Section: General Medicine

Original Research Article

A STUDY OF NON-INVASIVE PREDICTORS OF ESOPHAGEAL VARICES IN PATIENTS WITH CHRONIC LIVER DISEASE IN A TERTIARY CARE HOSPITAL

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Abstract

Background: Esophageal varices are one of the most dreaded complications of portal hypertension in patients with CLD. 20-40% of patients with EV develop variceal bleeding. **Aim:** The study aims to analyse the prevalence of non-invasive predictors in cases of portal hypertension with varices proved by endoscopy and to correlate the severity and grading of esophageal varices to the level of non-invasive predictors. **Materials and Methods:** This Prospective observational study was conducted at the government Thoothukudi medical college hospital for one year (Jan 2019- Jan 2020). All the data were collected from the persons admitted to the government TKMCH with symptoms and signs of chronic liver disease /cirrhosis. Seventy-five patients were included in the study, and the baseline medical histories were elicited, followed by a complete physical examination of the patients. **Result:** In our study, among 75 patients, 84% of the patients are males, and only 16% are female. The commonly affected age group in our study is between 41-50, contributing to 49.3%, age group between 31-40 years contributes to 30.7% of the total study population. The most common etiology for liver disease in our study is alcohol (76%), hepatitis b infection (8%) and less commonly autoimmune (2.7%) and cryptogenic etiologies. Most patients have grade 2 varices (45.3%) followed by Grade 3 varices (40%). There is a correlation between platelet count, fibroscan, PC/SD ratio and endoscopy varices. **Conclusion:** The study highlights the importance of early detection and managing chronic liver disease to prevent complications such as varices and UGI bleeding.

INTRODUCTION

Esophageal varices are one of the most dreaded complications of portal hypertension in patients with CLD. 20-40% of patients with EV develop variceal bleeding. EV can be diagnosed and confirmed by endoscopy.[1,2] As endoscopy is an invasive procedure that most patients will deny and is costly, this has very poor patient compliance.+ To overcome these problems and reduce endoscopy-induced variceal bleeding in patients at risk of bleeding, studies need to identify other modalities to predict EV by non-invasive methods.

Endoscopic screening for esophageal varices in all patients with cirrhosis is recommended to detect the presence and severity of varices and identify those at high risk of bleeding. However, this approach is associated with several challenges, including the limited availability of endoscopy units and the cost and discomfort associated with the procedure. Furthermore, patients with cirrhosis require regular surveillance endoscopy, which can significantly burden the patient and the healthcare system. Non-invasive predictors have been developed to identify cirrhosis patients at high risk of varices and variceal bleeding. These predictors include clinical parameters such as age, gender, and etiology of liver disease, as well as laboratory and radiological parameters such as platelet count, spleen diameter, and fibroscan score.[4]

The non-invasive methods that can be used as the predictors are platelet count, spleen size, right lobe of liver diameter, prothrombin time, spleen stiffness and

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liver stiffness. Our study includes platelet count, spleen size, and liver and spleen stiffness.

Aim

To analyse the prevalence of non-invasive predictors in cases of portal hypertension with varices proved by endoscopy and to correlate severity and grading of esophageal varices to the level of non-invasive predictors.

MATERIALS AND METHODS

This Prospective observational study was conducted at the government Thoothukudi medical college hospital for one year (Jan 2019- Jan 2020). All the data were collected from the persons admitted to the government Thoothukudi medical college hospital with symptoms and signs of chronic liver disease /cirrhosis.

After obtaining institutional ethical committee approval, informed consent was obtained from the patients admitted to the medical gastroenterology and medicine ward who participated in the study during the study period. Seventy-five patients were included in the study, and the baseline medical histories were elicited, followed by a complete physical examination of the patients.

Inclusion criteria: Age >18 years, patients who were diagnosed to have cirrhosis-portal hypertension with esophageal varices at TKMCH proved clinically, biochemically, radiologically and endoscopically were included.

Exclusion criteria: Age, HIV patients, patients on surgical treatment for portal hypertension, patients who are not willing to participate in the study, patients with psychiatric illness, pregnant and lactating mothers, and patients with fever, antiplatelet drug therapy, and malignancy were excluded.

All the patients included in the study were undergone complete blood count, which includes haemoglobin and platelet count, coagulation profile that includes prothrombin time and INR, liver function tests (alanine transaminase, aspartate transaminase, total protein, albumin globulin levels), blood urea, serum creatinine, serum electrolytes, blood sugar levels, viral markers(HBV, HCV), ultrasonography of abdomen (assesses spleen diameter, portal vein diameter, amount of ascites, liver parenchymal abnormalities), upper GI video endoscopy, fibroscan to evaluate the stiffness of the liver. All the parameters were compared with the grading of varices assessed by endoscopy using AASLD three-size classification.

Data were entered into MS excel and calculated.

RESULTS

Table 1: Demographic data of the study

		Frequency	Percentage
Gender	Male	63	84%
	Female	12	16%
Age	<30	4	5.3%
	31-40	23	30.7%
	41-50	37	49.3%
	51-60	10	13.3%
	>61	1	1.3%
Etiology	Alcohol	57	76%
	Autoimmune	2	2.7%
	Cryptogenic	10	13.3%
	Hep-B	6	8%
Endoscopy	Grade 1 varices	11	14.7%
	Grade 2 varices	34	45.3%
	Grade 3 varices	30	40%
Platelet	<50000	4	5.3%
	50000-1 Lakh	40	53.3%
	1 Lakh-1.5 Lakh	26	34.7%
	>1.5 Lakh	5	6.7%
CTP Class	A	6	8%
	B	46	61.3%
	C	23	30.7%

In our study, among 75 patients, 84% of the patients are males, and only 16% are female. The commonly affected age group in our study is between 41-50, contributing to 49.3%, age group between 31-40 years contributes to 30.7% of the total study population.

The most common etiology for liver disease in our study is alcohol (76%), hepatitis b infection (8%) and less commonly autoimmune (2.7%) and cryptogenic etiologies. Most patients have grade 2 varices (45.3%) followed by Grade 3 varices (40%). Most patients had a platelet count between 50000-100000(53.3%). Four patients had <50000 platelet count. 6.7% of patients had normal platelet count >150000. Most patients fall under class B, around 61%; class C around 31%; and class A, around 8% [Table 1].

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Table 2: Mean laboratory values among patients

	Minimum	Maximum	Mean	Std. Deviation
Age	19.00	61.00	42.80	7.58
Hb	5.90	11.50	9.06	1.16
Platelet	33000.00	168000.00	97106.67	29271.13
Bilirubin total	1.10	7.70	3.29	1.54
SGOT	41.00	336.00	128.71	52.39
SGPT	18.00	154.00	64.17	30.10
ALP	25.00	198.00	81.65	33.73
PT	14.00	25.00	19.37	2.74
Albumin	1.20	3.10	2.45	0.39
Spleen size	113.00	177.00	144.55	11.53
Fibroscan	21.70	65.60	36.44	11.00
PC/SD Ratio	197.70	1380.10	683.59	237.24

Mean Hb 9.0 (SD 1.1), mean fibroscan value 36.44kpa (SD 11), mean PC/SD ratio 683.5 (SD 237). The mean albumin value was 2.45 (SD 0.39), mean total bilirubin value was 3.29 (SD 1.54) [Table 2].

Table 3: CTP class comparison with endoscopy

		Endoscopy			Total	P value
		Grade 1 varices	Grade 2 varices	Grade 3 varices		
CTP class	A	3	2	1	6	0.065
	B	7	22	17	46	
	C	1	10	12	23	
Total		11	34	30	75	

In our study, 46 patients had CTP scores between 6-9 (class B), 23 patients had CTP scores of 10 or more (class C). 12 patients with class C had grade 3 varices. Seventeen patients with class B CTP scores had grade 3 varices. Only one patient in class A had grade 3 varices. CTP score and endoscopic variceal grading have statistical insignificance (p-value 0.065) [Table 3].

Table 4: Mean parameters among the study populations

		Mean	Std Deviation	95% Confidence Interval for Mean		P-value
				Lower Bound	Upper Bound	
Fibroscan values	Grade 1 varices	24.90	2.84	22.99	26.81	<0.0001
	Grade 2 varices	31.61	7.10	29.13	34.08	
	Grade 3 varices	46.14	8.56	42.94	49.34	
PC/SD ratio	Grade 1 varices	1052.74	218.50	905.95	1199.52	<0.0001
	Grade 2 varices	742.11	106.12	705.09	779.14	
	Grade 3 varices	481.92	128.69	433.87	529.98	
Platelet count and endoscopy	Grade 1 varices	141000.00	24669.82	124426.59	157573.41	<0.0001
	Grade 2 varices	104941.18	13967.37	100067.73	109814.62	
	Grade 3 varices	72133.33	17508.09	65595.70	78670.96	
Spleen size and variceal grading	Grade 1 varices	134.82	7.26	129.94	139.70	<0.0001
	Grade 2 varices	142.12	11.31	138.17	146.06	
	Grade 3 varices	150.87	9.57	147.29	154.44	
Platelet count and CTP class	A	119666.67	39888.18	77806.59	161526.74	0.01
	B	100608.70	25752.22	92961.23	108256.16	
	C	84217.39	28735.40	71791.27	96643.51	
Fibroscan with CTP class	A	31.65	12.74	18.28	45.02	0.003
	B	33.96	8.62	31.40	36.52	
	C	42.64	12.59	37.20	48.08	

In Patients with grade 3 varices mean fibroscan value is 46.14 kpa (SD 8.5), whereas for grade 1 varices mean fibroscan value was 24.9 kpa (SD 2.8). In patients with grade 2 varices mean fibroscan value is 31.61kpa. This comparison between fibroscan and endoscopic variceal grading has statistical significance with a p-value <0.0001.
In Patients with grade 3 varices mean PC/SD ratio was 481.9(SD 128.6), whereas in grade 1 varices mean PC/SD ratio was 1052.7(SD 218.5). This comparison between the PC/SD ratio and endoscopic variceal grading has statistical significance with a p-value <0.0001.
In Patients with grade 3 varices mean Platelet count was 72133.3(SD 17508), whereas for grade 1 varices mean Platelet count was 141000(SD 24669.8). This comparison between platelet count and endoscopic variceal grading has statistical significance with a p-value <0.0001.

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In Patients with grade 3 varices mean spleen diameter was 150.87(SD 9.5), whereas for grade 1 varices mean spleen diameter was 134.8(SD 7.2). This comparison between spleen diameter and endoscopic variceal grading has statistical significance with a p-value <0.0001.
The mean platelet count in patients with CTP class C is 84217.3(SD 28735.4). In CTP class B, the mean platelet count is 100608.7(SD 25752.2). CTP Class A, the mean platelet count is 119666.6. This comparison is statistically significant with a p-value of 0.01.
In patients with CTP class C, the mean fibroscan value is 42.6(SD 12.5), CTP class B, the mean fibroscan value is 33.9 (SD 8.6). CTP class A, the mean fibroscan value is 31.65(SD 12.74). This comparison is statistically significant, with a p-value of 0.003 [Table 4].

Table 5: Cut-off values for detecting varices grades

		Fibroscan	Platelets	PC/SD ratio	Spleen size
Grade 1 varices	Area under curve	8%	95%	94%	17%
	Sensitivity	72.00%	82%	82%	91%
	Specificity	2.00%	74%	75%	3%
	Cut off value	23.3	102500	756.9	124.5
Grade 2 varices	Area under curve	29%	72%	73%	42%
	Sensitivity	88.00%	91%	85%	74%
	Specificity	17.00%	66%	68%	74%
	Cut off value	24.45	88500	629.3	136.5
Grade 3 varices	Area under curve	93%	4%	3%	76%
	Sensitivity	93.00%	73%	70%	90%
	Specificity	82.00%	2%	2%	66%
	Cut off value	35.95	66000	425.9	141.5

Our study's platelet count cut-off value for high-grade varices is 66000, with a sensitivity of 73%. The cut-off value for the presence of grade 1 varices is 102500, with a sensitivity of 82% and a specificity of 74%.
Our study's cut-off value for high-grade varices is 425.9, with a sensitivity of 70%. The cut-off value for detecting grade 1 varices is 756.9, with a sensitivity of 82% and a specificity of 75%. It is statistically significant and has a modest correlation with the grading of varices (R-value -0.716) [Table 5].

Table 6: Correlation of parameters between endoscopy

			Endoscopy	
	Platelet	Correlation Coefficient	-0.714	Moderate correlation
		P value	<0.0001	
	Fibroscan	Correlation Coefficient	0.651	Moderate correlation
		P value	<0.0001	
	PC/SD ratio	Correlation Coefficient	-0.716	Moderate correlation
		P value	<0.0001	
	Spleen size	Correlation Coefficient	0.41	Mild Correlation
		P value	<0.0001	

There is a moderate correlation in platelet count with endoscopy varices (r=-0.714, p<0.0001). There is a moderate correlation in fibroscan with endoscopy varices (r=0.651, p<0.0001). There is a moderate PC/SD ratio correlation with endoscopy varices (r=-0.716, p<0.0001). There is a mild correlation in PC/SD ratio with endoscopy varices (r=-0.716, p<0.0001) (Table 6, Figure 5,6,7,8).

Table 7: Correlation of PC/SD ratio with CTP class

PC/SD ratio	**Correlation Coefficient**	-0.448
	P value	<0.0001

There is a correlation in PC/SD ratio with CTP class (r=-0.448, p<0.0001) [Table 7, Figure 9].

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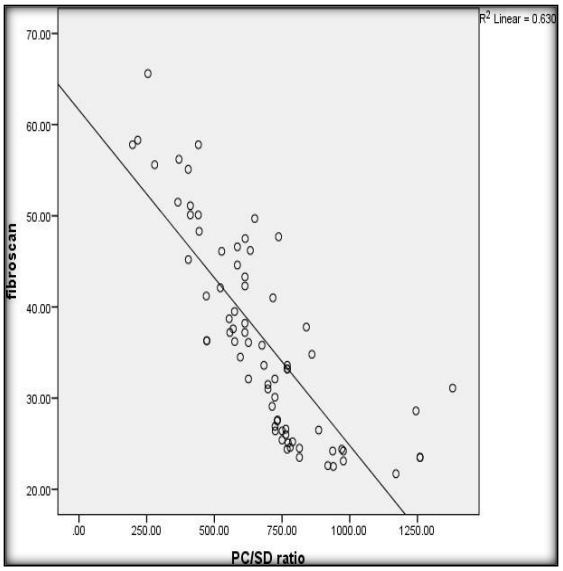

Figure 1: Fibroscan and PC/SD ratio correlation

Comparison of fibroscan and PC/SD ration showed Pearson correlation -0.794 (good correlation) with a p-value <0.0001 [Figure 1].

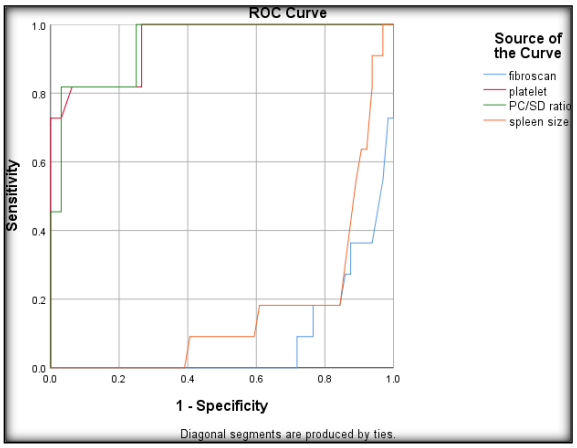

Figure 2: Cut-off values for detecting grade 1 varices

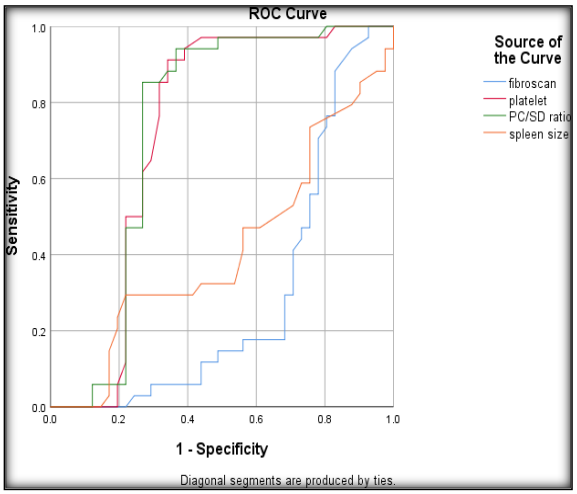

Figure 3:

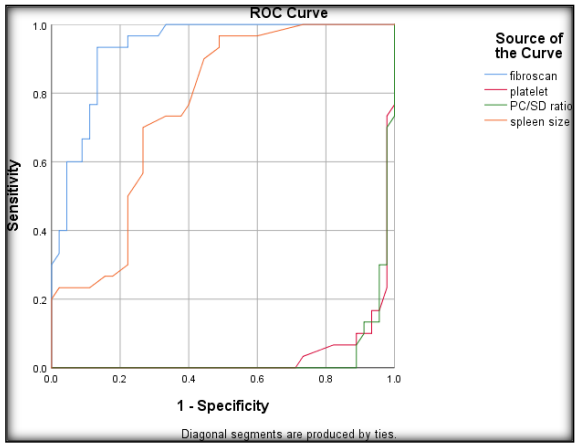

Figure 4: Cut-off values for detecting grade 3 varices

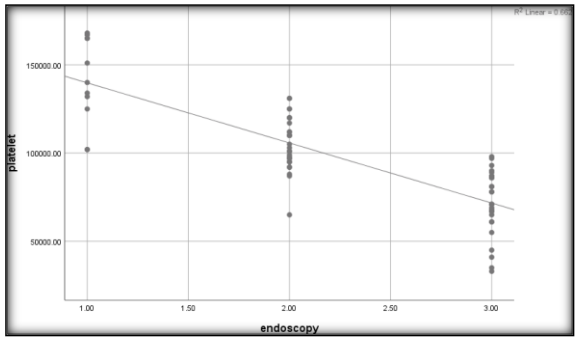

Figure 5: Correlation of platelet count with varices

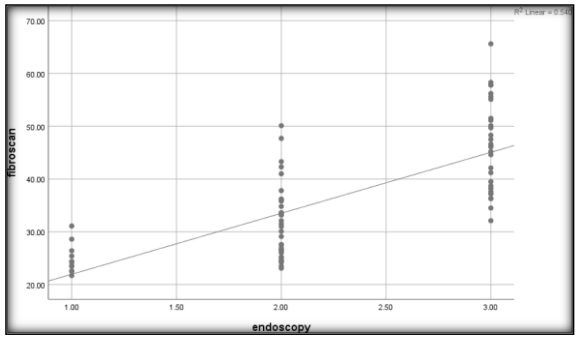

Figure 6: Correlation of fibroscan with endoscopic varices

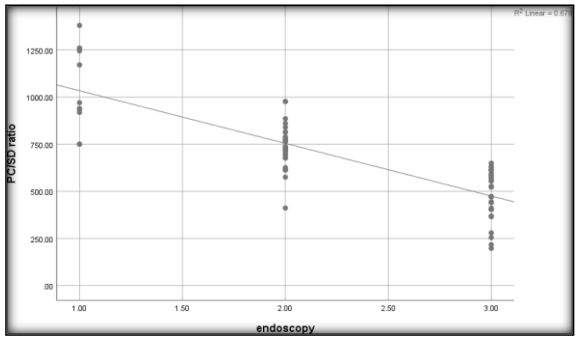

Figure 7: Correlation of fibroscan with endoscopic varices

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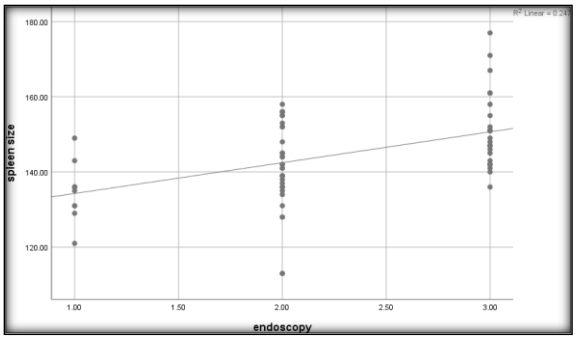

Figure 8: Correlation of spleen size with varices

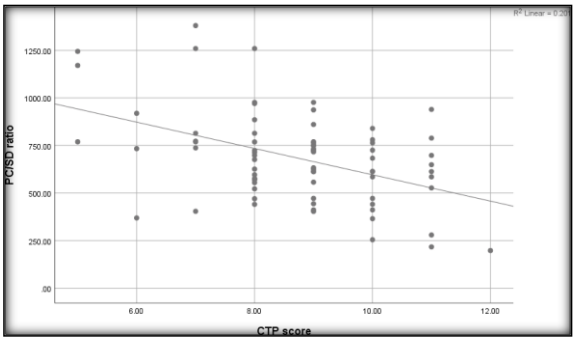

Figure 9: Correlation of PC/SD ratio with CTP class

DISCUSSION

Most of the patients in our study are predominantly 41-50 years of age (49.3%), as in many of the previously done studies. El-Makarem et al.[5] reported 36-60 years, and Baig et al.[6] found 40-60years (mean age 51). In Cherian et al.[7] the mean age is 42(17-73) years; in Al- Hamoudi et al.[8] the common age group are between 57.2±15.3 years.

In our study, 5/6 patients are male (84%), and the remaining are female patients (16%) because the predominant population in our study are alcoholics. This result is consistent with many studies, Alempijevic et al.[9] reported 74/12, and Montasser et al.[10] reported 56/19.

Most of the patients are alcoholic (76%), and others include cryptogenic (13.3%), hepatitis B (8%), and autoimmune (2.7%). This result is consistent with previous studies Baig et al.[6] 73/13/39/4 (alcohol/cryptogenic/hep-B/autoimmune), Cherian et al.[7] 97/35/23/45 (alcohol/hep-B/hep-C/others). According to Giannini et al.[11] 105/41/35/8/2 (hep-B/alcohol/PBC/cryptogenic/autoimmune), the common cause is hepatitis B, followed by alcohol.

The lower the platelet count higher the grade of varices. The mean platelet count in patients with grade 3 varices is 72133.3 cells/mm (SD-17508). 40% of patients had grade 3 varices. The mean platelet count in patients with grade 1 varices is 141000 (SD-24669.8). These results from our study are statistically significant as the p-value is <0.0001, and platelet count significantly correlates with the severity of varices (R-value -0.714).

In patients with a CTP class B score, the mean platelet count is 100608.7; in class C, the mean platelet count is 84217, with a P value of 0.01. Platelet count had a significant relationship with CTP score and endoscopy. The platelet count cut-off value for the presence of high-grade varices in our study is 66000, with a sensitivity of 73%. The cut-off value for grade 1 varices is 102500, with a sensitivity of 82% and specificity of 74%. In Giannini et al.[11] the mean platelet count is 85000 (p-value <0.0001). According to El-Makarem et al.[5] the presence of EV correlated significantly with the severity of cirrhosis as measured by CTP. Also, in that study, the patients with EV had low platelet count, high CTP, and low PC/SD ratio.

Almost all the patients had spleen enlargement (>130mm). About 58% had spleen diameters between 130-150mm. 33% had a diameter >150mm. The cut-off value for detecting grade 3 varices is 141.5cm with a sensitivity of 90% and specificity of 66%. Cut off for detecting grade 1 varices is 124.5mm with a sensitivity of 91% and specificity of only 3%. According to Sen et al.[12] a cut-off value of SD is 120mm for alcoholic cirrhosis, with a sensitivity of 74% and specificity of 55%. Giannini et al. 3,39, the mean SD value is 153 mm (p value< 0.0001).

The mean PC/SD ratio in patients with grade 3 varices is 481.9 (SD 128.6), and in patients with grade 1 varices, 1052.7 (SD 218.5). These values from our study are statistically significant as the P value is 0.0001. Our study's cut-off value for high-grade varices is 425.9, with a sensitivity of 70%. The cut-off value for detecting grade 1 varices is 756.9, with a sensitivity of 82% and specificity of 75%. It is statistically significant and has a modest correlation with the grading of varices (R-value -0.716). According to Giannini et al.[11] 39 PC/SD ratio can be used as the sole predictor of varices (PC/SD ratio 909, sensitivity 91.5%, specificity 67%), Baig et al.[6] cut off of PC/SD ratio 1014 (sensitivity 98%, specificity 88.6%), El-Makarem et al.[5] cut off are 939.7 (sensitivity 100%, specificity 86.3%). Cherian et al.[7] cut-offs are 666 (sensitivity 66.3%, specificity 80.4%).

The mean fibroscan value in detecting grade 3 varices is 46.14, and in detecting grade 1 varices 24.9kpa. The mean fibroscan value in patients with class B CTP score is 33.96 (SD 8.6). In class C, the CTP score is 42.64 kPa (SD 12.5). Fibroscan significantly correlates with the severity of varices (R-value 0.651) and CTP scores with a p-value of <0.0001 and 0.003. Our study's cut-off value for detecting grade 3 varices is 35.95kPa (AUROC 93%, sensitivity 93%, specificity 82%). The cut-off value for detecting grade 1 varices is 23.3kPa with a sensitivity of 72%. Al-hamoudi et al.8, the cut-off value for varices 16.9kPa (sensitivity 83.6%) for non-viral cirrhosis, 19.9kPa (sensitivity 83.4%) for viral cirrhosis, which is less than that of our values. The studies with cut-off values more than our study values are Saad et al.[13] proposed a cut-off value of 29.7kPa (sensitivity 95%, specificity 67%). Stefanescu et al.[14] the

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fibroscan cut-off value is 30.8kPa (sensitivity 68.32%); Sharma et al.[15] the cut-off value is 27.3kPa (sensitivity 91%, specificity 72%).

CONCLUSION

Based on the study results, it can be concluded that chronic liver disease, most commonly caused by alcohol, is highly prevalent in males, with most patients in the age group of 41-50. Patients with chronic liver disease typically present with splenomegaly and moderate anaemia. Varices are also a common complication, with most patients having grade 2 or 3 varices and a significant proportion experiencing UGI bleeding. Platelet count, spleen diameter, and fibroscan score are non-invasive predictors that can help assess the grading of varices and the risk of variceal bleeding. The study highlights the importance of early detection and managing chronic liver disease to prevent complications such as varices and UGI bleeding. Non-invasive predictors can aid in the early identification and grading of varices, facilitating prompt and appropriate management.

Limitations

The study was done in a single academic centre, and the sample size is small compared to the total prevalence of liver diseases. Even though the variables in our study in combination yield good predictive values, we cannot define the sensitivity and specificity of the parameters. So further large-scale studies to rectify these limitations are suggested in India for further evaluation.

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