ACUTE UPPER GASTROINTESTINAL BLEEDING IN PATIENTS WITH CIRRHOSIS: ENDOSCOPIC FINDINGS

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ABSTRACT

Objective: To determine the endoscopic findings in liver cirrhosis patients presenting with upper gastrointestinal bleeding.

Methodology: A descriptive observational study of 152 patients, of either gender, having liver cirrhosis presenting with acute upper gastrointestinal bleeding was conducted in the Department of Medicine, Lady Reading Hospital Peshawar, from July 2020 to December 2020. Demographic details were noted and relevant investigations were carried out. After resuscitation and stabilization, all patients were subjected to upper gastrointestinal endoscopy by a consultant gastroenterologist to detect endoscopic lesions causing upper gastrointestinal bleeding (UGIB). SPSS version 21 was used for data entry and analysis; post-stratification chi-square (χ^2) with $p \leq 0.05$ was considered statistically significant.

Results: The mean age of 152 patients was 50.95±16.44 years, including 96 (63.2%) males and 56 (36.8%) females. Oesophageal varices were found in 133 (87.5%) patients, gastric varices in 41 (27%) and portal gastropathy in 57 (37.5%) patients. Non-variceal lesions included peptic ulcer disease in 21 (13.8%) patients and gastritis in 19 (12.5%) patients. Only 5 (3.3%) patients had normal endoscopic study. Oesophageal varices were more common in males (72% versus 28%; p=0.001) whereas, gastric varices were more common in female patients (56% versus 44%), which was statistically significant (p=0.003).

Conclusion: Portal hypertension related lesions were the most common underlying etiology in the study patients of liver cirrhosis, presenting with UGIB. The findings on endoscopy included oesophageal varices (87.5%), portal gastropathy (37.5%) and gastric varices (27%). Non-variceal lesions were peptic ulcer disease (13.8%) and gastritis (12.5%). Male gender had significant association with esophageal varices and female gender with gastric varices.

Keywords: Upper gastrointestinal bleeding; Cirrhosis; Esophageal varices; Gastric Varices; Portal gastropathy; Peptic ulcer disease

INTRODUCTION

Acute upper gastrointestinal bleeding (UGIB) is an important and serious medical emergency with significant morbidity and mortality. It is a life threatening condition with mortality of around 15%.[1] Increasing age, in-hospital bleed and comorbidity are significant risk factors associated with mortality in UGIB. Ingestion of NSAIDs and Helicobacter pylori infection are risk factors for bleeding in peptic ulcer disease (PUD).[1,2] Prevalence of UGIB is 100/100,000 population/year.[3] UGIB is defined as hemorrhage arising from the gut proximal to the ligament of Treitz.[3] Portal hypertension in cirrhosis leads to formation of gatro-oesophageal varices culminating into life threatening complications like bleeding. UGIB in cirrhotic patients may be variceal or non-variceal.[4] Variceal hemorrhage is common, occurring in 50-70% of cirrhotic patients whereas non-variceal bleeding occurs in 30-40% of such patients. The non-variceal lesions in cirrhosis patients include gastric ulcer (24.4%), duodenal ulcer (20.6%), gastropathy (14.4%), Mallory-Weiss tear (11.3%) and mucosal erosions (10.6%).[1,4] Worldwide, bleeding peptic ulcer is the leading cause of UGIB in 50% of all patients followed by variceal bleed.[3] However, variceal bleeding is the major cause of bleeding in liver cirrhosis patients, especially in developing countries. Ulcer bleeds are usually mild and self-limiting in majority of the cases whereas variceal bleeds are severe in nature and usually need endoscopic interventions for control.[5,6] Re-bleeding is also common and, despite endoscopic intervention, occurs in 7-16% patients, especially in bleeding PUD and varices.[2]

Clinical presentation and endoscopic findings vary and depend upon the amount, duration, and site of the

bleed and underlying pathology.[7] UGIB may manifest as hematemesis in 40-50% and melena in 70-80%. Hematochezia usually represents a lower GI blood loss; however massive UGIB may result in hematochezia in 10% patients.[5] Oesophagogastrodoudenoscopy (OGD) is a primary diagnostic and therapeutic tool to assess, stratify and manage UGIB. Definitive diagnosis of variceal bleed in cirrhosis patients with UGIB needs endoscopy.[8] It enables to take tissue for biopsy from suspicious lesions in the upper gastrointestinal tract (GIT); to stop bleeding like variceal band ligation, injection sclerotherapy, coagulation or cauterization of the bleeding site. OGD is relatively safe procedure.[4]

Liver cirrhosis patients with UGIB are studied at the local and national level with varying study results.[8-13] For example, frequency of Variceal bleeds in cirrhosis patients reported as 92.9%[8], 73.6%[9], 50%[10], 53.8%[11], 45.9%[12] and 26%[13]. Owing to the scarcity of local studies on the subject, despite the huge burden of cirrhosis liver with complications and the discrepancy in results, we planned the study to determine the various causes leading to UGIB in these patients. It would be helpful for the primary physician encountering such emergency to suspect/identify the most likely underlying etiology and thereby manage or refer the patient to relevant facility at the earliest to help reduce mortality. The objective of this study was, therefore, to determine the endoscopic findings in liver cirrhosis patients, presenting with UGIB to the largest tertiary care hospital of the province. Findings of this study will be a valuable addition to the local and national statistics.

METHODOLOGY

This was an observational study conducted in the Department of Medicine, Lady Reading Hospital Peshawar, from July 2020 to December 2020. Non-probability consecutive sampling technique was used to enroll the patients. All adult patients, of either gender, having liver cirrhosis with clinically observed UGIB in vomitus and/or melena, fulfilling inclusion criteria were included. Patients in shock, previous history of gastrointestinal malignancy or surgery, those with established lower gastrointestinal cause for hematochezia, patients on anti-ulcer therapy; and those not willing for the procedure were excluded.

A total of 152 patients were included in the study after taking ethical approval from the Institutional Ethical Review Board. Sample size of 152 cases was calculated using WHO Sample Size Calculator, with 95% confidence level, 5% margin of error and 11% proportion of PUD among patients with upper GI bleed in liver cirrhosis.[8] All patients were examined by consultant physician; detailed history taken, patient resuscitated and stabilized. Relevant investigations carried out like complete blood count, liver and renal functions tests with serum electrolytes, viral hepatitis serology and abdominal Ultrasound examination. Patients were explained about the purpose and benefits of the study/procedure and written informed consent was taken. Demographic details were noted. OGD was performed by consultant gastroenterologist to detect endoscopic findings as a cause of UGIB. All findings were entered on predesigned proforma. OGD is a procedure used to visually examine upper gastro-intestinal tract with a tiny camera at the end of a long, flexible tube, the high definition video Endoscope.

Operational definitions: Cirrhosis was defined as a chronic progressive disease of the liver resulting from hepatocellular injury with ultra-sonographic features of altered echo-texture/shrunken liver with irregular margins, nodularity and portal hypertension with/without splenomegaly and ascites. Upper Gastrointestinal Bleeding was defined as clinically evident and significant bleeding presenting as hematemesis and/or melena (dark tarry loose stool) or as hematochezia (red blood) passed as massive blood loss, derived from a source proximal to the ligament of Treitz. Oesophageal/Gastric varices are dilated sub-mucosal veins, more than 1 mm in diameter in the oesophagus or stomach. Varices with endoscopic red sign, that is, red whale or white nipple sign" was considered as significant endoscopic sign of Variceal bleed. Chronic peptic ulcer was identified at endoscopy as a circumscribed mucosal breach of ≥5mm in diameter with an exudate, in the oesophagus, stomach or duodenum.[14] Gastritis is inflammation of gastric mucosa which may be erosive or non-erosive. Portal gastropathy refers to the gastric mucosal and sub-mucosal congestion of capillaries and venules secondary to portal hypertension (portal pressure more than 12 mmHg).

Data was entered and analyzed using SPSS version 21. Mean and standard deviations were calculated for numerical variables like age. Frequency and percentages were calculated for categorical variables like gender, hepatitis B and hepatitis C status and endoscopic findings. Data were stratified for age, gender, hepatitis B and hepatitis C status and endoscopic findings. Post-stratification, chi-square test was applied; p-value ≤0.05 was taken as significant. Results were presented in the form of tables.

RESULTS

A total of 152 patients were included in the study. Age of the patients ranged from 18 to 80 years with mean age of 50.95±16.44 years. Demographics and study statistics are presented in Table 1, which shows 96(63.2%) male patients; oesophageal varices in 133(87.5%) and peptic ulcer disease in 21(13.8%) patients. More than one type of lesion causing UGIB was seen in many patients on endoscopy; that is, many patients had a combination of oesophageal and gastric varices and so on, as shown in the tables.

Economically 43% patients belonged to poor class and 57% to middle class. Stratification of endoscopic findings with gender revealed oesophageal varices in 72% male and 28% female patients (p=0.001) whereas gastric varices were more common in female patients, 56% vs 44%, which was statistically significant (p=0.003), as shown in Table 2. However, there was no significant difference of various endoscopic lesions in different age groups, as shown in Table 3.

DISCUSSION

Variceal bleeding was the most common cause of bleeding in our study patients. Among the total of 152 liver cirrhosis patients presenting with UGIB, the mean age was 50.95 years ±16.44 SD and majority (63.2%) were males. Osophageal varices were the most common endoscopic finding in 87.5% of all patients with UGIB. Portal gastropathy was seen in 37.5% patients. Among the non variceal causes, PUD was found in 13.8% patients as a cause of UGIB in cirrhosis patients. Oesophageal varices were predominantly found in male patients (72% versus 28%, p=0.001) and gastric varices predominantly in female patients (56% versus 44%, p=0.003). This was statistically significant. However there was no significant difference of various endoscopic lesions in different age groups (p>0.05). Our results are comparable with other local studies done in Pakistan. Afzal et al from Gujrat[15] found that 90.48% of 830 patients had oesophageal varices; Jamil et al[9] reported 73.6% bleeding varices from Islamabad; 65% variceal bleed reported from Sukkur[16] and 69.6% varices from Rawalpindi.[17] Shah et al reported 53.8% portal hypertension related UGIB and 35.6% PUD related UGIB in their patients in Nawabshah Sind[11]; whereas Ahmed at al in Karachi[10] found variceal bleeding in 50% patients. Other local studies from Rawalpindi[6,18] also reported similar results. Malghani et al from Multan also reported similar results of variceal bleed significantly seen in male patients.[19]

Similarly, regional and international studies also reported similar results of high frequency of variceal bleeds in patients with cirrhosis. A Czech Republic[20] study showed that 72.3% patients bled due to underlying portal hypertension (57.7% oesophageal varices) and 25.5% had non variceal bleed (18.2% had PUD) whereas 2.2% had normal endoscopy. An Italian study of 465 patients with cirrhosis by D'Amico et al[21] reported bleeding varices in 72% patients. Gabr et al reported 75.5% variceal bleed and 24.5% PUD as non-variceal cause of UGIB in their cirrhotic patients in Nile Delta, Egypt.[22] Another Egyptian study of 918 patients of UGIB by El Badry[23] showed portal hypertension in 55.5% and PUD in 27.1% as underlying cause of bleeding. Mahajan et al [7] from India

Table 1: Descriptive statistics of cirrhosis patients with UGIB (n=152)

Characteristics		Number of Patients	Percentage
Gender	Male	96	63.2
	Female	56	36.8
Age Groups	18-40 years	38	25
	41-60 years	67	44
	61-80 years	47	31
Endoscopic Findings	Hepatitis B Virus	40	26.3
	Hepatitis C Virus	92	60.5
	Hepatitis B & C Co-infection	10	6.6
	Non-B, Non-C	10	6.6
	Oesophageal Varices	133	87.5
	Gastric Varices	41	27.0
	Portal Gastropathy	57	37.5
	Peptic Ulcer Disease	21	13.8
	Gastritis	19	12.5
	Normal endoscopy	05	03.3

Table 2: Correlations of endoscopic findings with gender (n=152)

Endoscopic Findings	Gender		Total	p-value
	Male	Female		
Oesophageal Varices	96 (72.2%)	37 (27.8%)	133 (87.5%)	0.001
Gastric Varices	18 (43.9%)	23 (56.1%)	41 (27%)	0.003
Portal Gastropathy	35 (61.4%)	22 (38.6%)	57 (37.5%)	0.730
Peptic Ulcer Disease	12 (57.1%)	09 (42.9%)	21 (13.8%)	0.541
Gastritis	10 (52.6%)	09 (47.4%)	19 (12.5%)	0.312

Table 3: Correlations of endoscopic findings with age groups (n=152)

Endoscopic Findings	Age distribution			Total	p-value
	18-40 years	41-60 years	61-80 years		
Esophageal Varices	35 (26.3%)	60 (45.1%)	38 (28.6%)	133 (87.5%)	0.23
Gastric Varices	10 (24.4%)	18 (43.9%)	13 (31.7%)	41 (27%)	0.99
Portal Gastropathy	14 (24.6%)	23 (40.4%)	20 (35.1%)	57 (37.5%)	0.66
Peptic Ulcer Disease	06 (28.6%)	10 (47.6%)	05 (23.8%)	21 (13.8%)	0.74
Gastritis	07 (36.8%)	06 (31.6%)	06(31.6.0%)	19 (12.5%)	0.37

reported portal hypertension related variceal bleed in 53.62% and PUD in 17.56%.of their patients of UGIB. Another south Indian study[24] reported varices in 51.4% patients, mostly elderly men. Study from Nepal[25] also reported results of UGIB comparable to our findings. Alema et al from Uganda[26] reported oesophageal varices as the most frequent cause of UGIB.

On the other hand, contrary to our study results, Khan et al from Peshawar[12] reported 45.7% variceal bleed in their 350 patients with UGIB. The most likely reason for this discrepancy was the study of the general population, including non-cirrhotic patients, presenting with UGIB. Another study by Hina et al[13] reported 26% variceal bleed and 20.7% gastritis as a cause acute UGIB in 270 predominantly (76.1%) male patients. An Indian study from sub Himalayan region showed that UGIB due to PUD was more frequently seen in middle-aged men, commonly presenting as melena.[27] An Iranian study[28] reported PUD as the most common (45.5%) cause of UGIB; variceal bleed accounted for 19.5% whereas GI malignancy contributed as 14.7% for the bleed. Alatawi et al reported non-variceal cause for the UGIB in 83.56%, variceal bleed in 9.57% and normal endoscopy in 6.84% patients in Tabuk area of Saudi Arabia.[29] A Nigerian study[30] of the elderly patients also revealed PUD as the most common cause of UGIB (45.8%), followed by oesophago-gastric varices (16.1%) and 26.2% had normal endoscopy findings. In Mexico[1], gastro-duodenal ulcers were the source of non variceal UGIB in 50.6% patients of hepatic cirrhosis, with mean age of 56.5 ± 14.4 years and male predominance with a high mortality of 13.8%. Rockey et al[4] in a study of 1034 patients from the US found that 54% of cirrhotic patients had UGIB.

Most of the western studies generally reported PUD as the major cause of UGIB[2,3], whereas most studies from the developing world reported bleeding varices as the most common cause.[8] The difference is mainly due to high incidence of chronic viral hepatitis due to HBV and HCV in developing countries. Risk factors include sharing razors, syringes/needles and tattooing; dental and surgical procedures by quacks with unsterilized equipment, lack of safe transfusions of blood products and sexual transmission. Delayed diagnosis and lack of effective management of viral hepatitis due to various reasons also contribute to the high incidence of variceal bleeds.

Patients with liver cirrhosis not only bleed from varices, but also from other non-variceal lesions that occur in the general population, such as gastro-duodenal ulcers, erosions and arterio-venous malformations. Non-variceal upper gastrointestinal bleeding may be the source of UGIB in 30–40% of cirrhosis patients.[1,4,20] There is a higher incidence of peptic ulcer in cirrhosis as compared to the general population. Extremely varying results have been reported regarding PUD as a cause of UGIB. In our patients, 13.8% had peptic ulcer which is comparable to the incidence in general population. It is also in conformity with the results of other studies.[7,8,13,17,18,20,21]

Contrary to our findings, other studies have reported high incidence of bleeding peptic ulcers as underlying cause of UGIB; 50.6% by González-González[2], 45.8% by Jemilohun[30], 45.5% from Iran[28], 39.4% from India[27], 35.6% by Shah et al[11], 32.85% by Alatawi et al[29], 27.1% from Egypt[23] and 24.8% from Nepal.[25] On the other hand, very low incidence of 2.3% of PUD as a cause of UGIB has been reported by Afzal et al[15], 5.8% by Muhammad et al[16] and 7.3% by Ahmad et al [6] from Rawalpindi. The reasons for the wide variations include sample size of the studies, patient's selection, inclusion of 'general' population of UGIB, inclusion of only cirrhosis liver patients of UGIB and so on. The frequent use of antiulcer medications by the medical practitioners in individuals with dyspepsia symptoms may contribute to the lower incidence of peptic ulcer as a cause of bleeding in our patients.

It was a single-center, tertiary-care hospital study and hence its results findings cannot be generalizable to patients in community, particularly those residing in far flung areas of the province with inadequate and limited access to medical facility. Therefore, studies are needed at primary healthcare/community level to draw the actual picture of the problem.

CONCLUSION

Portal hypertension related lesions were the most common underlying etiology in our study patients of liver cirrhosis presenting with UGIB. The findings on endoscopy included oesophageal varices (87.5%), portal gastropathy (37.5%) and gastric varices (27%). Non-variceal lesions were peptic ulcer disease (13.8%) and gastritis (12.5%). Only 5(3.3%) patients had normal endoscopic study. Male gender had significant association with oesophageal varices and female gender with gastric varices.

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Author's Contribution

MARA conceive the idea, designed the study, and helped in data collection and write-up of the manuscript. USR and MFA contributed in Data collection and write up and editing of the manuscript. MKH helped in data collection, Data analysis, and reviewed the manuscript for final approval. Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest

Authors declared no conflict of interest

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None

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.