

## Original Article

# DETECTION OF ESOPHAGEAL VARICES IN LIVER CIRRHOSIS USING PLATELET COUNT AS A NON-INVASIVE PARAMETER

Muhammad Imran, Javeid Iqbal and Raffad

**Background:** Bleeding of the esophageal varices is a major complication of portal hypertension. At least two-thirds of patients with cirrhosis develop esophageal varices, and about 30% of patients with cirrhosis experience variceal bleeding.

**Objective:** To determine the diagnostic accuracy of platelet count to predict the presence of esophageal varices in patients with liver cirrhosis taking endoscopic findings as gold standard.

**Material & Methods:** This cross-sectional observational study was carried out over a period of six months from December, 2008 to June, 2009 in five medical wards (I, II, III, IV, and Special) of Services Hospital, Lahore. Total 180 cases were chosen in this study. Initially, non-invasive parameters were used to diagnose varices; later, endoscopy was performed to confirm the diagnosis.

**Results:** Mean age of the patients observed was  $50.5 \pm 10.9$  years. Sensitivity, specificity, PPV, NPV and diagnostic accuracy of platelet count was 99.2%, 92.2%, 97.1%, 97.3% and 97.2% respectively.

**Conclusion:** Results of current study indicate that patients of chronic liver disease can be screened for esophageal varices using platelet count as a non-invasive parameter.

**Keywords:** Esophageal varices, liver cirrhosis, platelet count

## Introduction

Esophageal varices are the most significant complication of portal hypertension, which may be associated with 20% of cirrhotic patients.<sup>1</sup> The prevalence of esophageal varices in cirrhosis is from 50% to 61%.<sup>2,3</sup> In Pakistan, prevalence of esophageal varices is 65% and that of large varices is 15% in cirrhotic patients.<sup>4</sup> The risk of bleeding from varices is 25%-35% with majority of the initial bleeding occurring within one year of detection. The mortality from each episode of variceal bleeding is 17%-57%.<sup>5</sup> Bleeding episodes can be predicted by the presence of red sign (cherry red spots) on the varices and by its size. The incidence of bleeding can be reduced with nonselective beta-blockers. It is also suggested that prophylactic endoscopic variceal ligation can decrease the incidence of first variceal bleeding and mortality in patients with liver cirrhosis who have large varices. Therefore, annual endoscopic screening is highly recommended for patients with small esophageal varices while the procedure should be conducted once every two years for patients suffering from liver cirrhosis without diagnosed varices. Nevertheless, repeated endoscopic examinations are unpleasant for patients, and have cost impact on health care, while only half of cirrhotic patients have esophageal

varices, and only 30% have large varices.<sup>5</sup>

Noninvasive assessment of esophageal varices may improve the management of patients with cirrhosis and decrease both the medical and financial burden related to screening.<sup>6</sup>

In a study done by Sarwar et al, it was concluded that serum albumin less than 2.95g/dL, platelet count less than 88,000/ $\mu$ L and portal vein diameter more than 11mm were associated with presence of varices.<sup>3</sup> It has been observed in another study that a platelet count of 82,000/ $\mu$ L (90.9% sensitivity, 41.7% specificity), portal vein diameter of 1.15 cm (75% sensitivity; 54.5% specificity) and an antero posterior splenic measurement of 10.3 cm (83.3% sensitivity; 63.6% specificity) were predictive factors for esophageal varices in liver cirrhosis.<sup>7</sup>

Platelet count, portal vein diameter and antero posterior splenic measurement can be used as non-invasive parameters to detect esophageal varices in cirrhotic patients. They may be proposed as safe and reproducible means to improve the management of cirrhotic patients who undergo screening endoscopy for esophageal varices as endoscopic exploration of varices in cirrhotic patients increases cost and involves a certain degree of invasiveness and discomfort for patients. Early endoscopic intervention for varices could be applied to those who

bleeding. Very few studies have been done to determine the association of platelet count with esophageal varices in our setup. The aim of this study therefore, is to explore the use of platelet count in diagnosing esophageal varices.

### Material & Methods

This cross-sectional observational study was carried out over a period of six months from December 2008 to June 2009 in five medical wards (I, II, III, IV, and Special units) of Services Hospital, Lahore. A total of 180 patients were recruited through non-probability purposive sampling from amongst the patients (>15 and <60 years) admitted at Services Hospital, a tertiary care health facility in Lahore, Pakistan. Only those patients demonstrating evidence of cirrhosis of liver on abdominal ultrasound (coarse echo texture) were included. Following were excluded: patients with a history of previous bleed or melena, active variceal bleeding, already on prophylaxis for esophageal varices, treated with band ligation or sclerosing agents for esophageal varices, co-morbid ischemic heart disease, bone marrow disorders, autoimmune diseases or those receiving interferon or drugs causing thrombocytopenia.

An informed consent was taken from all the patients and confidentiality ensured. Risks and benefits were explained to the subjects. All the patients who fulfilled the inclusion criteria were interviewed and subjected to clinical examination, laboratory investigations including platelet count, ultrasonography and upper gastrointestinal endoscopy. Initially, non-invasive parameters were used to diagnose varices; later, endoscopy was carried out to confirm the diagnosis. The cut off value for platelet count was taken as <82000/ $\mu$ L. Ethical approval for the study was received from the Review Committee of the Center for Health Research, Lahore. The study was conducted in compliance with 'ethical principles for medical research involving human subjects' of Helsinki Declaration.<sup>8</sup>

All the data were entered and analyzed using SPSS version 10.0. Ages of the patients were presented by calculating mean and standard deviation and gender (male, female) were presented by calculating frequency and percentages. Sensitivity, specificity, negative predictive value, positive predictive value and diagnostic accuracy of platelet count were calculated for the diagnosis of esophageal varices taking endoscopy as gold standard.

### Results

The calculated sample size of 180 cases had 9% margin of error, 95% confidence level with sensitivity and specificity of portal vein diameter and prevalence of esophageal varices being 75%, 54.5% and 50% respectively.

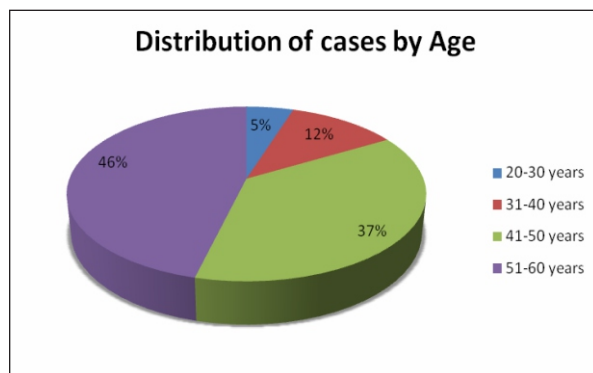
The mean age of the sample was  $50.2 \pm 10.5$  years. The maximum age was 60 and minimum age was 20 years. Most of the patients belonged to group 41 year to 60 years (83.3%) as illustrated in Figure-1. Out of 180 patients, 97 patients (53.9%) were male and 83 patients (46.1%) were female.

The study showed that 138 patients with platelet count below 80,000/ $\mu$ L had varices on gold standard as depicted by **Table-1**.

It was observed that platelet count can be used as non-invasive screening tool for predicting esophageal varices with diagnostic accuracy of 97.2% and it has 99.2% sensitivity and 90.2% specificity. Moreover, platelet count has 97.1% positive predictive value and 97.3% negative predictive value for diagnosing esophageal varices.

**Table-1:** Comparison of platelet count vs. upper GI endoscopy (n = 180)

Platelet Count	Endoscopy (Gold Standard)		Total
	Positive	Negative	
Positive	138 (True Positive)	04 (False Positive)	142
Negative	01 (False Negative)	37 (True Negative)	38
Total	139	41	180



**Fig-1:** Distribution of cases by age.

### Discussion

Most cirrhotic patients develop esophageal varices, with a lifetime incidence as high as 90%.<sup>9,10</sup> Approximately one third of cirrhotic patients with esophageal varices (EV) develop an episode of esophageal hemorrhage, and subsequently have high

to minimizing complications. An endoscopic examination is currently considered to be the gold standard. However, screening all patients with endoscopy to guide therapy may significantly increase the cost.

Non-invasive indicators of varices are desired to reduce the need for screening endoscopy in all patients with cirrhosis. Studies show that platelet count, splenomegaly, platelet count/spleen diameter ratio, advanced Child-Pugh class, serum albumin, and high portal vein diameter measured by ultrasonography may be useful non-invasive predictors of EV for patients with cirrhosis.<sup>11</sup>

In this study an attempt was made to find out sensitivity, specificity, negative predictive value, positive predictive value and diagnostic accuracy of platelet count in the diagnosis of esophageal varices taking endoscopy as gold standard.

The findings of our study have considerable consistency with the results of different local and international studies conducted in the past in which different variables have been taken into consideration as non-invasive markers to detect the esophageal varices. Various parameters which have been studied include serum albumin, prothrombin time, platelet count, portal vein diameter, splenic index, antero-posterior diameter of spleen.<sup>4</sup>

In one recent study cirrhotic patients without esophageal varices on initial endoscopy were followed up with annual or biannual surveillance. During the follow up it was proven that the platelet count/spleen diameter ratio is an effective means for ruling out the presence of esophageal varices even in the long term follow-up of the patients.<sup>12</sup> In this study all patients were followed up and endoscopies were done, and patients with higher baseline platelet count/ spleen diameter ratio were found less likely to develop esophageal varices. In our study we have not gone through the follow-up of endoscopies, making it less invasive and more convenient for the patients.

In another recent study by Prihatini et al<sup>7</sup> using bivariate analysis it was found that a platelet count of 82,000/uL (90.9% sensitivity; 41.7% specificity), portal vein diameter of 1.15 cm (75% sensitivity; 54.5% specificity) and an anteroposterior splenic measurement of 10.3 cm (83.3% sensitivity; 63.6% specificity) were predictive factors for esophageal varices in liver cirrhosis. Our data also showed that platelet count can be used as non-invasive parameter to detect esophageal varices in cirrhotic patients. Our results are comparable with study.

In a local study, it was concluded that using the

standard criteria of portal vein diameter 13 mm, I.N.R 1.5 and platelet counts 100,000/uL for the diagnosis of portal hypertension, about 70% patients had endoscopic evidence of esophageal varices.<sup>13</sup>

Another study showed that three non-invasive markers, ie, prothrombin index below 60%, alkaline phosphatase activity over 110 IU/L, and hyaluronate over 100 g/L were the best markers for the prediction of esophageal varices. The diagnostic accuracy for medium to large esophageal varices using these three factors was 86%.<sup>14</sup>

Comparing the results of the previous and objectively similar studies, the results of our study are relatively encouraging.

Like other studies, our study also has certain limitations. Prediction models may vary with the nature of the patient population from which these are derived. Our patients represent only those with chronic liver disease attending a teaching hospital and it will not apply to the patients attending basic health units and district hospitals. Further studies, covering these aspects, will be necessary.

Secondly, we did not test the predictive ability of this study in an independent prospective validation cohort, as was done in an Italian study.<sup>15</sup>

Thirdly, the presence of varices on endoscopy is subject to inter-observer variation. Our current method was easy to conduct and has comparable accuracy with other models used in the past which comprised of single and multiple variables in predicting the esophageal varices. The study utilized non-invasive blood tests, which every patient had to undergo to diagnose chronic liver disease with its complications, so non-invasive markers are not only simple but also practical to be used in clinical practice.

## Conclusion

Results of current study indicate that patients of chronic liver disease of any etiology can be screened for esophageal varices using platelet count as noninvasive parameter. Screening the patients of chronic liver disease by these parameters for varices will decrease burden of endoscopies and it will be possible to prevent first episode of variceal bleeding in these patients by various pharmacological and non-pharmacological strategies.

*Department of Medicine*  
*SIMS/ Services Hospital, Lahore*  
**[theesculapio@hotmail.com](mailto:theesculapio@hotmail.com)**  
**[www.sims.edu.pk/esculapio.html](http://www.sims.edu.pk/esculapio.html)**

## References

1. Suzuki AA, Mendes FB, Lindor KB. Diagnostic model of esophageal varices in alcoholic liver disease. *Euro J Gastroenterol Hepatol* 2005; 17:307-9.
2. Thomopoulos KC, Labropoulou KC, Mimidis KP, Katsakoulis EC, Iconomou G, Nikolopoulou VN. Non-invasive predictors of the presence of large esophageal varices in patients with cirrhosis. *Dig Liver Dis* 2003; 35: 473-8.
3. Giannini E, Botta F, Borro P, Risso D, Romagnoli P, Fasoli A et al. Platelet count/spleen diameter ratio: proposal and validation of a non-invasive parameter to predict the presence of esophageal varices in patients with liver cirrhosis. *Gut* 2003; 52:1200-5.
4. Sarwar S, Khan AA, Alam A, Butt AK, Shafqat F, Malik K et al. Non-endoscopic prediction of presence of esophageal varices in cirrhosis. *J Coll Physicians Surg Pak* 2005; 15: 528-31.
5. Alempijevic T, Bulat V, Djuranovic S, Kovacevic N, Jesic R, Tomic D et al. Right liver lobe/albumin ratio: Contribution to non-invasive assessment of portal hypertension. *Gastroenterol* 2007; 13: 5331-5.
6. Gartia-Tasao G. Current management of complications of cirrhosis and portal hypertension. *Gastroenterol* 2001; 120:726-48.
7. Prihatini J, Lesmana LA, Manan C, Gani RA. Detection of esophageal varices in liver cirrhosis using non-invasive parameters. *Acta Med Indones* 2005; 37:126-31.
8. WMA (2004). World Medical Association Declaration of Helsinki: ethical principles of medical research involving human subjects. [Available at: <http://www.wma.net/e/policy/b3.htm>].
9. Lay CS, Tsai YT, Teg CY. Endoscopic variceal ligation in prophylaxis of first variceal bleeding in cirrhotic patients with high-risk esophageal varices. *Hepatol* 1997; 25: 1346-1350 [CrossRef][Medline]
10. D'Amico G, Pagliaro L, Bosch J. Pharmacological treatment of portal hypertension: an evidence-based approach. *Semin Liver Dis* 1999; 19:475-505 [Medline]
11. Hong WD, Zhu QH, Huang ZM, Chen XR, Jiang ZC, Xu SH, et al. Predictors of esophageal varices in patients with HBV-related cirrhosis: a retrospective study. *BMC Gastroenterol* 2009; 9:11.
12. Giannini EG, Botta F, Borro P, Dulbecco P, Testa E, Mansi C et al. Application of the platelet count/spleen diameter ratio to rule out the presence of oesophageal varices in patients with cirrhosis: a validation study based on follow-up. *Dig Liver Dis* 2005; 37:779-85.
13. Gill ML, Atiq M, Sattar S, Khokhar N. Non-endoscopic parameters for the identification of esophageal varices in patients with chronic hepatitis. *J Pak Med Assoc* 2004; 54:575-7.
14. Vanbiervliet G, Barjoan-Marine E, Anty R, Piche T, Hastier P, Rakotoarisoa C et al. Serum fibrosis markers can detect large esophageal varices with a high accuracy. *Eur J Gastroenterol Hepatol* 2005; 17: 333-8.
15. Bressler B, Pinto R, El-Ashry D, Heathcote EJ. Which patients with primary biliary cirrhosis or primary sclerosing cholangitis should undergo endoscopic screening for esophageal varices detection. *Gut* 2005; 407-10.