Section: General Medicine

Original Research Article

# A HOSPITAL BASED CROSS SECTIONAL STUDY TO CORRELATE THE SERUM ALBUMIN CONCENTRATION AND SERUM–ASCITES ALBUMIN GRADIENT (SAAG) WITH THE ESOPHAGEAL VARICES (EV) IN PATIENTS WITH PORTAL HYPERTENSION DUE TO CHRONIC LIVER DISEASE (CLD)

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## Abstract

**Background:** The liver regulates most chemical levels in the blood and excretes a product called bile, which helps carry away waste products from the liver. CLD is gradually becoming a public healthy priority in India, CLDs accounted for 2.1% of all deaths in India in year 2016. One of the major complications of CLD reported was esophageal variceal bleeding, the reported mortality from variceal bleeding ranges from 17% to 57%. The objective is to investigate the correlation between level of serum-ascites albumin gradient (SAAG) and the presence of esophageal varices (EV) and their grades in patients with portal hypertension due to chronic liver disease. **Materials and Methods:** This hospital based cross sectional study was conducted on 94 patients admitted in Medicine wards and ICU of Tertiary Care Centre of Central India. Duration of Study was from November 2020- October 2022. **Result:** No patients had low SAAG (1.1g/dl). None of the patients with low SAAG had EV and 85 (90%) patients among high SAAG had EV. The presence of esophageal varices in high SAAG is directly related to degree of SAAG (P=0.0001). The size of the EV demonstrates significant statistical association (p = 0.0000) with the degree of SAAG in patients with high SAAG. The presence of esophageal varices and the size of the EV was not related to the serum albumin (P=0.19) concentration in our study. **Conclusion:** In patients with CLD with portal hypertension the presence of EV is associated only with patients with high SAAG. The presence of EV in patients with high SAAG is directly related to the degree of SAAG.

## INTRODUCTION

Cirrhosis, a chronic liver disease, is characterized by diffuse fibrosis and distortion of the normal acinar and/or lobular architecture of liver with or without degeneration, regeneration or nodule formation.[1] Cirrhosis results in a decrease in hepatic cellular mass. In India, the aetiology of cirrhosis of the liver is varied, the most common condition is HBV (Hepatitis B Virus) infection followed by alcohol and hepatitis C infection,[2,3] NAFLD burden is similarly increasing in India with an upward moving body mass index and diabetes incidence. The prevalence of hepatitis B infection in India is 2.4%.[4]

Cirrhosis eventually leads to the development of portal hypertension which affects various organs of the body, causing morbidity and even deaths in some patients. Portal hypertension presents with ascites, gastrointestinal bleed and splenomegaly.

Most dreaded complication of portal hypertension, oesophageal variceal bleeding, is responsible for high mortality in cirrhotic patients.[5]

Oesophageal varices have a high prevalence rate of 60- 80% in cirrhotic patients and it is a major cause of bleeding in 25-30% of the patients. Every year 5% new cases of oesophagalvarices are seen and every year, nearly 5-10% of these patients progress to large varices from small varices.[6]

Previous literature recommends that all cirrhotic patients should be screened for the presence of oesophagealvarices at the time of diagnosis. However, performing an endoscopic evaluation of all cirrhotic patients for screening may not be the affordable approach, more so in resource crunch situations like India. A cost-effective method of

screening would be possible if cirrhotic patients could be identified for varices based on clinical and biochemical variables.[6]

In order to reduce the increasing burden that endoscopy units will have to bear, some studies have attempted to identify characteristics that non-invasively predict the presence of varices. In the view of the above, the present study was undertaken to determine the correlation and association between the level of SAAG and serum albumin concentration with the complications of portal hypertension, mainly the presence and grade of oesophagealvarices (EV) found on upper gastrointestinal endoscopy. This would permit the use of the SAAG and serum albumin concentration as a preliminary indirect parameter that would indicate the presence of EV as a manifestation of portal hypertension.

Hence this study was conducted to investigate the correlation between level of serum-ascites albumin gradient (SAAG) and the presence of esophageal varices (EV) and their grades in patients with portal hypertension due to chronic liver disease.

## MATERIALSANDMETHODS

This hospital based cross sectional study was conducted on 94 patients admitted in Medicine wards and ICU of Tertiary Care Centre of Central India. Duration of Study was from November 2020-October 2022.

**Inclusion Criteria**

All patients aged above 18 years with chronic liver disease and portal hypertension diagnosed by Presence of chronic liver disease as evidenced by: abdominal ultrasound and liver profile derangement. Presence of portal hypertension as evidenced by: the presence of splenomegaly, portal-systemic collateral pathways, biphasic or reversal flow in portal vein, portal vein diameter > 13 mm.Presence of ascites detected by clinical examination and confirmed by abdominal ultrasound.

**Exclusion Criteria**

Causes of ascites other than chronic liver diseaseeg. congestive heart failure, renal failure, tuberculosis.

**Sample Size Estimation**

With reference to the study done by viswanthareddy et al. On "A study to correlate the serum–ascites albumin gradient (SAAG) with the esophageal varices in patients with portal hypertension".

- p = 0.909
- Absolute prescision (d) = 8%
- Desired confidence level = 95%
- Sample size (n) = 94
- Formula:

Sample size- 94.

Sample Technique: 94 patients with portal hypertension due to chronic liver disease attending/admitted in tertiary care centre of central India selected randomly till the sample size during study period and fulfilling the inclusion criteria were included and SAAG and serum albumin were compared with esophageal varices.

**Method of Collection of Data**

Approval from Institutional Ethics Committee (IEC) will be sought. Permission will be taken from the Head of the department of medicine. The purpose of the study will be explained to the study subjects. Informed written consent in local language will be taken before enrolment for study.

Meticulous history, clinical examination, laboratory investigations were carried out in all cases of chronic liver disease. CLD and Ascitis was confirmed by an abdominal ultrasound.

**Investigations Done on Patients**

Liver function tests, Renal function tests, Hepatitis viral markers (HBsAg and anti HCV), Ascitic fluid analysis-cell type, cell count, albumin, sugar, Abdominal ultrasonography, Upper Gastrointestinal Endoscopy.

**Statistical Analysis**

Data will be entered in the Microsoft Excel Sheet and analyzed using appropriate statistical tests.

## RESULTS

Among the study subject, 31(33%) were aged between 41 to 50 yrs, 21(22.3%) were aged between 51 to 60 yrs, 18(19.1%) were aged between 31 to 40 yrs and belongs to older age group ≥60yrs, 5(5.3%) were aged between 21 to 30 yrs and 1(1.1%) were aged belongs to ≤20yrs. The mean and S. D age was 48.57 ±11.36. The youngest patients were 20 years female patient and older patients were 75 years male patient respectively.

Among the study subjects, majority of study participants were males 76(80.9%) and rest 18(19.1%) were females. The youngest patients was female and oldest patients was male respectively.

Among the study subject, 32(34%) were hematemesis in predominant symptoms are presents and majority of 62(64%) were hematemesis in predominant symptoms are absents.

Among the study subject, 28(29.8%) were hepatic encephalopathy in predominant symptoms are presents and majority of 66(70.2%) were hepatic encephalopathy in predominant symptoms are absents.

Among the study subject, majority of patients have grade-3 50(53.2%), 39(41.5%) were grade-2 and rest of patients were grade-1 5(5.3%).

**Table 1: Distribution of patients according to cause of CLD**

| Cause of CLD | Number of patients | Percentage (%) |
|---|---|---|
| HCV | 1 | 1.1 |
| AUTOIMMUNE | 1 | 1.1 |
| WILSONS DISEASE | 2 | 2.1 |


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| | | |
|---|---|---|
| ALCOHOLIC + HBsAg | 2 | 2.1 |
| HBsAg | 9 | 9.6 |
| CRYPTOGENIC | 12 | 12.8 |
| ALCOHOLIC | 67 | 71.3 |
| Total | 94 | 100.0 |

Among the study subject, 67(71.3%) were alcoholic chronic liver disease, 12(12.8%) were cryptogenic chronic liver disease, 9(9.6%) were HBsAg chronic liver disease, 2(2.1%) were alcoholic and HBsAg multiple chronic liver disease, 2(2.1%) were Wilsons disease and both HCV, autoimmune were 1(1.1%) respectively.
Among the study subject, 11(11.7%) had an HBsAg chronic liver disease and rest of 83(88.3%) were HBsAg chronic liver diseases are absents.
Among the study subject, 1(1.1%) had an HCV chronic liver disease and majority of (88.3%) were HCV chronic liver diseases are absents.
Among the study subject, 9(9.57%) were normal platelets counts in lacs and majority of cases was platelets counts are abnormal 85(90.84%). The mean and S. D of the platelets counts in lacs 9589.61. Minimum and maximum platelets count (in lacs) were 350000 and 346000 respectively.
Among the study subject, 47(50%) were majority of serum albumin cases between 2.5 to 2.9, 31(33%) were serum albumin cases belongs to more than or equal to 3 and rest of 16(17%) were serum albumin cases between 2 to 2.4 respectively. The mean and S. D of serum albumin cases was 2.7±0.321 and minimum, maximum serum albumin cases was 2 and 3.50 respectively.

**Table 2: Distribution of patients according to serum albumin**

| Serum Albumin(g/dl) | Number of patients | Percentage (%) |
|---|---|---|
| 2 to 2.4 | 16 | 17.0 |
| 2.5 to 2.9 | 47 | 50.0 |
| ≥3 | 31 | 33.0 |
| Total | 94 | 100.0 |

Among the study subject, 51(54.3%) were majority of SAAG cases between to 1.6 to 2, 29(30.9%) were SAAG cases between 1.1 to 1.5 and rest of 14(14.9%) were SAAG cases belongs to more than or equal to 2.1 respectively. The mean and S. D of SAAG cases were 1.7±0.288 and minimum, maximum SAAG cases was 1.20 and 2.50 respectively.

**Table 3: Distribution of patients according to SAAG (gm/dl)**

| SAAG in gm/dl | Number of patients | Percentage (%) |
|---|---|---|
| <1.1 | 0 | 0 |
| 1.1 to 1.5 | 29 | 30.9 |
| 1.6 to 2 | 51 | 54.3 |
| ≥2.1 | 14 | 14.9 |
| Total | 94 | 100.0 |

Mean ± S.D =1.7±0.288, Range=Max-Min= 2.50 -1.20
Among the study population, 37(39.4%) were grade1 EV, 25(26.6%) were grade 2 EV, 23(24.5%) were grade 2 EV and 9(9.6%) were no EV cases respectively.

**Table 4: Distribution of patients according to EV**

| Ascites | Number of patients | Percentage (%) |
|---|---|---|
| GRADE 1 | 37 | 39.4 |
| GRADE 2 | 23 | 24.5 |
| GRADE 3 | 25 | 26.6 |
| No | 9 | 9.6 |
| Total | 94 | 100.0 |

**Table 5: Relationship between theserum albumin and EV grades**

| EV Grade | Serum albumin g/dl | | | Total(n=94)% | Chi-square | p-value |
|---|---|---|---|---|---|---|
| | 2 to 2.4 | 2.5 to 2.9 | ≥3 | | | |
| Grade-1 | 3 | 23 | 11 | 37(39.4%) | 8.57 | 0.19 Statistically not significant |
| Grade-2 | 4 | 10 | 9 | 23(24.5%) | | |
| Grade-3 | 5 | 11 | 9 | 25(26.6%) | | |
| No | 4 | 3 | 2 | 9(9.6%) | | |
| Total | 16 | 47 | 31 | 94 | | |

Among the study subject 94, 37 patients were grade-1 in that 17(45.9%) were SAAG between 1.1 to 1.5, 20(54.0%) were SAAG between 1.6 to 2 and no case in more than or equal to 2.1. 23 patients were grade-2 in that 4(17.3%) were SAAG cases between 1.1 to 1.5, majority of cases 15(65.2%) were SAAG cases between 1.6 to 2, 4(17.4%) were SAAG cases belongs to more than or equal to 2.1. 25 patients


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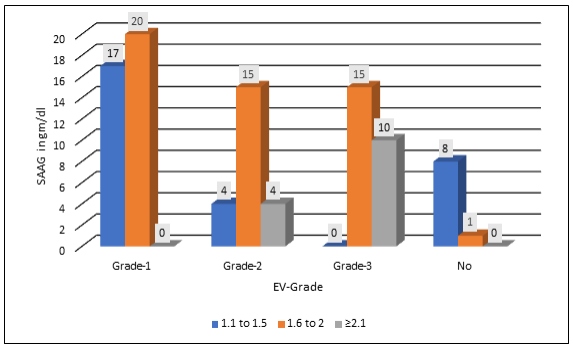
were grade-3 in that majority of cases 15(60%) were SAAG cases between 1.1 to 1.5, 10(40%) were SAAG cases belongs to more than or equal to 2.1. 9 patients were no grades in that 8(88.8%) were SAAG cases between 1.1 to 1.5, 1(11.1%) were SAAG cases between 1.6 to 2 and there was no SAAG cases more than or equal to 2.1.On applying chi-square test to find the relationship between SAAG and EV-grades was statistically significant at p (<0.001).

Among the study subject 94, 37 patients were grade-1 in that 3(8.10%) were serum albumin between 2 to 2.4, majority of cases 20(54.0%) were serum albumin between 2.5 to 2.9 and 11(29.7%) were serum albumin cases belongs to more than or equal to 3. 23 patients were grade-2 in that 4(17.3%) were Serum albumin cases between 2 to 2.4, majority of cases 10(43.8%) were serum albumin cases between 2.5 to 2.9, 9(39.1%) were serum albumin cases belongs to more than or equal to 3. 25 patients were grade-3 in that 5(20%) were serum albumin cases between 2 to 2.4, 11(44%) were serum albumin cases between 2.5 to 2.9 ,9(36%) were serum albumin cases belongs to more than or equal to 3. 9 patients were had no grades in that 4(44.4%) were serum albumin cases between 2 to 2.4, 3(33.3%) were serum albumin cases between 2.5 to 2.9 and 2(22.2%) were serum albumin cases was more than or equal to 3.On applying chi-square test to find the relationship between serum albumin and EV-grades was statistically not significant at p (≠0.05).




**Graph 1: Relationship between the SAAG with EV grade**

Ninty four patients were enrolled in to the study, of which 76 (80.9%) were males and 18 (19.1%) were females. Hematemesis was present in 32 (34%) patients and 28 (29.8%) patients had hepatic encephalopathy. 39(41.5%) patients had grade2 ascites and 50 (53.2%) had grade 3 ascites. Alcoholic liver disease is the cause of chronic liver disease in most of the patients (71.3%).

No patients had low SAAG (1.1g/dl).85(90.4%) patients among high SAAG had EV. Among patients with high SAAG 29 patients had SAAG between 1.1-1.5g/dl, 51 patients had SAAG between 1.6-2.0g/dl and 14 patients had SAAG >2.1g/dl. 21 (72.4%) of 29 with SAAG between 1.1-2-1.5g/dl had EV, 50 (98%) of 51 with SAAG between 1.6-2.0g/dl had EV and 14 (100%) of 14 with SAAG between had EV. The presence of esophageal varices in high SAAG is directly related to degree of SAAG (P<0.001) [Table 5]. The size of the EV demonstrate significant statistical association (p = 0.00) with the degree of SAAG in patients with High SAAG [Table 5].

Among the study subject 94, 37 patients were grade-1 in that 3(8.10%) were serum albumin between 2 to 2.4, majority of cases 20(54.0%) were serum albumin between 2.5 to 2.9 and 11(29.7%) were serum albumin cases belongs to more than or equal to 3. 23 patients were grade-2 in that 4(17.3%) were Serum albumin cases between 2 to 2.4, majority of cases 10(43.8%) were serum albumin cases between 2.5 to 2.9, 9(39.1%) were serum albumin cases belongs to more than or equal to 3. 25 patients were grade-3 in that 5(20%) were serum albumin cases between 2 to 2.4, 11(44%) were serum albumin cases between 2.5 to 2.9 ,9(36%) were serum albumin cases belongs to more than or equal to 3. 9 patients were had no grades in that 4(44.4%) were serum albumin cases between 2 to 2.4, 3(33.3%) were serum albumin cases between 2.5 to 2.9 and 2(22.2%) were serum albumin cases was more than or equal to 3.On applying chi-square test to find the relationship between serum albumin and EV-grades was statistically not significant at p (≠0.05).

## DISCUSSION

Severe upper gastrointestinal bleeding as a complication of portal hypertension develops in about 30-40% of patients with cirrhosis. Due to the increasing prevalence of chronic liver diseases, variceal haemorrhage is associated with significant morbidity, mortality and health care costs. Numerous studies have demonstrated the efficacy of beta blockers for primary prevention of variceal bleeding in patients with high-risk varices indicating the importance of screening for the presence of EVs.

In 2007, the American Association for the Study of Liver Diseases stated that screening esophagogastroduodenoscopy (EGD) for the diagnosis of esophageal and gastric varices is recommended when the diagnosis of cirrhosis of liver is made according to the AASLD guidelines. Baveno IV consensus conference on portal hypertension recommended that all cirrhotic patients should be screened for the presence of esophageal varices when liver cirrhosis is diagnosed (EASL).

Therefore, there is a particular need for a non-invasive predictor for the presence of EVs to ease the medical, social and economic burden of the disease. Previous studies have documented good predictive value of various non-endoscopic variables for the presence or absence of varices. In our study we considered only simple, commonly available, reproducible parameters.

Torres et al,[7] found that esophageal varices were present in 17 of 25 (68%) patients with high SAAG and in none of six (0%) patients with low SAAG (p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= 0.028) and in patients with non alcoholic liver disease.

AboHamila8 graded esophageal varices in patients with high SAAG as follows: In SAAG values between 1.10 - 1.49 g/dl, one patient (20%) had grade I EV, two patients (40%) had grade II EV and two patients (40%) had grade III EV. In SAAG values between 1.50 - 1.99 g/dl, two patients (40%) had grade I EV, two patients (40%) had grade II EV and one patient (20%) had grade III EV. In SAAG values of ≥ 2.0 g/dl, one patient (10%) had grade I EV, two patients (20%) had grade II EV, four patients (40%) had grade III EV and three patients (30%) had grade IV EV. They found no significant relation between the degree of SAAG and the grading of EV.

In our study there was an association between the level of SAAG and the presence 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 has association and had a good correlation with the size of oesophageal varices.[8]

Khan et al,[9]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.

In our study we also found that serum albumin concentration was not related to presence of EV in chronic liver disease patients with portal hypertension. However, the level of serum albumin presented no association and had no correlation with the size of oesophageal varices.

## CONCLUSION

In patients with CLD with portal hypertension the presence of EV is associated only with patients with high SAAG. The presence of EV in patients with high SAAG is directly related to the degree of SAAG. The size of the EV in patients with high SAAG is associated with the degree of SAAG. The presence of EV is does not correlate with serum albumin level. The size of the EV did not demonstrate significant statistical association with the level of serum albumin.

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