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A Study of Non Invasive Predictors of Esophageal Varices in Patients of Cirrhosis of Liver

Mohd. Junaid Khan[1], Anurag Prasad[2], Shrey Srivastav[3]
[1]Department of General Medicine, SMS&R Sharda University, Greater Noida, Uttar Pradesh, India
[2]Professor, Department of General Medicine, SMS&R Sharda University, Greater Noida, Uttar Pradesh, India
[3]Assistant Professor, Department of General Medicine, SMS&R Sharda University, Noida, Greater Uttar Pradesh, India

Corresponding Author: **Anurag Prasad**

Abstract:

Background: Cirrhosis is the end stage of every chronic liver disease characterized by fibrosis and the replacement of normal liver architecture into structurally abnormal nodules which interferes with liver function and results in portal hypertension. Upper Gastro-intestinal (UGI) endoscopy still remains the gold standard for screening and diagnosing esophageal varices , but it has its own limitation like, it is an invasive procedure, expensive and needs expertise too, which may be not available in all hospital settings at all times. The present study will be undertaken to find the correlation between serum nitric oxide levels, platelet count, spleen longitudinal diameter and its ratio with presence of esophageal varices in patients. It is simple, quick and reproducible so that unnecessary UGI endoscopy can be limited.

Key Words: Esophageal varices, Non- invasive markers, Cirrhosis, Liver, Nitric oxide, UGI Endoscopy, Chronic Liver Disease, Platelet count, Splenic diameter, Platelet count/spleen diameter

Material and Method: A cross-sectional study was conducted at Sharda Hospital, Greater Noida, with a sample of 50 randomly selected subjects with diagnosis of cirrhosis of liver on USG. Blood investigations, serum nitric oxide levels by ELISA kits, and Platelet count /spleen longitudinal diameter (PC/SD) ratio were taken and correlation with upper GI endoscopy were done to look for presence or absence of esophageal varices. The receiver operating characteristics curve (ROC) was used to find the sensitivity, specificity, NPV and PPV of the predictor variable. A p-value of <0.05 was considered statistically significant.

Results: The study comprised 84% males and 16% females, with a mean age of 49.52 years $\pm$ 17.112 years. Common presenting complaints included abdominal distension (46.0%), yellowish discoloration of the eyes (28.0%), and blood in

vomitus (26.0%). The primary cause of cirrhosis was alcohol-related (76.0%), followed by non-alcoholic steatohepatitis (NASH) (24.0%).

The mean serum nitric oxide level was 49.24 in patients with esophageal varices compared to those having no esophageal varices was 50 with p value of 0.767. The mean longest splenic diameter was suggestive of poor discriminative ability in identifying esophageal varices (p-value= 0.328) The mean platelet count/spleen diameter ratio (PC/SD) was 599.402 and in esophageal varices group it was 560 and in controls it was 776 with p value of 0.156 and AUC of 0.423, this ratio exhibited high sensitivity of 90.24%, indicating a strong ability to identify positive cases of esophageal varices.

Conclusion: The study highlights the potential of non-invasive measures in predicting the presence and severity of esophageal varices in patients with liver cirrhosis. The findings demonstrate significant correlations between serum nitric oxide levels, platelet count, splenic diameter, and the platelet count/spleen diameter ratio with the presence of esophageal varices. Larger studies are needed to prove serum nitric oxide levels accuracy in predicting esophageal varices, the platelet count and PC/SD ratio exhibited higher predictive values.

Introduction
Cirrhosis represents the final stage of chronic liver diseases, characterized by fibrosis and the transformation of the normal liver architecture into abnormal nodules, which disrupt liver function and result in portal hypertension [1].
Portal hypertension, a key complication of cirrhosis, is associated with changes in both the splanchnic and systemic circulation, leading to the development of portosystemic collateral vessels, particularly in the lower esophagus and stomach [2]. In both humans and animal models with portal hypertension, secondary hemodynamic changes occur. These include reduced systemic vascular resistance and mean arterial pressure, along with increased cardiac output and splanchnic blood flow. Current research suggests that increased nitric oxide production plays a major role in the development of these hemodynamic alterations [3]. Studies have demonstrated that nitric oxide levels are significantly elevated in patients with a high hepatic venous pressure gradient (HVPG >12 mm Hg) in cirrhosis [4]. This condition leads to the formation How to cite this article of esophageal varices, a major and often fatal complication [5]. Factors contributing to the development of varices in cirrhosis patients include increased portal vascular resistance, systemic and splanchnic vasodilation, and structural changes in the venous anatomy of the lower esophagus.
Varices develop in about 50% of patients with portal hypertension, and the severity of variceal bleeding depends on the extent of variceal dilation. While the exact cause of variceal rupture is not fully understood, several risk factors for variceal hemorrhage have been identified. These include larger varices, higher

intravariceal pressure, increased variceal wall tension (especially in large varices marked by red spots during endoscopy), and poor liver function. A high portal pressure during the post-bleeding phase is now recognized as a predictor of rebleeding. Despite advances in treatment, mortality from acute variceal bleeding remains high, reaching up to 20% [6], and it is the second leading cause of death among cirrhotic patients [1,7].

Predicting the presence of gastroesophageal varices without intervention remains a challenge. Identifying esophageal varices as the source of upper gastrointestinal bleeding in an emergency situation, without prior history or invasive procedures, is difficult. At the time of diagnosis, only about half of cirrhotic patients present with varices, and the management of variceal hemorrhage requires specific interventions. Rebleeding is common, occurring in 30% to 50% of cases [6].

Upper gastrointestinal (UGI) endoscopy is currently the gold standard for diagnosing and grading esophageal varices, but it has limitations. Endoscopy is invasive, costly, and operator-dependent, and frequent screenings may reduce patient compliance and increase healthcare costs [8]. In light of these challenges, non-invasive methods have been proposed to predict the presence and severity of esophageal varices, limiting endoscopy to high-risk patients. Various clinical and biochemical markers have been explored as predictors of varices in cirrhotic patients [9].

Thrombocytopenia (platelet count <150,000 /μL) is one such predictor and is present in approximately 64 76% of cirrhosis patients with portal hypertension [10]. Since both thrombocytopenia and esophageal varices are common in cirrhosis, and both are associated with portal hypertension, several studies have investigated the relationship between thrombocytopenia and the grades of esophageal varices as a non-invasive marker. Findings from different studies indicate that platelet count is inversely correlated with variceal severity [12].

Anatomically, the splenic vein drains into the superior mesenteric vein, which joins the portal vein. As a result, any pathology affecting portal blood flow can also influence the spleen. Several studies have investigated the role of splenic elastography in liver disease, correlating splenic stiffness with the stage of liver fibrosis [13].

 In chronic liver disease, reduced platelet counts may result from various factors, such as reduced platelet lifespan, decreased thrombopoietin production, or the myelotoxic effects of alcohol or hepatitis viruses. However, splenomegaly in cirrhotic patients is primarily caused by vascular disturbances linked to portal hypertension. Consequently, the platelet count-to-spleen diameter ratio has been used as a combined parameter, considering thrombocytopenia related to hypersplenism in portal hypertension [14].

This study was undertaken to assess the relationship between serum nitric oxide levels, platelet count, spleen diameter, and the platelet count/spleen diameter ratio in relation to the presence of esophageal varices in cirrhotic patients. These measures are simple, quick, and reproducible, potentially reducing the need for unnecessary UGI endoscopies.

Methodology and Materials

Study Design and Data Source:

This was a cross-sectional study conducted at the Department of General Medicine, Sharda Hospital, Greater Noida, Uttar Pradesh to assess relationship of non-invasive measures (Serum Nitric Oxide levels, Platelet Count, Splenic Longitudinal Diameter and its Ratio) with the occurrence of esophageal varices and its bleeding tendency in cirrhosis of liver patients. The study was approved by the institutional ethics committee, and it spanned from August 2022 to March 2024.

Study Population:

The sample size for this study was determined using the Cochrane's Formula: , where Z corresponds to a 95% confidence level (1.96), P is the prevalence of cirrhosis without previous portal hypertensive bleeding in India (0.5 or 50%), and d is the precision (14%). Using these values, the calculated sample size was 50 patients, which was considered adequate to meet the study objectives.

The study included patients above 18 years of age who were diagnosed with cirrhosis of the liver based on ultrasound findings of nodular or irregular liver margins. Patients unwilling to participate, those with hepatocellular carcinoma, portal vein thrombosis, a previous history of portal hypertensive bleeding, Budd-Chiari syndrome, or other non-cirrhotic causes of portal hypertension were excluded from the study.

Data Collection:

Written consent was acquired after the patient or patient party were explained about the study, its advantages, procedures and disadvantages. Demographic data such as age and sex were recorded. History of other co-morbid conditions such as, hypertension, diabetes mellitus, personal history such as habits of alcohol consumption, smoking, were noted. A thorough physical examination was conducted for vitals (pulse rate, blood pressure and respiratory rate) followed by systemic examination. The diagnosis of cirrhosis of liver with Ultrasound (USG) findings of nodular/irregular margins of liver was considered, blood investigations, serum nitric oxide levels and correlation with upper GI endoscopy were done to look for presence or absence of esophageal varices.

On the day of admission relevant history, physical examination along with platelet count by automated cell counter, serum nitric oxide levels by Enzyme-linked

immunosorbent assay (ELISA) kits and Platelet count /spleen longitudinal diameter (PC/SD) ratio were taken. Patient in the study underwent ultrasonography and upper gastrointestinal endoscopy on subsequent days to see the splenic diameter and varices grading and bleeding spots respectively.

Statistical Analysis:

Data were entered into a pre-designed proforma and analyzed using SPSS v21. Descriptive statistics were applied to summarize data as frequency, percentage, proportion, mean, and standard deviation. The chi-square test was used to assess differences between categorical variables. Receiver Operating Characteristic (ROC) curves were used to determine sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) for predictor variables. A p-value of less than 0.05 was considered statistically significant.

Results

The mean age of the participants was 49.52 years (SD = 17.112 years). The majority of participants were male 42(84.0%). The minimum reported age was 32 years (25th percentile), while the maximum age was 64 years (75th percentile). Common presenting complaints included abdominal distension 23(46.0%), yellowish discoloration of the eyes 14(28.0%), and blood in vomitus 13(26.0%). The primary cause of cirrhosis was alcohol-related 38(76.0%), followed by non-alcoholic steatohepatitis (NASH) 12(24.0%). All viral markers were negative in the study population.

For serum nitric oxide (NO), the mean was 49.24 (Standard deviation, SD = 12.054), with a minimum of 40.00 (25th percentile) and maximum of 61.00 (75th percentile). It was 49.24 (SD = 12.054) in patients with esophageal varices compared to those having no esophageal varices was 50 (SD=10.794) with p value of 0.767. But this was not significant as the sample size may be small to detect the difference.

The longest splenic diameter had a mean of 147.58 mm (SD = 23.396 mm), ranging from 135.25 mm (25th percentile) to 163.00 mm (75th percentile). In esophageal varices group it was 146.05 mm (SD=24.715) and 154.6 mm (SD=15.224) in no varices with p value of 0.328 suggestive poor discriminative ability in identifying esophageal varices. The mean platelet count was 86520.00 (SD = 59382.276), with a minimum of 41500.00 (25th percentile) and maximum of 102000.00 (75th percentile). In the esophageal varices group it was 79,829 and in controls it was 117000 with p value of 0.089 reflecting inadequate prediction capabilities of esophageal varices.

Finally, the PC/SD ratio had a mean of 599.402 (SD = 411.5030), ranging from 299.525 (25th percentile) to 689.700 (75th percentile). In esophageal varices group it was 560 and in controls it was 776 with p value of 0.156 and Area Under

Curve (AUC) of 0.423, this ratio exhibited high sensitivity of 90.24%, indicating a strong ability to identify positive cases of esophageal varices. Esophageal varices were present in 41 (82.0%) of the participants, with varying severity and associated findings. [TABLE 1]

Table 1: Mean Serum, Longest Splenic Diameter, Platelet Count and PC/SD ratio in different groups (p-value is considered significant if (p<0.05,0.001)

		N	Mean	Std. Deviation	P value
Serum NO	No Esophageal Varices	9	50.33	10.794	0.767
	Esophageal Varices	41	49.00	12.424	
	Total	50	49.24	12.054	
Longest Splenic Diameter	No Esophageal Varices	9	154.56	15.224	0.328
	Esophageal Varices	41	146.05	24.715	
	Total	50	147.58	23.396	
Platelet Count	No Esophageal Varices	9	117000.00	76121.613	0.089
	Esophageal Varices	41	79829.27	53905.891	
	Total	50	86520.00	59382.276	
PC/SD ratio	No Esophageal Varices	9	776.611	511.6272	0.156
	Esophageal Varices	41	560.502	382.7086	
	Total	50	599.402	411.5030	

Table 2 shows the association of UGI endoscopy findings and diagnosis of esophageal varices. Antral erosions with ooze were reported in 2(22.2%) participants with no esophageal varices and 0 (0.0%) participants with varices. Duodenal ulcers were reported in 2(22.2%) with no varices and 0(0.0%) with varices. Large esophageal varices with mild PHG were reported in 0(0.0%) with no varices and 4(9.8%) with varices. Large esophageal varices requiring banding occurred in 0(0.0%) with no varices and 13(31.7%) with varices. Severe Portal

hypertensive gastropathy (PHG) was reported in 5(55.6%) with no varices and 0(0.0%) with varices. Small esophageal varices were reported in 0(0.0%) with no varices and 24(58.5%) with varices.

Table 2: Association of UGI endoscopy and diagnosis of esophageal varices

	UGI Endoscopy		Diagnosis		
			No Esophageal Varices	Esophageal Varices	Total
	Antral Erosions with ooze	n	2	0	2
		%	22.2%	0.0%	4.0%
	Duodenal ulcers	n	2	0	2
		%	22.2%	0.0%	4.0%
	Large Esophageal varices , Mild PHG	n	0	4	4
		%	0.0%	9.8%	8.0%
	Large esophageal varices (banding)	n	0	13	13
		%	0.0%	31.7%	26%
	Severe PHG	n	5	0	5
		%	55.6%	0.0%	10.0%
	Small Esophageal varices	n	0	24	24
		%	0.0%	58.5%	48%
Total		n	9	41	50
		%	100.0%	100.0%	100.0%

Table 3 shows the association of ultrasound abdomen findings and diagnosis of varices. Chronic liver disease (CLD) alone was reported in 0 (0.0%) with no varices and 3 (7.3%) with varices. CLD with ascites and splenomegaly was seen in 2 (22.2%) with no varices and 20 (48.8%) with varices. CLD with ascites and umbilical hernia was reported in 0 (0.0%) with no varices and 2 (4.9%) with varices. CLD with collaterals and ascites occurred in 0 (0.0%) with no varices and 1 (2.4%) with varices. CLD with gross ascites was seen in 0 (0.0%) with no varices and 1 (2.4%) with varices. CLD with gross ascites and splenomegaly was reported in 5 (55.6%) with no varices and 3 (7.3%) with varices. CLD with gross splenomegaly occurred in 0 (0.0%) with no varices and 2 (4.9%) with varices. CLD with mild ascites was seen in 0 (0.0%) with no varices and 1 (2.4%) with varices. CLD with peripancreatic collaterals, ascites and splenomegaly was reported in 0 (0.0%) with no varices and 2 (4.9%) with varices. CLD with portal hypertension

(HTN) collaterals occurred in 0 (0.0%) with no varices and 2 (4.9%) with varices. CLD with right pleural effusion was seen in 0 (0.0%) with no varices and 2 (4.9%) with varices. CLD with splenomegaly alone was reported in 2 (22.2%) with no varices and 2 (4.9%) with varices.

Table 3 : Association of USG Abdomen and diagnosis

			Diagnosis		
USG Abdomen			No Esophageal Varices	Esophageal Varices	Total
CLD	n		0	3	3
	%		0.0%	7.3%	6.0%
CLD,Ascites,Splenomegaly	n		2	20	22
	%		22.2%	48.8%	44.0%
CLD,Ascites,Umblical hernia	n		0	2	2
	%		0.0%	4.9%	4.0%
CLD,Collaterals,Ascites	N		0	1	1
	%		0.0%	2.4%	2.0%
CLD,Gross Ascites	n		0	1	1
	%		0.0%	2.4%	2.0%
CLD,Gross Ascites,Splenomegaly	n		5	3	8
	%		55.6%	7.3%	16.0%
CLD,Gross Splenomegaly	n		0	2	2
	%		0.0%	4.9%	4.0%
CLD,Mild Ascites	n		0	1	1
	%		0.0%	2.4%	2.0%
CLD,Peripancreatic collaterals,Ascites,Splenomegaly	n		0	2	2
	%		0.0%	4.9%	4.0%
CLD,Portal HTN collaterals	n		0	2	2
	%		0.0%	4.9%	4.0%
CLD,Rt pleural effusion	n		0	2	2
	%		0.0%	4.9%	4.0%
CLD,Splenomegaly	n		2	2	4
	%		22.2%	4.9%	8.0%

Total		n	9	41	50
		%	100.0%	100.0%	100.0%

The analysis of "Serum NO" (Figure 1A) in relation to diagnosing "Esophageal Varices" revealed an optimal cutoff value of 67. The Area Under the Curve (AUC) was calculated at 0.481, indicating that "Serum NO" did not perform much better than random guessing in distinguishing between the presence and absence of "Esophageal Varices." The sensitivity at this cutoff was remarkably low at approximately 9.76%, but the specificity reached 100%, indicating that all non-cases were correctly identified. Both the positive predictive value (PPV) and the negative predictive value (NPV) were assessed, with PPV at 100%, suggesting that all patients predicted to have the condition did indeed have it. In contrast, the NPV was quite low at about 19.57%, reflecting the poor ability to correctly identify those without the condition.

The "Longest Splenic Diameter" (Figure 1B) presented an optimal cutoff at 155 mm with an AUC of 0.360, suggesting poor discriminative ability in identifying "Esophageal Varices." The sensitivity at this threshold was 34.15%, and the specificity was 77.78%, showing moderate ability to identify true negatives. The PPV was high at 87.5%, indicating that most patients above the threshold likely had the condition. However, the NPV was low at 20.59%, pointing to a poor rate of correctly identifying negative cases.

Figure 1: ROC Curve of (A) Serum NO (B) Longest splenic diameter
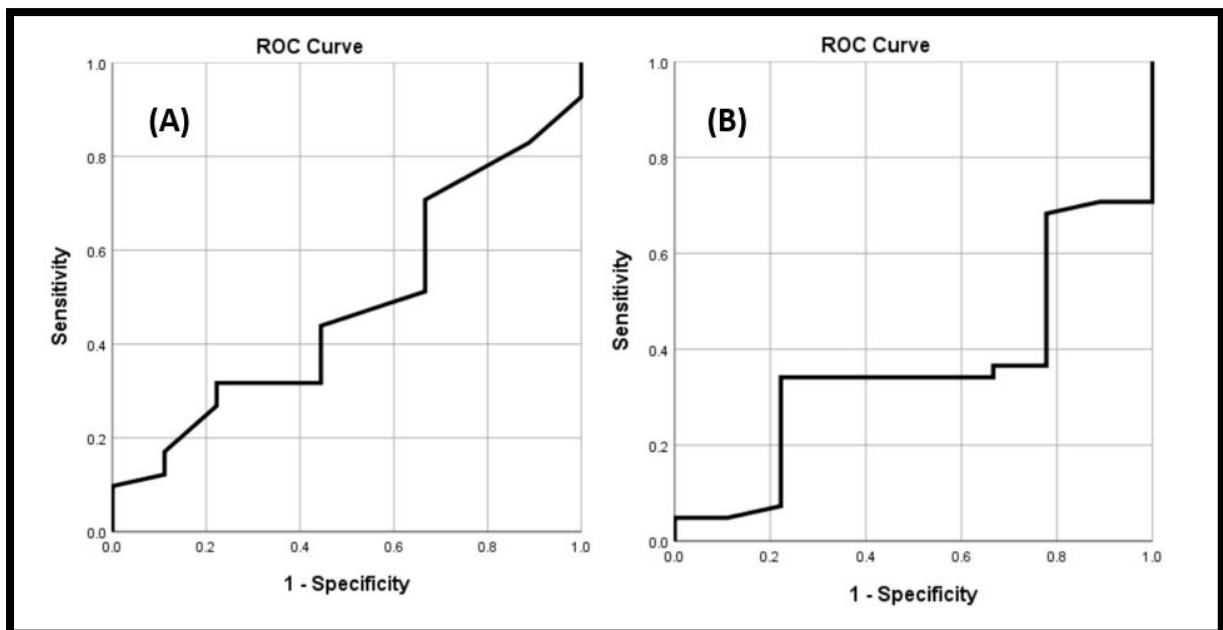
The analysis based on "Platelet Count" (Figure 2A) determined an optimal cutoff of 84,000, with an AUC of 0.390, reflecting inadequate prediction capabilities for "Esophageal Varices." The sensitivity was around 43.90%, and specificity was 66.67%, suggesting a modest ability to discern patients without the condition. The PPV was considerably high at 85.71%, implying that a large proportion of those predicted to have the condition actually had it. Nevertheless, the NPV remained low at 20.69%, underscoring the difficulty in correctly identifying those without "Esophageal Varices."

For the "PC/SD ratio (Figure 2B)," the determined optimal cutoff was 255.0, with an AUC of 0.423. This ratio exhibited high sensitivity of 90.24%, indicating a strong ability to identify positive cases of "Esophageal Varices." However, the specificity was notably low at 22.22%, reflecting poor performance in ruling out non-cases. The PPV and NPV were 84.09% and 33.33%, respectively, suggesting a decent predictive value for positive cases but a relatively poor predictive value for negative cases.

Figure 2: ROC Curve of (A) Platelet Count (B) PC-SD ratio
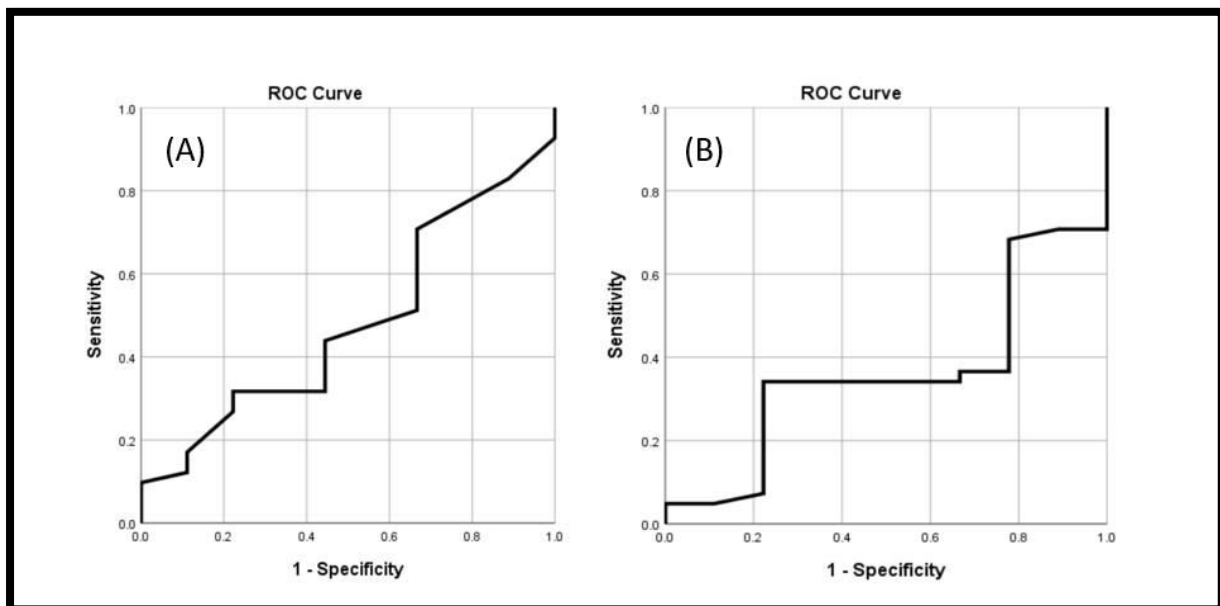
Discussion

The primary aim of this study was to assess the relationship between non-invasive measures (serum nitric oxide levels, platelet count, splenic longitudinal diameter, and their ratio) with the occurrence of esophageal varices and their bleeding tendency in patients with liver cirrhosis.

In the present study, the mean age of the patients was 49.52 years (SD = 17.112 years). This finding is slightly lower than that reported by Elsalam et al., where the mean age was 54.39 years (SD = 7.46 years) [11]. Arya et al. found a median age of 41.36 years (SD = 13.39 years), which is closer to the findings of Duah et al.,

who reported a mean age of 45 years (SD = 12.28 years) [15]. These variations in mean age could be attributed to differences in study populations, geographical regions, and inclusion criteria.

This study depicted that the majority of the participants were male (84.0%), with only 8 female participants (16.0%). This male predominance aligns with several other studies. Elsalam et al. reported that 66.36% of their participants were men, while Arya et al. found that 60% of their patients were male [11,15]. The overall trend across studies suggests a higher prevalence of liver disease among males, which could be due to higher alcohol consumption and other risk factors predominantly affecting men.

In the present study, 46.0% of the patients had abdominal distension, 28.0% had yellowish discoloration of the eyes, and 26.0% had blood in vomitus. Gebregziabiher et al. found that ascites was present in 74.3% of their patients, and jaundice was observed in 31.1% of the patients. Hossain et al. reported that 95.0% of their patients had body swelling, 64.0% had yellowish discoloration, 1.0% had vomiting of blood, and 1.0% had passage of black tarry stool. Additionally, they found that 65.0% had jaundice, 90.0% had anemia, 9.0% had clubbing, 96.0% had edema, 6.0% had caput medusa, and 6.0% had flapping tremor. These variations in clinical features highlight the diverse presentation of liver disease and its complications across different populations [16-17].

The present study found that 76.0% of the cases were alcohol-related, while 24.0% were due to non-alcoholic steatohepatitis (NASH). Gebregziabiher et al. identified hepatitis B infection and hepato-splenic schistosomiasis as the most common causes of cirrhosis, each accounting for 26% of cases. Hossain et al. reported that hepatitis B virus (HBV) was the etiology in 45% of their patients, while the etiology could not be determined in 38% of the cases. The differences in the etiology of cirrhosis across studies could be influenced by regional variations in risk factors such as viral hepatitis prevalence and alcohol consumption patterns [16-17].

In the present study, the mean serum nitric oxide (NO) level was 49.24 (SD = 12.054) in patients with esophageal varices compared to those having no esophageal varices was 50 (SD=10.794) with p value of 0.767. But this was not significant as the sample size may be small to detect the difference. However, Sherif et al reported higher levels of serum nitric oxide levels in patients with esophageal varices [18]. A possible explanation is that the differences in the severity of inflammation and fibrosis may cause varying serum nitrate levels, and the etiology of chronic hepatitis may explain the discrepancy between some previously reported studies and our results. Cirrhosis is considered as the most advanced stage of chronic liver disease. In viral cirrhosis, there is a significant increase in the serum nitrate levels.

The longest splenic diameter had a mean of 147.58 mm (SD = 23.396 mm) in esophageal varices group it was 146.05 (SD=24.715) and mean of 154.6 (SD=15.224) with p value of 0.328 suggestive poor discriminative ability in identifying esophageal varices (OE). Arya et al. reported a statistically significant larger splenic size (14.17 ± 3.51 cm) and splenic area (86.64 ± 53.19 cm²) compared to controls. Hossain et al. found a mean spleen diameter of 131.2 mm (SD = 26.5 mm) with a range of 90 to 210 mm. The mean platelet count in the present study was 86,520 (SD = 59,382.276) and in esophageal varices group it was 79,829 and in controls it was 117000 with p value of 0.089 reflecting inadequate prediction capabilities of esophageal varices , the platelet count/spleen diameter (PC/SD) ratio had a mean of 599.402 (SD = 411.503) and in esophageal varices group it was 560 and in controls it was 776 with p value of 0.156 and AUC of 0.423, this ratio exhibited high sensitivity of 90.24%, indicating a strong ability to identify positive cases of esophageal varices . Arya et al. found that 80% of their patients had esophageal varices (EV), similar to the present study where 82.0% had EV. Duah et al. reported that 90.60% of their patients had OV, with 82.22% having large varices. Gebregziabiher et al. observed that 85.4% of their participants had EV, with 49.45% having large varices. Hossain et al. found that 45.0% had medium EV, 27.0% had small EV, and 19.0% had large EV. Kothari et al. reported that 65.84% had large EV, 27.23% had small EV, and 6.93% had no EV. These findings indicate the prevalence of esophageal varices among patients with liver disease, underscoring the importance of regular monitoring [11-17].

The findings of this study contribute to the existing body of knowledge on the demographic characteristics, clinical features, and diagnostic markers of liver disease. The comparisons with other studies underscore the variability in patient profiles and the importance of tailored diagnostic criteria. Future research should focus on refining these diagnostic markers to improve sensitivity and specificity across diverse populations.

This study has some limitations that need to be considered when interpreting the findings. The sample size was relatively small, with only 50 patients, which may have limited the ability to detect statistically significant differences, particularly in key comparisons such as serum nitric oxide levels, spleen diameter, and platelet count between patients with and without esophageal varices. A larger sample size may have improved the statistical power and provided more conclusive results. Additionaly , the study was conducted at a single center, Sharda Hospital, Greater Noida, which may limit the generalizability of the findings to other populations. The patients included were primarily male (84.0%), and the majority had alcohol-related cirrhosis (76.0%). This demographic skew might not represent the broader population of cirrhosis patients, especially in regions where other causes of liver disease, such as viral hepatitis, are more prevalent.

Conclusion

The study highlights the potential of non-invasive measures in predicting the presence and severity of esophageal varices in patients with liver cirrhosis. The findings demonstrate significant correlations between serum nitric oxide levels, platelet count, splenic diameter, and the platelet count/spleen diameter ratio with the presence of esophageal varices. Although serum nitric oxide and the longest splenic diameter showed limited sensitivity and specificity, larger study is needed to prove serum nitric oxide levels accuracy in predicting esophageal varices, the platelet count and PC/SD ratio exhibited higher predictive values. These non-invasive markers can be valuable in identifying patients at risk for esophageal varices and tailoring their management to reduce the need for invasive procedures like endoscopy. Further research is necessary to refine these diagnostic markers and improve their accuracy across diverse populations.

Financial and Competing Interests Disclosure:

The authors declare no conflict of Interest

References

1. Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W: Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. Hepatology. 2007,

2. MacMathuna PM: Mechanisms and Consequences of Portal Hypertension. Drugs. 1992,

3. McCormick PA: Pathophysiology and Prognosis of Oesophageal Varices: Scandinavian Journal of Gastroenterology. 1994, 29:1-5.

4. Huang X, Thansamay S, Yang K, Luo T, Chen S: Measurement of Exhaled Nitric Oxide in Cirrhotic Patients with Esophageal and Gastric Varices. BioMed Research International. 2019,

5. D'Amico G, Luca A: 3 Natural history: Clinical-haemodynamic correlations. Prediction of the risk of bleeding. Baillière's Clinical Gastroenterology. 1997, 11:243-56.

6. Escorsell À, Pavel O, Cárdenas A, et al.: Esophageal balloon tamponade versus esophageal stent in controlling acute refractory variceal bleeding: A multicenter randomized, controlled trial. Hepatology. 2016,

7. Carbonell N, Pauwels A, Serfaty L, Fourdan O, Lévy VG, Poupon R: Improved survival after variceal bleeding in patients with cirrhosis over the past two decades. Hepatology. 2004,

8. Rye K, Scott R, Mortimore G, Lawson A, Austin A, Freeman J: Towards Noninvasive Detection of Oesophageal Varices. International Journal of Hepatology. 2012, 2012:1-9.

9. Ponnusamy R, Cherian J, Deepak N, Somasundaram A, Jayanthi V: Non-invasive predictors of esophageal varices. Saudi J Gastroenterol. 2011, 17:64.

10. Sheikh M, Raoufi R, Atla P, Riaz M, Oberer C, Moffett M: Prevalence of cirrhosis in patients with thrombocytopenia who receive bone marrow biopsy. Saudi J Gastroenterol. 2012, 18:257.

11. Abd-Elsalam S, Habba E, Elkhalawany W, et al.: Correlation of platelets count with endoscopic findings in a cohort of Egyptian patients with liver cirrhosis. Medicine. 2016, 95:3853.

12. Abbasi A, Butt N, Bhutto AR, Munir SM: Correlation of thrombocytopenia with grading of esophageal varices in chronic liver disease patients. J Coll Physicians Surg Pak [Internet. 2010:369-72.

13. Colecchia A, Montrone L, Scaioli E, et al.: Measurement of Spleen Stiffness to Evaluate Portal Hypertension and the Presence of Esophageal Varices in Patients With HCV-Related Cirrhosis. Gastroenterology. 2012, 143:646-54.

14. Giannini E: Platelet count/spleen diameter ratio: proposal and validation of a non-invasive parameter to predict the presence of oesophageal varices in patients with liver cirrhosis. Gut. 2003, 52:1200-5.

15. Arya S, Dixit R, Harish C S, Prakash A, Puri AS: Our experience with liver and spleen elastography in the prediction of oesophageal varices. South African Journal of Radiology. 2024, 28:..

16. Gebregziabiher HT, Hailu W, Abay Z, Bizuneh S, Meshesha MD: Accuracy of non-invasive diagnosis of esophageal varices among cirrhotic patients in a low-income setting. Heliyon. 2023, 9:23229.

17. Rahim MA, Hossain E, Ahammed F, Saha SK, Foez SA, Abdullah AS: Screening of Esophageal Varices by Noninvasive Means in Chronic Liver Disease. Euroasian Journal of Hepato-Gastroenterology. 2018, 8:18-22. 10.5005/jp-journals-10018-1252

18. El-Sherif AM, Abou-Shady MA, Al-Bahrawy AM, Bakr RM, Hosny A-MM: Nitric oxide levels in chronic liver disease patients with and without oesophageal varices.-Hepatol-Int.-2008,-2:341-5.