D, Saraya A. Factors influencing development of portal hypertensive gastropathy in patients with portal hypertension. Gastroenterology 1992;102(3):994–9.

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Address for Correspondence:

Khurram Saleem, Department of Medicine, University College of Medicine and dentistry, Lahore-Pakistan
Cell: +92 306 435 4221
Email: khurramsaleem@hotmail.com