Section: General Medicine

Original Research Article

THE DIFFERENT NON-INVASIVE PREDICTORS FOR THE PRESENCE OF LARGE OESOPHAGEAL VARICES IN PATIENTS WITH ALCOHOLIC LIVER DISEASE WITH CIRRHOSIS

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ABSTRACT

Background: Alcohol-related liver disease is the most common cause of chronic liver disease in India and a major etiological factor for cirrhosis worldwide. Esophageal varices are a serious complication of cirrhosis, and variceal bleeding contributes significantly to morbidity and mortality. Although endoscopic screening is the gold standard for detecting esophageal varices, it is invasive, resource-intensive, and not readily available in many peripheral healthcare settings. Hence, identification of reliable non-invasive predictors for large esophageal varices is clinically important to guide early primary prophylaxis.

Materials and Methods: This prospective case–control study was conducted over six months (April–September 2015) at Rajiv Gandhi Government General Hospital, Chennai, after institutional ethical clearance. A total of 106 adult patients with alcoholic liver disease and cirrhosis were enrolled. Detailed clinical evaluation, laboratory investigations, and ultrasonography were performed. All patients underwent upper gastrointestinal endoscopy, and esophageal varices were graded using Paquet's classification. Child–Turcotte–Pugh (CTP) scoring was calculated for all patients. The association between non-endoscopic clinical, laboratory, ultrasonographic parameters, CTP score, and the presence of large esophageal varices was statistically analyzed using SPSS and SAS software.

Results: Of the 106 patients, 11% had no varices, 66% had small varices (Grade I–II), and 23% had large varices (Grade III–IV). Large esophageal varices were more prevalent in the middle-aged group (41–65 years) and predominantly in males. Clinical features such as pallor, icterus, spider naevi, ascites, splenomegaly, and hepatic encephalopathy were significantly more common in patients with large varices. Laboratory parameters including low hemoglobin, thrombocytopenia, hypoalbuminemia, and prolonged INR showed a strong association with large varices ($p < 0.05$). Mean portal vein diameter increased progressively with variceal grade and showed a significant correlation with large varices ($p < 0.001$). Most patients with large varices belonged to Child–Pugh Class B or C, with a statistically significant association ($p < 0.001$).

Conclusion: Non-invasive clinical features, laboratory parameters, increased portal vein diameter on ultrasonography, and Child–Pugh Class B/C are sensitive and accessible predictors for the presence of large esophageal varices in patients with alcoholic cirrhosis. These parameters can help identify high-risk patients in settings where endoscopy is not readily available, enabling early initiation of primary prophylaxis and potentially reducing morbidity and mortality.

Keywords: Alcoholic liver disease, cirrhosis, esophageal varices, non-invasive predictors, Child–Pugh score, portal vein diameter.

INTRODUCTION

Alcohol related liver disease is the commonest liver disease in India and is on the raising trend and remains one of the major etiological factor for cirrhosis worldwide.[1,2]

Esophageal varices remains a serious complication in patients with alcoholic cirrhosis. The rate of development of the varices is around 5-8% per year with the annual rate of increase in size from small to large being 10-15%. Rupture of the esophageal varices accounts for one-third of all the cases of Upper gastro intestinal bleed with a high mortality rate of around 20 %.[3]

A meta-analysis of 11 randomised controlled trials comparing the efficacy of beta-blockers with placebo showed a 10% reduction of the first variceal bleeding with the reduction in the mortality rate from 28.4% in the control group to 23.9% in those treated with beta-blockers.[4] Therefore the present guidelines recommend use of beta-blockers at the primary prevention level to reduce the risk of progression and its rupture in patients with esophageal varices. Furthermore, studies shows that the satisfactory response to beta blockers is not only associated with decreased risk of bleeding but also has a positive impact on the natural course of the disease by decreasing the complications associated with it by lowering the risk of development of ascites, spontaneous bacterial peritonitis and hepatorenal syndrome thereby improving the survival in these patients.[5]

As per the current recommendations, all cirrhotic patients are advised to undergo initial endoscopic screening to grade the varices and to identify those at high risk of bleeding and to initiate measures to curtail its rupture which impose a significant burden on the endoscopy units, delay in the initiation of the primary prophylaxis , decreased patient compliance for invasive procedure and pose difficulty in the periphery health care centres where endoscopy is not readily accessible.[6] Use of non-invasive tools to predict the severity of oesophageal varices on the first encounter of the patients with alcoholic liver disease will be useful to guide to those treating Physicians without immediate endoscopic access to initiate appropriate and timely primary prophylaxis measures and thereby decrease the burden on the health care facility and the morbidity and mortality of the patients.

Aim & objectives:

A study on "The different non-invasive predictors for the presence of large oesophageal varices in patients with alcoholic liver disease with cirrhosis"

- To assess the significance of the different non-endoscopic variables for the presence of large oesophageal varices in patients with alcoholic liver disease.
- To use the Child Pugh score value as a predictor for oesophageal varices and to calculate its value in assessing the severity and management of the varices.

MATERIALS AND METHODS

A Prospective case control study conducted over 6 months from April 2015 to September 2015 in Rajiv Gandhi Government General Hospital, Chennai after obtaining the ethical clearance from the Institutional ethical committee. The sample size of 106 was calculated by analyzing with Power analysis test with the prevalence rate of alcoholic liver disease as 20% in south India and found to be statistically significant2. After an informed and written consent, detailed history and physical examination were done in all the patients and were subjected to AUDIT Questionnaire for assessing the significance of alcohol intake in these patients. The patients were then subjected to laboratory and radiological investigations to assess the alcoholic liver disease and cirrhosis. After obtaining the consent explaining the risk and benefit of the procedures, all the patients were then subjected to upper esophageal endoscopy to study for the presence of varices and its severity and are then graded based on Paquet grading of esophageal varices into Grade I-IV based on the endoscopic findings.

Japanese Classification	**US Classi-fication**	**VA Trial Classi-fication**	**Paquet Classi-fication**
Absent	Absent	Absent	No varices (not graded)
Grade 1: Small, straight varices disappearing with insufflation	small	<5 mm	Grade I: Small, straight varices
Grade 2: Medium-sized varices occupying <1/3 of the esophageal lumen	medium	5-9 mm	Grade II: Enlarged, tortuous varices occupying < 1/3 of the lumen
Grade 3: Large varices occupying > 1/3 of the esophageal lumen	large	>9 mm	Grade III: Large, coil-shaped varices occupying > 1/3 of the lumen
			Grade IV: Very large varices occupying most of the lumen, often with red color signs

A Child-Pugh Turcott scoring to assess the prognosis of cirrhosis and its correlation to the presence and severity of the varices was done for all the patients.[8]

Child-Pugh classification of cirrhosis:

Factor	**1**	**2**	**3**
Serum Bilirubin (mg/dL)	<2	2.0-3.0	>3.0

Serum Albumin (g/dL)	>3.5	3.0-3.5	<3.0
Prothrombin Time (Sec)	0-4	4-6	>6
INR	<1.7	1.7-2.3	>2.3
Ascites	None	Easily controlled	Poorly controlled
Hepatic Encephalopathy	none	Minimal	Advanced

Class A –Score of 5-6.
Class B – Score of 7-9.
Class C – Score of 10 and above.

Inclusion criteria:

- Patients with age more than 18 years with alcoholic liver disease (Associated with significant intake of alcohol)

Exclusion criteria:

- Pregnancy and Age <18 years.
- Patients with liver disease due to causes other than alcohol (Infection, NASH, other hepatotoxins, etc.)
- Those with alcoholic liver disease with previous history of varices or upper gastro intestinal bleed or any therapeutic intervention for the same
- Patients with upper gastrointestinal bleed with no significant alcohol intake or alcoholic liver disease with gastric varices
- Patients with haematological disorders or on drugs (anti-platelets, anti-coagulants or hepatotoxic drug or who were treated with Beta-blockers either currently or in the past) were excluded from the study.

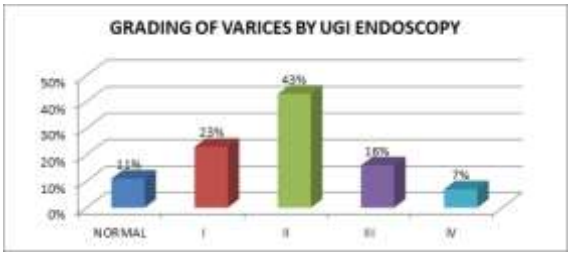
Statistical data analysis: Descriptive and inferential statistical analysis had been carried out in the present study. Results on continuous measurements were presented as Mean + SD (Min-Max) and results on categorical measurements were presented in Number (%). Significance was assessed at 5% level of significance. Independent sample test and paired sample T test (ANOVA) has been used to find the significance of study parameters on categorical scale between two or more groups after checking for normal distribution of all the variables. All results were analyzed using SAS 9.2, SPSS 15.0 which are commercially available statistical software.

RESULTS

The following parameters were analyzed and tabulated for comparison:

- Various Clinical features and signs analyzed for the presence of esophageal varices and its severity.
- Association of laboratory parameters for the presence of large esophageal varices.
- Significance of USG measurement of Portal vein diameter for the presence of large esophageal varices.
- Significance of the Child Pugh Turcott Score and its association with the evaluation of esophageal varices and its severity in patients with alcoholic liver disease with cirrhosis.

Incidence of esophageal varices in the study group

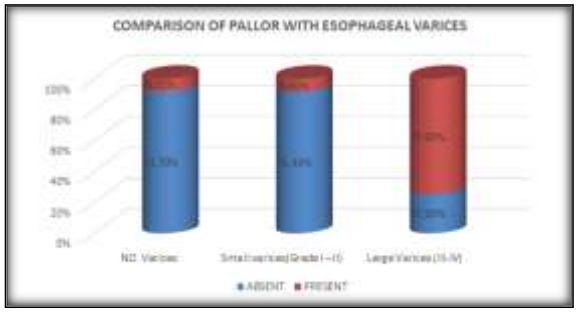


Of the 106 patients studied, 11% had no varices while 66% had small varices (Grade I-II) and 23% had large varices (Grade III-IV).

In our study of 106 patients, majority of the patients falls under middle age group of 41-65 years (54.7%) with the mean of 43.2 years.

Majority of the patients in the study (66%) had small varices of Grade I-II. Patients of the Middle age group had the highest prevalence of large Esophageal Varices (32.7%). In the study, males were 101 attributing to 95.3% and females were 5 contributing to 4.7%.

Clinical signs analysis: Pallor

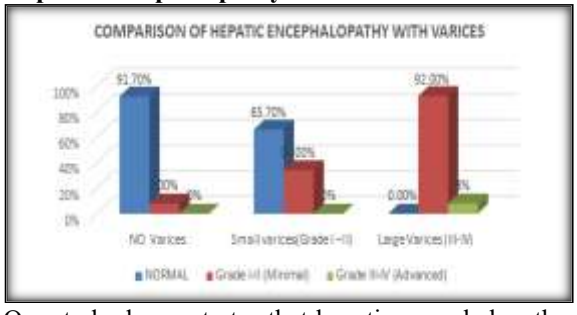


In the study population, 38.6% of patients with small varices and 91.7% of the patients with large varices had pallor implying the greater prevalence of pallor in patients with large varices.

ICTERUS & SPIDER NAEVI

Study showed among the patients with small varices 8.60% had icterus while in the large varices group the incidence was 75% implying presence of icterus in patients with larger varices group. Spider naevi was seen in 12.3% of the patients under study and its prevalence in patients with large varices was 54.2%.

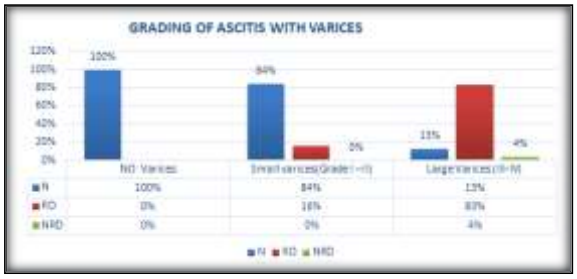
Hepatic Encephalopathy



Our study demonstrates that hepatic encephalopathy was seen in 8%of the individuals with no varices, 34% of the patients with small varices and 92% of the patients with large varices implying the increased

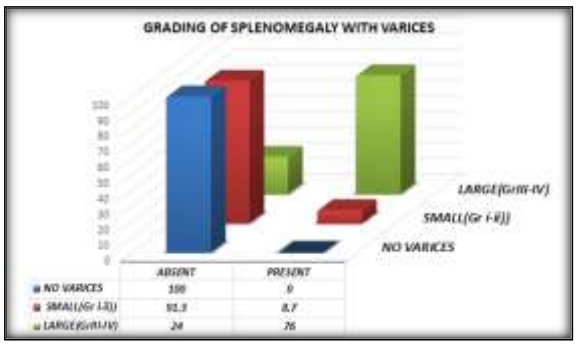
incidence of hepatic encephalopathy at higher grades of varices.

ASCITES:



16% of the patients with small varices had ascites while in patients with large varices 83% had ascites responsive to diuretic while 4% had ascites that is resistant to diuretic.

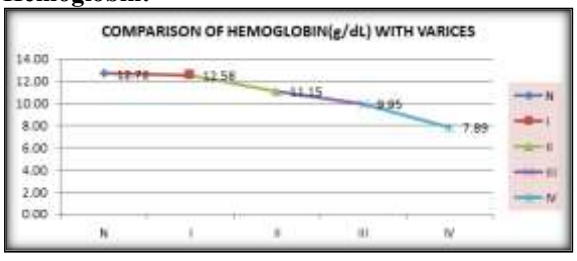
SPLENOMEGALY:



The study on the splenomegaly with the presence of varices showed 8.65% of the patients with small varices had splenomegaly while 76% of the patients with grade III varices had splenomegaly while all the patients with grade IV varices had splenomegaly implying the presence of splenomegaly in higher grades of varices.

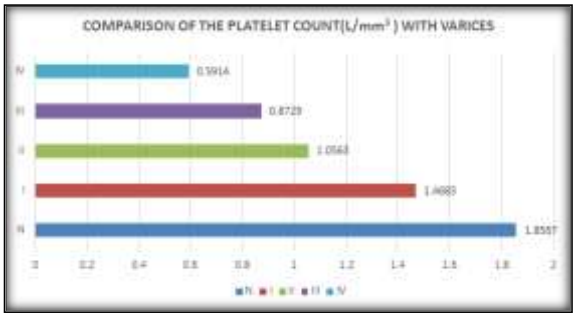
Laboratory investigations:

Hemoglobin:

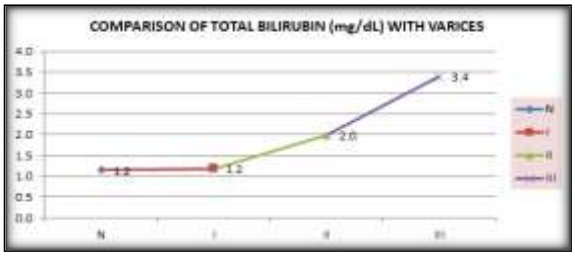


In the study population, 57 had no pallor (53.8%) and 49 had pallor (46.2%). On comparing the presence of pallor to the presence of varices 38.6% of patients with small varices (Grade I - II) and 91.70% of the patients with large varices (Grade III - IV) had pallor. From the study, it is seen that patients with higher degree of varices had pallor.

Platelet count: In our study, mean platelet count in No varices group (1.8 L/cu.mm.), grade I (1.16L/cu.mm.), grade II (1.05 L/cu.mm.), grade III (0.87 L/cu.mm.), grade IV (0.59 L/cu.mm.) signifying the presence of thrombocytopenia as a sensitive marker for esophageal varices and its severity.

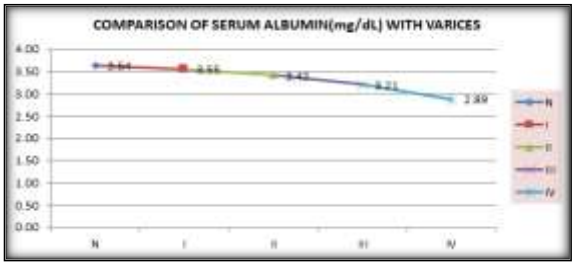


Total bilirubin:



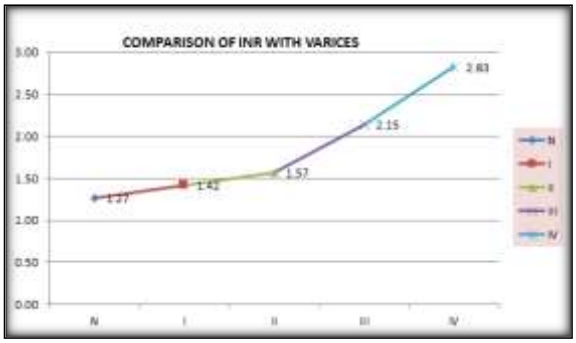
Patients with higher grades of varices had higher values of serum bilirubin.

S. Albumin:



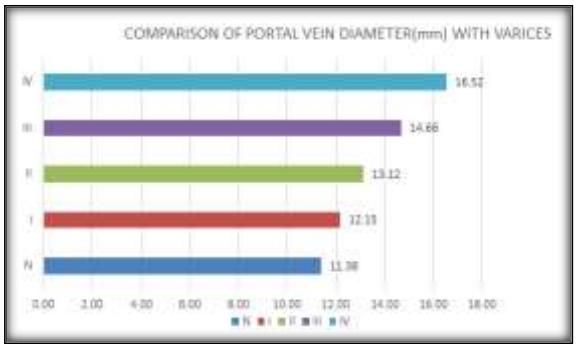
Patient with no varices group had a mean albumin of 3.64 g/dL, grade I (3.55 g/dL), grade II (3.42 g/dL), grade III (3.21 g/dl), and grade IV (2.89 g/dl) indicating presence of hypoalbuminemia in higher grades of varices.

INR:

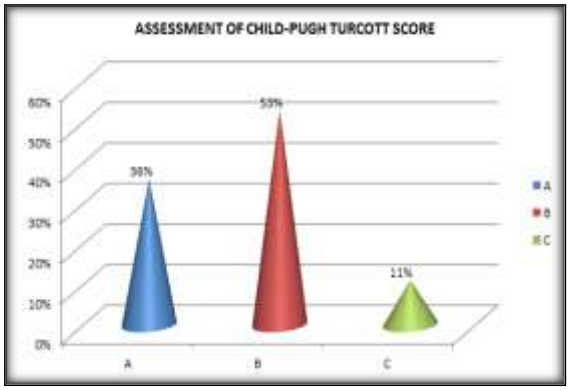


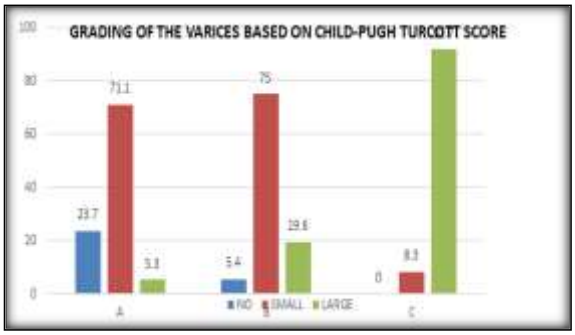
Patients with higher grades of varices had prolongation of INR implying clotting factor abnormality in patients with higher varices group.

Ultrasonogram findings: The relationship of portal vein diameter to the presence of varices shows mean PVD (in mm) in the No varices group (11.38), gr I(12.15), gr II(13.12), gr III (14.66), gr IV (16.53) implying a significant co relationship of portal venous diameter to the presence of varices and its severity.



Child-Pugh Turcot score:





35.8 % were in Class A of which 23.7% had no varices, 71.1% had small varices and 5.3% of patients had large varices.
52.8% were in Child Pugh Class B of which 75% had small varices and 19.6% had large varices.
11.3% were in Child Pugh Class C of which 91.7% had large varices, while small varices were found in 8.3% of the individuals indicating higher degrees of Child Pugh score (B/C) in patients with Large Esophageal Varices with a p value of <0.001 and Chi Square value of 39.096*.

Table 1: Different non-endoscopic parameters for large esophageal varices.

Esophageal Varices		N	Mean	Std. Deviation	Std. Error Mean	95 % Confidence interval		P Value
Hemoglobin g/dl	Small varices(Grade I –II)	70	11.64	1.46	0.17	11.30	11.98	P<0.001
	Large Varices (III-IV)	24	9.35	1.76	0.36	8.64	10.05	
Platelet count in lakhs	Small varices(Grade I –II)	70	1.20	0.40	0.05	1.10	1.29	P<0.001
	Large Varices (III-IV)	24	0.79	0.19	0.04	0.72	0.87	
S. Albumin _g/dl	Small varices(Grade I –II)	70	3.46	0.20	0.02	3.42	3.51	P<0.001
	Large Varices (III-IV)	24	3.12	0.41	0.08	2.95	3.28	
INR_no_unit	Small varices(Grade I –II)	70	1.52	0.30	0.04	1.45	1.59	P<0.021
	Large Varices (III-IV)	24	2.35	0.91	0.19	1.98	2.71	
Portal_Vein_Diameter_in_mm	Small varices(Grade I –II)	70	12.79	1.01	0.12	12.56	13.03	P<0.001
	Large Varices (III-IV)	24	15.21	1.90	0.39	14.45	15.97	

DISCUSSION

Our study was conducted to study the different non-endoscopic variables to predict the presence of oesophageal varices and its severity in patients with alcoholic liver disease with cirrhosis.

The following results were obtained from our study:

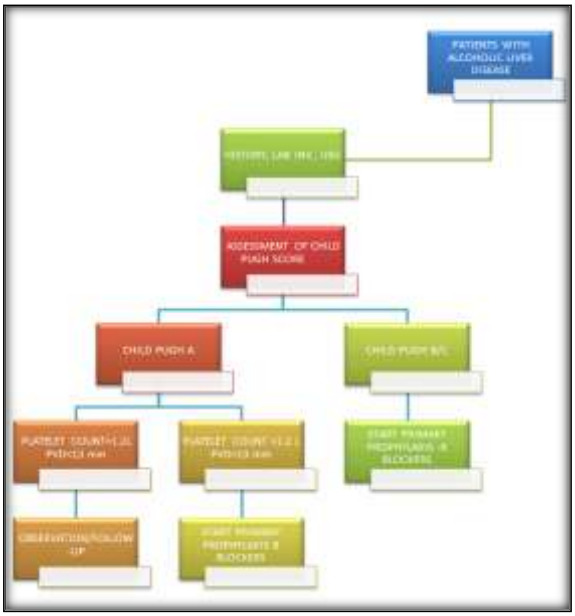
- In our study, the highest prevalence of large esophageal varices falls under Middle Age group (41-65 years).
- Alcoholic cirrhosis of liver was more common in males than females probably due to the lower incidence of alcohol in females in South India.
- Majority of the patients with large esophageal varices had clinical signs of pallor, icterus, spider naevi signifying that the above parameters can be taken as markers for the presence of large varices in patients with alcoholic cirrhosis as comparable to the earlier national study, Arul Prakash Sarangapani, Chitra Shanmugham,et al.[9]
- Majority of the patients with varices fall under grade I-II of hepatic encephalopathy. Advanced stages of hepatic encephalopathy were seen in patients with large varices.
- Ascites was commonly seen in patients with large varices and most of the cases were responsive to

diuretics while a small percentage of cases in the large varices group were diuretic resistant.

- Presence of Splenomegaly and Thrombocytopenia were a consistent finding in patients with large esophageal varices and had a significant association with a p value of <0.001.
- Patients with large varices had low hemoglobin, hypoalbuminemia, and prolongation of INR. Majority of the large varices falls under Child Pugh Class B/C with a significant p value of <0.001.
- Ultrasound assessment of portal venous diameter in the study population showed a significant p value of <0.001 correlating its association with the presence of oesophageal varices and its severity as comparable to the earlier study, D. La Breque, A.G.Khan, S.K.Sarin et al.[9]

CONCLUSION

Clinical, Laboratory and increased Portal Vein Diameter by Sonography with Child Pugh Score B/C can be used as sensitive and accessible indicators for the presence of large oesophageal varices in patients with alcoholic liver disease with cirrhosis. From the study, an algorithm approach to a patient with alcoholic cirrhosis is as follows comparable to the earlier study(10).



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