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Correlation of serum albumin levels with the grading of esophageal varices

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ABSTRACT

Background: Variceal bleed is one of the major complications seen in patients with cirrhosis of liver of various etiologies and endoscopy is a gold standard for its diagnosis which is an invasive procedure. There are other modalities of non-invasive methods to determine the degree of varices and estimation of serum albumin levels in one among them. **Aims and Objectives:** The aims of this study were as follows: (1) To measure serum albumin levels in patients with cirrhosis of liver and (2) to correlate serum albumin levels with grading of esophageal varices. **Materials and Methods:** A cross-sectional study was conducted on a total of 100 patients in Bangalore during the study period from October 2016 to September 2017. Case record form with follow-up chart was used to record the duration of disease, history of treatment and complications. Patients underwent biochemical investigations and endoscopy. The presence of varices and their size was obtained from endoscopy reports. **Results:** Study includes 100 patients that majority belonged to the age group 40–49 years (46%). Serum albumin levels of <2.8 mg/dL was seen in high number of study subjects (76%). Forty patients had albumin levels of <2.8 mg/dL with grade 3 OGD scopy, followed by 23 patients with Grade 1 esophagogastroduodenoscopy (OGD scopy). The association between albumin and OGD scopy grades was found to be significant (P=0.027). **Conclusion:** We conclude that low albumin levels predict higher grades of esophageal varices. It can identify the subset of patients who require prophylactic endoscopic management. Estimating serum albumin levels are non-invasive that can screen the patient for esophageal varices. Thus, this reduces the economic burden on the patients and the cost of management of esophageal varices.

Key words: Albumin; Cirrhosis; Varices; Endoscopy

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INTRODUCTION

Portal hypertension in liver cirrhosis results from the anatomical changes and the development of contractile element in the liver vascular bed secondary to progressive formation of regenerative nodules and hepatic fibrosis.[1,2] The increase in portal pressure triggers splanchnic vasodilation, increased cardiac output, and fluid/salt retention leading to a hyperdynamic circulation and increased to portal flow. Formation of collaterals between the portal and systemic systems such as those found in the gastric cardia and lower esophagus (gastroesophageal varices) may relieve some of the pressure and pose a risk for rupture and bleeding.[2] Development of esophageal varices is one of the major complications of portal hypertension.[3] The prevalence of gastroesophageal varices ranges from 0 to 40% in compensated cirrhosis to 70–80% in decompensated liver disease, while their growth and progression occur at an estimated 7% per year.[2,4] The 1-year rate of first variceal hemorrhage is 5% for small varices and 15% for large varices.[5] In 1996, the American Association for the study of liver disease stated that all cirrhotic patients should be screened for the presence of esophageal varices when portal hypertension is diagnosed. Recently, the Baveno III consensus conference on portal hypertension recommended that all the cirrhotic patients should be screened for the presence of esophageal varices when liver cirrhosis is diagnosed.[6] Repeat endoscopy is

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recommended at 2–3 years interval in patients without varices and at 1–2 years interval in patients with small varices to evaluate the development or progression of varices.[7]

Nevertheless, repeated endoscopic examinations are unpleasant for patients and have cost impact on health-care insurance, while only half of cirrhotic patients have esophageal varices, and up to 30% have large varices. Therefore, the sensitivity and specificity of numerous non-invasive parameters have been investigated for assessment of presence and size of esophageal varices and risk prediction for bleeding.

Many studies have shown that biochemical, clinical, and ultrasonographic parameters alone or together have good predictive power for non-invasively assessing the presence of esophageal varices. Predicting the presence of esophageal varices by non-invasive means might increase compliance and would permit to restrict the performance of endoscopy to those patients with a high probability of having varices. Upper GI endoscopy is deemed to be the gold standard against which all other tests are compared, but is not without its limitations. Thrombocytopenia, ascites, and splenomegaly are independent predictors of large esophageal varices in cirrhotic patients. The study suggests that endoscopy could be avoided safely in cirrhotic patients with none of these predictive factors, as large varices are absent in this group of patients. Here, we estimate serum albumin levels and correlate it with the degree of esophageal varices in cirrhotic patients.

Aims and objectives

The aims of this study were as follows:

1. To measure serum albumin levels in patients with cirrhosis of liver
2. To correlate serum albumin levels with grading of esophageal varices.

MATERIALS AND METHODS

A study was conducted on a total of 100 patients in Bangalore during the study period from October 2016 to September 2017. Data were collected from a total of 100 patients presenting to the department of general medicine ward/intensive care unit fulfilling the inclusion criteria.

After obtaining approval and clearance from the Institutional Ethics Committee (No.BMC/PGs/289/2016-17), the patients fulfilling the inclusion criteria were enrolled for the study after obtaining informed consent. Case record form with follow-up chart was used to record the duration of disease, history of treatment, and complications. Patients underwent biochemical investigations which included prothrombin time, international normalized ratio, platelet count, serum albumin, total bilirubin, Child-Pugh score, presence of ascites by clinical examination and radiography, and endoscopic findings. The presence of varices and their size was obtained from endoscopy reports. Endoscopic grading of varices was done as follows:

- Grade I: Small, straight esophageal varices.
- Grade II: Enlarged, tortuous esophageal varices occupying less than one-third of the lumen.
- Grade III: Large, coil-shaped esophageal varices occupying more than one third of the lumen.

Inclusion criteria

All patients aged 18 years and above diagnosed to have cirrhosis of liver were included in the study.

Exclusion criteria

The following criteria were excluded from the study:

- Previous history of portal hypertensive bleeding
- Patients with hepatocellular carcinoma
- Patients with portal vein thrombosis
- Patients with previous or current treatment with β-blockers, diuretics, or other vasoactive drugs.

Method of statistical analysis

Data were entered into Microsoft Excel data sheet. Categorical data were represented in the form of frequencies and proportions. Continuous data were represented as mean and standard deviation. Chi-square and Fisher-Exact was used for categorical variable and t-test was used for continuous variable. $P<0.05$ was considered statically significant.

RESULTS

Demographic data

In the present study, majority of the study subjects belonged to the age group 40–49 years (46%), followed by 30–39 years (17%), 50–59 years (15%), 60–69 years (12%), and <30 and >70 (5% each). The mean age of the study subjects was 47.11±11.33 years, as depicted in Table 1.

Males were high in number (87%) than females (13%), as shown in Table 2.

As seen in Table 3, majority of the study subjects had platelet count of 0.51–1 lakh (38%), followed by 1.01–1.5 lakhs (35%), >1.5 lakhs (24%), and <0.5 lakhs (3%).

The albumin value of <2.8 mg/dL was seen in a high number of study subjects (76%), followed by an albumin level of 2.8–3.5 mg/dL (23%) and >3.5 mg/dL (1%), as shown in Table 4.

Table 1: Age distribution

Age	Frequency	Percent
<30	5	5.0
30–39	17	17.0
40–49	46	46.0
50–59	15	15.0
60–69	12	12.0
≥70	5	5.0
Total	100	100.0

Table 2: Sex distribution

Gender	Frequency	Percent
Male	87	87.0
Female	13	13.0
Total	100	100.0

Table 3: Platelet count distribution

Platelet (×10^5 cu/mm)	Frequency	Percent
≤0.5	3	3.0
0.51–1	38	38.0
1.01–1.5	35	35.0
>1.5	24	24.0
Total	100	100.0

Table 4: Serum albumin levels in the study population

Albumin (mg/dL)	Frequency	Percent
<2.8 mg/dL	76	76.0
2.8–3.5 mg/dL	23	23.0
>3.5 mg/dL	1	1.0
Total	100	100.0

As shown in Table 5, 83 people (83%) were alcoholics and 17 were non-alcoholics. Among the 17 non-alcoholic patients, six patients had hepatitis B causing cirrhosis of liver.

As depicted in Table 6, the mean hemoglobin of the study subjects was 9.66±2.03 g/dL with the range of 4.9–16 g/dL. The mean total leucocyte counts of the study subjects were 11353±9459.55 with the range of 3100–85200 cells/cu mm. The mean platelets of the study subjects were 1.31±0.69 lakhs with the range of 0.25–4.56 lakhs. The mean total bilirubin of the study subjects was 7.87±8.32 with a range of 0.2–30. The mean direct bilirubin of the study subjects was 4.46±5.19 with a range of 0.05–20. The mean albumin levels of the study subjects were 2.38±0.62 with a range of 1.4–4. The mean SGOT of the study subjects was 94.83±62.94 with a range of 10–454. The mean SGPT of the study subjects was 44.12±42.01 with a range of 4–281. The mean ALP of the study subjects was 147.06±68.7 with a range of 39–349.

Majority of the study subjects had OGD grade 3 varices with platelet count of 0.51–1 lakhs (19) followed by

Table 5: Etiology of cirrhosis

Etiology	Frequency
Alcoholic	83
Hepatitis B	6
Cryptogenic	11

1.01–1.5 lakhs (15). The association between grading of varices by OGD scopy and platelet count was not found to be significant (P=0.498), as shown in Table 7.

Forty patients had albumin <2.8 mg/dL with grade 3 OGD scopy, followed by 23 patients with grade 1 OGD scopy. The association between albumin and OGD scopy grades was found to be significant (P=0.027), as depicted by Table 8.

DISCUSSION

Esophageal variceal bleeding is a potentially lethal complication in liver cirrhosis patients with incidence of variceal bleeding being 35–80%. The risk of mortality associated with first episode of variceal bleeding ranges from 17% to 57%. Therefore, early detection of esophageal varices and treating the patients with beta-blockers or variceal band ligation can minimize the complications. However, screening all patients with endoscopy may be an invasive and costly diagnostic procedure. Therefore, there is a need of non-invasive parameters for detection of esophageal varices to ease the economic, social, and medical burden of disease.

A number of studies based on laboratory and ultrasound based methods have been developed for non-invasive diagnostic evaluation of cirrhosis such as platelet count, spleenomegaly, platelet count/splenic diameter, serum albumin, right liver lobe diameter/albumin ratio, and advanced Child-Pugh class. Several studies suggest that platelet count may be useful in predicting esophageal varices. Zaman et al.,[8] reported that patients with platelet counts of <88,000/mm^3 have 5 times greater likelihood of having large esophageal or gastric varices as compared with the patients with higher platelet counts. Giannini et al.,[9] showed that platelet count/spleen diameter can be used as a non-invasive predictor of esophageal varices. Alempijevic et al.,[10] showed that right liver lobe diameter/albumin can also be used as non-invasive parameter for predicting esophageal varices. The pathophysiologic mechanisms are combined based on the integration of two non-invasive parameters, that is, right lobe of liver size and albumin into one ratio. We used serum albumin concentration as a parameter of liver function and correlated it with the grading of esophageal varices and found that hypoalbuminemia was associated with a higher grade of esophageal varices in cirrhotic patients.

Table 6: Variables in study population

Variables	Minimum	Maximum	Mean	Standard Deviation
Hemoglobin (g/dL)	4.9	16	9.66	2.03
Total Leucocyte Counts (cells/cu mm)	3100	85200	11,353.90	9,459.55
Platelets (×10^5 cells/cu mm)	0.25	4.56	1.31	0.69
TB (mg/dL)	0.2	30	7.87	8.32
DB (mg/dL)	0.05	20	4.46	5.19
Albumin (mg/dL)	1.4	4	2.38	0.62
SGOT (IU/L)	10	454	94.83	62.94
SGPT (IU/L)	4	281	44.12	42.01
ALP (U/L)	39	349	147.06	68.70

TB: Total Bilirubin, DBL: Direct Bilirubin, SGOT: Serum glutamic oxaloacetic Transaminase, SGPT: Serum glutamic pyruvic transaminase, ALP: Alkaline phosphatase

Table 7: Platelet count versus grading of esophageal varices

Platelet	OGD scopy				Total	P-value
	Grade 0	Grade 1	Grade 2	Grade 3		
≤0.5	0	3	0	0	3	0.498
0.51–1	4	12	3	19	38	
1.01–1.5	5	12	3	15	35	
>1.5	4	9	0	11	24	
Total	13	36	6	45	100	

Table 8: Correlation of albumin with esophageal varices

Albumin	OGD SCOPY				Total	P-value
	Grade 0	Grade 1	Grade 2	Grade 3		
<2.8 mg/dL	9	23	4	40	76	0.027*
2.8–3.5 mg/dL	3	13	2	5	23	
>3.5 mg/dL	1	0	0	0	1	
Total	13	36	6	45	100	

*Significant

Age distribution

Our study included age groups above 18 years, majority belonging to the age group 40–49 years (46%), followed 30–39 years (17%) and 50–59 years (15%). Least common age group being <30 years and >70 years (5% each). The mean age of the study subject was 47.11±11.33. Mean age of present study was comparable to that of Prof Said et al.[11]

Sex distribution

Majority of the patients were male which constitutes 87 (87%), while females were 13%. This is comparable to that of Prof Said et al.,[11] and Alempijevic et al.,[10] as all these studies constitute majority of male subjects.

Etiology of cirrhosis

Majority of the patient had alcohol as the etiology of cirrhosis which constitutes 83%. Among non-alcoholic 6% patient had hepatitis B as the cause of cirrhosis of liver.

Platelet count versus esophageal varices

Majority of the study subjects had platelet count of 0.51–1 lakh (38%), followed by 1.01–1.5 lakhs (35%), >1.5 lakhs (24%), and <0.5 lakhs (3%). Majority of the study subjects had OGD grade 3 with platelet count of 0.51–1 lakhs (19) followed by 1.01–1.5 lakhs (15). This is comparable with the study conducted by Madhotra et al.,[7] where the platelet count in patients with esophageal varices ranged from 0.53 to 1.05 lakhs. However, the association between grades of OGD scopy and platelet count was not found to be significant (P=0.498).

Albumin versus esophageal varices

The albumin value of <2.8 mg/dL was seen in high number of study subjects (76%), followed by albumin value of 2.8–3.5 mg/dL (23%) and >3.5 mg/dL (1%). With mean value being 2.38. This is comparable with the study conducted by Prof Said et al.,[11] which had a mean value of 2.54. However, the association between albumin and OGD scopy grades was found to be significant (P=0.027).

Limitations of the study

Sample size was a small and single-center study.

CONCLUSION

From our study, we conclude that low albumin levels predict higher grades of esophageal varices. It can identify the

subset of patients who require prophylactic endoscopic management. Estimating serum albumin levels are non-invasive that can screen the patient for esophageal varices. This, thus, reduces the economic burden on the patients and the cost of management of esophageal varices.

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Authors Contribution:
AHR- Design of study, literature review and drafting manuscript; **SI-** Concept, coordination, statistical analysis and interpretationl; **VSB**- Prepared first draft of manuscript, Interpretation of results, manuscript preparation.

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