Audit of Clinical Profile and Outcomes of Acute Variceal Bleed in a Tertiary Care Hospital

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Abstract

Aims   The main purpose of this article is to conduct audit of clinical profile and outcomes of patients presenting with acute variceal bleed in a tertiary care hospital.

Methods and Material   This was a retrospective study of patients presenting with variceal bleed in a tertiary care center. Data were generated through a computerized electronic record system. Data of patients admitted for acute variceal bleed from August 2018 to December 2018 were collected and considered for analysis. Statistical analysis was done using the software Statistical Package for the Social Sciences (SPSS) 22.0 version.

Results   Overall, 107 cases were analyzed. In 89.7% (96) cases, cirrhosis of liver was a cause of variceal bleed. Besides, 77.6% (83) patients had large esophageal varices. Five patients (4.7%) required glue injection. Rebleed rate in present study was 0.9%. Mortality due to variceal bleed was 9.3% (10). Acute rebleed (p = 0.002), low mean arterial pressure (MAP; p = 0.001), low platelet count (p = 0.001), high serum creatinine (p = 0.001), high serum total bilirubin (p = 0.001), high international normalized ratio (INR; p = 0.001), and higher model for end stage liver disease (p = 0.001) were associated with increased risk of mortality. Door to endoscopy time (<12 hours or 12–24 hours) did not affect the mortality rate (p = 0.699). Terlipressin given 24 hours after endotherapy is equally effective as terlipressin given 5 days after endotherapy.

Conclusion   Mortality due to acute variceal bleed can be reduced with timely intervention. Low MAP, low platelet count, higher serum bilirubin and creatinine, and higher INR are predictors of increased mortality due to variceal bleed. Endoscopy done within 12 to 24 hours of presentation did not affect the outcome.

Keywords
► upper GI endoscopy
► gastroesophageal varices
► cirrhosis of liver

Introduction

Variceal bleed is one of the most commonly encountered emergencies in patients with cirrhosis. In-hospital mortality remains as high as 20% in spite of advances in management.[1] Baveno VI consensus statement and the National Institute for Health and Care Excellence (NICE) guidelines on acute upper gastrointestinal (UGI) bleeding are widely used in managing patients of variceal bleed.[2,3]

There is a discrepancy in the epidemiological profile, management protocols, and outcomes worldwide. A nationwide survey on management and outcomes on variceal bleed in the UK considered prevalence of variceal bleed as a cause for UGI bleed, timing of presentation to hospital, etiology of varices, patients in whom endoscopy could be done within 24 hours of presentation, percentage of patients requiring anesthesia for UGI endoscopy, high risk stigmata, need for endoscopic therapy, etc.[4] The National Confidential Enquiry

into Patient Outcome and Death (NCEPOD) report in the UK pointed out the delays in endoscopy, clinical as well as organizational care, and need for out of hours dedicated gastrointestinal (GI) bleed services.[5] In-hospital mortality of patients with cirrhosis and variceal bleeding decreased threefold over the past two decades, in concurrence with an early and combined use of pharmacological and endoscopic therapies and short-term antibiotic prophylaxis.[6]

In spite of improved outcomes after variceal bleed, the necessity to optimize the management strategies persists. There are gray areas in managing variceal bleed such as duration of terlipressin therapy after variceal band ligation (VBL), use of proton pump inhibitors, referral for transjugular intrahepatic portosystemic shunt (TIPSS) after VBL, primary prophylaxis for gastric variceal bleed, antibiotics in variceal bleed, etc.[7] A tool kit developed to provide safer services in UGI bleed also recommends that all hospitals must collect a minimum dataset to measure service provision against auditable outcomes.[8] This underscores the importance of reporting data from all over the world. Several studies have done an audit of management, outcomes, and prognostic indicators.[9,10] Indian data in this regard, particularly variceal bleed management and outcomes, are scarce. We decided to conduct an audit of cases with variceal bleed who have undergone endoscopic therapy.

Materials and Methods

Study Design

It was a retrospective study of patients presenting with variceal bleed in a tertiary care center. Data were generated through a computerized electronic record system. Data of patients admitted for acute variceal bleed during August 2018 to December 2018 were collected and considered for analysis. All patients underwent endotherapy within 24 hours of presentation. As a departmental protocol, all patients received terlipressin on admission and every sixth hourly, which was continued for 24 hours after endotherapy. All patients received antibiotics before and after endotherapy till discharge or death. Patients with diagnosis of hepatorenal syndrome, spontaneous bacterial peritonitis, multiorgan dysfunction, sepsis, hepatic encephalopathy, etc., were excluded from analysis to avoid bias in mortality results. Esophageal varices were classified into small (<5 mm) and large varices (>5 mm), which is approved by the American Association for the Study of Liver Diseases. Gastric varices were classified according to Sarin's classification.

Variceal hemorrhage was defined as bleeding from an esophageal or gastric varix at the time of endoscopy or the presence of large esophageal varices with blood in the stomach and no other recognizable cause of bleeding.

An episode of bleeding was clinically significant when there is a transfusion requirement for two units of blood or more within 24 hours of time zero, together with a drop in systolic blood pressure of 20 mm Hg and/or pulse rate >100 beats per minute at time zero (time zero is the time of admission to the first hospital to which the patient was taken).

The acute bleeding episode is defined by an interval of 120 hours (5 days) from time zero. Evidence of any bleeding after 120 hours was the first rebleeding episode. Variceal rebleeding was defined as the occurrence of a single episode of clinically significant rebleeding from portal hypertensive sources from day 5. Clinically significant rebleeding was defined as recurrent melena or hematemesis in any of the following settings: (1) hospital admission; (2) blood transfusion; and (3) 30 g/L drop in hemoglobin.

Complete hemogram, lever function test, renal function test, and prothrombin time/international normalized ratio (PT/INR) were done using standard methods. UGI endoscopy was done by trained gastroenterologists.

Statistical Analysis

In the present study, the collected data were subjected to following statistical analysis. Descriptive statistics used were mean, standard deviation, frequency, and proportion. Inferential statistics including chi-squared test, Cramer's V, and independent-samples *t*-test were used for analyzing the various constraints among the study population. All the statistical methods were performed through the Statistical Package for the Social Sciences (SPSS) for windows package (version 22.0).

Results

During the study period, 107 patients were satisfying inclusion criteria and their data were recorded. Descriptive parameters are tabulated in ►**Table 1**.[2]

Results clearly revealed (►**Table 2**) that majority of the cases (89.7%, *n* = 96) diagnosed were due to cirrhosis of liver. Etiological distribution of cirrhosis of liver is shown in ►**Fig. 1**. Alcohol (75 out of 96, i.e., 78.1%) was the major contributor for cirrhosis. Most of the cases (77.6%, *n* = 86) of esophageal varices were found to be large (>5 mm). Glue injection was required in five (4.7%) cases. Only one patient (0.9%) rebled. Majority (90.7%, *n* = 97) of the cases were discharged. Majority of patients were in B and C of the Child–Turcotte–Pugh (CTP) class (84.1%, *n* = 90) and very few of the cases were in CTP class A (15.9%, *n* = 17). Gastric varices were seen in 35 patients (37.7%) with gastroesophageal varices 1 (GOV1) being the most common subtype (14%, *n* = 15) followed by combination

Table 1 Baseline characteristics

Parameter	Mean ± SD (CI)
Age (y)	48 ± 14.85 (11–81)
Hospital stay (d)	3.83 ± 2.08 (1–17)
Door to endoscopy time (d)	12.21 ± 5.91 (1–25)
Mean arterial pressure (mm Hg)	90.73 ± 15.36 (50–123.33)
Hemoglobin (g/dL)	7.71 ± 2.18 (2.6–13)
Platelet count (lacs per mL)	1.05 ± 0.66 (0.27–3.34)
Serum creatinine level (mg/mL)	0.97 ± 0.47 (0.70–4.13)
Serum total bilirubin (mg/mL)	3.06 ± 3.30 (0.30–1.92)
INR	1.63 ± 0.52 (0.96–2.90)

Abbreviations: CI, confidence interval; INR, international normalized ratio; SD, standard deviation.

of GOV1 and GOV2 (10.3%, $n = 11$). GOV2 was the least common subtype (1.9%, $n = 2$). Type 2 isolated gastric varices and ectopic varices were not seen in any of the cases.

Significant associations (►Table 3) were observed between diagnosis and outcome ($p = 0.013$), where majority of the cases with cirrhosis of liver discharged; however, more of mortality cases had noncirrhotic portal fibrosis ($p = 0.001$). Low mean

arterial pressure (MAP), low platelet count, higher serum creatinine, higher total bilirubin (TB), higher INR, and higher model for end-stage liver disease (MELD) were associated with increased risk of mortality (►Fig. 2; ►Table 4).

►Table 3 also revealed nonsignificant association between CTP class and outcome as well as no difference between discharged and mortality cases in their Hb values.

Discussion

Out of 107 cases analyzed, 9.3% ($n = 10$) died. This is comparable to other (10%) reported studies done on a larger sample size (10–15%).[11] Overall percentage of patients with gastric varices was 32.7%, which is higher than a usual of around 20% in patients with cirrhosis.[12] It is recommended that an acute variceal bleed should undergo endoscopic therapy in less than 12 hours.[13,14] Forty-nine out of 107 (45.7%) patients in our study have undergone endoscopic variceal ligation (EVL) within this time span. Patient's poor general condition requiring treatment and stabilization before endoscopy and delay on part of patient's attenders to give consent for the procedure were reasons for remaining patients in whom endoscopy was done after 12 hours. All patients have undergone endoscopy within 24 hours of presentation. Moreover, door to endoscopy time does not seem to affect the survival in our study ($p = 0.699$).

With advancement of liver disease, chances of variceal bleed also increase from 0% for CTP class A up to 30% for CTP class C.[15,16] We report that majority of our patients were of CTP class B and C (84.1%, $n = 80$). Proportion of CTP class C patients in expired group is 80% compared with 44% in alive group. Relatively well-compensated groups (CTP A and B) were 55% compared with 20% in expired group. p-Value being insignificant (0.08) might be due to smaller sample size. Larger sample size is needed for better validation of the p-value.

Only one among the 107 patients had rebleed in hospital and the p-value was statistically significant for rebleed in expired patients

Table 2 Percent distribution of diagnostic and treatment variables

Variables		No of patients, $n = 107$ (%)
Diagnosis	Cirrhosis of liver	96 (89.7)
	EHPVO	7 (6.5)
	NCPF	4 (3.7)
Esophageal varices	Large	83 (77.6)
	Small	24 (22.4)
Outcome	Discharged	97 (90.7)
	Died	10 (9.3)
CTP	A	17 (15.9)
	B	39 (36.4)
	C	51 (47.7)
GV type in positive cases	GOV1	15 (14.0)
	GOV2	2 (1.9)
	GOV1 + GOV2	11 (10.3)
	IGV1	7 (6.5)
Gastric varices		35 (32.7)
GLUE-INJ		5 (4.7)
Diabetes Mellitus		20 (18.7)
Rebleed		1 (0.9)

Abbreviations: CTP, Child–Turcotte–Pugh; EHPVO, extrahepatic portal venous obstruction;, GLUE-INJ, glue injection; GOV, gastroesophageal varices; GV, gastric varices; IGV, isolated gastric varices; NCPF, noncirrhotic portal fibrosis.
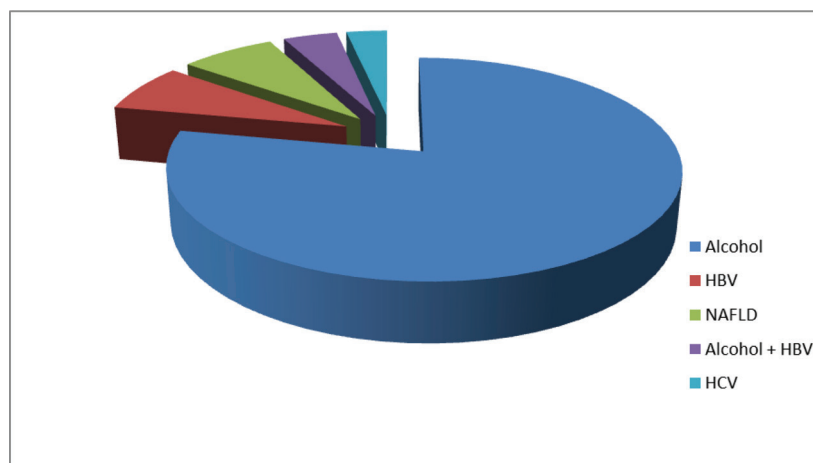

Fig. 1 Etiological distribution of cirrhosis. Alcohol, 75; HBV, 7; NAFLD, 7; Alcohol + HBV, 4; HCV, 3. HBV, hepatitis B virus; HCV, hepatitis C virus; MAP, mean arterial pressure; MELD, model for end-stage liver disease; NAFLD, nonalcoholic fatty liver disease; PLT, platelet; TB, total bilirubin.

Table 3 Analysis of variables in discharged and expired patients

Variable		Outcomes, n = 107 (%)		p-Value[a]
		Discharged, n = 97	Died, n = 10	
Age		47.90 ± 15.15	49.00 ± 12.24	0.824
		(Mean ± SD)	(Mean ± SD)	
	<30 y	11 (11.2)	0 (0)	0.414
	31–60 y	70 (72.2)	9 (90.0)	
	>60 y	16 (16.5)	1 (10.0)	
Gender	Male	74 (76.3)	9 (90)	0.322
	Female	23 (23.7)	1 (10.1)	
Diagnosis	Cirrhosis of liver	88 (90.7)	8 (80.0)	0.013
	EHPVO	7 (7.2)	0	
	NCPF	2 (2.1)	2 (20.0%)	
Esophageal varices	Large	74 (76.3)	9 (90.0)	0.322
	Small	23 (23.7)	1 (10.0)	
Door to endoscopy	<12 h	45 (46.4)	4 (40.0)	0.699
	>12 h	52 (53.6)	6 (60.0)	
Rebleed	Yes	0 (0.0)	1 (10.0)	0.002
	No	97 (100.0)	9 (90.0)	
CTP	A	17 (17.5)	0 (0.0)	0.082
	B	37 (38.1)	2 (20.0)	
	C	43 (44.3)	8 (80.0)	

Abbreviations: CTP, Child–Turcotte–Pugh; EHPVO, extra hepatic portal venous obstruction; NCPF, noncirrhotic portal fibrosis; SD, standard deviation.
[a]p-Value calculated using chi-squared test.
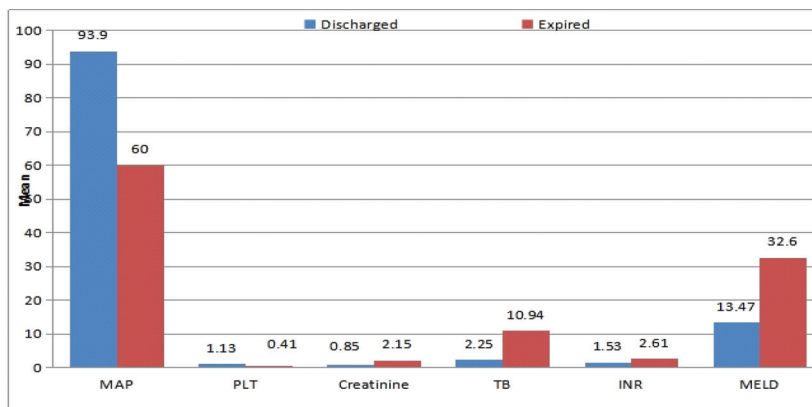
MAP – Mean arterial pressure, PLT – platelet, TB – Total bilirubin, MELD - Model for End stage Liver Disease

Fig. 2 Parameters associated significantly with increased risk of mortality due to variceal bleed in present study. INR, international normalized ratio; MAP, mean arterial pressure; MELD, model for end-stage liver disease; PLT, platelet; TB, total bilirubin.

In a similar multicentered retrospective study done on a larger sample size by Chalasani et al, age, blood pressure, hemoglobin, bilirubin, creatinine, INR, MELD score, etc., parameters were studied and were comparable to our results.[9,17] MAP, low platelet counts, high serum creatinine, high TB, high INR, higher MELD, and rebleed emerged as predictors of in-hospital mortality in our study. Age, sex, door to endoscopy time of 12 to 24 hours, CTP class, duration of hospital stay, and hemoglobin on admission were not statistically different across survived and expired cases.

Main strength of our study is that it shows that the mortality due to variceal bleed can be minimized if patients are timely managed. Even though 5 days of intravenous terlipressin is recommended, it has not shown to be beneficial in improving survival.[7] It also adds to the cost of treatment. This is particularly important in developing countries like India. We have treated patients with terlipressin for 24 hours with comparable survival rate. In this regard, our study highlights that treating patients with terlipressin for 24 hours is not only cost effective but also proved to be equally beneficial in reducing mortality.

Table 4 Analysis of investigations in discharged and expired patients

Variable	Outcomes, n = 107 (Mean ± SD)		p-Value
	Discharged, n = 97	Died, n = 10	
MAP (mm Hg)	93.90 ± 12.09	60.00 ± 7.86	0.001
Hemoglobin (g/dL)	7.81 ± 2.24	6.85 ± 1.40	0.189
Serum platelet (lacs per mL)	1.13 ± 0.66	0.41 ± 0.07	0.001
Serum creatinine	0.85 ± 0.15	2.15 ± 0.85	0.001
Total bilirubin	2.25 ± 1.69	10.94 ± 4.71	0.001
INR	1.53 ± 0.44	2.61 ± 0.30	0.001
Hospital stay	3.91 ± 2.15	3.10 ± 1.29	0.247
MELD	13.47 ± 3.96	32.60 ± 4.50	0.001

Abbreviations: INR, international normalized ratio; MAP, mean arterial pressure; MELD, model for end stage liver disease; SD, standard deviation.

This was a retrospective study done on a relatively small sample size and hence there are limitations in extrapolating the inferences to all patients with variceal bleed in whom endotherapy was done. Since there were limitations in accessing the data on risk stratification for risk factors like hepatocellular carcinoma (HCC), portal vein thrombosis, and other factors like obliteration or nonobliteration of varices after EVL, evaluation of the development of post-EVL ulcers could not be done. Since our study focused on mortality due to variceal bleed, it does not give any idea about the all-cause mortality. Fibroscan has a limited sensitivity in patients with ascites and obesity.[18] Moreover, the cut-off value of F2 and F4 fibrosis varies with the etiology.[19] Hence, we could not study the association of degree of fibrosis and mortality. Patients in whom endotherapy was unsuccessful could not undergo TIPSS, balloon-occluded retrograde transvenous obliteration, or endoscopic ultrasound-guided coiling due to unavailability of these modalities in our institute, which possibly could have further reduced bleeding-related mortality.

Owing to the dearth of parallel studies, particularly from India, our study throws light on the need for a thorough assessment of patients, risk stratification, and data recording and publication to set the standard operating procedure protocol suitable in Indian context in future.

Conclusion

In conclusion, the mortality rate due to variceal bleed was 9.3% in our study. Rebleeding occurred in as low as 0.9%. Alcohol-related cirrhosis of liver was the most common etiology of variceal bleed. Low MAP, low platelet count, higher serum creatinine, higher TB, higher INR, and MELD were associated with increased risk of mortality whereas age, sex, door to endoscopy time, grade of varices, CTP grade, and hemoglobin on admission did not emerge as predictors of mortality in the present study. However, we recommend more number of prospective studies in this regard on a larger sample size.

Conflict of Interest
None declared.

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