

## **Etiological Spectrum, Clinical Profile And Prognostic Factors In Variceal Upper Gastrointestinal Bleeding.**

Vipin Goyal<sup>1</sup>, Shinu Singla<sup>2</sup>

<sup>1</sup>Doctorate of Medicine, Medical Gastroenterology

<sup>2</sup>Doctorate of Medicine, Neurology

Sri Aurobindo Medical College & PG Institute, Indore

**Corresponding Author:** Shinu Singla, Doctorate of Medicine, Neurology, Sri Aurobindo Medical College & PG Institute, Indore

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### **Abstract**

**Introduction:** Acute UGI bleed is defined as bleed occurring proximally to ligament of trietz common emergency presentation accounting for mortality rate of 10%. Worldwide, peptic ulcer disease is the commonest cause. Variceal bleeding has 30% in-Hospital mortality and 60% mortality in the 1<sup>st</sup> year.

**Material and Methods:** 2-year prospective observational study was performed on 201 patients presenting with hematemesis. Out of 201 patients, 125 (62.4%) patients were having varices and 76 (37.6%) had no varices. The patients with non-variceal bleed were excluded. Detailed history, examination and laboratory tests were performed. Appropriate statistical analysis on the data was performed.

**Results:** Mean age of the variceal population was 44.9years. Alcoholic cirrhosis (38%) was the commonest cause in variceal. Patients at presentation having tachycardia and hypotension had significantly increased risk of mortality both in variceal. Patients requiring endoscopic intervention had significantly increased mortality.

**Conclusion:** We found variceal bleed to be the commonest cause of hematemesis. Mean age of the

variceal bleed patients was 5<sup>th</sup> decade. We observed alcoholic cirrhosis as the commonest cause of variceal bleed and alcohols of cirrhosis. Tachycardia and hypotension on presentation and those requiring endoscopic intervention have poor prognosis.

**Keywords:** Variceal bleed, Mortality

### **Introduction**

Upper gastrointestinal bleed (UGIB) is defined as the bleed occurring proximally to ligament of trietz.<sup>[1,2]</sup> Acute UGIB is a common medical emergency with a mortality rate of around 10%.<sup>[3]</sup> A study in united kingdom estimated the incidence rate of around 50-150 per 100,000 population. UGIB can present as hematemesis or melena. Hematemesis is defined as vomitus containing blood while melena is used as the term for the black tarry stools, formed by degradation of the hemoglobin to hematin by the intestinal bacteria. Melena requires > 60 ml of blood leaked proximally to ligament of trietz and requires more than 8 hrs of intestinal transit time.<sup>[4]</sup> In 80% of patients UGI bleed is self limited without specific therapy.<sup>[1]</sup> The mortality rises to 30-40% in the remaining 20% of the patients who continue to bleed.

Worldwide, peptic ulcer disease is the commonest cause accounting for nearly 50-70% of the cases of UGI bleed, followed by esophageal varices (6-39%), Mallory weiss (2-8%) and drug induced (mostly NSAID). Other causes include neoplasm, gastroduodenal erosions and arteriovenous malformations.<sup>[5]</sup> Variceal bleeding has 30% in hospital mortality and 60% 1 year mortality.<sup>[6]</sup>

### **Material and Methods**

This is a hospital based, prospective observational study done in all patients presenting to emergency with acute UGIB during April 2016 to March 2018. Since the study was an observational study to collect the existing data, no attempt was made to make changes in the existing method of managing these patients and an attempt was made to collect all the available data prospectively. Patients were resuscitated initially followed by history regarding the complaints of the patient were recorded. Clinical examination was done to look for pallor, icterus, pedal edema, splenomegaly, ascites and signs for liver failure. Ryle's tube was inserted and rectal examination was done to look for melena. Relevant blood investigations were done. Viral markers were done in cirrhotic patients. Special tests like contrast echo, urinary 24 hour sodium, urinary 24 hour protein were also performed. Radiological investigations like ultrasound (USG), chest x-ray and computed tomography (CT) abdomen were done whenever necessary.

In all patients, associated comorbidities were also recorded. Patients diagnosed having variceal bleeding received vasopressors like octreotide or terlipressin and antibiotics were started. Blood and blood products were transfused whenever necessary. Upper gastrointestinal (UGI) Endoscopy was done using video scope (Olympus, GIF Type Q 150, Tokyo, Japan). Endoscopic variceal ligation or sclerotherapy was done in patients having

variceal bleeding. Glue therapy was done in patients with bleeding gastric varices. Patients with recurrent bleeding, not responding to endoscopic treatment was considered for TIPS or shunt surgery. Any morbidity or mortality occurring in the patients was also recorded.

Patients having cirrhosis with history of alcohol intake of 80 gm/day for more than 5 yrs was taken as alcoholic cirrhosis. Patients having esophageal varices with altered echo texture of liver on ultrasound were considered as cirrhotics. If ultrasound showed portal cavernoma formation or portal vein thrombosis in the absence of altered echo texture of liver was considered as extra hepatic portal vein obstruction (EHPVO). If patients had periportal echoes with normal liver echo texture, diagnosis of non-cirrhotic portal vein thrombosis (NCPF) was made. Complications occurring as a result of bleed or surgery were considered as morbidity.

### **Study Analysis**

Univariate analysis for the associations between clinical parameters and the morbidity and mortality of UGIB was carried out using the  $\chi^2$  test or Fisher's exact test for categorical variables. Continuous variables were compared using Student's *t* test. A *p* value < 0.05 was considered statistically significant. Multivariate Analysis with Logistic regression to identify independent parameters was performed and is presented with odds ratio and 95% confidence interval. Statistical analysis was done using SPSS version 17.0.

### **Results**

Study included 201 patients presenting with hematemesis out of which 125 patients were patients having varices and 76 were found to have no varices. Non-variceal bleed patients were excluded from the study.

The mean age of the variceal bleed patients was 44.9 years. Males constituted about 68.8% and females about

31.2% of this study. History of alcohol intake was present in 32.8% patients and NSAID intake in 1 patient. Diabetes was present in 12.8% patients, 6.4% patients had hypertension and 1 patient had history of asthma. History of jaundice was present in 24% patients and history of melena was present in 67.2% patients.

104 (83.2%) patients have underlying cirrhosis while 21 (16.8%) had extra hepatic portal vein thrombosis. Out of 104 cirrhotic patients, 5.7% patients belonged to CHILD A, 65.5% to CHILD B and 28.9% to CHILD C patients. Ascites was present in 60 patients of which, 40% had gross ascites, 33.3% had mild ascites, 20% patients have moderate ascites and 6.7% patients have minimal ascites while 44 cirrhotic patients had no ascites. SBP was found in 18.3% patients out of the 60 patients having ascites. Splenomegaly was observed to be present in 36.8% patients. (TABLE 1)

On endoscopy, esophageal varices are present in 98.4% patients while 2 patients didn't had esophageal varices. Out of 123 patients having ascites, 12.2% had grade 1, 17.1% had grade 2, 69.1% had grade 3 and 1.6% had grade 4 varices. Gastric varices were present in 14.4% patients out of whom 27.8% had GOV1F1, 5.6% had GOV1F2, 38.9% had GOV2F1 and 22.2% had GOV2F2. Hemorrhagic gastritis, gastric ulcer and duodenal ulcer was present in 4% each of these patients. 2 patients had Forrest class 2 and 3 patients had Forrest class 3, those having duodenal ulcer. GAVE (gastric antral vascular ectasia) was present in 2.4% patients. PHG (Portal hypertensive gastropathy) was present in 94 patients out of which 55.3% had mild and 44.7% had severe. 48% patients required blood transfusion. Tachycardia developed in 47.2% patients and 17.6% patients had hypotension. Of patients having varices, EVL was done in

66.4% cases, sclerotherapy in 2.4% and glue in 4% while no intervention was required in 27.2% cases. (TABLE 2)

Alcohol was found to be the commonest cause of cirrhosis. Etiological diagnosis of varices in cirrhotics were alcohol in 30.4%, Hepatitis B in 19.2%, NCPF in 15.2%, NASH in 10.4%, Hepatitis C in 7.2%, autoimmune in 5.6%, Wilson in 2.4% and BCS in 1 patient while non-cirrhotics (EHPVO) accounted for 16.8% patients. (TABLE 3)

Of the 104 cirrhotic patients, 33.7% patients developed hepatic hydrothorax, HRS in 1 patient and HPS developed in 1 patient. Rebleeding was observed in 14.4% patients within 3 months. HCC was diagnosed in 6.4% of 125 variceal bleed patients. (TABLE 4)

Various mortality factors were observed and analysed in patients having varices. Alcohol intake didn't significantly increased during hospitalization as compared to non-alcoholics ( $p=0.47$ ). Patients having cirrhosis have twice the likelihood of mortality as compared to non-cirrhotics but was insignificant ( $p=0.19$ ). Patients having CHILD C score had significantly higher mortality as compared to CHILD A ( $p=0.024$ ). Patients having ascites as compared to those with no ascites and patients having gross ascites had significantly higher mortality than those having mild ascites ( $p=0.001$  and  $p<0.001$ , respectively). Patients having PHG was not found to significantly increase mortality as compared to those not developing PHG ( $p=0.41$ ). Patients requiring blood transfusion had significantly increased mortality and the mortality was found to increase with increase in number of transfusions ( $p<0.0001$ ). Diabetes or hypertension were not found to increase mortality ( $p=0.32$ ). Patients those presented with rebleed within 3 months had significantly higher rate of death as compared to those who don't bleed ( $p=0.001$ ). Patients at presentation developing tachycardia and

hypotension had significantly increased risk of mortality as compared to those who don't ( $p=0.002$  and  $p=0.012$  respectively). (TABLE 5)

Table 1: Various clinical parameters

<b>MEAN AGE</b>	44.9 years
<b>GENDER</b>	No of patients (%age)
Male	86 (68.8%)
Female	39 (31.2%)
<b>JAUNDICE</b>	30 (24%)
<b>MELENA</b>	84 (67.2%)
<b>CIRRHOSIS</b>	104 (83.2%)
Child A	6 (5.7%)
Child B	68 (65.5%)
Child C	30 (28.9%)
<b>ASCITES</b>	60 (48%)
Mild	20 (33.3%)
Moderate	12 (20%)
Gross	24 (40%)
Minimal	4 (6.7%)
Nil	44 (42.5%)
<b>SBP</b>	11 (18.3%)
<b>SPLENOMEGALY</b>	46 (36.8%)
<b>BLOOD TRANSFUSION REQUIRED</b>	60 (48%)
<b>TACHYCARDIA</b>	59 (47.2%)
<b>HYPOTENSION</b>	22 (17.6%)
<b>INTERVENTION</b>	<b>91 (72.8%)</b>
EVL	83 (91.2%)
SCLEROTHERAPY	3 (3.3%)
GLUE	5 (5.5%)
NO INTERVENTION	34 (27.2%)

Table 2: Endoscopic findings in variceal bleed patients

ENDOSCOPY FINDINGS	No.	(%age)
<b>GASTRITIS</b>	<b>5</b>	<b>4%</b>

<b>GASTRIC ULCER</b>	<b>5</b>	<b>4%</b>
<b>DUODENAL ULCER</b>	<b>5</b>	<b>4%</b>
<b>GAVE</b>	<b>3</b>	<b>2.4%</b>
<b>ESOPHAGEAL VARICES</b>	<b>123</b>	<b>98.4%</b>
GRADE 1	15	21.2%
GRADE 2	21	17.1%
GRADE 3	85	69.1%
GRADE 4	2	1.6%
<b>GASTRIC VARICES</b>	<b>18</b>	<b>14.4%</b>
GOV1F1	5	27.8%
GOV1F2	1	5.6%
GOV2F1	7	38.9%
GOV2F2	4	22.2%
<b>PHG</b>	<b>94</b>	<b>75.2%</b>
MILD	52	55.3%
SEVERE	42	44.7%
<b>PORTAL HYPERTENSIVE DUODENOPATHY</b>	<b>7</b>	<b>4.8%</b>

Table 3: Etiological diagnosis

DIAGNOSIS	No.	%age
ALCOHOLIC CIRRHOSIS	38	30.4%
HBV RELATED CIRRHOSIS	24	19.2%
NCPF	19	15.2%
NASH RELATED CIRRHOSIS	13	10.4%
HCV RELATED CIRRHOSIS	9	7.2%
AUTOIMMUNE RELATED CIRRHOSIS	7	5.6%
WILSON RELATED CIRRHOSIS	3	2.4%
BUDD CHIARI SYNDROME RELATED CIRRHOSIS	1	0.8%
EHPVO	11	8.8%
<b>Total</b>	<b>125</b>	<b>100%</b>

**Table 4: Complications developing in cirrhotic patients**

COMPLICATIONS	No.	%age
HEPATORENAL SYNDROME	1	0.96
HEPATOPULMONARY SYNDROME	1	0.96
HEPATIC HYDROTHORAX	35	33.7
REBLEED	18	14.4
HEPATOCELLULAR CARCINOMA	8	6.4

**Table 5: Various clinical parameters affecting mortality**

Parameters	Mortality		P Value
	Parameter Present	Parameter Absent	
ALCOHOLIC	6/38	11/87	0.47
CIRRHOSIS	16/17	1/87	0.19
CHILD SCORE		0.024	
A OR B	7/74		
C	10/30		
ASCITES	15/60	2/44	0.001
PHG	12/94	5/31	0.41
REQUIRED BLOOD TRANSFUSION	17/60	0/65	<0.0001
DIABETES	4/16	13/109	0.32
HYPERTENSION	3/11	14/114	0.3
REBLEED	14/18	3/107	0.001
TACHYCARDIA	12/59	5/66	0.002
HYPOTENSION	11/22	6/103	0.012

**Discussion**

We studied 201 cases of UGIB presenting as hematemesis out of which 125 cases are of variceal bleed. We observed

that the most common cause of UGIB is esophageal varices accounting for 61.2% cases, a finding supported by recent studies by Dewan et al<sup>[7]</sup> Jaka et al<sup>[8]</sup> Suba et al<sup>[9]</sup> Sarwar et al<sup>[10]</sup> and Shrestha et al.<sup>[11]</sup> The explanation is due to fall in the incidence of non variceal bleed due to overuse of proton pump inhibitors in the society with relative increase in variceal bleed. Some studies have reported that non-variceal bleed (peptic ulcer disease) is the most common cause of UGIB.<sup>[12,13]</sup>

The mean age in our study was found to be 44.9 years which corresponds to the study done by Jain J et on UGIB patients and observed the mean age to be 46.2 years.<sup>[14]</sup> A study done by Schiller et al observed mean age to be much higher i.e. 6<sup>th</sup> decade.<sup>[15]</sup> We observed that the rate of alcohol intake in patients with variceal bleeding was 30% which was much higher than 1.6% in the general populations observed by Deshmukh et al in age >18 years.<sup>[16]</sup> A study by Komori et al on gastric varices found alcohol as a cause in 47.6% of the patients.<sup>[17]</sup> Male were found to be twice more commonly present with variceal bleeding as compared to females, a finding also observed by Dewan et al and Komori et al.<sup>[7,17]</sup>

We observed that the most common type of gastric varices is on the greater curvature (60%) which is in contrast to the study done by Sarin et al.<sup>[18]</sup> We observed that the most common cause of cirrhosis was alcohol (30%) while a study on gastric varices done by Komori et al observed that Hepatitis C was the most common cause of cirrhosis constituting about 43% cases.<sup>[17]</sup> We observed that the most common stage of cirrhosis was CHILD class B as was observed in the study done by Komori et al.<sup>[17]</sup>

We developed shock in 17.8% patients, a finding also seen in study done by Dewan et al who observed shock in 21.7% UGIB patients.<sup>[7]</sup> Rebleeding was found to be in 15% cases in our study which was slightly lesser than

23.8% observed by Komori et al.<sup>[17]</sup> The mortality rate in our study was found to be 13.6% while a the study done by Dewan et al observed mortality rate of 4.2%.<sup>[7]</sup> This higher death rate may be due to only variceal bleed patients in our study which have higher mortality rate than the non-variceal bleeding patients.

We observed that the cirrhotic patients having higher CHILD score had higher mortality. We observed that the cirrhotic patients having ascents had higher mortality than non-ascitic cirrhosis. These finding is because the decompensated cirrhosis had higher mortality than non-decompensated cirrhosis. Shock, requirement of blood transfusion and rebleed were found to be independent markers of mortality in our study.

We recognize the limitations of the present study. The mostimportant of them being that sample size though adequate for detection of endoscopic lesions was inadequate for the subgroup analysis. The present study was a single center study and hence not reflects the whole population. The end-point of the study was endoscopic diagnosis and the patients were not followed subsequently.

### Conclusion

We found variceal bleed to be the commonest cause of hemetemesis. Mean age of the patients due to variceal bleed was 5<sup>th</sup> decade. We observed alcohol as the commonest cause of cirrhosis while alcoholic cirrhosis as of variceal bleeding. Shock, requirement of blood transfusion and rebleed were found to be independent markers of mortality in our study.

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