

Platelet Count to Spleen Diameter Ratio as a Noninvasive Marker of Oesophageal Varices in Hepatic Cirrhosis

B.K. Agrawal¹, A. Garg², H. Parashar³, T. Pruthi⁴, S. Tayal⁵

¹Department of Medicine, MM Institute of Medical Sciences and Research, Maharishi Markandeshwar Deemed to be University, Mullana, Haryana, India. ²Department of Medicine, MM Institute of Medical Sciences and Research, Maharishi Markandeshwar Deemed to be University, Mullana, Haryana, India. ³Department of Medicine, MM Institute of Medical Sciences and Research, Maharishi Markandeshwar Deemed to be University, Mullana, Haryana, India. ⁴Department of Medicine, MM Institute of Medical Sciences and Research, Maharishi Markandeshwar Deemed to be University, Mullana, Haryana, India. ⁵Department of Medicine, MM Institute of Medical Sciences and Research, Maharishi Markandeshwar Deemed to be University, Mullana, Haryana, India.

ABSTRACT

BACKGROUND

Cirrhosis, a chronic liver disease is an important health problem. The common aetiological factors are hepatitis B, hepatitis C, alcohol consumption and non-alcoholic fatty liver disease. Oesophageal varices are an important complication of hepatic cirrhosis, its prevalence in a cirrhotic being nearly 80%. Variceal haemorrhage can be fatal, and it has been recommended that every patient with cirrhosis should be screened for oesophageal varices at the time of presentation. This may not be feasible in resource crunch setting. There is a need for simpler methods which may help suspect or diagnose oesophageal varices. In this study platelet count to spleen diameter ratio, as has been suggestive in some studies, has been analysed to find out as to whether it can be used as a marker of presence of oesophageal varices.

METHODS

One hundred and fifty patients of cirrhosis of liver were included in this study. All patients underwent upper gastrointestinal endoscopy for the presence of oesophageal varices. Total platelet count (per cubic millimetre) to splenic diameter (in millimetre) ratio was calculated for each patient.

RESULTS

It was observed that there exists a correlation between the ratio of platelet count and bipolar spleen diameter for the prediction of oesophageal varices. A cut off value of P/S ratio of 909 correlated well with the presence of varices. The subject with advanced disease as per Child Pugh classification had lower P/S ratio.

CONCLUSIONS

Platelet count to spleen diameter ratio can be used as a sensitive marker for the prediction of oesophageal varices in patients with cirrhosis of liver.

KEY WORDS

Cirrhosis of Liver, Oesophageal Varices, Platelet Count, Spleen Diameter

Corresponding Author:
Dr. Bimal K. Agrawal,
Office of the Principal,
MM Institute of Medical Sciences and
Research, Mullana-133207, Ambala,
Haryana, India.
E-mail: onlybimal@gmail.com

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BACKGROUND

Cirrhosis, a chronic liver disease, is characterized by diffuse fibrosis and distortion of the normal acinar and/or lobular architecture of liver with or without degeneration, regeneration or nodule formation.¹ Cirrhosis results in a decrease in hepatic cellular mass and studies have proven that cirrhosis is reversible when disturbances have been removed. In India, the aetiology of cirrhosis of the liver is varied, the most common infectious condition is HBV² (Hepatitis B Virus) infection followed by alcohol and hepatitis C infection.³ The prevalence of hepatitis B infection in India is 4.7%.⁴ Cirrhosis eventually leads to the development of portal hypertension which affects various organs of the body, causing morbidity and even deaths in some patients. Portal hypertension presents with ascites, gastrointestinal bleed and splenomegaly. Most dreaded complication of portal hypertension, oesophageal variceal bleeding,⁵ is responsible for high mortality in cirrhotic patients.

Oesophageal varices have a high prevalence rate of 60-80% in cirrhotic patients and it is a major cause of bleeding in 25-30% of the patients. Every year 5% new cases of oesophageal varices are seen and every year, nearly 5-10% of these patients progress to large varices from small varices. Previous literature recommends that all cirrhotic patients should be screened for the presence of oesophageal varices at the time of diagnosis. However, performing an endoscopic evaluation of all cirrhotic patients for screening may not be the affordable approach, more so in resource crunch situations like India. A cost-effective method of screening would be possible if cirrhotic patients could be identified for varices based on clinical and biochemical variables. In this study, platelet count to spleen diameter (P/S ratio) has been evaluated as a single noninvasive test for prediction of oesophageal varices.

METHODS

The study protocol was approved by the Institutional Ethics Committee prior to enrolling any patient for the study. One hundred fifty patients of cirrhosis were included in the study fulfilling the inclusion and exclusion criteria. It is a prospective study of all patients consecutively diagnosed with cirrhosis of liver in a tertiary care hospital during the period November 2013 to August 2015 were included. All patients were subjected to platelet count estimation, spleen diameter and upper gastrointestinal endoscopy for oesophageal varices detection. Diagnosed subjects were graded according to Child-Pugh classification.¹ Spleen diameter was obtained via USG abdomen in all subjects. Upper GI endoscopy performed in all subjects using STORZ Karl STORZ XENON 100 flexible endoscope. Oesophageal varices were graded according to Paquet grading and size classification. P/S diameter ratio was calculated and correlated with the presence of oesophageal varices. A value of 909 for this ratio of P/S diameter was considered as a cut off point for this study, as has been validated by Giannini et al.⁶ Extrahepatic or non-cirrhotic causes of oesophageal varices were excluded. The patient's undergone treatment like band ligation, sclerotherapy, trans-jugular intrahepatic

portosystemic shunt were also excluded. Statistical analysis was done by using descriptive statistics (Mean, percentage and standard deviation) and inferential statistics using Chi square test, sensitivity, specificity, negative predictive value, positive predictive value.

RESULTS

In this study, the mean age of the subjects was 48.76 ± 9.0 years; the majority of subjects (83%) were males. The maximum number of patients belonged to Child-Pugh Class B (56.7%). Ascites and pedal oedema were the most frequent clinical presentation and most common sign encountered was splenomegaly (Table 1).

Child-Pugh Classification	A	B	C
No of subjects (N=150)	15(10%)	85(56.7%)	50(33.3%)
Icterus	5	30	10
Pedal Oedema	0	65	55
Ascites	5	80	55
Splenomegaly	0	55	35
Encephalopathy	0	5	35

Table 1. Distribution of Subjects as Per Child-Pugh Classification

With advancing stage, a decrease in platelet count was observed and p-value for the correlation between child Pugh score and mean platelet count came out to be 0.027. A maximum number of patients belonged to Class C and maximum bipolar splenic diameter was recorded in Class C with significant difference among the stages (p = 0.424). P/S diameter ratio was found to be maximum in Class A and the minimum ratio was found in Class C with a p-value of 0.023 (Table 2). As the Child-Pugh Class increased, the percentage of patients with oesophageal varices also increased with a maximum in class C (100%).

Child-Pugh Classification	A (N=15; 10%)	B (N=85; 56.7%)	C (N=50; 33.3%)	p-Value
Platelet Count (cells/cumm)	140000	121764	98000	0.027
Spleen Diameter (mm)	128	146	148	0.424
P:S ratio	1107	862	602	0.023
Oesophageal Varices	2	16	10	

Table 2. Parameters According to Child-Pugh Class

Paquet grade of oesophageal varices also worsened with the escalation in Child-Pugh class. Column grading of oesophageal varices also showed worsening with increasing Child-Pugh score with a significant p-value of 0.018 (Table 3).

Child-Pugh Class	Number of Subjects	Paquet's Grades of Oesophageal Varices					Oesophageal Varices Column grading		
		0	I	II	III	IV	Absent	Small	Large
A	15	5	10	0	0	0	5	10	0
B	85	5	10	35	30	5	5	45	35
C	50	0	0	5	45	0	0	5	45

Table 3. Child-Pugh Class, Paquet's Grading System and Size Grading System

The correlation of P/S ratio for the presence of oesophageal varices came out to be clinically significant with p-value 0.011. In the subjects, with P/S diameter ratio value ≤ 909 (115 subjects), the percentage of larger varices was more. By Paquet grading, 4.35 % of subjects had grade 4 and 65.2% subjects had grade 3 varices. Grade 1 varices were

detected in 4.35% and grade 2 in 26.08%. When size (column) classification was used, 69.6% of subjects had large varices and 30.4% had small varices.

In the other subset of subjects with P/S ratio >909 including 35 subjects, 10 (28.6%) subjects did not have any oesophageal varices, 15 (42.9%) had Paquet grade I, II (28.6%) had grade II and none had grade III/ IV varices. By size (column) grading out of 35 subjects, 10 (28.5%) subjects did not have any oesophageal varices. Small oesophageal varices were observed in 25 (71.4%) subjects only. These findings were statistically significant with $p = 0.002$ for Paquet staging and $p = 0.001$ for column grading (Table 4).

P/S Diameter	Number of Subjects	Oesophageal Varices		Paquet Grading				
		Absent	Present	0	I	II	III	IV
>909	35	10	25	0	5	30	75	5
≤ 909	115	0	115	10	15	10	0	0
Total	150	10	140	10	20	40	75	5

Table 4. Correlation of Platelet Count to Spleen Diameter Ratio with the Presence of Oesophageal Varices and Paquet Grading

P value = 0.008, Sensitivity = 100%, Specificity = 28.57%, Positive Predictive Value = 82.14%, Negative Predictive Value = 100%

In our study 140 subjects had oesophageal varices out of 150. In these patients, the mean value of P/S ratio was found to be 842 whereas in 10 subjects who did not have varices had the mean value of 1272. This difference was found to be highly statistically significant ($p = 0.011$).

Oesophageal Varices	Number of Subjects	P/S Ratio (Mean±SD)
Present	140	844±234
Absent	10	1272±314
Total	150	875±305

Table 5. Correlation of Oesophageal Varices with Platelet Count to Spleen Diameter Ratio

DISCUSSION

The hypothesis proposed for this study was that there exists a correlation between the ratio of platelet count and bipolar spleen diameter for the prediction of oesophageal varices. Based on previous studies, a reference cut off the value of this ratio was taken as 909 and was hypothesized that subjects with a value less than this predictably have oesophageal varices.

A similar trend of a number of subject inclusions was seen in the study by G. H. Sether et al,⁷ who had 13.27% Child-Pugh Class A, 60.18% Child-Pugh Class B and 26.55% Child-Pugh Class C subjects out of total 113 patients. Identical subject subsets were included in the study by Zaman et al⁵ with the maximum being in Child-Pugh class B. Higher number of subjects were reported in Child class A in the studies by M.H. Chang et al⁸ and P. Cales et al.⁹

The results of the present study suggested that platelet count reduced as the subject progressed from compensated towards decompensated cirrhosis of the liver (class A to class C). The positive correlation of platelet count reduction to Child-Pugh class progression was seen in our study wherein the Child-Pugh Class A, B and C the mean platelet counts were 140000, 121764 and 98000, respectively (Table 2). Similarly, Garcia- Tsao et al,¹⁰ Pilette et al¹¹ and K. C. Thromopoulos et al¹² in their studies reported a low platelet count in the patients of cirrhosis of the liver. They also found an increase

in the magnitude of thrombocytopenia with more pronounced decompensation of the disease process.

In our study, it was observed that as the Child-Pugh class progressed, the value of P/S ratio reduced (Table 2). This correlation had high statistical significance (p -value = 0.023). The study of Amin K et al,¹³ had similar results with P/S diameter ratio value in Child class A 1137.66, Child class B 728.23 and Child class C 670.84.

In our study, when Child-Pugh class was correlated with the presence of oesophageal varices, the association was found as 100% in Child-Pugh Class C, 94.1% in Child-Pugh Class B and 66.7% in Child-Pugh Class A (Table 5). Similar results were reported by Mahassadi et al¹⁴ with a higher incidence of oesophageal varices in child class C whereas Emam et al¹⁵, found the incidence of varices to be more in Child-Pugh class A subjects (64.3%).

In the present study, we found that as the Child-Pugh class increases the grades of oesophageal varices increase as well. Child-Pugh class C subjects were found to have higher grades of varices by both grading systems (Table 3). As per Paquet's grading system grade III, oesophageal varices were found in 0%, 35.3% and 90% subjects in Child-Pugh class A, B and C respectively. When graded by size (column) grading, large varices were seen in 0%, 41.2% and 90% of subjects in Child Class A, B and C respectively. These results were statistically significant for column grading (p -value = 0.018). Similarly, Nishaat et al,¹⁶ Dib ret al¹⁷ and Samada et al.¹⁸ Also reported a higher incidence of large oesophageal varices with decompensated cirrhosis of the liver. Increase in the oesophageal variceal size with the higher Child-Pugh score was reported by Cales, Desmolratetal⁹ as well.

The P/S ratio cut off of 909 used in our study was the one determined by Giannini et al⁶ in predicting large varices. In our study, all the subjects with P/S ratio ≤ 909 had oesophageal varices. This ratio value of 909 was found to be highly statistically significant in predicting the presence of oesophageal varices (p -value 0.008).

In our study, the sensitivity of P/S ratio for prediction of oesophageal varices was found to be 100%. A similar result was obtained in the studies by Giannini et al⁶ (91.5%) and Sarangapani et al (88.5%) and slightly lower sensitivity were reported by de Mattos et al¹⁹ (77.5%). The specificity in the present study for this cut off of 909 was 28.57%. Higher values were reported by Sarangapani et al²⁰ (83%) and Giannini et al⁶ (67%) whereas lower by de Mattos et al¹⁹ (45.5%). The positive predictive value in our study was 82.14%. Similar values have been obtained by Angela Zambam de Mattos et al¹⁹ (79.5%), E. Giannini et al⁶ (87%), Sarangapani et al²⁰ (83.5%) and Schwarzenberger et al²¹ (74%). The highest positive predictive value was found in a study by Agha et al²² (93.8%). In our study, the negative predictive value was found to be 100%. Similar results have been reported by Giannini et al⁶ (87%), Sarangapani et al²⁰ (90.5%) and Schwarzenberger et al²¹ (73%) along with Agha et al²² (100%). A lower negative predictive value was reported by Mattos et al¹⁹ (42.6%).

Many researchers have predicted different cut off values for this ratio and found different results as well. Baig et al²³ reported a cut-off value of 1014, which gave positive and negative predictive values of 95.4% and 95.1 %, respectively. F. Barrera et al,²⁴ in their study of 67 patients with the cut off value 830.8, found 77.8% negative predictive value. Makarem et al²⁵ found 100% sensitivity and 100% negative predictive

value for a cut off of 939.7. Barikbin et al²⁶ in their study including 55 subjects had 93% negative predictive value for a cut off 921. Similar results were obtained in studies by Emam et al¹⁵ (Cut off 900), Agha et al²³ (Cut off 571) and Nashaat et al¹⁶ (Cut off 820). In the study by Amin K. et al¹³ the mean P/S ratio for the patients with oesophageal varices was found to be 704.28 and those without varices was 1162.41. These findings were similar to our study. The proposed hypothesis, that the propensity for finding oesophageal varices increases as the ratio reduces further, stands true in these studies.

CONCLUSIONS

As Child-Pugh class progressed, there was also a fall in P/S ratio which was statistically highly significant (p-value=0.023). Further, it was also seen that oesophageal variceal grading also worsened with increasing Child-Pugh class. All the subjects with P/S ratio \leq 909 had oesophageal varices. The value of 909 was found to be statistically highly significant in predicting the presence of oesophageal varices (p-value= 0.008). The sensitivity of P/S ratio for the screening of oesophageal varices was found to be 100%. The specificity in the present study for this cut off of 909 was 28.57%. Thus, it can be concluded that a cut off value of 909 for P/S ratio can be taken as a non-invasive marker to differentiate high- and low-risk patients in screening oesophageal varices in patients of cirrhosis of liver.

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