Study of the Right Liver Lobe Size /albumin Ratio as a Noninvasive Predictor of Oesophageal Varices Compared to: Spleen Size, Platelet count and Platelet count/spleen Diameter Ratio in Post Hepatitis C Virus Liver Cirrhosis in Egypt

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Abstract: Back ground and aim: Hepatic C Virus (HCV) is considered the most common aetiology of chronic liver disease in Egypt.Portal hypertension is a major complication of liver cirrhosis, and leads to the development of portosystmic shunts. Oesophageal varices are the most important among these shunts. Bleeding from oesophageal varices is the most serious complication of cirrhosis, with a high risk of death. The prevention of variceal bleeding is very important, non-selective beta blockers and prophylactic band ligation decrease the risk of bleeding by 50%. The current guide lines recommend screening of all cirrhotic patients by endoscopy, to identify patients at risk of bleeding so prophylactic treatment should be started to them. But repeated endoscopic examinations are unpleasant for patients, and carries high cost impact and more burden on endoscopic units, while only 50% of cirrhotic patients have esophageal varices, and up to 30% have large varices. For these reasons many non-invasive predictors for the presence and size of varices have been studied. The aim of this study to evaluate prospectively the right liver lobe size /albumin ratio and to compare it with spleen size, platelet count and platelet count/spleen diameter ratio as noninvasive predictors of oesophageal varices in post hepatitis C virus liver Cirrhosis in Egypt.Patients and methods:This prospective study included one hundred patients with post hepatitis C virus liver Cirrhosis. All studied subjects underwent a detailed history taking, clinical examination and a biochemical workup, including total bilirubin, aspartate aminotransferase, alanine aminotransferase, serum albumin, prothrombin activity, complete blood count and viral markers for hepatitis C and hepatitis B viruses. Child-Pugh score was calculated for all patients. An upper gastrointestinal endoscopy and abdominal ultrasound were performed for all patients. The platelet count to spleen diameter ratio and the right liver lobe to albumin ratio were calculated.Results: All the 4 predictors showed high statistically significant correlation with the presence and the grade of oesophageal varices (P values <0.001) Among the 4 noninvasive predictors the platelet count/spleen diameter ratio gave the highest accuracy at a cut-off value of 1326.58 (sensitivity 96.34% and specificity 83.33%) followed by the RT liver lobe/albumin concentration ratio at a cut-off value of 44.2 (sensitivity 91.46% and specificity 77.78%) followed by the spleen size at a cut-off value of 131.5mm(sensitivity 90.24% and specificity 83.33%) then lastly the platelet count at a cut-of value of 131000/mm^3(sensitivity 84.15% and specificity 83.33%).

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Key words: Noninvasive predictors of oesophageal varices, The right liver lobe/albumin ratio, The platelet count/spleen diameter ratio, Oesophageal varices, Post HCV liver cirrhosis.

1. Introduction:

Egypt has a very high prevalence of hepatitis C virus (HCV) and a high morbidity and mortality from chronic liver disease(1).HCV is considered the most common aetiology of chronic liver disease in Egypt, where prevalence of antibodies to HCV (anti-HCV) is 10-fold greater than in the United States and Europe (2).

Portal hypertension is a major complicationof liver cirrhosis, and leads to the development of portosystmic shunts. Oesophageal varices are the most important among these shunts due to its clinical effects and play a major role in transforming the disease from a pre-clinical to a clinical phase.Longitudinal studies have shown thatoesophageal and/or gastric varices eventually develop in all cirrhotic patients (3,4)and that once they have developed they tend to increase in size and to bleed (4). The yearly rate of development ofnew varices is about 5–10% (3,5); the rate of growth of varices from small to large ranges between 5% and 30% in different studies [5–8]. Bleeding from oesophageal varices is the most serious complication of cirrhosis, with a high risk of death [9].The mortality from each episode of variceal bleeding is17%-57% (4, 10, 11). On endoscopic examination the presence of red spots on the varices equals high risk of bleeding which is also related to the size of varices (12, 13).

The prevention of variceal bleeding is very important, non-selective beta blockers and prophylactic band ligation decrease the risk of bleeding by 50% (14,15). It is recommended that all cirrhotic patients should undergo endoscopic screening for the presence of varices (16–21), patients who has large or medium sized varices should be treated to prevent bleeding.

Patients who don't have varices and with compensated cirrhosis should repeat endoscopy every 2-3 years, andevery 1-2 years for those with small varices (17). It is also recommended for patients with decompensated cirrhosis to repeat endoscopy every 1 year even if there is no varices (17,19). But repeatedendoscopic examinations are unpleasant for patients, and carries high cost impact and more burden on endoscopic units, while only 50% of cirrhotic patients have esophageal varices, and up to 30% have large varices. For these reasons many non-invasive predictors for the presence and size of varices have been studied.

This study attempts to evaluate prospectively the right liver lobe size /albumin ratioand to compareit with spleen size, platelet count and platelet count/spleen diameter ratio as noninvasive predictors of oesophageal varices in post hepatitis C virus liver Cirrhosis in Egypt

2. Materials and methods:

This prospective study included one hundred patients with post hepatitis C virus liver Cirrhosis who were under investigations and treatment at the Gastroenterology & Hepatology outpatient clinics or those who were admitted to the Internal Medicine departments of the Cairo university hospitals.

Diagnosis of cirrhosis was based on physical findings, laboratory investigations and imaging findings. Patients who previously underwent injection sclerotherapy, band ligation, surgeryfor oesophageal varices, and those who were receiving beta blockers were excluded from the study. All patients with liver cirrhosis due to causes other than HCV were also excluded.

All studied subjects underwent a detailed history taking, clinical examination anda biochemical workup, including total bilirubin, aspartateaminotransferase, alanine aminotransferase, serum albumin, prothrombin activity, complete blood count and viral markers for hepatitis C and hepatitis B viruses. Child-Pugh score was calculated for allpatients using the 5 parameters (ascites, albumin, bilirubin, prothrombin activity and encephalopathy) (22). An upper gastrointestinal endoscopy and abdominal ultrasoundwere performed in all patients.

The right liver lobe diameter in the midclavicular line and the maximum spleen bipolar diameter were measured and the values were recorded. The platelet count to spleen diameter ratio and the right liver lobe to albumin ratio were calculated.

All endoscopies were performed in a single endoscopy unit by an experienced endoscopist and a grading classification I – IV was used (23). Grade I was used for varices in thelevel of mucosa, grade II for varices smaller than 5 mm filling less than 1/3 of the oesophageal lumen, grade III for varices larger than 5 mm filling more than 1/3 of the oesophageal lumen and grade IV for varices occupied more than 2/3 of esophageal lumen.

All the data were recorded, analyzed and correlated.

Data were statistically described in terms of range, mean ± standard deviation (± SD), median, frequencies (number of cases) and percentages when appropriate. Comparison of quantitative variables between the study groups was done using Mann Whitney *U* test for independent samples when comparing 2 groups and Kruskal Wallis analysis of variance (ANOVA) test with Mann Whitney *U* test for independent samples as posthoc multiple 2-group comparisons when comparing more than 2 groups. For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5. Accuracy was represented using the terms sensitivity, specificity, +ve predictive value, -ve predictive value, overall accuracy, the likelihood ratio of a positive test and the likelihood ratio of a negative test. Receiver operator characteristic (ROC) analysis was used to determine the optimum cut off value for the studied diagnostic markers. A probability value (*p* value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel 2007 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

3. Results:

48 men and 52 women were included in the study, all with post HCV liver cirrhosis. The main clinical characteristicsof all patients are shown in table 1

The mean values of platelet (PLT) count, spleen diameter, PLT count/spleen diameter ratio and the right liver lobe diameter/albumin concentration ratio were correlated to the presence and grade of varices and they all highly significantly correlated to the presence and grade of varices as shown in table 2 and table 3.

The sensitivity, specificity and accuracy of PLT count, spleen diameter, PLT count/spleen

diameter ratio and the right liver lobediameter/albumin concentration ratio as noninvasive predictors of oesophageal varices were studied by applying the ROC curve to detect the cut off values with the best sensitivity and specificity.

Among the 4 noninvasive predictors the platelet count/spleen diameter ratio gave the highest accuracy at a cut-off value of 1326.58 followed by the RT liver lobe/albumin concentration ratio at a cut-off value of 44.2 followed by the spleen size at a cut-off value of 131.5mm then lastly the platelet count at a cut-of value of 131000/mm^3 as shown in table 4 and figures 1-5.

Table 1: showing the patients clinical characteristics

Main clinical characteristics of all patients	
Total number	100
Gender (M/F)	48/52
Age (mean ±SD)	49.23 ± 7.996
Age (range)	20 - 70
Child class.(A/B/C)	20/31/49
Varices present (yes/no)	82/18
Grade of varices(I/II/III/IV)	7/15/35/25
Varices type (small/large)	22/60
Mean PLT count,mm^3 (mean ±SD)	117070 ± 66145.883
Mean spleen diameter, mm (mean ±SD)	150.92 ± 23.371
Mean PLT count/spleen ratio(mean ±SD)	843.262 ± 616.250
Mean right liver lobe diameter, mm (mean ±SD)	147.74 ± 4.263
Mean albumin concentration,gm/dl (mean ±SD)	2.543 ± 0.9699
Mean right lobe/ albumin ratio (mean ±SD)	66.578 ± 23.735

Table 2: Correlation between all parameters with and without varices

Varices presence		PLT count	Spleen diameter	PLT/spleen ratio	Right lobe/albumin ratio
No	Mean	215,055.56	121.22	1,838.389	41.187
	SD	69,772.295	13.584	707.1507	8.8507
Yes	Mean	95,560.98	157.44	624.820	72.152
	SD	41,519.919	19.745	301.3943	22.3031
P		<0.001	<0.001	<0.001	<0.001

Table 3: Correlation between all predictors and grades of varices

Grade of varices		PLT count	Spleen diameter	PLT/spleen ratio	Right lobe/albumin ratio
I	Mean	167,428.57	136.29	1,204.285	42.192
	SD	59,969.040	15.966	364.5529	5.6384
II	Mean	99,466.67	149.87	668.750	56.054
	SD	37,015.183	16.296	246.9659	16.0342
III	Mean	96,000.00	160.60	600.033	72.150
	SD	31,167.479	14.136	199.6266	15.5372
IV	Mean	72,480.00	163.48	470.914	90.201
	SD	25,932.798	24.395	237.9270	20.3913
P		<0.001	0.007	<0.001	<0.001

Table 4: Comparison of accuracy of the 4 parameters in predicting the presence of oesophageal varices

Predictor	AUROC	Cut off point	Sensitivity (%)	Specificity (%)	(+)ve PV(%)	(-)ve PV(%)	Accuracy (%)	LR+	LR-
PLT count	0.912	131000	84.15	83.33	95.83	53.57	84.00	5.05	0.19
Spleen size	0.934	131.5	90.24	83.33	96.10	65.22	89.00	5.41	0.12
PLT count/spleen ratio	0.927	1326.58	96.34	83.33	96.34	83.33	94.00	5.78	0.04
Right liver lobe/Albumin conc.ratio	0.912	44.22	91.46	77.78	94.94	66.67	89.00	4.12	0.11

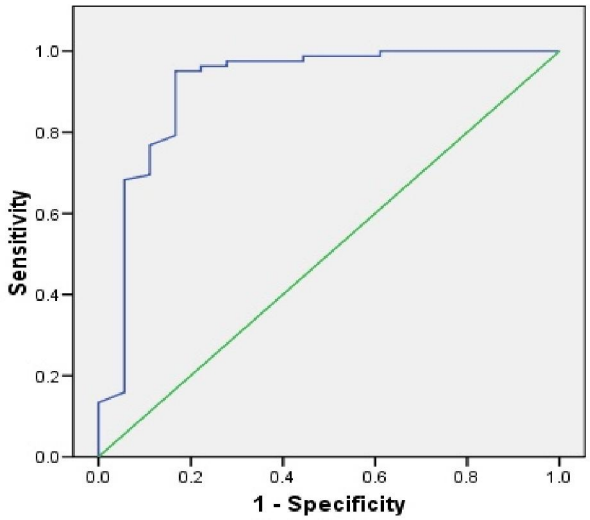

Figure1: ROC curve for sensitivity and specificity of platelet count for the prediction of varices

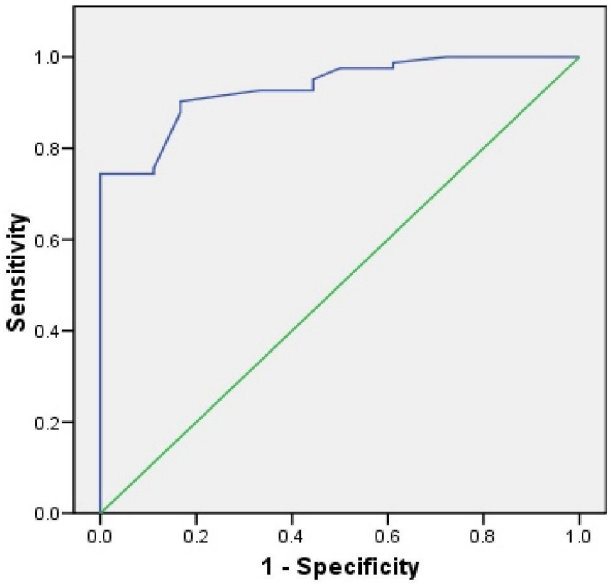

Figure 2: ROC curve for sensitivity and specificity of spleen size for the prediction of varices.

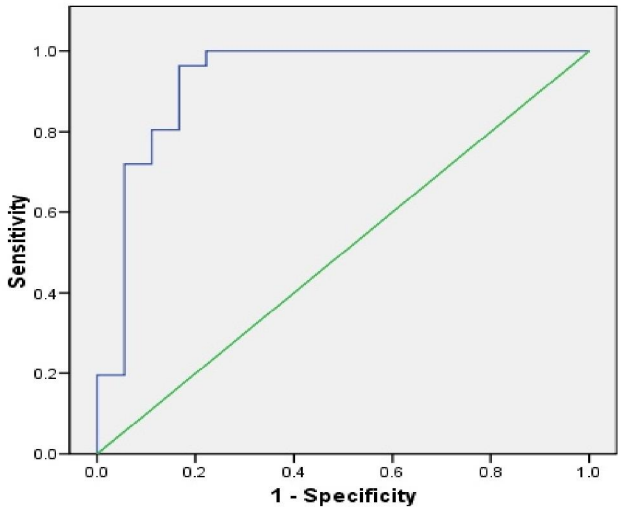

Figure 3: ROC curve for sensitivity and specificity of platelet count/spleen diameter ratio for the prediction of varices.

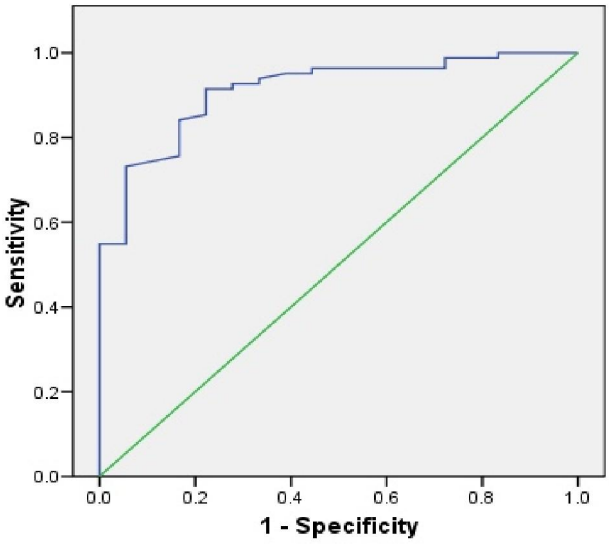

Figure 4: ROC curve for sensitivity and specificity of RT liver lobe size/albumin concentration ratio for the prediction of varices.

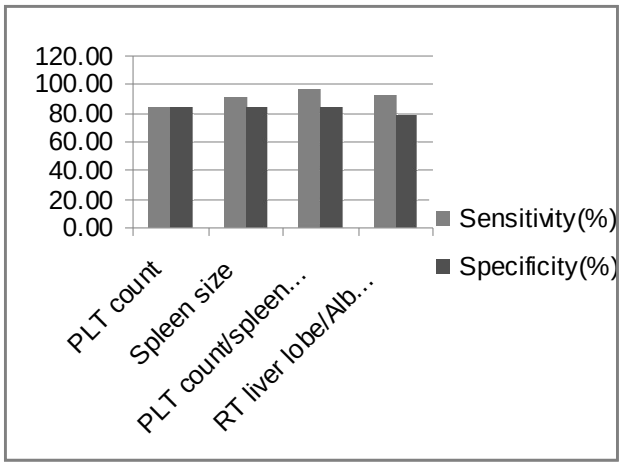

Figure 5: Comparison between sensitivity & specificity of the 4 parameters in predicting the presence of oesophageal varices

4. Discussion:

Bleeding oesophageal varices is still the leading cause of death in patients with cirrhosis. In recent studies, mortality rates vary between 11% and 20% within six weeks of the bleeding episode (24-27).

Endoscopy is still the gold standard method for diagnosis of oesophageal varices and is recommended every two to three years incirrhotic patients without varices, and every one to two years in patients with small varices (14,28,29).Several studies have been performed to find noninvasive parameters that can predict the presence of oesophageal varices in liver cirrhosis to reduce the cost andburden on endoscopy units(28).

The prevention of bleeding from oesophageal varices is an important goal. Identification of patients who are at risk of variceal bleeding is the first step in prevention of bleeding so the patients can be selected to start prophylactic treatment.

The prevalence of oesophageal varices among cirrhotics is variable, ranging from 24% to 80% (30). The value of diagnosing oesophageal varices by a noninvasive predictor is to save endoscopy to patients who have high probability of having varices.

In the present study as shown in tables 2-4 and figures 1 and 2 like many other previous studies (31-37) have shown that platelet count and spleen diameter correlate well with the presence of oesophageal varices.However, in cirrhoticpatients, the presence of thrombocytopenia may be due to several factors other than portal hypertension, as shortened mean platelet lifetime, decreased thrombopoietin production or myelotoxiceffects of hepatitis C viruse (38). The presence of splenomegaly in cirrhotic patients is mainly related to portal hypertension.

In 2003Giannini et al (28) introduced the use of the platelet count/spleen diameter ratio as a predictor of oesophageal varices. This ratio links thrombocytopenia to splenomegaly to introduce a variable that takes into consideration that thrombocytopenia is mainly due to hyperslenism secondary to portal hypertension.In his study with a cut-off value of 909 the sensitivity was 100% and specificity was 93%. In 2006 Giannini et al(39) reported the results of a multicenter study to validate the use of platelet count/spleen diameter ratio in the prediction of oesophageal varices. In this study the cut-off value of 909 showed sensitivity 92% and specificity 67%.Many studies (23, 39- 42) have been done using different best cut-off values to investigate thisparameter as a noninvasive predictor for oesophageal varices.

In the present study the cut-off value of 1326.58 for the platelet count /spleen diameter ratiowas used which showed sensitivity 96.34% and specificity 83.33% as shown in table 4 and figure 3.
In 2007 Alempijevic et al (24) investigated the right liver lobe diameter/albumin concentration ratio as a noninvasive predictor of oesophageal varices and at a cut-off value of 44.25 the sensitivity was 83.1% and the specificity was 73.9%. In the present study at a cut-off value of 44.22 for the right liver lobe diameter/albumin concentration ratio, the sensitivity was 91.46% and the specificity was 77.78% as shown in table 4 and figure 4.

5. Conclusion:

Among the noninvasive parameters studied in this study, the platelet count/spleen diameter ratio had the highest accuracy for diagnosing oesophagealvarices (sensitive to 96.34% and specificity 83.33%). For the right liver lobe diameter/albumin concentration ratio, the sensitivity was 91.46% and the specificity was 77.78% and can be considered as a noninvasive predictor of oesophageal varices that can provide accurate information as well as the platelet count/spleen diameter ratio.

The use of the 4 studied predictors in this study can help the physicians to restrict endoscopy on those who are highly suspected to have oesophageal varices to start the prophylactic therapy and not to use the endoscopy for all the patients.

Of course endoscopy still is the gold slandered for the diagnosis of oesophageal varices, but the use of the noninvasive predictors specially

platelet count/spleen diameter ratio and the right lobe liver size/albumin concentration ratio will be of a great help to reduce the number of endoscopies in patients with post hepatitis C virus liver cirrhosis in Egypt. More studies are required in a larger sample of post hepatitis C cirrhosis patients for validation of the right lobe liver size/albumin concentration ratio as a noninvasive predictor of oesophageal varices as well as the platelet count/spleen diameter ratio and to determine a cut-off value that can be safely recommended for the noninvasive diagnosis oesophageal varices.

The limitation of the present study includes: relatively small number of patients, liver biopsy was not done and the diagnosis of cirrhosis was based on clinical and laboratory results.

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