CORRELATION OF THROMBOCYTOPENIA WITH GRADING OF ESOPHAGEAL VARICES IN PATIENTS WITH CIRRHOSIS

SAMIA KAUSAR[1], KIRAN FATIMA[1], ZUNERA JAHANZEB[2], MUHAMMAD FAROOQ[1]
[1]Islamic International Medical College, Riphah International University Islamabad. HBS medical college, Rawalpindi

ABSTRACT

Objective: To determine the relationship of severity of thrombocytopenia with various grades of esophageal varices in patients with cirrhosis.

Methods: A cross sectional observational study conducted at Medicine Department of Islamic International Medical College & Pakistan Railway General Hospital from 1st September, 2018 to 31st August, 2020.

The record of 100 patients with cirrhosis having concomitant thrombocytopenia and esophageal varices was retrospectively analyzed. The information about clinical, hematological, biochemical, ultrasound and endoscopic findings was retrieved from medical record. On the basis of platelet count, four groups were made. Group I consisted of patients with a platelet count ≤ 20,000/ µl, group II 21,000-49,000/ µl, group III 50,000-99,000/ µl, and group IV 100,000- 149,000/ µl. Esophageal varices were reclassified as small and large varices group depending on the size. Correlation of thrombocytopenia with grading of esophageal varices was calculated using spearman's correlation.

Results: Out of 100 patients, 76% had large varices and 24% had small varices. Thrombocytopenia was more severe in patients with large varices group when compared with small varices group. There was significant negative correlation between thrombocytopenia and grading of esophageal varices (r= -.691; P < 0.001).

Conclusion: The severity of thrombocytopenia increased with increase in the size of esophageal varices. Low platelet count can strongly predict large varices in patients with cirrhosis.

Key words: Cirrhosis, Esophageal varices, Thrombocytopenia, UGIB.

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Correspondence to: Samia Kausar
Associate Professor, Department of Medicine, Islamic International Medical College, Railway General Hospital, Rawalpindi, Pakistan.

Email: samia.kausar@riphah.edu.pk

INTRODUCTION

Cirrhosis results from chronic inflammation of varied etiology leading to progressive fibrosis and disruption of hepatic architecture. Gradual decline in functional liver cell mass manifest in multiple hematological abnormalities like thrombocytopenia, leucopenia and anemia. Progressive fibrosis consequently increases hepatic venous pressure gradient (HPVG) and portal hypertension manifest as esophageal varices and splenomegaly. HPVG increases with severity of cirrhosis and when greater than 12 mm of Hg, increases the risk of variceal bleed. About one third of cirrhosis related deaths result from variceal haemorrhage[1-2].

Thrombocytopenia seen in 76% cases of cirrhosis, reflects degree of fibrosis, reduced liver functional capacity and bad prognosis[3]. A more advanced stage of cirrhosis is associated with severe thrombocytopenia because of combination of increased splenic sequestration of platelets, higher portal pressure, and decreased thrombopoietin production. As hepatic venous pressure gradient (HPVG) rises, variceal size increases and platelet count falls. Thrombocytopenia is correlated with the size of esophageal varices[4].

At the time of diagnosis 30% patients with cirrhosis have varices which increase up to 90% in 10 years. Almost 50% will have upper gastrointestinal bleed (UGIB) from esophageal varices at some point. Mortality is 57% per year in those who bleed compared with 3.4% per year who never bleed with varices[5]. Risk of variceal bleeding increases with advanced cirrhosis, grades of esophageal varices, HVPG and red whale sign on varices[6-7]. Both beta blockers and band ligation reduce HPVG, risk of bleeding and improve survival [8]. Early detection of varices and prevention of variceal hemorrhage by primary prophylaxis is extremely important[9]. Endoscopy is a gold standard safe procedure for quick diagnosis and therapeutic option if required but still invasive procedure and many patients do not consent for it because of discomfort and cost. Many patients with early cirrhosis may not have varices and thus endoscopy can be avoided. There is need for noninvasive index test for esophageal varices especially in low-risk patients who can be spared for endoscopy and identify high risk patient who need primary prophylaxis to prevent variceal bleed. We aimed to study the correlation of thrombocytopenia with size of esophageal varices.

METHODS

We performed this retrospective cross-sectional analysis at Pakistan Railway Hospital Rawalpindi from 1st September, 2018 to 31st August, 2020. Patient having cirrhosis with both esophageal varices and thrombocytopenia were included. Patients with portal vein thrombosis, hepatocellular carcinoma, IV drug user, current alcohol intake, beta blocker, nitrate drug treatment were excluded from study. We took permission from the institutional review committee of Riphah International University.

Patient's demographic data regarding age, sex, medical record number was recorded. Laboratory finding with complete blood count, liver function tests including serum bilirubin, AST, ALT, ALP, serum albumin and prothrombin time were retrieved from medical records. Abdominal ultrasound finding including shrunken liver, ascites, portal vein size, splenomegaly were noted. To determine etiology of cirrhosis information about HBsAg, anti HCV, Serum ceruloplasmin, eye examination for kayser fleischer ring for Wilson disease, iron studies for haemochromatosis, autoantibodies for autoimmune liver disease, and antimitochondrial antibodies for primary biliary cirrhosis were entered on structured performa. Cirrhosis was diagnosed with combined clinical, hemotological, biochemical and radiological findings and its severity was assessed by Child-pugh score. Endoscopic examination was done by single trained examiner using Olympus GIF 130 endoscope after informed consent. Esophageal varices were graded using Paquet classification[10.]

Grade I: Small varices disappear on air insufflations

Grade II: Larger, straight, does not disappear on insufflations.

Grade III: Medium size, partly occupying the lumen.

Grade IV: Large, tortuous, grapes like filling the lumen.

Patient were divided into two groups, small varices group (grade I, II) and large varices group (grade III, IV).

Platelet count less than 150,000/µl was taken as thrombocytopenia. Patients were divided into four groups depending on the platelet count. Group I platelet count ≤ 20,000/ µl, group II with count 21,000-49,000/ µl, group III 50,000-99,000/ µl, and group IV 100,000-149,000/ µl.

Parametric data was analyzed by SPSS 21. Correlation of thrombocytopenia with esophageal varices grade was studied by applying spearman's rank correlation test. The P value of < 0.01 was taken significant.

RESULTS

Table 1: Thrombocytopenia and esophageal varices correlation. Total number =100

Platelet count	Small varices group	Large varices group	Number of patients
<20,000	0	15 (15%)	15 (15%)
20,000-49,000	3 (10%)	27 (90%)	30 (30%)
50,000-99,000	10 (28.57%)	25 (71.42%)	35 (35%)
100,000-149,000	13 (65%)	7 (35%)	20 (20%)
Total	26	74	100

A total of 100 cirrhotic patients with esophageal varices and thrombocytopenia were included in the study. There were more males 65% as compared with females 35% in this study. The mean age was 48 ± 10.98 with age range of 23-85 years. Regarding etiology of cirrhosis 88% were HCV positive, 5% were HBV positive, both HBsAg and anti HCV were seen in 2% and no cause was found in 5% cases. There were 24 patients in Child class A, while 35 and 40 patients in Child class B and C respectively. As regard the size of esophageal varices, grade I and II varices were noted in 14 and 10 patients, while grade III and IV were present in 36 and 40 patients respectively. The correlation between thrombocytopenia with grade of esophageal varices is presented in Table 1. Greater degree of

thrombocytopenia was associated higher grade of varices. The spearman's rank correlation test was applied which showed significant negative correlation between the two.

Table 2: spearman's correlation between platelet count and esophageal varices grade.

Grades of esophageal varices		
Platelet count	R	P value
	-0.695	<0.001

DISCUSSION

We observed statistically significant negative correlation between thrombocytopenia and size of esophageal varices. Large varices found to be associated with severe thrombocytopenia. Moreover, degree of thrombocytopenia and size of varices increased with severity of chronic liver disease.

Screening endoscopy is recommended in all patient with cirrhosis at the time of diagnosis. Various noninvasive tests have been used as triage test to avoid or delay endoscopy in patients at low risk for varices like thrombocytopenia, spleen length, aspartate aminotransferase AST to platelet count ratio index (APRI), platelet count to spleen length ratio, FIB-4 score. These tests used either alone or along with measurement of liver stiffness and or spleen stiffness using transient elastography, have been focus of many studies[11-12]. Thrombocytopenia is an independent risk factor and non-invasive predicator for varices. Lahmidani et al. verified that platelet count of less than equal to 100,000 is associated with varices[13]. Similar observation was made by Abdul lslam et.al. He found that platelet count of 149,000 has sensitivity of 82% and sensitivity of 39% for prediction of esophageal varices. Normal platelet count in cirrhosis is associated with low risk of upper GI bleed from varices.

Thrombocytopenia not only predicts any varices in cirrhosis there exist negative correlation between thrombocytopenia and grade of esophageal varices. In study done in Egypt thrombocytopenia was more prevalent in patients with esophageal varices compared with patients without varices. Lower platelet counts were noted in patient with grade II and III varices than in patients with grade I varices[14]. Similar results were reported by Abdul lslam that large varices size was associated with lower platelet count[15]. Ding et.al showed that thrombocytopenia ≤ 100,000/µl along with liver stiffness ≥25k Pa was suggestive of large varices[16].

In a study done in Pakistan by Mahmood et.al, large varices were found in 47.81% of patients with cirrhosis, and thrombocytopenia was 88.05% sensitive and 59.85% specific for predicting large varices. Lower platelet count showed significant association with large varices[17]. Zubia et al found thrombocytopenia and spleen diameter are significant Indicators for large varices but platelet-count/spleen-diameter ratio is definitely more reliable[18]. We found results in agreement with above studies. Similar results were reported from India [19.] Other studies results suggest that noninvasive predictor probably assist in stratifying patients but still not replacement for endoscopic diagnosis [20].

So, thrombocytopenia is reliable noninvasive indicator of any varices particularly large varices. When patients have normal platelet count and low liver stiffness only less than 4% have large varices[12]. So, in patients with normal count, endoscopy can be avoided reducing financial burden as well as load on endoscopy units.

We verified the significant association between severity of chronic liver disease and the size of esophageal varices. Patients with large varices mostly belonged to class child B and C. This fact has been validated in previous studies[4,17]. So patients with thrombocytopenia and higher child class are more likely to have large varices and at high risk for upper GI bleed. Pakistan has high rate of hepatitis C infection almost 5% and majority of our patients had hepatitis C related chronic liver disease[21]. Hepatitis C virus, now regarded as a marker of thrombocytopenia in addition to causing cirrhosis, directly causes immune destruction of platelets.

Screening endoscopy limited to high-risk group by using noninvasive markers thereby reducing medical, social, and economic costs in resource poor countries like Pakistan. It will be helpful for general practitioners especially working in remote areas to stratify high and low risk patients and timely referral for endoscopic management in tertiary care hospitals.

CONCLUSION

Thrombocytopenia and variceal size were inversely related. Lower the platelet count greater the size of varices. Thrombocytopenia can strongly predict large varices in patients with cirrhosis.

Limitation of our study is a small sample size. Therefore, results needs to be validated on large population. Easy, noninvasive, cheap alternative to endoscopy will definitely reduce health care cost.

Authors alone are responsible for the contents of the article. We communicate no conflict of interest.

ETHICAL APPROVAL

The study was approved by the Institutional Review Committee of Islamic International Medical College via Reference No. Riphah/IRC/20/212 Dated: July 23, 2020.

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AUTHOR'S CONTRIBUTIONS

SK, MF: Concept, design, data analysis, manuscript writing, accuracy, integrity of data

KF, ZJ: Concept, design, data analysis, manuscript writing, data collection