Platelet Count to Spleen Diameter Ratio in the Prediction of Varices in Cirrhosis in Indian Patients - An Analytical Cross Sectional Study

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ABSTRACT

Introduction: Portal hypertension, development of esophageal varices and bleeding from the varices are leading causes of mortality in patients with cirrhosis liver. Upper gastrointestinal endoscopy is the gold standard to demonstrate the presence of gastroesophageal varices. Various non invasive tests have been tried as alternate methods to predict the presence of esophageal varices. Among these the ratio of platelet count to spleen diameter is a widely accepted one. The objective of this study was to check the usefulness of this ratio and also to find out other non invasive parameters which can predict the presence of varices in our population.

Material and Methods: We studied 60 consecutive patients diagnosed to have cirrhosis. The study setting was Government Medical College of Thrissur district in the state of Kerala, India. The inclusion criteria were patients above the age of 18 years with a diagnosis of cirrhosis (made by clinical findings, biochemical and radiological investigations) and willing to undergo upper gastrointestinal endoscopy. Cirrhosis due to all causes was included in the study. The exclusion criteria were those cases of cirrhosis with history of gastrointestinal bleeding in the last 6 months, those who had undergone endoscopic treatment for varices in the past, and those who were on beta-blocker prophylaxis. We studied whether a ratio of platelet count to spleen diameter less than 909 could be used in our population to predict the presence of varices.

Results: Platelet count to spleen diameter ratio of less than 909 did not achieve statistical significance in this study. By regression analysis, elevated bilirubin and splenomegaly more than 10.5cm were found to be useful to predict the presence of varices (OR 9.95 95% CI 1.32-74 and OR 6.18 95% CI 0.99-38 respectively). Spleen size more than 93 mm in bipolar diameter had 91.7% sensitivity, 50% specificity,88% PPV,60%NPV,1.83LR+ and 0.16 LR- to predict the presence of varices. PC/SD ratio below 1097 had 60% sensitivity 75% specificity, 90.6% PPV, 32%NPV, 2.4+LR and 0.5-LR to predict the presence of varices.

Conclusion: Platelet count to spleen diameter ratio is not found to be useful in our population to predict the presence of varices in patients with cirrhosis.

Keywords: Bipolar spleen diameter cirrhosis, gastro esophageal varices, platelet count, platelet count /spleen diameter ratio, noninvasive test

INTRODUCTION

Portal hypertension, development of esophageal varices and bleeding from the varices are leading causes of mortality in patients with cirrhosis liver. Upper gastrointestinal endoscopy is the gold standard to demonstrate the presence of gastroesophageal varices. As the prevalence of varices in cirrhosis is 60-80%[1] and severe variceal bleeding develops in around 40% of cirrhotics[2], it follows that upper gastrointestinal endoscopy has a crucial role in the management of cirrhotics.

As per guidelines[3] endoscopy needs to be performed frequently. Patients in our population, often are not able to afford the cost of frequent interventional procedures. Tests which are more affordable and non invasive at the same time would be a great help to such people.One of the endoscopic features which forsee the likelihood of variceal bleeding is the size of the varices. Hence if there are non invasive parameters which can predict the size of the varices, it would be an added advantage. Various non invasive tests have been tried as alternate methods to predict the presence of esophageal varices. One of the most studied among them is the ratio of the platelet count to bipolar spleen diameter. The objective of this study was to check the usefulness of this ratio and also to find out other non invasive parameters which can predict the presence of varices in our population.

MATERIAL AND METHODS

This is an analytical cross-sectional study to see the usefulness of the ratio of the platelet count to spleen diameter for the prediction of gastro esophageal varices in patients with cirrhosis of any etiology and also to see whether other parameters can be of use for this purpose. We studied 60 consecutive patients diagnosed to have cirrhosis. The study setting was Government Medical College of Thrissur district in the state of Kerala, India. The inclusion criteria were patients above the age of 18 years with a diagnosis of cirrhosis (made by clinical findings, biochemical and radiological investigations) and willing to undergo upper gastrointestinal endoscopy. Cirrhosis due to all causes was included in the study. The exclusion criteria were those cases of cirrhosis with history of gastrointestinal bleeding in the last 6 months, those who had undergone endoscopic treatment for varices in the past, and those who were on beta-blocker prophylaxis.

The physical examination findings and investigation results were entered into a proforma.The data collected included age,gender,history of alcohol intake, previous history of gastrointestinal bleed, history and evidence of endoscopic procedures in the past, clinical evidence of jaundice, ascites, encephalopathy, biochemical investigations including hemogram, tests of liver and renal function, serum electrolytes, blood sugar, viral markers, prothrombin time, ultrasound of the

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3491

abdomen and endoscopy findings. Child Pugh score and MELD scored were used to grade the severity of liver disease. Child Pugh score of 5 and 6 were included in class A, scores of 7, 8 and 9 in class B, scores 10 and above in class C. Based on MELD score, the patients are classified into five groups as follows-Score of 9 or less, 10-19, 20-29, 30-39 and 40.We grouped those patients with score of more than 20 into one category and the significance of score greater than 20 to predict varices was studied. EDTA anticoagulated blood sample collected from the patients were analysed in automated 3-part differential haematology analyzer Sysmex XP 100. Samples were analyzed within 1hour.Platelet count less than 1.5lakhs was considered as thrombocytopenia. Upper gastrointestinal endoscopy was done by a single gastroenterologist for all the patients. The gastroenterologist who performed the scopy was blinded to the physical findings and investigation results. Ultrasound scanning was done by a single sinologist who was also blinded to the other results. Ultrasound was done with GE LOGIC S8 machine. Portal vein size more than 13mm was taken as abnormal. Maxim bipolar diameter of spleen was taken. Bipolar diameter up to 10.5cm was taken as normal. Ratio of the platelet count expressed in thousands per mm^3 to spleen diameter in mm was determined. Cut off value of 909 was used to predict the presence of varices. All the investigations were done within an interval of one week. These parameters were studied in all aetiologies of cirrhosis and all stages of liver disease. The study was given clearance by the ethical committee of the institution.

STATISTICAL ANALYSIS

Statistical analysis was done using SPSS software. Quantitative variables were expressed as mean ± standard deviation. Qualitative data were expressed as number and percentages. Statistical tests used included chi-square test, correlation, binary logistic regression. The validity of the tests was assessed using sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio. P value (less than 0.05) and 95% confidence interval were used to determine the significance of the tests.

RESULTS

We studied 60 patients with cirrhosis. There were 56 (93.3%) males and 4 (6.7%) females in the study group. The mean age was 55 ± 9 years, (males 54 ±9 years, females 67± 6 years).
Among the 60 patients, 32 (53.3%) had ascites, 31 (51.7%) had jaundice 17 (28.3%) had encephalopathy, 2 (3.3%) had spontaneous bacterial peritonitis.
Among the 60 patients alcoholic liver disease was the etiology of cirrhosis in 51(85%) patients. The other causes were autoimmune hepatitis 1(1.7%) and nonalcoholic fatty liver disease 3 (5%). No obvious cause could be made out in 5 (8.5%). Upper GI endoscopy showed the presence of varices in 48 (80%) of cases, of which 23(38.3%) had small varices (grade 1) and 37(61.7%) had large varices (grade 2 and grade 3) (table-1). Patients with varices had significantly higher bilirubin level, Child Pugh score, MELD score, larger spleen size than patients without varices (table-2).
On doing regression analysis, elevated bilirubin and splenomegaly more than 10.5 cm had significant association with the presence of varices (OR 9.95 95% CI 1.32-74 and OR

6.18 95% CI 0.99-38 respectively).
ROC analysis yielded new values which had more sensitivity and specificity in predicting varices (table-3). Serum total bilirubin >1.75mg% had 83% sensitivity and 75% specificity in predicting varices. Child Pugh class A was significantly associated with the absence of varices 50% sensitivity and 87.5% specificity 95%CI 1.56-10.2 Child Pugh class B and C had 87.5% sensitivity and 50% specificity in predicting varices. MELD score more than 16 had 67% sensitivity and 83% specificity to predict varices. The size of the spleen more than 93 mm in bipolar diameter had 91.7% sensitivity, 50% specificity, 88% PPV, 60% NPV, 1.83LR+ and 0.16 LR- to predict the presence of varices. PC/SD ratio below 1097 had 60% sensitivity 75% specificity, 90.6% PPV, 32%NPV, 2.4+LR and 0.5-LR to predict the presence of varices.
With regression analysis of these variables spleen size more than 9.3 cm was significantly associated with prediction of large varices. (p 0.03 OR 6.71 95%CI 1.16-38) (table-4).

DISCUSSION

Ratio of the platelet count to bipolar spleen diameter is one of the most studied non invasive tests to predict the presence of varices in patients with cirrhosis. In this study neither the platelet count nor the ratio of the platelet count to maximum bipolar spleen diameter less than 909 as suggested by Giannini et al[4] had significant association with the presence of varices. In view of the smaller size of the spleen, which is more significant we searched for another cut off value for the PC/SD ratio which might be more applicable in our population. A cut off value of 1097 was found to have more sensitivity but less specificity than the value of 909 in predicting varices, though this value did not achieve statistical significance. Other studies have also found the ratio less than 909 to be useful, but with lower sensitivity in the prediction of varices.[5-9] Another Indian study also has found a higher value of the PC/SD ratio to be predictive.[10]
There are also studies which have not found PC/SD ratio to be useful,[11-13] In a meta analysis the pooled sensitivity of the ratio less than 909 was 89%, specificity 74%[14]
Non invasive parameters like total bilirubin, higher MELD and CPT score, and larger bipolar spleen diameter are good predictors of presence of varices, irrespective of the grading of varices. Even after regression analysis elevated bilirubin and enlarged spleen continue to be good predictors for the same purpose. We are of the opinion that a bipolar spleen diameter more than 9.3cm is a much better predictor of portal hypertension than 10.5cm.The reason why we obtained lower values of spleen diameter could be the smaller stature of our population (Kerala

Category		n (%)
Child Pugh	Class A	12 (20%)
	Class B	30 (50%)
	Class C	18(30%)
MELD score	9 or less	13 (21.7%)
	10-19	30(50%)
	20-29	12(20%)
	30-39	5(8.3%)
	40	nil

Table-1: Showing the Child Pugh and MELD score of the study subjects

3492

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Variable		Varices present	No varices	p	OR	95% CI
Age		54 ±9.7	57±11	0.39		
Sex	Males	45(80.4%)	11(19.6%)	0.79	1.07	0.6-1.9
	Females	3(75%)	1(25%)			
Ascites		28(87.5%)	4(12.5%)	0.12	2.2	0.77-6.7
Encephalopathy		15(88.2%)	2(11.8%)	0.31	1.9	0.48-8
Platelet <1.5 lak /mm³		41(82%)	9(18%)	0.54	1.17	0.76-1.79
Platelet <1lak/mm³		17(85%)	3(15%)	0.49	1.09	0.85-1.4
Total Bilirubin >1mg%		46(88.5%)	6(11.5%)	<0.001	3.58	1.06-11.7
Mean total bilirubin mg%		3.8 ±2.5	1.5±1.1			
AST>40U/l		38(80.9%)	9(19.1%)	0.65	1.07	0.75-1.5
ALT >40U/l		18(78.3%)	5(21.7%)	0.8	0.97	0.7-1.2
Albumin <3.5g/dl		42(82.4%)	9(17.6%)	0.27	1.23	0.76-1.99
S Sodium<135mmol/l		28(82.4%)	6(17.6%)	0.6	1.07	0.82-1.39
Child Pugh						
Class A		18(100%)	0	0.001	6.16	1.88-20.2
Class B		24(80%)	6(20%)			
Class C		6(50%)	6(50%)			
MELD score						
9 or less		7(53.8%)	6(46.2%)	0.003	5	1.6-16
10-19		24(80%)	6(20%)			
20-29		12(100%)	0			
30-39		5(100%)	0			
40		0				
Portal vein >13mm		12(80%)	3(20%)	1	1	0.7-1.33
Spleen size >105mm		38(88.1%)	5(11.6%)	0.01	1.5	0.99-2.26
Mean spleen size mm		121 ± 23	103.4 ±22			
PC/SD ratio <909		19(90.5%)	2(9.5%)	0.1	1.21	0.96-1.5
Mean PC/SD ratio		1089 ± 408	1340 ±510			

Table-2: Univariate analysis of the predictive factors for presence of varices

Test	Sensitivity %	Specificity %	PPV	NPV	+LR	-LR	AUC	95%CI	New cut off
Bilirubin >1 mg%	95.8	50	88.46	75	1.9	0.1	0.828	.69-.96	1.75
Child C	37.75	100	100	28.5			0.779	.64-.91	B and C
MELD≥20	35.4	100	100	27.9			0.818	.695-.94	16
Spleen >10.5cm	79.1	58.3	88.37	41.1	1.8	0.36	0.701	.53-.87	9.3
PC/SD<909	39.5	83.3	90.4	83.3	2.29	0.73	.65	.48-.81	1097

Table-3: Diagnostic features of the various tests in the prediction of varices

Test	Sensitivity %	Specificity %	PPV	NPV	+LR	-LR	p	95%CI
Bilirubin >1 mg%	94	26	67	75	1.27	0.23	0.02	.79-9.1
Spleen >9.3cm	94.5	34.7	70	80	1.42	0.17	0.003	1-12
Child C	40.5	86.9	83.3	47.6	2.8	0.69	0.02	1.1-2.3
MELD >20	40.5	91.3	88.23	48.8	4.4	0.6	0.008	1.2-2.4

Table-4: Diagnostic features of the various tests in the prediction of large varices

is a state located in South India). We have also observed that bipolar spleen diameter above 9.3 cm is a good predictor for the presence of large varices in our population. Various other studies have tested parameters like platelet count, hypoalbuminemia in the evaluation of varices.[15]

A major limitation of this study is the small sample size. We plan to study a larger cohort to validate the new spleen size as a marker of portal hypertension and also to see if a different value of the PC/SD ratio would be applicable in our situation.

CONCLUSION

There is no substitute for upper gastrointestinal endoscopy for the evaluation of varices in cirrhosis. Platelet count to bipolar spleen diameter ratio cannot be used as a good non invasive test to predict the presence of varices in our population.

But certain parameters could be of help, albeit with reduced sensitivity and specificity, thus reducing the number of endoscopies needed to be done in the management of cirrhotics. Certainly more studies are needed to clarify matters further.

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