Platelet Count to Spleen Length Ratio as a Predictor of Esophageal Varices in Patients with Cirrhosis of Liver

Dr P.Sathish Sreenivas[1], Dr L.Sandhyarani[2], Dr B.Raghuveer[3], Dr A.Venkata Raja[4], Dr P.S.S.V.Haritha[5]

[1]*[Associate professor(designated),General medicine,RMC,Kakinada]*
[2]*[Associate professor(designated),General medicine,RMC,Kakinada]*
[3]*(Junior resident, General medicine)*
[4]*(Junior resident, General medicine)*
[5]*(Senior resident, General medicine)*
Corresponding Author:- Dr L.Sandhya rani

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I. Background

Portal hypertension is a common finding in the course of chronic liver disease and accounts for the most severe complications of liver cirrhosis, such as gastroesophageal variceal bleeding, ascites, and hepatorenal syndrome (1).

Portal hypertension is determined as the elevation of Hepatic Venous Pressure Gradient (HVPG) to > 5 mm Hg and is clinically identified by splenomegaly, ascites, and prominent veins over the abdomen (2).

Variceal haemorrhage, as a complication of portal hypertension, is an immediate lifethreatening problem with 20 - 30 % mortality rate, with each episode of bleeding (2).

Intra-hepatic causes account for 95 % of cases of portal hypertension and are represented by significant forms of cirrhosis.

Significant portal hypertension is present in > 60% of cases of patients with cirrhosis.

It is a common practice to screen cirrhotics with endoscopy for esophageal varices(3).

Approximately one-third of patients with cirrhosis have varices at the time of diagnosis.

In a resource-poor country like India, it is difficult to screen every cirrhotic patient with endoscopy for esophageal varices.2

Majority of patients with cirrhosis are below the poverty line, and cannot afford an endoscopy.

An indirect tool to predict the presence of esophageal varices plays an important role in such situations where it can be used as a triage.

Many studies were done in this regard to determine indirect markers of esophageal varices. MELD score, Mean Platelet Count, PT/INR, Mean Spleen Length, Platelet Count and Spleen Length Ratio, Aspartate transferase and Platelet Ratio Index (APRI), etc. were studied for prediction of esophageal varices.

Platelet and spleen length are the most affected parameters due to portal hypertension.

This study aims to determine the value of Platelet Count and Spleen Length Ratio for predicting the severity of esophageal varices in cirrhosis with portal hypertension, thus helping in identification and immediate treatment of high-risk varices.

II. Materials And Methods

Place of study: Department of General Medicine, Rangaraya Medical College, Kakinada, Andhra Pradesh, India.

Study period: February 2018 to July 2019

Type of study: a Cross-Sectional study

Study population: 55 patients admitted to medical wards with history, clinical examination and investigations suggestive of cirrhosis of liver without any prior history of upper Gastro-intestinal bleed, propranolol usage, or portal shunt surgery were included. Informed consent was taken from the patients included in the study after explaining the nature and type of the study.

The diagnosis of cirrhosis with portal hypertension is made by a thorough history, clinical examination and required investigations. All these details are noted. Blood and other investigations necessary for aetiology were also done.

INCLUSION AND EXCLUSION CRITERIA
Inclusion Criteria:
All patients with a diagnosis of hepatic cirrhosis of any aetiology were included.
Exclusion Criteria:
1. Patients with hepatocellular carcinoma
2. Patients with a history of esophageal variceal bleeding
3. Patients with a previous history of variceal ligation, sclerotherapy, and/or portal
hypertension surgery.
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Investigations like Complete Blood Picture including Platelet Count, Renal Function Tests, Liver Function Tests Like Serum Bilirubin , Serum Total Proteins, Serum Albumin, Alanine Transaminase (ALT), Aspartate Transaminase (AST), Alkaline Phosphatase (ALP), PT/INR (Prothrombin Time), Hepatitis B surface antigen, Hepatitis C antibody, Ultrasound Abdomen, Serum Electrolytes, Ascitic Fluid Analysis, Upper Gastro-Intestinal Endoscopy were performed.

III.   Statistical Analysis And Results

All the data obtained are tabulated using Microsoft Excel Software.The data is analysed using the Statistical Package for Social Sciences Software (SPSS)
The present study includes 55 patients with cirrhosis of the liver who were admitted in the Department of General Medicine, Government General Hospital, Kakinada.
Sex distribution:
Out of 55 patients, 50 (91%) were male, and 5 (9%) were female.
Age distribution:
Mean age of presentation in the present study is 44.96 years and median is 43 years with a standard deviation of 13.053. Minimum age of presentation is 20 years, and the maximum age of presentation is 85 years. Most common age is 38 years in 5 patients. Maximum cases (17 patients) are between 31- 40 years of age.
Aetiology of cirrhosis:
The aetiology of cirrhosis in the majority of patients in this study is alcoholism in 48 patients (87.27%). Cirrhosis due to Hepatitis B was found in 3 patients, and due to Hepatitis C in 1 patient.

Cause	Number (%)
Alcoholism	48(87.27%)
Hepatitis B	3(5.45%)
Hepatitis C	1(1.81 %)
Unidentified etiology	3(5.45%)

The division into groups based on the presence or absence of varices:
For comparison, the sample is divided into two groups based on the presence or absence of varices.

GROUP	VARICES +/-	NUMBER(%)
A	With varices	33 (60%)
B	Without varices	22 (40%)

The p-value is 0.095 (>0.05) for the above comparisons; thus, the difference is not statistically significant. Hence, the age distributions of the two subgroups of the sample population are comparable to each other.

SERUM BILURUBIN LEVELS IN THE STUDY
The mean serum bilurubin value in the present study was 5.59 mg/dl with a SD of 5.64 and a minimum value being 0.4 mg/dl and maximum value being 25.3 mg/dl

SERUM BILURUBIN	GROUP A(N=33) WITH VARICES	GROUP B(N=32) WITHOUT VARICES
Mean	5.50	5.73
Median	3.60	4.15
SD	5.53	5.92
Minimum value	0.4	0.9
Maximum value	21.5	24.4
P value	0.88	0.88

There is no statistically significant difference between 2 groups with respect to serum Bilirubin

SERUM CREATININE LEVELS IN STUDY

The mean serum creatinine level in the study was1.25 mg/dl with median being 0.85 mg/dl with an SD of 1.52

SERUM CREATININE	GROUP A(N=33) with varices	GROUP B (N=22) without varices
Mean	1.19	1.34
Median	0.8	0.87
SD	1.63	1.37
Minimum value	0.6	0.5
Maximum value	10	6.9
P value	0.70	0.70

There is no statistically significant difference between 2 groups with respect to serum
Creatinine

SERUM ALBUMIN LEVEL IN THE STUDY

The mean serum albumin level in the study was 2.2 gm/dl with median being 2.20 SD being 0.65 with minimum value being 1.5 gm/dl and maximum value of 4.6
There is no statistically significant difference between 2 groups with respect to serum
Albumin

PLATELET COUNTS IN THE STUDY

The mean platelet count in the study was 1,41,154.54 with median being 1.23 lakh with a SD of 68,228.21 with minimum value being 58,000, maximum value being 3.5 lakh

PLATELET COUNT	GROUP A (N=33) with varices	GROUP B (N=22) without varices
Mean	102560.61	199045.45
Median	90000.00	190000
SD	44293.72	56031.85
Minimum value	58000	121000
Maximum value	306000	350000
P value	<0.001	<0.001

There is a statistically significant difference between 2 groups with respect to platelet count

ASCITES IN THE STUDY

This study assessed radiological parameters like the amount of free fluid in the abdomen, portal vein diameter, and spleen length for prediction of varices.
Amount of fluid is categorized as mild ascites, moderate ascites and gross ascites.
The significance of ascites for prediction of varices is done by Chi-Square test.
Amount of fluid/ascites did not show any statistically significant difference between the two groups with a level of significance more than 0.05 (p = 0.307).

PORTAL VEIN DIAMETER IN STUDY

The mean portal vein diameter in the study was 12.58 mm with median 13.00 mmand SD of 1.39.The maximum value of portal vein diameter in the study was 15.00 and minimum value was 10.00
There is no statistically significant difference between the 2 groups with respect to portal vein diameter

SPLEEN LENGTH IN THE STUDY

The mean spleen length in the study was 141.54 mm with median 124.00 mm and SD of 18.20.The maximum value in the study was 180 mm and minimum value was 96 mm

SPLEEN LENGTH(MM)	GROUP A(N=33) with varices	GROUP B (N=22) without varices
MEAN	149.18	130.09
MEDIAN	148	135
SD	12.401	19.714
MINIMUM VALUE	122	96
MAXIMUM VALUE	180	160
P VALUE	<0.0001	<0.0001

There is a statistically significant difference between 2 groups with respect to spleen length

PLATELET COUNT/SPLEEN LENGTH RATIO(PC/SL)

The mean PC/SL ratio in the study was 1043.88 with median 869.56 and SD of 587.62.The maximum value in the study was 2812.50 and minimum value was 333.33

PC/SL RATIO	GROUP A(N=33) WITH VARICES	GGROUP B(N=22) WITHOUT VARICES
MEAN	699.07	1561.10
MEDIAN	628.57	1468.72
SD	342.84	491.65
MINIMUM VALUE	333.33	864.28
MAXIMUM VALUE	2318.18	2812.50
P VALUE	<0.0001	<0.0001

There is a statistically significant difference between 2 groups with respect to pc/sl ratio

PPV & NPV VALUES IN STUDY

CUT OFF<651.31	LARGE VARICES	SMALL VARICES	TOTAL
TEST POSITIVE	10	4	14
TEST NEGATIVE	1	18	19
TOTAL	11	22	33

Prevalence (33.33 % for large varices among Group A) adjusted Positive Predictive Value is 71.12 %, and Negative Predictive Value is 94.81 %.

By the ROC curve, the cut-off obtained is < 651.315. When the Platelet count/spleen length ratio is less than 651.31, it is associated with the presence of large varices. It showed a sensitivity of 81.82

Thus, Platelet count, spleen length and Platelet Count/Spleen Length ratio are found to be independent predictors of esophageal varices. Platelet count/spleen length ratio has a statistically significant value in predicting esophageal varices. The ratio has also shown a statistically significant value in the detection of large varices.% and specificity of 90.91%

IV. Discussion

Though Platelet Count and Spleen Length are affected by portal hypertension, Platelet Count is also affected by Spleen Length. This is due to splenic sequestration of Platelets. A novel parameter is required which overcomes this disadvantage of splenic sequestration of Platelets .Giannini et al. first described that Platelet Count/Spleen Length Ratio could be used as the Platelet Count corrected to the level of splenomegaly. (41) Later many studies were done to assess the significance of Platelet Count/Spleen Length Ratio in the identification of varices. All these studies showed a statistically significant association of a low value of this ratio for the presence of varices.

Various methods used different cut-off for the ratio. Gianni et al. (41) study used the ROC curve (Receiver Operating Characteristics curve) to obtain a cut-off for identification of varices with maximum sensitivity and specificity for the given data.

The cut-off obtained is 909. Other studies used this cut-off to study the significance, while some studies used ROC curves to obtain a new ratio.

The cut-off obtained by ROC curve is 957.14 with maximum sensitivity and specificity. This cut-off obtained for PC/SL ratio by ROC curve is higher than that obtained by Giannini et al.,(41) but lower than that obtained by WW Baig et al. (45) using the same method.

With the cut-off of 957.14, sensitivity(90.91%) and specificity (95.45%) were calculated, which were obtained after 60% prevalence adjusted, as observed in the study.

The sensitivity obtained for 957.14 is low compared to other studies but is higher than the sensitivity obtained in the study of Sarangapani et al. (46)

Sarangapani et al. (46) used PC/SL ratio cut-off of 909 as observed in Giannini et al.,(41). To use a test as screening/triage, the sensitivity of that test should be high.

Though the sensitivity obtained in this study is low compared to major studies like Giannini et al. (41) and Agha et al. (44), it is still high.

The specificity obtained in this study is 95.45% which is higher than all other studies.

This study showed good efficiency, which is more than the efficiency obtained in the study done by Schwarzenberger et al. (74%). The efficiency obtained in the study done by Agha et al. is higher (98.4%).

This study showed that PC/SL ratio could be used as a predictor of varices.

To study the usefulness of PC/SL ratio for grading of varices, Group A is further divided into two groups, those who have small varices, and those who have large varices (As the management of medium and large varices is similar). According to Baveno Consensus criteria, small esophageal varices are those that minimally protrude into the lumen or those that flatten with insufflation, whereas large varices are those that fill more than 50% of the lumen or show confluence/touch each other.

This study did not show the significance of Platelet count/Spleen length ratio for the grading of varices (p-value = 0.578). The study done by Alempijevic et al. showed a statistically significant value of Platelet

Count/Spleen Length ratio and Right lobe of liver/serum albumin in detecting the presence and grading of varices. (22)

LIMITATIONS OF THE STUDY

1. The study sample is small, which may not reflect the actual burden of the disease.
2. The main aetiology of cirrhosis in the present study is alcohol. Previous studies were done mainly in Hepatitis C patients. Separate studies should be undertaken for each cause of cirrhosis to identify the usefulness of the Platelet Count/Spleen Length Ratio.
3. The study has very less number of female patients as the prevalence of alcoholism among female patients in the study area is low.
4. Patients included in the study presented late with decompensated cirrhosis.
The study should be extended to compensated cirrhosis patients also.
5. This study is an observational study without any active therapeutic interventions. This study did not study Platelet Count/Spleen Length Ratio as a prognostic factor for progression of varices or regression of varices with treatment.

V. Conclusions And Summary

1. This study showed that low Platelet Count, increased Spleen Length and low Platelet Count/Spleen Length ratio are independent risk factors for esophageal varices.
2. Platelet Count/Spleen Length Ratio has high sensitivity and specificity in the prediction of varices. Hence, this can be used as a triage to perform endoscopy in high-risk patients first or to start Beta-Blocker therapy in high-risk patients.
3. Negative Predictive Value of PC/SL Ratio in this study is little less as compared to other studies.
4. Platelet count /spleen length ratio also useful in predicting presence of large varices. However, it is not useful for grading of varices.
5. Ascites, Portal Vein diameter, Serum Albumin did not show any correlation with the presence of varices.

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