Original article

Risk factors associated with early variceal rebleed after endoscopic variceal band ligation in cirrhotic Hepatitis B and C patients with variceal bleed

Atif Nasrullah[1], Muhammad Kashif[2], Haris Nasrullah[3], Arif Mahmood Siddiqui[4]

[1]Registrar Medical Unit II, Jinnah Hospital Lahore, [2]Assistant Professor of Medicine CMH Lahore Medical College, Combined Military Hospital Lahore, [3]Medical Officer BHU Jamu Bola Gujrat-Pakistan, [4]Head of Department Medical Unit-II, Jinnah Hospital Lahore

Correspondence to: Dr. Muhammad Kashif, Email: mkashif7290@gmail.com

ABSTRACT

Background: Chronic liver disease is endemic in Pakistan with esophageal variceal bleeding as one of the important complications and is treated with EVBL. The early esophageal variceal rebleeding is one of the ignored factors which carries the high mortality and morbidity.

Patients and methods: This case-control study was conducted in the Gastroenterology Department at Jinnah Hospital, Lahore, from February 2016 to February 2017. The Study included total 100 patients and out of these 50 were rebleeding cases while 50 were controls (without esophageal rebleed). Cases and control were matched for age, sex, Presence of hepatitis B and C and cirrhosis. The endoscopic findings of any active bleed and white nipple sign was recorded.

Results: In this study, association of risk factors for prediction of early variceal rebleed after banding in cirrhotic hepatitis B and C patients with variceal bleed was recorded as 58% (n=29) in cases and 12% (n=6) for active bleeding, O.R was 10.12, 68% (n=34) in cases and 14% (n=7) in controls had nipple sign, O.R was 13.05, Hb level <9 g/dl was recorded in 88% (n=44) in cases and 40% (n=20) in controls, O.R 11.00, PT>18 sec was recorded in 96% (n=48) in cases and 4% (n=2) in controls, O.R was 576.

Conclusion: Active bleeding and nipple sign, Hb level <9 g/dl and PT >18 sec are found to have strong association for prediction of early variceal rebleed after EVBL in cirrhotic hepatitis B and C patients.

Keywords:

Cirrhosis, Variceal bleed, Endoscopic variceal band ligation, Rebleeding, risk factors, Association

INTRODUCTION

Worldwide about 350,000 to 500,000 deaths occur each year from hepatitis C related complications, while more than 780,000 die each year due to hepatitis B related disease.[1] In Pakistan hepatitis B and C are endemic viral infection and a total population of about 13 million affected with hepatitis B and C.[2]

About one third of the patients with varices develop acute variceal bleeding.[3] Variceal bleed is a life threatening complication of cirrhosis with about 20% mortality.[4] Current treatment for variceal bleed is medical which consists of vasoconstrictor drugs, endoscopic variceal band ligation.[5,6] Without treatment about 60% of patients rebleed within one year.[7] While risk of rebleed is 19% with treatment.[8,9] Different factors have been measured in various studies to show the increased incidence of rebleed; among them is increased Model for End-stage Liver Disease and serum sodium (MELD-Na) score, decreased albumin variceal size, esophageal varices (EV) column, puts patient at an increased risk of early variceal rebleed.[10-12] Multiple studies show the effect of different factors on rebleed but there is no widespread agreement on particular set of factors. Results of different studies often contradict each other.[12-14] Wang and coauthors reported that Child-Pugh grade B, total bilirubin (Tbil), creatinine and the collective volume of blood transfusion were associated with increased risk of rebleed.[13] Hunter and Hamdy found that mean Model for End-stage Liver Disease (MELD) score was remarkably high in rebleed group in comparison to control group. Active bleeding was found in 8% of control group during endoscopy and 53.3 % in rebleed group, while 10.6% had white nipple sign in control group, and 73.3% of rebleed group. In conclusion, MELD score (> 18), active bleeding and white nipple sign at time of endoscopy are important factors for early variceal rebleed and mortality.[14] The rationale of this study is that both Hepatitis B and C are endemic in Pakistani population and its complications including variceal bleed and rebleed are common. These are associated with increased morbidity and mortality requiring continuous

Conflict of interest: The authors declared no conflict of interest exist.

Citation: Nasrullah A, Kashif M, Nasrullah H, Siddiqui AM. Risk factors associated with early variceal rebleed after endoscopic variceal band ligation in cirrhotic Hepatitis B and C patients with variceal bleed. J Fatima Jinnah Medical Univ. 2020; 14(1): 30-33.

DOI: https://doi.org/10.37018/penc3048

Table 1. Association of risk factors for prediction of early variceal rebleed after endoscopic variceal band ligation in cirrhotic Hepatitis B and C patients with variceal bleed (n=100)

Risk factors	Cases (*n*=50)		Controls (*n*=50)		OR
	No. of patients	%	No. of patients	%	
Active bleeding	29	58	6	12	10.12
Nipple sign	34	68	7	14	13.05
Hb level <9 g/dl	44	88	20	40	11.00
PT > 18 sec	48	96	2	4	576.00

monitoring. This study aims to look into factors responsible for early rebleed after endoscopic variceal band ligation (EVBL) possibly leading to delineate guidelines for management of such high risk patients and will help us to provide optimum care to those who are at increased risk of rebleed. Objective is to highlight the association of common risk factors with rebleed and if an association is found then measure can be taken to prevent it, as no local study exist on this till present date to best of our knowledge.

PATIENTS AND METHODS

This case control study was conducted in Gastroenterology Department, Jinnah Hospital, Lahore from February 2016 to February 2017 after taking approval from the Ethical Review Board (ERB), Jinnah Hospital Lahore. The study included cirrhotic hepatitis B and C patients from both genders with an age range of 25-65 years. Patient with any other reason of cirrhosis and previous history of injection sclerotherapy were excluded from the study. Sample size of 100 cases (50 in each group) was calculated with 90% power of test, 5% level of significance and taking expected percentage of Hb level <9 g/dl in both groups i.e. 35%[12] in control group *vs*. 92%[12] in study group. They were divided into cases (who rebleed after EVBL) and controls (who do not rebleed after (EVBL) informed written and verbal consent was taken from all the patients. 5 ml venous blood was sent to laboratory and haemoglobin level and prothrombin time were noted as per operational definition (patients assessed whether they have HB levels <9g/dl. And prothrombin time was assessed whether they have PT >18 seconds. The endoscopic findings were noted for any active bleed and white nipple sign and recorded as per operational definition. Early variceal rebleed was defined as bleeding from gastrointestinal tract after 24 hour to 14 days of band ligation in the form of > 1 episode of haematemesis or malena (>100 ml blood) and Hypovolemic shock measured clinical in presence by (systolic Blood pressure <90 mm hg, and Decrease in Hb of 2g/dl assessed after 24 hour). The White nipple sign was a platelet fibrin plug which was seen as white nipple like projection from varix noted from endoscopic data.

RESULTS

A total of 100 cases (50 in each group) fulfilling the inclusion/exclusion criteria were enrolled to evaluate risk factors for prediction of early variceal rebleed after EVBL in patients with chronic liver disease secondarily to hepatitis B and C patients with variceal bleed. Age of the patients was recorded as 26% (n=13) in cases and 28% (n=14) in controls were between 25-40 years while 64% (n=37) in cases and 72% (n=36) in controls were between 41-65 years of age, mean+sd was calculated as 55.24+5.53 and 56.32+5.35 years respectively. Gender distribution shows that 52% (n=26) in cases and 58% (n=29) in controls were male while 48% (n=24) in cases and 42% (n=21) in controls were females. Mean Hb level in both groups was recorded as 7.23+2.47 in cases and 10.41+2.96 in controls. Mean prothrombin time in both groups was recorded as 23.45+5.29 in 48 cases and 9.16+3.60 in 2 controls. Association of risk factors for prediction of early variceal rebleed after EVBL in cirrhotic hepatitis B and C patients with variceal bleed was recorded as 58% (n=29) in cases and 12% (n=6) for active bleeding, O.R was 10.12, 68% (n=34) in cases and 14% (n=7) in controls had nipple sign, O.R was 13.05, Hb level <9 g/dl was recorded in 88% (n=44) in cases and 40% (n=20) in controls, O.R 11.00, PT>18 sec was recorded in 96% (n=48) in cases and 4% (n=2) in controls, O.R was 576.00 (Table 1). The data is stratified and presented for active bleeding and nipple sign with regards to age in Table 2.

DISCUSSION

One of the most important complication associated with high mortality in patients with chronic liver disease is bleeding from esophageal varices. Reportedly 5 –15% of cirrhotic patients presents with upper gastrointestinal bleed each year. The main factor which

Table 2: Stratification for active bleeding and nipple sign with regards to age

Age groups	Active bleeding		p-value	Nipple sign		p-value
	Yes	No		Yes	No	
25 - 50						
A	9	4	0.003	10	3	0.001
B	2	12		2	12	
51 - 65						
A	20	17	0.00	24	3	0.000`
B	4	32		5	31	

predicts the bleeding from the varices is the size of varices. Large varices are associated with highest risk of first bleeding (15% per year). Endoscopic variceal band ligation (EVBL) has proved to be the most successful method for prevention of variceal bleeding. Despite that, early rebleed after EVBL (rebleeding between 24 hours to 14 days post procedure) is also lethal.[2] This study was planned with the view that both Hepatitis B and C are endemic in Pakistani population and its complications including variceal bleed and rebleed are common, increased morbidity and mortality is associated with it requiring continuous monitoring.

In this study, mean age was found as 55.24+5.53 and 56.32+5.35 years in cases and controls, 52% (n=26) in cases and 58% (n=29) in controls were male while 48% (n=24) in cases and 42% (n=21) in controls were females, mean Hb level in both groups was recorded as 7.23+2.47 in cases and 10.41+2.96 in controls, mean prothrombin time in both groups was recorded as 23.45+5.29 in cases and 9.16+3.60 in controls. Association of risk factors for prediction of early variceal rebleed after EVBL in cirrhotic hepatitis B and C patients with variceal bleed was recorded as 58% (n=29) in cases and 12% (n=6) for active bleeding, O.R was 10.12, 68% (n=34) in cases and 14% (n=7) in controls had nipple sign, O.R was 13.05, Hb level <9 g/dl was recorded in 88% (n=44) in cases and 40% (n=20) in controls, O.R 11.00, PT>18 sec was recorded in 96% (n=48) in cases and 4% (n=2) in controls, O.R was 576.00.

Active bleeding was found in 8% of control group during endoscopy and 53.3 % in rebleed group (p = 0.003), while 10.6% had white nipple sign in control group, and 73.3% of rebleed group (p=0.05). In conclusion MELD score (>18), active bleeding and white nipple sign at time of endoscopy are important factors for early variceal rebleed and mortality.[14] Another study reveals that hemoglobin levels less than < 9 g/dl was present in 35% of non rebleeding group and 92% of bleeding group[12] (p<0.01), While PT >18 sec as present in the 1.3% of non rebleeding group patients and 92% of rebleeding group (p<0.01),[12] our findings are in agreement with the above studies.

Very limited studies are available to address this issue, however, in our study we ruled out the factors responsible for early rebleed after EVLB possibly leading to delineate guidelines for management of such high risk patients and helpful for us to provide optimum care to those who are at increased risk of rebleed. This study shows the association of common risk factors with rebleed and measures should be taken to prevent it, these findings are primary in local setup as no local study exist on this till present date to best of our knowledge. Further trials are also required to validate our findings.

CONCLUSION

Active bleeding and nipple sign, Hb level < 9 g/dl and PT > 18 seconds are found to have strong association for prediction of early variceal rebleed after endoscopic variceal band ligation in cirrhotic hepatitis B and C patients with variceal bleed. Patients having these risk factors may be considered as high risk and should be monitored and managed accordingly.

REFERENCES

1. WHO. Hepatitis C, B fact sheets. Geneva: World Health Organization; 2019 [cited 16 March 2020]. Available from: https://www.who.int/news-room/fact-sheets/detail/hepatitis-c
2. WHO. 15 million people affected with hepatitis B and C in Pakistan: Government announces ambitious plan to eliminate hepatitis. Geneva: World Health Organization; 2019 [cited 16 March 2020]. Available from: https://www.who.int/hepatitis/news-events/pakistan-hepatitis-elimination-plan/en/
3. Mehmood S, Raza H, Abid F, Saeed N, Rehman HM, Javed S et al. National prevalence rate of hepatitis B and C in Pakistan and its risk factors. J Public Health (Berl.) (2019). https://doi.org/10.1007/s10389-019-01119-8
4. Jameson JM, Fauci AS, Kasper DL, Hauser SL, Longo DL. Harrison's Principles of Internal Medicine, 20th ed. America: McGraw Hill; 2018; 2410-2411.
5. Bosch J, Sauerbruch T. Esophageal varices: Stage-dependent treatment algorithm. J Hepatol. 2016; 3(64): 746–748.

6. National Institute for Health and Clinical Excellence. Acute upper gastrointestinal bleeding: Management. London: Royal College of Physicians (UK); 2012.
7. Bari K, Garco-Tso G. Traeatment of portal hypertension. World J Gastroenterol. 2012; 18(11): 1166-1175.
8. Ahme S, Hoque M.N, Bhuiyan T.M. Outcome of Esophageal Variceal Ligation in Cirrhotic Patients: Experience in a Tertiary Care Hospital in Dhaka. BIRDEM Med J. 2019; 9(1): 63-69.
9. Ray G. Long-term outcome of endoscopic variceal band ligation of esophageal varices in patients with chronic liver disease. Indian J Gastroenterol. 2019; 38(1): 69-76.
10. Topal F, Karakaya Z, Çakır A. Prediction of hospital mortality by MELD Na+ score for esophageal variceal bleeding. ACAM. 2020; 11(4): 314-318.
11. Groza I, Acalovschi M, Pasca S. et al. 'Factors predictive of relapse in variceal upper gastrointestinal bleeding. A prospective study in patients with liver cirrhosis. Int J Bioflux Soc. 2017; 9(4): 116-123.
12. Liang Xu, Feng Ji, Qin-Wei Xu, Mie-Qing Zhang. Risk factors for predicting early variceal rebleeding after endoscopic variceal ligation. World J Gastroenterol 2011; 17(28): 3347-3352.
13. Mei-tang W, Xiu-qiang MA, Jian HE. Prognostic factors factors associated with rebleeding in cirrhotis inpatients complicated with esophageal variceal bleeding. Chin Med J. 2011; 124(10): 1493-1497.
14. Hunter SS, Hamdy S. Predictors of early re-bleeding and mortality after acute variceal hemorrhage. Arab J Gastroenterol. 2013; 14(02): 63-67.