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FREQUENCY AND SEVERITY OF THROMBOCYTOPENIA IN PATIENTS WITH LIVER CIRRHOSIS

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ABSTRACT

Background: Thrombocytopenia is the most prevalent hematological disorder in patients with liver cirrhosis and is often related to portal hypertension, hypersplenism and late-stage liver disease.

Objective: To determine the frequency, severity and clinical correlates of thrombocytopenia in patients with liver cirrhosis.

Methods: The study design was descriptive cross-sectional method conducted in Medical Units I, II and III GIMS, Gambat from January 2025 to June 2025 in General medicine Out Patient Department. The sampling technique was non-probability consecutive sampling with 247 patients with cirrhosis of liver included. Demographic, clinical, laboratory and ultrasound findings were recorded. Thrombocytopenia was defined as platelet count <150,000/mm3, which was divided into mild, moderate and severe grades. Analysis of data was done by SPSS version 26.0.

Results: The mean age of patients was 48.6 ± 12.4 years. Out of 247 patients, 147 (59.5%) were males and 100 (40.5%) were females. Two hundred (81.0%) of these patients had thrombocytopenia. Mild thrombocytopenia was observed in 84 (34.0%), moderate in 81 (32.8%) and severe in 35 (14.2%) patients. Splenomegaly, ascites, esophageal varices, gastrointestinal bleeding, Child-Pugh class C and jaundice were found to be significantly associated with thrombocytopenia. On ultrasound examination, the liver surface was nodular, and the liver echotexture was coarse, with splenomegaly and ascites and portal vein dilatation.

Conclusion: Thrombocytopenia was extremely common in liver cirrhosis and was significantly associated with advanced cirrhosis and complications of portal hypertension.

KEYWORDS: Liver cirrhosis, thrombocytopenia, platelet count, portal hypertension, splenomegaly, ascites.

INTRODUCTION

Liver cirrhosis is a chronic liver disease that is characterised by the progressive diffuse fibrosis of the liver, architectural distortion, portal hypertension and progressive decline in liver function. Thrombocytopenia is one of the common and significant hematological abnormalities in cirrhosis. It can occur early in the course of chronic liver disease and tends to increase in severity as the liver disease progresses and portal hypertension ensues. Recent studies have demonstrated that thrombocytopenia is very common in patients with liver cirrhosis and that the incidence of thrombocytopenia and its severity may differ depending on the stage of the disease, the etiology and clinical complications [1].

Thrombocytopenia in cirrhosis has a multifactorial genesis. The major mechanisms are splenic sequestration as a result of portal hypertension and hypersplenism, decreased production of thrombopoietin by the liver, suppression of bone marrow, immune-mediated platelet destruction, nutritional deficiencies, marrow toxic effect of alcohol, and viral effects in chronic hepatitis. Thrombocytopenia may be caused by more than one of these mechanisms in combination, and thus not only be a laboratory abnormality, but also be a sign of advanced liver disease and systemic involvement [2]. Besides, there are complex modifications of hemostasis, including platelets, coagulation factors, anticoagulant proteins, endothelial function, and fibrinolysis. Thus, the platelet count is far from the whole picture of bleeding risk but severe thrombocytopenia is still a significant clinical issue in everyday management [3].

Thrombocytopenia means practical issues when considering patients with cirrhosis who need to undergo diagnostic or therapeutic procedures such as endoscopy, liver biopsy, paracentesis, central venous access or surgery. Low platelet counts can lead to delays in surgical interventions, need for platelet transfusion, and

challenges in clinical decision making especially if counts are in the severe range [4]. The platelet transfusion has been used traditionally to correct severe thrombocytopenia prior to invasive procedures, however, it has some drawbacks, including the short duration of effect, transfusion reactions, refractoriness, the risk of infection, and limited availability. Thus, recent therapeutic approaches have been the use of thrombopoietin-receptor (TP0XX) agonists in certain patients with chronic liver disease and severe thrombocytopenia who are undergoing elective procedures [5].

Thrombocytopenia remains a difficult periprocedural complication to manage in cirrhosis because various factors influence the risk of bleeding such as type of procedure, severity of liver disease, renal dysfunction, infection, anemia, portal hypertension and overall clinical condition. The current recommendations are that it be individualized risk assessment and not routine correction of all abnormal coagulation parameters [6]. In practice, however, the platelet count remains a valuable and readily available measure of disease severity, procedure-related risk and need for further evaluation or intervention [7].

Important clinical correlates of patients with cirrhosis and a thrombocytopenia include the presence of splenomegaly, ascites, gastrointestinal bleeding, varices, jaundice, coagulopathy and deranged liver function tests. Thus, the presence and degree of thrombocytopenia may be useful in clinicians to detect more advanced disease and more portal-hypertension burden [8]. Furthermore, recently emerging data indicate that, in certain patients, the use of thrombopoietin-receptor agonists (TRAs) can enhance platelet counts and limit the need for platelet transfusion, but must be carefully administered for reasons of thrombosis and cost [9]. Systematic evidence also suggests that agents like lusutrombopag are effective in raising platelets prior to invasive procedures for patients with chronic liver disease and severe thrombocytopenia, further emphasizing the importance of properly characterizing the severity of the thrombocytopenia in these patients [10].

Although often associated with liver cirrhosis, the incidence, severity grading and association of clinical features of thrombocytopenia is not frequently reported in local clinical settings. Understanding thrombocytopenia and its associates can be helpful for clinical recognition of high-risk patients in the earlier stages and for safer management. The present study was designed to assess the incidence, the frequency of occurrence and the clinical association of thrombocytopenia in liver cirrhosis.

METHODS

The study was descriptive cross-sectional study, which was done in Medical Units I, II, III GIMS Gambat and General Medicine Out Patient Department. The study was conducted in a six-month period from January to June 2025.

Sample size was determined using sample size calculator for frequency in a population on OpenEpi. With the expected prevalence of thrombocytopenia in liver cirrhosis patients being 80.7% and 95% confidence level and 5% margin of error, the minimum sample size required was 240. Finally, the patients with liver cirrhosis were selected by non-probability consecutive sampling method and totalled 247 patients.

Patients who were clinically, biochemically, radiologically or endoscopically diagnosed with liver cirrhosis were enrolled in the study regardless of gender. Patients having thrombocytopenia due to causes other than cirrhosis, such as hematological malignancy, aplastic anemia, immune thrombocytopenic purpura, chemotherapy, chronic kidney disease, chemotherapy, or current use of drugs affecting platelet count, were excluded from the study.

Information regarding demographics and clinical details was then collected on a predesigned proforma, after obtaining informed consent. The data collected were age, sex, duration of liver disease, presenting symptoms, clinical findings and associated complications of cirrhosis. Complete blood count, platelet count, liver function test and coagulation profile were checked and analyzed. If available, the radiological findings including splenomegaly and ascites were also documented.

Thrombocytopenia was a platelet count <150,000/microliter. It was then classified as mild, moderate and severe based on platelet count. Mild thrombocytopenia was considered a platelet count of 100,000 to 149,999/mm^3, moderate thrombocytopenia a platelet count of 50,000–99,999/mm^3, and severe thrombocytopenia a platelet count of less than 50,000/mm^3.

The data were coded and analysed using SPSS 26.0. Quantitative variables like age, disease duration, platelet count were expressed as mean and standard deviation. All qualitative variables like gender, severity of thrombocytopenia, clinical symptom, radiological finding, clinical correlate were expressed as frequencies and percentages. Chi square test was used as appropriate to determine association of thrombocytopenia with clinical variable. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 247 patients with liver cirrhosis were included in the study. The mean age of the patients was 48.6 ± 12.4 years. Out of 247 patients, 147 (59.5%) were males and 100 (40.5%) were females. Disease duration was less than five years in 158 (64.0%) patients, while 89 (36.0%) patients had disease duration of five years or more. Hepatitis C was the most common underlying cause of cirrhosis, observed in 139 (56.3%) patients, followed by hepatitis B in 52 (21.1%) patients. According to Child-Pugh classification, 50 (20.2%) patients were in class A, 115 (46.6%) were in class B and 82 (33.2%) were in class C, as shown in **Table 1.**

Table 1: Baseline Demographic and Clinical Characteristics of Patients with Liver Cirrhosis (n=247)

Variable	Frequency / Mean ± SD
Age, years	48.6 ± 12.4
Male	147 (59.5%)
Female	100 (40.5%)
Disease duration <5 years	158 (64.0%)
Disease duration ≥5 years	89 (36.0%)
Hepatitis C-related cirrhosis	139 (56.3%)
Hepatitis B-related cirrhosis	52 (21.1%)
NASH / cryptogenic cirrhosis	35 (14.2%)
Alcohol / other causes	21 (8.5%)
Child-Pugh class A	50 (20.2%)
Child-Pugh class B	115 (46.6%)
Child-Pugh class C	82 (33.2%)

Thrombocytopenia was present in 200 (81.0%) patients, while 47 (19.0%) patients had normal platelet counts. Among the total study population, mild thrombocytopenia was found in 84 (34.0%) patients, moderate thrombocytopenia in 81 (32.8%) patients and severe thrombocytopenia in 35 (14.2%) patients. The mean platelet count was 104.2 ± 45.8 $\times 10^3/\mu L$, as shown in **Table 2.**

Table 2: Frequency and Severity of Thrombocytopenia among Patients with Liver Cirrhosis (n=247)

Platelet Category	Definition	Frequency / Mean ± SD
Normal platelet count	≥150,000/mm³	47 (19.0%)
Overall thrombocytopenia	<150,000/mm³	200 (81.0%)
Mild thrombocytopenia	100,000–149,999/mm³	84 (34.0%)
Moderate thrombocytopenia	50,000–99,999/mm³	81 (32.8%)
Severe thrombocytopenia	<50,000/mm³	35 (14.2%)
Mean platelet count, $\times 10^3/\mu L$	—	104.2 ± 45.8

The association of thrombocytopenia with major clinical correlates was assessed. Splenomegaly was present in 157 (78.5%) patients with thrombocytopenia compared with 14 (29.8%) patients without thrombocytopenia, and this association was statistically significant ($p<0.001$). History of gastrointestinal bleeding, Child-Pugh class C and jaundice were also significantly associated with thrombocytopenia, as shown in **Table 3.**

Table 3: Association of Thrombocytopenia with Major Clinical Correlates in Patients with Cirrhosis

Clinical Correlate	Thrombocytopenia Present n=200	Thrombocytopenia Absent n=47	p-value
Splenomegaly	157 (78.5%)	14 (29.8%)	<0.001
Ascites	119 (59.5%)	14 (29.8%)	<0.001
Esophageal varices	113 (56.5%)	8 (17.0%)	<0.001
History of gastrointestinal bleeding	57 (28.5%)	6 (12.8%)	0.025
Child-Pugh class C	77 (38.5%)	5 (10.6%)	<0.001
Jaundice	86 (43.0%)	12 (25.5%)	0.032

Laboratory parameters showed progressive deterioration with increasing severity of thrombocytopenia. Mean platelet count decreased from 186.5 ± 29.4 $\times 10^3/\mu L$ in patients with normal platelet count to 37.9 ± 8.6 $\times 10^3/\mu L$ in patients with severe thrombocytopenia. Hemoglobin, total leukocyte count and serum albumin showed a decreasing trend with worsening thrombocytopenia, while total bilirubin and INR increased across thrombocytopenia severity groups. These differences were statistically significant, as presented in **Table 4.**

Table 4: Laboratory Profile According to Severity of Thrombocytopenia (n=247)

Laboratory Parameter	Normal n=47	Mild n=84	Moderate n=81	Severe n=35	p-value
Platelet count, $\times 10^3/\mu L$	186.5 ± 29.4	126.8 ± 13.8	73.6 ± 14.2	37.9 ± 8.6	<0.001
Hemoglobin, g/dL	11.8 ± 1.5	10.9 ± 1.7	10.1 ± 1.6	9.6 ± 1.5	<0.001
Total leukocyte count, $\times 10^3/\mu L$	6.9 ± 1.8	6.0 ± 1.6	5.2 ± 1.4	4.8 ± 1.3	<0.001

Total bilirubin, mg/dL	1.8 ± 0.8	2.3 ± 1.0	2.8 ± 1.2	3.4 ± 1.5	<0.001
Serum albumin, g/dL	3.5 ± 0.5	3.1 ± 0.6	2.8 ± 0.5	2.6 ± 0.5	<0.001
INR	1.22 ± 0.18	1.36 ± 0.26	1.55 ± 0.32	1.74 ± 0.41	<0.001

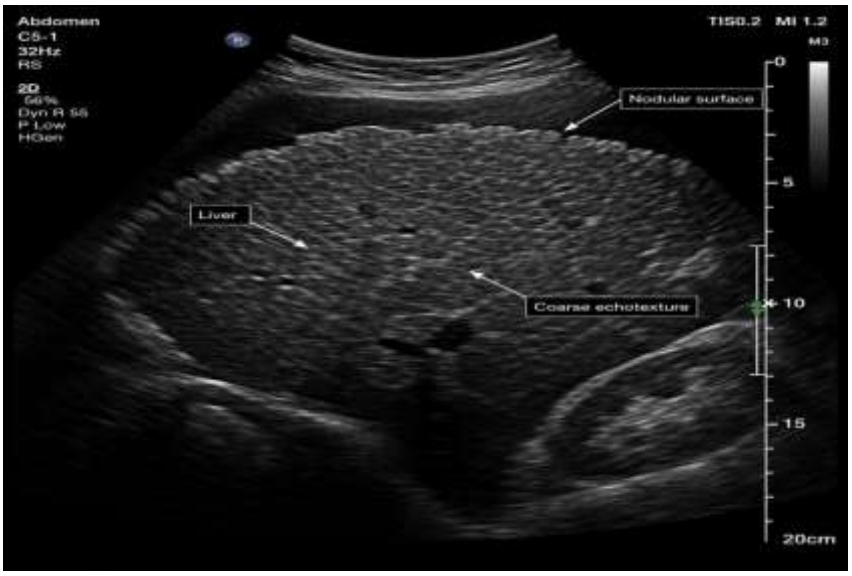

Figure 1: Representative Ultrasound Image of Cirrhotic Liver it shows a cirrhotic liver with coarse hepatic echotexture and an irregular nodular surface. These findings are consistent with chronic liver parenchymal disease and structural distortion due to cirrhosis.

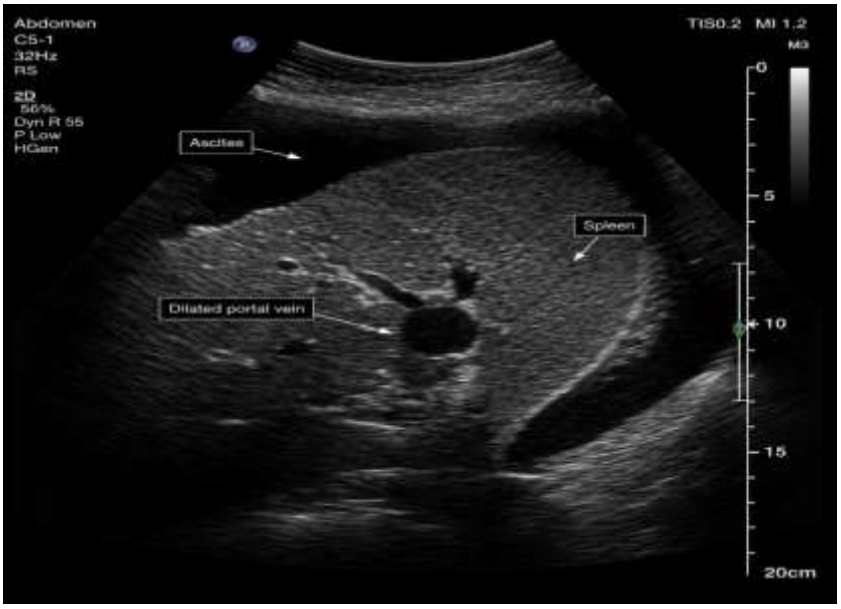

Figure 2: Representative Ultrasound Image of Portal Hypertension-Related Changes; it shows splenomegaly, ascites and a dilated portal vein. These ultrasound findings suggest portal hypertension-related complications in patients with liver cirrhosis.

DISCUSSION

The present study assessed the prevalence, severity and clinical significance of thrombocytopenia in 247 liver cirrhotic patients. Reduced platelet count was a common haematological disorder in cirrhosis, being present in 200 (81.0%) patients with thrombosis. Eighty-four patients (34.0%) had mild, 81 (32.8%) had moderate and 35 (14.2%) had severe thrombocytopenia. These findings confirmed the importance of platelet count as an easily obtainable and simple parameter in cirrhotic patients and suggested that, since thrombocytopenia is often a consequence of portal hypertension, splenic sequestration and advanced liver disease. A study also highlighted the need for recognition of portal hypertension and its clinical manifestations in cirrhosis, as this has a significant impact on prognosis, guiding clinical decisions and planning. [11]. Splenomegaly, ascites, esophageal varices and gastrointestinal bleeding, Child-Pugh class C and jaundice were significant factors associated with

thrombocytopenia in this study. These results indicated a correlation between low platelet count and more severe disease and portal hypertension related complications. This was in keeping with the current advice that conventional coagulation tests should not be used alone in assessing the bleeding and thrombotic risk of patients with cirrhosis. The EASL guidelines also stated that hemostatic abnormalities in cirrhosis are complex and should be understood on the context of the clinical condition of the patient [12].

Thrombocytopenia was frequently observed in the present study, which could be attributed to several factors. These involve hypersplenism as a consequence of portal hypertension, decreased production of thrombopoietin by the diseased liver, bone marrow suppression, immune-mediated platelet destruction and systemic inflammation. Similar mechanisms have also been found in the recent literature on the hematological abnormalities observed in cirrhosis, in which thrombocytopenia is one of the earliest and most frequently observed blood abnormalities in chronic liver disease [13]. Another notable trend in the present study was the severity of the thrombocytopenia. The patients with severe thrombocytopenia had deranged laboratory parameters, such as decreased hemoglobin, decreased leukocyte count, decreased serum albumin and increased INR and bilirubin. This indicated that the more severe the thrombocytopenia, the more severe was the liver dysfunction and the more general was the haematological failure. Although recent guideline reviews have demonstrated that platelet thresholds have evolved over time and that platelet count does not always have to be corrected, severe thrombocytopenia is clinically relevant in patients who are at high-risk and prior to certain procedures [14].

The clinical significance of the association between thrombocytopenia and gastrointestinal bleeding and esophageal varices was also highlighted in this study. While platelet count alone is not the only predictor of bleeding risk in cirrhosis, hypoplaetetism could be suggestive of portal hypertension and advanced cirrhosis, which may be associated with a greater risk of variceal complications. There is recent evidence that cirrhosis is a rebalanced, but fragile, hemostatic state and that patients may develop bleeding or thrombosis depending on the type of clinical stressors, infection, renal dysfunction, severity of disease and procedure-related factors [15]. Bleeding associated with procedures is a significant concern in the cirrhotic who have a platelet count low. A significant number of patients in the current study were moderately to severely thrombocytopenic, and this could impact upon the approach to endoscopy, biopsy, paracentesis or surgery. Another large prospective multicentre study found that the bleeding risk in hospitalized patients with liver disease was associated with several clinical parameters and not only with an abnormal platelet count and coagulation profile. This will help justify the importance of thorough clinical evaluation than reflexively correcting any lab abnormality [16].

The results of ultrasound obtained in this study also confirmed association between thrombocytopenia and portal hypertension. All patients displayed coarse hepatic echotexture, with nodular liver surface, splenomegaly, ascites, portal vein dilatation and portosystemic collaterals being all frequent. These sonographic findings are characteristic of a chronic liver disease with portal hypertension. Recent reviews have also discussed that other hematological abnormalities and structural problems of chronic liver disease are frequently associated with thrombocytopenia in cirrhosis [17]. In the current study, the portal hypertension-related ultrasound parameters were correlated with the degree of thrombocytopenia. Splenomegaly, ascites, portal vein dilatation and portosystemic collaterals were more common in those with severe thrombocytopenia. The significance of this is that low platelet count might be useful for selecting patients who should be carefully screened for varices and complications of portal hypertension. Recent studies have also demonstrated that thrombocytopenia can impact outcomes in cirrhotic patients with acute variceal bleeding, and can be linked to the failure of endoscopic management of variceal bleeding in high-risk groups [18].

The results have implications for management. In patients with cirrhosis and thrombocytopenia, the platelet count should be the first step in assessing a patient's risk for bleeding, but should also be accompanied by assessment of disease severity, portal hypertension, bleeding history, renal function and infection risk and plans for procedures. There is also expert consensus that thrombocytopenia in cirrhosis should be managed in a structured manner and that severity of the platelet count should be determined, bleeding risk assessed and that therapeutic options should be used in appropriate patients with selected measures [19]. The results of this study were also in favor of the pathophysiological association of thrombocytopenia, portal hypertension and chronic liver disease. As cirrhosis progresses, splenic sequestration, decreased thrombopoietin production, and systemic mechanisms may all contribute to decreasing the platelet count. Thus, it is important to note that thrombocytopenia could be an important clinical and laboratory marker, not only for the presence of hematological disturbance, but also for the burden of portal hypertension in the cirrhotic patient [20].

Limitations of study: There were shortcomings in this study. The study was descriptive, cross-sectional, and single center, therefore no causal relationships could be determined. Mock/discrete clinical categories were employed and long-term follow-up of bleeding events or mortality/ treatment response was not conducted. Additionally, advanced non-invasive markers of portal hypertension, and thrombopoietin levels were not evaluated. These results should be confirmed by further multicentre studies using a larger number of patients. The strong point of this study was that the number of patients with liver cirrhosis in medical units and OPD was clinically relevant (247 patients). In addition to the incidence and severity of thrombocytopenia, its association with clinical, laboratory and ultrasound findings was evaluated. Future studies should involve follow-up of the patients to see if thrombocytopenia is a predictor of variceal bleeding, bleeding at the procedure, decompensation or death. Routine platelet assessment should be used along with ultrasound findings and clinical severity scores for better risk categorisation in cirrhotic.

CONCLUSION

Thrombocytopenia was very common in patients with liver cirrhosis, was often mild to moderate, and a small but clinically significant number of patients had severe thrombocytopenia. This was significantly correlated with splenomegaly, ascites, esophageal varices, gastrointestinal bleeding, Child-Pugh class C, jaundice and abnormal ultrasound findings. These results ended up determining that thrombocytopenia was a significant clinical indicator of complications related to portal hypertension and advanced cirrhosis.

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