ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 09 | September - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

MORTALITY ASSOCIATED WITH VARICEAL BLEED IN CIRRHOSIS PATIENTS ATTENDING A TERTIARY CARE CENTRE IN SOUTH KERALA.

Medicine

Joshi S.C.	Ex DNB Trainee (Gastroenterology), KIMS Trivandrum, Kerala. Presently working as Associate professor in department of Medicine, Government Medical college Haldwani, Uttarakhand .
Dr. Godawari Joshi *	Associate professor in department of Obst. & Gynae, Government Medical college Haldwani, Uttarakhand. *Corresponding Author
Nair A.K.	Senior Consultant in department of Gastroenterology , KIMS Trivandrum, Kerala.
Khiangate Banjamin	Ex DNB Trainee (Gastroenterology), KIMS Trivandrum, Kerala.
Raviraj Sunil	Ex DNB Trainee (Gastroenterology), KIMS Trivandrum, Kerala.

ABSTRACT

Background : Acute variceal bleeding is a most common complication of portal hypertension. Despite advancement in management of variceal bleeding still carries a very high morbidity and mortality. The present study was undertaken to study mortality associated with variceal bleed in cirrhotic patients attending a tertiary care hospital.

Method : This prospective study was conducted between June 2016 to may 2018. Total 60 patients included in the study who admitted with acute variceal bleeding episode with underlying cirrhosis.

Results : Majority of patients were male (76 %). The mean age of patients was 54 +/- 13.7. Most common etiology of cirrhosis was Alcohol related liver disease (51.7%). Most common presenting symptom was hematemesis with melena(41.7%). Majority of patients presented with recurrent bleeding episodes (61.7%). 18.3% Patients had rebleeding episode within 5 days of admission. Total 21 (35 %) patients died during study period. Univariate analysis showed advance age, presence of ascites, Encephalopathy, high creatinine, bilirubin and INR were important predictors of mortality. In multivariate analysis only significant predictors was serum creatinine (OR 43.1 (CL 3.05 to 608.64)).

Conclusion: Patients with cirrhosis are always at risk of variceal bleeding. The survival after a bleeding episode was influenced by age, comorbidities, in hospital complications, ascites, high CTP and MELD score , beta blocker therapy

KEYWORDS

Cirrhosis , Portal Hypertension, variceal bleeding , esophageal varices

INTRODUCTION

Cirrhosis is major health problem worldwide. Alcoholism, Chronic viral hepatitis, and nonalcoholic steatohepatitis (NASH) account for major etiologies. The natural history cirrhosis characterized by an asymptomatic compensated phase, followed by a progressive decompensated phase.[1] Moreover, ascites is most frequently the first sign to appear and transition from compensated to a decompensated stage occurs at a rate of 5-7% per year.[1] Varices usually develop when the HVPG (Hepatic Venous Pressure Gradient) rises above 12 mmHg to decompress the portal vein pressure. New varices develop at a rate 5% at one year and 28% at three year, and progression of small varices at a rate of 12% at one year and 31% at three years.[2] It has been seen that 30% of patients of compensated cirrhosis and 60% of patients with decompensated cirrhosis have varices at the time of diagnosis.[3] The risk of hemorrhage has been related to the size and appearance of the varices as well as degree of hepatic dysfunction. Each episode of acute variceal hemorrhage is associated with 30% mortality[3, 4] In addition survivors of an episode of active bleeding have a 70% risk of recurrent hemorrhage within one year of the bleeding episode.[5] The risk peaks noted during the first 5 to 10 days, the period in which 40% of all re-bleedings occur. Afterwards, it decreases slowly, equaling at week six.[5] Prognostic factors of mortality in acute variceal hemorrhage included presentation with hematemesis, failure to control bleeding within five days, raised bilirubin, encephalopathy, shorter interval of admission to hospital, plasma urea, bleeding starting in hospital, recent use of steroid drugs within seven days of bleeding, age >60 years, HVPG, concomitant HCC and need of transfusions.[6] Being a tertiary care Centre, our hospital was catering a large population of south Kerala and peripheral areas of Tamilnadu state. No recent data was available from our region on mortality associated with variceal bleeding in cirrhosis and still there is a paucity of Indian literatures regarding mortality in variceal bleeding with ascites. So, we conducted this study to determine the mortality in all cirrhotic patients admitting with variceal bleeding.

MATERIALAND METHODS

This study was conducted at a tertiary care hospital in department of Medical Gastroenterology during April 2016 to March 2017 Kerala Institute of Medical Sciences, Trivandrum in South Kerala. It was a Prospective Descriptive Study and was approved from Institutional Ethics committee. Total 73 patients presenting with variceal bleed enrolled in the study. All patients were explained in detail about the purpose of the study and informed consent was taken from each patient. All variceal bleeding patients, diagnosed as having liver cirrhosis based on clinical, laboratory, imaging, and endoscopic features. Thirteen Patients were lost during follow up and whose survival data could not be obtained. All patients were followed up to one year after recruitment. All the data were collected and subjected to conventional statistical analysis. SPSS 17 software was used. Categorical and continous variable expressed as frequency/ Percentage and mean ± SD. Logistic regression done with one year mortality as the dependent variable (Yes or No). After univariate analysis the variables with a "p" value less than or equal to 0.1 were be included in the final model. ROC curves were drawn for each of the following parameters: MELD Na score, INR, Platelet count, serum creatinine, Haemoglobin, Bilirubin. Sensitivity, specificity and likelihood ratios were calculated at each cut off. Area under the curve were calculated after drawing the ROC curves.

OBSERVATION:

Majority of patients were from > 6th decade of life 20 (33.3 %) Amith S. Kumar et al,(28).. Mean age was 54 ± 13.7 years. Most of the patients were males 46 (76.7 %), followed by females 14 (23.3 %). Male to female ratio was 3.2: 1. Majority of patients were graduate/postgraduate 32(53.3 %), followed by up to intermediate 17 (28.3 %). Almost half of the patients were in lower middle class 30 (50 %), followed by upper middle class 18 (30 %). Shown in table (1). Most common etiology of cirrhosis of liver was alcohol 31 (51.7 %), followed by NASH 8 (13.3 %) and viral 7 (11.7 %), shown in Table (2). Out of 60 patients, 39 (65%) had cirrhosis with ascites. Mild to moderate ascites was noted in 21(35 %), 15 (25 %) patients, respectively. Tense ascites was noted in only 4 patients (6.7 %). Cirrhosis with HCC noted in 7 (11.7 %) patients. Out of 60 patients, 33 (55%) had associated comorbidities. Hepatic Encephalopathy was noted in 48 patients (80 %), maximum patients were in Grade I Hepatic Encephalopathy, 28 (46.7 %), followed by Grade II 14 (23.3%). Spontaneous Bacterial Peritonitis was noted in 11 patients (18.3 %), shown in Table (3).

Majority of patients, 39 (65%) were in Child class-C, followed by Child class-B, 18 (30 %). Most common presentation was hematemesis with melena 25 (41.7 %), followed by hematemesis 18 (30%). Majority of patients presented with recurrent variceal bleeding episodes 37(61.7 %). More than > 4 units of PRBC transfusion required in 16 patients (26.7%). Most common source of bleeding was esophageal varices 50 (83.3 %), followed by gastric varices 9 (15 %). Most common endoscopic intervention was done EVL, in 41 patients (68.3 %) followed by sclerotherapy in 7 patients (11.7 %), shown in Table (4) In hospital mortality was 16.7 %. One-year mortality in variceal bleeding patients was 35 %. The table (5) shows higher age, presence of ascites, encephalopathy, higher creatinine, bilirubin and INR are significant predictors of mortality at one-year. Higher albumin, Haemoglobin and Platelet count were significant protective factors. In a multivariate logistic regression analysis, the only significant predictor of mortality was serum creatinine (OR 43.1 (CI 3.05 to 608.64)). ROC analysis showed a MELD score above 21 has a sensitivity of 95% in predicting mortality in the first year.

DISCUSSION :

The large burden of chronic liver disease in Kerala is due to high incidence of alcohol abuse, nonalcoholic hepatitis (NASH) followed by 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.[8] In our study alcohol was the most common etiology of cirrhosis of liver (51.7%) followed by NASH (13.3%). Probably high consumption of alcohol and different dietary habits may be a one of reason for large burden of disease. Existing literature indicates that the mortality rate with each variceal bleeding episode is ranges from 8 % to 50 %.[1, 7] In our study, In- hospital and one-year mortality were 16.7 %, and 35 %, respectively and it was comparable with other studies. K Thomopulos et al,[9] reported in-hospital, and 1-year mortality, 12.1%, and 32.6%, respectively. Kumar AS et al,[8] reported in-hospital mortality 19.87% in their study. More recently, Chalasani et al,[10] in a large study over a period of 3 years, reported in- hospital mortality 14.2%. A decreasing trend of mortality associated with variceal bleeding is noted in several studies.[11,12,13]. It is probably because of improved survival due to use of non-selective beta-blockers, endoscopic band ligation and other effective therapies for primary and secondary prophylaxis. In our study, univariate analysis revealed several predictors of mortality: higher age, presence of ascites, encephalopathy, higher creatinine, bilirubin and INR were significant predictors of mortality at one-year, but higher albumin, haemoglobin and Platelet count were significant protective factors. In a multivariate logistic regression analysis, the only significant predictor was serum creatinine (OR 43.1 (CI 3.05 to 608.64)). In our study higher age was associated with high mortality and majority of patient died in > 60 years of age group (P < 0.028). In a series Sempere L et al[14] noted that the that age ≥ 65 years was significantly associated with early mortality after a bleeding episode. In a another study conducted by Chojkier M et al,[15] found that in-hospital status of the patient, co-morbid conditions and greater transfusion requirements with in first 24 hours, showed a striking association with mortality. This increased mortality was probably related to duration of progression of liver disease, and the greater difficulty of management of recurrent decompensation. In our study we found that presence of ascites was associated with higher mortality (P < 0.020). G D' Amico et al,[1] described one year mortality rate in stage 4 disease 57 %. In the Danish National Health registry in alcoholic cirrhosis, one-year survival rate was 51 % in ascites with variceal bleeding.[16]. In our study higher serum creatinine value was an independent predictor of mortality, raised bilirubin and INR were also showed a significant association at one-year mortality. Ismail Faisal W et al[17] in a retrospectively analysis found that serum creatinine > 1.5 mg/dl at the time of admission, Serum bilirubin >3 mg/dl, were significant predictor of mortality. Another large retrospective study Malinchocs model[18] showed serum bilirubin level >3 mg/dL and serum creatinine level >1.7 mg/dL were an important predictor of mortality.[19] Patch et al, in their study found INR, serum creatinine and bilirubin, platelet count were an important predictor of mortality. Magliocchetti and colleagues,[8] correlated, albumin level, in variceal hemorrhage with survival. In our study Hepatic Encephalopathy was also an important predictor of mortality in variceal bleeding patient (P < 0.016). In a study by Chalasani et al and Amith S. Kumar et al,[8, 19] reported Encephalopathy as a important factor predicting mortality. In our study ROC analysis, showed CTP Score and MELD Na score were an important predictor of mortality. A MELD score above 21 had a sensitivity of 95% in predicting mortality in the first year. Wang MT et al,[20] noted in their study that higher Child Class B and C were the predictors of mortality in cirrhotic patients with variceal bleed. K.Thomopulos et al,[9] in their study showed that Child Class C on admission was an independent predictors of 6 week mortality. In a prospective study Hunaysh AY,[21] demonstrated that CTP and MELD were the predictive factors associated with re-bleeding within 6 weeks period and high MELD score (>19) was an independent predictor of mortality. In a series of Bambha K et al,[22] found that MELD score ≥ 18 were early predictor of mortality and every 1-point increase in the MELD score, there was a 5% increased risk of re-bleeding within 5 days of hospital admission and that patients with a higher MELD (>18) had a significantly increased risk of rebleeding. In our study we also noted that higher CTP score and MELD score associated with increased mortality. A MELD score above 21 had a sensitivity of 95% in predicting mortality in the first year.

CONCLUSIONS:

Acute variceal bleeding is a fatal complication of portal hypertension and associated with increased morbidity, mortality, hospital stay and cost of health care for patients. Several factors associated with mortality in acute variceal bleeding, so early identification and intensive care management of these factors can lead to decrease in morbidity and mortality.

TABLES

Table-1: Socio-Demographic Profile.

Age group (years)	Frequency	Percent
≤ 40	7	11.7
41 - 50	17	28.3
51 - 60	16	26.7
> 60	20	33.3
Total	60	100.0
Sex	**Frequency**	**Percent**
Male	46	76.7
Female	14	23.3
Total	60	100.0
Education	**Frequency**	**Percent**
High school	11	18.3
Intermediate	17	28.3
Graduate/Post graduate	32	53.3
Total	60	100.0
Socio-Economic Status (SES)	**Frequency**	**Percent**
Upper class	7	11.7
Upper middle class	18	30.0
Lower middle class	30	50.0
Lower class	5	8.3
Total	60	100.0

Table : 2 , Etiology (N=60)

Characteristics	Frequency	Percentage
Alcohol	31	51.7
NASH	8	13.3
Viral	7	11.7
Cryptogenic	6	10.0
Wilson	4	6.7
Autoimmune	2	3.3
Hemochromatosis	1	1.7
Drug induced	1	1.7

Table-3: Clinical characteristics of study subjects. (N=60)

Variables	Frequency	Percentage	
Cirrhosis/ Cirrhosis with ascites	Cirrhosis	21	35.0
	Cirrhosis + Ascites	39	65.0
Ascites	None	21	35.0
	Mild	20	33.3
	Moderate	15	25.0
	Massive(tense)	4	6.7
Hepatocellular carcinoma (HCC)	Cirrhosis alone	53	88.3
	Cirrhosis + HCC	7	11.7
Comorbidities	Cirrhosis alone	27	45.0
	Cirrhosis + comorbidities	33	55.0

Hepatic Encephalopathy	None	12	20.0
	Grade I	28	46.7
	Grade II	14	23.3
	Grade III	5	8.3
	Grade IV	1	1.7
SBP	Present	11	18.3
	Absent	49	81.7

Table-4: Clinical characteristics of study subjects. (N=60)

Variables	Frequency	Percentage	
Child class	A	3	5.0
	B	18	30.0
	C	39	65.0
Presenting symptoms	Hematemesis	18	30.0
	Melena	17	28.3
	Hematemesis + Melena	25	41.7
Variceal Bleeding episode	First	23	38.3
	Recurrent	37	61.7
Blood transfusion (PRBC in first 24 hours)	>4PRBC	16	26.7
	<4PRBC	25	41.7
	No transfusion	19	31.7
Source of Bleeding	Esophageal varices	50	83.3
	Gastric varices	9	15.0
	Both	1	1.7
	Ectopic	2	3.3
Endoscopic diagnosis	Active bleeding from varix	31	51.7
	Clot overlying a varix	13	21.7
	White nipple on a varix	16	26.7
Endoscopic therapy /Intervention applied	EVL	41	68.3
	Sclerotherapy	7	11.7
	Both	4	6.7
	Sangstaken tube	3	5.0
	Esophageal Stenting	3	5.0
	BRTO	1	1.7
	No intervention done	1	1.7
Re-bleeding within 5 days	Rebleeding	11	18.3
	No rebleeding	49	81.7
In hospital complications	Complications	20	33.3
	No complications	40	66.7
On B- blocker	Blocker	46	76.7
	Not	14	23.3
Hospital stay	<48 hours	7	11.7
	>48 hours	53	88.3

Table-5: Descriptive statistics for continuous variables.

Characteristic	Value
CTP Score, mean (SD)	10.4 (2.3)
MELD Na, mean (SD)	23.4 (7.1)
Systolic Blood pressure, (mm of Hg), mean (SD)	91.0 (17.2)
Hemoglobin level, (gm/dl), mean (SD)	7.5 (1.9)
WBC count (per cubic mm), mean (SD)	12218.3 (6858.5)
Platelet Count (thousands), mean (SD)	63.6 (28.3)
Bilirubin, (mg/dL), median (range)	2.9 (0.1-13.7)
Albumin, (gm/dl), mean (SD)	2.8 (0.6)
INR, mean (SD)	2.0 (0.5)
Sodium (meq/L), mean (SD)	130.9 (5.8)
Creatinine, (mg/dL), median (range)	0.9 (0.6-3.6)

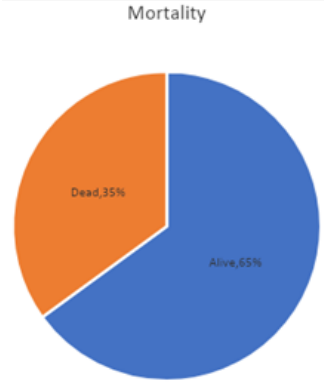

Fig. Percentage distribution of one year mortality.

Table-6, Predictors of Mortality; Logistic regression. Mortality (Yes or No) as dependent variable.

Variable	Odds ratio	CI of OR	P value
Age	1.05	1.01 to 1,10	0.028
Sex	2.29	0.67 to 7.75	0.184
Ascites	5.14	1.30 to 20.34	0.020
Albumin	0.09	0.02 to 0.34	0.0005
Haemoglobin	0.61	0.42 to 0.89	0.0094
Platelet Count	0.97	0.95 to 0.99	0.0077
Creatinine	20.27	2.68 to 153.13	<0.0001
Bilirubin	1.36	1.08 to 1.71	0.003
INR	4.61	1.38 to 15.41	0.0076
Encephalopathy	2.22	1.16 to 4.25	0.016

Table -7, ROC (ROC-Receiver operating characteristics) Analysis

Variable	AUC	Cut-off	Sensitivity	Specificity
MELD Na	0.803 (0.68 to 0.90)	21	95.2	53.8
Creatinine	0.824 (0.70 to 0.91)	0.9	81.0	71.8
INR	0.712 (0.58 to 0.82)	1.87	81.0	57.0
Haemoglobin	0.689 (0.56 to 0.80)	8.2	100	41.0
Platelets	0.712 (0.58 to 0.82)	50000	66.7	68.2
Bilirubin	0.72 (0.59 to 0.83)	3.0	71.4	69.2

REFERENCES

1. D'Amico G, Garcia TG, Pagliaro L. Natural history and prognostic indicator of survival in cirrhosis: A systemic review of 118 studies. Journal of Hepatology.2006; 44:217-231.
2. Merli M, Nicolini G, Angelonis S, Renaldi V, De Santis A, Merkel C et al. Incidence and natural history of small esophageal varices in cirrhosis patients. J Hepatol.2003;38:266.
3. Smith JL, Graham hemorrhage DY. Variceal hemorrhage: A critical evaluation of survival analysis. Gastroenterology.1982;82:968.
4. de Dombal FT, Clarke JR, Clamp SE, Malizia G, Kotwal MR, Morgan AG. Prognostic factor in Upper G I bleeding.Endoscopy1986;18 Suppl 2:6-10.
5. Graham DY, Smith JL. The course of patients after variceal hemorrhage. Gastroenterology.1981;80:800.
6. Gado A, Ebeid B, Abdelmohsen A, Axon A. Predictor of mortality in patients with acute upper gastrointestinal hemorrhage who underwent endoscopy and confirmed to have variceal hemorrhage. Alexandria Journal of Medicine.2015;51:295-304.
7. Sharara AI, Rockey DC. Gastroesophageal variceal hemorrhage. N Engl J Med.2001;345:669-681
8. Amith S. kumar and Raminderpal S. Siba. Predictors of in-hospital mortality among patients presenting with variceal gastrointestinal bleeding. Saudi J Gastroenterol.2015; 21(1):43-46.
9. Thompoulos K, Theocharis G, Mimidis K, Lampropoulou-karatza C, Alexandridis E, Nikolopoulou V. Improved survival of patients presenting with acute variceal bleeding. Prognostic indicator of short References 60 term and long term mortality. Digestive and liver Disease.2006;38 (12):899-904.
10. Chalsani N, Kahi C, Francois F, Pinto A, Marathe A, Bini EJ, et al. Improved patient survival after acute variceal bleeding: a multicenter, cohort study. Am J Gastroenterol.2003;98:653-659.
11. Pauwels A, Fourdan O, Carbonell N. Mortality from digestive hemorrhage for the last fifteen years. Gastroenterol Clin Biol.1998;22:(Suppl 2): A27. References 58
12. Del Olmo JA, Pena A, Serra MA. Predictors of morbidity and mortality after the first episode of upper gastrointestinal bleeding in liver cirrhosis. J Hepatol.2000;32:19-24.
13. Carbonell N, Pauwels A, Serfaty L, Fourdan O, Levy VG, Poupon R. Improved survival after variceal bleeding in patients with cirrhosis over the past two decades. Hepatology. 2004;40:652-659.
14. Sempere L, Palazón JM, Sánchez P J. Assessing the short and long-term prognosis of patients with cirrhosis and acute variceal bleeding. Revista Española dfermedades Digestivas.2009;101:236-248.
15. Chojkier M, Laine L, Conn HO, Lerner E. Predictors of outcome in massive upper gastrointestinal hemorrhage. J Clin Gastroenterol.1986;8:16-22
16. Asrani SK, Kamath Patrick S. Predictors of Outcomes in Patients with Ascites, Hyponatremia, and Renal Failure. Clinical Liver Disease.2013;2:132-135.
17. Ismail FW, Mumtaz K, Shah HA, Hamid S, Abbas Z, Abid S et al. Factors predicting in hospital mortality in patients with cirrhosis hospitalized with gastroesophageal variceal hemorrhage. Indian Journal of Gastroenterology.2006;25:240- 243.
18. Malinchoc M, Kamath PS, Gordon FD, Peine CJ, Rank J, Borg PC. A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. Hepatology.2000;31:864-871.
19. Chalasani N, Clark WS, Martin LG, Kamean J, Khan MA, Patel NH, et al. Determinants of mortality in patients with advanced cirrhosis after TIPS. Gastroenterology. 2000;118:138-144.
20. Wang MT, Liu T, Ma XQ, He J. Prognostic factors associated with rebleeding in cirrhotic in- patients complicated with esophageal variceal bleeding. Chinese Medical Journal. 2011; 124: 1493-1497.
21. Hunaysh AY. Prediction of Early Re-bleeding and Mortality after Acute Esophageal Variceal Hemorrhage among Yemeni Patients in Major Hospitals Sana'a. Open Journal of Gastroenterology.2016;6:214-227
22. Bambha K, Kim WR, Pedersen R, et al. Predictors of early re-bleeding and mortality after acute variceal haemorrhage in patients with cirrhosis. Gut.2008;57(6):814–820.