



NON INVASIVE PARAMETERS- VALIDITY FOR THE PREDICTION OF ESOPHAGEAL VARICES IN CIRRHOTIC PATIENTS

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ABSTRACT

Aim & Background: Approximately 5–15% of cirrhotics per year develop varices, and it is estimated that the majority of patients with cirrhosis will develop varices over their lifetime. Variceal hemorrhage is an immediate life-threatening problem with a 20–30% mortality associated with each episode of bleeding. Present study is planned to predict the presence of esophageal varices by means of simple biochemical and ultrasonographical parameters which may be cost effective.

Methods: We analyzed four parameters including platelet count alone, portal vein diameter, and spleen diameter and platelet count / spleen diameter ratio in 50 cirrhotic patients (male: female ratio 30:20) for the prediction of esophageal varices.

Results: We found the sensitivity, specificity, positive predictive value, negative predictive value of each parameter as given below. For platelet count alone with a cut off value of 90.27×10^3 /cu.mm is (33%, 100%, 100% and 27%), Portal vein diameter alone with cut off value of 14.23mm is (69.23%, 81.8%, 93.11% and 42.8%), Spleen diameter alone with a cut off value of 143.7 mm is (74.35%, 63%, 87.87% and 41.17%) and Platelet count and spleen diameter ratio with a cut off value of $0.93 (\times 10^3)$ is 79.5%, 72.73%, 91.18% and 50%.

Conclusion: Even though all the non invasive parameters can predict the presence of esophageal varices, the negative predictive value of all non invasive parameters were very low. These parameters cannot exclude the presence of esophageal varices. So the non invasive parameters cannot be an alternative for upper GI endoscopy.

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INTRODUCTION

Cirrhosis is the most common cause of portal hypertension and clinically significant portal hypertension is present in >60% of patients with cirrhosis. Portal hypertension is a significant complication of decompensated cirrhosis which is responsible for the development of ascites and bleeding from esophagogastric varices, two complications that signify decompensated cirrhosis.¹ Approximately 5–15% of cirrhotic per year develop varices, and it is estimated that the majority of patients with cirrhosis will develop varices over their lifetime. In patients with cirrhosis who are being followed chronically, the development of portal hypertension is usually revealed by the presence of thrombocytopenia; the appearance of an enlarged spleen; or the development of ascites, encephalopathy and/or esophageal varices with or without bleeding. Variceal hemorrhage is an immediate life-threatening problem with a 20–30% mortality associated with each episode of bleeding. Simple biochemical and ultrasonographical parameters may predict the presence of esophageal varices which may be cost effective.

Aim: To study the clinical, biochemical and ultrasonographical parameters which would non-invasively predict the presence of esophageal varices in patients with liver cirrhosis.

MATERIALS AND METHODS

We analyzed 50 cirrhotic patients with a male: female (30: 20), aged between 20yrs to 60 yrs, were selected from the Medical OPD and Medical ward, Bhopal medical college and all the patients were undergone the following investigations platelet count, serum Bilirubin, serum albumin, Prothrombin time (INR), ultrasonography for spleen diameter and portal vein diameter and upper GI endoscopy for esophageal varices. All the patients were classified according to child-Pugh's classification.

Inclusion Criteria

1. Age more than 20 years and below 60 yrs.
2. All patients with cirrhosis of the liver detected by USG and clinical parameters.

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Exclusion Criteria

1. Age below 20 years and above 60 years.
2. Hepatocellular carcinoma detected by USG.
3. Primary Hematological disorder.
4. Active UGI bleed on admission.
5. Taking β -Blocker for primary prophylaxis of esophageal varices.
6. Taking alcohol in the past 6 months.
7. History of pyrexia in the past 4 weeks.

The following parameters were defined

Cirrhosis: Detected by USG (Altered Coarse Echo texture of the liver parenchyma with surface micronodularity in the setting of chronic liver disease).

Splenomegaly: Spleen bipolar diameter more than 100 mm by USG.

Normal platelet count: $150-450 \times 10^3 / \text{cu.mm}$.

Platelet count / spleen diameter ratio: platelet count $\times 10^3$ / spleen diameter in mm.

Size of Esophageal varices

Large: Varices in the lower 3rd of the esophagus that occupied at least a third of the lumen or protrudes into the esophageal lumen and touch each other (presence of confluence) and did not flatten with air insufflations.

Small: Varices in the lower 3rd of the esophagus and occupied less than a third of the esophageal lumen or minimally protrude into the lumen.

Statistical Analysis

All the data were analyzed in the SPSS 11.5 version for windows. Mean, Standard deviation, Pearson’s correlation efficient were used to identify the significance of this study.

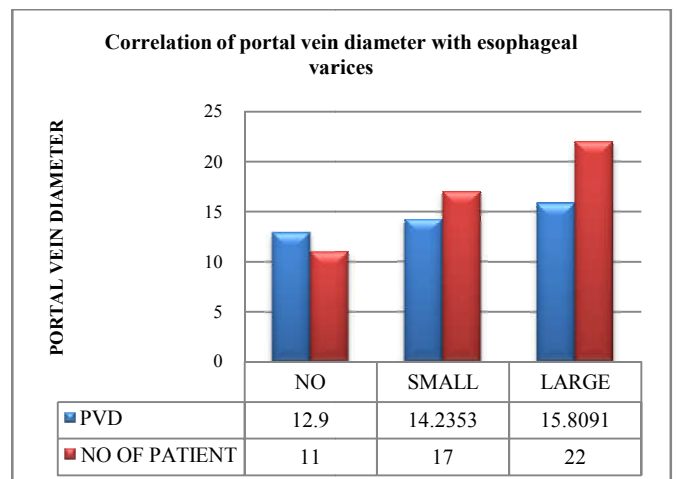
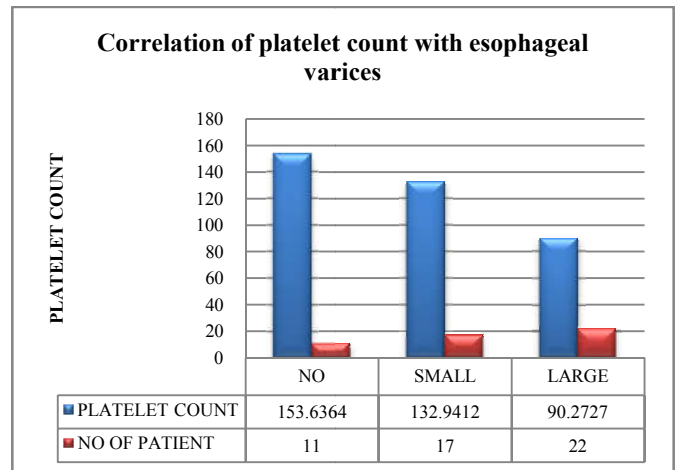
RESULTS

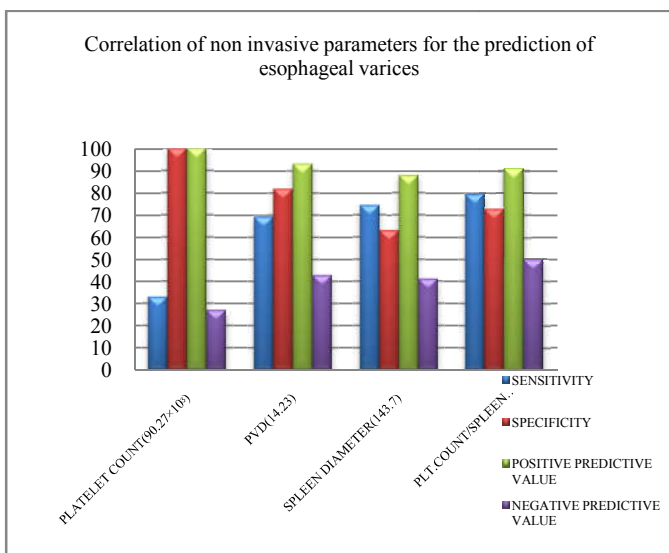
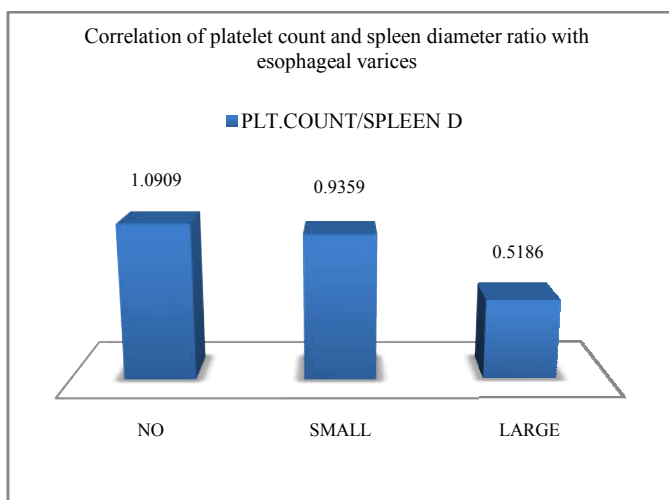
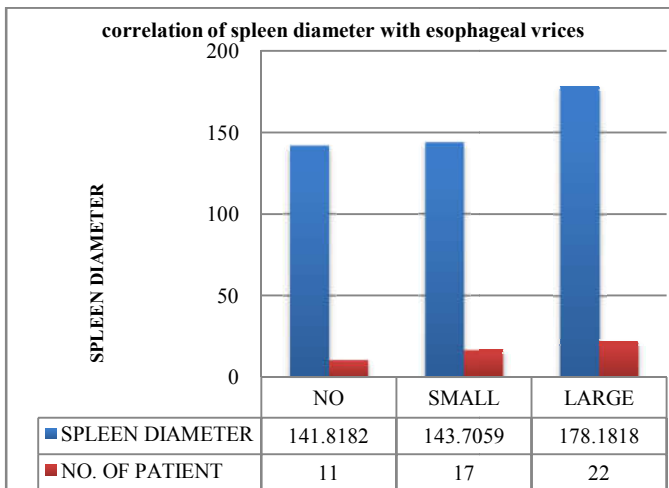
In our study, Out of 50 patients, 13 patients (26%) were in the Child-Pugh’s classification A, 23 patients (46%) were in the class B and 14 patients (28%) were in the class C. On correlation of platelet count alone with esophageal varices, cirrhotic patients with no esophageal varices showed the mean platelet count of 153.64 with SD ± 28.02 , patients with small esophageal varices showed the mean platelet count of 132.94 with SD ± 16.49 and patients with large esophageal varices showed the mean platelet count of 90.27 with SD ± 19.32 . The correlation was significant with a Pearson correlation coefficient $r = -0.801$ with a 2-tailed significance of sig. (2-tailed) of 0.000. (Correlation is significant at the 0.01 level (2-tailed)). Platelet count alone with a mean value of $132.9 (\times 10^3 / \text{cu.mm})$ can predict the esophageal varices with a sensitivity of 74.36%, specificity of 72.73%, positive predictive value of 90.62% and negative predictive value of 44%.

On correlation of portal vein diameter alone with esophageal varices, cirrhotic patients with no esophageal varices showed the mean portal vein diameter of 12.9 with SD ± 1.93 , patients with small esophageal varices showed the mean portal vein diameter of 14.24 with SD ± 2.20 and patients with large esophageal varices showed the mean portal vein diameter of 15.80 with SD ± 2.05 . The correlation was significant with a Pearson correlation coefficient $r = -0.570$ with a 2-tailed significance of sig. (2-tailed) of 0.000. (Correlation is significant at the 0.01 level (2-tailed)). Portal vein diameter alone with a mean of 14.23mm can predict the esophageal

varices with a sensitivity of 69.23%, specificity of 81.8% and positive predictive value of 93.11% and negative predictive value of 42.8%. On correlation of spleen diameter alone with esophageal varices, cirrhotic patients with no esophageal varices showed the mean spleen diameter of 141.82 with SD ± 19.52 , patients with small esophageal varices showed the mean spleen diameter of 143.70 with SD ± 15.64 and patients with large esophageal varices showed the mean spleen diameter of 178.18 with SD ± 22.12 . The correlation was significant with a Pearson correlation coefficient $r = 0.679$ with a 2-tailed significance of sig. (2-tailed) of .000. (Correlation is significant at the 0.01 level (2-tailed)). Spleen diameter alone with a mean of 143.7 mm can predict the esophageal varices with a sensitivity of 74.35%, specificity of 63.63%, positive predictive value of 87.87%, and negative predictive value of 41.17%.

On correlation of platelet count and spleen diameter ratio with esophageal varices, patients with no esophageal varices showed the mean platelet count /spleen diameter ratio of 1.09 with SD ± 0.20 patients with small esophageal varices showed the mean platelet count /spleen diameter ratio of 0.94 with SD ± 0.16 and patients with large esophageal varices showed the mean platelet count /spleen diameter ratio of 0.52 with SD ± 0.15 . The correlation was significant with a Pearson correlation coefficient $r = -0.900$ with a 2-tailed significance of sig. (2-tailed) of 0.000. (Correlation is significant at the 0.01 level (2-tailed)). Platelet count and spleen diameter ratio with a mean value of $0.93 (\times 10^3)$ can predict the esophageal varices with a sensitivity of 79.5%, specificity of 72.73%, positive predictive value of 91.18% and negative predictive value of 50%.





DISCUSSION

We found the sensitivity, specificity, positive predictive value, negative predictive value of each parameter as given below. For platelet count alone with a cut off value of 90.27×10^3 /cu.mm is (33%, 100%, 100% and 27%), Portal vein diameter alone with cut off value of 14.23mm is (69.23%, 81.8%, 93.11% and 42.8%), Spleen diameter alone with a cut off value of 143.7 mm is (74.35%, 63%, 87.87% and 41.17%) and Platelet count and spleen diameter ratio with a cut off value of $0.93 (\times 10^3)$ is 79.5%, 72.73%, 91.18% and 50%.

Our results matched with the study of Schwarzenberger et.al² where he found negative predictive value of only 73% and a positive predictive value of 74%, using platelet count/spleen diameter ratio with a cut-off value of 909, and he also concluded the platelet count/spleen diameter ratio with a cut-off value of 909 may not be accurately diagnostic in predicting the presence of esophageal varices and hence concluded that Upper GI endoscopy is only diagnostic method to screen for the presence of varices.

We used the portal vein diameter as a non invasive parameter for the prediction of esophageal varices which were not used in the other studies.

Edoardo G Giannini et.al³ found the platelet count/spleen diameter ratio had 86.0% (95% CI, 80.7–90.4%) diagnostic accuracy for EV, which was significantly greater as compared with either accuracy of platelet count alone (83.6%, 95% CI 78.0–88.3%, $P = 0.038$) or spleen diameter alone (80.2%, 95% CI 74.3–85.3%, $P = 0.018$). The 909 cutoff had 91.5% sensitivity (95% CI 85.0–95.9%), 67.0% specificity (95% CI 56.9–76.1%), 76.6% positive predictive value, 87.0% negative predictive value, 2.77 positive likelihood ratio, and 0.13 negative likelihood ratio for the diagnosis of EV.

E Giannini et al⁴ found in his study that cut off value 909 for platelet count/spleen diameter had 100% negative predictive value for esophageal varices diagnosis and this finding was reproducible and of value in compensated cirrhosis group and he also concluded that it is cost effective compared to endoscopy.

WW. Baig et al⁵ conducted a study on feasibility of Platelet count to spleen diameter ratio for the diagnosis of esophageal varices and found that there was highest accuracy for platelet count to spleen diameter for diagnosing esophageal varices noninvasively, Eventhough it can not replace endoscopic method, It can be used as an alternative where endoscopic facility is not available.

Alejandro Gonzalez-Ojeda et al⁶ concluded that for screening esophageal varices platelet count/spleen diameter ratio may be a useful parameter in patients with hepatic cirrhosis. Cutoff value of ≤ 884.3 for platelet count /spleen diameter, had 84% sensitivity, 70% specificity, and positive and negative predictive values of 94% and 40%, respectively to detect esophageal varices independent of the grade.

Nina Dib et al⁷ did a study on Noninvasive diagnosis of portal hypertension in cirrhosis and its application in prevention of varices and concluded even though noninvasive methods of screening oesophageal varices are useful, it cannot be a complete substitute to conventional endoscopy in our clinic practice. Roberto de Franchis et al⁸ conducted a study on noninvasive or minimally invasive diagnosis of oesophageal varices and found that the platelet count/spleen diameter, CT scan and video capsule endoscopy might increase the compliance of patients for screening but it can never be equivalent to endoscopy.

Sambit Sen et al⁹ studied non invasive prediction of oesophageal varices using platelet count, spleen diameter in two group of patients hepatitis C related cirrhosis and alcohol induced cirrhosis patients and finalized that it is more useful in first group than second group.

Tamara Alempijevic et al¹⁰ did a study on non invasive diagnosis of esophageal varices and their grading in cirrhosis

using right liver lobe diameter/albumin and platelet count/spleen diameter ratios were accurate.

Konstantinos C *et al*¹¹ conducted a study on three noninvasive parameters low platelet count <90000/ μ l, spleen diameter >160 mm and child pugh class B and C and found they were significant predictors of esophageal varices.

Lahmidani Nada *et al*¹² analysed five variables (platelet count, ascites, prothrombin time, splenic and portal vein diameter and concluded that large varices is associated with abundant ascites, prothrombin time, splenic and portal vein diameter whereas platelet count <100000 is associated with presence of varices in cirrhosis due to hepatitis B and C.

Sharma SK *et al*¹³ did a study analysing five parameters (pallor, palpable spleen, platelet count total leukocyte count and liver span by USG and found that palpable spleen and low platelet count were independent predictors of esophageal varices and this may be used to reduce the cost and discomfort due to endoscopy. T A Zimbwa *et al*¹⁴ by doing a study Platelet count/spleen diameter ratio as a predictor of oesophageal varices in alcoholic cirrhosis found that with cut off value of 909 there was 100 % sensitivity and specificity for prediction of esophageal varices in alcoholic cirrhosis and it is also reproducible. Grace Marie *et al*¹⁵ conducted a study and concluded that platelet count/spleen diameter ratio cut off value < 160 had high predictive value for diagnosing esophageal varices non invasively with sensitivity of 88.4% , specificity 80.2%, positive predictive value 79.2 % and negative predictive value of 89%.

CONCLUSION

Even though noninvasive parameters can predict the presence of Esophageal varices, the negative predict value of all parameters are very low. The cut off value of all the noninvasive parameters can't rule out the esophageal varices. So the noninvasive parameters can not be an alternative of upper GI endoscopy.

Study Highlights

What is Current Knowledge

VARICEAL HEMORRHAGE is an immediate life-threatening problem with a 20–30% mortality associated with each episode of bleeding

Screening with UPPER GI ENDOSCOPY in all cirrhotic patients would be costly especially in developing countries.

What Is New Here

Non Invasive Parameters like platelet count, portal vein diameter, spleen diameter and platelet count/spleen diameter ratio may be an alternative for the prediction of esophageal varices.

High risk patients selected from these parameters can be given prophylactic treatment with beta blockers and undergone upper GI endoscopy.

It may reduce the burden of endoscopic screening and may be cost effective also.

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