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A Study on Non-Invasive Predictors of Large Esophageal Varices in Patients with Cirrhosis

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Abstract
Context: *Esophageal varices are porto-systemic collaterals and they form as a consequence of portal hypertension (a progressive complication of cirrhosis) preferentially in the sub mucosa of the lower esophagus. Due to thelimitations in using UGIE like cost, unpleasant feeling, want of good expertise, bleeding and infection, some noninvasive means have been proposed for prediction of esophageal varices in order to restrict UGIE to the population with high riskof variceal bleeding.The noninvasive predictive variables include platelet count, Child Pugh class , albumin level, albumin globulin ratio, AST/platelet ratio index[APRI], bilirubin level, serum transaminases, hemoglobin level, total counts, platelet count/spleen diameter ratio, prothrombintime,spleen size, portal vein diameter, splenic diameter, ascites.*
Aims and Objectives: *To identify and study noninvasive investigative parameters (clinical, biochemical and radiological) that could predict the presence and grades of esophagealvarices in cirrhosis patients.*
Setting & design of study*:ObservationalCross sectional study*
Materials And Methods*: The present study was conducted on 50 patients admitted witha diagnosis of cirrhosis of liver at general medicine and medical gastroenterology wards of Government Rajaji Hospital, Madurai during the period of February 2016 to July 2016.History was taken on details and duration of alcoholism, jaundice, ascites, oliguria, pedal edema and gastrointestinal bleed. Presence or absence of jaundice, ascites, splenomegaly and hepatic encephalopathy were noted. Platelet count, prothrombin time and INR,liver function tests including serum bilirubin, serum transaminases, serum albumin was estimated. Modified Child-Turcotte-Pugh (CTP) class was calculated for each patient. At ultra-sonogram abdomen and Doppler study of portal venous system, the portal vein and spleen diameter along with echo texture of the liver,spleen size and direction of blood flow and ascites were noted. The portal vein diameter and platelet count / spleen diameter ratio were determined. At UGI endoscopy, the esophageal varices were graded as large (Grade III-IV) or small (Grade I-II), based on Paquet's grading system.*
Results: *Child Pugh class B/C,presence of higher grades of ascites,low platelet count,low serum albumin,high total bilirubin,elevatedprothrombintime,higher portal vein diameter,higher spleen size ,lower platelet count /spleen diameter ratio emerged as significant predictors for the presence of large varices.*
Keywords: *Large esophagealvarices, cirrhosis, Child Pugh class B/C .*

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I. Introduction

Esophageal varices are porto-systemic collaterals and they form as a consequence of portal hypertension (a progressive complication of cirrhosis), preferentially in the sub mucosa of the lower esophagus. Rupture and bleeding from esophageal varices are major complications of portal hypertension and are associated with a high mortality rate. Current guidelines recommend using upper gastrointestinal endoscopy (UGIE) to screen all cirrhotic patients at diagnosis for identification of varices at a high risk of bleeding. Even though UGIE is believed to be the gold standard to diagnose esophageal varices, the use of UGIE has its own limitations. Due to these problems in using UGIE, some noninvasive means have been proposed for prediction of esophageal varices in order to restrict UGIE to the population with high risk of variceal bleeding. Noninvasive identification of esophageal varices is usually based on regular laboratory parameters and clinical signs relevant to liver fibrosis and function, portal hypertension and hypersplenism. The noninvasive predictive variables include platelet count, ChildPugh class, albumin level, albumin globulin ratio AST/platelet ratio index[APRI], bilirubin level, serum transaminases, hemoglobin level, total counts, platelet count/spleendiameter ratio, prothrombintime,spleen size, portal vein diameter, splenic diameter, ascites. The common features of these

noninvasive means that prediction of esophageal varices is reproducible, cost effective, simple and quick with no additional burden to patients.

II. Materials And Methods

Study Population

The present study an observational cross-sectional study was conducted on 50 patients admitted witha diagnosis of cirrhosis ofliver at general medicine and medical gastroenterology wards of GovernmentRajaji Hospital, Madurai during the period of February 2016 to July 2016.

Inclusion Criteria

50 patients admitted with a diagnosis of cirrhosis of liver to the general medicine and medical gastroenterology wards of Government RajajiHospital,Madurai.Diagnosis of cirrhosis was based on clinical, biochemical and ultra-sonographic findings.

Exclusion Criteria

Individuals presenting with variceal bleed, those with a past history of bleed ,those who had undergone sclerotherapy or band ligation for esophageal varices, those with portal vein thrombosis, hepatoma and those on current or past treatment with beta-adrenergic receptor blockers were excluded.

Methodology

History was taken on details and duration of alcoholism, jaundice, ascites, oliguria, pedal edema and gastrointestinal bleed. Presence or absence of jaundice, ascites, splenomegaly and hepatic encephalopathy were noted. Platelet count, prothrombin time and INR,liver function tests including serum bilirubin, serum transaminases, and serum albumin were estimated. Modified Child-Turcotte-Pugh (CTP) class was calculated for each patient. At ultra-sonogram abdomen and Doppler study of portal venous system, the portal vein and spleen diameter along with echo texture of the liver,spleen size and direction of blood flow and ascites were noted. The portal vein diameter and platelet count / spleen diameter ratio was determined. At UGI endoscopy, the esophageal varices were graded as large (Grade III-IV) or small (Grade I-II), based on Paquet's grading system.

Ethical committee approval was obtained.

III. Statistical Analysis

All data were entered in Excel 2007 and statistical analysis was performed using the statistical software SPSS 16.0.Data were expressed as frequency (with percentages) and median values (with range (min, max)). For continuous variables, Mann Whitney U-test was performed to find the differences between two groups and for categorical variables Pearson's chi-square test was performed.Resultswere defined as statistically significant when the P value (2-sided) was less than 0.05.

IV. Results And Discussion

Our study was done to assess various noninvasive predictors that could predict the presence of large esophageal varices.Out of 50 total patients,28 had small varices and 22 had large varices.In small varicesgroup,median age was 48 (17 -72),in large varices group median age was 50(26-73).In small varices group,20 patients were male and 8 patients were female,in large varices group,17 patients were male and 5 patients were female.Alcohol was the most common etiology and out of 19 patients 12 had large varices.In no/small varices group,75% were in CTP –A,17.9% were in CTP-B and 7.1% belonged to CTP-C class.In large varices group, 13.6% were in CTP-A, 31.8% were in CTP-B , 54.5% were in CTP-C class.P value <0.01,significant so presence of large gastroesophagealvarices correlated with the severity of liver disease, as Child Pugh class C has maximum no of large varices.Large varices were associated with increasing grade of ascites ,p value<0.001 median platelet count in large varices group was 90,100,median platelet count in small varices group was 2 lakh.With a p value <0.001, low platelet count was significantly associated with large varices. Large varices were significantly correlated with increasing bilirubin levels,median value- 2.8 mg/dl.(p value- 0.001). Large varices were significantly correlated with low albumin levels,median value -2.2 mg/dl.(p value- 0.001).Large varices were significantly correlated with elevated prothrombintime,median value – 3.6 sec prolonged .(p value- 0.004).Large varices were significantly correlated with increasing portal vein diameter,median value- 15.6 mm (p value- 0.001).Large varices were significantly correlated with increasing spleen size,median value -182.5 mm (p value- 0.001).Large varices were significantly correlated with lower values of platelet count/spleen diameter ratio.,with a median value of 454.1(p value- 0.001).Large esophageal varices are a dangerous clinical consequence of liver cirrhosis. Since variceal screening causes considerable endoscopic burden andcost, seeking a less expensive, noninvasive means for accurate prediction of large esophageal varices has great clinical importance. Several studies in the past have shown independent parameters like splenomegaly, ascites, spider naevi, Child's grade,platelet count, prothrombin time/activity, portal

veindiameter, platelet count/ spleen diameter ratio,serum albumin, and serum bilirubin as significant predictors for the presence of esophageal varices.

Correlation of varices grade with prothrombin time

	Varices Grade			
	Small (Grade I-II) or no varices		Large varices (Grade III-IV)	
	N=28		N=22	
	Median	Range	Median	Range
Prothrombin Time (seconds prolonged)	2.0	(0.4 – 13.0)	3.6	(0.8 – 12.0)
p-value	p=0.004 (Significant)			

Correlation of varices grade with platelet count

	Varices Grade			
	Small (Grade I-II) or no varices		Large varices (Grade III-IV)	
	N=28		N=22	
	Median	Range	Median	Range
Platelet Count	200000	(42000 – 442000)	90100	(28000 – 245000)
p-value	p<0.001 (Significant)			

The present study further corroborates the results of earlier studies. Giannini et al,proposed the platelet count-spleen diameter ratio of ≤ 909, as an accurate non-invasive marker for the presence of esophagealvarices. This was further validated in a multicentre trial. The study population comprised predominantly of patients with hepatitis C related cirrhosis. A similar study by Agha et al, from Pakistan, made identical observations in the same subset of patients. Sen et al, found the platelet count-spleen diameter ratio of ≤ 650 as a sensitive non-invasive marker [Area under curve (AUC) of 0.81] in HCV related cirrhosis.

Non endoscopic assessment for presence and grades of varices from India are few. Amarapurkar et al, report that splenomegaly alone was a significant predictor for the development of large esophagealvarices. Sharma et al, in a prospective study, observed that splenomegaly and platelet count were the independent predictors for the presence of large varices. They could derive a predictor function based on this observation, which had an AUC of 0.76.From the present study, Child Pugh class B/C,presence of higher grades of Ascites,low platelet count,low serum albumin,high total bilirubin,elevatedprothrombintime,higherportal vein diameter,higher spleen size ,lower platelet count /spleen diameter ratio emerged as significant predictors for the presence of large esophageal varices.

V. Conclusion

Child Pugh class B/C, presence of higher grades of ascites,low platelet count,low serum albumin,high total bilirubin,elevatedprothrombintime,higher portal vein diameter,higher spleen size ,lower platelet count

/spleen diameter ratio emerged as significant predictors for the presence of large esophageal varices. Presence and Grade of varices was correlated with severity of liver diseases as in large varices group, 13.6% were in CTP-A, 31.8% were in CTP-B , 54.5% were in C

VI. Summary

A cross sectional observational study was done at Government Rajaji Hospital, Madurai among 50 cirrhosis of liver patients for assessing various noninvasive predictors that could predict the presence of large esophageal varices. From the present study, Child Pugh class B/C,presence of higher grades of ascites,low platelet count,low serum albumin,high total bilirubin,elevatedprothrombintime,higher portal vein diameter,higher spleen size ,lower platelet count /spleen diameter ratio emerged as significant predictors for the presence of large varices. We believe that these predictors may be of help to the physicians practicing in areas where endoscopy facilities are not readily available, in helping them to initiate appropriate primary pharmacological prophylaxis in these patients. Accurate identification of patients at the highest risk of bleeding allows stratification in an attempt to avoid unnecessary preventive measures in 60-75% of patients who will never have variceal bleeding in future. In a limited resources setting like ours,where financial constraints are a major problem,predicting the presence and grade of varices by non-invasive methods help to avoid unnecessary upper G.I endoscopies.

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