Validity of Platelet Count/Spleen Diameter Ratio for the Noninvasive Diagnosis of Esophageal Varices in Cirrhotic Patients

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ABSTRACT

Objective: The objective of the study is to determine the validity of platelet count/Spleen Diameter ratio for the noninvasive diagnosis of esophageal varices in cirrhotic patients.
Study Design: Cross sectional survey.
Setting: Medical Unit 4, Services Institute of Medical Sciences, Services Hospital, Lahore.
Duration: The study was completed over a period of 6 months.
Subjects and methods: One hundred and fifty patients who had coarse echotexture of liver on abdominal ultrasound fulfilling the criteria were selected. Platelet count was calculated after taking blood sample. Spleen diameter was calculated using abdominal ultrasound in millimeters (mm). These patients were then subjected to upper gastrointestinal endoscopy after informed consent and presence or absence of esophageal varices was documented.
Results: Platelet count/spleen diameter ratio as a non invasive marker for the presence or absence of EV has a sensitivity of 96.07%, specificity is calculated to be 93.75%, positive predictive value of 97.02% and negative predictive value of 91.83%. **Conclusion:** Study showed that platelet count spleen diameter ratio is a simple and reproducible means for non invasive diagnosis of EV, and its application may decrease the need for performing upper gastrointestinal endoscopy for diagnosis of **EV.**
Key words: Cirrhosis, Esophageal Varices, Platelet, Spleen diameter

INTRODUCTION

Cirrhosis is a serious and irreversible disease. It is a consequence of chronic liver disease characterized by replacement of liver tissue by fibrotic scar tissue as well as regenerative nodules, leading to progressive loss of liver function[1].

It is a major cause of mortality and morbidity worldwide. It is also a common cause of mortality amongst Pakistani population and frequent reason for admission in hospitals. Cirrhosis develops in about 10-20% within 5-30 years. The most common cause being viral hepatitis as compared to developed countries where alcohol is more common. It is generally irreversible disease, and treatment focuses on preventing the progression and its complications. In advanced stages of cirrhosis the only option is liver transplantation[2].

Cirrhosis is often an indolent disease; approximately 40% of the patients with cirrhosis are asymptomatic[3] until the development of decompen-sation, characterized by bleeding from varices due to portal hypertension, ascites, spontaneous bacterial peritonitis (SBP), or hepatic encephalopathy[4].

Mortality rates in patients with alcoholic liver disease are considerably higher than in patients with other forms of cirrhosis[5].

A major cause of cirrhosis-related mortality and morbidity is the development of variceal hemorrhage, a consequence of portal hypertension. The reported prevalence of esophageal varices in patients with chronic liver disease varies from 24% to 81%.[6] Variceal hemorrhage occurs in 25%-40% of patients with cirrhosis, and is associated with a mortality rate of up to 30% [7] and up to 70% of those who survive have one or more additional episodes of bleeding within six weeks of admission[8].

Accurate identification of patients with an increased risk of bleeding allows for primary prophylaxis to prevent variceal bleeding.[9] Prophylactic use of beta- blockers has been shown to decrease the incidence of first variceal bleeding and death in patients with cirrhosis, and is currently the standard of care in patients who are at high risk for variceal hemorrhage[10].

The risk of bleeding from esophagogastric varices is determined by the extent of portal hypertension, liver dysfunction, and endoscopic findings[11]. Hemorrhage due to EV is a poor prognostic sign[12].

Screening for EV represents an important part of the diagnostic work up of cirrhotic patients[13]. Diagnostic yield of upper Gastrointestinal (GI) endoscopy is undoubtedly very high if the patient selection is done in a meticulous way[14]. Upper GI endoscopy is the gold standard for the diagnosis of EV[15].

In future, this social and medical burden is expected to increase due to ever increasing number of patients with chronic liver disease and their improved survival.[16] With significant improvements in the early diagnosis and treatment of variceal hemorrhage, mortality from acute variceal bleeding has been decreasing, it still remains high (20%–35%) depending on the severity of liver disease and age of the patient[17].

Recent guidelines recommend periodic screening for esophageal varices by endoscopy in patients with cirrhosis[18].

Surveillance for varices can involve multiple EGDs over the course of a patient's lifetime, and is associated with costs, inconvenience, discomfort, and risks. EGD is an invasive technique that usually requires conscious sedation; therefore, many patients are reluctant to undergo this procedure and, in fact, might be noncompliant with screening and surveillance recommendations[19]. EGD might be limited to a subgroup of patients only, if a simple non-invasive test to detect EV was available to select those at risk of bleeding, which will reduce both the medical and financial burden on hospitals related to screening[20].

As mentioned above, bleeding from varices occurs in 25 to 35% of cirrhotic patients and is associated with significant morbidity and mortality and elevated hospital costs. Endoscopic exploration of varices increases costs and involves a certain degree of discomfort and invasiveness for patients[21].

The possibility of identifying EV in cirrhotic patients by non-invasive means is attractive because it will allow for the restriction of performance of screening endoscopy[22].

MATERIALS AND METHODS

This cross-sectional descriptive study was conducted in Medical unit 4, Services Institute of Medical Sciences, Lahore over a period of 06 months. One hundred and fifty patients who had coarse echotexture of liver parenchyma on abdominal ultrasound and age ranges between 12-60 years were included in the study, based on the selection criteria. Non-probability purposive sampling technique was used. All those male and female patients between 12-60 years of age showing coarse echotexture of liver parenchyma on abdominal ultrasound were included in the study. Patients presenting with variceal bleed, received any therapeutic intervention for their varices like banding or injection sclerotherapy, taking non selective beta blockers and/ or nitrates and patients who refused to undergo upper GI EGD were excluded from the study.

Patients who had coarse echo texture of liver parenchyma on abdominal ultrasound will be selected from emergency department. In the selected patients, platelet count will be calculated and splenic diameter will be measured with the help of abdominal ultrasound and Platelet count/Spleen diameter ratio will be calculated and cut off value will be applied and documented. These patients will then be booked for diagnostic upper gastrointestinal endoscopy at a later date after informed consent. Upper GI EGD will be performed in these selected patients after full preparation and presence or absence of EV will be documented in each case. The validity of platelet count/spleen diameter ratio will then be assessed using the cut off value of 909 for diagnosing presence or absence of EV in each patient.

Data was collected and compiled in the computer and analyzed using SPSS version 10 for Windows. Demographic variables included were age and was expressed as mean and $\pm$SD, and gender was presented as percentages and frequency tables. Platelet count/Spleen diameter ratio (with the cut off value of 909 showing presence or absence of esophageal varices) was the qualitative variable, and presence or absence of esophageal varices on Endoscopy was the qualitative variable and was presented as frequencies and as percentages. The Sensitivity, Specificity, Positive predictive value (PPV), Negative predictive value (NPV) and diagnostic accuracy for platelet count/spleen diameter ratio was calculated considering EGD findings (presence or absence of EV) as a gold standard.

RESULTS

A total of 150 patients who had coarse echotexture of liver parenchyma on abdominal ultrasound and had age between 12-60 years were selected from the emergency department of Services Hospital Lahore.

Table 1 shows that amongst the 150 patients, 54% were male and 46% were females. Overall percentage of males was more than that of females.

Table 2 shows age distribution of patients. According to it 05 patients were up to 20 years of age, 04 patients were between 21-30 years of age, 17 patients were between 31-40 years of age, 58 patients were between 41-50 and 66 patients were between 51-60. Mean age was 50.99 ± SD of 12.99. Figurative representation is shown in figure 1.

Table 3 shows another independent variable which is platelet count/splenic diameter ratio .According to the table, 101 patients (67.30%) had platelet count/splenic diameter ratio of less than 909 and 49 patients (32.7%) had platelet count/splenic diameter ratio of more than 909.figure 2 shows it in a in a pie chart. Table 4 shows group of patients according to the presence or absence of esophageal varices. According to the table, 119 patients had esophageal varices (79.3%) and 31 patients did not had esophageal varices (20.7%). Bar chart is shown in figure 3.

Table 1: Distribution of subjects according to their gender (n=150)

Gender	Frequency	%age
Male	81	54
Female	69	46

Table 2: Distribution of subjects according to their age (n=150)

Age in years	Frequency	%age
Less than 20	05	3.3
21-30	04	2.7
31-40	17	11.3
41-50	58	38.7
51-60	66	44.0
Mean ± SD	50.99 ± 12.99	

Minimum age: 15 years, Maximum age 60 years

Fig 1: Age distribution

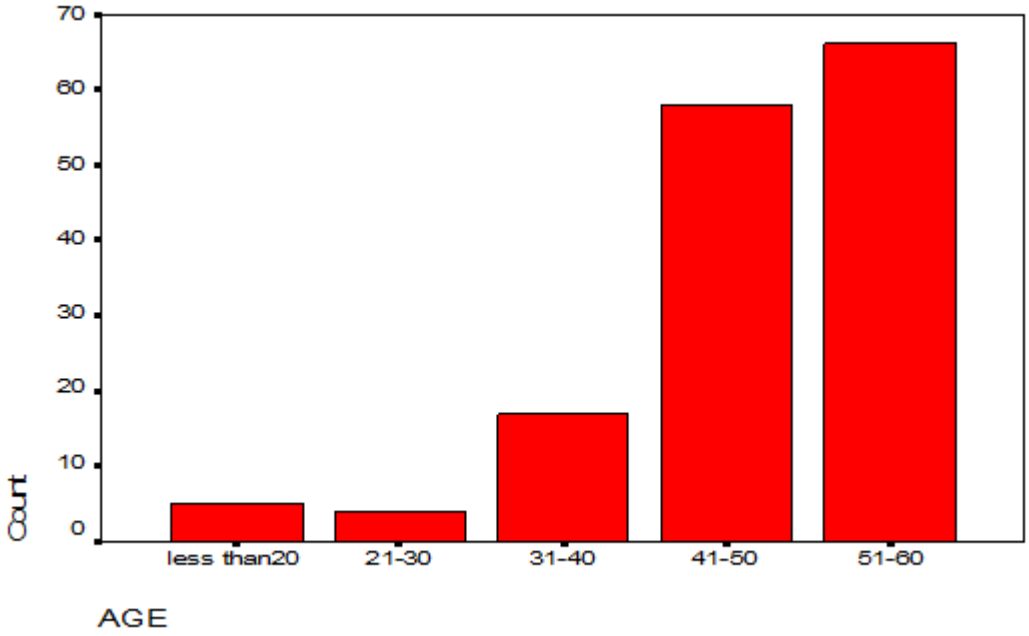

Table 3: Distribution of subjects according to platelet count/spleen diameter ratio (n=150)

Plt/sp ratio	Frequency	%age
<909	101	67.3
>909	49	32.7
Total	150	100

Fig. 2: Distribution of subjects according to platelet count/spleen diameter ratio

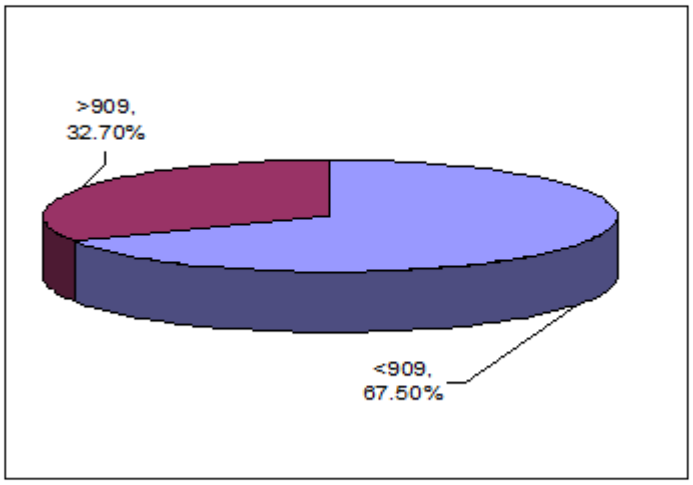

Table 4: Distribution of subjects according to EV (n=150)

EV	Frequency	%age
Present	119	79.3
Absent	31	20.7
Total	150	100

Fig. 3: Distribution of subjects according to EV

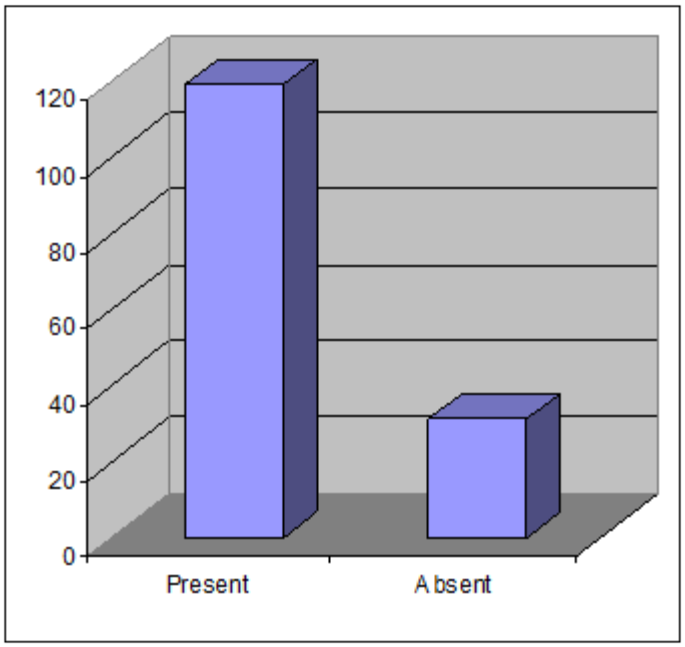

Table 5: Distribution of subjects according to positivity (n=150)

Positivity	Frequency	%age
True positive	98	64.9
True negative	45	30.0
False positive	3	2.0
False negative	4	2.6
Total	150	100

Table 6: Cross-tabulation between Platelet count/Spleen diameter ratio and EV

Plt/spl ratio	EV present	EV absent	Total
<909	98	3	101
>909	4	45	49
Total	102	48	150

Table 5 shows groups of patients according to positivity of patients. According to this table , 98 patients (64.9%) were true positive, 3 patients (2.0%) were false positive, 45 patients (30.0%) were true negative. 4 patients (2.6%) were false negative.

In table 6, a cross tabulation is shown between platelet count/spleen diameter ratio and presence or absence of EV. This table shows the frequency of presence or absence of EV with respect to the platelet count/spleen diameter ratio. It's clear after studying the table that out of 101 patients with platelet count /spleen diameter ratio of <909, EV were present in 98 patients, and in 3 patients EV were absent. It is also clear from the table that a total of 49 patients had platelet count/spleen diameter ratio >909, 4 out of these 49 had EV present and, EV were absent in 45 patients.

The research inferred that the sensitivity of this non invasive marker as a tool for determining the presence or absence of EV is 96.07%, specificity is calculated to be 93.75%, positive predictive value of 97.02% and negative predictive value of 91.83%.

DISCUSSION

In this study, it has been shown that implementing the platelet count/spleen diameter ratio for the noninvasive diagnosis of EV in patients with cirrhosis is both practical and reproducible. Diagnostic accuracy for presence or absence of EV of the platelet count/spleen diameter ratio was significantly better than accuracy of either platelet count or spleen diameter alone[23]. It was confirmed that the platelet count/spleen diameter ratio has a very high NPV, and therefore can be confidently applied. Therefore, applying the platelet count/spleen diameter ratio criteria to screen patients who may benefit from endoscopy and prophylactic treatment is likely to be more cost-effective than wasting this diagnostic and therapeutic modality.

It is important to determine the presence of EV in cirrhotic patients because variceal bleeding is one of the most dreaded complications of portal hypertension. Although with recent advancements, the prognosis and outcome of variceal bleeding has improved but it still carries a substantial mortality. Cirrhotic patients should undergo upper GI EGD to detect EV. This enables us to diagnose EV, so that early treatment could be initiated and life threatening complications could be withheld[24]. It is uncertain till date that how often patients should be screened for varices, and there are few data on the relationship of varices to nonendoscopic variables. Studies have been done to identify clinical, laboratory and imaging characteristics that may non-invasively predict the presence or absence of EV with a high degree of accuracy, either reducing or eliminating the need for screening EGD[25].

In this study an attempt was made to ascertain the validity between the presence or absence of EV and platelet count/spleen diameter ratio expressed as value of less than or greater than 909. It was found that there is a significant relationship between these two variables in cirrhotic patients.

There have been different studies conducted in the past in which different variables have been taken into account to be used as the non invasive markers for the presence or absence of EV. Different parameters used in different studies have included ascites, spider naevi, hepatic encephalopathy, serum bilirubin levels, prothrombin time, [26] splenomegaly[27], serum albumin concentration, thrombocytopenia, portal vein diameter. [28]. The inference of this study is very much comparable to the other alternative studies done in the past.

It is a useful and practical study in many ways. One of the merits of this study is the complete non invasive nature of this variable. Moreover, it is easy to use and had comparable accuracy with other models used in the past, which also comprised of multiple variables combined together and were similarly used in predicting severity of esophageal varices[26].

This study has an advantage of using simple and non-invasive diagnostic tool like abdominal ultrasound which is a cheap and readily available diagnostic modality with a fairly high degree of accuracy. Platelet count used as a non invasive predictor could be measured easily by a simple blood testing which is readily available and cheap test.

In the present study conducted, patients who were considered false positive (i.e. patients with platelet count/spleen diameter ratio < 909 but without EV) were more likely to have EV later as compared

to those patients who had higher platelet count/spleen diameter ratio. This is an important finding that could enable to determine the patients at risk of bleeding.

The presence and severity of EV by splenic index in cirrhotic patients has been assessed in the past in which CT scan of the abdomen was used as a diagnostic mortality to calculate splenic index. The study concluded that the SI in patients with EV was greater than in patients without EV[29].

To make this non invasive technique more reliable, platelet count, portal vein diameter and anteroposterior splenic measurements have been studied in the past as non invasive parameters to detect EV in cirrhotic patients[30]. The study also concluded that the platelet count, portal vein diameter and splenic diameter can be used as non invasive predictors of the presence of EV with a fair degree of specificity and sensitivity.

Like other studies, our study also has certain boundaries. Prediction models may vary with the nature of the patient population from which these are derived.

Our study group represented a select group of patients with liver cirrhosis attending a tertiary care center and included patients with relatively advanced disease. This model would be expected to have the best predictive value in a population similar to the one from which it is derived. Thus, it would be best applied in patients attending large hospitals and may not perform as well in primary care settings. Further studies will be necessary regarding this aspect.

Second, we did not test the predictive ability of this model in an independent prospective validation cohort. Unfortunately, this has not been performed in any of the previous studies either, except in a recent study[31].

Third, the variable being predicted EV, is not completely objective and is subject to interobserver variation. The model may thus need prospective validation in patients attending various medical centers. Moreover we do not know that whether any cirrhotic patients could have EV without appreciating course echotexture of liver which is the only marker of cirrhosis in our study. Even echotexture of liver can be subjected to interobserver variation.

Moreover the fact that platelet count/spleen diameter ratio was used to assess the presence or absence of EV rather than large EV can be considered a drawback of the study. This is due to the fact that currently any form of prophylactic treatment like beta blockers is only recommended for patients with large EV[20,23].

CONCLUSION

Our study shows that platelet count/spleen diameter ratio is independent predictor of the presence and absence of EV in patients with cirrhosis of the liver. This parameter can be used to calculate a predictor function, which showed moderate efficacy in predicting the presence of EV. This predictor function needs further study in patients with liver cirrhosis to validate its efficacy. If its efficacy is confirmed, it may permit institution of prophylactic measures like beta-adrenergic antagonists for preventing primary variceal bleeding in patients with liver cirrhosis, without the need for costly and invasive investigations like EGD.

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