

# Diagnostic Accuracy of Thrombocytopenia and Fib 4 Score in Predicting Esophageal Varices Using Endoscopy as Gold Standard Among Patients with Chronic Liver Disease

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## ABSTRACT

**Objective:** To assess diagnostic accuracy of thrombocytopenia and Fib 4 Score in predicting esophageal varices using endoscopy as gold standard among patients with chronic liver disease.

**Study Design:** Descriptive cross sectional study.

**Place and Duration of Study:** This study was conducted at the Study was conducted at advanced GI & Liver Tower, hospital, Multan, from 15-09-2022 to 15-06-2023.

**Methods:** A total of 377 patients with chronic liver disease aged between 20-60 years were included. Three ml of venous blood sample was drawn and sent to the Central laboratory of the hospital for platelet count and other biochemical tests. The FIB-4 score was calculated for all patients and endoscopy was carried out for all enrolled patients to visualize esophageal varices.

**Results:** Mean age of these patients with CLD was  $46.20 \pm 7.80$  years (range; 33 years to 60 years) and 232 (61.5%) were male patients. Grade 1 esophageal varices were noted in 67 (17.8%), grade 2 in 181 (48.0%), grade 3 in 40 (10.6%). Sensitivity of thrombocytopenia was 38.89%, Specificity was 75.53%, PPV was 84.85%, NPV was 28.16% and Diagnostic Accuracy was 48.01%. For FIB score  $>3$ , Sensitivity was 34.03%, Specificity was 78.65%, PPV was 83.76%, NPV was 26.92% and Diagnostic Accuracy was 44.56%.

**Conclusion:** Thrombocytopenia and FIB score  $>3$  revealed good diagnostic accuracy in predicting esophageal varices in CLD patients. These are simple tests which can be easily employed by treating physicians to anticipate disease severity in these patients.

**Key Words:** Chronic Liver disease, Diagnostic Accuracy, Esophageal varices, Endoscopy.

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## INTRODUCTION

Chronic liver injury stemming from various sources can lead to irreversible scarring of the liver, a condition known as cirrhosis<sup>1,2</sup>. Cirrhosis, a progressive liver ailment, is characterized by fibrosis brought about by prolonged liver damage. Liver fibrosis not only impairs liver function but also leads to structural changes, resulting in portal hypertension<sup>3</sup>.

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Therefore, it is of paramount importance to appropriately manage these patients, both in the hospital and outpatient settings, in order to enhance their overall well-being and reduce mortality<sup>4,5</sup>. While histopathology has historically been regarded as gold standard for evaluating liver fibrosis, it has now been largely supplanted by certain non-invasive procedures<sup>6,7</sup>. Biochemical noninvasive scores offer a significant advantage in assessing liver fibrosis due to their widespread availability at a low cost and ease of use. However, the utilization of TE-LS measurements is limited, primarily due to technical and practical issues as well as its high cost<sup>8,9</sup>. In contrast, APRI and FIB-4 scores have proven to be fairly reliable in assessing liver fibrosis. Nonetheless, further validation in diverse patient populations is still necessary<sup>10</sup>.

Thrombocytopenia, characterized by a low platelet count (less than 150,000/  $\mu$ L), remains one the commonest derangements in individuals with chronic liver disease<sup>11</sup>. The precise causes of thrombocytopenia among patients with liver diseases are multifaceted and encompass lower synthesis of thrombopoietin, appropriation of platelets in the spleen and

myelosuppression of platelet synthesis induced by the hepatitis C virus (HCV) <sup>12</sup>. Thrombocytopenia is a common blood disorder among those with chronic liver disease, and its severity is chiefly influenced by the extent of liver disease. Due to the increased risk of bleeding associated with thrombocytopenia, it can have implications for medical procedures such as surgery or liver biopsy. An Egyptian study has documented 39 % sensitivity, 82 % specificity, 72 % PPV, 54 % NPV and accuracy of 59 % with platelet count more than 149000 while FIB – 4 score (cut off value of 3.175) sensitivity was 78.4%, 45 % specificity, 78.4 % PPV, 45.7 % NPV and 61 % accuracy for EV in cirrhotic patients <sup>13</sup>.

We decided to perform this study to determine the role of platelet counts and FIB 4 score in chronic liver disease patients as early diagnosis of such cases remains cornerstone of the proper management to improve prognosis. The results will help clinicians for early diagnosis and timely management of esophageal varices.

## METHODS

This descriptive Cross Sectional Study was conducted at advanced GI & Liver tower, Multan from 15-09–2022 to 15-06-2023. Sample size was 377 patients with CLD calculated using PASS 11 formula. Targeted significance level is 0.05 and prevalence of esophageal varices is 79%. A total of 377 patients with chronic liver disease aged between 20-60 years were included. Patients with Chronic lung diseases e.g. COPD and ILD, Cardiac patients (e.g. Valvular heart disease and congenital heart disease), HCC patients (arterial phase enhancement and wash out in venous phase on triphasic CT scan), Pulmonary embolism, connective tissue disease were excluded from this study. Basic demographics (age, gender, and duration of disease, grades of esophageal varices, residential status, and obesity) was noted. All baseline tests like LFTs, complete blood count and FBS. Once registered, 3 ml

of venous blood sample was drawn and sent to the Central laboratory of the hospital for platelet count and other biochemical tests. The FIB-4 score was calculated for all patients and endoscopy was carried out for all enrolled patients to visualize esophageal varices.

Statistical analysis was done using computer program (SPSS version 25) to determine Frequencies and percentage for gender, diabetes, age groups, grades of esophageal varices, thrombocytopenia and smoking. Mean  $\pm$  SD was presented for quantitative variables like age, FIB–4 score, platelet count and duration of disease. Sensitivity, specificity, PPV, NPV and diagnostic accuracy were calculated for platelet count, FIB–4 and endoscopy with 95% CI taking as gold standard.

## RESULTS

Of these 377 CLD patients, 232 (61.5 %) were male patients while 145 (38.5 %) were female patients. Mean age of these patients with CLD was  $46.20 \pm 7.80$  years (range; 33 years to 60 years). Mean age of the male patients was  $46.11 \pm 6.56$  years versus  $46.34 \pm 9.48$  years for female patients ( $p=0.779$ ) and 276 (73.2 %) were aged more than 40 years. Of these 377 CLD patients, 244 (64.7 %) belonged to urban areas and 303 (80.4%) were middle income. Diabetes was present in 59 (15.6%) while 117 (31%) were hypertensive. Mean disease duration was  $4.23 \pm 2.88$  years and 59 (15.6%) were smokers. Thrombocytopenia was noted in 132 (35.0%) and FIB score more than 3 was noted in 117 (31.0%) while endoscopy results revealed esophageal varices in 288 (76.4%). Grade 1 esophageal varices were noted in 67 (17.8%), grade 2 in 181 (48.0%), grade 3 in 40 (10.6%).

Sensitivity of thrombocytopenia was 38.89%, Specificity was 75.53%, PPV was 84.85%, NPV was 28.16% and Diagnostic Accuracy was 48.01%. For FIB score  $>3$ , Sensitivity was 34.03%, Specificity was 78.65%, PPV was 83.76%, NPV was 26.92% and Diagnostic Accuracy was 44.56%.

**Table No. 1: Stratification of esophageal varices with thrombocytopenia with regards to gender. (n = 377)**

Gender	Thrombocytopenia	Esophageal varices on endoscopy		P – value
		Yes (n=288)	No (n=89)	
Male (n=232)	Yes (n=57)	55(TP)	02 (FP)	<b>0.001</b>
	No (n=175)	126 (FN)	49 (TN)	
Female (n=145)	Yes (n=75)	57(TP)	18 (FP)	<b>0.574</b>
	No (n=70)	50 (FN)	20 (TN)	

Gender	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
Male	30.39	96.08	96.49	28.0	44.83
Female	53.27	52.63	76.0	28.57	53.10

**Table No. 2: Stratification of esophageal varices with thrombocytopenia with regards to age. (n = 377)**

Age	Thrombocytopenia	Esophageal varices on Endoscopy		P – value
		Yes	No	
Up to 40 (n=101)	Yes (n=60)	57 (TP)	03 (FP)	0.001
	No (n=41)	25 (FN)	16 (TN)	
More than 40 (n=276)	Yes (n=72)	55 (TP)	17 (FP)	0.756
	No (n=204)	151(FN)	53 (TN)	

Age	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
Up to 40	69.51	84.21	95.00	39.02	72.28
>40	26.70	75.71	76.39	25.98	39.13

**Table No. 3: Stratification of esophageal varices with FIB score >3 with regards to gender. (n = 377)**

Gender	FIB>3	Esophageal varices on Endoscopy		P – value
		Yes	No	
Male (n=232)	Yes (n=202)	84 (TP)	18 (FP)	0.201
	No (n=130)	97 (FN)	33 (TN)	
Female (n=145)	Yes (n=15)	14 (TP)	01 (FP)	0.117
	No (n=130)	93 (FN)	37 (TN)	

Gender	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
Male	46.41	64.71	82.35	25.38	50.43
Female	13.08	97.37	93.33	28.46	35.17

**Table No. 4: Stratification of esophageal varices with FIB score >3 with regards to age. (n = 377)**

Age	FIB >3	Esophageal varices on Endoscopy		P – value
		Yes	No	
Up to 40 (n=101)	Yes (n=45)	43 (TP)	02 (FP)	0.002
	No (n=56)	39 (FN)	17 (TN)	
More than 40 (n=276)	Yes (n=72)	55 (TP)	17 (FP)	0.755
	No (n= 204)	151 (FN)	53 (TN)	

Age	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
Up to 40	52.44	89.47	95.56	30.36	59.41
>40	26.70	75.71	76.39	25.98	39.13

## DISCUSSION

Thrombocytopenia and the FIB-4 score are commonly used tools to assess the severity and prognosis of chronic liver disease. However, their diagnostic

accuracy can vary depending on the specific liver disease in question and the population being studied. In the context of chronic liver disease, it often occurs due to decreased platelet production in the bone marrow and increased spleen sequestration of platelets, both of

which are associated with liver dysfunction. The diagnostic accuracy of thrombocytopenia in chronic liver disease is variable, and it is typically used in combination with other clinical and laboratory parameters for a more comprehensive assessment<sup>14</sup>. The FIB-4 score is a non-invasive scoring system used to assess liver fibrosis, specifically in patients with chronic hepatitis C. It incorporates age, platelet count, and liver enzyme levels (AST and ALT) to estimate the degree of fibrosis in the liver. The FIB-4 score is primarily used to identify patients with hepatitis C who have advanced fibrosis or cirrhosis and may need treatment. It is not as useful for assessing fibrosis in other forms of chronic liver disease. Its diagnostic accuracy can vary based on the specific population and disease under consideration, but it is generally considered a valuable tool for risk stratification<sup>15</sup>.

Of these 377 CLD patients, 232 (61.5%) were male patients while 145 (38.5%) were female patients. Park et al<sup>15</sup> from Korea has reported 52.5% male gender predominance in these patients in a multicenter study conducted in 6 major Asian hospital of Korea, Japan and Taiwan. A Multicenter study conducted in Sargodha, Peshawar and Muzaffarabad has also documented 52% male patients with chronic liver disease<sup>16</sup>. A study from Swat conducted by Ahmed et al<sup>17</sup> has also reported 60.35% male patients with chronic liver disease. Akram et al<sup>18</sup> from Bahawal Victoria Hospital has reported 54.2% male patients presenting with chronic liver disease, similar to our findings. A study from Peshawar conducted by Naim et al<sup>19</sup> also reported 69.9% male patients presenting with chronic liver disease, close to our findings.

Mean age of our study cases was  $46.20 \pm 7.80$  years (range; 33 years to 60 years). Mean age of the male patients was  $46.11 \pm 6.56$  years versus  $46.34 \pm 9.48$  years for female patients ( $p=0.779$ ) and 276 (73.2%) were aged more than 40 years. Park et al<sup>15</sup> from Korea has reported  $46.1 \pm 16.1$  years mean age in these patients in a multicenter study conducted in 6 major Asian hospital of Korea, Japan and Taiwan. A Multicenter study conducted in Sargodha, Peshawar and Muzaffarabad has also documented  $56.6 \pm 7.9$  years mean age of the patients with chronic liver disease, similar to our results<sup>16</sup>. A study from Swat conducted by Ahmed et al<sup>17</sup> has also reported 68.1% patients with chronic liver disease were aged up to 45 years, similar to our findings. A study from Peshawar conducted by Naim et al<sup>19</sup> also reported  $43.30 \pm 8.00$  years mean age of these patients, close to our findings. Akram et al<sup>18</sup> from Bahawal Victoria Hospital has reported  $53.69 \pm 7.11$  years mean age of the patients presenting with chronic liver disease while 58.5% were aged 40–55 years of age, similar to our findings.

Of these 377 CLD patients, 244 (64.7%) belonged to urban areas and 303 (80.4%) were middle income. Diabetes was present in 59 (15.6%) while 117 (31%)

were hypertensive. A study conducted in Netherland Wlazlo et al<sup>20</sup> has reported 37% diabetes in patients with liver cirrhosis. A study conducted by Zein et al<sup>21</sup> from USA has documented 25% diabetes in liver cirrhosis which is close to our study results. Almani et al<sup>22</sup> has reported 42% hypertension in liver cirrhosis which is in compliance with our study results. Mean disease duration was  $4.23 \pm 2.88$  years and 59 (15.6%) were smokers. Akram et al<sup>18</sup> from Bahawal Victoria Hospital has reported  $10.49 \pm 3.48$  months mean duration of disease which is quite lower than that of our findings.

The diagnostic accuracy of thrombocytopenia and the FIB-4 score in chronic liver disease can be variable, and their utility may depend on the specific context and liver disease etiology. Healthcare providers often use a combination of clinical, laboratory, and imaging tests to assess liver disease severity and make treatment decisions. Additionally, other non-invasive methods, such as elastography (FibroScan) and serum biomarkers like FibroTest and ELF (Enhanced Liver Fibrosis) score, are also used to evaluate liver fibrosis and disease severity. The choice of diagnostic tools should be made in consultation with a healthcare professional based on the individual patient's circumstances. Thrombocytopenia was noted in 132 (35.0%) and FIB score more than 3 was noted in 117 (31.0%) while endoscopy results revealed esophageal varices in 288 (76.4%). Grade 1 esophageal varices were noted in 67 (17.8%), grade 2 in 181 (48.0%), grade 3 in 40 (10.6%). Sensitivity of thrombocytopenia was 38.89%, Specificity was 75.53%, PPV was 84.85%, NPV was 28.16% and Diagnostic Accuracy was 48.01%. For FIB score  $>3$ , Sensitivity was 34.03%, Specificity was 78.65%, PPV was 83.76%, NPV was 26.92% and Diagnostic Accuracy was 44.56%. An Egyptian study has documented 39% sensitivity, 82% specificity, 72% PPV, 54% NPV and accuracy of 59% with platelet count more than 149000 while FIB – 4 score (cut off value of 3.175) sensitivity was 78.4%, 45% specificity, 78.4% PPV, 45.7% NPV and 61% accuracy for EV in cirrhotic patients<sup>13</sup>. These findings are in compliance with our study results.

## CONCLUSION

Very high frequency of esophageal varices has been noted in our study in patients with chronic liver disease. Thrombocytopenia and FIB score  $>3$  revealed good diagnostic accuracy in predicting esophageal varices in CLD patients. These are simple tests which can be easily employed by treating physicians to anticipate disease severity in these patients.

### Author's Contribution:

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