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Research Article

**FREQUENCY OF RE-BLEEDING AFTER SUCCESSFUL ENDOSCOPIC
MANAGEMENT OF ESOPHAGEAL VARICES IN CIRRHOTIC
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Bushra Ali⁵, Dr. Arif Amir Nawaz⁶**¹. Demonstrator Anatomy Department, Fatima Memorial Medical and Dental College, Lahore². Medical Officer Hayat Memorial Hospital, Lahore³Sheikh Zayed Medical College/Hospital, Rahim Yar Khan⁴. Resident Gastroenterology Department, Fatima Memorial Hospital, Lahore⁵. Assist prof. Gastroenterology Department, Fatima Memorial Medical and Dental College, Lahore⁶. Prof. Gastroenterology Department, Fatima Memorial Medical and Dental College, Lahore**Abstract:**

In nearly 50% of cirrhotic patients gastroesophageal varices are present at the time of diagnosis. Each episode of esophageal bleeding is associated with 30-70% risk of mortality. Patients treated with EVBL had a decreased risk of first bleeding episode by 64% and mortality by 45%.

Objective: *To assess the rebleeding rate in 4 weeks after successful endoscopic variceal band ligation in cirrhotics.*

Methods: *The retrospective observational analysis of endoscopic band ligation procedures, performed in Fatima Memorial Hospital, Lahore during the period January 2016– February 2018, was made. 80 endoscopic band ligation procedures were included in the study. Patients with rebleeding were recorded presenting in four weeks.*

Results: *80 cases with history of cirrhosis and previous band ligation were chosen for the study. Out of which 49 (61.3%) were male and 31 (38.8) were female with median age of 51.32±12.57. Cause of liver cirrhosis was identified as 63(78.8%), 5(6.3%) and 12(15%) for hepatitis C, hepatitis B and Non B, Non C respectively. Out of 80, 13(16.2%) patients presented with rebleeding in 4 weeks post band ligation. 12(92.3%) out of 13 patients with rebleeding had child pugh class C and had more than 2 columns of esophageal varices.*

Conclusion: *Endoscopic variceal band ligation was found to be an effective modality in reducing the frequency of rebleeding in cirrhotic patients. Re-bleeding after variceal banding was 16.2 %. Major factors contributing to re-bleeding were number of columns of esophageal varices and severity of liver cirrhosis.*

Keywords: *Cirrhosis of liver, Esophageal variceal banding, Re-bleeding.*

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INTRODUCTION:

Portal hypertension (PH), defined as hepatic venous pressure gradient of more than 5 mmHg, is one of the major complications of the liver cirrhosis. Clinical complications of portal hypertension, including gastroesophageal varices, become evident once hepatic venous pressure gradient exceeds 10 mmHg [1]. In nearly 50% of cirrhotic patients gastroesophageal varices are present at the time of diagnosis. Primary prophylaxis is recommended with either non selective beta blocker (NSBB) or endoscopic variceal band ligation (EVBL) on the basis of patient's preference/tolerance. Both of these modalities are superior to no-treatment in patient with evidence of medium and large size varices [2]. Each episode of esophageal bleeding is associated with 30-70% risk of mortality [3]. The standard of care in these patients is combination of medical therapy and endoscopic band ligation to prevent rebleeding [4]. Secondary prophylaxis is recommended in the form of nonselective beta blockers (NSBB) and endoscopic variceal band ligation (EVBL) after initial episode of variceal hemorrhage [5]. Combination therapy with NSBB and EVBL is more effective than EVBL alone ((RR = 0.65, 95%CI: 0.45-0.93) [6]. There are many factors which predict bleeding in liver cirrhosis i.e. size of varices, red wale marks on endoscopy and decompensated cirrhosis (Child Pugh B/C). Among them, size of varices is the most significant predictor of first bleeding episode (15% per year). After EVBL, the time period between 24 hours and 14 days is crucial as the spontaneous band slippage during this period can be catastrophic, the greatest risk of rebleeding is within five days of admission in the hospital [7,8]. For effective treatment, early diagnosis should be made in these patients [9]. Studies have shown that in comparison to untreated group, patients treated with EVBL had a decreased risk of first bleeding episode by 64% and mortality by 45% [10]. Once patient present with rebleeding the management is same as acute variceal hemorrhage including hemodynamic resuscitation and endoscopic examination. Endoscopic therapies like band ligation, sclerotherapy and detachable snares can be applied on individual basis. Patients with variceal bleeding refractory to endoscopic upper GI bleeds should be considered for transjugular intrahepatic portosystemic shunt (TIPSS) procedure [11]. Keeping in view of the high mortality in patients with variceal hemorrhage and effectiveness of endoscopic intervention, as evident in western literature, it's worthwhile to study this in our

population. Objective of the study was to assess the rebleeding rate in 4 weeks after the band ligation in a tertiary care center of Lahore.

METHODS:

The retrospective observational analysis of endoscopic band ligation procedures, performed in Fatima Memorial Hospital, Lahore during the period January 2016 to February 2018, was made. 80 endoscopic band ligation procedures were included in the study. Non probability consecutive sampling technique was used. Both males and females were included who have evidence of cirrhosis on the basis of clinical history, examination, biochemical and radiological investigations, had first episode of upper gastrointestinal bleeding secondary to esophageal varices and had undergone band ligation. Patients with other causes of upper GI bleeding, with two or more previous bleeding episodes and patients who undergone surgical procedures for varices or transjugular intrahepatic portosystemic shunt procedure were excluded from the study.

Data collected for the gender and age of the patient, etiology of cirrhosis and size of esophageal varices. Less than or equal to 5 mm varices were graded as small sized while more than 5 mm varices were graded as large size varices. Rebleeding was considered in the patient who presented again with hematemesis, melena or drop in hemoglobin of more or equal to 2 grams/dl within 4 weeks of the index endoscopic band ligation. Patients presented with rebleeding were managed according to the standard treatment protocols.

Collected information of the patients was entered into SPSS version 21 and analyzed. Results were presented as mean \pm standard deviation for quantitative variables and frequencies (percentages) for qualitative variables. P value ≤ 0.05 was taken as significant.

RESULTS:

80 cases with history of cirrhosis and previous band ligation were chosen for the study. Out of which 49 (61.3%) were male and 31 (38.8) were of female gender. Causes of liver cirrhosis were identified as 63(78.8%), 5(6.3%) and 12(15%) for hepatitis C, hepatitis B and Non B, Non C respectively. Out of 80, 13(16.2%) patients presented with rebleeding in 4 weeks post band ligation.

Table 1

Variables	Value
Age (years)	51.32±12.57
Gender (%)	
Male	49 (61.3)
Female	31 (38.8)
Etiology (%)	
HCV	63 (78.8)
HBV	5 (6.3)
Non B, Non C	12 (15)
Child-Pugh Class, n (%)	
A	6 (7.5)
B	12 (15.0)
C	62 (77.5)

Table 2

Variable		Recurrent bleeding(n)		P value
		Yes	No	
Child pugh score	A	0	6	0.01
	B	1	11	
	C	12	50	
Number of variceal columns	1-2	1	29	0.02
	3-4	12	38	

DISCUSSION:

Development of portosystemic collaterals is one of the major consequences of portal hypertension, gastroesophageal region being the most common site of these collaterals. Esophagogastric variceal hemorrhage is one of the fatal complications of end stage liver disease. In newly diagnosed patient with cirrhosis, having no varices at the time of diagnosis, annual rate of development of varices is around 5-7%[1]. 12% of patients with esophagogastric varices suffer bleeding episode within 1 year. There is 5% risk of initial bleeding in small size varices while 15% risk in large varices within one year [12,13]. Advanced cirrhosis and varices with red wale marks pose a high risk of variceal hemorrhage [14] Variceal hemorrhage is one of the major cause of death in liver cirrhosis, with 15-20% of 6-week mortality rate and it constitute one of the main indication for liver transplantation in patients with end stage liver disease [15,16]. Endoscopic band ligation which is a modification of the technique that has been used in hemorrhoids, first time described in 1988 by Stiegmann and Goff in human, has now become standard of care for esophageal varices and it appeared to be superior to sclerotherapy in terms of better efficacy and superior safety profile [17-19]. Despite of the availability of such effective therapies, approximately two third of the patients will develop

recurrent bleeding after successful hemostasis if further preventive measures are not taken. Factors which can contribute in recurrence variceal bleed include high portal pressure, poor liver function, size of the varices, treatment technique used and presence of infection and portal vein thrombosis [8,20,21]. Patients with variceal hemorrhage refractory EVBL should be referred for the advanced procedure like TIPSS and other novel techniques should be utilized like self-expandable metallic stents (SEMSs), hemostatic powder and endoscopic ultrasonography (EUS)-guided angiotherapy [22-25].

We observed in our study that re-bleeding following successful control of the initial bleeding episode with band ligation occurred in 13(16.2%) patients which is consistent with frequency as compared to study done by Abbasi A et al i.e., 19.1% [26]. In another local study [27] the risk of rebleeding was found to be 6.4%(14 out of 220 patients had rebleeding), the frequency in that study is low as compared to our study and the difference in frequency could be because of the patients included in our study have more advanced liver disease as more than 75% patients had child pugh score C. Other possible explanation of the high frequency could be the length of follow up as we included the patients presenting with rebleeding up to 4 weeks and in that study the

follow up time was 3 weeks. Furthermore they excluded the patients with portal vein thrombosis and HCC. Our observations were consistent with the frequency of bleeding seen in various international studies (ranging from 9% to 19%) [28-34]. The variation in frequencies in these studies is probably due to different study populations with different etiologies of cirrhosis and different severity of liver disease.

Total 13 patients developed rebleeding out which 12 (92.3%) patients had Child Pugh Class C. One patient (7.3 %) developed rebleeding among child class B patients while none of the patient re-bled with Child A cirrhosis. Our findings were consistent with D Amico et al [8] who found the fact that patients with advanced liver disease have greater chances of re-bleed.

Another major factor contributing re-bleeding after successful EVBL was number of variceal columns. In our study, 12(92.3%) out of 13 patients who presented with rebleeding had more than 2 columns of esophageal varices. While in other group of patients with 2 or less than 2 columns, only one patient developed re-bleeding which comprises 7.3% of total patients presented with rebleeding. Our findings are consistent with the observations found by Farwa et al²⁷, they studies 220 patients and observed that patients with more than two columns of varices had more chances of re-bleeding in cirrhotic patients.

Limitations of our study are a small sample size and a shorter follow up period. Other confounding factors like presence of hepatocellular carcinoma/portal vein thrombosis and ongoing alcohol use were not separately considered which can alter the frequency of re-bleeding.

CONCLUSION:

In this study, EVBL was found to be an effective modality in reducing the frequency of rebleeding in cirrhotic patients. Severity of liver disease and number of variceal columns were independent risk contributing to re-bleeding.

REFERENCES:

1. R. J. Groszmann, G. Garcia-Tsao, J. Bosch et al., "Beta-blockers to prevent gastroesophageal varices in patients with cirrhosis," *The New England Journal of Medicine*, vol. 353, no. 21, pp. 2254–2261, 2005.
2. Garcia-Tsao G, Abraldes JG, Berzigotti A, et al. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. *Hepatology* 2017;65:310–335.
3. Laura Mašalaitė, Jonas Valantinas, Juozas Stanaitis. Recurrence of esophageal varices after endoscopic band ligation: single centre experience. *ACTA MEDICA LITUANICA*. 2012. Vol. 19. No. 2. P. 59–66
4. Jing-Run Zhao, Guang-Chuan Wang, Jin-Hua Hu. Risk factors for early rebleeding and mortality in acute variceal hemorrhage. *World J Gastroenterol* 2014 December 21; 20(47): 17941-17948
5. de Franchis R; Baveno VI Faculty. Expanding consensus in portal hypertension: Report of the Baveno VI Consensus Workshop: Stratifying risk and individualizing care for portal hypertension. *J Hepatol* 2015;63:743-752.
6. Christos Triantos, Maria Kalafateli. Endoscopic treatment of esophageal varices in patients with liver cirrhosis. *World J Gastroenterol* 2014 September 28; 20(36): 13015-13026
7. Xu L et al. Risk factors for predicting early variceal rebleeding after endoscopic variceal ligation. *World J Gastroenterol* 2011 July 28; 17(28): 3347-3352
8. D'amico G, de Franchis R. Upper digestive bleeding in cirrhosis. Post-therapeutic outcome and prognostic indicators. *Hepatology* 2003;38:599–612.
9. Kapoor A et al. Endoscopic diagnosis and therapy in gastro-esophageal variceal bleeding. *Gastrointest Endosc Clin N Am*. 2015 July ; 25(3): 491–507. doi:10.1016/j.giec.2015.03.004
10. Salim A, Malik K. Early initiation of beta blockers following primary endoscopic therapy for bleeding oesophageal varices in cirrhotics. *J Ayub Med Coll Abbottabad* 2017;29(2):186–9
11. Anastasios A. Mihas And Arun J. Sanyal. Recurrent variceal bleeding despite endoscopic and medical therapy. *Gastroenterology* 2004;127:621–6
12. Merli M, Nicolini G, Angeloni S, et al. Incidence and natural history of small esophageal varices in cirrhotic patients. *J Hepatol* 2003;38:266-72.
13. D'Amico G, Pagliaro L, Bosch J. Pharmacological treatment of portal hypertension: an evidence-based approach. *Semin Liver Dis* 1999;19:475-505.
14. North Italian Endoscopic Club for the Study and Treatment of Esophageal Varices. Prediction of the first variceal hemorrhage in patients with cirrhosis of the liver and esophageal varices. A prospective multicenter study. *N Engl J Med* 1988;319:983-9.
15. Bosch J, Garcia-Pagan JC. Prevention of variceal

- rebleeding. *Lancet* 2003;361:952-4.
16. Villanueva C, Piqueras M, Aracil C, et al. A randomized controlled trial comparing ligation and sclerotherapy as emergency endoscopic treatment added to somatostatin in acute variceal bleeding. *J Hepatol* 2006;45:560-7.
 17. Steigmann G, Goff GS. Endoscopic esophageal varix ligation: Preliminary clinical experience. *Gastrointest Endosc* 1988;34:113-17.
 18. Stiegmann GV, Goff JS, MichaletzOnody PA, et al. Endoscopic sclerotherapy as compared with endoscopic ligation for bleeding esophageal varices. *N Engl J Med* 1992;326: 1527-32.
 19. Lo GH, Lai KH, Cheng JS, et al. A prospective, randomized trial of sclerotherapy versus ligation in the management of bleeding esophageal varices. *Hepatology* 1995;22:466-71.
 20. de Franchis R, Dellera A, Fazzini L, Zatelli S, Savojardo V, Primignani M. Evaluation and follow-up of patients with portal hypertension and oesophageal varices: how and when. *Dig Liver Dis* 2001; 33: 643-646
 21. Mihas AA, Sanyal AJ. Recurrent variceal bleeding despite endoscopic and medical therapy. *Gastroenterology* 2004; 127: 621-629
 22. Marot A, Trepo E, Doerig C, et al. Systematic review with meta-analysis: self-expanding metal stents in patients with cirrhosis and severe or refractory oesophageal variceal bleeding. *Aliment Pharmacol Ther* 2015;42:1250-1260.
 23. Yau AH, Ou G, Galorport C, et al. Safety and efficacy of Hemospray® in upper gastrointestinal bleeding. *Can J Gastroenterol Hepatol* 2014;28:72-76.
 24. Garcia-Pagan JC, Caca K, Bureau C, et al. Early use of TIPS in patients with cirrhosis and variceal bleeding. *N Engl J Med* 2010;362:2370-2379.
 25. Artifon ELA, Marson FP, Khan MA. Endoscopic ultrasonography-guided hemostasis techniques. *Gastrointest Endosc Clin N Am* 2017;27:741-747.
 26. Abbasi. A, Bhutto.AR, Bhatti KI, Mahmood K, Lal Keshav Outcome of band ligation in oesophageal varices: *J Pak Med Assoc* 2013;63:983-7.
 27. Farwah, J, Hassan, G. Frequency of Re-bleeding after Esophageal Variceal Banding in Cirrhotic patients at 3 weeks. *Pakistan Journal of Medical and Health Sciences*. 2017;11(3): 832-836.
 28. Lay CS, Tsai YT, Teg CY, Shyu WS, Guo WS, Wu KL, et al. Endoscopic variceal ligation in prophylaxis of first variceal bleeding in cirrhotic patients with high-risk esophageal varices. *Hepatology* 1997; 25: 1346-50.
 29. Sarin SK, Lamba GS, Kumar M, Misra A, Murthy NS. Comparison of endoscopic ligation and propranolol for the primary prevention of variceal bleeding. *N Engl J Med* 1999; 340: 988-93.
 30. Lo GH, Chen WC, Chen MH, Lin CP, Lo CC, Hsu PI, et al. Endoscopic ligation vs. nadolol in the prevention of first variceal bleeding in patients with cirrhosis. *Gastrointest Endosc* 2004, 59: 333-8.
 31. Harewood GC, Baron TH, Song LM. Factors predicting success of endoscopic variceal ligation for secondary prophylaxis of esophageal variceal bleeding. *J Gastroenterol Hepatol* 2006; 21:237-41.
 32. Lo GH, Lai KH, Cheng JS, Lin CK, Hsu PI, Chiang HT. Prophylactic banding ligation of high-risk esophageal varices in patients with cirrhosis: a prospective, randomized trial. *J Hepatol* 1999; 31: 451-6.
 33. Lo GH, Lai KH, Cheng JS, Lin CK, Huang JS, Hsu PI, et al. Emergency banding ligation versus sclerotherapy for the control of active bleeding from esophageal varices. *Hepatology* 1997; 25: 1101-4.
 34. De BK, Ghoshal UC, Das T, Santra A, Biswas PK. Endoscopic variceal ligation for primary prophylaxis of oesophageal variceal bleed: preliminary report of a randomized controlled trial. *J Gastroenterol Hepatol* 1999; 14: 220-4.