

RESEARCH ARTICLE DOI: 10.53555/jptcp.v30i18.3456

# ACUTE VARICEAL BLEED IN CIRRHOTIC PATIENTS: FACTORS INFLUENCING CLINICAL OUTCOME

Soban Abu Khifs<sup>1</sup>, Zoobia Hussain<sup>2\*</sup>, Rubab Munawar<sup>3</sup>, Zara Sagheer<sup>4</sup>, Muhammad Shaheryar Khan<sup>5</sup>, Ammar Farooq<sup>6</sup>, Swetha Sakthivel<sup>7</sup>

<sup>1</sup>House Officer, Ayub Teaching Hospital, Abbottabad - Pak
<sup>2\*</sup>Lecturer Pathology, Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur - AJK
<sup>3</sup>Medical Officer, RHC Mallot, Bagh- AJK
<sup>4</sup>Medical Officer, CMH Rawalakot - AJK
<sup>5</sup>Sharif Medical City Hospital, Lahore - Pak
<sup>6</sup>Divisional Headquarters Teaching Hospital, Mirpur – AJK
<sup>7</sup>Royal College of Surgeons - Ireland

#### \*Corresponding Author: Zoobia Hussain

\*Lecturer Pathology, Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur - AJK Email: zkmart94@gmail.com

#### Abstract

**Objective:** The purpose of this study was to identify the clinical outcome and contributing factors of acute variceal haemorrhage in cirrhotic individuals.

Study Design: Retrospective study

**Place and Duration:** The study was conducted by collecting data from medicine departments of different hospitals during the period from July 2022 to June 2023.

**Methods:** Total 215 patients with variceal bleed were presented in this study. Based on laboratory, clinical and imaging results, cirrhosis was diagnosed. The Baveno III consensus report was used to identify acute variceal haemorrhage, inability to control bleeding, and rebleeding. Rate of mortality related to uncontrolled bleeding was assessed.

**Results:** There were 142 (66.04%) males and 73 (33.95%) females among all cases. 37 (17.2%) cases had age 18-30 years, 72 (33.5%) had age 31-40 years, 55 (25.6%) patients had age 41-50 years and 51 (23.7%) cases had age >50 years. We found failure to control bleed in 27 (12.5%), rebleeding in 31 (14.4%) cases. Diabetes was found in 88 (40.9%) cases. There were 58 instances (26.04%) of hepatocellular carcinoma and 35 cases (16.3%) of portal vein thrombosis (PVT). The presence of diabetes mellitus and active bleeding at the time of endoscopy were predictors of failure to control bleed, while the presence of diabetes mellitus and serum bilirubin >3 mg/dL were predictors of in-hospital re-bleed. Mortality was found in 19 (8.8%) cases.

**Conclusion:** The presence of diabetes mellitus, active bleeding during endoscopy, and bilirubin levels that are greater than 3 mg/dL were revealed to be negative prognostic markers for initial control of variceal haemorrhage as well as recurrent bleed in patients with cirrhosis.

Keywords: Variceal bleeding, DM, Mortality, Cirrhosis

#### INTRODUCTION

Variceal haemorrhage happens in thirty percent of people who have liver cirrhosis and portal hypertension, and if it is left untreated, there is a mortality rate of fifty percent after one year.[1,2] The risk of an early rebleed is highest within the first 48–72 hours, and more than half of all early rebleed episodes occur within the first 10 days after an active bleed has been stopped.[3-5] It is unknown what causes variceal haemorrhage in people with liver cirrhosis who are from the Indian subcontinent. According to an early observation made at our institute in 2003, the likelihood of experiencing a further bleed after the index bleed was relatively low.[6] This experiment had a bias in support of a reduced rebleed rate as a result of the participation of variceal bleeders who had previously received sequential sclerotherapy.

Several different prognostic models have been developed in order to accomplish the goal of predicting the outcome of upper gastrointestinal bleeding, often known as UGIB. Although the Rockall and Glasgow Blatchford ratings are often employed in UGIB, it has been demonstrated that they are not effective for predicting predicted results in patients who have AVB. These measures have only been validated for use in determining clinical outcomes for patients who have nonvariceal UGIB (NVB).[6] Child-Pugh scores and the MELD score, which evaluates end-stage liver disease, are widely used to anticipate prognosis in cirrhotic patients. Both of these scores measure the severity of end-stage liver disease. However, because these models were not developed with the purpose of predicting patients' prognoses for AVB, it is possible that AVB patients cannot make use of them. Patients who have AVB have a significantly increased chance of developing bacterial septicemia, circulatory dysfunction, and other cirrhosis consequences. These complications can ultimately lead to acute or chronic liver failure.[8] Mortality rates in cirrhotics following a first variceal bleed climb to between 15 and 80% and rise with rising Child scores. These rates vary from 15 to 80%.[9] The three major causes of death are haemorrhaging that cannot be controlled, infections, and kidney failure. High MELD scores, renal failure, hepatic venous pressure gradients above 20 mm Hg, and endoscopic evidence of a continuous bleed are all characteristics that are related with higher mortality and a poor prognosis. Other factors include liver venous pressure gradients above 20 mm Hg.[10,11] There is a possibility that the CPT and MELD prognostic ratings, which are currently being utilised, do not provide an appropriate representation of the potential for acute variceal bleeding.

The severity of UGIB might vary greatly from person to person. The ability to accurately predict clinical outcomes is still receiving a significant amount of attention. This is due to the fact that early prognostication may assist in effectively stratifying and treating patients who are at a higher risk. In addition, patients with cirrhosis who are admitted to the intensive care unit (ICU) for any reason are a particularly high-risk population, with an in-hospital mortality rate ranging from 20 to 100 percent. This is because the ICU is a setting that is designed to treat patients who are critically ill. [12]. The in-hospital mortality rate for cirrhotic patients who were hospitalised to the intensive care unit (ICU) with acute variceal bleed (AVB) was found to be 39% after an analysis was performed on all of the patients.[13] Recently, research and assessment have been conducted on alternative statistical methods such as the Classification And Regression Tree (CART) analysis in preparation for their potential application in the medical domains. Numerous studies conducted up to this point have proved that this approach is useful in the process of generating accurate prognostic models for a wide range of medical subspecialties.[14] However, Child-Pugh, MELD, and CART have not all been implemented on the same patient dataset at the same time. The CART analysis for short-term and long-term survival has only been supplied by two early data studies for the purpose of prognostic assessment of bleeding cirrhotic patients.[15]

This study was carried out with the purpose of determining the factors that influence the clinical outcome of acute variceal bleeding in cirrhotic patients.

#### MATERIALS AND METHODS

This retrospective study was conducted in the department of medicine of multiple hospitals during the period from July 2022 to June 2023. The data comprised of 215 cirrhotic cases. Patients with

cirrhosis who were experiencing acute bleeding due to variceal haemorrhage were considered for inclusion in the trial. Cirrhosis was diagnosed after reviewing the patient's medical history, analysing the patient's clinical data, and obtaining imaging results (Ultrasound abdomen, CT scan or MRI) that were consistent with the diagnosis. Esophagogastroduodenoscopy demonstrated the presence of bleeding from a varix (active bleeding, endoscopic red sign or absence of any other cause except the esophageal varices). Patients' first clinical characteristics were documented, such as their levels of shock, biochemical profiles, endoscopic findings, and imaging results.

Everyone in the database received the gold level of care as determined by the Baveno consensus workshops. At admission, all patients were given terlipressin a vasoactive agent, blood, and the prophylactic antibiotics ceftriaxone (91%) or cefotaxime (9%). In the event of uncontrolled bleeding or rebleeding, we used endoscopic band ligation during hospitalization and Sengstaken-Blakemore balloon tamponade as rescue therapy (rescue transjugular intrahepatic portosystemic shunt was not accessible at our centres). By the fifth day following index admission, we had incorporated betablockers into our secondary prophylaxis. According to the report of the Baveno VI consensus workshop on broadening consensus in portal hypertension, 6-week mortality was the major outcome of interest in this study. Mortality at 5 days and rebleeding were the secondary outcomes examined.

The demographic characteristics of the sample population were described using descriptive statistics. The t-test and the Mann-Whitney U test were used to do comparisons between groups with continuous variables reported as means with standard deviations. All data was analysed using SPSS 24.0.

### RESULTS

There were 142 (66.04%) males and 73 (33.95%) females among all cases. 37 (17.2%) cases had age 18-30 years, 72 (33.5%) had age 31-40 years, 55 (25.6%) patients had age 41-50 years and 51 (23.7%) cases had age >50 years.(table 1)

Table-1. Gender and age of the enrolled cases					
Variables	Frequency Percentage				
Gender					
Male	142	66.04			
Female	73	33.95			
Age					
18-30 years	37	17.2			
31-40 years	72	33.5			
41-50 years	55	25.6			
>50 years	51	23.7			

**Table-1:** Gender and age of the enrolled cases

We found failure to control bleed in 27 (12.5%), re-bleeding in 31 (14.4%) cases.(table 2)

Table-2: Frequency of re-bleeding					
Variables	Frequency	Percentage			
Failure to control Bleeding					
Yes	27	12.5			
No	188	87.5			
Re-bleeding					
Yes	31	14.4			
No	184	85.6			

Diabetes was found in 88 (40.9%) cases. There were 58 instances (26.04%) of hepatocellular carcinoma and 35 cases (16.3%) of portal vein thrombosis (PVT).(table 3)

Variables	Frequency (215)	Percentage
Other Diseases		
DM	88	40.9
Hepatocellular carcinoma	58	26.04
PVT	35	16.3

**Table-3:** Frequency of DM, PVT and hepatocellular carcinoma

The presence of diabetes mellitus and active bleeding at the time of endoscopy were predictors of failure to control bleed, while the presence of diabetes mellitus and serum bilirubin >3 mg/dL were predictors of in-hospital re-bleed.(table 4)

<b>Tuble 11</b> Treaterors of fundice and te bleeding in hospital					
Predictors	Frequency	Percentage			
Failure to control bleed					
DM	12	5.6			
Active bleeding during endoscopy	15	6.97			
Re-bleeding					
DM	14	6.5			
Serum bilirubin >3 mg/dL	17	7.9			

**Table-4:** Predictors of failure and re-bleeding in hospital

Mortality was found in 19 (8.8%) cases.(figure-1)

Figure-1: Association of mortality



## DISCUSSION

The purpose of this study was to evaluate the 5-days outcomes of a single-center cohort of patients who experienced acute variceal haemorrhage during routine clinical care. This study's primary objective was to suggest an innovative and complementary predictive strategy for estimating 5-day mortality in this context. Patients with acute variceal haemorrhage have fared better in recent years compared to historical cohorts, as shown by this study's findings. Compared to the 60% mortality rate found in the foundational study by Graham and Smith, our 8.8% mortality rate after 5 days (excluding instances with HCC) is consistent with that of more recent and well-conducted investigations.[16,17]

Child-Pugh and MELD scores have recently been compared in investigations of patients with cirrhosis and variceal haemorrhage. All of these studies demonstrated that Child-Pugh and MELD scores were similarly effective at predicting mortality.[18] A recent retrospective study by Flores-Rendón AR, et al. demonstrates that MELD is more accurate than CP at predicting bleeding-related mortality in the hospital. However, no distinctions were found in the examination of total mortality.[19] Our findings are consistent with these in showing that there are no major distinctions between these 2 prognostic scores when it comes to predicting death. In addition, our findings corroborate the importance of well-known risk variables (Child-Pugh and MELD score and early

occurrence of rebleeding in hospital), which are mostly related to baseline liver function and overall patient clinical condition.

In this study 215 patients were included. There were 142 (66.04%) males and 73 (33.95%) females among all cases. 37 (17.2%) cases had age 18-30 years, 72 (33.5%) had age 31-40 years, 55 (25.6%) patients had age 41-50 years and 51 (23.7%) cases had age >50 years. Findings were comparable to the previous studies.[20,21] We found failure to control bleed in 27 (12.5%), re-bleeding in 31 (14.4%) cases. The presence of diabetes mellitus and active bleeding at the time of endoscopy were predictors of failure to control bleed, while the presence of diabetes mellitus and serum bilirubin >3 mg/dL were predictors of in-hospital re-bleed. Endoscopic sclerotherapy has been associated with a high rebleeding rate (30%-50%).[22,23] Factors that contribute to this condition include advanced age (over 60), low haemoglobin (less than 8 g/dL), big varices, a clot on the varices, active bleeding from the varices, renal failure, and ascites.[24] The rebleeding rate at 18 months in today series was 29.4%, which is comparable to the multicentric report of 26.5% over a median time of 23 months») from the North Italian Endoscopic Club (NIEC).[25,26] identical to the NIEC study, the risk factors for variceal rebleed in this particular series were identical to those of the initial bleed, and there was little variation in the interval among the first and second and third bleeds.

Individuals for prophylactic medication with non-select beta blockers (NSBBs) include patients with small varices who haven't yet bled but are at greater danger for bleeding. The recommended treatment procedures for the primary avoidance of variceal bleeding in individuals with short- to large-sized varices are NSBBs or endoscopic band ligation. On the other hand, nitrates, shunt surgery, and sclerotherapy are all contraindicated [27]. Endoscopic band ligation may be helpful for patients who are resistant to NSBBs or who are ineligible for pharmacological treatment [28].

According to our research, the risk of death increases when endoscopic intervention lasts less than 12 hours. The patients who underwent urgent endoscopy within 24 hours were sicker than those who underwent elective endoscopy, which could be a potential reason for this finding. At our facilities, an on-call endoscopist along with assistance staff are not always on hand to provide emergency EGD. Patients deemed sufficiently stable for medical care, particularly those in over the weekend, may want to consider having an endoscopy during a weekday.

## CONCLUSION

The presence of diabetes mellitus, active bleeding during endoscopy, and bilirubin levels that are greater than 3 mg/dL were revealed to be negative prognostic markers for initial control of variceal haemorrhage as well as recurrent bleed in patients with cirrhosis.

## REFERENCE

- 1. Prediction of the first variceal hemorrhage in patients with cirrhosis of the liver and esophageal varices. A prospective multicenter study. The North Italian Endoscopic Club for the Study and Treatment of Esophageal Varices. N Engl J Med 1988; 319:983-9.
- 2. Gores GJ, Wiesner RH, Dickson ER, et al. Prospective evaluation of varices in primary biliary cirrhosis. Gastroenterology 1989; 96:1552-9.
- 3. Smith JL, Graham DY. Variceal hemorrhage: a critical evaluation of survival analysis. Gastroenterology 1982; 82(5 pt 1):968-73.
- 4. Sclerotherapy after first variceal hemorrhage in cirrhosis. A randomized multicenter trial. The Copenhagen Esophageal Varices Sclerotherapy Project. N Engl J Med 1984; 311:1594-600.
- 5. Muthurulandi K, Randhir J, Murali A, et al. Bleed and rebleed pattern in portal hypertension. Indian J Gastroenterol 2003; 22 Suppl 1: Al -132.
- 6. Reed EA, Dalton H, Blatchford O *et al.* Is the Glasgow Blatchford score useful in the risk assessment of patients presenting with variceal haemorrhage? *Eur. J. Gastroenterol. Hepatol.* 2014; **26**: 432–7.
- 7. Malinchoc M, Kamath PS, Gordon FD, Peine CJ, Rank J, ter Borg PCJ. A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. *Hepatology*. 2000; **31**: 864–71.

- 8. Moreau R, Jalan R, Gines P *et al.* Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. *Gastroenterology*. 2013; **144**: 1426–37, 1437.e1-9.
- 9. Carey WD. Predictors of variceal bleeding: solving the puzzle. Am J Gastroenterol 1990;85(10):1426–1427
- Bambha K, Kim WR, Pedersen R, Bida JP, Kremers WK, Kamath PS. Predictors of early rebleeding and mortality after acute variceal haemorrhage in patients with cirrhosis. Gut 2008;57(6):814–820
- 11. Vuachet D, Cervoni JP, Vuitton L, et al. Improved survival of cirrhotic patients with variceal bleeding over the decade 2000-2010. Clin Res Hepatol Gastroenterol 2015;39(1):59–67
- 12. Das V, Boelle PY, Galbois A, et al. Cirrhotic patients in the medical intensive care unit: early prognosis and long-term survival. Crit Care Med 2010;38(11):2108–16.
- 13. Kamath PS , Kim WR ; Advanced Liver Disease Study Group. The model for end-stage liver disease (MELD). Hepatology 2007;45(3):797–805.
- 14. Lyles T , Elliott A , Rockey DC . A risk scoring system to predict in-hospital mortality in patients with cirrhosis presenting with upper gastrointestinal bleeding. J Clin Gastroenterol 2014;48(8):712–20.
- 15. Marmo R , Koch M , Cipolletta L , et al. Predictive factors of mortality from nonvariceal upper gastrointestinal hemorrhage: a multicenter study. Am J Gastroenterol 2008;103(7):1639–47; quiz 1648.
- 16. Graham D.Y., Smith JL.The course of patients after variceal hemorrhage Gastroenterology, 80 (1981), pp. 800-809
- 17. Bambha K., Kim W.R., Pedersen R., *et al*.Predictors of early re-bleeding and mortality after acute variceal haemorrhage in patients with cirrhosis Gut, 57 (2008), pp. 814-820
- 18. Lee J.Y., Lee J.H., Kim S.J., *et al*.Comparison of predictive factors related to the mortality and rebleeding caused by variceal bleeding: Child Pugh score, MELD score and Rockall score.Taehan kan Hakhoe Chi, 8 (2002), pp. 458-464
- 19. Flores-Rendón A.R., González-González J.A., Garcí–a-Compean D., *et al*.Model for end stage of liver disease (MELD) is better than the Child-Pugh score for predicting inhospital mortality related to esophageal variceal bleeding.Ann Hepatol, 7 (2008), pp. 230-234
- 20. Majid, S., Azam, Z., Shah, H.A. *et al.* Factors determining the clinical outcome of acute variceal bleed in cirrhotic patients. *Indian J Gastroenterol* **28**, 93–95 (2009).
- 21. Yan Zhao, Mudan Ren, Guifang Lu, Xinlan Lu, Yan Yin, Dan Zhang, Xin Wang, Wenhui Ma, Yarui Li, Guohong Cai, Yiguang Lin, Shuixiang He, "The Prognosis Analysis of Liver Cirrhosis with Acute Variceal Bleeding and Validation of Current Prognostic Models: A Large Scale Retrospective Cohort Study", *BioMed Research International*, vol. 2020, Article ID 7372868, 7 pages, 2020.
- 22. Berclaz R, de Peyer R, Miazza B, et al. [Endoscopic sclerotherapy and esophageal varices]. Schweiz Med Wochenschr 1988; 118:1476-81. French.
- 23. Grace ND. A hepatologists view of variceal bleeding. Am J Surg 1990;160: 26-31.
- 24. de Franchis R, Primignani M. Why do varices bleed? Gastroenterol Clin North Am 1992; 21:85-101.
- 25. Lebrec D, De Fleury P, Rueff B, Nahum H, Benhamou JP. Portal hypertension, size of varices, and risk of bleeding in alcoholic cirrhosis. Gastroenterology 1980; 79:1139-44.
- 26. Beppu K, Inokuchi K, Koyanagi N, et al. Prediction of variceal hemorrhage by esophageal endoscopy. Gastrointest Endosc 1981; 27: 213-8.
- 27. Triantos C, Kalafateli M. Primary prevention of bleeding from esophageal varices in patients with liver cirrhosis. World J Hepatol. 2014;6: 363–369. pmid:25018847
- Garbuzenko DV, Arefyev NO. Primary prevention of bleeding from esophageal varices in patients with liver cirrhosis: An update and review of the literature. J Evid Based Med. 2020;13: 313–324. pmid:33037792