

ORIGINAL RESEARCH ARTICLE

**Association between platelet count and grades of oesophageal varices in patients of cirrhosis of liver with portal hypertension**

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**Abstract**

**Background:** Cirrhosis is the end-stage of different chronic liver diseases, which is a major cause of mortality and morbidity worldwide. The majority of patients with cirrhosis are likely to develop oesophageal varices, with patients at risk of variceal bleeding. Thrombocytopenia is a common complication affecting cirrhotic patients which can be used to predict the presence of oesophageal varices. The present study was conducted to determine the correlation of thrombocytopenia with oesophageal varices grading in chronic liver disease patients as well as to determine if platelet count can predict the presence of oesophageal varices in a patient of cirrhosis of liver with portal hypertension.

**Materials & Methods:** This study was conducted on 50 cirrhotic patients in the department of Medicine, Government Medical College, Amritsar. The study protocol was approved by the institutional ethics committee. The patients were enrolled in the study after obtaining written informed consent. All the patients were interviewed and clinically examined. Upper gastrointestinal endoscopy, Child-Pugh scoring and platelet count was calculated for every patient. The results were then analyzed.

**Results:** The mean age was  $46.8 \pm 12.65$  years with a slight male preponderance (56% male vs 44% female patients). The mean platelet count was  $103292.00 \pm 57441.38$  lakhs/cumm. Platelet count was  $<0.50$  lacs/ $\mu$ l in 6 (12%) patients,  $0.50-0.99$  lacs/ $\mu$ l in 22 (44%) patients,  $1.0-1.4$  lacs/ $\mu$ l in 12 (24%) patients,  $1.5-2.0$  lacs/ $\mu$ l in 8 (16%) patients, and  $>2.0$  lacs/ $\mu$ l in 2 (4%) patients. On correlation of platelet count with grades of oesophageal varices it was evident that 56% patients had their platelet count less than 1 lac/ $\mu$ l out of which 12 patients had grade II varices followed by 7 patients with grade III varices (p value=0.0012; highly significant).

**Conclusion:** The present study found that there is significant negative correlation between platelet count and grades of oesophageal varices. Low platelet count is associated with higher grades of oesophageal varices. This suggest that platelet count can be used as a predictor to predict the grade of oesophageal varices. The platelet count is a non-invasive parameter with high accuracy for prediction of oesophageal varices.

**Keywords:** Cirrhosis, Portal hypertension, Oesophageal varices, Platelet count, thrombocytopenia

## Introduction

Liver cirrhosis is often considered as the end-stage of different chronic liver diseases.<sup>[1]</sup> It is a major cause of mortality and morbidity worldwide.<sup>[2]</sup> In the GBD Study 2017, the estimated number of people with compensated cirrhosis was 112 million worldwide, corresponding to an age-standardized global prevalence of compensated cirrhosis of 1,395 cases per 100,000 population.<sup>[3]</sup>

This disease entity is often neglected until the various related complications (e.g., variceal haemorrhage, spontaneous bacterial peritonitis, ascites, or hepatic encephalopathy) start appearing. The majority of patients with cirrhosis are likely to develop oesophageal varices, with about one-third of these patients at risk of at least one bleeding episode due to the varix rupture.<sup>[4]</sup> Thrombocytopenia (defined as platelet count < 150,000/ $\mu$ L) is a common complication affecting as many as 76% of cirrhotic patients.<sup>[5]</sup> The present study was conducted to determine the correlation of thrombocytopenia with oesophageal varices grading in chronic liver disease patients as well as to determine if platelet count can predict the presence of oesophageal varices in a patient of cirrhosis of liver with portal hypertension.

## Materials and methods

This descriptive observational study was conducted on 50 patients of liver cirrhosis admitted in the department of Medicine, Guru Nanak Dev Hospital, Government Medical College, Amritsar (Punjab). The study protocol was approved by the institutional ethics committee. Written informed consent was obtained from the patients before enrolment in the study.

### Inclusion criteria-

- Patients with cirrhosis of liver without any past history of upper (or) lower gastrointestinal bleed.
- Patients who gave written informed consent to participate in the study.

### Exclusion criteria-

- Patients with present or previous history of variceal bleed.
- Patients on previous/current treatment with beta blockers/ diuretics/ antiplatelet drugs.
- Patients underwent sclerosis (or) band ligation of oesophageal varices, TIPSS (or) surgery for portal hypertension.
- Patients who had fever associated with thrombocytopenia in the past, or fever in the past 15 days.
- Patients who were on drugs associated with thrombocytopenia.

All patients in the study were subjected to complete clinical evaluation. Biochemical tests, like liver function tests, complete blood counts, renal function tests, prothrombin time and ultrasonography of the abdomen to confirm the presence of cirrhosis and to record the spleen bipolar diameter, portal vein size, ascites and presence of collaterals were performed. Child-Pugh score was calculated for all patients. Upper gastrointestinal endoscopy was also done in all patients to confirm the presence of varices and for its grading. All endoscopies were performed in a single endoscopy unit using a video endoscope.

The platelet count was calculated for all patients in the study. The platelet count was compared between the two groups of patients with and without oesophageal varices. The results of observations of individual patients were tabulated and analyzed using appropriate statistical tests.

## Results

**Baseline data of patients:** The mean age was  $46.8 \pm 12.65$  years with majority of the patients (52%) belonging to 36-45 years age group. There was a slight male preponderance (56%

male vs 44% female patients). Majority of the patients (66%) had a medical history of chronic liver disease, followed by cardiovascular disease (16%), diabetes mellitus (10%), and chronic kidney disease (8%). Hypertension was present in all the patients. Alcohol intake was present in 40 patients (80%), while 32 (64%) patients had a history of smoking.

Hepatic encephalopathy was present in all the patients. The subtype distribution was as follows- Type 0 (76%), Type I (16%), Type II (6%), and Type III (2%). Majority of the cirrhotic patients (58%) had Child Pugh Score B, followed by Child Pugh Score A (30%) and Child Pugh Score C (12%). Other complications of cirrhosis included ascites and oesophageal varices. Mild ascites was present in 12 (24%) patients, moderate ascites in 16 (32%) patients, and severe ascites in 22 (44%) patients. With respect to oesophageal varices, grade 0 varices were present in 7 (14%) patients, grade I varices in 9 (18%) patients, grade II varices in 18 (36%) patients, grade III varices in 12 (24%) patients, and grade IV varices in 4 (8%) patients.

**Clinical and laboratory investigations:**

Analysis of vitals revealed that the mean systolic blood pressure and mean diastolic blood pressure was 126.18±27.95 mm Hg and 83.52±12.84 mm Hg, respectively. The mean pulse rate was 92.12±19.34 beats/ min, and Spo2 was 93.00±5.00%.

Haemogram of the patients was done. The mean hemoglobin was 11.49 ± 1.62 g/dL, mean total blood count was 11304.00 ± 5739.31 cells/cumm, and mean platelet count was 103292.00 ± 57441.38 lakhs/cumm. Platelet count was <0.50 lacs/µl in 6 (12%) patients, 0.50-0.99 lacs/µl in 22 (44%) patients, 1.0-1.4 lacs/µl in 12 (24%) patients, 1.5-2.0 lacs/µl in 8 (16%) patients, and >2.0 lacs/µl in 2 (4%) patients.

Liver function tests of the patients revealed that the mean serum bilirubin was 3.22±0.50 mg/dL. The mean serum albumin was 2.98±0.58 mg/dL. The mean Alanine Amino Transferase (SGPT), Aspartate Amino Transferase (SGOT), and Alkaline phosphatase was 115.96 ± 14.03 U/L, 113.80 ±10.00 U/L, and 58.00 ± 9.00 U/L, respectively. The mean prothrombin time was 21.98 ± 5.56 seconds.

**Correlation of grades of oesophageal varices with platelet count:** On correlation of platelet count with grades of oesophageal varices it was evident that 56% patients had their platelet count less than 1 lac/µl out of which 12 patients had grade II varices followed by 7 patients with grade III varices (p value=0.0012; highly significant). These findings suggest that grading of oesophageal varices was inversely correlated with platelet count.

Parameters	Variables	Total
Age (years)	25-35	18 (36%)
	36-45	26 (52%)
	46-55	2 (4%)
	56-65	4 (8%)
Gender	Male	28 (56%)
	Female	22 (44%)
Medical	Chronic Liver	33

history	Disease	(66%)	
	Cardiovascular Disease	8 (16%)	
	Chronic Kidney Disease	4 (8%)	
	Diabetes Mellitus	5 (10%)	
Hypertension	Present	50 (100%)	
Personal history	Alcohol intake	40 (80%)	
	Smoking	32 (64%)	
Hepatic encephalopathy	Type 0	38 (76%)	
	Type I	8 (16%)	
	Type II	3 (6%)	
	Type III	1 (2%)	
	Type IV	0	
Child Pugh Score	Child Pugh Score A	15 (30%)	
	Child Pugh Score B	29 (58%)	
	Child Pugh Score C	6 (12%)	
Ascites	Mild	12 (24%)	
		Moderate	16 (32%)
		Severe	22 (44%)
Oesophageal Varices		Grade 0	7 (14%)
		Grade I	9 (18%)
		Grade II	18 (36%)
		Grade III	12 (24%)
		Grade IV	4 (8%)
Platelet count (lacs/ $\mu$ l)		<0.50	6 (12%)
		0.50-0.99	22 (44%)
		1.0-1.4	12 (24%)
		1.5-2.0	8 (16%)
		>2.0	2 (4%)

**Table 1: Baseline characteristics of patients**

**Table 2: Clinical and biochemical findings of patients**

Parameters	Variables	Values
Vitals	SBP (mmHg)	126.18±27.95
	DBP (mmHg)	83.52±12.84
	Pulse beats/min	92.12±19.34
	Spo2%	93.00±5.00
Complete Haemoglobin	Hemoglobin (g/dL)	11.498 ± 1.627
	Total Count (cells/cmm)	11304.00 ± 5739.318
	Platelets (lakhs/cmm)	103292.00 ± 57441.380
Liver function tests	Serum bilirubin (mg/dL)	3.22 ± 0.50
	Serum albumin (g/dL)	2.98 ±0.58
	Alanine Amino Transferase (SGPT) (U/L)	115.96 ± 14.03
	Aspartate Amino Transferase (SGOT) (U/L)	113.80 ±10.00
	Alkaline phosphatase (U/L)	58.00 ± 9.00
	Prothrombin time (sec)	21.98 ± 5.56

**Table 3: Correlation of grades of oesophageal varices with platelet count**

Variables	Values	Grade 0	Grade I	Grade II	Grade III	Grade IV	Total	p-value	R-value
Platelet Count (lacs/µl)	<0.50	1	1	1	3	0	6	0.0012 (S)	0.165
	0.50-0.99	4	1	11	4	2	22		
	1.0-1.4	2	3	3	3	1	12		
	1.5-2.0	0	4	3	1	0	8		
	>2.0	0	0	0	1	1	2		
	Total	7	9	18	12	4	50		

**Discussion**

**Patient’s demographics:**The mean age of the patients was 46.8±12.65 years. Majority of the patients (52%) belonging to 36-45 years age group. There was a slight male preponderance (56% male vs 44% female patients). Baig et al (2008) reported a mean age of 51 years (range 20-80).<sup>[6]</sup> Cherian et al (2011) reported the mean age of the patients reported was 42 years (range 17-73).<sup>[7]</sup> Similar to the present study, Priyadarshi et al (2020) reported majority of male patients (85%).<sup>[8]</sup>

**Baseline characteristics:**With respect to oesophageal varices, grade 0 varices were present in 7 (14%) patients, grade I varices in 9 (18%) patients, grade II varices in 18 (36%) patients, grade III varices in 12 (24%) patients, and grade IV varices in 4 (8%) patients. Similar findings were reported by some previous studies (Priyadarshi et al., 2020; Afsar et al., 2021).<sup>[8,9]</sup> Priyadarshi et al reported that majority of the patients had grade 2 varices followed by 23% patients who had varices of grade 3.<sup>[8]</sup> Afsar et al also found that grade I oesophageal varices were found in 23.6% (n=26) patients, whereas grade II, grade III and grade IV were found in 24.5% (n=27), 33.6 (n=37) and 18.2% (n=20) of patients, respectively.<sup>[9]</sup>

**Clinical and biochemical findings of patients:**The mean platelet count was  $103292.00 \pm 57441.38$  lakhs/cumm. Platelet count was  $<0.50$  lacs/ $\mu$ l in 6 (12%) patients,  $0.50-0.99$  lacs/ $\mu$ l in 22 (44%) patients,  $1.0-1.4$  lacs/ $\mu$ l in 12 (24%) patients,  $1.5-2.0$  lacs/ $\mu$ l in 8 (16%) patients, and  $>2.0$  lacs/ $\mu$ l in 2 (4%) patients. Afsar et al (2021) reported that platelet count was  $<50,000$  /uL in 35.5% (n=39) of patients,  $50,000-99,000$ /uL in 26.4% (n=29),  $100,000-150,000$ / $\mu$ l in 12.7% (n=14), and  $>150,000$ /uL in 25.5% (n=28) patients.<sup>[9]</sup> Chalasani et al (1999) found that a platelet count  $<88,000$ / $\mu$ l was an independent risk factor for the presence of large varices.<sup>[10]</sup> In retrospective analysis of 143 patients with compensated cirrhosis, Schepis F et al (2001) reported oesophageal varices in 63 patients (44%) with platelet count  $<1$  lac/ $\mu$ l as predictor of oesophageal varices.<sup>[11]</sup> Zaman et al (1999) reported that groups without varices had a higher mean platelet count (mean platelet count  $1,28,500$ / $\mu$ l) than the group with small varices (mean platelet count  $1,07,800$ / $\mu$ l) and platelet count of  $<90,000$ / $\mu$ l increased the risk of having oesophageal varices by nearly 2.5-fold.<sup>[12]</sup>

**Correlation of grades of oesophageal varices with platelet count:**On correlation of platelet count with grades of oesophageal varices it was evident that 56% patients had their platelet count less than 1 lac/ $\mu$ l out of which 12 patients had grade II varices followed by 7 patients with grade III varices (p value=0.0012; highly significant). These findings suggest that grading of oesophageal varices was inversely correlated with platelet count.

This is in agreement with the findings of a previous study stated that the severity of thrombocytopenia increased as the grading of oesophageal varices increased (Abbasi et al., 2010).<sup>[13]</sup> Similarly, a study conducted in India also had the same results; lower platelet count was significantly associated with large varices (Priyadarshi et al., 2020).<sup>[8]</sup>

Many studies earlier used platelet count along with other non-invasive parameters like platelet count/ spleen diameter ratio, AST Platelet Ratio Index (APRI) to predict the grades of oesophageal varices and need of endoscopy in cirrhotic patients (Kothari et al., 2019).<sup>[14]</sup> It was found that these markers were useful in predicting the grades of oesophageal varices (González-Ojeda et al., 2014; Kothari et al., 2019).<sup>[14,15]</sup> In the present study, platelet count was used as a marker as it is not only non-invasive, but also inexpensive, resource effective, does not need special expertise, and is easily available.

The present study was fraught with some limitations: it was a single center study including all patients of cirrhosis of liver with portal hypertension irrespective of the cause. Only platelet count was used to predict the grade of varices, some studies have shown that platelet count and spleen size ratio is more accurate in predicting the size and grade of varices. Impending or recent bleeding signs like cherry red spots were not included in the study. In future, multicenter studies with specific cause of cirrhosis with portal hypertension, using imminent bleeding signs also along with grades of varices and using platelet count and spleen size ratio are suggested.

### Conclusion

The present study found that there is significant negative correlation between platelet count and grades of oesophageal varices. Low platelet count is associated with higher grades of oesophageal varices. This suggest that platelet count can be used as a predictor to predict the grade of oesophageal varices. The platelet count is a non-invasive parameter with high accuracy for prediction of oesophageal varices. Cirrhotic patients with normal platelet counts (above 150,000), especially in financially deprived developing countries, can avoid screening endoscopy, because they are at low risk for a variceal bleed and presence of large oesophageal varices in these patients is much less common than in those with thrombocytopenia. So, therefore, this parameter can be used in predicting propensity to oesophageal varices non-invasively and thus help in starting prophylactic therapy earlier to prevent bleeding and other complications of varices.

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## References

1. Wong MC, Huang J. The growing burden of liver cirrhosis: implications for preventive measures. *Hepatology international*. 2018 May;12:201-3.
2. Schuppan D, Afdhal NH. Liver cirrhosis. *Lancet*. 2008 Mar 8;371(9615):838-51.
3. Sepanlou SG, Safiri S, Bisignano C, Ikuta KS, Merat S, Saberifiroozi M, et al. The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *The Lancet gastroenterology & hepatology*. 2020 Mar 1;5(3):245-66.
4. Nusrat S, Khan MS, Fazili J, Madhoun MF. Cirrhosis and its complications: evidence based treatment. *World J Gastroenterol*. 2014;20(18):5442.
5. Uong P, Chey V, Unn K, Nov N, Kang K, Un S, et al. Correlation of Platelet Count with Grading of Esophageal Varices in Cirrhotic Patients. *Open Journal of Gastroenterology*. 2023 Jan 9;13(1):12-27.
6. Baig WW, Nagaraja MV, Varma M, Prabhu R. Platelet count to spleen diameter ratio for the diagnosis of oesophageal varices: Is it feasible? *Can J Gastroenterol*. 2008;22(10):825-8.
7. Cherian JV, Deepak N, Ponnusamy RP, Somasundaram A, Jayanthi V. Non-invasive predictors of esophageal varices. *Saudi J Gastroenterol*. 2011;17:64-8.
8. Priyadarshi BP, Khan IK, Kumar V, Verma AK, Midha T, Singh M. Study the association between platelets count and grades of oesophageal varices in patients of cirrhosis of liver with portal hypertension. 2020.
9. Afsar A, Nadeem M, Shah SA, Hussain H, Rani A, Ghaffar S. Platelet count can predict the grade of esophageal varices in cirrhotic patients: a cross-sectional study. *F1000Research*. 2021;10.
10. Chalasani N, Imperiale TF, Ismail A. Predictors of large esophageal varices in patients with cirrhosis. *Am J Gastroenterol*. 1999;94:3285-91.
11. 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 Feb;33(2):333-8.
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 Nov 1;94(11):3292-6.
13. Abbasi A, Butt N, Bhutto AR. Correlation of thrombocytopenia with grading of esophageal varices in chronic liver disease patients. *J CollPhysSurg Pakistan*. 2010;20:369-72.
14. Kothari HG, Gupta SJ, Gaikwad NR, Sankalecha TH, Samarth AR. Role of non-invasive markers in prediction of esophageal varices and variceal bleeding in patients of alcoholic liver cirrhosis from central India. *The Turkish Journal of Gastroenterology*. 2019 Dec;30(12):1036.
15. González-Ojeda A, Cervantes-Guevara G, Chávez -Sánchez M, Dávalos -Cobián C, Ornelas-Cázares S, Macías-Amezcuca MD, et al. Platelet count/spleen diameter ratio to predict esophageal varices in Mexican patients with hepatic cirrhosis. *World J Gastroenterol*. 2014 Feb 28;20(8):2079-84.