Original Article

Predictors of In-hospital Mortality Among Patients Presenting with Variceal Gastrointestinal Bleeding

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ABSTRACT

Background/Aim: The recent years have witnessed an increase in number of people harboring chronic liver diseases. Gastroesophageal variceal bleeding occurs in 30% of patients with cirrhosis, and accounts for 80%–90% of bleeding episodes. We aimed to assess the in-hospital mortality rate among subjects presenting with variceal gastrointestinal bleeding and (2) to investigate the predictors of mortality rate among subjects presenting with variceal gastrointestinal bleeding. **Patients and Methods:** This retrospective study was conducted from treatment records of 317 subjects who presented with variceal upper gastrointestinal bleeding to Government Medical College, Patiala, between June 1, 2010, and May 30, 2014. The data thus obtained was compiled using a preset proforma, and the details analyzed using SPSSv20. **Results:** Cirrhosis accounted for 308 (97.16%) subjects with bleeding varices, with extrahepatic portal vein obstruction 9 (2.84%) completing the tally. Sixty-three (19.87%) subjects succumbed to death during hospital stay. Linear logistic regression revealed independent predictors for in-hospital mortality, including higher age (P = 0.000), Child–Pugh Class (P = 0.002), altered sensorium (P = 0.037), rebleeding within 24 h of admission (P = 0.000), low hemoglobin level (P = 0.023), and serum bilirubin (P = 0.002). **Conclusion:** Higher age, low hemoglobin, higher Child–Pugh Class, rebleeding within 24 h of admission, higher serum bilirubin, and lower systolic blood pressure are the independent predictors of in-hospital mortality among subjects presenting with variceal gastrointestinal bleeding.

Key Words: Cirrhotics, predictors of mortality, variceal bleeding

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Gastrointestinal bleeding is one of the common, yet difficult to manage situations in an emergency department. Among the numerous causes of gastrointestinal bleeding, variceal bleeding accounts for the majority. Gastroesophageal variceal hemorrhage is a major complication of portal hypertension resulting from cirrhosis of the liver.[1] It causes gastrointestinal bleeding in 50%–60% cirrhotic patients. Rebleeding in upper gastrointestinal bleeding occurs in 7%–16%, despite endoscopic therapy. Rebleeding is especially high in variceal bleeding and peptic ulcer bleeding. Mortality ranges between 3% and 14% and there does not seem to be any change in this figure in the past 10 years. Mortality increased with increasing age and is significantly higher in patients who are already admitted in hospital for comorbidity.[2]

Gastroesophageal variceal hemorrhage is associated with higher morbidity, mortality, and hospital costs than other causes of upper gastrointestinal tract bleeding.[3,4] Approximately 30%–50% of patients with liver cirrhosis die within 6 weeks of the first variceal bleeding episode.[5,6]

The heavy burden of chronic liver disease in Punjab is due to high incidence of alcohol abuse and chronic viral hepatitis. According to the latest statistics, the state of Kerala stands first in per capita consumption of liquor at 8.3 L, followed by Punjab 7.9 L.[7] In a recent study conducted in Punjab, population prevalence of hepatitis C virus (HCV) infection was found to be 5.2%, with the highest prevalence noticed in the 41–60 years age group.[8] Early identification of predictors of mortality and intensive management can lead to decrease in mortality and morbidity.

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PATIENTS AND METHODS

This retrospective study was conducted from treatment records of 317 subjects who presented with variceal upper gastrointestinal bleeding to Government Medical College, Patiala, a tertiary care teaching hospital, between June 1, 2010, and May 30, 2014. All patients with gastroesophageal variceal hemorrhage were managed in emergency department as per hospital protocol using splanchnic vasoconstrictors such as terlipressin and octreotide, when indicated. Variceal band ligation is the treatment modality of choice, except when visibility is poor due to torrential bleeding, in which case ethanolamine oleate sclerotherapy is performed. In patients with significant rebleeding, defined as frank hematemesis, new onset of melena, fresh blood in nasogastric tube aspirate, or hemodynamic compromise, with a drop in hemoglobin level of >2 g/dL, re-endoscopy was done.

Diagnosis of cirrhosis was based on biochemical parameters and imaging studies and liver biopsy, where available. Extrahepatic portal vein obstruction was diagnosed on ultrasound Doppler scanning or computed tomography. Ascites was graded as "absent," "easily controlled" (if not associated with distress or easily treated with diuretics), or "tense" (if associated with respiratory or abdominal distress).

In patients with multiple admissions for variceal hemorrhage, each admission was treated separately. In case of death in the second or subsequent admission, the patient's data were analyzed as "survivor" in the initial admission(s) and as "nonsurvivor" in the last admission. In-hospital mortality was defined as death occurring while admitted at hospital for the particular episode of variceal bleeding.

A comparison between the chosen variables and mortality was performed. Univariate analysis included the Fisher's exact test or Chi-square test for categorical variables and the analysis of variance for continuous variables. Multivariate logistic regression using the stepwise selection method was performed starting from the variables with $P < 0.1$ in the univariate analysis. The accuracy was determined from the area under the receiver operating characteristic (ROC) curve using the SPSS version 20.0.

ROC curves compare sensitivity versus specificity across a range of values for the ability to predict a dichotomous outcome. Area under the ROC curve is another measure of test performance.

RESULTS

Cirrhosis accounted for 308 (97.16%) subjects with bleeding varices; with extrahepatic portal vein obstruction 9 (02.84%) completing the tally. Sixty-three (19.87%) subjects succumbed to death during hospital stay. Forty-nine (77.77%) subjects among those who died were males. Twenty-one subjects had 2 admissions and 12 had 3 admissions each.

Among the subjects who lost their lives, 16 harbored hepatitis B virus (HBV) infection, 22 had HCV infection, 39 had alcoholic liver disease as the cause of cirrhosis. Four subjects had HBV and HCV coinfection, 17 had alcoholism and HCV infection in common, and 12 had alcoholism and HBV infection in common.

After univariate analysis among survivors (S) and nonsurvivors (NS); predictors of mortality included rebleeding within 24 h of admission (P value = 0.000), Child–Pugh Class B and C (P = 0.000), altered sensorium (P = 0.005), spontaneous bacterial peritonitis (P = 0.000), older age group [60.30 ± 11.10 years (NS) versus 49.97 ± 11.24 years (S), P = 0.000], lower hemoglobin (Hb) levels [8.02 ± 2.01 g/dL (NS) versus 8.96 ± 2.07 g/dL (S), P = 0.001], serum bilirubin [2.98 ± 1.17 mg/dL (NS) versus 2.02 ± 1.24 mg/dL (S), P = 0.000], serum creatinine [1.62 ± 0.49 mg/dL (NS) versus 1.37 ± 0.58 mg/dL(S), P = 0.002], prothrombin time-International normalized ratio (PTINR) [1.19 ± 0.39 (NS) versus 1.09 ± 0.30 (S), P = 0.037], serum ascites albumin gradient (SAAG) [1.22 ± 0.419(NS) versus 1.11 ± 0.30(S) g/dL, P = 0.014], pulse rate [104.03 ± 8.48/min (NS) versus 95.60 ± 12.72/min(S), P = 0.000] and systolic [99.59 ± 11.45 mmHg(NS) versus 104.83 ± 10.52 mmHg(S), P = 0.001], and diastolic blood pressure [60.54 ± 9.55 mmHg(NS) versus 64.39 ± 9.733 mmHg (S), P = 0.005].

After linear logistic regression [Table 1], independent predictors for in-hospital mortality included higher age (P = 0.000), Child–Pugh Class (P = 0.008), rebleeding within 24 h of admission (P = 0.012), spontaneous bacterial peritonitis (P = 0.001), and high serum bilirubin (P = 0.002).

DISCUSSION

Gastrointestinal hemorrhage is a major complication of cirrhosis and portal hypertension, and is responsible for

Table 1: Linear logistic regression-significant predictors

Parameters	*P*
Age	0.000
Spontaneous bacterial peritonitis	0.001
Altered sensorium	0.037
Child-Pugh class	0.008
Rebleeding within 24 h of admission	0.012
Serum bilirubin	0.002

significant morbidity and mortality. The present study notes a mortality rate of 19.87% [Table 2]. Literature from Asian and Western studies alike report mortality rate between 7% and 35%.[9-13] The high mortality rate among the subjects suffering from variceal hemorrhage is a major cause of alarm in our institute as the prevalence of chronic liver disease in Punjab, India, has been on rise along with its complications.

Predictive factors reported for a poor prognosis in various cohorts of patients with variceal gastrointestinal bleeding include serum bilirubin,[13-15] international normalized ratio,[16] rebleeding after admission,[13] Child–Pugh Class,[17] serum albumin,[17] serum creatinine,[13,15,16] white blood cell count,[15,16] platelet count,[16] encephalopathy,[13,14,17] need for ventilation,[16] moderate-to-severe ascites,[16] and alanine aminotransferase levels.[14]

Early identification and appropriate management of variceal bleeding in individuals presenting with signs that predict mortality in the contemporary literature would give the medical practitioner the extra edge and time to save precious human lives [Table 3].

RECEIVER OPERATING CHARACTERISTIC CURVE

The area under the ROC curve describes test accuracy. Age and serum bilirubin levels with an area under curve of 0.743 and 0.756, respectively, claims the highest test accuracy for predicting mortality. Other significant predictors and area under curve were as follows: Altered sensorium (0.624), spontaneous bacterial peritonitis (0.669), CTPS class (0.668), rebleeding within 24 h (0.615) [Table 4 and Figure 1].

Table 2: Review of literature-mortality rate in subjects presenting with variceal bleeding

Study	Mortality rate (%)
Chojkier *et al.*[9]	35
Afessa and Kubilis[10]	21
Chalsani *et al.*[11]	14.2
Del Olmo *et al.*[12]	7.4
Ismail *et al.*[13]	8.7
Present study	19.87

CONCLUSION

Older age, low hemoglobin, higher Child–Pugh Class, rebleeding within 24 h of admission, spontaneous bacterial peritonitis, and higher serum bilirubin are the independent predictors of in-hospital mortality among subjects presenting with variceal gastrointestinal bleeding. Early identification and management of these predictors will aid in reducing mortality among subjects presenting with variceal bleeding.

Study limitations

The study was conducted as a retrospective design and the sample size was small.

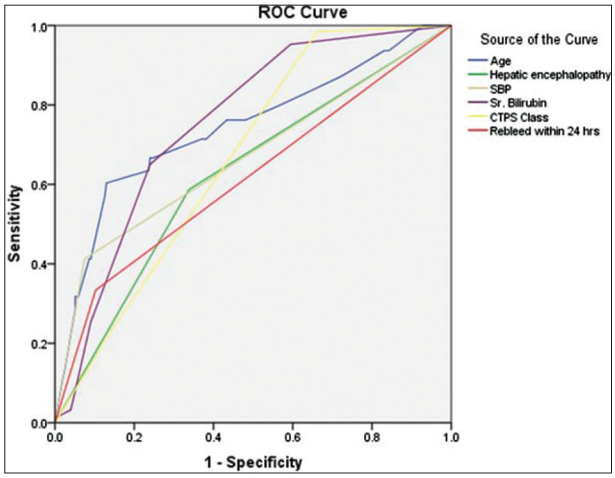

Figure 1: ROC curve

Table 3: Review of literature-predictors of mortality among subjects presenting with variceal bleeding

Parameters	Present study	Magliocchetti *et al.*[17]	Patch *et al*[16]	Chalasani *et al.*[14]	Malinchoc *et al.*[15]	Ismail *et al.*[13]
Serum bilirubin	+	–	–	+	+	+
Older age	+	–	–	–	–	–
Prothrombin time-international normalized ratio	–	–	+	–	–	–
Rebleeding within 24 h	+	–	–	–	–	+
Spontaneous bacterial peritonitis	+	–	–	–	–	–
Serum albumin	–	+	–	–	–	–
Serum creatinine	–	–	+	–	+	+
White blood cell count	–	–	+	–	–	–
Platelet count	–	–	+	–	–	–
Child-Pugh class	+	+	–	–	–	–
Encephalopathy	+	+	–	+	–	+

Table 4: Test accuracy

Parameters	Area under the curve	Standard error	95% confidence interval	
			Lower bound	Upper bound
Age	0.743	0.038	0.667	0.818
Altered sensorium	0.624	0.040	0.546	0.703
Spontaneous bacterial peritonitis	0.669	0.043	0.586	0.752
Serum bilirubin	0.756	0.031	0.695	0.816
CTPS class	0.668	0.033	0.604	0.733
Rebleeding within 24 h	0.615	0.043	0.532	0.699

CTPS=Child-Turcotte pugh score

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