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Original article

Correlation between serum-ascites albumin concentration gradient and endoscopic parameters of portal hypertension

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Abstract
Objective: We sought to determine the correlation between the level of serum-ascites albumin concentration gradient (SAAG) and the complications of portal hypertension (PHTN), manifested by the presence and grade of esophageal varices (EV).
Material and methods: Our study included 32 patients with ascites, demonstrated by ultrasonography, who had measurement of the SAAG. All had upper gastrointestinal endoscopy with assessment of the presence and size of EV. High SAAG was considered to be present when SAAG was >= 1.1 g/dl and Low SAAG when it measured < 1.1 g/dl.
Results: We found that 25 of 32 (78.13%) patients had High SAAG and 7 of 32 (21.87%) had Low SAAG. Esophageal varices were present in 18 of 25 (72%) patients with High SAAG and in none of 7 (0%) patients with Low SAAG (p =< 0.001). Among patients with High SAAG, EV were present in four of 8 patients (50%) with SAAG values of 1.10-1.49g/dl; in four of seven patients (57.1%) with SAAG values of 1.50-1.99g/dl; and in ten of ten (100%) with SAAG values of >= 2.0g/dl (p = 0.037). The size of the esophageal varices had no association with the level of SAAG in patients with High SAAG (p = 0.426).
Conclusions: In patients with ascites the presence of esophageal varices is associated only with patients with High SAAG. The presence of EV in patients with ascites and High SAAG is directly related to the degree of SAAG. The size of the EV in patients with ascites and High SAAG is not associated with the degree of SAAG.

Keywords: Ascites, Serum-ascites albumin concentration gradient (SAAG), Esophageal varices (EV), Portal Hypertension (PHTN)

Ascites, defined as fluid accumulation in the peritoneal cavity, may accompany several diseases. Patients who suffer from ascites present a diagnostic and therapeutic problem[1-3]. Biochemical, microbiological and cytological analysis of ascitic fluid are very important for differential diagnosis among the diseases causing ascites. Traditionally, ascites has been classified as being either transudative or exudative, based upon the ascitic fluid total protein concentration[4,5], the ascitic fluid to serum ratio of total protein[6,7], or the ascitic fluid to serum ratio of lactic dehydrogenase[8] . Unfortunately, none of these parameters has been found to be completely discriminating. Several studies have demonstrated the superiority of the serum-ascites albumin concentration gradient (SAAG) in the discrimination of ascitic fluid, compared with the exudate-transudate concept. It was shown that such a classification has a validity rate of 90% or more in detecting the ascites of portal hypertension[9-11]. The SAAG is minimally invasive method that is highly precise and allows for classification of ascitic fluids according to the absence or presence of portal hypertension (PHTN)[1,10,11,13-17].

It is pointed out in the literature that the SAAG is an indicator of PHTN[1,10,11,13-17], and that a direct relationship probably exists between SAAG and different PHTN measurements such as the portal pressure gradient[13], net portal pressure[14], or corrected portal pressure[11]. These measurements are obtained only by invasive methods, which are not feasible in most centres in the resource-constrained countries. The indirect way to assess PHTN is by detection of oesophageal varices (EV).

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A number of potential modalities exist to assess the status of EV including barium radiography, ultrasonography and upper gastrointestinal endoscopy. The upper gastrointestinal endoscopy is currently the best reliable method available to diagnose presence of EV and hence, PHTN[18].

In the view of the above, the present study was undertaken to determine the correlation and association between the level of SAAG and the complications of PHTN, mainly the presence and grade of oesophageal varices (EV) found on upper gastrointestinal endoscopy. This would permit the use of the SAAG as a preliminary indirect parameter that would indicate the presence of EV as a manifestation of portal hypertension.

Materials and methods

This was a prospective and observational study of 32 patients diagnosed with ascites who were hospitalized at Kathmandu Medical College Teaching Hospital, Kathmandu between June 2003 and April 2005. All patients had a diagnosis of ascites confirmed by ultrasonography and all of them were older than age 18 years. Exclusion criteria included pregnancy, haemodynamic instability, bleeding disorders and other medical contraindications to perform upper gastrointestinal endoscopy.

An attending physician in medical ward evaluated all patients. Blood was drawn from the antecubital vein and ascitic fluid was obtained by paracentesis, performed using the standard technique[3]. Determination of the concentration of albumin in both the serum and the ascitic fluid were carried out simultaneously. The concentration of albumin in serum and ascitic fluid was determined using the Bromcresol Green method[1,10]. With these results, the SAAG was calculated. According to previous reports we considered a SAAG value of >= 1.1g/dl as High SAAG and a SAAG value of < 1.1g/dl as Low SAAG, the High SAAG being associated with PHTN[1-3,10,13,14,16,17].

After giving informed consent all patients underwent an upper gastrointestinal endoscopy at the endoscopy unit of Kathmandu Medical College Teaching Hospital. This procedure was performed with fiberoptic endoscopes. Patients were premedicated with 1ml of intravenous Hyoscine Butrybromide (Buscopan) and Xylocaine 1% spray was given as a topical anaesthetic. During upper gastrointestinal endoscopy all patients were assessed for the presence and size of EV. The varices were graded according to the Japanese classification[17,19,20] (Table 1).

PHStat2 software was used for statistical analysis. X^2 test was used for statistical analysis. A p value below 0.05 was considered statistically significant. Microsoft Excel was used for diagrammatic representation of data.

Table 1: Japanese Classification of Oesophageal Varices*

Grade I	The varices can be depressed by the endoscope
Grade II	The varices cannot be depressed by the endoscope and are separated by normal mucosa
Grade III	The varices are confluent around the circumference of the oesophagus and cannot be depressed by the endoscope

* Reference: N Engl J Med, 1988; 319:983-9

Results

Of the 32 patients examined, 25 (78.13%) had High SAAG, whereas 7 (21.87%) had Low SAAG. The diagnoses in the group with High SAAG were alcoholic liver cirrhosis in 16 patients (64%), non alcoholic liver cirrhosis in 4 patients (16%), congestive cardiac failure in 3 patients (12%), and fulminant hepatic failure in 2 patients (8%). In the group with Low SAAG 4 patients (57.1%) had peritoneal tuberculosis, two patients (28.6%) had carcinoma of stomach, and one patient (14.3%) had ovarian carcinoma (Table 2). Oesophageal varices were found in 18 of the 25 patients with High SAAG (72%), in contrast with none in the seven patients with Low SAAG (0%) (p =< 0.001) (Table 3. Fig.1).

Table 2: Causes of ascites according to the SAAG of ascitic fluid

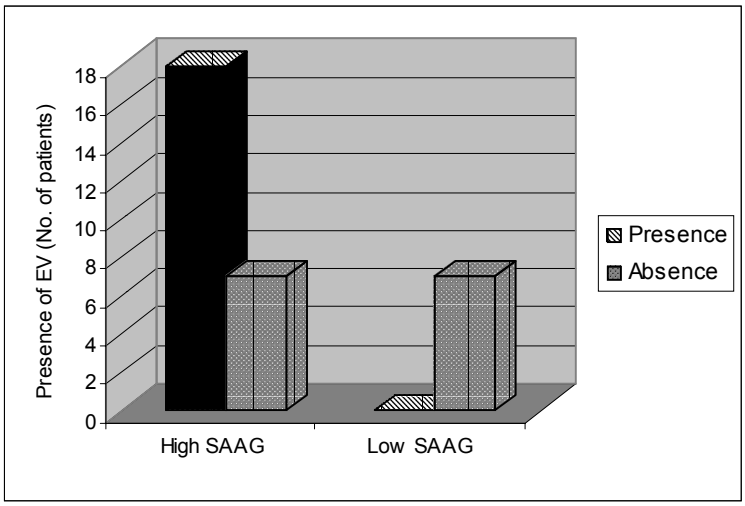
High SAAG		
Causes	Patients	%
Hepatic cirrhosis		
Alcoholic	16	64
Nonalcoholic	4	16
Cardiac ascites	3	12
Fulminant hepatic failure	2	8
Total	25	100
Low SAAG		
Causes	Patients	%
Peritoneal tuberculosis	4	57.1
Carcinoma of stomach	2	28.6
Ovarian carcinoma	1	14.3
Total	7	100

Table 3: Patients distribution according to the SAAG and the presence or absence of oesophageal varices

	High SAAG No. of patients (%)	Low SAAG No. of patients (%)	Total (%)
Oesophageal varices			
Presence	18(72)	0(0)	18(56.3)
Absence	7(28)	7(100)	14(43.7)
Total	25(100)	7(100)	32(100)

x^2= 11.52, d.f=1, p=< 0.001

Fig. 1: Patient's distribution according to the SAAG and the presence or absence of oesophageal varices



Of the 25 patients with High SAAG 18 (72%) presented with EV. Of this group, four of 8 patients (50%) had SAAG values between 1.10 and 1.49g/dl, four of seven patients (57.1%) had SAAG values between 1.50 and 1.99g/dl, and ten of ten patients (100%) had SAAG values >= 2.0g/dl. In patients without EV, four of 8 patients (50%) had SAAG values between 1.10 and 1.49g/dl, three of

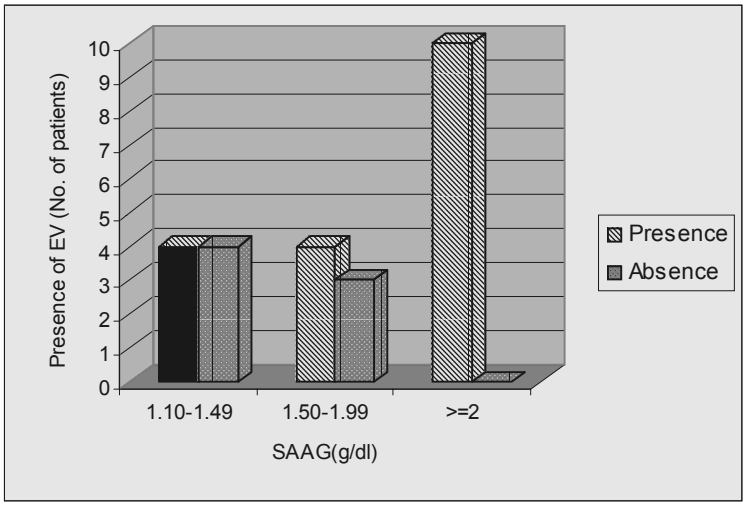
seven patients (42.9%) had SAAG values between 1.50 and 1.99 g/dl, and none of ten patients (0%) had SAAG values >=2.0g/dl. The presence of EV in patients with High SAAG was directly related to the degree of SAAG (p = 0.037) (Table 4, Fig. 2).

Table 4: Patients distribution according to the presence or absence of oesophageal varices and the degree of SAAG in patients with High SAAG

	SAAG values (g/dl), No. of patients (%)			Total (%)
	1.10-1.49	1.50-1.99	>= 2	
Oesophageal varices				
Presence	4(50)	4(57.1)	10(100)	18(72)
Absence	4(50)	3(42.9)	0(0)	7(28)
Total	8(100)	7(100)	10(100)	25(100)

x^2= 6.57, d.f=2, p=0.037

Fig. 2: Patients distribution according to the presence or absence of oesophageal varices and the degree of SAAG in patients with High SAAG



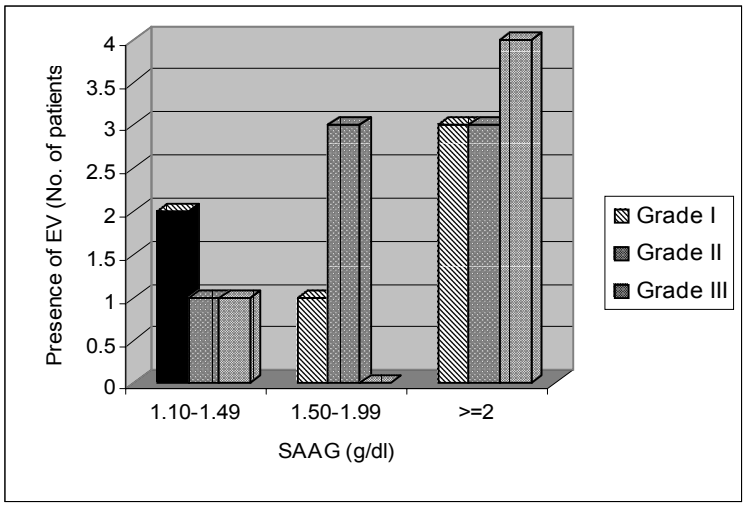
The size of the EV in patients with High SAAG, according to the degree of SAAG and using Japanese classification, was as follows: in SAAG between 1.10 and 1.49g/dl, two patients (50%) had grade I EV, one patient (25%) had grade II EV, and one patient (25%) had grade III EV; in SAAG between 1.50 and 1.99g/dl, one patient (25%) had grade I EV, three patients (75%) had grade II EV, and none (0%) had grade III EV; in SAAG >=2.0g/dl, three patients (30%) had grade I EV, three patients (30%) had grade II EV, and four patients (40%) had grade III EV. The size of the EV did not demonstrate significant statistical association (p = 0.426) with the degree of SAAG in patients with High SAAG (Table 5, Fig. 3).

Table 5: Patients distribution according to the size of oesophageal varices and the degree of SAAG in patients with High SAAG

	SAAG values (g/dl), No. of patients (%)			Total (%)
	1.10-1.49	1.50-1.99	>= 2	
Size of EV				
Grade I	2(50)	1(25)	3(30)	6(33.3)
Grade II	1(25)	3(75)	3(30)	7(38.9)
Grade III	1(25)	0(0)	4(40)	5(27.8)
Total	4(100)	4(100)	10(100)	18(100)

x^2= 3.85, d.f= 4, p= 0.426

Fig 3: Patients distribution according to the size of oesophageal varices and the degree of SAAG in patients with High SAAG



Discussion

Previous research indicates that the measurement of the portal pressure gradient (PP-GRAD) and the portal pressure (PP) are the most appropriate haemodynamic parameters for evaluating the development of PHTN and its complications[21,22,23,24]. The SAAG has been found to correlate with different PHTN measurements, such as PP-GRAD[13], net portal pressure[14], or corrected portal pressure[11]. In 1990, Kajani et al. investigated the correlation in patients with alcoholic cirrhosis and with cirrhosis due to other causes seperately[11]. In this study, a correlation was found between SAAG and either portal pressure or oesophageal varices in alcoholic cirrhosis. But in the patients with non-alcoholic cirrhosis, no correlation was found between SAAG and portal pressure, while the correlation between SAAG and the varix degree was found to be weaker.

In spite of these controversial results, the SAAG is able to define the presence or absence of PHTN with an accuracy of 96.7%[1-3,10,17]. This test is accurate despite ascitic fluid infection, diuresis, therapeutic paracentesis, albumin infusion, and aetiology of liver diseases[1-3]. In a study performed by Hoefs et al. in 1983, it was shown that an excellent correlation exists between portal hypertension and SAAG[13]. In this study, a numeric formula was established for the first time between portal hypertension and SAAG. While it was established in this formula that $p < 0.05$, the numeric formula was as follows: PP-GRAD = 7.08 X (SAAG+3.62).

In our study in patients with ascites there was an association between the level of SAAG and the development of oesophageal varices. With oesophageal varices present only in patients with

High SAAG, there was a higher probability of finding EV in patients with higher values of High SAAG. However, the level of High SAAG presented no association and had a poor correlation with the size of oesophageal varices.

In summary, taking into account the correlation between SAAG and PP-GRAD, the simple and minimally invasive technique of measuring SAAG may prove useful as an indirect indicator in estimating PHTN and its complications, such as EV. However, the SAAG should be viewed as a preliminary and indirect measurement of PHTN due to different correlations and limitations between SAAG and PHTN measurements, as described earlier.

Based upon our findings, we conclude that the presence of EV in patients with ascites is only associated with patients with High SAAG. Likewise, the presence but not the size of the EV in patients with ascites and High SAAG is directly related to the degree of SAAG.

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