

Role of Non-Invasive Methods to Predict the Presence of Gastro-Esophageal Varices among the Patients Present With Chronic Liver Disease

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Abstract

Original Research Article

Background: Liver disease particularly chronic liver disease is one of the major public health problem, accounting for significant morbidity and mortality worldwide. Among the different complications, gastro-esophageal variceal bleeding is the deadliest complications of advanced liver disease and have been described in 50% of patients with liver cirrhosis. Moreover, the presence of gastroesophageal varices (GEV) has important implications for the prognosis and the severity of the disease. An estimate suggest that mortality due to variceal bleeding is around 20%. **Objective:** The objective of this study was to determine the role of non-invasive methods to predict the presence of gastroesophageal varices among patients with chronic liver disease. **Methods:** It was a hospital based cross-sectional study and conducted at the Department of Gastroenterology and department of Medicine in Dhaka Medical College Hospital, for six month period. Written informed consent was taken from the subject and ethical issues was ensured. Total 146 CLD individual was selected according to inclusion and exclusion criteria. Each patient was interviewed individually by the principal investigator. All these was registered, documented and analyzed in the statistical program Statistical Package for Social Science (SPSS) version 22.0. The data was systematically described and summarized and presented through descriptive statistics. In all cases significance level will be set at $p < .05$. Findings were expressed by graph and chart whichever is relevant. Thus the study was assessed the usefulness of non-invasive methods to predict the presence of Gastro-esophageal varices among the patients who present with chronic liver disease. **Results:** The mean age of the CLD patients was 44.62 ± 13.87 years, minimum age 20 and maximum 78 years. Majority of the patients were male 78.8% and female 21.2%. Male: Female ratio was 3.7:1. In present study clinical presentation of CLD patients were showed 82.2% patients had splenomegaly, 63.0% patients had anemia, 55.5% patients had testicular atrophy, 53.4% patients had ascites, 48.6% patients had hyperpigmentation, 42.5% patients had leuconychia, 41.8% patients had edema, 30.1% patients palmar erythema, 29.5% patients Caput Medusa, 28.8% patients had muscle wasting, 17.8% patients jaundice, 14.4% patients had flapping, 13.7% patients ha clubbing. The presence of gastro-esophageal varices by Fibroscan at a cut off value 18.1 kpa with sensitivity, specificity, PPV, NPV, accuracy respectively 80%, 87.5%, 98.1%, 35.0% can predict the gastro-oesophageal varices (AU ROC – 82.5%). Gastro-esophageal varices were predicted by platelet count at a cut off value ≥ 166000 with sensitivity, specificity, PPV, NPV was 83.8%, 81.2%, 97.3%, 36.1% respectively can predict the gastro-oesophageal varices (AU ROC – 89.2%). Enlarged spleen size cut-off value 14.1 cm had an acceptable sensitivity 82.3% specificity, 87.5% with a high NPV 98.2%. **Conclusion:** In conclusion, noninvasive strategies probably save costs and avoid unnecessary gastroscopies; however, there are a considerable number of patients undiagnosed with these methods. In our study, platelet count, spleen size and fibroscan are the best noninvasive methods. These methods can be useful in our daily practice to decide which patients could avoid a gastroscopy.

Keywords: Gastroesophageal Varices (GEV), Liver Cirrhosis, Esophageal Varices (EV), Transient Elastography, Non-Invasive Predictors.

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INTRODUCTION

Gastroesophageal varices (GEV) is a serious consequences of portal hypertension in patients with advanced chronic liver disease (CLD) as portal hypertension is a key event in the evolution of CLD

when severe fibrosis or cirrhosis develops. Once portal pressure exceeds 10 mmHg (clinical significant portal hypertension – CSPH), patients are at risk of experiencing severe complications such as variceal haemorrhage (VH) [1, 2]. GEV are abnormally dilated collateral veins within the wall of the esophagus and

stomach that project directly into the lumen and are prone to haemorrhage [3]. Approximately 30-40% of compensated cirrhotic patients develop GEV at a rate of 7-8% per year and progression from small to large varices occurs at a rate of 10%-12% per year [4]. VH occurs at a rate of around 10%-15% per year and depends on the severity of liver disease, size of varices and presence of red wale marks (areas of thinning of the variceal wall) [5, 6]. Estimated mortality of VH ranges between 15% and 25% [7-9]. Moreover, in the compensated stage of CLD median survival of the patients exceeds 12 years, it is only 1.8 years in patients who develop decompensation [10]. All over, cirrhosis of liver constitutes the fifth-leading cause of adult deaths and ranks eighth in economic cost among the major illnesses [11]. In addition, the incidence of first VH ranges from 20 to 40% within two years and the chance of recurrent bleeding is 30 to 40% within the next two to three days and in up to 60 % within one week. Thus, the prevention of VH remains at the forefront of long-term management of cirrhotic patients [12]. The American Association for the Study of Liver Disease and the Baveno IV Consensus Conference on portal hypertension recommended that all cirrhotic patients should be screened for the presence of GEV when liver cirrhosis is diagnosed [13]. Although, endoscopy is the gold standard method for the diagnosis of GEV, the performance of this invasive procedure is appreciated only for the subgroup of cirrhotic patients with high risk of having GEV [14]. However, the first line techniques for diagnosis of cirrhosis and portal hypertension include physical examination, laboratory parameters, transient elastography (TE) and Doppler-US [15]. Although physical examination alone is not as much as sensitive method for detecting portal hypertension, spider naevi is independently predictive of CSPH as well as GEV [15, 16]. Similarly, progressive spleen enlargement may predict GEV formation and growth [16]. In addition, platelet count is also independently correlated with the prevalence and grade of GEV in several studies, suggesting that it could be of help in avoiding unnecessary endoscopies [14, 17]. Again, another noninvasive quantitation of liver stiffness (LS) by ultrasound based TE using Fibro Scan has revolutionary role in the early diagnosis of liver cirrhosis [18], and high values of liver stiffness at TE are strongly predictive of the presence of CSPH, as well as varices. Moreover, several studies have shown that biochemical, clinical and ultrasonographic parameters alone or together have good predictive power for noninvasively assessing the presence of GEV [12]. According to the LSPS (liver stiffness measurement x spleen diameter/platelet ratio score) model, patients with a cut-off <3.5, gastroscopy could be avoided with a negative predictive value (NPV) of 94.7% [19]. On the other hand, patients with a cut-off >5.5 has a positive predictive value (PPV) of 94%. Another proposed index called Variceal Risk Index (VRI) that included as well LS, platelet count and spleen diameter and classified correctly 65.4-76.5% of cirrhotic patients [20]. Due to

invasive in nature, several initiatives are noticed over the last few years to invent noninvasive methods to predict the presence of GEV. But the result of the studies are inconclusive and sometimes controversial. More recently, a sequential algorithm based on LS, platelet count and ultrasound parameters have been used in few sites. But none of these non-invasive strategies have been evaluated specifically in patients with Chronic Liver Disease. In Bangladesh, very few studies are noticed regarding this topics. Therefore the purpose of the study is to evaluate the noninvasive methods to predict the presence of GEV among the patients present with CLD.

OBJECTIVES

General Objective

1. To determine the sensitivity and specificity of non-invasive methods to predict the presence of gastroesophageal varices (GEV) in patients with CLD.

Specific Objectives

2. To assess the clinical characteristics of the CLD patients.
3. To assess the socio-demographic characteristics of the respondents.
4. To assess the endoscopic findings of the patients with chronic liver disease.

METHODOLOGY

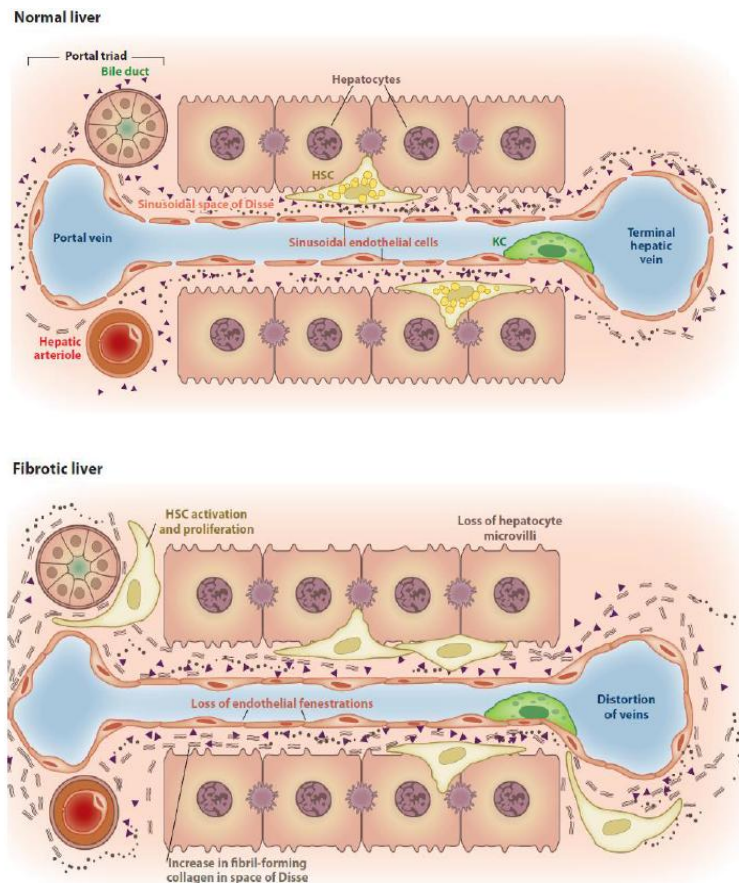
It was a hospital based cross-sectional study and conducted at the Department of Gastroenterology and department of Medicine in Dhaka Medical College Hospital, for six month period. Written informed consent was taken from the subject and ethical issues was ensured. Total 146 CLD individual was selected according to inclusion and exclusion criteria. Each patient was interviewed individually by the principal investigator. All these was registered, documented and analyzed in the statistical program Statistical Package for Social Science (SPSS) version 22.0. The data was systematically described and summarized and presented through descriptive statistics. In all cases significance level will be set at $p < .05$. Findings were expressed by graph and chart whichever is relevant. Thus the study was assessed the usefulness of non-invasive methods to predict the presence of Gastro-esophageal varices among the patients who present with chronic liver disease.

Knowledge on Causation

The main causes of cirrhosis are Guha & Iredale [21]: (1) Alcoholic liver disease (ALD), (2) Hepatitis B (HBV), (3) Hepatitis C (HCV), (4) Non-alcoholic steatohepatitis (NASH), (5) Haemochromatosis, (6) Auto-immune hepatitis (AIH), (7) Primary biliary cirrhosis (PBC) and (8) Primary sclerosing cholangitis (PSC). The natural history of cirrhosis can be divided into a preclinical and a

subsequent clinical phase. The preclinical phase is usually prolonged over several years; once clinical events occur, such as, ascites, encephalopathy, variceal bleeding or the development of hepatocellular carcinoma the remaining course of the disease is much shorter and usually fatal. For liver cirrhosis there still is no curable treatment available except for liver transplantation. Cirrhosis of the liver is typical for a late stage of any disease to the liver. The necro-inflammation and fibrogenesis leads to pronounced distortion of the liver resulting in death unless a liver transplant is performed. The predominant causes of liver disease are excessive intake of alcohol, viral hepatitis B and C, non-alcoholic fatty liver followed by a number of cases of Cryptogenic liver disease. Over time a transition from liver disease into liver cirrhosis occurs with a scarring reaction characterized by accumulation of an altered extracellular matrix rich in fibrillar collagens. The reaction is driven by a variety of inflammatory mediators such as growth factors and cytokines released by the liver tissue with hepatic myofibroblasts in a central role. The process of cirrhosis of the liver causes a slow cascade of reactions with

initially no symptoms and fully compensated developing into several symptoms and decompensated [22]. A description of stages from 1-4 describes the development with no symptoms at stage 1. At stage 2 the blood flow through the liver decreases, and the blood pressure in the portal vein increases, the blood is forced to find alternative routes through the liver. To compensate, capillarisation of sinusoids and intrahepatic shunts develops together with the possibility of oesophageal varices characterizing stage 2 of compensated liver cirrhosis. From this stage the condition deteriorates with a rapid increase in mortality. In decompensated stages of cirrhosis both ascites and varices develops as well as reduced function of the liver resulting in jaundice, encephalopathy and hepatorenal syndrome (HRS). HRS is a complex condition of the kidneys mainly caused by peripheral arterial vasodilatation due to excessive release of nitric oxide (NO) as the portal vein pressure increases resulting in increased renal vasoconstriction. Development of HRS is detrimental for human functioning causing death within a few weeks unless the liver is replaced [23].



Diagrammatic features of cirrhosis of Liver

Figure-1 Features of cirrhosis. Cells of the liver lobes is divided into Parenchymal and non-parenchymal. The top part of figure shows a healthy liver part. A low density membrane ensures the metabolic exchange between Sinusoidal cells and space

of Disse. Upon injury (bottom part), large amounts of extracellular matrix is secreted and deposited in the space of Disse impairing bidirectional metabolic exchange between venous blood and Hepatocytes. Figure taken from [22].

RESULTS AND OBSERVATIONS

This observational cross sectional study was conducted in the Department of Gastroenterology and Medicine, Dhaka Medical College Hospital, Dhaka from April 2018 to September 2018 to determine the sensitivity and specificity of non-invasive methods to

predict the presence of gastroesophageal varices (GEV) in patients with CLD. A total of 146 patients with chronic liver disease irrespective of age and sex were selected by non-randomized purposive sampling technique.

Table-1: Age distribution of the patient (n=146)

Age group (years)	No of the Patient	Percentage (%)
18-30	25	17.1
31-40	36	24.7
41-50	33	22.6
51-60	30	20.5
61-70	13	8.9
>70	9	6.2
Total	146	100.0
Mean±SD	44.62±13.87	
Range	(20-78) years	

Table-1 shows that 36(24.7%) in the age group 31-40 years followed by 33(22.6%) in 41-50 years. The mean age of the study group was

44.62±13.87 years, minimum age 20 and maximum 78 years.

Table-2: Sex distribution of the patients (n=146)

Sex of the patient	No of the Patient	Percentage%
Male	115	78.8
Female	31	21.2
Total	146	100.0

Table-2 shows the distribution by sex. Maximum patients were male 78.8% and rest 21.2% patient was female. Male: Female ratio was 3.7:1.

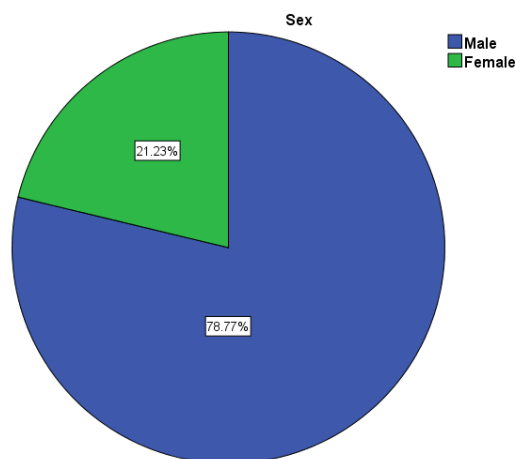


Fig-2: Sex distribution of the study patients

Table-3: Distribution of the study subjects by occupation (n=81)

Occupation	No of the Patient	Percentage (%)
Service holder	34	23.3
Business	38	26.0
House wife	28	19.2
Others	46	31.5
Total	146	100.0

Table-3 showed 23.3% patients were service holder, 26.0% patients were business, 19.2% patients were housewife and 31.5% patients were other occupation.

Table-4: Distribution of the study subjects by residence (n=146)

Residence	No of the Patient	Percentage%
Rural	86	58.9
Urban	60	41.1
Total	146	100.0

Table-4 showed that maximum patients 58.9% come from rural and 41.1% patients come from urban area.

Table-5: Distribution of the study patients by education (n=146)

Education	Frequency	Percentage (%)
Illiterate	44	30.1
Primary	52	35.6
SSC	25	17.1
HSC	12	8.2
Graduate and above	13	8.9
Total	146	100.0

Table-5 shows, distribution of the study subjects according to educational status, it was found that the maximum study subjects 35.6% primary, 30.1%

were illiterate, 17.1% respondents were SSC, 8.2% patients were HSC and 8.9% patients were graduate and above.

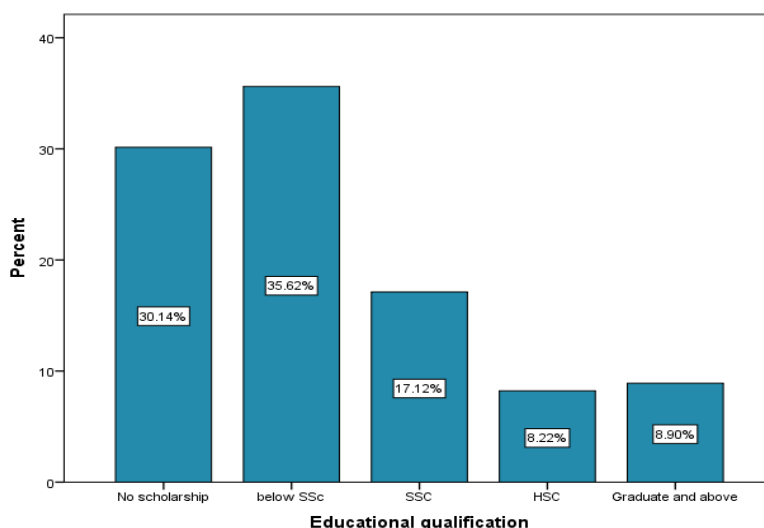


Fig-3: Bar diagram showing the educational qualification of the study subjects

Table-6: Distribution of the study patients by marital status (n=146)

Marital status	Frequency	Percentage (%)
Unmarried	15	10.3
Married	131	89.7
Total	146	100.0

Table-6 shows the marital status of the study subjects, maximum (89.7%) were married and 10.3% patients were unmarried.

Table-7: Distribution of the study subjects according to socioeconomic status (n=362)

Monthly income	Frequency	Percentage (%)
Less than 10000 Tk.	44	30.1
10000-20000 Tk.	49	33.6
20000-40000 Tk.	45	30.8
More than 40000 Tk.	8	5.5
Total	146	100.0

Table-7 shows, distribution of the respondents according to economical status. It was found that the maximum respondents 33.6% had monthly income

10,000-20000 Tk. followed by 30.1% had monthly income of less than 10000 Tk. and 30.8% respondents had monthly income 20000-40000 Tk.

Table-8: Distribution of the study CLD patients by clinical presentation (n=146)

Clinical presentation	Frequency	Percentage (%)
Splenomegaly	120	82.2
Anemia	92	63.0
Testicular atrophy	81	55.5
Ascites	78	53.4
Hyperpigmentation	71	48.6
Leuconychia	62	42.5
Edema	61	41.8
Palmar erythema	44	30.1
Spider naevi	43	29.5
Muscle wasting	42	28.8
Jaundice	26	17.8
Flaping tremor	21	14.4
Clubbing	20	13.7

Table-8 shows clinical presentation, 82.2% patients had splenomegaly, 63.0% patients had anemia, 55.5% patients had testicular atrophy, 53.4% patients had ascites, 48.6% patients had hyperpigmentation,

42.5% patients had leuconychia, 41.8% patients had edema, 30.1% patients palmar erythema, 29.5% patients spider naevi, 28.8% patients had muscle wasting, 17.8% patients jaundice, 14.4% patients had flapping.

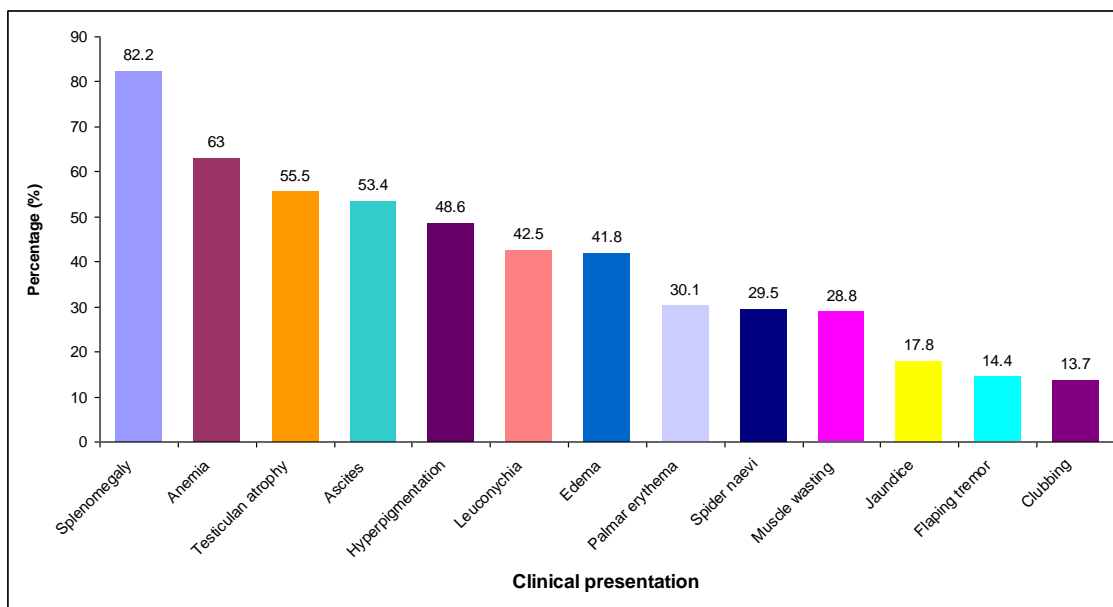


Fig-4: Bar diagram showing the clinical presentation of the study patients

Table-9: Distribution of the study CLD patients by ultrasonographic findings (n=146)

Ultrasonographic findings	Mean±SD
Spleen diameter (cm)	11.68±2.21
PVD (mm)	10.51±1.32

Shows in mean spleen diameter 11.68±2.21 and mean PVD was found 10.51±1.32 (Table-9).

Table-10: Distribution of the study CLD patients by endoscopy findings (n=146)

Endoscopy findings	Frequency	Percentage (%)
Presence of varices		
Yes	130	89.0
No	16	11.0
Total	146	100.0
Grading of varices		
Grade I	18	13.8
Grade II	35	26.9
Grade III	55	42.3
Grade IV	22	15.1
Total	130	100.0
Other findings		
Congestive gastropathy	104	80.0
Ulcer	5	3.8
Polyp	2	1.5
Gastritis	4	3.1

Table-10 showed majority of the patients had varices 130(89.0%). Among 130 varices maximum Grade III 42.3% followed by Grade II 26.9%, Grade IV 15.1% and Grade I 13.5%. Majority of the patients had congestive gastropathy 105(80.0%), ulcer 5(3.8%), polyp 2(1.5%) and gastritis 4(3.1%).

Receiver-operator characteristic (ROC) curve of spleen size for prediction of esophageal varices

The area under the receiver-operator characteristic (ROC) curves for the esophageal varices

is depicted in the following table. Based on the receiver-operator characteristic (ROC) curves spleen size had the best area under curve. Receiver-operator characteristic (ROC) were constructed using spleen size value of the patients having esophageal varices with a best combination of sensitivity and specificity for esophageal varices, which gave a spleen size cut off value of ≥ 14.1 cm, with 82.3% sensitivity and 87.5% specificity as the value and for identifying the esophageal varices.

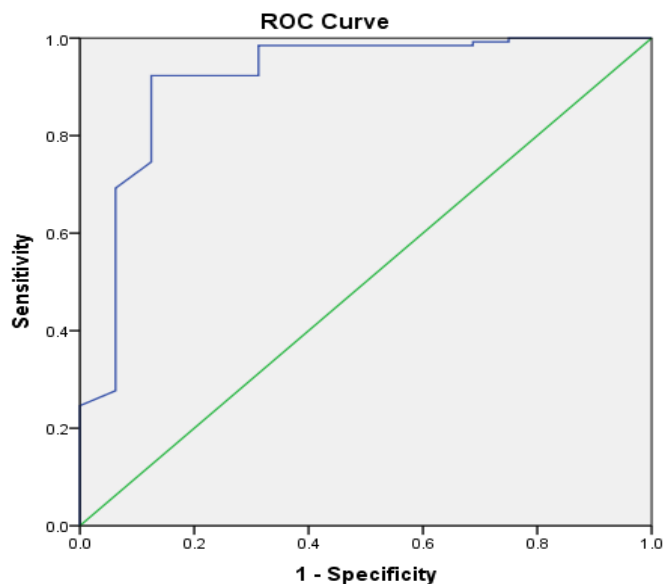


Fig-5: ROC curve for spleen size in predicting esophageal varices

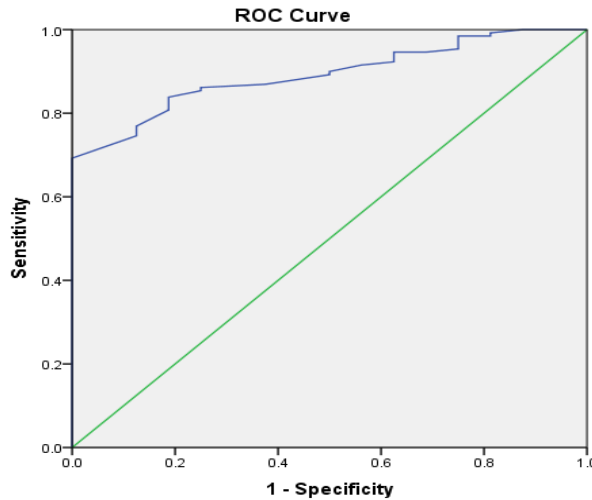
Table-11: Test Result Variable(s): Spleen size with varices.

AUC	Std. Error	p-value	95% CI		Cut of value	Sen	Spec	NPV	PPV
			Lower	Upper					
0.916	0.047	<0.0001	0.824	1.000	14.1	92.3%	87.5%	98.4%	58.3%

Receiver-operator characteristic (ROC) curve of Platelets count for prediction of esophageal varices

The area under the receiver-operator characteristic (ROC) curves for the esophageal varices is depicted in the following table. Based on the receiver-operator characteristic (ROC) curves platelets count had the best area under curve. Receiver-operator

characteristic (ROC) were constructed using Platelets count value of the patients having esophageal varices with a best combination of sensitivity and specificity for esophageal varices, which gave a Platelets count cut off value of <126000/ cmm, with 74.6% sensitivity and 87.5% specificity as the value and for identifying the esophageal varices.



Diagonal segments are produced by ties.

Fig-6: ROC curve for platelet count in predicting esophageal varices

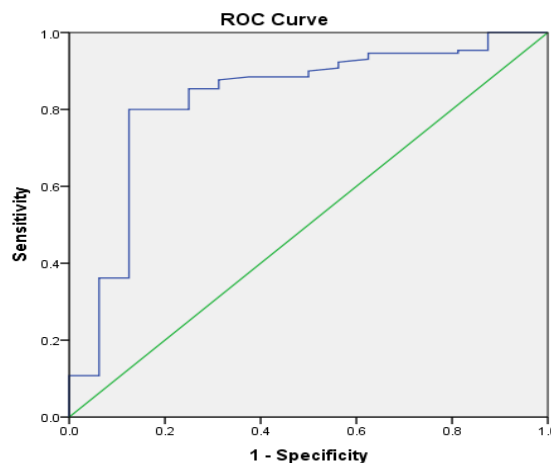
Table-12: Test Result Variable(s): Platelets with varices

AUC	Std. Error	p-value	95% CI		Cut of value	Sen	Spec	NPV	PPV
			Lower	Upper					
0.892	0.030	<0.001	0.834	0.950	126000	74.6%	87.5%	32.9%	94.3%

Receiver-operator characteristic (ROC) curve of fibro scan for prediction of esophageal varices

The area under the receiver-operator characteristic (ROC) curves for the esophageal varices is depicted in the following table. Based on the receiver-operator characteristic (ROC) curves fibro scan had the best area under curve. Receiver-operator characteristic (ROC) were constructed using fibro scan

value of the patients having esophageal varices with a best combination of sensitivity and specificity for esophageal varices, which gave a fibro scan cut off value of ≥ 17.85 cm, with 81.5% sensitivity and 75.0% specificity as the value and for identifying the esophageal varices.



Diagonal segments are produced by ties.

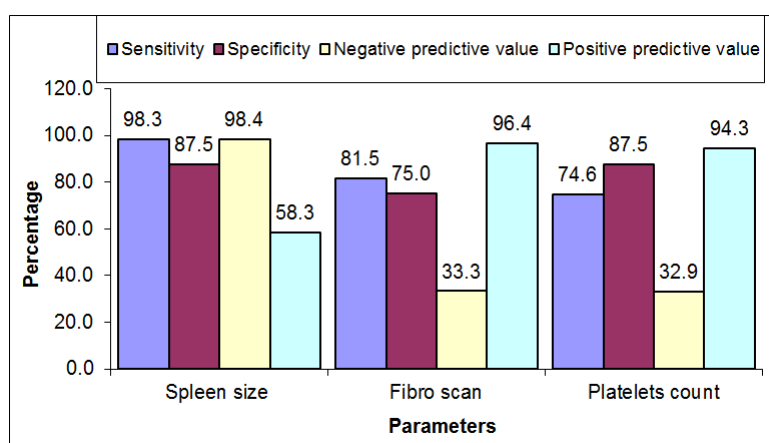
Fig-7: ROC curve for fibroscan size in predicting esophageal varices

Table-13: Test Result Variable(s): Fibro scan with varices.

AUC	Std. Error	p-value	95% CI		Cut of value	Sen	Spec	NPV	PPV
			Lower	Upper					
0.824	0.062	<0.001	0.703	0.944	17.85	81.5%	75.0%	33.3%	96.4%

Table-14: Sensitivity, specificity, positive and negative predictive values for identifying the esophageal varices evaluated by different non-invasive methods

Parameters	Cut of value	Sensitivity	Specificity	Negative predictive value	Positive predictive value
Spleen size	14.10	92.3%	87.5%	98.4%	58.3%
Fibro scan	17.85	81.5%	75.0%	33.3%	96.4%
Platelets count	126000	74.6%	87.5%	32.9%	94.3%

**Fig-8: Bar diagram shows the Sensitivity, specificity, positive and negative predictive values**

DISCUSSION

In the present study the mean age of the CLD patients was 44.62 ± 13.87 years, minimum age 20 and maximum 78 years. Majority of the patients were male 78.8% and female 21.2%. Male: Female ratio was 3.7:1. Ahsan *et al.*, [24], found 28% in between 46-55 years age group which coincide with our study. 73% were male and 27% female. Male female ratio was 2.7:1. Mahtab *et al.*, [25], found male female ratio of 2.97:1, which almost coincide with our study. In our study clinical presentation of CLD patients were showed 82.2% patients had splenomegaly, 63.0% patients had anemia, 55.5% patients had testicular atrophy, 53.4% patients had ascites, 48.6% patients had hyperpigmentation, 42.5% patients had leuconychia, 41.8% patients had edema, 30.1% patients palmar erythema, 29.5% patients Caput Medusa, 28.8% patients had muscle wasting, 17.8% patients jaundice, 14.4% patients had flapping, 13.7% patients had clubbing. Sharma and Aggarwal [26], found splenomegaly 52%, pallor 68%, jaundice 52%, pedal edema 80%, spider vaevi 22%, ascites 19%, encephalopathy 52% in patients with cirrhosis of the liver. Mahfuzzaman *et al.*, [27], cirrhotic patient with splenomegaly, thrombocytopenia and increase spleen had more possibility to have OV. Different studies in recent years also found similar findings [28, 29]. Several studies have reported that splenomegaly could be a good predictor of LEV for cirrhotic patients [26,

30]. In present study endoscopic findings were showed varices 130(89.0%). Among 130 varices maximum Grade II 42.3% followed by Grade II 26.9%, Grade IV 15.1% and Grade I 13.5%. Out of 130 varices majority of the patients had congestive gastropathy 105(80.0%), ulcer 5(3.8%), polyp 2(1.5%) and gastritis 4(3.1%). Schepis *et al.*, [31], reported using endoscopy, EV were detected in 63 of the 143 patients examined (44%). Medium and large EV were observed in 28 of the 63 subjects (44%) with EV. In present study the presence of gastro-esophageal varices by fibroscan at a cut off value 17.8 kpa with sensitivity, specificity, PPV, NPV, accuracy respectively 81.5%, 75%, 33.3%, 94.6% can predict the gastro-oesophageal varices (AU ROC – 82.5%). Foucher *et al.*, [32], reported a cut off value (27.5 kPa) for the presence of esophageal varices grade II/III with sensitivity 88%, specificity 53%, PPV 45% and NPV 90%. Kazemr *et al.*, [33], reported that liver stiffness measurement value < 19 kpa was highly predictive of the absence of esophageal varices grade II with sensitivity 84%, PPV 47% and NPV 93%. In contrast, Vizzutti *et al.* [34], found no correlation between LSM and the size of the varices. In present study the predicted gastro-esophageal varices by platelet count at a cut off value ≥ 126000 with sensitivity, specificity, PPV, NPV was 74.6%, 87.5%, 32.9%, 94.3% respectively can predict the gastro-oesophageal varices (AU ROC – 89.2%). In accordance Pilette *et al.*, (1999) reported that the best threshold for the diagnostic accuracy of platelet count was

160000/cmm providing a sensitivity of 80% and a specificity of 58%. The ROC curve also showed that the presence of large EV is improbable if cirrhotic patients have a platelet count ≥ 260000 /cmm (negative predictive value $\geq 91\%$). In the group of patients with cirrhosis, global diagnostic accuracy was 71%, and platelet count was isolated at the first step and prothrombin index at the 2nd step either for all EV or large EV. Thus, platelet count appeared to be the best single marker of EV or large EV, since other markers added little information [35]. Platelet count has also been shown to be an independent marker in two other studies with multivariate analysis [28, 36, 37], reported the platelet count/spleen diameter ratio to be the only independent variable associated with presence of OV on multivariate analysis and identified a cut-off value of 909, giving a PPV of 96% and NPV of 100%. Sen *et al.*, [38], found the platelet count-spleen diameter ratio of ≤ 650 as a sensitive non-invasive marker [Area under curve (AUC) of 0.81] in HCV related cirrhosis. Cherian *et al.*, [39], reported on univariate analysis, a platelet count-spleen diameter ratio of ≤ 666 was significantly associated with the presence of esophageal varices in a predominant alcohol related cirrhosis subset. Llop *et al.*, [40], demonstrated the presence of GEV was related with platelet count ($p=0.02$), TE ($p=0.001$) and spleen diameter ($p=0.003$). The multivariate analysis confirmed, although discreetly, TE OR 1.04 (IC 1.01-1.08). They analysed different single methods to predict the presence of GEV in patients with cACLD. Previous studies have shown that platelets are a good predictor of the presence of GEV in patients with liver cirrhosis with high sensitivity and specificity [37, 41]. These results were confirmed partially in our study, a platelet count 260000 had a good sensitivity 74.6%, specificity 87.5%. In present study, enlarged spleen size cut-off value 14.1 cm had acceptable sensitivity 92.3% specificity, 87.5% with a NPV 98.4%, PPV 58.3%. Giannini *et al.*, [37], reported spleen diameter ratios were significantly different between NOV and OV patients, spleen size (cut of point > 12.1 cm, 90.9% accuracy) had the highest accuracy for identifying patients with OV. Giannini *et al.*, [37], used ROC curves to assess the platelet count (cut off value > 112000)/spleen diameter ratio (cut off value > 12.1 cm) cut off with the best sensitivity and specificity for a diagnosis of OV (sensitivity=100% (95% CI 100–100); specificity=93% (95% CI 82–98). The prevalence adjusted positive and negative predictive values for a platelet count/spleen diameter ratio < 909 were 96% and 100%, respectively. Moreover, accuracy of the platelet count/ spleen diameter ratio cut off as evaluated by the c index was 0.981 (95% CI 0.943–0.996). Both spleen diameter and platelet count cut offs with the best sensitivity and specificity for a diagnosis of OV. Sharma and Aggarwal [26], showed that to predict the presence of EV using simple and non-invasive tools like clinical examination for the presence of a palpable spleen and platelet count with a fairly high degree of accuracy. Thus, these two

measures could accurately predict the presence or absence of EV in nearly 70% of patients.

CONCLUSION

In conclusion, noninvasive strategies probably save costs and avoid unnecessary gastroscopies; however, there are a considerable number of patients undiagnosed with these methods. In our study, platelet count, spleen size and fibroscan are the best noninvasive methods. These methods can be useful in our daily practice to decide which patients could avoid a gastroscopy.

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