

Correlation between Serum Albumin Level and Degree of Esophageal Varices in Patients with Liver Cirrhosis

Dewa Gde Agung Budiyasa, Yuna Ariawan, I Ketut Mariadi,
I Dewa Nyoman Wibawa, Nyoman Purwadi, I Gusti Agung Suryadarma
Division of Gastroentero-hepatology, Department of Internal Medicine,
Faculty of Medicine, University of Udayana/Sanglah General Hospital, Denpasar

ABSTRACT

Background: It has not been clear about how often the patient should have esophago-gastroduodenoscopy (EGD) screening for esophageal varices (EV) detection and there is only some data that demonstrates the correlation between the degree of EV and non-endoscopic variables. It is assumed that the presence of EV detected through examination of serum albumin level may trim down the unnecessary endoscopy. This study was aimed to recognize the correlation between albumin level and the degree of EV in patients with liver cirrhosis.

Method: A retrospective analysis was performed for 61 patients with liver cirrhosis who had EGD at Sanglah hospital between January and December 2008. Spearman test was used to analyze the correlation between albumin level and the degree of EV.

Results: There were 61 patients of 45 (73.8%) male and 16 (26.2%) female. The range age of patients was 13–77 years (average 49.98 ± 1.62 years). Serum albumin level ranged between 1.10–3.60 mg/dL, the average value was 2.21 ± 0.451 mg/dL. We also found 8 (13.1%) patients without EV, 14 (23.0%) patients with EV grade I, 21 (34.4%) patients with grade II and 18 (29.5%) patients with grade III. A negative correlation was found between serum albumin level and the degree of EV ($r = -0.587$; $p = 0.000$, $p < 0.01$).

Conclusion: Serum albumin level can predict the presence and the degree of EV in patients with liver cirrhosis.

Keywords: albumin, degree of EV, liver cirrhosis

ABSTRAK

Latar belakang: Belum jelas seberapa sering pasien harus melakukan esofago-gastroduodenoskopi (EGD) untuk skrining varises, dan hanya sedikit data yang menunjukkan hubungan derajat varises dan variabel non-endoskopik. Dugaan adanya varises esofagus (VE) melalui kadar albumin serum dapat mengurangi endoskopi yang tidak perlu. Tujuan penelitian ini untuk mengetahui korelasi antara albumin dan derajat VE pada pasien sirosis hati.

Metode: Suatu analisis retrospektif dilakukan pada 61 pasien sirosis hati yang melakukan pemeriksaan EGD di Rumah Sakit Sanglah pada bulan Januari-Desember 2008. Tes Spearman digunakan untuk menganalisis korelasi antara albumin dan derajat VE.

Hasil: Terdapat 61 pasien terdiri dari 45 (73,8%) laki-laki, dan 16 (26,2%) perempuan, dengan usia antara 13–77 tahun dengan rerata $49,98 \pm 1,62$ tahun. Kadar albumin antara 1,10–3,60 mg/dL, rerata $2,21 \pm 0,45$ mg/dL. Ditemukan pula berturut-turut pasien tanpa VE 8 (13.1%), derajat I 14 (23.0%), derajat II 21 (34.4%), dan derajat III 18 (29,5%) orang. Terdapat korelasi negatif antara albumin serum dan derajat VE ($r = -0,587$; $p = 0,000$; $p < 0,01$).

Kesimpulan: Albumin serum dapat memprediksi ada dan derajat VE pada pasien sirosis hati.

Kata kunci: albumin, derajat VE, sirosis hati

INTRODUCTION

Esophageal varices (EV) are a major complication of liver cirrhosis due to portal hypertension. It is assumed that the prevalence is approximately 50% of patients with cirrhosis and the rate of incidence is assumed to be increasing at 5% per year. Moreover, the progression of EV from small to large varices is about 20% after 1 year period. EV bleeding is the most serious and life-threatening complication in patients with liver cirrhosis. The risk of bleeding of 25-35% in a year has been detected. The mortality rate of each bleeding episode is 17-57% and almost 70% patients without treatment died within 1 year of their first bleeding.¹ The occurrence of bleeding may be predicted by the red sign or red cherry spots on the varices and by the size of varices. The risk of bleeding may be reduced by using non-selective beta blockers and endoscopic variceal ligation has been shown to be an effective prophylaxis, particularly against the first variceal bleeding.^{1,2} Therefore, regular screening by endoscopy is very recommended for patients without or with small-sized varices and such procedure should be performed in every 2 years. The American Association for the Study of Liver Disease recommend screening in all patients with cirrhosis to recognize the presence of EV when a diagnosis of cirrhosis is made.² However, repeating endoscopy is not convenient for patients and it brings high-cost burden; therefore, other parameters, particularly the non-invasive one should be considered to predict the presence and the degree of EV in patients with liver cirrhosis.

There are some non-invasive parameters for predicting the presence and the degree of EV, which are the biochemical, clinical and ultrasonography parameters. Those parameters could be performed separately or in combination. Among them, the parameters that mostly applied to predict the presence of EV are splenomegaly, thrombocytopenia, Child-Pugh score, ascites, portal flow pattern, platelet count-splenic size ratio, gall bladder wall thickness, serum ascites albumin gradient, and right lobe liver diameter-albumin ratio.¹⁻¹⁰ Other parameter has also been used including the serum albumin level. Albumin itself is a part of Child-Pugh score used for predicting the severity of liver disease. Hypoalbuminemia in liver cirrhosis probably may be caused by some issues including decreased production that liver parenchyma is replaced by scar tissue, increased removal by the reticuloendothelial system or the spleen and increased albumin loss through the gastrointestinal system (portal hypertensive gastropathy or enteropathy), and all of them are associated with portal hypertension.⁶

An experimental animal study demonstrated that portal hypertension may induce hypoalbuminemia. The serum albumin level increased by 20% when

the portal vein pressure decreased after the transjugular intrahepatic portosystemic shunt had been performed. The study demonstrated that there is a correlation between portal hypertension and hypoalbuminemia.⁹ A study by Khan et al found that there was a significant correlation between serum albumin level and the presence of EV ($r = -0.494$; $p < 0.01$). The study was conducted in patients with liver cirrhosis caused by hepatitis B and C virus only. Serum albumin level was determined as < 3.5 mg/dL to predict the presence of esophageal varices. Moreover, a study by Sarwar et al and Schepis et al, found that the patient with serum albumin level < 2.95 mg/dL may have greater probability of having EV and greater possibility of more severe EV.^{9,11} Therefore, our study would like to find the correlation between serum albumin level and the degree of EV in patients with liver cirrhosis.

METHOD

A retrospective analysis was performed for 61 patients with liver cirrhosis who had their endoscopy procedure at Sanglah hospital between January and December 2008. Diagnosis of liver cirrhosis was established based on clinical sign and symptoms, appropriate laboratory results and ultrasonography findings. Symptoms of liver cirrhosis usually include swollen belly and swollen legs, fatigue, loss of appetite, easily sated, losing weight, epigastric discomfort, bloating, nausea and muscles weakness, abdominal pain on the right upper quadrant, black stool and blood vomiting. Signs of liver cirrhosis due to failure in liver function and clinical signs because of portal hypertension. Laboratory result may reveal anemia, signs of hypersplenism, abnormal hemostasis, abnormal liver function test, hypoalbuminemia, hyperglobulinemia, electrolyte disturbances and abnormal serological marker for hepatitis virus. Ultrasonographic study includes observation on liver angled edge, surface contour, homogeneity and the occurrence of any mass. In advanced cirrhosis, the ultrasonography may show a small and nodular liver, irregular surface contour, and increased echogenicity in liver parenchyma.¹²

Serum albumin level was determined by a time endpoint method using the Synchron Cx[®] System. Basically, in the reaction the albumin was combined with bromocresol purple (BCP) to form a colored complex. The ratio used in the system was one part of sample to 100 parts of reagent. The system monitored the change in absorbance and it was directly proportional to the concentration of albumin in the sample, with chemical reaction of: albumin + BCP \rightarrow albumin-BCP complex.¹³ The serum albumin level used in the study were albumin measurements upon

hospital admission and if the patients had not been admitted to the hospital, then we used the latest serum albumin level before the endoscopy was performed.

There are some methods to determine the degree of esophageal varices (EV) such as Japanese classification, Franchis classification or others. In our study, it was determined by subjective evaluation method.¹⁰ Grade I included small varices that were only detectable on performing a Valsava maneuver; grade II referred to small varices approximately 1-3 mm in diameter that were visible both during inspiration and expiration; grade III were varices of moderate size with 3-6 mm in diameter, and grade IV indicated large varices over 6 mm. The inclusion criteria of our study were patients who had been confirmed to have liver cirrhosis with clinical signs and symptoms, laboratory results and suitable ultrasonographic findings and patients who had their esophagogastroduodenoscopy between January and December 2008 at Sanglah hospital, Denpasar. The exclusion criteria were patients with history of albumin transfusion prior to the EGD, history of sclerotherapy or band ligation treatment, history of treatment for portal hypertension, history of treatment using diuretics, had thrombosis of portal vein as revealed by the abdominal ultrasonography, who had hematemesis melena previously, who had infection or other abnormalities that may affect the serum albumin level.

Data are presented in the form of graphs, tables, histogram, and scatter plot diagram. Correlation between serum albumin level and the degree of EV was determined by using Spearman test. Statistically significant level was considered when the value of $p < 0.05$ with CI 95%.

RESULTS

Of patients with liver cirrhosis who had the EGD, there were 61 eligible patients including 45 (73.8%) male 16 (26.2%) female patients with age ranged of 13–77 years and the mean age of 49.98 ± 1.621 years. Patient characteristics and laboratory results are presented on Table 1.

EGD findings revealed that EV were found in 53 patients with varices of fundus in 24 patients and cardia in 2 patients; the patients without EV were patients with only fundal varices; while all patients with varices of cardia may also have the EV. There was a negative correlation between serum albumin level and the degree of EV ($r = -0.587$; $p = 0.000$).

Table 1. Characteristic of patient

Characteristic	n (%)	Mean \pm SD
Sex		
Male	45 (73.8)	
Female	16 (26.2)	
Age (years)		49.98 \pm 1.62
10-19	1 (1.6)	
20-29	2 (3.3)	
30-39	14 (23.0)	
40-49	15 (24.6)	
50-59	15 (24.6)	
60-69	13 (31.3)	
≥ 70	1 (1.6)	
Albumin (mg/dL)		2.21 \pm 0.45
< 2.8	56 (91.8)	
2.8-3.5	4 (6.6)	
> 3.5	1 (1.6)	
Degree of EV		
Without EV	8 (13.1)	
Grade I	14 (23.0)	
Grade II	21 (34.4)	
Grade III	18 (29.5)	
Grade IV	0 (0.0)	
Laboratory examination		
Hemoglobin (3.1-16.9 mg/dL)		9.53 \pm 0.37
Platelet (7-631 x 1,000/L)		141.78 \pm 13.98
Serum bilirubin (0.32-26.30 mg/dL)		4.03 \pm 0.72
AST (15-1,544 IU/L)		117.23 \pm 27.73
ALT (10-947 IU/L)		81.96 \pm 21.39

EV: esophageal varices; AST: aspartate aminotransferase; ALT: alanine aminotransferase

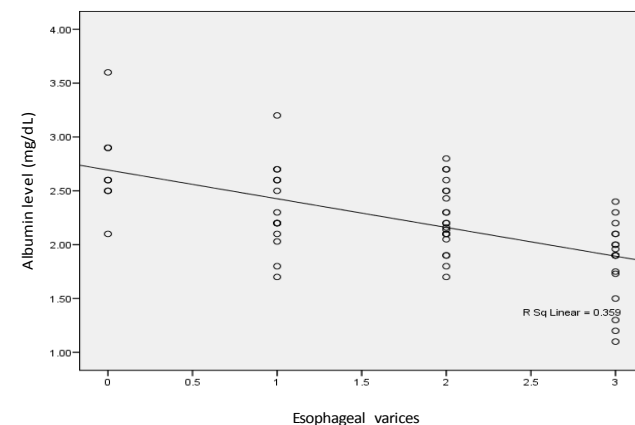


Figure 1. Scatter plot diagram of correlation between albumin and the degree of esophageal varices

DISCUSSION

Some previous studies indicated that there was a significant correlation between the degree of EV and serum ascites albumin gradient (SAAG), as well as with the right liver lobe diameter/albumin ratio.^{1-3,6,8-11} It could be understood since both SAAG and the right liver lobe diameter/albumin ratio indicated the severity of portal hypertension. Furthermore, portal hypertension may cause EV; therefore any changes of both measurements would be correlated to the degree of EV. Often, there are only limited data of our patients so that we need an easier parameter to predict the occurrence and severity of EV including the serum albumin level.

Albumin (50-60% of total plasma proteins), globulin, and fibrinogen are the greatest part of plasma proteins with an increase of 24-56% death risk for each 2.5 g/dL decrement in serum albumin level. Albumin is an integral part of Child-Pugh score that could predict the severity of liver disease. Liver produces albumin as much as 130-200 mg/kgBW/day. There are multifactor mechanisms hypoalbuminemia in liver cirrhosis. It probably may be caused by decreased production that liver parenchyma is replaced by scar tissue, increased removal by the reticuloendothelial system or the spleen and increased albumin loss through the gastrointestinal system such as portal hypertensive gastropathy or enteropathy.⁶ Most patients in our study (91.8%) had serum albumin level of < 2.8 mg/dL and they were likely to have severe liver disease (Child Pugh score C). The albumin level ranged between 1.10 and 3.60 mg/dL with the mean value of 2.21 ± 0.45 mg/dL. We did not performed measurement of the Child Pugh score due to limited financial support and considering that our study was a retrospective study.

The degree of EV indicates the severity of portal hypertension, the higher degree of EV, the more severe the portal hypertension. However, the severity of portal hypertension does not suggest the severity of liver disease. In contrast, the degree of EV may be used to predict the probability of bleeding occurrence. Our study was using subjective method for criteria on degree of EV performed by different operator but still using exactly the same criteria. To predict the presence of EV, some previous studies have used different limits of albumin levels. Schepis et al and Sarwar et al, used limit of albumin level < 2.95 mg/dL; while Khan et al used < 3.5 mg/dL. All of them demonstrated significant correlations.^{6,9,11} This study did not use any certain limits and the correlation between EV and albumin was evaluated by Spearman test. A study by Khan et al, indicated that higher frequency of hypoalbuminemia above age 30 (27.4%) suggests worsening of albumin levels as the disease advances with growing age.⁶ Bressler et al, found hypoalbuminemia of < 4 mg/dL as an independent risk factor for EV with odd ratio of 6.02.¹⁴

In this study, we found that most patients were at 40-59 years of age; however, there was no significant correlation between age and albumin level ($r = -0.218$, $p = 0.091$). It may be caused by different study population, the cause of liver disease itself, or by the multifactorial cause of hypoalbuminemia. In addition, there was no significant correlation between age and the degree of EV; therefore, the age could not be used to predict the degree of portal hypertension ($r = 0.005$; $p = 0.970$; $p < 0.01$).

The correlation between albumin level and degree of EV has been demonstrated by some studies.

Khan et al, conducted a cross-sectional prospective study in patients with chronic liver disease caused by hepatitis B and C. About 197 patients were categorized into 2 groups consisted of group A with albumin level < 3.5 mg/dl and group B with normal albumin level. EV was found in 63 patients. The sensitivity of albumin as a predictor of EV was 53.2%, the specificity was 91%, and odds ratio was 11.57. The Spearman test suggested a significant negative correlation ($r = -0.494$) between serum albumin level and the degree of EV.⁶ Moreover, Sarwar et al, had studied 101 patients with liver cirrhosis who had never have EV bleeding. They found that serum albumin level < 2.95 mg/dL, platelet counts of < 88 K/uL, and portal vein diameter > 11 mm were associated with the presence of EV and the patients were more likely to have severe degree of EV.⁹ We conducted this study in 61 patients with liver cirrhosis who had fulfilled the criteria without considering the cause of cirrhosis. This study found a significant negative correlation between serum albumin level and the degree of EV ($r = -0.587$; $p = 0.000$; $p < 0.01$). Thus, without considering the etiology of liver cirrhosis, the albumin level could still be used to predict the degree of EV severity.

CONCLUSION

There was a negative correlation between serum albumin level and the degree of EV in patients with liver cirrhosis and therefore, the serum albumin level could be used as a predictor for determining the degree of EV.

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Correspondence:

Dewa Gde Agung Budiayasa
 Division of Gastroentero-hepatology, Department of Internal Medicine
 Sanglah General Hospital
 Jl. Sanglah, Denpasar Indonesia
 Phone/Facsimile: +62-361-244177
 E-mail: budyasadewa@yahoo.com
