ORIGINAL ARTICLE

PREDICTORS OF RE-BLEEDING AFTER OESOPHAGEAL VARICEAL BANDING IN CIRRHOTIC PATIENTS AT 4 WEEKS

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Background: Acute upper gastrointestinal bleeding is a serious complication in cirrhotic patients. Without recommended management, recurrent bleeding happens in 30–40% within the next 2–3 days, and up to 60% within 1 week. Aim was to determine predictors of re-bleeding after oesophageal variceal banding in cirrhotic patients for 4 weeks. It was a descriptive study, conducted at the Department of Medicine, Sheikh Zayed Hospital, Rahim Yar Khan. Six months from June 21 to December 21, 2021. **Methods:** A total of 93 patients with active oesophageal variceal bleeding were included in this study. Upper gastrointestinal (UGI) endoscopy was performed to look for bendable varices (grades 1–4) and band ligation was applied. Patients were followed for 4 weeks for the history of hematemesis or Malena, fall in haemoglobin of 2 grams per decilitre or more and endoscopic rebleeding findings. **Results:** Out of 93 patients, 67(72.0%) were males, while 26(28.0%) were females. The Mean age of the patients was 45.66±16.61 years. According to Child-Pugh Classification, the majority of the patients 45(48.4%) had Child-Pugh Class-A, while 33 (35.5%) were Child B and 15 (16.1%) patients belonged to Child-Pugh Class C. Red wale sign was noted in 22 patients (23.7%). Among 93 cirrhotic patients who presented with variceal bleeding, 9 (9.7%) had re-bleeding within 4 weeks. Amongst 9 patients, 8 patients (88.9%) had red wale sign, grade II or above oesophageal varices and belonged to severe liver disease with child class B or C. **Conclusion:** Endoscopic variceal band Ligation is an effective treatment modality for the control of oesophageal variceal bleeding. Re-bleeding after band ligation was 9.7%. The major contributing factors to re-bleeding were the severity of cirrhosis, grades and columns of oesophageal varices, number of bands ligation and findings of red wale sign. Increasing age and duration of cirrhosis were contributing predictors of increased re-bleeding risk.

Keywords: Cirrhosis of liver; Oesophageal varices; Variceal band ligation; Red wale marking

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INTRODUCTION

Cirrhosis of the Liver is a serious irreversible disease and currently the 11th most common cause of death globally with one million deaths per year.[1] It is also a common cause of morbidity and mortality amongst the Pakistani population and a prominent reason for admissions in our hospitals, making it a major health burden.[2] Portal hypertension is a chief consequence of cirrhosis. Approximately 59% of cirrhotic patients develop oesophageal varices, and one-third of these patients experience oesophageal variceal bleeding (EVB) with a mortality risk of 17–42% with each bleeding episode.[3]

Recurrent bleeding is common without prophylactic treatment; the risk varies between 8–35% within 2 years of follow-up[4]. In another series, the risk of recurrent bleeding was as high as 60% with a mortality rate of 33%.[5] In a local study, re-bleeding was seen in 33(19.1%) of the 173 patients analyzed after variceal band ligation.[6] Prevention of re-bleeding is therefore a major goal in patients in whom the initial bleeding episode has been successfully controlled.[7]

Acute variceal bleeding is managed with endoscopic therapy[7] and endoscopic variceal band ligation is now the treatment of choice. Endoscopic band ligation controls bleeding by causing thrombosis and scaring off the vessel.[7] Band ligation has also been used successfully for the treatment of re-bleeding. Various studies were aimed at predicting the risk factors of re-bleeding. In one study, major risk factors identified for re-bleeding were Child-Pugh Class B or C, grades of varices, number of bands applied, and volume of blood in hematemesis.[8] Variceal re-bleeding is associated with a greater mortality rate and limited work has been done to identify the incidence and frequency of early re-bleeding after band ligation and predict associated factors with rebleeding in our population. The rationale of this study is to assess risk factors of re-bleeding after oesophageal variceal band ligation to see the effectiveness of therapy in our population. The objective of the study was to predict re-bleeding risk factors after oesophageal variceal band ligation in cirrhotic patients within 4 weeks.

Variceal bleeding: Presence of blood in vomiting (hematemesis), black-coloured stools (Malena) or presence of blood in a nasogastric tube in the last 24 hours and upper gastrointestinal (UGI) endoscopy showing ruptured esophagogastric varices.

Re-Bleeding: Re-Bleeding is defined as new hematemesis or melena within 4 weeks of banding and/or a decrease in haemoglobin level more than 2 gm/dl (grams per decilitre), as compared to pre-discharge levels of the patient on complete blood count (CBC).

Red wale marking: It is defined as dilated venules appearing like red patches or strips on the surface of varices, assessed during upper gastrointestinal endoscopy.

Cirrhosis: Cirrhosis is an irreversible change in normal liver tissue characterized by diffuse hepatic fibrosis and nodule formation, in response to chronic liver injury. This is detected radiologically on ultrasound abdomen as coarse texture of liver, clinically (ascites, encephalopathy and hematemesis) and laboratory indicators of liver dysfunction (decrease serum albumin, rise in total bilirubin and prolonged prothrombin time) that are altogether scored as Child-Pugh Classification.

MATERIAL AND METHODS

This descriptive study was carried out in the Department of Medicine, Sheikh Zayed Hospital, Rahim Yar Khan. The study was conducted over six month's period from June 21, 2021 to December 21, 2021. With a confidence level of 95%, and 6.4% of the anticipated population proportion for this study is 93 patients with an expected percentage of rebleeding in 17% of cases after variceal banding. The sampling technique was non-probability consecutive sampling.

Inclusion Criteria

1. Both male and female patients from 18 to 65 years of age.
2. Liver cirrhosis patients for at least 6 months (due to any aetiology) presented with variceal bleeding as per operational definition.
3. Bandable esophagogastric varices especially in structure, according to grades (1,2,3,4) of oesophageal varices assessed by the specialists during endoscopy.

Exclusion Criteria

1. History of treatment for variceal bleeding in the past.
2. Patients with non-cirrhotic portal hypertension
3. Patients with portal vein thrombosis
4. Patients with a history of intake of NSAIDS and antiplatelet drugs.
5. Upper GI Bleed due to any other cause apart from portal hypertension i.e., peptic ulcer bleed
6. Patients with a history of Tran's jugular intrahepatic portosystemic shunts (TIPS) or surgical decompression for portal hypertension.

After approval of the research study from the Institutional Ethical Review Board, consecutive 93 patients from the Department of Medicine, Sheikh Zayed Hospital, Rahim Yar Khan fulfilling the inclusion criteria were selected. The purpose of the study was explained to each patient and informed consent was taken. All the data such as age, gender, aetiology, Child-Pugh classification, and any episode of re-bleed was collected. All patients were screened to confirm the aetiology of cirrhosis of the liver (Viral Hepatitis screening HbsAg, Anti-HCV, liver function tests, prothrombin time, serum albumin), undergo clinical examination (to look for stigmata of chronic liver disease i.e., ascites, encephalopathy, palmar erythema, spider nevi, anaemia, jaundice,) and ultrasound abdomen done, and classified based on Child-Pugh Classification.

Upper GI endoscopy was performed to look for bandable varices (grades 1–4), number of varices, any red sign (red patches, varices on varices) for re-bleed and band ligation was done accordingly. Patients were followed for re-bleed as per operational definition at 04 weeks. When oesophageal varices were discovered on upper GI endoscopy, they were graded according to their size from Grades I – IV, as in Figure-1.

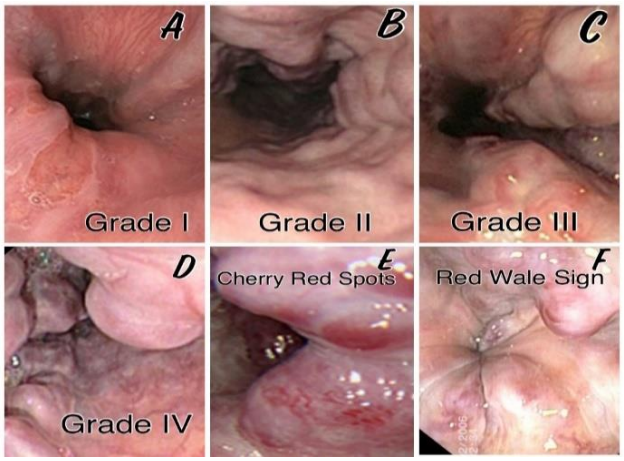

Figure-1. A) Small, straight oesophageal varices (grade 1); B) enlarged, tortuous and beady oesophageal varices occupying less than one-third of the lumen (grade 2); C) Medium calibre coil-shaped varices (3-6mm diameter) occupying up to one-third of the lumen (grade 3); D) Large calibre white oesophageal varices, larger than 6mm that look like mucosal folds (grade 4); E) Grade 3 oesophageal varices with cherry red spots and red wale marks; F) Large oesophageal varices with red wale signs

Data analysis was computer-based by statistical software SPSS version 22. Mean and standard deviation was calculated for the age of patients, grade and number of varices. Data stratification of re-bleed within 4 weeks was done for qualitative variables like age groups, gender, grades of varices, Child-Pugh classification, number of bands ligation along with absence or presence of red wale sign. Post-stratification chi-square test was applied. *p* value ≤0.05 will be significant. Data was presented in the form of tables 1-6.

RESULTS

A total of 93 patients with cirrhosis presenting with variceal bleeding were selected for this study. Among these patients, 67 (72.0%) were males, while 26 (28.0%) were females. The mean age of the patients was 45.66±16.61 years. According to Child-Pugh Classification, the majority of the patients 45 (48.4%) had Child-Pugh Class A, while 33 (35.5%) were Child B and 15 (16.1%) patients belong to Child-Pugh Class C.

Out of 93 patients, 62(66.7%) had two oesophageal varices, while 11(11.8%) had three oesophageal varices and 20 (21.5%) had four oesophageal varices respectively. Concerning grades of oesophageal varices, 20 (21.5%) patients had Grade II oesophageal varices and 10 (10.7%) had Grade III oesophageal varices. The majority of the patients 41 (44.1%) had a duration of disease of <1 year, while 41 (44.1%) and 11 (11.8%) patients had a duration of disease of 1–3 years and >3 years respectively. Sixty-two patients (66.7%) had 1-2 bands ligation, while 31 (33.3%) had 3–4 bands ligation. Red wale sign was observed in 22 (23.7%). Evidence of re-bleeding was observed in 9 (9.7%). According to stratification of re-bleed within 4 weeks concerning different variables, the difference was statistically insignificant with respect to gender (*p*=0.705) and age groups (*p*=0.324) in Table-1, 2, while the difference was statistically significant with respect to Child-Pugh class (*p*=0.041), Grades of oesophageal varices (*p*=0.000058), Red wale sign (*p*=0.001) and a number of bands ligation (*p*=0.000199) in Tables 3–6.

Table-1, 2: Stratification of re-bleed within 4 weeks with respect to Age / Gender

Age groups	Re-bleed within 3 weeks		Total	*p*-value
	Yes	No		
18-30 years	1	13	14	0.324
	7.1%	92.9%	100.0%	
31-45 years	1	27	28	
	3.6%	96.4%	100.0%	
>45 years	7	44	51	
	13.7%	86.3%	100.0%	
Total	9	84	93	
	9.7%	90.3%	100.0%	

Gender	Re-bleed within 3 weeks		Total	*p*-value
	Yes	No		
Male	6	61	67	0.705
	9.0%	91.0%	100.0%	
Female	3	23	26	
	11.5%	88.5%	100.0%	
Total	9	84	93	
	9.7%	90.3%	100.0%	

Table-3, 4: Stratification of re-bleed within 4 weeks with respect to Grades / Child-Pugh Class

Grades of oesophageal varices	Re-bleed within 3 weeks		Total	*p*-value
	Yes	No		
Grade-1	0	63	63	0.000058
	0%	100%	100.0%	
Grade-2	2	18	20	
	10%	90%	100.0%	
Grade-3	7	3	10	
	70%	30%	100.0%	
Total	9	84	93	
	9.7%	90.3%	100.0%	

Child-Pugh class	Re-bleed within 3 weeks		Total	*p*-value
	Yes	No		
Class-A	0	45	45	0.041
	0%	100%	100.0%	
Class-B	4	29	33	
	12.1%	87.9%	100.0%	
Class-C	5	10	15	
	33.4%	66.7%	100.0%	
Total	9	84	93	
	9.7%	90.3%	100.0%	

Table-5, 6: Stratification of re-bleed within 4 weeks with respect to Number of Bands Ligation/ Red Wale Sign

Number of bands ligation	Re-bleed within 3 weeks		Total	*p*-value
	Yes	No		
1-2	1	61	62	0.000199
	1.6%	98.4%	100.0%	
3	1	9	10	
	10%	90%	100.0%	
3-4	7	14	21	
	33.33	66.67	100.0%	
Total	9	84	93	
	9.7%	90.3%	100.0%	

Red wale sign	Re-bleed within 3 weeks		Total	*p*-value
	Yes	No		
Yes	8	14	22	0.001
	36.4%	63.6%	100.0%	
No	1	70	71	
	1.4%	98.6%	100.0%	
Total	9	84	93	
	9.7%	90.3%	100.0%	

DISCUSSION

The formation of Oesophageal varices is a common complication of cirrhotic portal hypertension. The prevalence of oesophageal varices in cirrhotic patients is around 60–80%, the incidence rises 5% per year, and the rate of progression from small to large varices is approximately 5–10% per year.[9] The risk of variceal bleeding is 25–35% in patients of

cirrhosis with portal hypertension[9] and each event of bleed carries a 30% mortality risk and 70% risk of recurrent bleeding within one year from the first episode of bleeding.[10] At the time of diagnosis of cirrhosis, oesophageal varices are present in about 60% of decompensated and 30% of compensated patients.[11] Nearly 90% of patients with cirrhosis develop oesophageal varices sometime in their lifetime, of which 30% bleed.[12]

Once varices have developed, they increase gradually in size and are presented as an episode of blood in vomitus (hematemesis) or black tarry stools (Malena). Similar to the result of our study, the study by the North Italian Endoscopy Club identified the variceal size, the degree of liver failure assessed by the Child-Pugh classification and endoscopic "red signs" as the major independent risk factors of the first variceal bleeding episode.[13]

Endoscopic variceal band ligation (EVBL) is effective in primary and secondary prophylaxis of bleeding oesophageal varices and is recognized as a standard treatment to secure haemostasis. It has considerably decreased the frequency of variceal bleeding, complications and mortality. EVBL has replaced endoscopic injection sclerotherapy (EIS) as the first-line treatment of choice for acute oesophageal variceal haemorrhage.[14,15] However, this treatment is mostly performed in the in-patient setting and has a high recurrence rate, also needs advanced technique and incurs high cost.[16,17]

In this study, the risk of re-bleeding following successful control of the initial bleeding episode with band ligation was observed in 9 (9.7%) patients which is quite low in frequency as compared to the study done by Abbasi A *et al*, i.e., 19.1%[18] and the difference in frequency is because they included every patient with an indication for band ligation but in this study, we excluded the patients with previous band ligation, portal vein thrombosis and non-cirrhotic portal hypertension.

In another study done by Harewood GC[19] rebleeding was reported to be 9.3% which is similar to the results of this study. In the present study, re-bleeding after oesophageal variceal banding in cirrhotic patients was 9.7%. One study from Turkey reported a re-bleeding rate of 6.1%.[20] In another study frequency of post–banding ulcer bleeding following EVBL in cirrhotic patients was found to be 7.9%[21] and 7.7% by Cho *et al*[22].

Other previous studies found rates of re-bleeding between 10% and 50%. Such wide variation in recurrent bleeding rates may be due to inclusion or exclusion criteria differences among studies, such as the interval between sessions or the number of bands placed during each session[23]. Other associated factors, such as the time elapsed since the first episode of bleeding, the definition of endpoints such as recurrent bleeding, history of alcoholism, and urgent considerations to manage the bleeding, may also affect the results of treatment.

In this study, the major factors contributing to re-bleeding were the grades of varices, the severity of cirrhosis, the number of bands ligation and the presence or absence of red wale sign. 8 out of 9 (88.9%) patients that had evidence of re-bleeding had findings of red wale sign at the initial endoscopy which is consistent with data from an international study by Slowik, Voytek, *et al*.[24] In 30 patients who had grade 2 or above oesophageal varices, 9 (30%) out of these patients had rebleeding, while 63 patients had grade 1 on initial endoscopy and had no evidence of re-bleeding. In total 93 patients; 15, 33 and 45 patients belonged to child C, B and A respectively showing that the risk of rebleeding is significantly greater in patients with severe liver disease Child-Pugh Class C or B. 7 out of 9 patients (77.8%) of rebleeding had variceal grade III and had 3–4 bands legations at the first place.

Age was another factor that was studied in the frequency of re-bleeding. Among patients, 51 (54.8%) patients had ages >45 years of age, 28 (30.1%) patients were between 31–45 years and only 14 (15.1%) patients were younger than 30 years however rebleeding risk increases with increasing age especially after 45 years of age. The frequency of re-bleeding was found in 6 (9%) out of 67 male patients and 3 (11.5%) out of 26 female patients. Age factor has not been studied as a risk factor for rebleeding in international studies.

The limitations of the study were a short follow-up interval. Patients were not followed up till the eradication of varices. Other confounding factors like the use of alcohol were not considered. The use of medications, other than NSAIDs and antiplatelet drugs, was not considered. Endoscopic variceal Band ligation is an operator-dependent procedure, and banding in our study was not done by a single operator which can also influence the results.

CONCLUSION

Endoscopic variceal Band Ligation is an effective modality of treatment for the control of oesophageal variceal bleeding. The major factors contributing to re-bleeding were the severity of cirrhosis, grades and columns of oesophageal varices, number of bands applied and findings of red wale signs. Increasing age and duration of cirrhosis were contributing predictors of increased re-bleeding risk.

Disclosure: None
Conflict of Interest: None

AUTHORS' CONTRIBUTION

SA: Acquisition, analysis, data interpretation, drafting, revision, final approval. Agreement to be accountable for all aspects of the work. JM, HUR: Conceptualization of the study design, revision, data acquisition & final approval. Agreement to be accountable for all aspects of the work. MUW, MKF: Design of work, data analysis, data interpretation, revision. Agreement to be accountable for all aspects of the work. SS: Data acquisition, drafting, final approval. Agreement to be accountable for all aspects of the work.

REFERENCES

1. Asrani SK, Devarbhavi H, Eaton J, Kamath PS. Burden of liver diseases in the world. J Hepatol 2019;70(1):151–71.
2. Almani SA, Memon AS, Memon AI, Shah I, Rahpoto Q, Solangi R. Cirrhosis of liver: Etiological factors, complications and prognosis. J Liaquat Uni Med Health Sci 2008;7(2):61–6.
3. Simonetto DA, Liu M, Kamath PS. Portal hypertension and related complications: diagnosis and management. Mayo Clin Proc 2019;94(4):714–26.
4. Augustin S, González A, Genescà J. Acute esophageal variceal bleeding: Current strategies and new perspectives. World J Hepatol 2010;2(7):261–74.
5. Biecker E. Portal hypertension and gastrointestinal bleeding: diagnosis, prevention and management. World J Gastroenterol 2013;19(31):5035–50.
6. Abbasi A, Bhutto AR, Bhatti KI, Mahmood K, Lal K. Outcome of band ligation in oesophageal varices. J Pak Med Assoc 2013;63(8):983–7.
7. Belbase NP, Jalan A, Upadhya HP, Mishra R, Karki M, Kumar S. Endoscopic Band Ligation in Patients with Variceal Bleeding. Birat J Health Sci 2018;3(1):320–4.
8. Zhou JN, Wei Z, Sun ZQ. Risk factors for early rebleeding after esophageal variceal ligation in patients with liver cirrhosis. Zhonghua Gan Zang Bing Za Zhi 2016;24(7):486–92.
9. Sarangapani A, Shanmugam C, Kalyanasundaram M, Rangachari B, Thangavelu P, Subbarayan JK. Noninvasive prediction of large esophageal varices in chronic liver disease patients. Saudi J Gastroenterol 2010;16(1):38–42.
10. Xavier RG, Tahir MH, Zulkifli MH, Han WH, Hassan A. The use of propranolol as primary prophylaxis in preventing an index bleed in patients with liver cirrhosis: a retrospective cohort study. Dig Med Res 2019;2:33.
11. D'amico G, Pagliaro L, Bosch J. The treatment of portal hypertension: a meta-analytic review. Hepatology 1995;22(1):332–54.
12. Grace ND. Diagnosis and treatment of gastrointestinal bleeding secondary to portal hypertension. American college of gastroenterology practice parameters committee. Am J Gastroenterol 1997;92(7):1081–91.
13. 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. N Engl J Med 1988;319(15):983–9.
14. Seo YS. Prevention and management of gastroesophageal varices. Clin Mol Hepatol 2018;24(1):20–42.
15. Santos MM, Tolentino LH, Rodrigues RA, Nakao FS, da Silveira Rohr MR, de Paulo GA, *et al*. Endoscopic treatment of esophageal varices in advanced liver disease patients: band ligation versus cyanoacrylate injection. Eur J Gastroenterol Hepatol 2011;23(1):60–5.
16. Latif S, Saleem HQ, Akhtar N, Shafique R, Pari A, Naseeb M, *et al*. Comparison of endoscopic band ligation alone versus propanalol plus endoscopic band ligation for control of rebleeding Oesophageal varices in patients with portal hypertension. J Khyber Coll Dentistry 2021;11(2):32–7.
17. Jha AK, Goenka MK. Endoscopic Band Ligation for the Hemostasis of Active Esophageal Variceal Hemorrhage: Technique, Tips, and Tricks. J Dig Endosc 2019;10(4):219–20.
18. Shrestha R, Thapa J, Yadav B, Thapa B, Paudel MS. Endoscopic detection and management of esophagogastric varices. Cureus. 2021 Aug 2;13(8).
19. Harewood GC, Baron TH, Wong Kee Song LM. Factors predicting success of endoscopic variceal ligation for secondary prophylaxis of esophageal variceal bleeding. J Gastroenterol Hepatol 2006;21(1):237–41.
20. Kuran S, Oğuz D, Parlak E, Asil M, Çiçek B, Kilic M, *et al*. Secondary prophylaxis of esophageal variceal treatment: Endoscopic sclerotherapy, band ligation and combined therapy--long-term results. Turk J Gastroenterol 2006;17(2):103–9.
21. Elhawari SA, Moustafa EA, Zaher T, Elsadek HM, Abd-Elazeim MA. Frequency and Risk Factors of Post Banding Ulcer Bleeding Following Endoscopic Variceal Ligation in Patients with Liver Cirrhosis. Afro-Egypt J Infect Endem Dis 2019;9(4):252–9.
22. Cho E, Jun CH, Cho SB, Park CH, Kim HS, Choi SK, *et al*. Endoscopic variceal ligation-induced ulcer bleeding: What are the risk factors and treatment strategies? Medicine (Baltimore) 2017;96(24):e7157.
23. Nguyen KC, Nguyen TH. Efficacy of endoscopic multi-site band ligation in eradicating esophageal varices. Gastrointest Endosc 2009;69(5):AB222.
24. Slowik V, Bernardez A, Wasserkrug H, Fischer RT, Daniel JF, Grammatikopoulos T. Use and safety of prophylactic endoscopy from a single center serving urban and rural children with portal hypertension. Sci Rep 2022;12(1):25.

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