

## ORIGINAL ARTICLE

# A STUDY OF THROMBOCYTOPENIA IN CHRONIC LIVER DISEASE AND ITS CORRELATION WITH DEVELOPMENT OF ESOPHAGEAL VARICES

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### Abstract:

**Background:** The aim and objective of this study was to evaluate relationship of platelet count and esophageal varices in chronic liver disease (CLD) admitted in the medicine unit and gastroenterology department of Dhaka Medical College Hospital. **Methods:** In this cross-sectional study, a total number of 100 randomly selected, clinically diagnosed patients of chronic liver disease were studied from June 2010 to November 2010 (6 months). All patients were assessed as per Child-Pugh class and had full blood count, HBsAg, Anti-HCV antibodies by ELISA, abdominal ultrasound and Endoscopy of upper gastrointestinal tract. Patients were divided into Group A (Platelet count <1,50,000) and Group B (platelet count>1,50,000). **Result:** 73 male (73%) and 27 female patients (27%) with age range of 16 to 75 years were evaluated. 24% patient were in between 45-55 years age group. 63% patient fall in child Pugh class A group, 32% fall in child Pugh class B & 5% fall in child Pugh class C. Esophageal varices were present in 32 patients (32%) and absent in 68 patients (68%). Group A had 31 patients (31% of the total) with 26 patients (83.87%) having esophageal varices. Group B had 69 patients (69% of the total) with 6 patients (8.70%) having esophageal varices. Sensitivity of thrombocytopenia as a marker of esophageal varices was 81.25% and specificity 92.64%, positive predictive value 83.87% and negative predictive value 91.3% and Odds ratio was 54.6. P value is <0.001. **Conclusion:** In this study, It was attempted to find out the relationship between thrombocytopenia and esophageal varices in CLD. In Group A that is platelet count <1,50,000, the incidence of EV was more than Group B (platelet count >1,50,000). Hence, thrombocytopenia is a good surrogate marker for the presence of esophageal varices in CLD.

**Key words:** Chronic liver disease, thrombocytopenia, esophageal varices.

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**Introduction:**

Chronic liver disease (CLD) is a common clinical problem in Bangladesh. Chronic liver disease is the tenth leading cause of death in adults with HBV and HCV being the most important underlying causes.<sup>1</sup> HBV infects nearly 350 million people worldwide. Of them 75-80% reside in Asia and Western Pacific. HBV is responsible for over 1 million deaths per year globally. CLD can occur at any age & often causes prolonged morbidity & an important cause of premature death. Chronic liver disease in the clinical context is a disease process of the liver that involves a process of progressive destruction and regeneration of the liver parenchyma leading to fibrosis and cirrhosis. Clinical features of cirrhosis derive from the morphologic alterations and often reflect the severity of hepatic damage rather than underlying liver disease. Fibrosis and distorted vasculature lead to portal hypertension and its sequel, including gastroesophageal varices and splenomegaly.

The patient whom we come across in the hospital ward is mostly in advanced stage with overt clinical manifestation and/or complication. Among them most important life threatening complication is vomiting out of blood (haematemesis) and malaena due to ruptured esophageal varices. Esophageal variceal bleeding is one of the most dreaded complications of chronic liver disease because of its high mortality. Variceal bleeding often occurs without obvious precipitating factor and usually presents with painless but massive hematemesis with or without malaena.<sup>2</sup> The prevalence of varices in patients with CLD is approximately 60-80% and the risk of bleeding is 25-35%. The incidence of esophageal varices (EVs) increases by nearly 5% per year, and the rate of progression from small to large varices is approximately 5 to 10 % per year<sup>3</sup>. The presence of gastroesophageal varices correlates with the severity of liver disease. The severity of cirrhosis can be scored using the Child-Pugh classification system. Pathogenesis of thrombocytopenia in case of chronic liver disease includes productive, consumptive or distributional mechanisms. Low platelet count can be explained by hypersplenism involved in the disease process. In the presence of portal hypertension, as much as 90% of the circulating thrombocytes are sequestered in the spleen, leading to a significant reduction in the circulating platelet count.

Thrombocytopenia (platelet count <150,000/microL) is also a common complication in patients with chronic liver disease (CLD) that has been observed in up to 76% of patients. Moderate thrombocytopenia (platelet count, 50,000/microL-75,000/microL) occurs

in approximately 13% of patients with cirrhosis.<sup>4</sup> Thrombocytopenia is an important predictor of esophageal varices in patients with chronic liver disease.<sup>5</sup> Garcia-Tsao et al in 1997 (180 patients), Pilette et al in 1999 (116 patients) and K. C. Thomopoulos et al in 2009 (184 patients) reported a low platelet count to be an independent risk factor for the presence of varices.<sup>7,8</sup>

The American Association for the Study of Liver Disease and the Baveno IV Consensus Conference on portal hypertension was held on April 10-11, 2015, Milan, Italy recommended that all patients having chronic liver disease should be screened for the presence of Esophageal varices<sup>9</sup>. Other investigators recommend 2-yearly endoscopy for patients with no varices and yearly endoscopy for patients with known small varices<sup>10</sup>. Investigators have attempted to identify characteristics that noninvasively predict the presence of varices. These studies have shown that biochemical, clinical, and ultrasonographic parameters alone or together have good predictive power for noninvasively assessing the presence of EV. Overall, the most common result of these studies was that parameters such as splenomegaly, thrombocytopenia, Childs Turcotte Pugh score, ascites, portal flow patterns, and platelet count—splenic size ratio were predictors for the presence of esophageal varices.

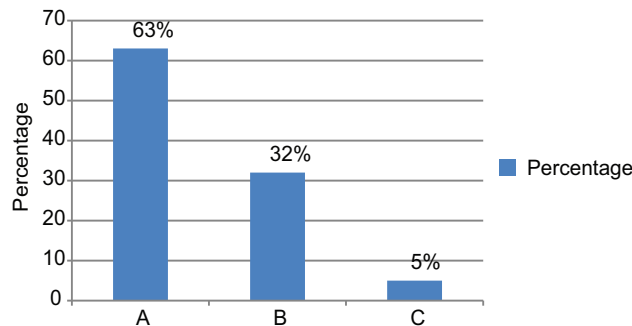
**Methods:**

In this cross-sectional study, a total number of 100 randomly selected, clinically diagnosed patients of chronic liver disease were studied for a period of June 2010 to November 2010 (6 months) at medicine units and gastroenterology department of Dhaka Medical College Hospital. All patients were assessed as per Child-Pugh class and had full blood count, HBsAg, Anti-HCV antibodies by ELISA, abdominal ultrasound and Endoscopy of upper gastrointestinal tract. Exclusion criteria were patients receiving sclerotherapy, band ligation of EV and prophylactic treatment for portal hypertension, patient with thrombocytopenia due to other cause (infective / hematological) evidenced by clinically and supporting investigations. This study was carried out to correlate between platelet and EV in CLD. Patients were divided into Group A (Platelet count <1,50,000) and Group B (platelet count >1,50,000). Statistical analysis was carried out by using SPSS v16.0 Windows statistical software. Descriptive statistics were used for the interpretation of the findings. Informed and written consent obtained from all patients or their guardian. Formal Ethical Clearance was obtained from the Research Review Committee of Dhaka Medical College and Hospital.

**Results:**

Seventy-three male (73%) and twenty seven female patients (27%) with age range of 16 to 75 years were evaluated. Out of 100 patients 24% were in between 46-55 years age group. 75% of CLD were due to Hepatitis B, 7% due to Hepatitis C, 18% due to others. 32% patients have EV and 68% patients do not have EV.

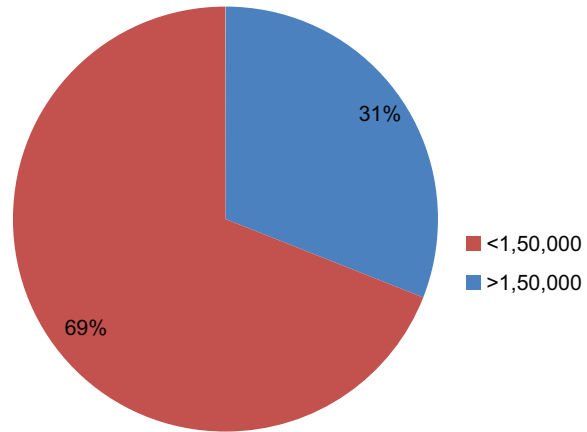
Figure-1 shows that majority of CLD patients 63% fall in child Pugh class A group, followed by 32% fall in child Pugh class B & 5% fall in child Pugh class C.



**Fig.-1:** Distribution of CLD patients in Child Pugh class.

Fig.-2 This figure shows that 31% of CLD patient have thrombocytopenia & 69% have not.

Table-I shows among 100pts of CLD pts 63 pts (63%) were in Child Pugh class A from which 74.60% have no varices. 32 pts (32%) were in Child Pugh class B from which 62.5% have no varices. 5pts (5%) were in



**Fig.-2:** Prevalence of thrombocytopenia in CLD patients.

Child Pugh class C from which 40% have Grade II varices.

Table-II shows that in group A 83.87% have EV while in group B only 8.70% have EV, So EV is more in group A in CLD patients. This Table shows P value is <0.001 that is association between thrombocytopenia and Esophageal varices is significant. The following table shows P value is <0.001 i.e association between thrombocytopenia & esophageal varices is significant. Sensitivity 81.25%, Specificity 92.64%, Positive predictive value(PPV) 83.87%, Negative predictive value(NPV) 91.30%, Odds ratio 54.6

**Table-I**

*Gradings of EV in different Child Pugh class*

Child Pugh class	NO EV (%)	Grade I (%)	Grade II (%)	Grade III (%)	Grade IV (%)	Total (%)
A	47(74.60)	8 (12.69)	5 (7.93)	1 (1.58)	2 (3.17)	63 (100)
B	20 (62.5)	2 (6.25)	1 (3.13)	2 (6.25)	7 (21.87)	32 (100)
C	1 (20)	0 (0)	2 (4)	1 (20)	1(20)	5 (100)
Total (%)	68 (68)	10 (10)	8(8)	4(4)	10(10)	100

**Table-II**

*Frequency of Esophageal varices in group A & group B in Chronic Liver Disease pts*

Platelet count	EV Present (%)	EV Absent (%)	Total(%)	P Value
Group A(<1,50,000)	26 (83.87)	5(16.13)	31(31)	
Group B(>1,50,000)	6(8.70)	63(91.30)	69(69)	<0.001
Total	32	68	100	

**Discussion:**

In this study all the patients were grouped in six age groups. Majority of the study subjects were in between 46-55 years age group 24% followed by 23% between 36-45 years age group. Pilette C et al in 1999 found 28% in between 46-55 years age group which coincide with our study.<sup>10</sup> 73% were male and 27% female. Male female ratio was 2.7:1. Mahtab et al<sup>11</sup> found male female ratio of 2.97:1, which almost coincide with our study. In this study 63% patient fall in child Pugh class A group, 32% fall in child Pugh class B & 5% fall in child Pugh class C. This study almost coincide with the study of Khan H et al<sup>5</sup> where 70.1% patient fall in child Pugh class A group, 24.9% patient fall in child Pugh class B group, 5.1% patient grouped in child Pugh class C group. Present study shows that 32% of CLD patients have EV & 68% patients did not have EV. Schepis et al found<sup>12</sup> 80 pt (55.9%) have EV, 63 pt (44.05%) did not have. This difference may be due to sample size and etiological difference.

In child pugh class A pts, 16pts out of 63 pts (25.40%) have varices among them 8 pts (12.69%) have grade I, 47 pts (74.60%) have no varices. In child pugh class B pts, 12pts out of 32 pts (37.50%) have varices among them 7 pts (21.88%) have grade IV, 20 pts (62.5%) have no varices. In child pugh class C pts, 4 pts out of 5 (80%) have varices among them 2 pts (4%) have grade II, 1 pt (20%) have no varices.

Our study shows that (Fig 3.8) 31 patients out of 100(31%) have thrombocytopenia (platelet count <1,50,000 –Group A) & 69 patient(69%) had platelet count >1,50,000(Group B). Among Group A (n=31), 26 patients (83.87%) have EV & 5 patient (16.13%) have no EV. Among Group B (n=69), 6 patient had EV (8.70%), while 63 patient (91.30%) have not (Table 3.17). Khan H et al<sup>8</sup> found thrombocytopenia in 57 patients (28.9%) out of 197 patients. Among them 51 patients (89.47%) have EV, while 140 patients (71.1%) had platelet count >1,50,000 with 12 having EV(8.57%).. Mohammad Khuram et al in (200 patients) found EV in 146 with 121 having thrombocytopenia (94.5%).<sup>13</sup> In our study is consistent with the previous studies that reported a low platelet count to be an independent risk factor for the presence of varices<sup>9,10</sup>

From this study, platelet count <1,50,000 is 81.25% sensitive & 92.64% specific for presence of EV with positive predictive value of 83.87% & negative predictive value of 91.3% and odds ratio is 54.6 & P value is <0.001(Table 3.18). This study almost coincide with the study of Khan H et al<sup>6</sup> which shows that platelet count <1,50,000 is 80.95% sensitive & 95.5% specific predictor of EV with positive predictive value of 89.47% and negative predictive value of 91.43%

and odds ratio of 90.67. Sarangapani et al<sup>3</sup> reported that platelet count <1,50,000 is 72.5% sensitive & 75% specific predictor of EV with positive predictive value of 63.8% & negative predictive value of 70.5%. In retrospective analysis of 143 patients with compensated cirrhosis, reported EV in 63 patients (44%) with platelet count of <100 x10<sup>9</sup>/L as predictor of EV<sup>12</sup>. Most of these studies did not have aetiologically uniform patient population. The limitations of the study were retrospective analysis and inclusion of liver transplant patients only.

Specificity of 95.5% and PPV of 89.47% suggest that thrombocytopenia is a good indicator of EV. However low sensitivity of thrombocytopenia & NPV of 91.3% indicates that absence of thrombocytopenia does not rule out EV.

**Conclusion:**

Patients with chronic liver disease frequently undergo endoscopy of upper GIT to detect EV. Doing endoscopy in all patients of CLD will increase socioeconomic and medical load because of the rising numbers of such patients. Therefore, there is a particular need for a noninvasive predictor for the presence of EV to ease the medical, social and economic burden of the disease. Many previous studies have documented good predictive value of various non-endoscopic variables for the presence or absence of varices, but available data in our country is limited. We consider simple, commonly available parameter platelet. From this study it is assumed that thrombocytopenia is a good non-endoscopic marker for the presence of esophageal varices.

**Conflict of Interest:**

The author stated that there is no conflict of interest in this study

**Funding:**

No specific funding was received for this study.

**Ethical consideration:**

The study was conducted after approval from the ethical review committee. The confidentiality and anonymity of the study participants were maintained

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