

# Diagnostic Accuracy of Serum Albumin for Diagnosis of Esophageal Varices among Patients of Chronic Liver Disease taking Endoscopy as Gold Standard

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## ABSTRACT

**Objective:** To determine the diagnostic accuracy of serum albumin for the detection of esophageal varices (EV) in cases presented with chronic liver disease taking Esophagogastroduodenoscopy (EGDs) as the gold standard.

**Methodology:** This cross-sectional study was conducted at the Department of Medicine, Sir Ganga Ram Hospital, Lahore in collaboration of Department of Gastroenterology, Services Hospital, Lahore, during a period of six months. After receiving informed consent, each patient's blood was drawn using a 5cc disposable syringe and sent to the hospital's laboratory for analysis of serum albumin levels. Esophageal varices were suspected as positive on albumin level <3.5mg. Then, patients were referred to and underwent EGD. All EGDs were done on every patient by a consultant gastroenterologist having a minimum experience of 5 years. Self-made study proforma was used for the data collection and SPSS version 26 was used for the data analysis.

**Results:** The patient's average age was 55.44±12.51 years. Males were found in majority 70.53%. Esophageal varices were noted positive among 41.1% of the cases out of a total 95 study subjects. The sensitivity and specificity of the serum albumin in the diagnosis of esophageal varices were found to be 80.55 percent and 83.05 percent, respectively, followed by a positive predictive value 74.35 percent, negative predictive value 87.5 percent, and the diagnostic accuracy was 82.10 percent by taking EGD as the gold standard.

**Conclusion:** Decreased serum albumin level was observed to be the non-invasive, useful predictor and as a good first-line diagnostic tool of esophageal varices among cases having chronic liver disease in clinical practice.

**Keywords:** Serum Albumin, Esophageal Varices, CLD, EGD

## INTRODUCTION

Portal hypertension (PHTN) is an increased hepatic sinusoidal pressure of >6mmHg. Cirrhosis seems to be the most frequent cause of portal hypertension, which is caused by excessive blood flow resistance at the hepatic sinusoidal region, resulting in esophageal varices.<sup>1</sup> Esophageal varices are swollen veins in the lower esophagus that is aberrant. When normal blood flow to the liver is impeded by the hepatic fibrosis tissues or a clot, the esophageal varices developed. Blood moves into tiny blood capillaries that are not meant to carry large amounts of blood to get past the blockages. Variceal bleeding occurs when blood vessels leak or break.<sup>2</sup> Gastric varices rupture leading to variceal bleeding, which is one of the most serious cirrhosis consequences. The literature has reported that >90% of cirrhotic patients develop EV out of which 30% may bleed.<sup>3</sup> The incidence of EV in cirrhotic patients is predicted to be between 60% and 80% dependent on the severity and etiology of liver diseases.<sup>4</sup> According to current guidelines, all the patients with liver cirrhosis should have screening endoscopy at the time of diagnosis to assess the cases with EVs who might benefit from primary prevention.<sup>5</sup> This method places a significant burden on endoscopy facilities, and the repetitive testing over time may reduce patient cooperation. Patients at high risk of esophageal varices could be identified noninvasively, limiting research to those who are most likely to benefit. Although upper GI endoscopy is considered the gold standard against which all other tests are measured, it does have limits.<sup>5</sup> There are several non-invasive indicators for determining the existence and severity of esophageal varices like, clinical features, ultrasound and biochemical parameters.<sup>6</sup> These factors could be used individually or in conjunction. Splenomegaly, Thrombocytopenia, splenomegaly, ascites, Child-Pugh score, platelet count-splenic size ratio, portal flow pattern, thickness of the gall bladder wall, serum ascites albumin gradient, and right lobe liver diameter-albumin ratio are the mostly used markers to predict the existence of EV.<sup>6-8</sup> In chronic liver disease caused by the hepatitis B and C viruses, hypoalbuminemia is a suitable surrogate marker for the presence of esophageal varices.<sup>9</sup> One study

reported that sensitivity of serum albumin for detection of esophageal varices i.e. 66% and specificity i.e. 80%.<sup>10</sup> But another study agreed with the results of this study and reported that the sensitivity and specificity of serum albumin level for detection of EV was 56% and 83.8% respectively.<sup>11</sup> Another study reported that the sensitivity and specificity of serum albumin level for the detection of EV were 53.2% and 91%, respectively.<sup>9</sup> This study determined the diagnostic accuracy of serum albumin for the detection of esophageal varices among individuals having chronic liver disease taking EGD as the gold standard. Studies has reported that some non-invasive methods are available which can detect esophageal varices, but in routine, these procedures are not adopted and patients must undergo EGD. EGD is an invasive procedure, which also has side effects and repeated EGD is also a risk of poor prognosis of patients in such critical condition which, which may lead to more severe outcome. In routine, in tertiary care hospitals, physicians rely on EGD, but in sub-urban areas or at peripheries, facilities EGD are not available. Through this study, we want to assess the diagnostic accuracy of serum albumin level, so that in the future we can implement the results of this study as earlier reported accuracy of serum albumin is variable in the different studies. This study may help to rule out the problem of EVs just assessment through albumin level in case results show high diagnostic accuracy instead of referring patients to some tertiary care hospital, which also have burden.

## MATERIAL AND METHODS

This cross-sectional study was conducted at the Department of Medicine, Sir Ganga Ram Hospital, Lahore in collaboration of the Department of Gastroenterology, Services Hospital, Lahore with a duration of six months. Non-probability, consecutive sampling method was employed. All the patients of age 20-60 years of either gender presenting with CLD were included. Patients having a history of esophageal band ligation, sclerotherapy and preventive treatment for portal hypertension (through medical record), patients with hypoalbuminemia due to congestive cardiac failure (EF<50%on echo), nephritic syndrome (24-hour urinary protein

>3.5gm/dl) or underweight (BMI<19kg/m2) and patients with extra-hepatic metastasis (on CT scan abdomen), thrombosis of splenic vein or portal vein were excluded. After receiving informed consent, each patient's 5cc blood sample was drawn using a 5cc disposable syringe and sent to the Hospital's laboratory for analysis of serum albumin levels. After taking reports from the laboratory, the esophageal varices were suspected as being positive for albumin level <3.5mg. All the expenses of the reports were done by the researcher. Suspected patients with esophageal varices based on albumin were referred to the Department of Gastroenterology, Services Hospital, Lahore for esophagogastroduodenoscopy. All EGDs were performed by a consultant gastroenterologist having minimum experience of more than five years. The presence of varices on esophagogastroduodenoscopy was labeled as positive if there were dilated sub-mucosal veins in the lower third of the esophagus and negative if sub-mucosal veins were normal. The data were entered and analyzed through SPSS version26.

**RESULTS**

There were 95 cases studied, whose average age was 55.44±12.51 years, with ranging in age from 30 to 70 years. Out of all study subjects 64(64.4%) cases were male and 31(32.6%) cases were females. The mean duration of CLD of the patients was 2.32±1.06 months. The average blood albumin concentration of the participants was 3.77±0.44 g/dl, according to the findings with minimum albumin level 2.1 g/dl and maximum 5 g/dl. Table. 1

In this study, esophageal varices were noted positive among 41.1% of the cases, while esophageal varices on EGD were observed positive among 37.3% of the participants out of a total 95 study subjects. The sensitivity and specificity of the serum albumin in the diagnosis of esophageal varices were found to be 80.55 percent and 83.05 percent, respectively, followed by a positive predictive value 74.35 percent, negative predictive value 87.5 percent, and the diagnostic accuracy was 82.10 percent by taking EGD as the gold standard. Table. 2

Table 1: Descriptive statistics of demographic variables n=95

Variables	Statistics	
Age	55.44±12.51 years	
Duration of CLD	2.32±1.06 years	
Serum Albumin level	3.77±0.44 g/dl	
Gender	Males	64(64.4%)
	Females	31(32.6%)

Table 2: Comparison of serum albumin with EGD for prediction of esophageal varices n=95

		EVs on EGD		Total
		Positive	Negative	
EVs on serum albumin	Positive	29	10	39
	Negative	7	49	56
Total		36	59	95
Sensitivity 80.55%	Specificity 83.05%	PPV 74.35%	NPV 87.5%	Diagnostic accuracy 82.10%

**DISCUSSION**

The lower esophageal region veins that are unusually swollen are known as esophageal varices.<sup>12</sup> Its occurrence in cirrhotic patients is expected to range from 60.0 percent to 80.0 percent, depending on the cause and severity of hepatic diseases.<sup>12</sup> In this study, esophageal varices on serum albumin were estimated 38.95% and on Esophagogastroduodenoscopy were observed 61.05% among CLD patients. In this study patient's average age was 53.92±14.61 years and out of all 64.4% were males and 32.6% were females. Consistently Thong VD et al<sup>13</sup> demonstrated that the mean age of the subjects was 54.59 ± 13.23 years, males were 60(75.0%) and females were 20(25.0%). In the study of Baloch, MZ et al<sup>12</sup> also reported that the average age of the cases was 53.63±14.61 years and males were 67(70.5%) cases and females were 28(29.5%). In the comparison of this study the Budiya DG et al<sup>6</sup> reported that there were 61 eligible individuals having cirrhosis of the liver who

had the EGD, with males 73.8% and females 26.2% ranging in age from 13 to 77 years with an average age of 49.98±1.621 years.

In this study, the sensitivity and specificity of the serum albumin in the diagnosis of esophageal varices were found to be 80.55 percent and 83.05 percent, respectively, followed by positive predictive value 74.35 percent, negative predictive value 87.5 percent, and the diagnostic accuracy was 82.10 percent by taking EGD as the gold standard. These findings were almost similar to the study of Baloch MZ et al<sup>8</sup> reported that the sensitivity of esophageal varices on serum albumin was 81.08 percent, with 84.48 percent specificity. Taking esophageal varices on EGD as the gold standard, the PPV value was 76.92 percent, the NPV value was 87.5 percent, and the diagnostic accuracy of esophageal varices on serum albumin was 83.16 percent. In the study of Khan J et al<sup>14</sup> demonstrated that in the group of low-level serum albumin, 42 cases out of 133 had esophageal varices, whereas in the normal group of albumin level only 7 cases had esophageal varices out of 87. Pasha HF et al<sup>15</sup> reported that serum ascites albumin gradient (SAAG) may predict the existence of esophageal varices with specificity 100% and PPV 100%, sensitivity 90.09%, and NPV 64.5% at a cut off value of 1.3 gm/dl, according to a receiver operating characteristic (ROC) curve. Recently, Moharm AE et al<sup>16</sup> reported that albumin-bilirubin score was seen significantly different among the groups tested and might be utilized as a marker for esophageal varices (p-0.046), at a cutoff value of -1.67, with sensitivity 52.9%, specificity 59.6%, PPV 64%, and NPV 47%. Furthermore, it is reported that the serum albumin was significantly lower in individuals with gastroesophageal varices, who also had a higher death rate and according to the researchers, serum albumin control is essential in preventing gastroesophageal variceal haemorrhage.<sup>16,17</sup> On the other hand, it has been reported that the serum ascites albumin gradient (SAAG) is a precise, minimally invasive approach that has already been established for classifying ascetic fluid depending on the presence or absence of PHT.<sup>13,18</sup> on-invasive measures for the prediction of EVs in patients newly diagnosed with cirrhosis have been investigated.<sup>13</sup> Consistently, Khan H, et al<sup>9</sup> reported that the hypoalbuminemia was found to be 53.2 percent sensitive and 91 percent specific as a predictor of the esophageal varices with PPV and NPV were both 73.3 percent. Noninvasive procedures that can accurately detect esophageal varices bleeding among cases of the liver cirrhosis could lead some patients to skip invasive upper endoscopy screening.<sup>19</sup>

**CONCLUSION**

As per study conclusion the decreased serum albumin was observed to be a non-invasive, useful predictor and as a good first-line diagnostic tool of esophageal varices among cases having chronic liver disease in clinical practice. Now we have got local estimates and now we are able to implement the use of serum albumin levels for the prediction of EVs and can prevent patients from the development of EVs and EV bleeding without undergoing for interventional procedure. Although further large-scale studies are recommended to observe the association between the severity of decreased albumin levels and esophageal varies among patients with chronic liver disease.

**REFERENCES**

1. Coelho-Prabhu N, Kamath PS. Current staging and diagnosis of gastroesophageal varices. Clin Liver Dis. 2010;14(2):195-208.
2. Feldman M, Friedman LS, Brandt LJ. Sleisenger and Fordtran's gastrointestinal and liver disease: pathophysiology, diagnosis, management, expert consult premium edition-enhanced online features: Elsevier Health Sciences; 2010.
3. Cordon JP, Torres CF, Garcia AB, Rodriguez FG, de Parga JMS. Endoscopic management of esophageal varices. World J Gastrointest Endosc. 2012;4(7):312-22.
4. Hong W-d, Dong L-m, Jiang Z-c, Zhu Q-h, Jin S-Q. Prediction of large esophageal varices in cirrhotic patients using classification and regression tree analysis. Clinics. 2011;66(1):119-24

5. Asser ML, Ooda SA, Zaki MA, Amin GA, El-Hassafi MY. Study of Serum N-Terminal-Pro C-Type Natriuretic Peptide and its Relation to the Risk of Variceal Bleeding in Cirrhotic Hepatitis-C Virus Patients. *J Gastrointest Dig Syst* 2018;8:2
6. Budiayasa DG, Ariawan Y, Mariadi IK, Wibawa ID, Purwadi N, Suryadarma IG. Correlation between serum albumin level and degree of esophageal varices in patients with liver cirrhosis. *Indonesian Journal of Gastroenterology, Hepatology, and Digestive Endoscopy*. 2011 Jan 4;12(1):23-7.
7. Alempijevic T, Bulat V, Djuranovic S, Kovacevic N, Jescic R, Tomic D, et al. Right liver lobe/albumin ratio: contribution to non-invasive assessment of portal hypertension. *World J Gastroenterol* 2007;13:5331-5.
8. Gulzar GM, Zargar SA, Jalal S, Alaie MS, Javid G, Suri PK, et al. Correlation of hepatic venous pressure gradient with variceal bleeding, size of esophageal varices, etiology, ascites and degree of liver dysfunction in cirrhosis of liver. *Indian J Gastroenterol* 2009;28:59-61
9. Khan H, Iman N-u. Hypoalbuminemia: a marker of esophageal varices in chronic liver disease due to hepatitis B and C. *Rawal Med J*. 2009;34(1):89-101.
10. Zein CO, Lindor KD, Angulo P. Prevalence and predictors of esophageal varices in patients with primary sclerosing cholangitis. *Hepatology*. 2004;39(1):204-10.
11. Hossain S, Islam Q, Siddiqui M, Hossain A, Jahan N, Rahman Y, et al. A Study of Hypoalbuminaemia in Chronic Liver Disease and its Correlation with Development of Esophageal Varices. *Bangl J Med*. 2011;22(1):17-20.
12. Baloch MZ, Pathan GN, Mujtaba S, Uqaili AA. Diagnostic accuracy of serum albumin for diagnosis of esophageal varices in patients of chronic liver disease. *Annals of PIMS-Shaheed Zulfiqar Ali Bhutto Medical University*. 2019 Sep 23;15(2):52-5.
13. Thong VD, Anh HT. Prediction of Esophageal Varices Based on Serum-Ascites Albumin Gradient in Cirrhotic Patients. *Gastroenterology Insights*. 2021 Jun;12(2):270-7.
14. Khan J, Rabbani A, Ali S, Dar UF, Riaz H, Nayyar U, Aslam A. Frequency of Esophageal Varices and Comparison of Serum Albumin levels with and without Esophageal Varices in Patients Presenting with Chronic Liver Disease. *PAKISTAN JOURNAL OF MEDICAL & HEALTH SCIENCES*. 2016 Jan 1;10(1):127-9.
15. Pasha HF. Prediction of Oesophageal Varices in Cirrhotic Patients by Serum-Ascites Albumin Gradient. *Zagazig University Medical Journal*. 2020 Jan 1;26(1):99-107.
16. Moharm AE, El-Kalla FS, Kobtan AA, El Khalawany WA. Combination of Albumin-Bilirubin Grade and Platelet Count as a Predictor of Esophageal Varices' Presence and Grading in Egyptian Patients with HCV Related Cirrhosis. *The Open Biomarkers Journal*. 2022 Feb 7;12(1).
17. Soga K, Tomikashi K, Miyawaki K, et al. MELD score, child-pugh score, and decreased albumin as risk factors for gastric variceal bleeding. *Hepatogastroenterology* 2009; 56(94-95): 1552-6
18. Hou, Y.; Yang, Z.; Yang, Y.; Gao, F.; Liu, X.; Zhang, Q.; Zhu, B.; Jiang, Y.; Wang, X. Serum-ascites albumin gradient: An independent predictor of esophageal variceal bleeding in cirrhosis patients with ascites. *Int. J. Clin. Exp. Med*. 2019, 12, 8645–8653.
19. Li S, Huang P, Jeyarajan AJ, Ma C, Zhu K, Zhu C, Jiang N, Li M, Shao T, Han M, Tan L. Assessment of Non-invasive Markers for the Prediction of Esophageal Variceal Hemorrhage. *Frontiers in Medicine*. 2021;8.