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Frequency, Determinants and Outcome of Upper Gastrointestinal Bleed among Patients with Liver Cirrhosis

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Abstract

Upper gastrointestinal bleed (UGIB) is among one of the common clinical manifestations encountered in emergency departments. UGIB can manifest in form of hematemesis, melena and/or hematochezia. This study was undertaken to study frequency and determinants of upper gastrointestinal bleed in patients with liver cirrhosis and to assess the outcome of patients of liver cirrhosis presenting with upper gastrointestinal bleed. This study was conducted among 100 patients with documented cirrhosis of liver admitted to different wards of Rajindra Hospital attached to Govt. Medical College, Patiala, India.. Patients of liver cirrhosis with presenting complaints of upper gastrointestinal bleed were recruited as the study group and the patients of liver cirrhosis without UGIB were assessed as the control group. Upper gastrointestinal endoscopy was done to identify cause of UGIB. Patients with UGIB were followed up at 0, 3 and 6 month interval to assess the outcome. UGIB was detected among 53 (53%) among 100 subjects enrolled in the study. Previous history of upper gastrointestinal Bleed, NSAIDs intake, Binge alcohol drinking, presence of red colour signs, presence of medium and large size varices, evidence of varices in esophagus and stomach, low platelet count, deranged coagulation profile (prothrombin time and INR) and increased portal vein diameter were determinants of upper gastrointestinal bleed. In conclusion, early identification of these determinants combined with logical prescription to those with cirrhosis of liver can aid in deceasing the frequency of upper gastrointestinal bleed.

Keywords: Gastrointestinal Hemorrhage, Hematemesis, Liver Cirrhosis, Melena, Portal Vein, Ulcer, Varicose Veins

Introduction

Cirrhosis is a chronic disease of the liver in which diffuse destruction and regeneration of hepatic parenchymal cells has occurred and diffuse increase in connective tissue has resulted in disorganization of the lobular architecture. The triad of parenchymal necrosis, regeneration and

scarring is always present regardless of individual clinical manifestations.[1] Variceal hemorrhage, hepatic encephalopathy, spontaneous bacterial peritonitis and ascites-the major complications of cirrhosis of the liver result from portal hypertension which is defined as an increase in hepatic sinusoidal pressure to 6 mm Hg or greater. Portosystemic collaterals decompress the hypertensive hepatic sinusoids and give rise to varices at the gastroesophageal junction and elsewhere.[2]A major cause of cirrhosis-related morbidity and mortality is the development of variceal hemorrhage, a direct consequence of portal hypertension.[3] Survivors of an episode of active bleeding have a 70 percent risk of recurrent hemorrhage within one year of the bleeding episode.[4]Variceal hemorrhage occurs in 25 to 40 percent of patients with cirrhosis.[5] Early identification of, determinants of upper gastrointestinal bleeding and intensive management can lead to decrease in mortality and morbidity.

Materials and Methods

The present observational study was conducted among 100 patients with documented cirrhosis of liver admitted to different wards of our institution. Patients of liver cirrhosis with presenting complaints of upper gastrointestinal bleed (UGIB) were recruited as the study group and the remaining were assessed as the control group. This was a case control study to record frequency and various determinants of UGIB.

Inclusion Criteria

Case group

1. Patients with documented liver cirrhosis.
2. Patients in age group > 14 years.
3. Patients presenting with upper gastrointestinal bleed manifested as hematemesis or melena.

Control group

1. Patients with documented liver cirrhosis.
2. Patients in age group > 14 years.
3. Patients presenting without upper gastrointestinal bleed

Patients with age group < 14 year and upper gastrointestinal bleed without liver cirrhosis were excluded from the study. Patients were verified for fulfilling inclusion criteria and ruled out for presence of exclusion criteria. Informed consent was taken from patients and family after briefing them about the study in their vernacular language. A detailed history, clinical examination and laboratory workup was done. Upper gastrointestinal endoscopy was done to identify the cause of UGIB. Detailed statistical analysis was performed using Chi Square Test for significance and continuous variables were analyzed by ANOVA for significance using SPSS version 20. The study group with UGIB was followed up at 0, 3 and 6 month interval to assess the outcome.

Binge alcohol drinking is defined as a state where 5 drinks for men and 4 drinks for women and must be consumed on one occasion at least once in a two-week period.

Thrombocytopenia was defined as platelet count of <150,000/mm3 and deranged coagulation profile as defined as INR of >1.2 and dilated portal vein diameter as diameter >12mm on ultrasound.

Results

Out of the total 100 patients with liver cirrhosis enrolled for the study 53 (53%) had UGIB. Among the patients with UGIB (53), 14 (26.41%) expired in total, out of which 6 (11.32%) patients expired during the hospital stay, 6 (11.32%) patients expired at 3 months and 2(3.77%) patients expired at 6 months according to follow up data. Out of 53 patients with UGIB, 19 (35.84%) patients had rebleeding, out of which 3 patients had rebleeding (5.66%) during the hospital stay, 7 (13.20%) had history of rebleeding at 3 months and 9 (16.98%) had history of rebleeding at 6 months according to follow up data. 4 patients were lost to follow up.

Table 1. Comparison of various parameters between cirrhotic patients with and without UGIB

Variable (% or Mean±SD)		With UGIB	Without UGIB	P value
Age (years)		53.91±10.992	53.26±11.683	0.775
Sex (male/female)		47/6	10/37	0.000
History of previous UGIB		79.24%	4.25%	0.000
NSAID'S intake		28.30%	6.38%	0.004
Binge Alcohol Drinking		71.69%	12.76%	0.000
Smoking		18.86%	29.78%	0.149
Child Turcotte Pugh Class	A	9.43%	21.27%	0.084
Child Turcotte Pugh Class	B	32.07%	46.80%	0.096
Child Turcotte Pugh Class	C	58.49%	31.91%	0.007
Red Colour Signs		69.81%	12.76%	0.000
Size of varices	Small (grade1)	47.16%	59.57%	0.149
	Medium (grade 2)	56.60%	21.27%	0.000
	Large (grade3)	71.69%	4.25%	0.000
Site of varices	Esophageal	60.37%	17.02%	0.000
	Gastric	15.09%	46.08%	0.001
Platelet Count (/mm3)		98849.06±30007.304	183595.74±77326.709	0.000
Blood Urea (mg/dl)		31.74±11.229	37.36±22.677	0.120
Serum Creatinine (mg/dl)		1.43±0.665	1.49±0.655	0.676
Serum Bilirubin (mg/dl)		4.060±0.9451	1.460±0.5157	0.000
SGOT		78.25±63.806	67.40±54.924	0.390
SGPT		111.49±111.113	96.13±91.359	0.455
Alkaline phosphatase		204.79±78.074	241.38±103.923	0.048
Prothrombin time (sec)		22.47±1.987	15.70±1.921	0.000
International Normalized ratio (INR)		2.00±0.000	1.04±0.204	0.000
Portal vein diameter (mm)		14.36±0.736	10.51±0.748	0.000

Discussion

Cirrhosis, the end result of the chimeric progression of multi hit liver damage, is on the rise in our community. The Punjabi culture of pomp and flair, being misread as a license to feed on intoxicants has lead the society into a fragile state, cirrhosis being one of the prominent end results. Males being the heavy drinkers are more prone to cirrhosis and its complications especially UGIB.

Patients with chronic liver disease (CLD) constitute a significant burden on the economy of the country. Patients with CLD frequently experience episodes of exacerbations including upper gastrointestinal bleeding precipitated by variety of established determinants or predictors.

Our study has demonstrated the frequency, determinants and outcome of UGIB. Identification and prevention of determinants of UGIB remains the corner stone of management. The present study aims to point out the major determinants prevalent in our community where the cases of cirrhosis and its complications are on exponential rise.

UGIB was detected among 53 (53 %) among 100 subjects enrolled in the study.

86.79% of the study group was in the age group of 30 – 69 years. Romcea et al[6] in a similar study noted similar frequency in the age group with 87.00% subjects falling in age group of 30 – 69 years.

In the present study a strong male preponderance was noted with 86.67% of males with UGIB. 47 (88.67%) males and 6 (11.37%) females had upper gastrointestinal bleed. Statistical evaluation showed p value of 0.000, indicating a statistically significant relation of difference in sex contributing to occurrence of UGIB. Singh et al[7] and Anand et al[8] in their studies noted that there was a male preponderance among the patients with UGIB with frequency of 85.53% and 83.88% respectively. Almost similar frequency was noted byLimquiaco et al[9] (73.11%), Kashyap et al[10] (78.40%), Romcea et al[6] (61.91%) and Benedeto-Stojanov et al[11] (65.38%). Male preponderance can be explained by the fact that majority of patients were male alcoholic cirrhotics and thus were prone to UGIB.

Etiology of variceal and non-variceal UGIB was sought for among the study group. Among 53 patients with upper gastrointestinal bleeding, 40 (75.47%) subjects were detected to have variceal bleeding and 13 (24.52%) were detected to have non-variceal bleeding. Out of 53 patients with UGIB, most common cause of UGIB was varices (esophageal and gastric) 40(75.47%) patients. Among patients with non-variceal UGIB, Portal Hypertensive Gastropathy was seen in 9.43% patients. Duodenal ulcer (5.66%), Gastric ulcer (3.77%) Gastric Vascular Ectasia 2 (3.77%) and Mallory Weiss Tear 1 (1.88%) were the other contributors in non-variceal UGIB. In a similar study conducted by Romcea et al[6], Variceal bleeding (73%) was more common as compared to non-variceal bleeding (27%). In the study conducted by Anandet al[8] in north India, Variceal bleeding was most common cause of UGIB followed by peptic ulcer disease, gastric erosions, Mallory Weiss tear, gastric tumor and duodenal polyp. However in the study conducted by Singh et al[7] in eastern India, bleeding from duodenal ulcer was most common followed by variceal bleeding.

Frequency of previous UGIB among patients with UGIB was noted as 79.24% in the present study(p=0.000). De Franchis et al[12] (70.00%) and Benedeto-Stojanov et al[11] (86.36%) have reported similar frequency of previous gastrointestinal bleed compared to the present study indicating history of previous UGIB as a significant determinant of recurrent UGIB.

History of NSAID's intake was documented among 28.30 % of patients presenting with UGIB (p=0.004). Contemporary literature mentions almost similar frequencies of – De Ledinghen et al[13] (25%), and Matei et al[14] (22.80%). While other studies mentions frequencies as follows - Kashyap et al[10] (56.26%), Anand et al[8] (19.28%) and Holvoet et al[15] (34.16%). This indicates use of NSAID is a major determinant of UGIB among patients presenting with UGIB.

History of binge alcohol drinking was documented among 71.69% of patients presenting with UGIB (p=0.000). Liao et al[16] in their study mentions a similar frequency of 78.37%. Anand et al[8] and Matei et al[14] in their studies noted the frequency of 53.50% and 4.50% respectively. Whereas Longstreth et al[17] in their study mentions a frequency of 18.00%. This indicates that the binge alcohol drinking is a major determinant of UGIB among patients presenting with UGIB.

History of smoking was documented among 18.86% of patients presenting with UGIB (p=0.149). A study conducted by Matei et al[14] mentions a similar frequency of 20.09% for history of smoking among patients with UGIB with p value 0.69 indicating non-significant association between smoking and patients with UGIB similar to present study.

Present study has noted that among 53 patients with cirrhosis of liver when graded according to Child Turcotte Pugh Score (CTPS) – Class A (9.43%), Class B (32.07%) and Class C (58.49%) (p value 0.007), with increasing degree of liver dysfunction chances of UGIB also increase. Similar results were noted by Svoboda et al[18] [Class A (23.30%), Class B (51.10%) and Class C (25.50%)] and Cerqueira et al[19] (p value 0.002).The NIEC study[20] also showed that higher degree of liver dysfunction according to CTP Class is a determinant of UGIB. Where as in a study conducted by Sarin et al[21], there was no significant difference in the rate of bleeding between patients belonging to Child's A (60%), B (50%), and C (56%) class of liver disease.

Presence of red colour signs was documented among 69.81% of patients presenting with UGIB (p=0.000). Other contemporary study conducted by Sarin et al[21], Benedeto-Stojanov et al[11] and Limquiaco et al[9] mentions a frequency of 93.05%, 85% and 98% respectively for presence of red colour signs on endoscopic evaluation among patients with UGIB indicating red colour signs are a major determinant of UGIB among the patients presenting with UGIB.

Present study documented that large (p=0.000) and medium (p=0.000) varices are more likely to bleed than small varices. Similar results were noted in the studies conducted by Sarin et al[21],Witzel et al[22], Pagliaroet al[23], Burrooughs et al[24], Benedeto-Stojanov et al[11] and NIEC[20]. The only exception is a study conducted by Koch et al[25], who found that 35% of patients with small varices bled, while only 20% of patients with large varices also bled.

Presence of esophageal varices was documented among 60.37% patients in present study and presence of gastric varices was among 15.09% patients with UGIB. Present study documented significant association of esophageal varices (p=0.000) and gastric varices (p=0.001) as a determinant of UGIB. Similar results were noted in the studies conducted by Odelowo et al[26], Seo et al[27] and Svoboda et al[18] indicating presence of varices in both esophagus and stomach was significantly associated with UGIB.

Mean platelet count was 98849.06±30007.304 (/ mm3) among patients presenting with UGIB (p=0.000) and 183595.74±77326.709 (/ mm3) among patients without UGIB. Limiquiaco et al[9] in their study noted a mean platelet count of 122570±55666 (/ mm3) among patients with UGIB, depicting a similar significant decrease in platelet count in UGIB group. Similarly, Umar et al[28] in their study has noted a mean platelet count of 86100±69645 (/ mm3) in patients with UGIB indicating significant relationship between thrombocytopenia and UGIB.

In present study, Mean INR was 2.00±0.000 among patients presenting with UGIB (p=0.000) and 1.04±0.204among patients without UGIB. Umar et al[28] in their study also noted a mean INR of 1.63±0.503 in patients with UGIB indicating significant relationship between deranged coagulation profile and UGIB. However, Limiquiaco et al[9] in their study noted a mean INR of 1.38±0.503 among patients with UGIB, depicting non-significant deranged coagulation profile in UGIB group.

In present study, Mean portal vein diameter was 14.36±0.736 mm among patients presenting with UGIB(p=0.000) and 10.51±0.748 mm among patients without UGIB. Umar et al[28] in their study noted a mean portal vein diameter of 12.24±3.023 mm among patients with UGIB, depicting a similar significant increase in portal vein diameter in UGIB group.

Present study notes a frequency of rebleeding (35.84%) and mortality (26.41%). Among the patients with UGIB(53), total mortality was 26.41%, out of which 11.32% patients expired during the hospital stay at 0 month, 11.32% patients expired during next 3 months and 3.77% patients succumbed to illness at 6 months according to follow up data. Total patients with rebleeding were 35.84% patients had rebleeding, out of which 5.66% had rebleeding during the hospital stay at 0 month, 13.20% had history of rebleeding at 3 months and 16.98% had history of rebleeding at 6 months according to follow up data. 4 patients were lost to follow up. In a study conducted by Katschinski et al[29], death occurred in 189 (8.5%) patients, and 243 (11%) patients experienced rebleeding. Zaltmanet al[30] showed Rebleeding in 9.1% of the patients and overall mortality rate of 15.34%. In study conducted by D'Amico et al[31], 6-week rebleeding was 17%, and mortality was 20%. Romcea et al[6] showed bleeding relapses in 45.16% of all upper gastrointestinal bleeding. 6.45% cases of recurrence of bleeding within 7 days from the first episode of bleeding were found, 11.05% cases in the first month, 12.90% cases after 6 months and 14.74%cases after the first year and mortality because of upper gastrointestinal bleeding was of 2.69% in the study group.

Conclusion

Thus, we conclude that previous history of upper gastrointestinal Bleed, NSAIDs intake, Binge alcohol drinking, presence of red colour signs, presence of medium and large size varices, presence of varices in esophagus and stomach, low platelet count, deranged coagulation profile (prothrombin time and INR) and increased portal vein diameter were determinants of upper gastrointestinal bleed. Prevention is better than cure. Early identification of these determinants combined with logical prescription to those with cirrhosis of liver can aid in deceasing the frequency of upper gastrointestinal bleed. Special emphasis has also to be laid to steps in preventing alcoholism and viral infections leading to cirrhosis of liver.

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