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PREDICTION OF ESOPHAGEAL VARICES BASED ON SERUM-ASCITES ALBUMIN GRADIENT(SAAG) IN CIRRHOTIC PATIENTS

Gastroenterology

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KEYWORDS

1.Introduction

Cirrhosis is the end stage of chronic liver disease. Ascites and esophageal varices (EVs) are the most common complications of portal hypertension (PHT), with an incidence of approximately 50% [1]. Since effective preventive modalities have been established for variceal haemorrhage, early detection of EVs is critical for primary prevention of bleeding. Upper gastrointestinal endoscopy (UGE) remains the gold standard for screening [2,3]. However, many studies have been conducted to predict PHT and EV with a diverse rate of accuracy. All patients with cirrhosis should undergo UGE screening to identify those at high risk of bleeding and who may benefit from primary prophylaxis, since EVs are an independent predictive factor and an early complication of cirrhosis. The test should also be repeated during the follow-up of patients with cirrhosis without EVs, who are at risk of bleeding, with or without decompensation [1]. Though UGiscopy is the gold standard to screen patients for variceal development; but has has many drawbacks such as being relatively expensive, invasive, and restrictive [4]. Such a screening test should be simple, rapid, reproducible, and inexpensive [5–7]. The serum ascites albumin gradient (SAAG) is a minimally invasive method that is precise and has been described in the classification of ascitic fluid(AF) based on the presence or absence of PHT [8]. Many Studies have been performed to identify non-invasive parameters for the prediction of EVs in patients newly diagnosed with cirrhosis [5]. SAAG can be considered an indirect parameter for the detection of EVs and is useful in regions where there are limitations to perform UGE. The aim of our study was to evaluate the role of SAAG in the prediction of EVs in cirrhotic patients with ascites.

2. Material and Methods

This was a descriptive cross-sectional study of data from the hospital records of patients in the Department of Gastroenterology, Sardar Vallabhbhai Hospital,Ahmedabad, conducted from December 2021 to May 2021.

Inclusion Criteria

All newly diagnosed cirrhotic patients with ascites were confirmed based on history and physical examination, biochemical parameters, and abdominal ultrasonography. Patients without any history of hematemesis and/or melena were included in the study.

Exclusion Criteria

Pregnant patients, those with bleeding from existing PHT or AIDS, and those currently on beta-blockers were excluded from the present study. Excluding cirrhosis,patient with ascites secondary to aetiology such as congestive heart failure, abdominal tuberculosis, hepatocellular carcinoma, renal failure, and intra-abdominal malignancy, as well as patients with albumin transfusion were excluded.

Study Methodology

All patients in this study underwent detailed clinical evaluation. Serum and ascitic fluid albumin levels were determined using standard laboratory techniques [1]. SAAG was calculated using the following formula: SAAG (g/dL) = (serum albumin) − (albumin level of ascitic fluid). The two values were measured at the same time. Patients with cirrhosis are often subjected to screening endoscopy for varices in order to plan prophylactic therapy and/or follow-up. Informed consent was obtained from the patients prior to inclusion in the study.

Statistical Analysis

Data were collected in a predetermined manner and results were analysed using the Statistical Package for Social Sciences (SPSS) program, version 20.0. The chi-square test ($\chi 2$) and Fisher's exact test were used to calculate differences between qualitative variables as indicated. Quantitative data are expressed as mean ± SD. Independent t-test was used to calculate the differences between quantitative variables in the two groups. One-way ANOVA F-test was used to calculate the differences between quantitative variables in more than two groups. All statistical comparisons were conducted with a significance level of $p \leq 0.05$, wherein a p value of < 0.001 indicated a highly significant difference, while a value > 0.05 indicated non-significant difference.

3. Results

Total 80 cirrhotic patients with ascites during the aforementioned period were enrolled in our study .There were 60 men and 20 women (M/F- 4/1).

The average age of the patients was 54.59 ± 13.23 years.The main causes of cirrhosis were alcohol intake (37.5%) and NAFLD(25.0%) followed by hepatitis B and hepatitis C virus (10%, 2.5%) infection
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Mean values ± SD of serum albumin, ascitic fluid albumin, platelet count and total bilirubin were 2.49 ± 0.52 g/dL, 0.53 ± 0.54 g/dL, 138.35 ± 86.54 G/L and 5.39 ± 7.12 mg/dL respectively (Table 1).

Table 1. Baseline characteristics.

Variable	Total (n = 80)
Age(y)	54.59 ± 13.23
Sex [No. (%)] Male	60 (75.0%)
Female	20 (25.0%)
Aetiology [No. (%)] Alcohol intake	30 (37.5%)
NAFLD	30 (37.5%)
HBV	8 (10.0%)
HCV	2 (2.5%)
Other	10 (15.0%)
Serum albumin (g/dL)	2.49 ± 0.52
Ascitic fluid albumin (g/dL)	0.53 ± 0.54
Total bilirubin (mg/dL)	5.39 ± 7.12
Platelet count (G/L)	138.35 ± 86.54
Ascites protein/fluid (g/dL)	1.15 ± 1.05
Child–Pugh Score Child–Pugh A	3 (3.75%)
Child–Pugh B	19 (23.75%)
Child–Pugh C	58 (72.50%)
Esophageal varices Absent	6 (7.5%)
I	28 (35.0%)
II	33 (41.2%)
III	13 (16.3)
SAAG (g/dL) 1.10–1.49	10 (12.5%)
1.50–1.99	34 (42.5%)
≥2	36 (45.0%)

Distribution according to the Child–Pugh classification showed that patients in class C had the highest rate at 72.5%, with only about a quarter of patients in classes A and B. The mean score was 10.48 ± 1.71. In our study, of total 74 patients with EVs (92.50%), of which the

majority had EVs grades II and III (46 patients, 62.16%). EVs were more frequent in cirrhotic patients with high SAAG values of ≥1.5 g/dL ($p < 0.0001$).(Table 2)

Table 2. SAAG with the presence of Evs.

SAAG (g/dL)	Absence of Esophageal Varices		Presence of Esophageal Varices		p Value
	n	%	n	%	
1.1–1.49	5	6.25	5	6.25	
1.5–1.99	1	1.25	33	41.25	<0.0001
≥2	0	0	36	45.0%	

Results of the univariate analysis showed that factors such as platelet count, peritoneal fluid albumin level, SAAG, and Child–Pugh score were related to the occurrence of EVs on endoscopy results (Table 3).

Table 3. Predictive factors of EVs (univariate analysis).

	Absence of Esophageal Varices	Presence of Esophageal Varices	p Value	r Value
Age (y)	46.50	55.24	0.120	0.175
Platelets (G/L)	233.33	130.65	0.004	−0.314
Prothrombin	19.23	21.99	0.367	0.102
INR	1.53	1.81	0.215	0.140
Serum albumin (g/dL)	2.55	2.49	0.769	0.033
Ascites albumin (g/dL)	1.22	0.47	0.001	0.362
Total bilirubin (mg/dL)	1.07	5.74	0.123	0.174
Child–Pugh score	8.17	10.66	<0.001	0.388
SAAG	1.33	2.012	<0.001	0.429

INR: International Normalised Ratio; SAAG: Serum-Ascites Albumin Gradient.

According to Multivariate analysis - SAAG ratio was an independent predictor of EVs on endoscopy results with $p < 0.05$.

The results of our study revealed that SAAG values > 1.75 g/dL could predict EVs with a sensitivity of 78.4%, specificity of 83.3%, PPV of 98.31%, and an AUC of 0.952.

In the analysis of the correlation of SAAG with the severity of EVs, values > 1.8 g/dL were associated with the risk of large EVs with sensitivity of 88.24%, and specificity of 50.79%.

The correlation coefficient (r) between SAAG and EVs was 0.429, which was statistically significant ($p < 0.001$).

4. Discussion

Average Age in our study was 54.59 ± 13.23 years old, and the highest rate (30%) was seen in patients between 50 and 59 years of age. This result was similar to that reported by Hou Y et al., who included cirrhotic patients with a mean age of 52.5 ± 10.3 years [8]. However, the age of our patients was higher than of those included in the study by Lawson-Ananissoh LM et al. [9].They included over 125 cirrhotic patients with a mean age of 48.70 ± 14.89 years. However, this difference was not significant, probably due to the differences in race and geography. The causes of cirrhosis can vary depending on the geography, population characteristics, living habits, and human and medical development..

Alcohol intake and NAFLD followed by viral hepatitis remain the leading causes of liver fibrosis, globally. There are many types of hepatitis virus but the most common are HBV and HCV. Our research showed that alcohol intake,NAFLD ,chronic viral hepatitis(HBV and HCV) were the top three causes of cirrhosis, accounting for 87% of the cases.

In our study, the average platelet count was 138.35 ± 86.54 G/L, and the lowest count was 11 G/L.

The mean INR value in our study was 1.79 ± 0.52.
The average total serum bilirubin level was 5.39 ± 7.12 mg/dL, and the highest value was 36.50 mg/dL.

Liver's most important synthetic function is Albumin synthesis. Normally, the body can produce approx 15 g of albumin per day. Albumin synthesis has been reported to decrease to approximately 4 g per day in Child–Pugh class C patients with cirrhosis. Our study predominantly included Child–Pugh class C patients; hence, the mean albumin concentration of the study sample was low. The mean albumin concentration in our study was 2.49 ± 0.52 g/dL, which was higher than that in the study by Dewa Gde AB et al., who reported a concentration of 2.21 ± 0.45 g/dL in cirrhotic patients [10]. Lawson-Ananissoh LM et al. reported that serum albumin levels of <3.5 g/dL in patients with abdominal cirrhosis accounted for 92.8% of the cases [9].

The mean albumin level in ascitic fluid in our study was 0.53 ± 0.54 g/dL, ranging from 0.1 to 2.8 g/dL. This result was similar to that in the study by Enas A et al., who reported peritoneal fluid albumin in the range of 0.2–3.3 g/dL, with an average of 1.37 ± 0.7 g/dL [11]. Hou Y et al. reported that peritoneal fluid albumin averaged 0.6 ± 0.47 g/dL [8].

Currently, endoscopy is considered a good method to determine EVs in cirrhotic patients according to the recommendations of global digestive associations [2,12,13]. The mean value of SAAG in this study was 1.94 ± 0.40 g/dL, ranging from 1.2 to 3.4 g/dL. This result was similar to that reported in the study by Iqbal N et al. (1.905 ± 0.7955 g/dL) [14] but lower than that reported by Hou Y et al. (2.14 ± 0.47 g/dL) [8]. The results of our study showed that five out of ten patients with SAAG values from 1.1 to 1.49 g/dL, 33/34 patients with values from 1.5 to 1.99 g/dL, and all patients with values ≥2 g/dL had EVs on their endoscopy results. This difference in SAAG values was statistically significant with the occurrence of EVs ($\chi 2 = 54.614$ and $p < 0.0001$). Lawson-Ananissoh LM et al. reported that 75% of the patients with SAAG values >1.5 g/dL will develop EVs [9]. However, Suresh I et al. showed that 50% of the patients with SAAG values from 1.1 to 1.49 g/dL and all patients with values >1.5 g/dL had EVs [15], and this result was similar to that of our study. Torres E et al. reported that approximately 40% of the patients with SAAG values < 1.5 g/dL demonstrated EVs on endoscopy results, in contrast to 66.7% and 100% of those with values from 1.5 to 1.99 g/dL and ≥2 g/dL, respectively [16].

Summarising the above study , it may be considered that the SAAG value is truly related to the degree of EVs as well as showed that the incidence of EVs was higher in patients with higher SAAG. In our study,all those patient with SAAG>2 g/dl had EV compared to those SAAG values from 1.1 to 1.49 g/dL,only 50 % of patient had EV.. Some studies reported that all patients with SAAG values ≥ 1.5 g/dL had EVs [17,18].

Our study revealed that the mean SAAG value in patients without and with EVs was 1.33 and 2.012 respectively. Multivariate analysis revealed that SAAG was an independent parameter to predict EVs ($p = 0.0104$), and the corresponding r value was 0.429. Previous studies by Iqbal N et al. have demonstrated that the degree of esophageal varicose veins was significantly related to the SAAG value with a Pearson relationship value of 0.631 ($p < 0.01$) [14]. Suresh I et al. reported that the r value was 0.607 [15]. However, Hou Y et al. and Shahed FHM et al. reported the r values as 0.244 and 0.358, respectively [8,17]. The correlation coefficients differed marginally in the above studies; however, they both concluded that there was a positive correlation between SAAG and EVs, and that higher SAAG values were associated with a greater likelihood of EVs.. In the study by Iqbal N et al., SAAG value ≥ 1.90 ± 0.796 g/dL was a predictor of the presence of esophageal veins [14], while that in the study by Torres E et al. was 1.435 ± 0.015 g/dL [16]. Prabakaran DB et al. reported that a SAAG cutoff of 1.48 g/dL resulted in a specificity and accuracy of 82% and 89% respectively in the prediction of EVs [19]. In addition, Sayyed J et al. and Gurubacharya DL et al. suggested that the cut-off point of SAAG was 1.5 g/dL [19,20]. The results of our study showed that SAAG values >1.75 g/dL demonstrated a sensitivity of 78.4%, specificity of 83.3%, PPV of 98.31%, and AUC of 0.925 in patients at increased risk for EVs.

Our result doesn't match with the result reported by Hou Y et al., who considered a cut-off point of 2.5 g/dL to predict EVs [8].

Although the method using SAAG values to predict EVs has high sensitivity and specificity, it cannot completely replace UGE. SAAG ratio is only an early warning and predictive tool that can help clinicians advise UGE or refer high-risk patients to an endoscopy

centre. Cirrhotic patients with SAAG values ≥1.8 should always undergo endoscopy, considering their risk for large EVs. also patients with SAAG value >1.9 had higher possibility of large EVs, which subsequently may lead to higher risk of bleeding,hence such patient should be timely refered for endoscopy..

However, the present study has few limitations . The following time was short to evaluate patients and this was a single centre study .

5. Conclusions

In conclusion, Cirrhotic patients with SAAG ratio values ≥1.8 have a higher risk of large EVs and those with values >1.9 who have higher possibility of bleeding must undergo timely upper GI endoscopy to prevent bleeding.

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