

Original Article

Correlation of Severity of Esophageal Varices with Platelet Count in Patients Of Chronic Liver Disease

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Abstract

Objective: The objective of this study was to ascertain if the platelet count of individuals with decompensated CLD and the grading of their esophageal varices were correlated.

Methods: This study used non-probability purposive sampling to undertake a descriptive cross-sectional analysis. There were 150 individuals with decompensated liver cirrhosis in all. Each patient received an endoscopy to grade their esophageal varices, and a platelet count was performed on each one. The spearman's rank-C correlation approach was utilized to establish correlation.

Results: 38.3% of patients with platelets count $< 50,000/\text{mm}^3$ and 61.7% of patients with third grade esophageal varices were found in this group of patients. Of the patients whose platelet counts ranged from 51,000 to 99,000/ mm^3 , 28.1% had second-grade esophageal varices, and 40.6% had third-grade varices. In patients with a platelet count between 100,000 and 149,00/ mm^3 , second- and third-grade esophageal varices affected 17.9% and 23.1% of patients, respectively. With a p-value of less than 0.001, the Spearman's rank correlation test showed a negative relationship between platelet count and esophageal varices' grading.

Conclusion: This research shows a statistically significant negative correlation between the grading of esophageal varices and platelet count. As a result, in scenarios when endoscopic resources are unavailable, the platelet count could serve as a predictor of esophageal varices.

Keywords: Chronic liver disease, WHO Esophageal varices

How to cite this:

Shafi N, Rauf HA, Khan FA, Imran M, Khan I, Qaisar W. Correlation of Severity of Esophageal Varices with Platelet Count in Patients Of chronic liver disease. *J Pak Soc Intern Med.* 2024;5(2): 502-506

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Introduction

Chronic liver disease is defined as abnormal liver function tests that last for more than six months.¹ Ten percent of the world's population, or 500 million individuals, suffer from chronic liver disease, as per the reports of World Health Organization (WHO). Of them, 20 million have liver cirrhosis and/or liver cancer.² Liver cirrhosis is an epidemic in Pakistan and Hepatitis C is its leading cause.³ In Pakistan, an estimated 10 million individuals have contracted Hepatitis C.⁴ Cirrhosis is a stage that many chronic liver disorders reach that is thought to be permanent. Cirrhosis is a life-threatening disease due to its strong association with lethal complications like gastrointestinal bleeding, porto-systemic encephalopathy, ascites, renal failure and hepatocellular carcinoma. Definitive management of cirrhosis usually results in significant reduction in morbidity and mortality which is evident from histological improve-

ment in certain reversible components of cirrhosis with regression of the disease, although complete resolution with a return to pre-disease histological features is improbable.⁵ The immunological response often takes months or years to manifest, during which time tissue repair and inflammation occur concurrently, ultimately resulting in fibrosis and cirrhosis.^{6,7} Three significant consequences associated with portal hypertension include ascites, hypersplenism, and gastro-esophageal varices with hemorrhage.^{8,9} Portal hypertension can result in esophageal varices. The frequency of esophageal varices in patients with cirrhosis stands at 30–70%, with 9–36% having "high-risk" varices. Individuals with cirrhosis experience a 5–8% yearly rate of esophageal varices, however only 1–2% of these individuals have varices big enough to be dangerously bleeding. Every year, between 4 and 30 percent of individuals with tiny varices will acquire big varices, increasing their risk of bleeding.¹⁰ The grading and severity of esophageal varices is asso-

ciated with the severity of CLD, or chronic liver disease. There is a greater likelihood of varices in patients with more severe diseases. 80% of children with Child Class C-CLD will get esophageal varices.^{11,12} All over the world research is going on to find out some non-invasive, cost-effective markers of the varices.¹³ In a retrospective study conducted by Arhip O et al. between 2007 and 2008, 126 patients with primary sclerosing cholangitis (HC) in the CHILD class A were included. The study's findings indicated that in patients with compensated HC, non-invasive prediction cannot rule out the endoscopic exam.¹⁴ The best noninvasive markers to predict esophageal varices (EVs) were thrombocytopenia, splenomegaly, and a fibroscan test. From January 2007 to March 2008, 106 individuals with liver disorders were examined in another research conducted by Sarangapani A et al. Relevant clinical indicators that were evaluated were splenomegaly, ascites, and Child-Pugh class.¹⁵ In addition to ultrasonographic features, laboratory data was also evaluated. There were 41% of cases of major varices. Large varices were independently predicted by multivariate analysis to be present in patients with palpable spleen, low platelet counts, splenic size greater than 13.8 mm, portal vein greater than 13 mm, and splenic vein greater than 11.5 mm. In addition, 110 individuals with cirrhosis were included in research conducted by Tanveer S et al.¹⁶ Based on platelet count, the patients were split into three groups. Groups I and II had platelet counts of less than 50,000/mm³, 100,000/mm³, and 150000/mm³, respectively, and 300,000/mm³. Between 22000 and 385000/mm³ were the different platelet counts. The spleen's average size was 12.53 ± 14 cm, yet it could be anywhere between 9 and 18 cm. Esophageal varices were discovered in 102 individuals. 17 cases were related to grade I varices, 20 to grade II varices, 40 to grade III varices, and 4 cases to grade IV varices. The majority of grade-III (22 patients) and grade IV (3 patients) esophageal varices were seen in patients whose platelet levels were below 50,000/mm³. It has been established that two dependable non-invasive markers of esophageal varices are a large splenic size and a low platelet count. These criteria can also be used to consistently detect large varices. This leads to a higher diagnostic rate of esophageal varices on upper gastrointestinal endoscopy in individuals with cirrhosis who have large spleens and low platelet counts.¹⁶ Abbasi A et al. found in another study that there is an inverse relationship between the severity of esophageal varices and the platelet count ($p < 0.001$, $r = 0.321$).¹⁷ While there is a correlation between low platelet count and EVs, but this correlation is not trustworthy as revealed by the study of Qamar AA et al.¹⁸ Further literature review shows that there is a wide variation in the cutoff level of platelets used in many studies¹⁹, so more studies are needed to find out cost effective reliable means for pre-

diction of high risk EVs. This study will further serve as a primary data source on the subject in our population which is demographically different from western population. Moreover it will suggest platelet count range which can reliably predict the presence of esophageal varices as there is no consensus on this range.

Methods

It is a descriptive cross sectional study that was conducted at the department of Medicine, Gulab Devi hospital Lahore for a period of six months from July 2021 to February 2022. The total sample size estimated 150 cases using 5% type I and 10% type II error taking expected correlation coefficient of platelet count with different grades of esophageal varices in chronic liver disease patients that $r = -0.321$. The sample was selected by adopting non probability purposive sampling. A specific criterion of inclusion was designed and by following that criteria all the patients with decompensated chronic liver disease and patients with thrombocytopenia were included in the study. Meanwhile, all the patients with age above 70 years and below 15 years of age were excluded from the study. Moreover, cancer patients, patients in which endoscopy is contraindicated, and patients with treatment with beta blockers were also excluded.

A total of 150 Cases selected as per the inclusion criteria were registered through Medical ICU, Gulab Devi Hospital, Lahore. Demographic characteristics [including age and sex were taken]. Informed consent was taken in written by patients or by attendants if patients were unable to. Platelet count was sent to the Gulab Devi hospital lab. Platelet count was to be determined by automated method. Patients suitable (according to criteria mentioned) underwent endoscopy. Platelet count of the patients were observed and assessed for the grades of EVs present. All information was collected according to a pre-designed Performa.

All of the gathered data was examined using SPSS version 22.0. Frequency distributions were used to display the qualitative data, which included gender (male or female) and the various grades of esophageal varices. The data was shown as mean and standard deviation for age and platelet count. The spearman's rank C correlation approach was used to establish correlation. The primary outcome was displayed as the correlation coefficient, or "r". A significant P value was defined as one that was less than or equal to 0.05.

Results

In this study, 150 patients with esophageal varices diagnosis were included. Four (2.7%) patients were in the 15–20 age group, eleven (7.3%) in the 21–30 age group, sixty (40%) in the 31–40 age group, fifty-two (34.7%)

in the 41–50 age group, thirteen (8.7%) in the 51–60 age group, and ten (6.7%) in the 61–70 age group. The patients were 42.07 + 10.96 years old on average. The range of ages was 15 to 68 years old (Table 1). Of the patients in the study, 46 (30.7%) were female and 104 (69.3%) were male. As seen in Figure 1, there were 1:2 female to male. The thrombocyte count was below 50,000/mm³ in 47 (31.3%) individuals and between 5,000 and 99,000/mm³ in 64 (42.7%) patients. The range of 100000 – 149000 /mm³ was the thrombocyte count in 39 (26%) patients. 82733.33± 45352.56/mm³ (range 3000 – 149000) was the mean thrombocyte count in the research population (Table 2). Of the 150 patients diagnosed with esophageal varices, 17(11.3%) had grade 0 varices, 26 (17.3%) had grade I varices, 43 (28.7%) had grade II varices, and 64 (42.7%) had grade III varices. Therefore, the patients who were included in the study were all affected by esophageal varices. (Figure 2)

Platelet count and esophageal varices' grades have been correlated. Of the 47 patients with a platelet count < 50000/mm³, grade II esophageal varices were present in 18 (38.3%) and grade III in 29 (61.7%) of the patients. Grade 0 or grade I esophageal varices were absent among the patients. Of the 64 patients whose platelet counts ranged from 51000 to 99000/mm³, 4 (16%) had grade 0 esophageal varices, 16 (25%) had grade II, 18 (28.1%) had grade II, and 26 (40.6%) had grade III. 37 patients (with platelet counts between 100,000 and 149,000/mm³ had esophageal varices of grade 0, 10, 25, 7, and 9 (23.1%) had esophageal varices of grade I, grade II, and grade III. An association between the thrombocyte count and the varices' grading was computed. An inverse relationship between platelet count and grading of esophageal varices was found using Spearman's rank correlation test (r=-0.949). The grading of esophageal varices rose as the platelet count fell, according to a significant connection with a p-value of less than 0.001. (Table 3)

Table 1: Demographic features of study sample (n=150)

Age (years)	No. of patients	Percentage
15-20	4	2.7
21-30	11	7.3
31-40	60	40
41-50	52	34.7
51-60	13	8.7
61-70	10	6.7
Mean ± SD	42.07 ± 10.96	
Range	12-68	

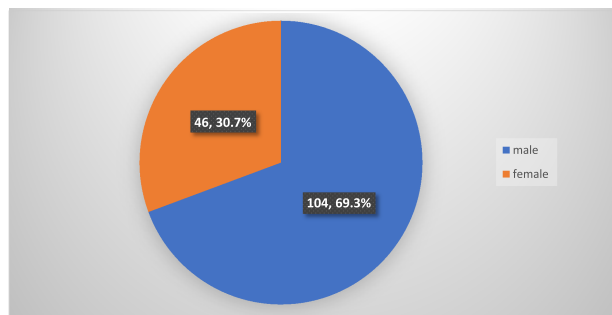


Figure 1: Gender Distribution

Table 2: Distribution of patients mean thrombocyte count (n=150)

Thrombocyte counts (/mm ³)		
Platelet count	No.	%
<50000	47	31.3
51000-99000	64	42.7
100000-149000	39	26
Mean ± SD	82733 ± 45352.56	
Range	30000-149000	

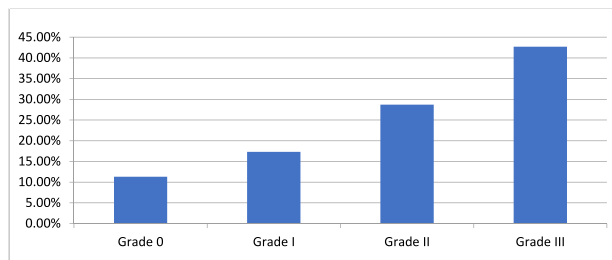


Figure 2: Distribution of patients by grades of thrombocytopenia (n=150)

Table 3: Assessment of relationship between platelet count and grades of esophageal varices

Thrombocyte count (/mm ³)	Severity of Esophageal varices			
	Grade 0 (n=17)	Grade I (n=26)	Grade II (n=43)	Grade III (n=64)
< 50000 (n=47)	0	0	18 (38.3%)	29 (61.7%)
51000 – 99000 (n=64)	4 (6.3%)	16 (25%)	18 (28.1%)	35 (40.6%)
100000–149000 (n=39)	13 (33.3%)	10 (25.7%)	7 (17.9%)	9 (23.1%)
Mean ± SD*	82733.33 ± 45352.56			
r	- 0.949*			
p-value	0.000**			

*Correlation is significant at the 0.01 level (2-tailed)

** Statistically significant (p < 0.05)

Discussion

Significant morbidity and mortality as well as increased hospital care expenses can result from venous gastrointestinal bleeding, a potentially fatal consequence of portal hypertension, particularly in those with chronic liver disease. Chronic liver disease patients frequently have a drop in their thrombocyte count. The primary objective of this investigation was to assess the relationship between the grade of esophageal varices and the platelet count. The findings of this investigation demonstrated an inverse relationship between the grade of esophageal varices and the platelet count. The patients in our study were $42.07 + 10.96$ years old on average. The patients in a local study were 49.49 ± 14.3 years old on average. This indicates that middle-aged individuals made up the majority of those impacted. People may have chronic liver disease at a younger age in poor nations such as Pakistan, where the most common cause is chronic hepatitis B and C infection. It was found in our study that men were impacted more often than women (30.7% vs. 69.3%). Abbasi A. et al.'s study revealed the same thing. Of the study population, 39.2% were female and 60.8% were male. In our research, the average platelet count was $82733.33 + 45352.56/\text{mm}^3$, whereas the mean platelet count in the study conducted by Abbasi A, et al.¹⁷ was $66715.69 \pm 30481.41/\text{mm}^3$. In their study, the mean platelet count was lower than that of ours. However, both of the results showed a lower than normal thrombocyte count. In our study, the range of platelets was $3000 - 320000/\text{mm}^3$ while in study by Tanveer S, et al¹⁶ the platelets were found in a range of 22000 to $385000/\text{mm}^3$. In our study, majority of patients 42.7% were found to be in grade III, then were found in grade II i.e., 28.7%. This pattern was not different in the study by Abbasi A, et al,¹⁷ where majority of the patients presented in grade III (34.3%) and IV (35.2%). In study by Tanveer S, et al,¹⁶ the majority of patients were in grade III i.e. 36.3%, followed by grade II i.e. 22.7. In their study, 15.5% patients were of grade I varices, and the lowest frequency was observed in grade 0 i.e. 3.6%. So, this can be observed that most of the patients presented with grade III in different studies. This may be due to the reason that all of these studies were conducted in tertiary care hospitals. In a developing country like Pakistan, where poverty and health illiteracy are very common, patients usually seek advice from quacks or local doctors. Unfortunately, they usually present very late to the tertiary care units. Therefore, this may be the reason for majority of the patients to be seen with grade III EVs.

In our study, the majority of patients (61.7%) with lowest platelet count ($<50000/\text{mm}^3$) had grade III esophageal varices followed by grade II (38.3%), while none of the patients in this group had esophageal varices of grade

0 or I. In the patients group with platelets count $50000 - 100000/\text{mm}^3$, 68.7% patients fell into esophageal grading II and III. In patients with platelets count $10000 - 150000/\text{mm}^3$ 59% patients had esophageal grading 0 and I. This indicates that the platelet count rises in response to a decrease in the severity of esophageal varices. The Spearman's rank correlation test was used to examine the relationship between the platelet count and the grading of esophageal varices. An inverse connection ($r = -0.949$) was found, indicating that the grading of esophageal varices increased as the platelet count dropped. Abbasi A et al. already came to the same conclusion in a local study: there is an inverse relationship between platelet count and esophageal varices' grading. ($R=0.321, p < 0.001$). This research was not without its limitations. It had a small population size and was single-centered. The reports were all completed at the same laboratory; the tests' dependability was not examined by contrasting the outcomes with those from other labs.

Conclusion

In conclusion, this study concluded that there exists an inverse correlation of platelet count with grading of esophageal varices which is statistically significant. So, the platelet count may be taken as marker for prediction of esophageal varices, where the facilities of endoscopy are not available.

Acknowledgement: The Department of Medicine at Gulab Devi hospital, Lahore and its administration.

Conflict of Interest: *None*

Funding Source: *None*

References

1. Kinoshita N, Shima T, Terasaki K, Oya H, Katayama T, Matsumoto J, Mitsumoto Y, Mizuno M, Mizuno C, Hirohashi R, Sakai K. Comparison of thrombocytopenia between patients with non-alcoholic fatty liver disease and those with hepatitis C virus-related chronic liver disease. *Hepato Res.* 2022; 52(8):677-86.
2. Younossi ZM, Yu ML, El-Kassas M, Esmat G, Castellanos Fernández MI, Buti M, Papatheodoridis G, Yilmaz Y, Isakov V, Duseja A, Méndez-Sánchez N. Severe impairment of patient-reported outcomes in patients with chronic hepatitis C virus infection seen in real-world practices across the world: Data from the global liver registry. *J Viral Hep.* 2022; 29(11):1015-25.
3. Yağanoğlu M. Hepatitis C virus data analysis and prediction using machine learning, *Data & Knowledge Engineering.* 2022; 142:102087.
4. Semmler G, Meyer EL, Kozbial K, Schwabl P, Hametner-Schreil S, Zanetto A, Bauer D, Chromy D, Simbrunner B, Scheiner B, Stättermayer AF. HCC risk stratification after cure of hepatitis C in patients with compensated advanced chronic liver disease, *J Hepatol.* 2022; 76(4): 812-21.

6. Murayama A, Ozaki A, Saito H, Sawano T, Tanimoto T. Are clinical practice guidelines for hepatitis C by the American Association for the Study of Liver Diseases and Infectious Diseases Society of America evidence based? Financial conflicts of interest and assessment of quality of evidence and strength of recommendations. *Hepatology*. 2022;75(4):1052-4.
7. Mazzaro C, Quartuccio L, Adinolfi LE, Roccatello D, Pozzato G, Nevola R, Tonizzo M, Gitto S, Andreone P, Gattei V, A review on extrahepatic manifestations of chronic hepatitis C virus infection and the impact of direct-acting antiviral therapy. *Viruses*. 2021; 13(11): 2249.
8. Chaudhari R, Fouda S, Sainu A, Pappachan JM, Metabolic complications of hepatitis C virus infection, *World J Gastroenterol*. 2021;27(13):1267.
9. Oru E, Trickey A, Shirali R, Kanters S, Easterbrook P, Decentralization integration, and task-shifting in hepatitis C virus infection testing and treatment: a global systematic review and meta-analysis. *Lancet Glob Health*. 2021; 9(4):e431-45.
10. Roudot-Thoraval F. Epidemiology of hepatitis C virus infection. *Clin Res Hepatol Gastroenterol*. 2021; 45(3): 101596.
11. Stuart JD, Salinas E, Grakoui A. Immune system control of hepatitis C virus infection. *Curr Opin Virol*. 2021; 46(1):36-44.
12. Holtzman D, Asher AK, Schillie S, The changing epidemiology of hepatitis C virus infection in the United States during the years 2010 to 2018, *Am J Public Health*. 2021; 111(5):949-55.
13. El-Mowafy M, Elgaml A, El-Mesery M, Sultan S, Ahmed TA, Gomaa AI, Aly M, Mottawea W. Changes of gut-microbiota-liver axis in hepatitis C virus infection. *Biol*. 2021; 10(1):55.
14. Arhip O, Cijevschi-Prelicean C, Manole A, Matei M. Clinical and biological correlations of esophageal varices in patients with compensated hepatic cirrhosis]. *Rev Med Chir Soc Med Nat Iasi*. 2010;114(5):671-6.
15. Sarangapani A, Shanmugam C, Kalyanasundaram M, Rangachari B, Thangavelu P, Subbarayan JK, Saudi Noninvasive prediction of large esophageal varices in chronic liver disease patients. *Gastroenterol*. 2010; 16(1): 38-42.
16. Tanveer S, Khan AQ, Pervez T, Arshad M, Taseer IH, Hepatic cirrhosis association of platelet count, splenomegaly and esophageal varices in patients. *Professional Med J*. 2011;18(3):426-9.
17. Abbasi A, Butt N, Bhutto AR, Munir SM. Correlation of thrombocytopenia with grading of esophageal varices in chronic liver disease patients, *J Coll Physicians Surg Pak*. 2010;20(3):369-72.
18. Qamar AA, Grace ND, Groszmann RJ, Garcia-Tsao G. Platelet count is not a predictor of the presence or development of gastroesophageal varices in cirrhosis†. *Hepatology*. 2008; 47(2): 153-9.
19. Rye K, Scott R, Mortimore G, Lawson A, Austin A, Freeman J. Review Article "Towards Noninvasive Detection of Oesophageal Varices" Liver Unit, Royal Derby Hospital, Uttoxeter Road, Derby DE22 3NE, UK
20. Olariu M, Olariu C, Olteanu D. Thrombocytopenia in Chronic Hepatitis C. *J Gastrointestin Liver Dis*. 2010; 19(2):381-5.