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Original Article

Post Banding Ulcer Haemorrhage: a Contributor to Morality in Patients with Liver Cirrhosis

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ABSTRACT

Objectives: To evaluate the frequency, risk factors and mortality of post-banding bleeding in cirrhosis.
Study Design: Retrospective longitudinal Study.
Place and Duration of Study: Department of Medicine, Fauji Foundation Hospital, Rawalpindi Pakistan, from Feb to Jul 2021.
Methodology: Esophageal variceal band ligation (EVBL) was done in 123 patients. The study cohort was divided into two groups: Group-1 without re-bleed and Group-2 with re-bleed. Blood chemistry, Child-Pugh and MELD score, including the indications of EVBL and risk factors, were also analysed. Regression analysis was performed.
Results: Re-bleed occurred in 10.6% (n=13) of patients. The mean duration between ligation and re-bleed was 8.75±2.8 days. Oesophageal ulcers were the most common cause of re-bleeding (38.5%). Mortality rates among the two groups were 21.8 %(n=24) and 30.8 %(n=4), respectively. The model for end-stage liver disease score (OR 2.177, CI 1.069-4.43, p .03), APTT (OR 0.593, CI 0.397-0.887, *p* .01) and Sodium (OR 1.345, CI 1.07-1.69, *p*<0.01) were detected as the predictors of re-bleed.
Conclusion: Although re-bleeding after banding occurs in a trivial number of patients, it contributes to mortality. Coagulopathy, high sodium and MELD score are major predictors.

Keywords: Endoscopy, Endoscopic variceal band ligation (EVBL), Model for end-stage liver disease score, Post banding ulcer haemorrhage,

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INTRODUCTION

Liver cirrhosis is the leading cause of mortality globally, accounting for 1.3 million deaths in 2017.[1] The most common complication is portal hypertension and varies. Varices are present in half of cirrhotic patients at diagnosis. Variceal bleeding is a common complication of cirrhosis. The incidence of bleeding is around 12% and depends upon the severity of varices.[2,3] Beta-blockers and endoscopic band ligation (EBL) are the first strategies to prevent haemorrhage from varices in primary and secondary prophylaxis. EBL is the method of choice to identify and control the bleeding source in case of bleeding.[4] Although it is effective in controlling the bleeding, it also has complications ranging from mild epigastric burning and chest pain to worsening portal hypertensive gastropathy.[5,6]

While there are no defined treatment strategies for post-EBL bleeding, recognising and managing its risk factors is important.[7] There bleed incurs significant mortality in patients undergoing EBL, as high as up to 50%. Various studies have determined the risk factors associated with this complication.[7,8] One study found that advanced liver damage and lower PT was associated with re-bleed.[9] EBL indication, portal vein thrombosis, and hepatocellular carcinoma were independently associated with re-bleed. The event culminates in higher mortality in these patients.[10] There is limited local data regarding this complication. The study aims to determine the frequency and risk factors of post-banding bleeding and its mortality in patients with liver cirrhosis.

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METHODOLOGY

The retrospective longitudinal study was conducted at Department of Medicine, Fauji Foundation Hospital, Rawalpindi Pakistan, from February to July 2021 after Approval from the hospital ethical review board (Letter No 502/RC/FFH/RWP, dated 1st Jan 2021).

Inclusion Criteria: Patients with portal hypertension aged 18 and 80 years who underwent EVBL for upper GI bleeding were included.

Exclusion Criteria: Patients on maintenance dialysis, those having congestive cardiac failure, those taking anti-coagulants, pregnant females and patients having upper GI bleed due to any cause other than portal hypertension were excluded. Endoscopy was done using the endoscope of the model Olympus XP 180,

Japan. Portal hypertension was diagnosed based on clinical, radiological and laboratory data.

Post-banding haemorrhage was taken as any upper GI bleed (hematemesis, melena, hematochezia) occurring within two weeks after EVBL. We further categorised it into post-banding ulcer, varices and indeterminate (where we found both ulcer and varices, but the source of bleeding was not sure).

Detailed data about demographics, biochemistry, CTP, MELD and endoscopic findings were retrieved from the hospital records at the time of index EVBL. Patients who presented with a recurrence of upper GI bleeding after the banding procedure were sought out. Patients were divided into two groups. Group-1 comprised patients without re-bleeding episodes, and Group-2 had re-bleeding episodes. Patients were followed, and mortality after one week was recorded. All the patients had been managed according to standard hospital protocols for upper GI bleed. Treatment included intravenous fluids, transfusions, Octreotide infusion, Tranexamic Acid, nasogastric tube placement for gastric drainage and endoscopy. In Group-2, we noted the time from index EVBL to re-bleed and findings of repeat endoscopy.

Statistical Package for Social Sciences (SPSS) version 24.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Chi-square and student t-tests were used for data analysis. Multiple logistic regression analysis was used to identify the risk factors for the recurrence of bleeding post-EVBL and mortality in both groups. For the parameters found significant in regression analysis, the Receiver-operating curve (ROC) was performed to determine the cut-off value, sensitivity and specificity.

RESULTS

A total of 123 patients were included in the analysis. 121(96.8%) of our study population consisted of females. The mean age was 57.67±9.17 years, ranging from 18-70 years. The most common cause of portal hypertension was hepatitis C virus infection in 96(78%) patients, hepatitis B and C coinfection in 11(8.9%) and Hepatitis B in 10(8.1%) patients, whereas in 6(4.87%) subjects it occurred with other diseases. Oesophageal varices were present in all the recruited patients, of which 29(23.6%) had F2 and 94(76.4%) had F3 varices. Gastric varices and portal hypertensive gastropathy occurred with a frequency of 21(17.1%) and 3(2.4%), respectively. Emergency EVBL was done in 63(50.4%) cases. Out of the total patients recruited, 28(21.8%) died. 13(10.6%) patients developed post-banding haemorrhage; all were females. Lab parameters were analysed and compared between the groups as shown in Table-I.

Table-I: Comparison of Continuous Variables between the Study Groups (n=123)

	Total (n=123)	Group-1 (n=110)	Group-2 (n=13)	*p*-value
Age (years)	57.67±9.17	58.17±9.16	53.38±8.49	0.07
WBC (n×103/µl)	7.36±9.25	7.59±9.74	5.43±1.8	0.42
Hb (g/dl)	10. 8±10.44	10.9±11.00	9.66±2.54	0.68
PLT (n×103/µl)	100.70±58.22	102.97±59.22	81.53±46.46	0.21
Bilirubin (µmol/l)	31.29±36.65	30.69±36.61	36.38±38.10	0.59
ALT (U/l)	68.04±44.14	67.11±45.33	75.84±32.70	0.50
ALP (U/l)	206.60±116.54	209.96±121.84	178.23±47.54	0.35
Albumin (g/l)	30.91±7.06	30.98±7.20	30.38±6.04	0.77
Urea (mmol/l)	8.6±7.95	8.7±8.27	7.75±5.50	0.68
Creatinine (µmol/l)	95.76±49.20	96.85±51.03	86.46±29.20	0.47
PT (seconds)	4.47±6.7	4.22±6.72	6.54±6.04	0.23
APTT (Seconds)	7.49±11.62	7.46±11.85	7.85±9.20	0.90
INR	1.36±0.55	1.33±0.56	1.52±0.49	0.25
Na	137.43±13.38	137.05±13.70	140.69±10.01	0.35
MELD	12.54±6.49	12.25±6.53	14.92±5.84	0.16
CTP	8.42±2.24	8.3±2.23	9.38±2.18	0.10

Platelets were low in Group-2 and bilirubin, sodium and creatinine were higher than in Group-1. Advanced liver damage, renal derangement, coagulopathy, CTP and MELD score and gender were all associated with mortality in patients with variceal bleeding (Table-II).

Lower WBC (cut-off value of 5.17×103/µl); higher sodium (cut-off value of 136mg/dl), APTT(cut-off value of 4.5 seconds) and MELD(cut-off value of 15.5) at the time of first EVBL were associated with the risk of re-bleeding. The area under the ROC curve (AUROC) was analysed to determine the accuracy of the tests for predicting the re-bleeding. MELD score was the most accurate to predict the risk with a cut-off value >15.5 (AUC of .91, sensitivity of 89.3% and specificity of 83.2%) (Figure-1)

Table-II: Predictive factors for Post-EVBL Bleeding (n=123)

	Univariate Regression Analysis			Multivariate Regression Analysis		
Parameters	*p*-value	Odds Ratio (OR)	95% Confiden ceinterval(CI)	*p*-value	Odds Ratio (OR)	95% Confidence interval(CI)
Haemoglobin	0.69	0.96	0.76-1.21	0.83	0.99	0.88-1.11
WBC	0.03	.565	0.34-.96	0.04	0.59	0.36-0.98
Platelets	0.21	0.99	0.98-1.01	0.61	0.59	0.36-0.97
Bilirubin	0.59	1.00	0.99-1.02	0.29	0.97	0.92-1.02
ALT	0.50	1.00	0.99-1.02	0.64	0.99	0.97-1.01
ALP	0.36	0.99	0.99-1.00	0.50	0.99	0.98-1.00
Albumin	0.77	0.99	0.91-1.07	0.90	0.99	0.83-1.17
Urea	0.68	0.98	0.89-1.08	0.42	1.16	0.81-1.65
Creatinine	0.48	0.99	0.98-1.01	0.07	0.94	0.88-1.01
Na	0.009	1.393	1.09–1.78	0.005	1.36	1.09-1.69
PT	0.25	1.04	0.97-1.11	0.75	2.08	0.02-215.37
APTT	0.011	.534	.33 - .866	0.01	0.60	0.40-0.89
CTP	0.10	1.22	0.95-156	0.77	0.88	0.39-2.02
MELD	0.029	2.328	1.09–4.973	0.025	2.09	1.09-3.97

The mean duration between the band ligation and re-bleed was 8.75±2.80 days. In these patients, endoscopy was done to ascertain the local cause of haemorrhage and achieve haemostasis. Oesophageal ulcers alone were detected in 5(38.5%), varices in 2(15.4%) and ulcers along with varices were present in 6(46.2%) patients. We further stratified the cause of re-bleed into post-banding ulcers and others(including indeterminate and varied). Out of 4 patients who died, 2(50%) had PBU. Out of 5 patients who had a post-banding ulcer (PBU), 2(40%) died; in other causes of rebleed 2(25%), patients died.

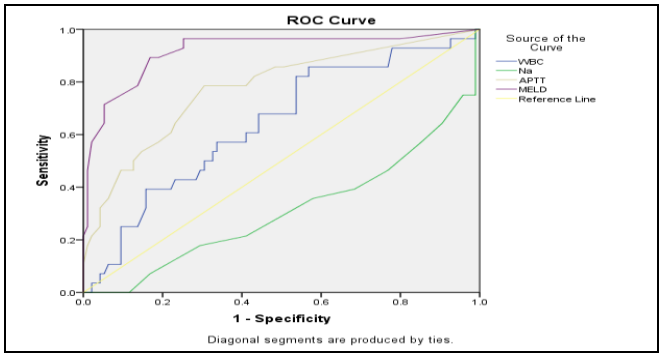

Figure-1: ROC Curve Analysis for factors Predicting Post EBL Bleeding

Although the rate of mortality was higher in patients with post-EVBL bleeding with the occurrence of 4(30.8%) vs 24(21.8%) in those without re-bleed, the difference was not statistically substantial with an OR 1.59, CI 0.45-5.62 and *p*-value of 0.47.

Serum sodium, APTT and MELD were the predictors of mortality in this group. Only the MELD score showed statistical significance in the ROC analysis of these factors. A MELD score of more than 17.5 was a predictor with AUC=.889, sensitivity of 75%, specificity of 100% (Figure-2).

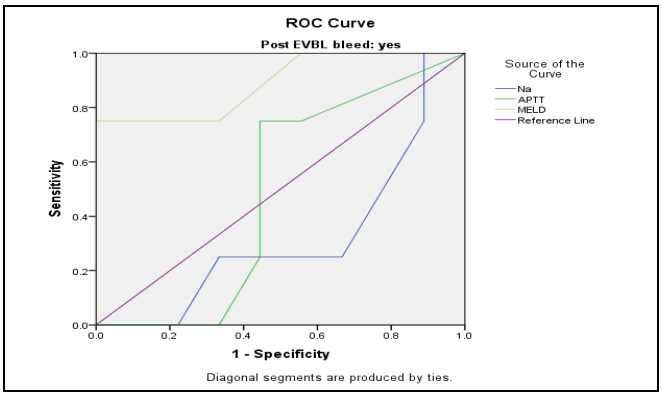

Figure-2: ROC Curve Analysis of Mortality Predictors in Patients with post EBL Bleeding

DISCUSSION

Post-EVBL bleeding is an unusual complication of portal hypertension. It contributes significantly to morbidity, mortality and health expenditure of patients with liver cirrhosis. This study aimed to determine the factors associated with mortality in post-EVBL bleed. The frequency of post-EVBL bleeding in our study was 10.4%, comparable to previous reports.[11] After EVBL, the thrombi start forming in the varices occluded by the bands, leading to vessel blockage. In a week or so, the occluded part of the vessel sloughs and the band slips, leaving the scar at the occlusion site.[12] Early band slippage may cause bleeding from the raw ulcer because it is more fragile than the surrounding mucosa. The mean interval between EBL and re-bleed was 8.7 days, almost matching the mean band slippage time of 7.5 days.[13,14]

Our study groups included similar age and gender profiles. We did not find a difference between the groups in baseline routine chemistry, liver or renal derangements, CTP and MELD scores. These complied with previous study.[15] At the same time, some works suggested that age and male gender were associated with post-banding bleeding.[16] Most of our patients were females, so our data may have a gender bias. Some works found that emergent EVBL was associated with an increased risk of bleeding complications.[12,17] However, we did not notice any effect of the banding indication on re-bleed, which is consorted by the work of Elhawari *et al*.[13]

Major predictors of post-banding bleeding in our study were coagulopathy indicated by APTT, relative leukopenia(Cut-off value 5.1) and advanced liver damage. MELD has been reported as a risk factor in different reports.[13] while some studies negated its effect. Kang *et al*. reported that MELD of >18 was associated with re-bleeding.[14] Hunter *et al*.also reported that a MELD score of 18 or more was associated with both post-EVBL bleed and mortality.[17]

In our study, serum sodium predicted re-bleeding and re-bleeding-related mortality. Bhambha *et al*. found sodium to be a risk factor for death at six weeks post-EBL (HR .92; 95% CI .88- .97) but not for re-bleeding within five days of EVBL(HR 1.0; CI .94-1.07).[18] Vanbiervliet *et al*. reported that lower PT portends a higher risk.[8] They also found hepatocellular carcinoma as a risk factor compared to our study. This may be due to the lower sample size, leading to the lower percentage of patients with HCC in our study population. In a recent study, Machlab *et al*. reported that none of the clinical lab or endoscopic parameters predicted the post-banding bleed.[19]

15% of our patients had concomitant gastric varices. They were not associated with re-bleed or mortality. Congruent with our results, one study reported that EV grade, GV, and PHG had no role in re-bleeding.[16] Whereas the results of Cho *et al*.contradict ours, they noted that the coexistence of gastric varices was associated with re-bleed risk.[9] However, most of their patients had grade 3 GVs, which was different here. This may be responsible for the difference.

The frequency of post-EBL bleeding in this study may be underestimated, as the patients with mild bleeding may have yet to report to hospital settings. All of our patients received pre and post-banding PPIs as standard protocol, which may decrease the risk of re-bleed. We did not evaluate the effect of other treatments like beta-blocker use, multiple ligation sessions, and no. of bands applied, which may significantly affect the incidence of post-banding bleeding. Further local studies addressing these issues are required.

CONCLUSION

Post-banding ulcer haemorrhage accounts for 40% of mortality in patients with post-EVBL bleeding. Although this doubles the death rate, when added to the mortality of index bleed for which ligation is done, our study did not find any association of post-banding ulcer with mortality within one week of the episode. Lower sodium and higher APTT and MELD predicted mortality. Identification of patients at high risk may help reduce re-bleeds and improve overall patient survival.

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Conflic of Interest: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

SP & OA: Conception, study design, drafting the manuscript, approval of the final version to be published.

BB & AB: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

SJA & SFH: Data acquisition, drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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