Original Article

Prediction of Esophageal Varices in Cirrhotic Patients with Serum - Ascites Albumin Gradient

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ABSTRACT

OBJECTIVE: To identify commonest SAAG "serum-ascites albumin gradient" value in patients with cirrhotic disease having esophageal varices and to discover values of serum ascites and serum albumin.

MATERIAL AND METHODS: This cross sectional was conducted on 100 cirrhotic patients with ascites to calculate SAAG level in serum and ascitis fluid the value of SAAG was examined (≥1.1 g/dl) and high SAAG was measured to be ≥1.1 g/dl and Low SAAG when it is <1.1g/dl to rank the esophageal varices. All the cases included in the study under went upper GI endoscopy.

RESULTS: From total 100 patients, male were 62 and female were 38. SAAG was 2.01 ± 0.52. Esophageal varices (EV) found in 87 patients and were absent in 13 patients. Grades of the esophageal varices highlighted significant correlation with degree of SAAG (p<0.01) with r =0.55 (p<0.01) of Pearson correlation coefficient. With uses of ROC curve a SAAG value i.e. ≥1.65 ± 0.014 g/dl was an correct marker of the occurrence of EV; cutoff points for the higher predictive value 98% were positive, and 96% were nagetive.

CONCLUSION: In the cirrhotic patients having ascites, the occurrence of EV is related only with SAAG and size of EV are mainly associated to the degree of SAAG. A SAAG value of ≥1.65 ± 0.014 g/dl is a helpful mean to predict the occurrence of EV in cirrhotic patients with ascites.

KEY WORDS: SAAG, Esophageal varices, Portal hypertension, Cirrhosis.

INTRODUCTION

The chronic Liver disease is a frequent disorder in south Asia. Increasing prevalence need to be evaluated and updated from time to time for Hepatitis B and C, progressively people are being affected by this dangerous disease.[1] In an area based study 31% of the cases had hepatitis B core antibodies and 4.3% had hepatitis B surface antigen (HBsAg) positive.[2] The mass of HCV associated chronic liver disease in Pakistan has also increased and additional current data shows about 60-70% patients with CLD to be positive for Anti HCV antibodies.[3] Patients with chronic liver disease eventually progress to cirrhosis of liver and its associated problems like portal hypertension. Development of esophageal varices is one of the major problems of portal hypertension.[4] In the cirrhotic patients chronic upper GI bleeding is common because of portal hypertension seen in about 30% to 40%.[5] Reports western studies reveals that variceal bleeding from upper part ranges between (17 to 57%) but in our cases it is (5 to 10%).[6]

In the near past fourth Baveno international consensus on portal hypertension advocated that total cirrhotic patients for varices should be monitored through diagnostic endoscopy.[7] Investigation of gastro esophageal varices (GEV) in cirrhotic patients enhances the cost and involves a confirmed degree of invasiveness and discomfort of patients.[8] Several retrospective studies shows probable non-invasive sign of esophageal varices in cirrhotic patients like SAAG and serum albumin levels.[9]

Several parameters similar to clinical ultrasonographic and biochemical values may be benefited having prognostic skill for non persistent evaluation of bleeding risk from varices.[10] Serum-ascitic albumin attentiveness gradient (SAAG) has been concluded in several studies like an oblique marker in approximating portal hypertension and its problems so it's a helpful mean in the forecasting of incidence of EV.[11-12] For SAAG involvement computation assessing the albumin concentrations of serum and ascitic fluid specimens got hold on parallel day and subtracting the ascitic fluid value from the values of serum. If SAAG is equal or greater than 1.1 gm/dl (11mg/L), the patient has covered portal hypertension, with regarding decreases the risk of bleeding upto (97%) with this correctness.[13] Estimation of SAAG is probably still in a tinny, un-assumingly operational laboratory and made available for new means to recognize of high risk patients for GI bleeding.

The aim of present study is to report the frequency of the range of serum-ascitic albumin gradient (SAAG) in the forecast of incidence of EV in the patients of cirhosis with ascites and to study connection between degree of SAAG, and incidence of ranking of EV. This will make possible to perform upper gastrointestinal

endoscopy in preffered patients thus keep away from needless interference and simultaneously not present the patients at risk of bleeding.

PATIENTS AND METHODS

This cross sectional study was conducted in the Department of Medicine, Liaquat University of Medical & Health Sciences (LUMHS), Jamshoro from March 2008 to February 2009. In this study 100 cirrhotic patients were included all having ascites, all the cases under went this study were diagnosed on the basis of pervious biopsy report having cirrhosis and ultrasonographic, biochemical and clinical examinations confirmed the diagnosis.

Exclusion criteria incorporated all those patients who were already being treated on medicine, all subjects getting medicines as prophylactic measure for bleeding variceal, patients not included in this study who went formerly had scelerotherapy or band ligation, patents suffering fron Hepatocellular carcinoma, previous portasystemic anastomosis or portal vein thrombosis and ascites because of etiologies other than cirrhosis.

All patient attending Medical OPD and Emergency Department of Liaquat University of Medical & Health Sciences, Jamshoro with recognized analysis of decompensated chronic liver disease with ascites, were admitted in the medical units for the purpose of study. Examination of cirrhosis was supported on former liver biopsy or on ultrasonographic, biochemical and clinical observation. A consensus form was ended and whole study protocol described to patients with written consent obtained. All patients undertaken a full physical examination followed by blood sampling for the investigations i.e. complete blood count, liver function test, liver biochemistry, serum albumin, prothrombin time and viral profile (HbsAg, Anti-HCV). Diagnostic paracentesis was done under aseptic measures within 30 minutes of taking blood samples. Ascitic fluid was sent in 10cc disposable syringe for detailed report and ascitic albumin to main LUMHS laboratory. Serum ascitic-albumin gradient was calculated. Abdominal ultrasound was performed to evaluate the echogenic texture of liver parenchyma, splenomegaly and ascites. Flexible upper gastrointestinal endoscopy of all patients was conducted in Department of Medicine, LUMHS, again after a written consent by the patient. Patients were evaluated for the incidence and evaluating EV throughout process. deFranchis classification' system was used for the grading of Esophageal varices with the following:[14]

F1 as small straight varices,

F2 as enlarged tortuous varices occupying less than one third of the lumen.

F3 as large coil-shaped varices occupying more than one third of the lumen.

All the collected data of 100 subjects was entered and analyzed on statistical program SPSS version 16.0. Frequency and percentages were computed for categorical variables like sex, age groups, clinical features, serum ascites-albumin gradient ratio, grading of esophageal varices and X^2 test was applied to compare the proportions between serum ascites-albumin gradient and EV. Mean and standard deviation were estimated for quantitative variables like age and serum ascites-albumin gradient. Regression analysis was applied to determine the positive and negative correlation between SAAG and degree of Esophageal-varices. A p-value of ≤ 0.05 was considered statistically significant level.

RESULTS

Out of 100 patients 62 (62%) were male and 38 (38%) female, mean age + SD of the patients was (44.59 ± 13.55 years). Causative agents were observed to be HCV in 53 (53%) patients and HBV in 34 (34%) patients, 5 patients (8%) had both HBV and HCV infection while in 5 (5%) patients the viral markers for HBV and HCV could not be detected.

Mean Albumin serum level $\pm$ SD was (2.87 ± 0.34 (1.9 to 3.5 g/dl), albumin ascitic level was (0.87 ± 0.52 (0.1 to 2.2 g/dl), and mean $\pm$ SD SAAG value was (2.01 ± 0.52). The patients were divided into groups according to SAAG values. 3 patients (3%) had SAAG value <1.10 g/dl. 11 patients (11%) had SAAG rangesb/w (1.10 and 1.49 g/dl). 33(33%) patients had SAAG rangeb/w(1.50 and 1.99 g/dl). 29(29%) patientshad SAAG rangeb/w(2.0 and 2.49 g/dl) and 24(24%) patients SAAG range was(≥2.5 g/dl).

EV were occur in 87 (87%) patients and were missing in 13 (13%) patients. Occurrence of EV in patients having SAAG ≥1.1 g/dl is statistically significant with $p < 0.001$. Out of the 87 patients having esophageal varices, 21 (22.6%) had grade F1, 38 (45.3%) had grade F2 and 28 (32.1%) had grade F3 varices.

All were distributed with the SAAG values and the size of varices was evaluated.3 patients found to have SAAG value <1.10 and EV were absent in all of them. 11 patients were found to have SAAG ranges between (1.1 and 1.49 g/dl), EV were not present in 7 (63.6%) of them while 4 (36.4%) had grade F1 varices. 33 patients SAAG ranges was between (1.50 and 1.99 g/dl), out of these 3 (9%) did not have varices, 5 (15.2%) had grade F1 varices while 15 (45.5%) had grade F2 varices and 10 (30.3%) had grade F3 varices. 29 patients were found with the SAAG range between (2.0 and 2.49 g/dl), out of these 7 (24.1%) had grade F1 varices, 16 (55.2%) had grade F2 varices and remaining 6 (20.7%) had grade F3 varices. 24 patients had SAAG values ≥ 2.5 g/dl,

TABLE I: DISTRIBUTION OF THE CASES ACCORDING TO DEGREE OF SAAG & GRADE OF EV

SAAG Group	No. of Patients	Esophageal varices (Grades)			
		Absent	F1	F2	F3
< 1.10	3	3 (100%)	-	-	-
1.10 - 1.49	11	7 (63.6%)	4 (36.4%)	-	-
1.50 - 1.99	33	3 (9%)	5 (15.2%)	15 (45.5%)	10 (30.3%)
2.00 - 2.49	29	-	7 (24.1%)	16 (55.2%)	6 (20.7%)
≥2.5	24	-	5 (20.8%)	7 (29.2%)	12 (50%)
Total	**100**	**13**	**21**	**38**	**28**

Grade of esophageal varices were significantly associated with the level of SAAG ($p<0.01$)

out of these 5(20.8%) had grade F1 varices while 7 (29.2%) had grade F2 varices, while 12 (50%) patients were found to have grade F3 varices. (Table I)

Mean SAAG values were also calculated according to esophageal varices. Mean value of SAAG was 1.3 g/dl ± 0.20 (SD) in 13 patients without esophageal varices. 21 patients had grade F1 varices with mean SAAG 2.0 g/dl ± 0.54 (SD). 38 patients had grade F2 varices with mean SAAG 2.1 g/dl ± 0.38 (SD) and 28 patients with grade F3 varices were found to have mean SAAG 2.3 g/dl ± 0.44 (SD). (Table II)

The grades of the esophageal varices demonstrated important statistical relationship with SAAG degree ($p<0.01$) with a Pearson association coefficient of $r = 0.55$ ($p<0.01$). With the use receiver operating Characteristics (ROC) curve a SAAG range of ≥1.65 ± 0.014 g/dl was an perfect marker of the occurrence of EV; Cutoff points for the greater predictive range were (98%) positive and (85 %) negative. (Figure I)

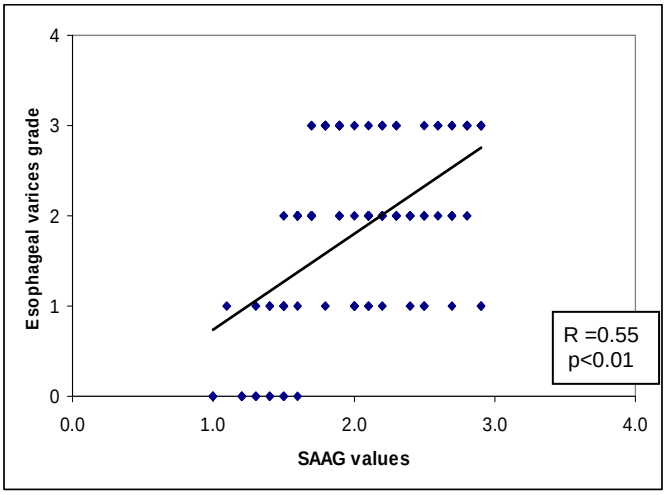
TABLE II: SAGG VALUE ACCORDING TO ESOPHAGEAL VARICES

Esophageal Varices	No. of Patients	SAAG Mean±SD
Absent	13	1.3 ± 0.20
F1	21	2.0 ± 0.54
F2	38	2.1 ± 0.38
F3	28	2.3 ± 0.44
P-value		0.001

DISCUSSION

Primary finding and prevention of esophageal varices in the patients of cirrhosis is critical complications. It is advised that all cirrhotic patients should be screened for varices at diagnosis. However our health system lack endoscopic facilities in all hospitals, therefore this

FIGURE I: CORRELATION BETWEEN SSAG VALUES AND GRADES OF ESOPHAGEAL VARICES



approach is not applicable in our setup.[15] Non-invasive markers of varices are desired to decrease the requir for screening endoscopy in cirrhotic patients.

SAAG is one of these minimally invasive indirect parameters that can predict the availability of esophageal varices as manifestation of portal hypertension. Few studies emphasize the value of SAAG in the determination of portal hypertension and so in the prediction of availability of esophageal varices.

By the report of Hoefs et al [16] on 56 patients showed that there is excellent correlation exists between portal hypertension and SAAG with p= 0.05 and r=0.73. Same results were found by Rector et al [17] in its study contain 18 alcoholic cirrhosis patients. Relationshipb/w portal hypertension and SAAG was (p=0.001 and r=0.8).

Demirel et al [18] performed a study on 45 patients to evaluate the relationship b/w SAAG and EV in cirrhotic patients. SAAG values were found to be above 1.1 g/

dl in all patients which supports my study and total patients with a SAAG range large than 2.0 had EV, but no relationship was found b/w SAAG and EV.

Study of Masroor et al [19] at Karachi showed a strong correlation between degree of SAAG and grading of esophageal varices. 50 cirrhotic patients were included in the study. All of them had SAAG ≥ 1.1 g/dl and esophageal varices were seen in 46 out of 50 patients. It showed that raised SAAG reflects great probabilities of occurence of EV in the cirrhotic patients. Further more the availability and size of esophageal varices is observed to be directly concerned to the degree of SAAG. These results strongly support our study. Torres et al [20] determined the correlation between SAAG and problems of portal hypertension patented by the occurrence and grades EV. 31 patients were added in the study, out of which 25 had elevated SAAG (≥ 1.1 g/dl) and 6 had low SAAG (<1.1 g/dl). EV was observed with high SAAG 17 of the 25 patients and with low SAAG 6 patients, which supports our study in which all the patients with esophageal varices had high SAAG (≥ 1.1 g/dl).

In our study, EV occur in 4 of 11 (28.6%) patients with SAAG value between 1.10-1.49 g/dl, in 30 of 33 (66.7%) patients with SAAG value between 1.50-1.99 g/dl, in 29 of 29 (100%) patients with SAAG value between 2.0-2.49g/dl and in 24 of 24 (100%) patients with SAAG values ≥2.5 g/dl. These values show that as the degree of SAAG increases, the probability of availability of esophageal varices also increases. Thus it proves that degree of SAAG is directly associated to the presence of esophageal varices.

Further more our study shows that grades of esophageal varices were significantly related with the degree ($p<0.01$) of SAAG with a Pearson relationship of $r = 0.55$ ($p<0.01$) so as the size (grade) of esophageal varices increases, the degree of SAAG also increases. This suggests that the size of esophageal varices is completely associated to the SAAG degree. This is in contrast to the study conducted by Torres et al which concluded that size of esophageal varices in patents with ascites and degree of SAAG not related with high SAAG. This conflict may be due to variations in different populations and due to deferent prevalence cirrhosis and severity liver disease as the studies of Demirel et al[18] & Torres et al [20] were conducted on Western population where the main causative factor of liver cirrhosis is alcoholism while our study included Pakistani patients in whom the chronic viral hepatitis B and C were the main causative factors for development of liver cirrhosis. Poor nutritional status of Pakistani patients may be another contributing factor. This fact is supported by similar results of study by Masroor et al [19] conducted on Pakistani population.

In addition, Torres et al [20] detected a range of SAAG ≥1.435 ± 0.015 g/dl as a require able mean to predict the occurence of EV. This value is very much similar to our study which gives the value of SAAG ≥1.65 ± 0.014 g/dl as accurate perfect markers of occurrence of EV.

CONCLUSION

Cirrhotic patients with occurrence of EV and ascites related only with High value of SAAG (≥1.1g/dl).Occurrence and size of EV in patients with ascites is directly associates to the SAAG degree and a SAAG value of ≥1.65 ± 0.014 g/dl is a helpful mean to predict the occurrence of EV in cirrhotic patients with ascites.

REFERENCES

1. Khokhar N. Spectrum of chronic liver disease in a tertiary care hospital. J Pak Med Assoc. 2002;52:56-58.
2. Luby SP, Qamruddin K, Shah AA, Omair A, Pasha O, Khan Aj, et al. The relationship between therapeutic injection and high prevalence of hepatitis C infection in Hafiz bad, Pakistan. Epidemiol Infect.1997; 119:349-56.
3. Umar M, Khaar HB, Anwar F, Aid M. Management of acute variceal bleeding by octreotide. J Rawal Med Coll. 2000,4:4-16.
4. Sethar GH, Ahmed R, Rathi SK, Shaikh NA. Platelet count / splenic size ratio: a parameter to predict the presence of esophageal varices in cirrhotics. J Coll Physicians Surg Pak. 2006;16:183-6.
5. Jensen DM. Endoscopic screening for varices in cirrhosis: findings, implications, and outcomes. Gastroenterology. 2002;122:1620-30.
6. Farooqi RJ, Farooqi JI , Rehman M , Ahmad H , Ahmad F, Gul S. Outcome after injection sclerotherapy for esophageal variceal bleeding in patients with liver cirrhosis and COPD. J Postgrad Med Inst. 2005;19:76-80.
7. Prevention of the formation of varices (pre-primary prophylaxis). In: De Franchis R, editor. Portal hypertension IV: proceedings of the fourth Baveno international consensus workshop. Massachusetts: Blackwell; 2006. p.103-151.
8. Adrover R, Cocozzella D, Borzi S, Montenegro L, Defelitto M, Bosia D, et al. When is the best time to perform upper digestive endoscopy to detect the presence of esophageal varices in patients with cirrhosis? Gastroenterology Hepatol. 2004;27:353-6.
9. Zaman A, Becker T, Lapidus J, Benner K. Risk factors for the presence of varices in cirrhotic patients without a history of variceal hemorrhage. Arch Intern Med. 2001;161:2564-70.

10. Sarwar S, Khan AA, Alam A, Butt AK, Shafqat F, Malik K, et al. Non-endoscopic prediction of presence of esophageal varices in cirrhosis. J Coll Physicians Surg Pak. 2005;15:528-31.
11. Gurubacharya DL, Mathura KC, Karki DB. Correlation between serum-ascites albumin concentration gradient and endoscopic parameters of portal hypertension. Kathmandu Univ Med J. 2005;3:327 -33.
12. Dittrich S, Yordi LM, de Mattos AA. The value of serum-ascites albumin gradient for the determination of portal hypertension in the diagnosis of ascites. Hepatogastroenterology. 2001;48:166-8.
13. Runyon BA. Management of adult patients with ascites due to cirrhosis. Hepatology. 2004;39:841-56.
14. Gill ML, Atiq M, Sattar S, Khokhar N. Non-endoscopic parameters for the identification of esophageal varices in patients with chronic hepatitis. J Pak Med Assoc. 2004;54: 575-7.
15. Farooqi JI, Ahmed H, Ikramullah Q, Ahmed F, Rehman M. Predictors of esophageal varices in patients of liver cirrhosis. J Postgrad Med Inst. 2007;21:60-4.
16. Hoefs JC. Serum protein concentration and portal pressure determine the ascitic fluid protein concentration in patients with chronic liver disease. J Lab Clin Med. 1983;102:260-73.
17. Rector WG Jr, Reynolds TB. Superiority of the serum-ascites albumin difference over the ascites total protein concentration in separation of transudative and exudative ascites. Am J Med. 1984;77:83-5.
18. Demirel U, Karincaoglu M, Harputluoglu M, Ates M, Seckin Y, Yildirim B, et al. Two findings of portal hypertension: evaluation of correlation between serum-ascites albumin gradient and esophageal varices in non-alcoholic cirrhosis. Turk J Gastroenterol. 2003;14:219-22.
19. Masroor M, Qamar R, Ahmed I, Danish S, Sattar A, Imran K, et al. Do we always need Endoscopy to predict varices. Med Channel. 2007;13:55-8.
20. Torres E, Barros P, Calmet F. Correlation between serum-ascites albumin concentration gradient and endoscopic parameters of portal hypertension. Am J Gastroenterol. 1998;93:2172-8.

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