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Hepatology

The Correlation between Serum Ascites Albumin Gradient and Oesophageal Varices in Chronic Liver Disease

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Abstract **Original Research Article**

Background: Oesophageal varices are abnormally enlarged veins in the tube that connect the throat and esophagus. Such condition occurs most often in people with serious liver diseases. On the other hand, chronic liver disease denotes the disease of the liver which lasts over a period of months or more. The serum ascites albumin gradient (SAAG) is a formula that is used to assist in determining the etiology of ascites. We don't have any research-based information regarding the correlation between serum ascites albumin gradient and Oesophageal varices in chronic liver disease. ***Aim of the study*:** The aim of this study was to assess the correlation between serum ascites albumin gradient and Oesophageal varices in chronic liver disease. ***Methods*:** This prospective observational study was conducted in the Department of Hepatology, BSMMU, Dhaka, Bangladesh during the period from January 2005 to December 2005. In total 50 patients with cirrhosis with ascites with high SAAG values (>1.1 gm/dl) were included as the study people. The age of the patients was 15 to 70 years. Both males and females were included in the study. All data were entered into a personal computer, thoroughly checked for any possible error, and then processed and analyzed by the SPSS program. The significance of the test was tested by the chi-square test. P-value of <0.05 was taken as statistically significant. Correlation analysis was done by the Pearson correlation test. ***Results*:** In this study, in the SAAG group 1.10-1.49 gm/dl, there were 15 patients, 8 patients (53.28%) of them had small varices, 4 patients (26.64%) had medium-sized varices and 2 patients (13.32%) had large-sized varices. In the SAAG group 1,50-1.99 gm/dl, there were 9 patients, 1 patient (11.11%) of them had small sized varices, 6 patients (66.66%) had medium sized varices and 2 patients (22.22%) had large-sized varices. In SAAG group >2 gm/dl, there were 26 patients. Nine (9) patients (34.2%) of them had small-sized varices, 5 patients (19%) had medium-sized varices and 12 patients (45.6%) had large sized varices**.** ***Conclusion*:** We can conclude that high SAAG (>I. I gm/dl) is an indicator of portal hypertensive changes in the upper gastrointestinal tract (Oesophageal varices and gastropathy) and there is a positive(weak) correlation between high SAAG values and grades of Oesophageal varices and portal hypertensive gastropathy. For getting more reliable information we would like to recommend conducting more studies in several places with larger-sized samples.

Key words: Ascites albumin, Oesophageal varices, Liver disease, SAAG.

I INTRODUCTION

Oesophageal varices are abnormally enlarged veins in the tube that connect the throat and esophagus. Such condition occurs most often in people with serious liver diseases. On the other hand, chronic liver disease denotes the disease of the liver which lasts over a period of months or more. The serum ascites albumin gradient (SAAG) is a formula that is used to assist in determining the etiology of ascites. We don't have any research-based information regarding the correlation between serum ascites albumin gradient and Oesophageal varices in chronic liver disease. In several studies recently carried out, it was emphasized that serum ascites albumin gradient (SAAG) based on the difference between albumin level of serum and ascitic fluid should be used to determine the aetiology of ascites cases instead of discrimination between transudate and exudates [1]. It was shown that such a classification has a validity rate of 96.7% in detecting ascites of portal hypertension in the adult population whereas distinguishing transudate from exudate based on criteria requiring total protein level in ascites above

2.5gm/di has a validity rate of 55.6% in presence of portal hypertension [2]. The osmotic pressure gradient between portal venous blood and the peritoneal cavity is a direct function of the corresponding capillary hydrostatic pressure gradient. The difference between serum and ascites albumin concentration (SAAG) is thought to reflect directly colloid osmotic pressure gradient and indirectly degree of portal hypertension. SAAG is a better discriminator of portal hypertension than ascites total protein concentration2. Indeed, in the workup of ascites SAAG is now considered a useful physiological clinical tool. Patients with SAAG >1.1 gm/dl are considered as high SAAG and indicate the presence of porta, hypertension while those with SAAG <1.1 gm/dl are considered as low SAAG and indicate the absence of portal hypertension. Net portal pressure is correlated strongly with SAAG in patients with cirrhotic ascites (r=0.81, p< 0.001) [2]. Serum-ascites albumin gradient, an index of serum-ascites oncotic pressure difference, correlates directly with the pressure gradient between portal capillaries and peritoneal cavity1. Portal hypertensive changes in upper gastrointestinal endoscopy arc Oesophageal varices, gastric varices, and portal hypertensive gastropathy. The Oesophageal varices are graded according to Japanese classification into three grades (Japanese research society for portal hypertension 1980). There are some red color signs present on Oesophageal varices. They are red wale markings, cherry-red spots, and haemato-cystic spots. Gastric varices are assessed according to position in stomach and type of varices into tortuous type, tumor type, and notched type. In a recent study by Torres et al., [3] the correlation between SAAG and Oesophageal varices was studied (p=0.001, r=0.54). In this study, a total of 31 patients was included. Among them, 25 patients had high SAAG. Among the patients of high SAAG value, 17 had Oesophageal varices (68%). Varices were present in 4 of 10 (40%) patients with SAAG value 1.10 to 1.49 gm/dl; in 4 of 6 patients (66.7%) with SAAG value 1.50 to 1.99 gm/dl and in 9 of 9 patients (100%) with SAAG values of >2 gm/dl. Grade-I was present in 1 patient (25%), Grade-II in 1 patient (25%), and Grade-Ill in 2 patients (50%) with SAAG value 1.10 to 1.49 gm/dl. Grade-I was present in 2 patients (50%), Grade-II in 2 patients (50%), and Grade-Ill in 0 patients with SAAG value 1.5 to 1.99 gm/dl. Grade-I was present in 2 patients (22.2%), Grade-II in 4 patients (44.4%), and Grade-Ill 3 patients (33.4%) with SAAG value >2gm/dl. Multiple studies have shown that SAAG is associated with portal venous pressure, EV, and differential diagnosis of ascites, over the past decade or so [4-6] Hoef's first introduced SAAG, reporting that SAAG can reflect portal vein pressure and improve the accuracy of ascites identification [7]. Many studies have recommended that cirrhotic patients be screened for the presence of esophageal varices (EV) when liver cirrhosis is diagnosed [8, 9]. However, endoscopy procedures are invasive and unpleasant, carrying rare but serious complications [10, 11]. In this study we have the aim to evaluate whether such a correlation exists between SAAG values and portal hypertensive changes (varices, gastropathy) in upper gastrointestinal endoscopy in cirrhotic patients with ascites.

II OBJECTIVES

General Objective

- To evaluate the use of high SAAG value as a preliminary indirect parameter of presence of portal hypertensive changes (varices, gastropathy) in upper gastrointestinal endoscopy.

Specific Objective

- To correlate the degree of high SAAG values with the grades or sizes of oesophageal varices.
- To correlate the degree of high SAAG values with the presence of gastric varix.
- To correlate the degree of high SAAG values with the grades of portal hypertensive gastropathy.

III METHODOLOGY & MATERIALS

This prospective observational study was conducted in the Department of Hepatology, BSMMU, Dhaka, Bangladesh during the period from January 2005 to December 2005. In total 50 patients with cirrhosis with ascites with high SAAG values (>1.1 gm/dl) were included as the study people. The age of the patients was 15 to 70 years. Both males and females were included in the study. According to the exclusion criteria of this study cirrhotic patients with ascites with low SAAG values (<l.l gm/dl), pregnant women, cases with a space-occupying lesion (SOL) in the liver or intra-abdominal tuberculosis or malignancy, patients received endoscopic treatment for Oesophageal varices previously and patients to whom endoscopy was contraindicated were excluded. After taking written consent from the patient, biochemical liver function tests and viral serological tests that is, serum bilirubin, ALT, AST, prothrombin time, serum albumin, HBsAg, Anti-HCV were done. Ultrasonography of the hepatobiliary system was done to detect the presence of features of chronic liver disease, presence of ascites and to exclude space-occupying lesions in the liver. Ascitic fluid was aspirated from the abdomen through the abdominal wall at the junction between the medial two-third and lateral one-third of the spinoumbilical line under aseptic precaution after asking the patient to evacuate the bladder in the procedure room. The ascitic fluid was sent for cytology, total protein and albumin, and malignant cell. At the same time, venous blood was drawn and sent for serum albumin concentration estimation. During endoscopy, the Oesophagus was surveyed for evidence of Oesophageal varices. If Oesophageal varices are present, then the number of Oesophageal varices, size of Oesophageal varices, and presence of any red signs over the varices were noted in the case record form. Then the stomach was surveyed for the presence of portal hypertensive gastropathy and gastric varix. If portal hypertensive gastropathy is

present, then the grade of portal hypertensive gastropathy was noted. If the gastric varices were present, the site of varices and type of varices were noted. All information was noted in the case record form. A detailed history of each patient was taken and preset data was filled for every patient. History of jaundice, blood transfusion, operation, dental procedure, haemetemesis and melaena, endoscopic treatment of oesophageal varices, ingestion of hepatotoxic drugs and alcohol were inquired for every patient. Physical examination was done systematically. All data were entered into a personal computer, thoroughly checked for any possible error, and then processed and analyzed by the SPSS program. The significance of the test was tested by the chi-square test. P-value of <0.05 was taken as statistically significant. Correlation analysis was done by the Pearson correlation test.

IV RESULT

In this study, the age range of the cirrhotic patients was 15-70 years, and the mean age was 39,61±14.54 years. Male was 42 (84%) and female were 8(16%) in number. The number of patients in child Grade-B was 11(22%) and child Grade-C was 39(78%). The SAAG values of the cirrhotic patients divided into three groups. The first group was 1.1-1.49 gra/dl, the number of patients in this group was 15 (30%). The second group was 1.5-1.99 gm/dl; the number of patients was 9 (18%). The third group was >2 gra/dl, the number of patients was 26 (52%). In SAAG 1.1-1.49 gm/dl, 14 of 15 patients (93.3%) had Oesophageal varices. In SAAG 1.5-1.99 gm/dl, 9 of 9 patients (100%) had Oesophageal varices and in SAAG > 2 gm/dl, 26 of 26 patients (10%) had. So, a total of 49 of 50 patients (98%) had Oesophageal varices. In this study, in the SAAG group 1.10-1.49 gm/dl, there were 15 patients, 8 patients (53.28%) of them had small varices, 4 patients (26.64%) had medium-sized varices and 2 patients (13.32%) had large-sized varices. In the SAAG group 1,50-1.99 gm/dl, there were 9 patients, 1 patient (11.11%) of them had small-sized varices, 6 patients (66.66%) had medium-sized varices and 2 patients (22.22%) had large-sized varices. In the SAAG group >2 gm/dl, there were 26 patients, 9 patients (34.2%) of them had small-sized varices, 5 patients (19%) had medium-sized varices and 12 patients (45.6%) had large-sized varices. In SAAG group 1.1-1.49 gm/dl, 26.66% of patients were included in child Grade-B and 73.33% in child Grade-C. In the SAAG group 1.5-1.99 gm/dl, 11.11% of patients were included in child Grade-B and 88.88% in child Grade-C. In the SAAG group >2 gm/dl, 23.07% patient were included in child Grade-B and 76.92% patients in child Grade-C. In this study we observed, due to the Hepatitis-B virus, small, sized varices were present in 11 patients (33.3%), medium-sized in 11 patients (33.3%), and large size in 10 patients (30.3%). In cirrhosis due to the Hepatitis-C virus, large-sized varices were present in 1 patient (100%). In cirrhosis due to Non-B Non-C(NBNC), small-sized varices were present in 6 patients (42.8%), medium-sized varices in 4 patients (28.5%), and large-sized varices in 4 patients (28.5%). In cirrhosis due to Wilson's disease, small-sized varices were present in 1 patient (50%) and large-sized varices in 1 patient (50%).

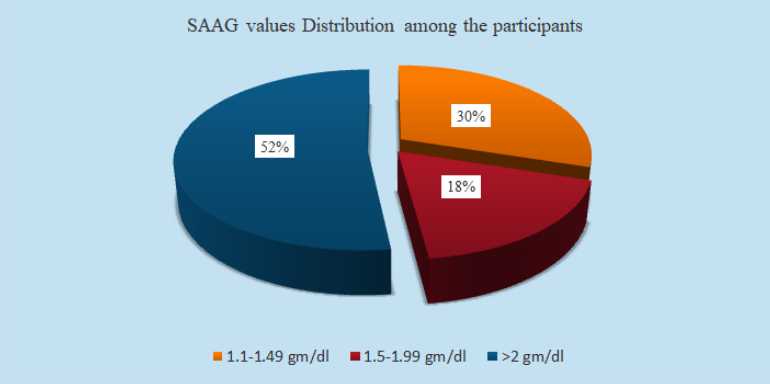

Figure 1: Distribution of SAAG values among the participants (N=50)

Table I: Distribution of Oesophageal varices in different SAAG group (N=50)

SAAG gm/dl	Frequency (%)	Oesophageal Varices			
		Present		Absent	
		n	%	n	%
1.1-1.49	15 (30.0)	14	93.3	1	6.6
1.5-1.99	9 (18.0)	9	100.0	0	0.0
>2	26 (52.0)	26	100.0	0	0.0
Total	50 (100.0)	49	98.0	1	2.0

Table II: Correlation between SAAG group and size of Oesophageal varices of the cirrhotic patients (N=50)

SAAG (gm/dl)	Frequency (%)	Size of Oesophageal varices				r	p- Value
		Absent	Small	Medium	Large		
		n (%)	n (%)	n (%)	n (%)		
1.1-1.49	15 (30.0)	1 (6.66)	8 (53.28)	4 (26.64)	2 13.32)	0.358	0.011
1.5-1.99	9 (18.0)	0(0.0)	1 (11.11)	6 (66.66)	2 (22.22)		
>2	26 (52.0)	0(0.0)	9 (34.2)	5 (19.0)	12 (45.6)		
Total	50 (100.0)	1 (2.0)	18 (36.0)	15 (30.0)	16 (32.0)		

Table III: Correlation between SAAG group and child grades of cirrhotic patients (N=50)

SAAG (gm/dl)	Frequency (%)	Child Grades		r	p- Value
		Frequency (n)			
		Grade-B	Grade- C		
1.1-1.49	15 (30.0)	4 (26.66)	11(73.33)	0.023	0.874
1.5-1.99	9 (18.0)	1 (11.11)	8 (88.88)		
>2	26 (52.0)	6 (23.07)	20 (76.92)		
Total	50 (100.0)	11 (22.0)	39 (78.0)		

Table IV: Distribution of different size of Oesophageal varices in different aetiology of cirrhosis (N=50)

Aetiology	Frequency (%)	Frequency (%)				r	p-Value
		Absent	Small	Medium	Large		
Hepatitis-B virus	33(66.0)	1 (3.03)	11 (33.3)	11 (33.3)	10 (30.3)	3.992	0.912
Hepatitis-C virus	1 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)		
Non-B Non-C	14 (28.0)	0 (0.0)	6 (42.8)	4 (28.5)	4 (28.5)		
Wilson's disease	2 (4.0	0 (0.0)	1 (50.0)	0 (0.0)	1 (50.0)		
Total	50 (100.0)	1 (2.0)	18 (36.0)	15 (30.0)	16 (32.0)		

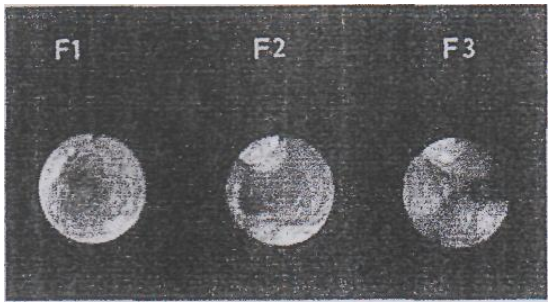

Figure 2: Form of Oesophageai varices

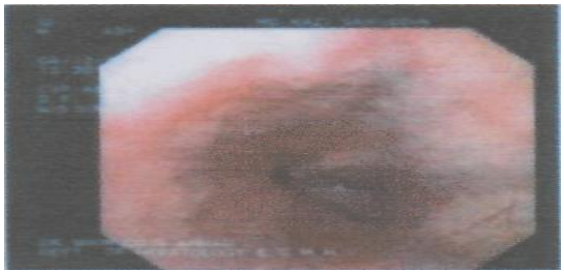

Figure 4: Small sized varices through endoscope at 3,9,12 o'clock positions

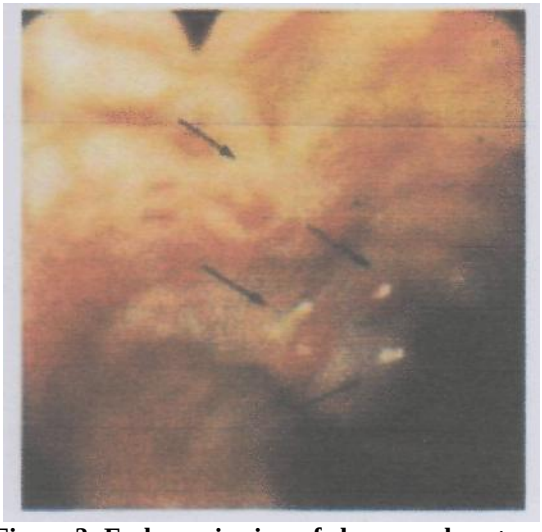

Figure 3: Endoscopic view of cherry-red spots on Oesophageal varices

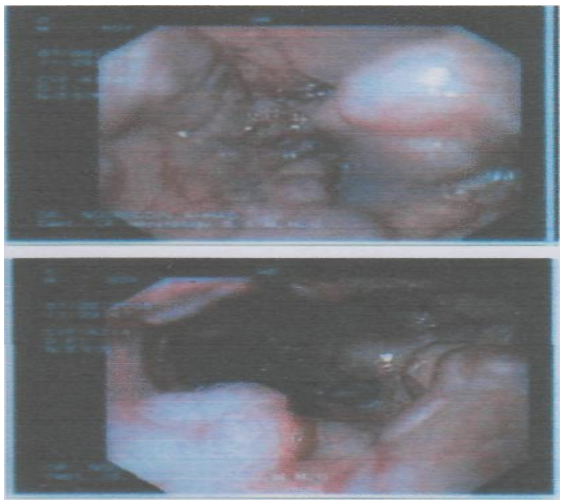

Figure 5: Medium and large sized Oesophageal varices through endoscope at 6,9 o'clock positions and at 3 o'clock position. Large sized varices are seen at 3 o'clock position in upper photograph and at 7 o'clock position

V DISCUSSION

Cirrhosis of the liver is a medical problem in Bangladesh. It is manifested by the development of ascites, oesophageal varices, gastric varices, and portal hypertensive gastropathy. Serum ascites albumin gradient (SAAG) is a physiological clinical diagnostic tool for the evaluation of ascites. High SAAG (>1.1 gm/dl) indicates the presence of portal hypertension which is detected by observing portal hypertensive changes in the upper gastrointestinal tract. Direct portal pressure measurement is an invasive and cumbersome procedure. So minimal invasive endoscopy helps us to detect the development of portal hypertension by observing changes in the upper gastrointestinal tract. There is a correlation between SAAG and portal hypertensive changes in the upper gastrointestinal tract in cirrhotic patients with ascites [7]. Several studies have been conducted in different parts of the world on alcoholic cirrhosis but studies on nonalcoholic cirrhosis are scanty. In this study, a numeric formula was established for the first time. Rector et al., studied 18 alcoholic cirrhotic patients. They also showed a similar correlation between SAAG and portal pressure (r=0.80, p=0.001) [12]. In this study, a correlation was found between SAAG and portal pressure (r=0.62) in alcoholic cirrhosis but no significant correlation was found between SAAG and portal pressure (r=0.39) while the correlation between SAAG and variceal grades was found to be weaker (r=0.02) in nonalcoholic cirrhosis. In a study done by Torres et al., [3] a correlation was found between SAAG and oesophageal varices (r=0.54, p=0.005). In this study total of 31 were included. Among them, 25 patients had high SAAG and 17 of them had Oesophageal varices (68%). Varices were present in 4 of 10 patients (40%) with SAAG values 1.10-1.49 gm/dl; in 4 of 6 patients (66.7%) with SAAG values 1.50-1.99 gm/dl; in 9 of 9 patients (100%) with SAAG values >2 gm/dl. In SAAG value U-1.49 gm/dl, one patient (25%) had small-sized varices, one patient (25%) had medium-sized varices and 2 patients (50%) large-sized varices. In SAAG value 1.5-1.99 gm/dl, two patients (50%) had small-sized varices, 2 patients (50%) had medium-sized varices and no patient had large-sized varices. In SAAG value >2 gm/dl, two patients (22.2%) had small-sized varices, 4 patients (44.4%) had medium-sized varices and 3 patients (33.4%) had large-sized varices. In this current study, there were 7 patients (21.2%) of child grade B and 26 patients (78.7%) of child grade C in cirrhosis due to hepatitis B virus; 1 patient (100%) of child grade C in cirrhosis due to hepatitis C virus; 4 patients (28.5%) of child grade B and 10 patients (71.4%) of child grade C in cirrhosis due to Non-B Non-C; 2 patients (100%) of child grade C in cirrhosis due to Wilsons disease. These findings are comparable with that of some other studies [13, 14]. Significance was noted between portal vein size (cm) and the presence of varices. Similar results were obtained in some other studies [15]. In our study, a total of 50 patients with cirrhosis of various aetiology were included. A correlation was studied between SAAG and portal hypertensive changes in the upper gastrointestinal tract like Oesophageal varices, gastric varices, and gastropathy. Oesophageal varices were present in 49 patients (98%), of them small-sized in 18 patients (36%), medium-sized in 15 patients (30%), large-sized in 16 patients (32%). Red signs over the Oesophageal varices were present in 12 patients (24%). Gastric varices were present in only 2 patients (4%). All these findings are comparable with findings of the previous studies done in other centers in the world. So, the study has shown that high SAAG value is an indicator of the presence of portal hypertensive changes especially Oesophageal varices and portal hypertensive gastropathy in the upper gastrointestinal tract and there is a weak positive correlation between SAAG values and grades of Oesophageal varices and PHG.

VI CONCLUSION AND RECOMMENDATIONS

Cirrhosis of liver is a medical disease in Bangladesh. It comprises 2-6% of our hospital admission. The unavoidable complication of cirrhosis of liver is development of portal hypertension. It leads to development of Ocsophageal varices, gastric varices and portal hypertensive gastropathy. Those are responsible for upper gastrointestinal bleeding in 2-9% of cases and one of the leading causes of death in cirrhosis. So, it is important to detect portal hypertensive changes in upper gastrointestinal tract as early as possible, thereby prophylaxis and treatment of portal hypertension keep cirrhotic patients' symptom free life. So, we can conclude that, high SAAG (>I. I gm/dl) is an indicator of portal hypertensive changes in upper gastrointestinal tract (Oesophageal varices and gastropathy) and there is a positive(weak) correlation between high SAAG values and grades of Oesophageal varices and portal hypertensive gastropathy. For getting more reliable information we would like to recommend for conducting more studies in several places with large sample size.

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