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Correlation of Portal Hypertensive Gastropathy with the Size of Esophageal Varices in Patients with Decompensated Chronic Liver Disease:

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Abstract:

Objectives: To determine the correlation of portal hypertensive gastropathy with esophageal variceal size. To determine the differences in gender of esophageal varices

Study design & setting: A cross-sectional study was done from January 2022- October 2022 on 440 patients reporting to JPMC, Karachi having portal hypertensive gastropathy and were assessed for severity of esophageal varices based on endoscopic findings.

Methodology: The new Italian Endoscopic Club criterion was used for portal hypertensive gastropathy (PHG) and the Japanese Research Society for Portal Hypertensive Gastropathy to describe the grading of esophageal varices.

Results: Of 440 patients 163 (37%) were female and 277 (63%) were males. The size of esophageal varices correlated with severity and a Spearman p<0.1% was seen which is significant. Male patients showed a significantly higher chance of having larger-sized varices.

Conclusions: The size of varices correlates to severe decompensated chronic liver diseases (DCLD). Hence, patients with advanced liver cirrhosis are likely to be at risk of severe upper GI bleeds.

Keywords: esophageal varices, liver cirrhosis, morbidity, portal hypertension

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INTRODUCTION:

Globally, liver cirrhosis along with its subsequent complications contribute to one million deaths per year making it the 11th most common cause of death as of 2019 (Chaudhary, 2020)[1]. Among the many complications that arise in decompensated chronic liver disease (DCLD), portal hypertensive gastropathy (PHG) and esophageal varices stand out as indicators of disease severity (Mauro, 2020)[2]. Esophageal varices are the dilated submucosal distal esophageal veins which connect the portal and systemic circulations. They form due to portal hypertension, as a result of cirrhosis, resistance to portal blood flow, and increased portal venous blood inflow. Oesophageal variceal rupture is the most common but fatal complication of cirrhosis.

The severity of liver cirrhosis being linked to the size of varices is reported in literature; larger varices are more likely to be found in advanced cirrhosis (Mikhailova, 2022)[3]. The increasing trend in hospitalizations for esophageal varices, particularly those with bleeding, has been noted in the United States (Elghezewi, 2023)[4]. Cirrhotic portal hypertension result in PHG. Its diagnoses are based on esophagogastroduodenoscopy (EGD) findings[5]. The term "Portal hypertensive gastropathy" is defined as a mosaic-like pattern or a diffuse, erythematous and reticular cobblestone pattern of gastric mucosa comprising of polygonal areas, inclusive of but not always superimposed red punctate lesions. The diameter of these lesions is >2 mm and are bordered with whitish depressed areas[6]. To

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classify PHG through endoscopic findings for severity is clinically imperative because severity is connected with bleeding risk increasing the risk of gastric hemorrhage in severe (38% to 62%) in comparison to mild cases (3.5% to 31%)[6].

The portal vein has circulation of over 1500 ml/min of blood. If there is an obstruction, results in elevated portal venous pressure. The body responds to the increased venous pressure by the development of collaterals. These collaterals divert blood from the portal venous system to the inferior and superior vena cava. The gastroesophageal collaterals drain into the azygos vein and lead to the development of esophageal varices. When these varices get enlarged, they rupture and produce severe hemorrhage. Bleeding from esophageal varices is the third most common cause of upper GI bleeding, after duodenal and gastric ulcers.

The exact prevalence of liver disease globally is not known but an approximate 1% of the population morbidity is estimated. UK National statistics state, liver ailments as the fifth most common cause of mortality[8]. The connection of esophageal varices to PHG remains controversial. Esophageal variceal existence has links to the increasing prevalence of PHG, interestingly, endoscopic grade 3 and 4 esophageal varices are connected with increasing severity of PHG [9]

Recent studies have emphasized the importance of considering gender association in the manifestation and progression of chronic liver disease (CLD). The influence of both sex and gender on the development and progression of CLD is further emphasized by the differences observed in the epidemiology, natural history, and patient outcomes of liver diseases in women (Guy 2013)[10]. These findings highlight the need for tailored approaches to the diagnosis and treatment of CLD, taking into account the unique risk factors and disease progression patterns in both men and women.

This study aims to dig into the correlation between PHG and the size of esophageal varices, illuminating associations that can guide clinical decision-making.[11]

METHODOLOGY:

The Jinnah Postgraduate Medical Center (JPMC) Institutional Review Board (IRB) granted approval for this study. The IRB letter number is F.2-81/2023-GENL/209/JPMC. This study is a retrospective, observational study conducted in the endoscopy suite of Medical Unit III, Ward 7, at Jinnah Postgraduate Medical Center.

The study population included all patients of liver cirrhosis above the age of 12 years who were diagnosed clinically and through radiological and laboratory investigations. Patients who had evidence of portal hypertensive gastropathy (PHG) on endoscopy and who provided consent were included in the study. Patients who had underlying malignancies such as hepatocellular carcinoma, pregnant females, and those who did not give consent for endoscopy were excluded from the study.

The sample size was determined by taking the prevalence of liver cirrhosis to be 23.72% and keeping the error limit at 5%. Using these parameters, the sample size was calculated to be 278 at a 95% confidence interval. The sample size calculation was performed using the OpenEpi calculator, a widely used tool for epidemiological studies.

Data of patients with decompensated chronic liver disease (DCLD) who underwent endoscopy in 2022 was obtained for the study. The endoscopic findings of these patients were recorded, focusing on the findings of PHG and the size of esophageal varices. The data collection process involved meticulous review and documentation of the patients' clinical and endoscopic records to ensure accuracy and completeness.

Data analysis was conducted using IBM-SPSS version 23.0. Counts with percentages were reported for the baseline and clinical characteristics of the studied patients, providing a comprehensive overview of the demographic and clinical profile of the cohort. Mean values with standard deviations were calculated for laboratory findings, offering a detailed description of the biochemical and hematological parameters of the patients.

To investigate the associations between PHG, the size of esophageal varices, and gender, the Pearson Chi-Square test was used. This statistical test is suitable for categorical data and helps to determine whether there are significant associations between the variables. Additionally, the Spearman Rank correlation was used to test the correlation between the size of esophageal varices and PHG. The Spearman Rank correlation is a non-parametric test that assesses the strength and direction of the association between two ranked variables.

p-values of less than 0.05 were deemed statistically significant, indicating that the observed associations were unlikely to have occurred by chance. The results of the statistical analyses were presented graphically using scatter plots and bar charts, which provided a clear and visual representation of the data.

The approval from the JPMC IRB ensured that the study was conducted in accordance with ethical guidelines and standards, safeguarding the rights and welfare of the participants. The inclusion criteria were designed to encompass a wide range of patients with liver cirrhosis while excluding those with confounding conditions such as malignancies and pregnancy. This approach ensured that the study population was representative of the typical patient population seen in the endoscopy suite at JPMC.

The retrospective nature of the study allowed for the analysis of existing data, which provided valuable insights into the clinical characteristics and endoscopic findings of patients with DCLD. By focusing on patients who had evidence of

PHG on endoscopy, the study aimed to shed light on the prevalence and severity of this condition in the context of liver cirrhosis.

The use of the OpenEpi calculator for sample size determination ensured that the study was adequately powered to detect significant associations, providing a robust basis for the statistical analyses. The detailed data analysis using IBM-SPSS version 23.0 allowed for comprehensive exploration of the relationships between PHG, esophageal varices, and gender, offering valuable insights into the pathophysiology and clinical management of liver cirrhosis.

Overall, this study provides a thorough and systematic examination of the clinical and endoscopic features of patients with DCLD at JPMC. The findings have important implications for the early detection, monitoring, and management of liver cirrhosis, highlighting the need for regular endoscopic surveillance and targeted therapeutic interventions to address complications such as PHG and variceal bleeding. The use of advanced statistical methods and graphical presentations ensures that the results are both rigorous and accessible, contributing to the growing body of knowledge on liver cirrhosis and its associated complications

RESULTS:

A total of 440 samples 163 (37%) were female and 277 (63%) were male gender, mean age was 51±12 years, mean SBP was 118±18 units, mean DBP was 74±10 units. Hepatitis C was the most common etiology 44.8% of CLD. Laboratory parameters showed mean hemoglobin (Hb) was 10.6±7.7 units, mean TLC was 7.1 ±3.7 units, mean platelet was 118±43 units, mean PT was 13±3 units, median INR was 1.16 (IQR= 1.05 – 1.32) units. 44.8% presented with hematemesis, 37% were melena and 3.2% with lower gastrointestinal bleed. Baseline characteristics are mentioned in table-1.

Table-2 showed the endoscopic findings of frequency of size of esophageal varices, scar of previous band ligation and severity of PHG. Out of total, 148 patients (33.6%) were found to have large sized esophageal varices, 17% had scar of previous band ligation, 19.1% had first session of esophageal varices bleeding (EVBL) in band ligation, 9 patients (2%) were found with large size fundal varix and the same number of patients underwent sclerotherapy and 305 (69.3%) cases were of severe PHG

Figure 1. displays the association of size of esophageal varices with severity of PHG. Patients with small sized and medium sized esophageal varices had 65.3% association with severe PHG whereas patients having large esophageal varices 77.7% had findings of severe PGH. The association was found to be statistically significant with $p<0.01$.

Table-4 reports the association of gender with size of esophageal varices and PGH. Among female patients, 51(31.3%) had large size esophageal varices and 112 (68.7%) were found to have severe PHG. On the other hand, 97 (35%) male patients had large sized esophageal varices and 193 (69.7%) male patients had severe PHG. Pearson Chi Square test did give a significant association of gender with size of esophageal varices $p<0.01$. However, association of gender with PHG was not found to be statistically significant.

Spearman rank correlation showed 15% positive correlation between size of esophageal varices and PGH and is statistically significant with $p=0.002$, the R-square showed 2.25% variation in PGH, was explained by size of esophageal varices.

DISCUSSION:

Analyzing a cohort comprising predominantly male individuals (63%), with 51 years being the mean age, this study unravels key insights into the demographic and clinical characteristics of patients grappling with decompensated chronic liver disease (DCLD). Notably, a substantial proportion (77.5%) of cases presented with undiagnosed DCLD, underscoring the challenges in early detection and management. Among the diagnosed cases, comorbid conditions such as diabetes mellitus and hypertension were prevalent, albeit with varying frequencies.

Etiologically, hepatitis C emerged as the predominant factor contributing to chronic liver disease (CLD), emphasizing the continued significance of viral hepatitis in disease burden. Hematemesis, melena, and lower gastrointestinal bleeding featured prominently as clinical manifestations, highlighting the multifaceted impact of CLD on patients' health. Hepatitis C is a significant contributor to CLD, with a high prevalence in Europe (Blachier, 2013)[13]. It is also associated with atherosclerosis and cardiovascular diseases, which can lead to complications such as heart failure and stroke (Adinolfi, 2014)[14]. The virus can cause considerable liver damage before its recognition, and it is a large cause of cirrhosis and hepatocellular cancer. The global prevalence of chronic hepatitis C is estimated at 2.8% (Mohd Hanafiah, 2013)[15]. Furthermore, it is linked to comorbidities such as steatosis, diabetes mellitus, and cardiovascular diseases (Negro, 2014)[16]. These findings underscore the multifaceted impact of CLD on patients' health, with hematemesis, melena, and lower gastrointestinal bleeding being prominent clinical manifestations (Blachier, 2013)[17].

The severity of portal hypertensive gastropathy (PHG), including esophageal varices, is a significant concern in liver cirrhosis patients, as it can lead to variceal bleeding and increased mortality (Lesmana, 2020)18. Gastric varices, in particular, are associated with higher mortality and a higher risk of re-bleeding (Wani, 2015)[19]. The incidence of varices is increasing due to factors such as alcohol consumption and obesity (Boregowda, 2019)20. Management of these conditions is crucial, with a focus on endoscopic interventions and newer treatment modalities (Boregowda,

Table 1: Baseline and Clinical Characteristics of Studied Patients (n=440)

Characteristics	**N (n%)**	
Gender		
Female	163 (37.0%)	
Male	277 (63.0%)	
Age (years)	Mean ±SD	51±12
Systolic blood pressure (SBP)	Mean ±SD	118±18
Diastolic blood pressure DBP	Mean ±SD	74±10
Etiology of CLD		
Hepatitis B	37 (8.4%)	
Hepatitis C	197 (44.8%)	
Hepatitis B and C	7 (1.6%)	
Autoimmune Hepatitis	1 (0.2%)	
Alcoholic Liver Diseases	6 (1.4%)	
Others	192 (43.6%)	
Hematemesis		
Yes	197 (44.8%)	
No	243 (55.2%)	
Melena		
Yes	163 (37.0%)	
No	277 (63.0%)	
Lower GI Bleed		
Yes	14 (3.2%)	

Table 2: Endoscopic findings of Esophageal varices and other studied parameters

Size of esophageal varices	Yes	Large	148 (17.0%)
		Small	116 (26.4%)
		Medium	101 (23.0%)
	No		75 (33.6%)
Scar of Previous Band Ligation	Yes		75 (17.0%)
	No		365 (83.0%)
Esophageal Variceal Band ligation (EVBL)	Yes	First session of EVBL	84 (19.1%)
		Second session of EVBL	11 (2.5%)
	No		344 (78.4%)
Size of fundal varix	Yes	Small	26 (5.9%)
		Medium	9 (2.0%)
		Large	9 (2.0%)
	No		396 (90.0%)
Sclerotherapy	Yes		9 (2.0%)
	No		431 (98.0%)
Portal hypertensive Gastropathy	Mild		37 (8.4%)
	Moderate		98 (22.3%)
	Severe		305 (69.3%)

2019; Triantafyllou, 2014)[21].

Analysis of esophageal varices size and PHG severity showed that large esophageal varices correlated significantly with severe PHG. Furthermore, gender-based disparities in variceal size and hepatic gastropathy severity surfaced, with statistical

Figure 1: Showing association of size of esophageal varices with PHG. (p<0.01)

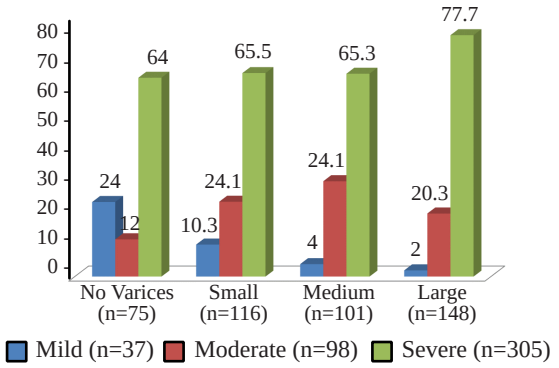
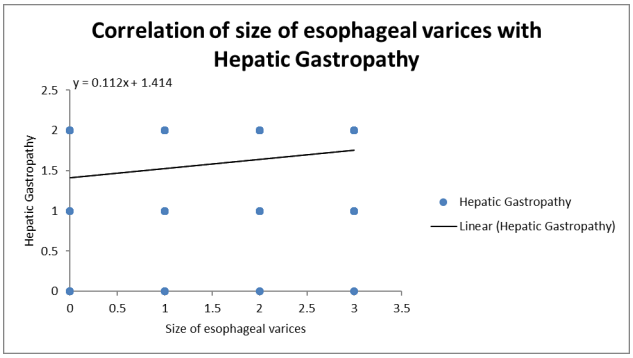


Table 3: Association of size of esophageal varices and PHG with gender

		Gender		**p-value**
		Female	**Male**	
		N (n%)	**N (n%)**	
Size of esophageal varices	No varices	36 (22.1%)	39 (14.1%)	<0.01*
	Small	53 (32.5%)	63 (22.7%)	
	Medium	23 (14.1%)	78 (28.2%)	
	Large	51 (31.3%)	97 (35.0%)	
Hepatic Gastropathy	Mild	17 (10.4%)	20 (7.2%)	0.47
	Moderate	34 (20.9%)	64 (23.1%)	
	Severe	112 (68.7%	193 (69.7%)	

Figure 2. Scatter Plot



significance accentuating the differential disease dynamics between male and female cohorts. An inpatient study based on around 553,000 patients with cirrhosis discovered in-hospital mortality to be lowered by 14% in females as compared to males (Rubin, 2020)[22]. A study in Norway reported reduced chances of variceal bleeding and mortality in female patients around 10% less than males (Haukeland, 2020)[23]. However, the differences between gender and correlation with gastric varices remain underrepresented in literature.

This explanation of correlations between PHG and the size of esophageal varices in liver cirrhosis improves our grasp of disease pathogenesis while paving the way for better

therapeutic intervention and prognostic stratification. Findings reported in our study may serve as a guide to clinicians on managing patients with liver cirrhosis.

The complex interplay between hepatitis C virus (HCV) infection and the progression of liver disease has been well-documented. HCV infection can cause significant liver damage before clinical recognition, leading to cirrhosis and hepatocellular carcinoma. The prevalence of HCV is notably high in certain regions, including Europe, where it continues to be a major public health concern (Blachier, 2013)[13]. The virus's ability to induce chronic liver inflammation and fibrosis underscores the importance of early detection and treatment. Additionally, the association of HCV with other comorbidities such as steatosis, diabetes mellitus, and cardiovascular diseases further complicates the clinical management of affected individuals (Negro, 2014)[16].

Clinical manifestations of CLD, such as hematemesis and melena, often reflect the underlying severity of the disease. These symptoms are indicative of complications like variceal bleeding, which is a direct consequence of portal hypertension—a common sequela of advanced liver disease. The management of variceal bleeding requires prompt endoscopic intervention and may involve the use of medications to reduce portal pressure. The increasing incidence of varices, driven by factors such as alcohol abuse and rising obesity rates, highlights the evolving landscape of CLD (Boregowda, 2019)[20].

The gender-based disparities observed in the size of esophageal varices and the severity of PHG suggest potential biological and hormonal influences on disease progression. Females appear to have a lower risk of in-hospital mortality and variceal bleeding compared to males, as demonstrated by the studies conducted by Rubin and Haukeland. These findings warrant further investigation to elucidate the underlying mechanisms and to explore whether gender-specific therapeutic approaches could enhance patient outcomes (Rubin, 2020; Haukeland, 2020)[22,23.]

The presence of large esophageal varices is a critical prognostic marker in liver cirrhosis patients. It signifies a higher likelihood of severe PHG and an increased risk of life-threatening bleeding events. The correlation between variceal size and PHG severity underscores the need for regular screening and surveillance in patients with cirrhosis. Endoscopic evaluation remains a cornerstone in the management strategy, allowing for timely intervention and prevention of complications.

The role of endoscopic interventions in the management of variceal bleeding is well-established. Techniques such as band ligation and sclerotherapy are commonly employed to control acute bleeding episodes and to prevent recurrence. Recent advancements in endoscopic technology and therapeutic modalities have improved the efficacy and safety of these procedures. However, the risk of re-bleeding and the potential for complications necessitate ongoing research to optimize treatment protocols and to develop novel therapeutic strategies (Triantafyllou, 2014)[21].

In conclusion, this study highlights the significant burden of undiagnosed decompensated chronic liver disease and the critical role of hepatitis C virus infection in its etiology. The findings underscore the importance of early detection, regular monitoring, and comprehensive management of CLD to mitigate complications such as variceal bleeding. Gender-specific differences in disease progression and outcomes further emphasize the need for personalized therapeutic approaches. The integration of advanced endoscopic techniques and emerging treatment modalities holds promise for improving patient care and outcomes in liver cirrhosis. Continued research and clinical vigilance are essential to address the evolving challenges posed by CLD and to enhance the quality of life for affected individuals.

CONCLUSION:

PHG has shown to have a significant positive correlation with the size of esophageal varices in our patients. Patients with advanced cirrhosis are at a high risk of upper gastrointestinal bleed secondary to large esophageal varices, leading to the inpatient mortality. Female patients were less likely to have larger varices which could lead to an explanation towards their lower inpatient mortality rates as compared to males. Further research is still required to explore the gender differences in this condition.

Authors Contribution:
Fatima Fakhir Musharraf: Interpretation of data and manuscript writing
Marium Fatima Waqar: design, data analysis and manuscript writing
Momina Mazhar: compilation of data, manuscript writing
Zeeshan Ali: Concept, design, data analysis / interpretation and review
Shabnam Naveed: interpretation of data and article review
S. Masroor Ahmad: interpretation of data and review of the article

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