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PROGNOSTIC MARKERS FOR ACUTE VARICEAL BLEED IN PATIENTS WITH CIRRHOSIS OF LIVER AND PORTAL HYPERTENSION

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ABSTRACT

Background and Aims: Variceal bleed is the most lethal complication of liver cirrhosis. Several factors and scoring systems have been known to predict the outcome of variceal bleed. The aim of the study was to assess the efficacy of current known factors and prognostic scoring systems in predicting short term outcome in patients presenting with variceal bleeding. **Materials and Methods:** The study was a prospective observational study that included 127 adult patients with cirrhosis and portal hypertension who presented with variceal bleeding. The outcomes measured were mortality and length of hospital stay ($</= 7$ days or > 7 days). A poor outcome was taken as mortality or hospital stay > 7 days. Categorical variables were expressed using frequency and percentage. Numerical variables were presented using mean and standard deviation. Chi-square test with continuity correction was used to study the statistical significance of the association of all categorical variables with the outcomes mortality and hospital stay. Student's t test was used to study the statistical significance of the comparison of all continuous demographic and clinical parameters between outcomes. **Results and Conclusion:** The study showed that total counts, platelet counts, INR did not have significant association with poor outcomes. Presence of hepatic encephalopathy, renal failure and a MELD score $>/= 14$ were found to have association with mortality in variceal bleed. CHILD C status, presence of hepatic encephalopathy, MELD score $>/= 14$, AIMS 65 score of $>/=2$ and Glasgow Blatchford Score (GB score) >8 were predictors of a prolonged hospital stay.

KEYWORDS: Cirrhosis, variceal bleed, prognostic markers.

INTRODUCTION

Cirrhosis is defined as the histological development of regenerative nodules surrounded by fibrous bands in response to chronic liver injury that leads to portal hypertension and end stage liver disease. Portal hypertension is a clinical syndrome defined by a portal venous pressure gradient exceeding 5 mm Hg.[1] Variceal haemorrhage, hepatic encephalopathy, and ascites, the major complications of liver cirrhosis, result from portal hypertension. Nature decompresses the hypertensive portal vein by diverting up to 90% of the portal flow through portosystemic collaterals back to the heart, resulting in flow mediated remodelling and enlargement of these vessels. A common location for portosystemic anastomoses is at the gastroesophageal junction where they lie immediately subjacent to the mucosa and present as gastric and oesophageal varices. Variceal haemorrhage is the most lethal complication of Cirrhosis.[2] Despite advancements in therapy, the mortality rate at 6 week is at least 20%.[2] It is managed with pharmacologic agents, endoscopic, radiologic and surgical techniques, in addition to the general measures. Various factors influence the outcomes in variceal bleeding. The commonly studied factors include the presence of hepatic encephalopathy, prothrombin time/ International Normalised Ratio (INR), Child Pugh Score, presence of acute renal failure and Model for End stage Liver disease (MELD) score. Various studies have proved the role of above factors in outcome of variceal bleed. The other currently existing scores used to assess the outcomes after variceal bleeding are AIMS 65 score and Glasgow Blatchford Score (GB score).

In this study, we have attempted to assess the efficacy of current known factors and prognostic scoring systems in predicting short term outcome in patients presenting with variceal bleeding secondary to cirrhosis of liver with portal hypertension.

MATERIALS AND METHODS

I. Selection and description of participants

The present study was a prospective observational study that included 127 adult patients with cirrhosis and portal hypertension who presented with variceal bleeding to a tertiary care hospital in India. Patients diagnosed to have other causes of upper gastrointestinal tract bleeding (such as peptic ulcer disease, reflux esophagitis, erosions, antral vascular ectasia) were excluded.

Ethical clearance was obtained for the study from

Institutional Ethics Committee of the hospital. Informed consent was obtained from the patients.

II. Technical Information

All clinical variables including demographics, biochemical and haematological investigations and other relevant data were recorded on a pre-designed proforma. All patients underwent upper endoscopy and therapy was initiated according to the endoscopic findings. All the endoscopic findings were described according to the American Association for the Study of Liver Diseases (AASLD) system of classification.

III. Statistics

Statistical analysis was performed using IBM SPSS version 20.0 software. Categorical variables were expressed using frequency and percentage. Numerical variables were presented using mean and standard deviation. Chi-square test with continuity correction was used to study the statistical significance of the association of all categorical variables with the outcomes mortality and hospital stay. Student's t test was used to study the statistical significance of the comparison of all continuous demographic and clinical parameters between outcomes. A p value of <0.05 was considered to be statistically significant.

Short term outcomes assessed

A good outcome was defined as survival or hospital stay $</= 7$ days.

A bad outcome was defined as death or hospital stay > 7 days.

RESULTS AND DISCUSSION

The baseline characteristics of all the patients are given in table 1.

Table 1.

Baseline Characteristics	Overall n=127
Age (Mean±SD) in years	58±9.8
Gender n(%) Male Female	109(85.8) 18(14.2)
Aetiology n(%) Alcoholic HBV related HCV related Cryptogenic Others	61(48) 7(5.5) 4(3.1) 49(38.6) 6(4.7)
Comorbidities n(%) Diabetes Hypertension Coronary Artery Disease Chronic Kidney Disease	66(52) 33(26) 5(3.9) 10(7.9)
CHILD Status n(%) A B C	28(22) 52(40.9) 47(37)
Hepatic encephalopathy n(%)	36(28.35)
Hepatic encephalopathy grading n(%) Grade 1 Grade 2 Grade 3 Grade 4	5(3.9) 15(11.8) 11(8.6) 5(3.9)
Ascites n(%)	73(57.5)
Blood culture n(%) Positive Negative	6(4.72) 121(95.28)
AIMS 65 score n(%) 0 1 2 3 4	20(15.75) 35(27.56) 30(23.62) 31(24.41) 11(8.66)

Glasgow-Blatchford score n(%)	
4-7	10(7.87)
8-11	29(22.83)
12-23	88(69.29)
Renal failure n(%)	40(31.5)
Rebleed n(%)	15(11.8)
Mortality n(%)	20(15.7)

Association of variables with mortality
Table 2 shows the comparison of variables between the patients who died during the hospital admission and those who did not.107 patients survived and 20 patients died during the hospital admission. It was noted that mortality was high in patients who were known hypertensives. The presence of hepatic encephalopathy and acute renal failure was more in the patients who died. A MELD score >/= 15 was also a predictor of mortality. Although the patients who died had a higher AIMS 65 score and GB score, it was not significant.

Table 2.

Variables	Alive(n=107)	Dead(n=20)	p value
Age (mean±SD)	58±9.5	58±11.21	0.77
Comorbidities n (%)			
Diabetes	53(49.5)	13(65)	0.204
Hypertension	24(22.4)	9(45)	0.035
CAD	4(3.73)	1(5)	1.000
CKD	7(6.54)	3(15)	0.403
CHILD C n(%)	36(33.6)	11(55)	0.074
Hepatic Encephalopathy n(%)	25(23.36)	11(55)	0.004
HE grading n(%)			
Grade 3	6(5.6)	5(25)	0.001
Grade 4	2(1.86)	3(15)	
Ascites n(%)	60(56)	13(65)	0.459
Total WBC count	10.53 ± 7.40	10.95 ± 5.56	0.809
Platelet	93.94 ± 50.82	115.40 ± 75.27	0.113
INR	2.05 ± 1.05	1.94 ± 0.87	0.671
Acute Renal Failure	26(24.2)	14(70)	< 0.05
MELD >/=15 n (%)	60(56.07)	17(85)	0.01
AIMS 65 SCORE n(%)			
>/= 2	57(53.27)	15(75)	0.058
GB score n (%)			
>8	97(90.65)	20(100)	0.051

Association of variables with duration of hospital stay
Table 3 shows the comparison of variables between the patients who had a stay of </= 7 days with patients who had a stay of > 7 days. 90 patients had a hospital stay of </= 7 days where as 37 patients had hospital stay of > 7 days. The mean age of patients who had a longer hospital stay was higher. The chance of patients with Child Pugh score C and hepatic encephalopathy having a longer hospital stay was more. A higher MELD score, higher AIMS 65 score and a higher GB score were also predictors of a longer hospital stay.

Table 3.

Hospital stay	</=7 days (n=90)	>7 days (n= 37)	p value
Age (mean±SD)	56.52±9.83	61±9.15	0.019
Comorbidities n (%)			
Diabetes	47(52.2)	19(51.3)	0.929
Hypertension	22(24.4)	11(29.7)	0.537
CAD	3(3.33)	2(5.4)	0.965
CKD	6(6.66)	4(10.8)	0.671
CHILD C n(%)	27(30)	20(54.05)	0.005
Hepatic Encephalopathy n(%)	19 (21.1)	17 (45.94)	0.005
HE grading n(%)			
Grade 3	6(6.66)	5(13.5)	0.001
Grade 4	3(3.33)	2(5.4)	
Ascites n(%)	45(50)	28(75.67)	0.459
Total WBC count	10.06 ± 6.972	11.90 ± 7.42	0.187
Platelet	94.93 ± 55.32	103.13 ± 56.54	0.452
INR	1.99 ± .99	2.14 ± 1.11	0.445
Acute Renal Failure	27 (30)	13 (35.13)	0.57
MELD >/=15 n (%)	50 (55.56)	27 (72.97)	0.05
AIMS 65 SCORE n(%) >/= 2	44(48.88)	28(75.67)	0.006
GB score n (%) >8	80(88.88)	37(100)	0.021

This study was done to assess the efficacy of current known factors and scoring systems in predicting short term outcome in patients presenting with variceal bleeding secondary to cirrhosis of liver with portal hypertension. Short term outcomes evaluated were mortality and duration of hospital stay.

In our study 15.7% patients died of variceal bleed. This was similar to that found by Chalasani et al.[3] who, in a large study over three years long, reported that in-hospital mortality was 14.2%. In this study older patients were found to have longer hospital stay though it had no association with mortality. This can be due to the age-related comorbidities. This is similar to the previous study by Liu C L et al. who found that age was an independent factor for longer hospital stay.[4] Magliocchetti et al. had found that presence of encephalopathy was a predictor of morality in patients with variceal bleeding.[5] This study also showed that the presence of hepatic encephalopathy was a predictor of mortality and longer hospital stay. Goh et al.[6] had found thrombocytopenia as a predictor of the presence of bleeding. The INR is an accurate measure of liver synthetic function and has been validated as a means of indicating liver decompensation and predicting mortality in the cirrhotic patient.[7] In our study, however total counts, platelets and INR had no significant association with outcome in variceal bleed. A previous study by Hshieh et al.[8] had showed INR not to be validated as a predictor of bleeding risk in cirrhotic patients. It was noted in the study that the presence of acute renal failure was a predictor of mortality. This finding is in keeping with that of a previous report showing that the development of renal failure after bleeding was an independent predictor of both short and long term mortality.[9]

The AIMS65 score consists of the following components: albumin level <3.0 g/dL (A), international normalized ratio (INR) >1.5 (I), altered mental status (M), systolic blood pressure ≤90 mm Hg (S), and age >65 years (65). In this study, patients with AIMS score ≥ 2 had chances of a prolonged hospital stay. In a study from the Middle East conducted by R B Thandassery et al.[10], the score predicted high in-hospital mortality, blood transfusion, intensive care unit (ICU) admission, and duration of hospital and ICU stay.

The Glasgow Blatchford Score (GB Score) takes into account heart rate, systolic blood pressure, haemoglobin, blood urea, presence of melaena, cardiac failure, syncope, history of hepatic disease. It is a tool to assess the prognosis of patients presenting with upper gastrointestinal bleed. In our study GB score had significant association with hospital stay. Patients with scores > 8 were found to have prolonged hospital stay.

In this study a MELD score >/= 15 was associated with both mortality and hospital stay. This finding was similar to the finding of Asrani et al. that a higher MELD was a predictor of 6 week mortality.[11]

A limitation of the study was that one month and three month mortality of the patients could not be followed up.

CONCLUSION
The study showed that total counts, platelet counts, INR did not have significant association with poor outcomes. Presence of hepatic encephalopathy, renal failure and a MELD score >/= 14 were found to have association with mortality in variceal bleed. CHILD C status, presence of hepatic encephalopathy, MELD score >/= 14, AIMS 65

score of >/=2 and GB score >8 were predictors of a prolonged hospital stay.

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