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NON ENDOSCOPIC PREDICTION OF OESOPHAGEAL VARICES WITH PLATELET COUNT, SPLENIC SIZE AND PLATELET COUNT/SPLENIC DIAMETER RATIO

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ABSTRACT

OBJECTIVE: *To identify the relationship of platelet count, splenic size and platelet/ splenic ratio with the presence of esophageal varices.*
DESIGN: *An observational, cross –sectional study.*
PLACE AND DURATION OF STUDY: *Medical unit one, Civil Hospital Karachi.*
PATIENTS AND METHODS: *One hundred (100) patients with cirrhosis of liver were studied. Patients were evaluated for cause of chronic liver disease(abdominal ultrasound, serum proteins and albumin, prothrombin time, complete blood count and liver function tests were performed) Upper Gastrointestinal endoscopy performed to look for the presence esophageal varices. It was noted if splenic size, platelets count and platelet/splenic ratio have its relation to the presence and absence of esophageal varices.*
RESULTS: *Out of hundred patients 65 were male and 35 females. The mean age between the subjects was 42.8 +/- 14.3 years. Seventy-two patients had anti-HCV antibodies, twenty-two had HBsAg, and no cause was identified in three patients. According to Child Pugh classification 17 patients had child A, 44 patients had class B and 39 had child class C. On Endoscopy 85 patients had esophageal varices, while 15 didn't have any varices. Regression analysis reveals splenic size, platelets count and platelets/splenic ratio significantly (p<0.001) correlated with presence or absence of esophageal varices. T test for comparison also showed p value less then <o.oo1.*
CONCLUSION: *Platelet count, splenic size and platelet/splenic ratio are important and independent parameters that can determine the presence of esophageal varices.*

KEY WORD: Esophageal varices, splenic size, platelet count, platelet count/splenic diameter ratio.

INTRODUCTION

Oesophageal varices are longitudinal, superficial, dilated and tortuous veins at the lower end of oesophagus which develop as a result of portal hypertension. About 30% of compensated and 60-70% patients with decompensated cirrhosis have varices at presentation[1, 2]. The oesophageal varices are prone to ulcerate and bleed. The risk of bleeding from the oesophageal varices is 30% in the first year[1, 2,] and about 10% of upper gastrointestinal bleeding is caused by oesophageal varices[1- 3]. In order to prevent variceal bleeding, prophylactic treatment is indicated only after Endoscopic visualization, because it is the only confirmatory method of diagnosing oesophageal varices[4, 5]. As Endoscopy is invasive, costly and unavailable at most of the health centers of our country, a need of non-invasive methods of detecting oesophageal varices is warranted.

The non invasive methods of detecting oesophageal varices currently studied are low platelet count (ranging from 67000 to 100,000) [2,4,6,8], increased splenic size[10- 13] and platelet /splenic ratio of 900[6, 7]. In addition increased Serum Ascitic Albumin Gradient(SAAG)[4, 5,9], increased portal vein diameter[10, 12,13] and Child-Turcotte-Pugh class[9, 11,12] have also been studied as other non invasive methods of detecting oesophageal varices.

The purpose of this study was to:

A- Determine the efficacy of platelet count, splenic size and platelet/splenic ratio in detection of oesophageal varices.

B- Diagnose the presence of oesophageal varices in patients with chronic liver disease Non Endoscopically, so that these patients can be put on primary prophylaxis against bleeding if endoscopic facilities are not available.

OBJECTIVES

To identify the relationship of platelet count, splenic size and platelet /splenic ratio with the presence of esophageal varices.

MATERIAL AND METHODS

It was an observational, cross-sectional study, carried out in medical wards of Civil hospital Karachi on one hundred patients. Patients with history of chronic liver disease diagnosed on clinical, biochemical or histopathological ground were enrolled in the study. Patients who were hemodynamically unstable or who had had previously undergone sclerotherapy or band ligation for esophageal varices, transjuglar porto-systemic shunts or surgery for portal hypertension were excluded from study. Patients with recent history of blood transfusion or alcohol abuse or those taking medicines for primary prophylaxis of variceal bleeding were also excluded from the study. All the patients admitted or booked for Endoscopy at medical unit 1 and fulfilling the selection criteria were selected for this study. The written and informed consent was taken before registering them for the study. The data was collected on a Performa specifically designed for this study. All the patients were clinically examined and findings of the result were recorded on the performa. The findings of laboratory investigations, Endoscopy and ultrasound were also recorded on the performa. For each patient complete blood picture with platelet count, ultrasound exam of abdomen for splenic size, ascites and portal vein diameter and calculation of platelet/splenic ratio was done. The patients underwent upper gastrointestinal Endoscopy for determining the presence/absence of varices. Other laboratory tests like screening for HBsAg and Anti HCV, liver function tests including Prothrombin time, Serum albumin and globulin ratio and ascitic fluid analysis were recorded if available.

The collected data was analyzed through computer with the help of SPSS programme version 13.0. Descriptive analysis was done for age, sex, viral profile, presence or absence of varices. The data was analyzed for platelet count, splenic size and platelet/splenic ratio. The data then was divided into two groups on the basis of presence or absence of thrombocytopenia, normal/increased splenic size on ultrasound, and platelet/splenic of ratio. The mean and standard deviation, percentages and ratio were calculated and are presented in the form of tables . The two groups were compared with other variables. For statistical significance value, chi-square test and test of proportion was applied. Multi variate analysis of variables with significant correlation was carried out using stepwise logistic regression analysis. Discriminant analysis was used for developing combined predictability of variables.

Threshold of different variables for the best compromised sensitivity-specific was determined using ROC curve

OBJECTIVE MEASUREMENTS

1-Platelet count from complete blood picture

2-Spleen size on ultrasound findings in millimeters

3-Platelet /splenic ratio calculated

4-Endoscopy was done on the MODEL-COLUMBUS G I F 16 Q for the presence or absence of esophageal varices.

TABLE 1

DESTRIPTIVE ANALYSIS OF ALL VARIABLES

	Mean	Std deviations
Age in years	42.8	14.3
Spleen size in mm	136.9	25.3
Portal vein diameter in mm	13	.25
Albumin g/dl	3.0	.64
A G ratio	.96	.25
SGPT IU/L	73	34.4
P.T difference	8.9	6.7
Platelet x 1000/dl	142.9	108.8
P S ratio	1047.3	732.3

RESULTS

One hundred patients with chronic liver disease fulfilling the inclusion criteria were enrolled in study. Of these sixty-five (65%) patients were male and thirty-five (35%) were females. Mean age of these patients was 42.8 +- 14.3. Seventy two (72) patients were reactive for anti HCV, Twenty-two (22) patients were reactive HBsAg, and three (3) patients had both these, while three (3) patients were not reactive for both the markers.

Patients were then classified according to the child Pugh classification, 17 patients were classified in class A, 44 patients had

TABLE 2

T TEST FOR COMPARISION OF TWO GROUPS PRESENCE AND ABSENCE OF VARICES

Parameter	Varices	No	Mean	Std	F	Significance	Significance 2 tailed
P S ratio	Yes	85	879.5	518	21.8	.000	.000
	No	15	1998	1018			.001
Platelets count	Yes	85	121	96	6.9	.01	.000
	No	15	249	121			.001
Spleen size in mm	Yes	85	138.5	25	06	.05	.005
	No	15	128	26			.008
P.V diameter mm	Yes	85	1.33	.237	.305	.5	.008
	No	15	1.14	.29			.32
Albumin g/dl	Yes	85	2.8	.50	10.8	.001	.000
	No	15	40.7	.15			.000

TABLE 3

CORRELATION BETWEEN ESOPHAGEAL VARICES AND SPLENIC SIZE, PLATELET COUNT AND PLATELETS SPLENIC RATIO

Nonparametric Correlations

			Varices	Spleen	Platelets	PS ratio
Kendall's tau_b	Varices	Correlation co efficient	1.00	-.145	.409	.309
		Significance		.091	.000	.000
	Spleen	Correlation co efficient	-.145	1.00	.117	.135
		Significance	.001		.05	.05
	platelets	Correlation co efficient	-.409	.117	1.00	.685
		Significance	.008	.008		.000
	P S ratio	Correlation co efficient	.430	-.135	.685	1.00
		Significance	.000	.006	.000	

child class B, and 39 patients had child Pugh class C. All these patients then underwent upper GI endoscopy which revealed that 85 patients were having presence of esophageal varices, while 15 patients had no varices on endoscopy. Platelet count done in these patients with varices had mean count of 121000+/_ 96000/ cmm, and without varices the mean count was 249500 +/-121000, splenic size in varices group was 138 mm+/- 25, non varices group had 105 +/- 26 cm, mean platelet/ splenic ratio in varices group had ratio of 879 +/- 518, in patients that didn't have esophageal varices the ratio was 1998 +/- 998. Portal vein diameter was 13 +/- 2.3mm in esophageal varices group and 10.0 +/- 2.9mm in non-variceal group. Mean albumin count was 2.84+/-0 .5 mg/dl and 4.0 +/-0 .15mg/dl in esophageal varices and no esophageal group patients respectively.

For comparison of two groups (1- presence of varices and 2- absence of varices) t-Test applied which showed significant difference with p value of <0.001 in two-group .

To check the correlation linear correlation test was applied which showed significant correlation of platelet count (p value < 0.001), splenic size diameter (p value <0.001) and platelet/splenic ratio (p-<0.001) for the detection of esophageal varices.

Area under ROC (receiver operating characteristic) was used for checking the sensitivity and specificity of these three variables. Platelet count of 76000 has 90% sensitivity and 100% specificity, splenic size of 120 mm has 70% sensitivity and specificity of 86% and platelet/splenic ratio of 870 have 70% Sensitivity and 90 % specificity for the detection of esophageal varices.

TABLE 4

Result of ROC curve

Number	Variables	Count	Sensitivity	Specificity
1	Platelet count	76000	90%	100%
2	Splenic size	120 mm	70%	86%
3	Plt/splenic size ratio	870	70%	90%

DISCUSSION

Patients with chronic liver disease over the years develop portal hypertension and its associated complication like esophageal varices, which not only affects the quality of life but may also lead to life threatening episodes of upper GI bleeding. Endoscopy remains the gold standard for screening and detection of esophageal varices, but it is costly, invasive and not available at many health centers specially in smaller cities and in rural setup. The prediction of esophageal varices by noninvasive methods in patients suffering from cirrhosis, with no previous history of upper GI bleed, is essential as the number of patients under going screening for the presence of esophageal varices is likely to increase in the near future, as a result of growing pool of patients with chronic liver disease. Identification of these predictors will provide relief in medical, social and economical costs. To date several studies have been performed regarding the non-invasive methods of detection of esophageal varices by different variables and in different combinations, Like platelet count, splenic size, serum albumin level, portal vein diameter, SAAG (serum ascetic albumin gradient) ratio, prothrombin time (P.T), and platelet count/splenic diameter ratio. Indirect echographic markers of portal hypertension and esophageal varices (ascites, portal vein diameter > or = 13 mm, spleen length, maximal and mean velociy of portal vein flow, respectively < 20 cm/s and < 12 cm/s) could be useful. Among these parameters, spleen length is an independent predictive marker of esophageal varices [20]. Thrombocytopenia have been seen in different studies as a strong risk factor for the presence of esophageal varices. Platelet count (68,000 to 160,000)[11-13,15-18] is repeatedly found to be a predictive marker of esophageal varices in multivariate analysis.

Pilette C [15] et all found figure of 160,000, Sharma SK [16] et all showed that low platelet count, Madhotra R et al [11] found 68,000, NG FH et al[10]found 150,000, Thromopoulus KC et al [17] founds 118,000, Scepis F et al [18] <100,000, Atif Zaman et al[9] found 90,000 and Shahid sawer et al[3] found platelet count of 88,000 is strongly associated with having esophageal varices.

We found that platelet count of 121,000 in chronic liver disease patients have strong prediction for having esophageal varices with significant p value, this finding matches many international and national studies.

Splenic enlargement (clinically palpable or increase on ultrasound examination) [9,11,13,16,17,19] found to have significant association for prediction of esophageal varices.

Thomopoulos KC et al[17] found 135 mm size on ultrasound.

Madhotra R et al[11] , Fagundes ED et al[19] detected enlarged spleen in their study, Atif Zaman et all[9] and Sharma SK et al[16] found enlarged spleen as predictor in their studies

for having esophageal varices in patients with esophageal varices.

In our study splenic size on ultrasound examination taken as parameter and figure of 138.5 found to have significant prediction of esophageal varices.

Platelet count/splenic size was calculated in our studies and figure of 879 found to have strong predction for presence of esophageal varices , while E Giani et al[7] detected ratio of 909 while Gul Hassan et al[14] also find this ratio as strong predictor of having esophageal varices in patients with chronic liver disease.

Additionally we also noted that hypoalbunemia (2.84mg/dl) was significantly associated with prediction of esophageal varices. This result matches with study conducted by Shahid Sarwer et al [3] (2.95mg/dl) and Fagundes ED et al[19] (hypoalbunemia).

In our study all three variable (platelets count, splenic diameter and platelet count/splenic size diameter ratio), showed strong correlation (with significant p value) with presence of esophageal varices in cirrhotic patients. Al these results were matched with international and local studies and found to have significant correlation.

There are few limitations in this study Number of patients in this study is only 100, so the results are to be seen in that context. Study was conducted on admitted patients, having advanced stage of chronic liver disease and were expected to have esophageal varices as suggested by number of variceal positive patients. It is difficult to compare the result with other studies; all have applied different methods for analysis. Investigations were laboratory based and Ultra sound finding were operator based so also chances of errors.

CONCLUSION

We conclude that three non-endoscopic parameters: low platelet count, splenomegaly and platelet count/splenic size diameter ratio, can significantly predict the presence of esophageal varices and can be used as surrogate markers for the presence of esophageal varices where endoscopic facilities not available. However endoscopy may still be required for diagnosing the esophageal and gastric varices and for therapeutic interventions. As such these patients can be put on prophylactic treatment to prevent variceal bleeding.

REFERENCES

1. McQuaid K. Alimentary tract. In: Tierney LM Jr, Mcphee SJ, Papadakis MA, editors. Current medical diagnosis & treatment: 44th ed. New York: Mc Graw-Hill; 2005; 518-628.
2. Azer SA. Esophageal varices[online] 2004.[cited 2006 Jan 10]. Available from: URL: http://www.emedicine.com/med/topic745.htm.
3. 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; 5: 528-31.
4. Chalasani N, Imperiale TF, Ismail A, Sood G, Carey M, Wilcox CM, et al. Predictors of large esophageal varices in patients with cirrhosis. Am J Gastroenterol 1999; 94: 3285-91.
5. Zafar S, Kashif MA, Butt AR, Shafiq F. Correlation of grade of esophageal varices with serum ascites-albumin gradient. Pakistan J Gastroenterol 2005; 19: 89-94.
6. Thabut D, Ratziu V, Trabut J-B, Poynard T. Prediction of oesophageal varices with platelet count/spleen diameter ratio or platelets alone. Gut 2004; 53: 913-5.
7. 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 oesophageal varices in patients with liver cirrhosis. Gut 2003; 52:1200-5.
8. Hegab AM, Luketic VA. Bleeding esophageal varices: how to treat this dreaded complication of portal hypertention. Postgrad Med 2001; 109: 75-89.
9. Zaman A, Becker T, Lapidus J, Benner K. Risk factors for the presence of varices in cirrhotic patients without a history of variceal hemorrhage. Arch Intern Med 2001; 161: 2564-70.
10. Ng FH, Wong SY, Loo CK, Lam KM, Lai CW, Cheng CS. Prediction of oesophagogastric varices in patients with liver cirrhosis. J Gastroenterol Hepatol 1999;14: 785-90.
11. Madhotra R, Mulcahv HE, Willner I, Reuben A. Prediction of esophageal varices in patients with cirrhosis. J Clin Gastroenterol 2002; 34: 81-5.
12. Zaman A, Hapke R, Flora K, Rosen Hr, Benner K. Factors predicting the presence of esophageal or gastric varices in patients with advanced liver disease. Am J Gastroenterol 1999; 94: 3103-5.
13. Prihatini J, Lesmana LA, Mannan C, Gani RA. Detection of esophageal varices in liver cirrhosis using non-invasive parameters. Acta Med Indones 2005; 37: 126-31.
14. Sethar GH, Ahmed R, Rathi SK, Shaikh NA. Platelet count/splenic size ratio: a parameter to predict the presence of esophageal varices in cirrhotics. J Coll Physicians Surg Pak 2006; 16:183-6.
15. Pilette C, Oberti F, Aube C, Rousselet MC, Bedossa P, Gallois Y, et al. Non-invasive diagnosis of esophageal varices in chronic liver diseases. J Hepatol 1999; 31:867-73.
16. Sharma SK, Aggarwal R. Prediction of large esophageal varices in patients with cirrhosis of the liver using clinical, laboratory and imaging parameters. J Gastroenterol Hepatol. 2007;22:1909-15.
17. Thomopoulos KC, Labropoulou-Karatza C, Mimidis KP, Katsakoulis EC, Iconomou G, Nikolopoulou VN. Non-invasive predictors of the presence of large oesophageal varices in patients with cirrhosis. Dig Liver Dis. 2003; 35: 473-8.
18. Schepis F, Cammà C, Niceforo D, Magnano A, Pallio S, Cinquegrani M, et al. Which patients with cirrhosis should undergo endoscopic screening for esophageal varices detection? Hepatology 2001; 33: 333-8.
19. Fagundes ED, Ferreira AR, Roquete ML, Penna FJ, Goulart EM, Figueiredo Filho PP, et al. Clinical and laboratory predictors of esophageal varices in children and adolescents with portal hypertension syndrome. J Pediatr Gastroenterol Nutr. 2008 ;46:178-83.
20. Dib N, Konate A, Oberti F, Calès P. [Non-invasive diagnosis of portal hypertension in cirrhosis. Application to the primary prevention of varices] Gastroenterol Clin Biol. 2005 ;29:975-87.