Original Research Article

A Study on Non-Endoscopic Predictors of Esophageal Varices in Patients With Chronic Liver Disease - A Prospective Study

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Received: 29-01-2023 / Revised: 27-02-2023 / Accepted: 02-04-2023

Abstract

Background: Esophageal varices are a serious consequence of portal hypertension in patients with liver diseases. Non-invasive markers of esophageal varices helps to reduce unnecessary endoscopies in patients with cirrhosis. **Aims and Objectives**: To evaluate various clinical, biochemical and ultrasonographic parameters in predicting the presence of large esophageal varices. **Materials and Methods**: Ninety-four in-hospital patients with chronic liver disease were studied. Detailed history and physical examination was done as per pre-fixed performa. Relavant haematological, biochemical and radiological investigations were done to confirm chronic liver disease and to record spleen diameter, portal vein diameter and ascites. Screening for esophageal varices was done by upper GI endoscopy. The severity of liver cirrhosis was judged by the Child Pugh score. **Results**: The prevalence of large esophageal varices was found to be 45(47.9%). 69 (73.4%) of the participants were male and 25(26.6%) were female with mean age 45 years. Alcohol was the most common etiology found. Ascites, hepatic encephalopathy, Child-Turcotte-Pugh score, low platelet count, serum bilirubin, PT/INR, spleen diameter and portal vein size were found statistically significant (p value<0.001) in univariate analysis in predicting the presence of large esophageal varices. However on multivariate analysis, low platelet count, splenomegaly and portal vein diameter found to have independent predictive value (p value<0.001). **Conclusion**: Low platelet count, splenomegaly and increased portal vein diameter were found to be the independent predictors of large esophageal varices in chronic liver disease patients. Hence using these noninvasive predictors for the detection of esophageal varices seems to be more cost effective than the "scope all strategy". This may help reduce the cost and discomfort for patients and the burden on endoscopy units.

Keywords: Chronic liver disease, Upper GI bleed, Noninvasive predictors

Introduction

Liver diseases are the leading cause of morbidity and mortality all over the world. It is the 11th leading cause of death and 15th leading cause of morbidity, accounting for 2.2% of deaths and 1.5% of disability adjusted life years worldwide in 2016[1].

The natural history of chronic liver disease is characterised by a long asymptomatic and compensated phase. During this phase, fibrosis progresses leading to cirrhosis. Liver cirrhosis is the final evaluative stage of any chronic liver disease. It results in the formation of fibrous tissue, disorganization of liver architecture and nodule formation, which interferes with liver function and results in portal hypertension[2].

The three primary complications of portal hypertension are gastroesophageal varices, ascites and splenomegaly. Esophageal varices develop in the context of increased portal blood pressure owing to increase portal vascular resistance. Esophageal varices are a dangerous clinical consequences of liver cirrhosis.The incidence of esophageal varices in cirrhotic patients is 5% at the end of one year and 28% at the end of three years. Small varices progress to large ones at a rate of 10-12% annually[3]. The size of esophageal varices is directly proportional to the risk of variceal rupture and bleeding. The annual risk of variceal bleeding among small and large varices is 5% and 15% respectively[3].

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Despite significant improvements, the mortality rate of first variceal hemorrhage is still high (48%)[4].Studies reported the significance of pharmacologic therapy for primary prevention of variceal bleeding; emphasizing the importance of screening endoscopy.Cirrhosis demands repeated endoscopies in the same patient for screening and follow-up. Patients with compensated cirrhosis and without varices should undergo endoscopy every 2-3 years[5]. Patients with small varices every 1-2 years. But this test is limited as it is invasive, costly and poorly accepted by patients. Hence there is a particular need for the identification of noninvasive parameters that strongly predict the presence of esophageal varices.

Materials and Methods

Study Design: Prospective study
Source of Data: Department of General Medicine, G.R. Medical College, Gwalior (M.P.) from Jan 2021 - Jun 2022.
Sample Size: The sample size was calculated using the formula

$$n = \frac{Z^2_{\alpha/2} \times PQ}{D^2}$$

The calculated sample size was 94 patients.

Study Population: The study included 94 patients with symptoms and signs of chronic liver disease who were admitted to the medicine ward of JAH and KRH. The Inclusion Criteria were patients over 18 years of age with chronic liver disease with portal hypertension. The

Exclusion Criteria were patients with active gastrointestinal bleeding, primary hematologic disorders, history of EVL, EST or TIPS, hepatocellular carcinoma detected by ultrasonography, previous surgical intervention for portal hypertension, advanced co-morbidity for endoscopy.

Data Collection: All patients underwent a detailed clinical examination at admission, and relevant history and physical examination including symptoms and signs of liver failure, hepatomegaly, splenomegaly, and abdominal vein collaterals were recorded. Ascites were graded as none, mild, moderate, and severe. Hematological and biochemical workup was performed, which included measurement of hemoglobin, total leukocyte count, platelet count, prothrombin time, and serum concentration of bilirubin (both direct and indirect), protein, albumin, alanine aminotransferase, and aspartate aminotransferase.

USG findings suggestive of chronic liver disease were noted, which included nodular irregular surface of the liver, distorted vascular pattern, ascites, and signs of portal hypertension (spleen diameter, portal vein diameter). Screening for esophageal varices was done by upper GI endoscopy. Upper GI endoscopy findings were noted as, None - No esophageal varices, Small - Minimally elevated veins above surface, Large - Tortuous veins occupying >1/3 rd of esophageal of esophageal lumen.

Due permission of Ethics committee was taken regarding the study participants and all ethical practices were followed.

Statistical Analysis: All data were entered into an Excel format and analyzed using SPSS Software. Numerical values were reported using mean and standard deviation or median. Categorical values were reported using number and percentages. A probability value (p) less than 0.05 was considered statistically significant.

Results

The study included 94 participants, out of which 69(73.4%)were males, and 25(26.6%) were female. More than 85% of participants belongs to 30 to 59 year age group (81) and only 10.6% enrolled participants belongs to ≥ 60 year age (10). Only 3.2% of participants (3) belongs to below the age of 30 year

Alcohol was the most common cause of CLD (49 cases), followed by Hepatitis B (15) and HCV (4). Other causes were responsible for 26 cases of CLD.

The biochemical parameters of cases were also studied, 28.7% (27) participants were having thrombocytopenia and 53.2% (50) participants were having raised prothrombin time. Serum bilirubin level was found raised in 47.9% (45) of CLD patients. Spleen size and portal vein size above the normal range was found in 63.8% (60) and 53.2% (50) of participants respectively.

Child-Pugh score distribution of participants were 23.4% (22), 29.8% (28) and 46.8% (44) belonging to Class A, B and C respectively. Hepatic encephalopathy was found in 12.8% (12) of participants.

In endoscopy 47.9% (45) of CLD patients were detected with large esophageal varices and 22.3% (21) with small esophageal varices.

Table 1: Demographic distribution of study participants

Age Group	Frequency	Percent
<20 year	2	2.1
20-29 year	1	1.1
30-39 year	28	29.8
40-49 year	34	36.2
50-59 year	19	20.2
≥60 year	10	10.6

Table 2: Distribution of cases according to etiology

		Frequency	Percent
Etiology	Alcohol	49	52.1
	Hepatitis B	15	16.0
	Hepatitis C	4	4.3
	Others	26	27.7

Table 3: Biochemical and ultrasonographic parameters of Cases

Platelet count	<1 Lac (below normal)	27	28.7
	≥1 lac (normal)	67	71.3
Serum bilirubin	<0.1 mg/dl (below normal)	0	0.0
	0.1-1.3 mg/dl (normal)	49	52.1
	>1.3 mg/dl (above normal)	45	47.9
Prothrombin time	<11 Sec (below normal)	0	0.0
	11-14 Sec (normal)	44	46.8
	>14 Sec (above normal)	50	53.2
Spleen Size	≤12 cm (below normal)	34	36.2
	>12 (above normal)	60	63.8
Portal Vein Size	<07 cm (below normal)	0	0.0
	07-13 cm (Normal)	44	46.8
	>13 cm (above normal)	50	53.2

Table 4: Endoscopy finding

Endoscopy finding	Frequency	Percent
Large	45	47.9%
Small	21	22.3%
Normal	28	29.8%

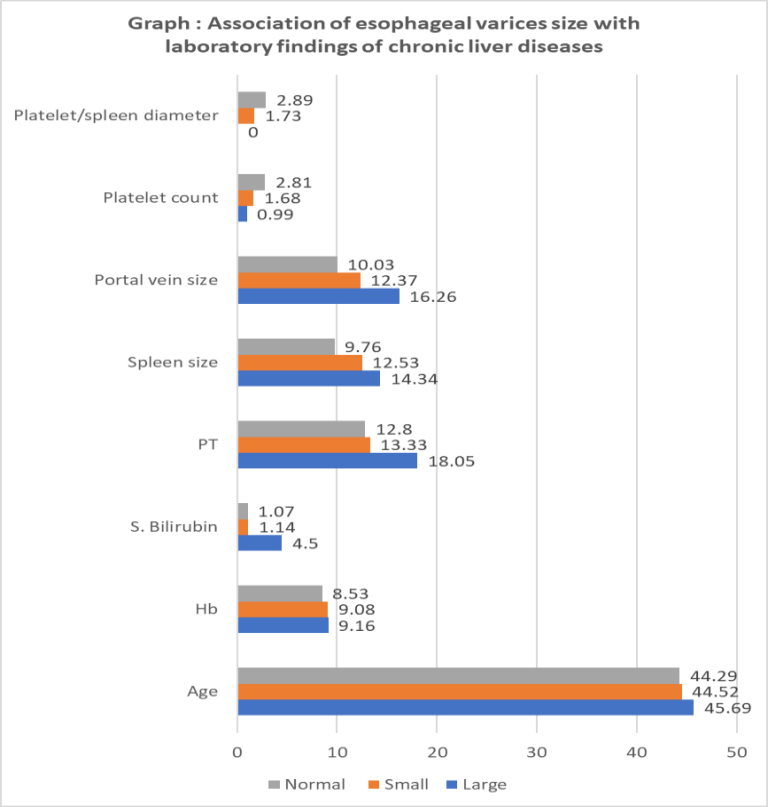
Table 5: Association of esophageal varices size with etiology and sign of chronic liver diseases

		Large	Small	Normal	p value
Etiology	Alcohol	20 (44.4%)	14 (66.7%)	15 (53.6%)	0.662
	Hepatitis B	9 (20%)	2 (9.5%)	4 (14.3%)	
	Hepatitis C	3 (6.7%)	0 (0%)	1 (3.6%)	
	Others	13 (28.9%0	5 (23.8%)	8 (28.6%)	
Ascites	Mild	0 (0%)	10 (47.6%)	9 (32.1%)	<0.001
	Moderate	21 (46.7)	8 (38.1%)	6 (21.4%)	
	Massive	24 (53.3%)	2 (9.5%)	1 (3.6%)	
	None	0 (0%)	1 (4.8%)	12 (42.9%)	
Encephalopathy	No	33 (73.3%)	21 (100%)	28 (100%)	0.001
	Yes	12 (26.7%)	0 (0%)	0 (0%)	
CTP Score	A	0 (0%)	3 (14.3%)	19 (67.9%)	<0.001
	B	1 (2.2%)	18 (85.7%)	9 (32.1%)	
	C	44 (97.8%)	0 (0%)	0 (0%)	

Ascites, encephalopathy and CTP Score was found significantly associated with size of esophageal varices.

Table 6: Association of esophageal varices size with laboratory findings of chronic liver diseases

Variable	Large	Small	Normal	p value
Platelet count	99315.56± 7516.95	168057.14± 46371.56	280785.71± 44909.72	<0.001
S. Bilirubin	4.5±3.58	1.14±0.83	1.07±1.68	<0.001
PT	18.05±5.67	13.33±2.01	12.89±1.59	<0.001
Spleen size	14.34±1.53	12.53±0.76	9.76±0.85	<0.001
Portal vein size	16.26±1.99	12.37±0.7	10.03±1.08	<0.001



Patients with low platelet count, raised serum bilirubin, raised prothrombin time, enlarged spleen size and portal vein size were having large esophageal varices.

Table 7: Multivariate analysis of esophageal varices endoscopic findings with dependent variables

Variables	Understandarized coefficients	95% confidence interval for B		t	Sig
		Lower bound	Upper bound		
Hb%	-0.029	-0.064	0.007	-1.590	0.116

Platelet count	4.268	0.000	0.000	-6.080	0.000
S. Bilirubin	-0.005	-0.027	0.017	-0.433	0.666
PT	-0.003	-0.017	0.012	-0.344	0.732
Spleen Size	-0.092	-0.133	-0.050	-4.348	0.000
Portal vein size	-0.078	-0.111	-0.045	-4.733	0.000
Platelet count/spleen diameter	0.000	0.000	0.000	1.469	0.145

On multivariate analysis only three parameters platelet count, spleen size and portal vein diameter were found to be statistically significant.

Discussion

In this study, data was obtained from 94 patients with portal hypertension . Alcohol was found as the most common etiology for chronic liver disease among study participants.

On univariate analysis, eight factors had predictive ability for the presence of large esophageal varices. The parameters found statistically significant in univariate analysis are ascites, hepatic encephalopathy, Child- Turcotte -Pugh score, low platelet count, serum bilirubin, PT/INR, spleen diameter and portal vein size (p value-<0.001). However on multivariate analysis, low platelet count, splenomegaly and portal vein diameter were found to have independent predictive value (p value-<0.001).

Comparing these findings to those of other studies, the results are largely consistent with previous research on the topic. Arulprakash Sarangapani *et al* (2010) analyzed 106 patients with liver diseases. Thrombocytopenia, large spleen size, portal vein size and platelet spleen diameter ratio were found to strongly predict large number of EVs. Another study by Poralla Sammaiah *et al*[7] studied among 100 patients, they stated portal vein diameter >13.9 m,Spleen size >16 cm and Platelet count of <98000/microL predicted the severity of esophagogastric varices indirectly.

Rishab Shrestha *et al* concluded that in chronic alcoholic liver disease patients low platelet count and increased spleen diameter are useful in predicting presence of esophageal varices.

The relationship of these predictors to the presence of large esophageal varices can be easily explained. A palpable spleen as well as large esophageal varices can be related to presence of a higher portal pressure. Similarly, the low platelet counts in patients with large esophageal varices reflects the higher rate of splenic sequestration and destruction of these cells.

However the study has certain limitations. The predicted variable, that is, the presence of large esophageal varices is not completely objective and can be subjected to interobserver variation. The study was performed in a tertiary care centre and patients of advanced disease were included hence the study may not perform well in primary care settings.[7,8]

Conclusion

The conclusion derived from this study are as follows: The clinical and biochemical parameters found to have predictive value in large esophageal varices are splenomegaly and low platelet count. However other parameters like jaundice, ascites, hepatic encephalopathy, serum bilirubin, PT/INR and Child-Turcotte-Pugh score failed to show independent predictive value. The ultrasonographic parameter found to have predictive value in large esophageal varices are increased splenic and portal vein diameter.

Use of these parameters may help identify patients with low probability of large esophageal varices who may not need upper GI endoscopy. This may help reduce the cost and discomfort for patients and the burden on endoscopy units.

Conflict of Interest: Nil Source of support: Nil

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