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## **Diagnostic accurateness of AST/ALT for esophageal variceal bleeding diagnosis considering endoscopy as gold standard**

**Umer Bin Tariq**

Department of Medicine, Nawaz Sharif Medical College, Gujrat Pakistan

**Iqra Shafqat**

Shaikh Zayed Hospital, Lahore Punjab, Pakistan

**M. Nabeel Mohsin**

Senior Registrar, Department of Internal Medicine, Mayo Hospital Lahore, Pakistan

Corresponding author email: [dr.nabeel2011@hotmail.com](mailto:dr.nabeel2011@hotmail.com)

**Urooj Yahya**

Assistant Professor Physiology department, Swat Medical College, Khyber Medical University, Peshawar Pakistan

**Aysha Mushtaq**

MBBS, MPhil Physiology, Demonstrator Islamic International Medical College, Rawalpindi, Punjab, Pakistan

**Imran Khawaja**

Senior Registrar Internal Medicine, Ayub Teaching Hospital, Abbottabad, Pakhtunkhwa, Pakistan

**Abstract**--Aim: To assess the diagnostic accurateness of AST/ALT  $\geq 1$  for detecting esophageal varices' considering endoscopy as gold standard. Study Design: A Cross-sectional study. Place and duration of study: The study was conducted at Lahore General Hospital and Hayatabad Medical Complex, Peshawar during the period from January 2022 to December 2022. Methodology: Using non-probability purposive sampling, 180 patients with liver cirrhosis between the ages of 18 and 65, of either sex, were selected. On endoscopy, esophageal varices were confirmed, and the AST/ALT Ratio was calculated. Results: Of the 180 patients in total, 120 (66.7%) were men and 60 (33.3%) were women. The sampled population's mean age was 51.20  $\pm$ 6.9 years. The average duration of CLD was 5.42 years with a range of 2 to 10 years. 118 (65.5%) patients had an AST/ALT ratio greater

than 1, 105 (58.3%) had varices detected during endoscopy, and 75 (41.7%) had no varices. The results showed that the sensitivity was computed to be 96.8%, the specificity to be 55.2%, the negative predictive value to be 90.2%, the positive predictive value to be 77.1%, the false negative rate to be 6.9% and the false positive rate to be 41.5%. Conclusion: AST/ALT Ratio > 1 is 96.8% sensitive but not specific (55.2%) for the detection of bleeding from esophageal variceal.

**Keywords**---AST/ALT Ratio, Chronic Liver Disease, Endoscopy, Esophageal varices, Alanine aminotransferase, Hepatic cirrhosis and Aspartate aminotransferase.

## **Introduction**

The severe and frequent complication of liver cirrhosis is bleeding from esophageal varices that can be fatal in individuals who exhibit symptoms of clinical decompensation, such as ascites, upper gastrointestinal bleeding, jaundice or encephalopathy<sup>1-2</sup>. Between 60 and 80% of cirrhotic individuals have esophageal varices, and variceal bleeding has a mortality incidence of 17% to 57%. 60% of people may experience bleeding again within two years<sup>3-4</sup>. The preferred diagnostic test for patients with upper GI bleeding brought on by esophageal varices is an endoscopy. It assists in diagnosis, provides data that supports in outcome prediction, and most significantly, it enables options for treatment that can halt bleeding and reduce the chance of rebleeding<sup>5</sup>. The study of numerous non-invasive parameters that can be used clinically to diagnose varices in cirrhotic individuals has advanced. These variables include the AST/ALT Ratio, spleen size, platelet counts and portal vein diameter<sup>6</sup>. Another non-invasive method, transient elastography, is also useful in identifying esophageal varices and portal hypertension. Numerous studies have employed the AST/ALT ratio as a non-invasive and simple technique to forecast the existence of cirrhosis and varices of the esophagus. HCV is the most frequent cause of cirrhosis in underdeveloped nations<sup>7-8</sup>. According to WHO, there are 130–170 million—or 2–3%—of the global population are HCV positive. In both developed and developing nations, HCV is the main reason for hospital admissions and liver transplants. The prevalence of HCV is around 2% in many industrialized nations, including Australia and several Western European nations, which is equal to the estimated prevalence in the United States. The rates of HCV infection are greater (3%) in nations in South Asia, Latin America, Middle East and Eastern Europe. With a prevalence incidence ranging from 4.5% to 8%, HCV is the 2<sup>nd</sup> most prevalent infection in our setting. Studies done among small sample size exhibit that blood donors, chronic liver disease, intravenous drug abusers and medical professionals have the HCV prevalence of about 40%<sup>9-10</sup>. The commutative pervasiveness of hepatitis C and hepatitis B among the people of Pakistan was 8.1%, or 5.1 and 2.1% of separate hepatitis C and hepatitis B, correspondingly, according to the study conducted by the PMDC in 2007-2008. This equals to 13 million people who are chronic hepatitis B and C carriers<sup>11</sup>. The unsafe therapeutic injections, transfusion of blood from donors without screening, IV drug abusers, and a few other hospital-associated operations are the main risk factors for the HCV infection transmission internationally. The liver parenchyma

is distorted and regenerating nodules forms in liver cirrhosis, a last stage of hepatic fibrosis that is typically irreversible in its later stages. The sole choice for treatment in these circumstances is liver transplantation<sup>12-13</sup>. A cirrhotic patient is more likely to experience decompensation if they consume alcohol, have any comorbid condition, use drugs, experience bleeding, are constipated, are dehydrated, or are obese<sup>14</sup>.

There was a mortality rate of up to 15–20% after a single episode of bleeding from varices before the advancement of modern therapeutic methods<sup>15</sup>. Studies have indicated that using endoscopic variceal band ligation or using nonselective beta blocker as primary prophylaxis lowers the incidence of first variceal haemorrhage and lowers the risk of mortality related with bleeding.

### **Methodology**

This cross-sectional study was held in the medicine department of Lahore General Hospital and Hayatabad Medical Complex, Peshawar for one-year duration from January 2022 to December 2022. Using non-probability purposive sampling, 180 patients with liver cirrhosis between the ages of 18 and 65, of either sex, were selected. On endoscopy, esophageal varices were confirmed, and the AST/ALT Ratio was calculated. Raised prothrombin time, deranged liver function tests, splenomegaly greater than 14 cm, portal vein diameter greater than 15 mm and the presence of ascites were used to diagnose liver cirrhosis. Endoscopy revealed dilated sub-mucosal veins as esophageal varices. If the AST/ALT Ratio was  $\geq 1$ , it was considered positive. Predictive accuracy was labelled as True negative if AST: ALT is less than 1 and negative endoscopy findings, True positive if AST: ALT  $\geq 1$  with positive endoscopy findings, False negative if AST: ALT is less than 1 with positive endoscopy findings and False positive if AST: ALT  $\geq 1$  with negative endoscopy findings. The study included patients of both genders between 16–60 years of age who had been diagnosed with cirrhosis of liver based on Child Turcotte Pugh Classes A, B, or C.

Patients with active bleeding from the varices, patients with hepatic encephalopathy, those who had undergone endoscopic variceal band ligation or sclerotherapy, patients who had trans-jugular intrahepatic portosystemic shunt placement, those who had undergone surgery for portal hypertension and patients who were taking medicines as the prophylaxis for variceal bleeding were all omitted from the study. Patients with cholelithiasis identified by abdominal ultrasonography, renal disease (serum creatinine  $>1.2$ gm/dl), with thrombocytopenia (platelet count less than 150,000/mm<sup>3</sup>) or those on hemodialysis were also not included for the study. The informed consent was taken from the participants and approval from the hospital's ethical committee was taken. Data were collected and age and gender were noted after which a thorough clinical examination was performed. For the AST and ALT analyses, blood samples were sent to the hospital laboratory. A consultant gastroenterologist then performed an endoscopic evaluation of these patients to check for the absence or presence of esophageal varices. To determine the required diagnostic accuracy, AST/ALT results were compared with endoscopic findings. SPSS version 22.0 was used to enter and analyse all of the gathered data. Gender and Child Pugh class were two qualitative factors that were reported

as frequencies and percentages. Age, AST, and ALT were quantitative variables that were provided as Mean S.D. Using a 2×2 table, PPV and NPV were obtained for accuracy, sensitivity, and specificity.

## Results

Of the 180 patients in total, 120 (66.7%) were men and 60 (33.3%) were women. The sampled population's mean age was 51.20 ±6.9 years.

Table-I shows the baseline characteristics of the patients

Gender	
Male	120 (66.7%)
Female	60 (33.3%)
Age (years)	
Minimum	18
Maximum	65
Mean±SD	51.20 ±6.9
Age Group distribution	
>40 years	162 (90%)
<40 years	18(10%)
CLD Duration in years:	
Maximum	10
Minimum	2
Mean±SD	5.42±3.10
Frequency based on disease duration:	
>5 years	85(47.2%)
<5 years	95 (52.8%)

The average duration of CLD was 5.42 years with a range of 2 to 10 years. 18 patients (10%) were under the age of 40, whereas 162 (90%) patients were over that age. 85 (47.2%) individuals had CLD for more than 5 years. 118 (65.5%) patients had an AST/ALT ratio greater than 1, 105 (58.3%) had varices detected during endoscopy, and 75 (41.7%) had no varices.

Table-II shows the Cross tabulation between Varices and AST/ALT Ratio >1 on Endoscopy

AST/ALT Ratio >1	Varices on Endoscopy		Total
	Yes	No	
Yes	a=102	b=16	118
No	c=3	d=59	62
Total	105	75	180

The results showed that the sensitivity was computed to be 96.8%, the specificity to be 55.2%, the negative predictive value to be 90.2%, the positive predictive value to be 77.1%, the false negative rate to be 6.9% and the false positive rate to be 41.5%.

Table-III shows the diagnostic accuracy of AST/ALT >1 considering endoscopy as gold standard

Outcome	Formula x 100	
Specificity	$\frac{d}{B+d}$	55.2%
Sensitivity	$\frac{a}{A+c}$	96.8%
NPV	$\frac{d}{C+d}$	90.2%
PPV	$\frac{a}{A+b}$	77.1%
False negative rate	$\frac{c}{C+d}$	6.9%
False positive rate	$\frac{b}{B+d}$	41.5%

## Discussion

Variceal bleeding events have significantly decreased due to improvements in endoscopic and radiographic procedures as well as novel pharmaceutical medications. Even yet, the clinical importance of a mortality rate of 15–23% due to esophageal varices bleeding is significant<sup>16</sup>. In cases of extensive esophageal varices, primary prophylaxis of the varices has been demonstrated to significantly lower the risk of haemorrhage from 50% to 15% before the episode of first bleed. In order to determine any variceal enlargement and the necessity for prophylactic treatment, existing guidelines advise variceal screening in all patients with cirrhosis at the time of diagnosis, followed by after every 2-3 years for subjects not having varices and once or twice a year for patients with small varices<sup>17</sup>. The best method for identifying variceal haemorrhage is still upper GI endoscopy. The effectiveness of the AST/ALT ratio as a rapid, non-invasive, repeatable, easy, and cost-effective method to predict esophageal varices has been examined in a number of researches. These investigations have demonstrated a significant difference in the specificity and sensitivity of the AST/ALT ratio, principally due to the diverse cirrhosis aetiologies and varying AST/ALT cut off values. An AST/ALT ratio greater than 1.12 was associated significantly with the existence of varices at the initial endoscopy, according to a study by Treeprasertsuk S et al<sup>18</sup>. (p=0.02, Odds Ratio = 3.9, CI95%, 1.2-12.0). This cutoff resulted in an AUROC of 0.699, specificity of 87%, sensitivity of 47.8%, NPV of 89.2% and PPV of 42.3%. Castéra L. et al. utilized a different cutoff of  $\geq 1.0$  in a second trial and reported a specificity of 89%, sensitivity of 68%, NPV 83% and PPV 77% with an AUROC 0.84 (0.70-0.89), for determining the esophageal varices presence<sup>19</sup>. In this analysis, age > 40 years (90%) and male sex (66.7%) were found to be the main

predictors of esophageal varices. The study's median age of 51.20 ±6.9 years is comparable to those of other published research. Cirrhosis typically strikes Pakistani people in their fifth or sixth decade of life, according to the disease's typical course<sup>20-21</sup>.

## Conclusion

AST/ALT Ratio > 1 is 96.8% sensitive but not specific (55.2%) for the detection of bleeding from esophageal variceal. A lower sample size is one of the study's limitations. Consequently, a larger cohort of patients must be used to validate the results. Further research must be done in this area, keeping endoscopy as the gold standard and using AST/ALT >1 as a non-invasive and simple method to diagnose variceal bleeding.

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