Original Research Article

Platelet count/spleen diameter ratio as a non-invasive parameter in the prediction of esophageal varices in patients with liver cirrhosis

Abstract:

Background:

Esophagogastroduodenoscopy (EGD) is the gold standard for detecting oesophageal varices (OVs) in cirrhotic patients. However, due to the possible limitations of EGD, there has been much interest in the use of non-invasive techniques for this purpose. This study aimed to evaluate the use of platelet count/ spleen diameter ratio (PC/SD) in the prediction of the presence and grading of OVs in cirrhotic patients.

Methods:

One hundred cirrhotic patients were included in this cross-sectional study and subjected to EGD after informed consent. Either absence or the grade of OVs if existent was correlated with values of thePC/SD ratio. Univariate and multivariate analyses of data and areas under the receiver operating characteristic curve (AUC) were used.

Results:

The PC/SD ratio was a good indicator in predicting the development of OVs (AUC of 0.897) with cut-off values of (987.28). Also, it correlated well with grades of oesophageal varices, a significant stepwise progressive decrease in PC/SD ratio was recorded through the grades of oesophageal varices as follows: Mean ± SD (882.59±390.43) (603.33±266.99) (503.76±190.80) (439.69±22.51) for grades I, II, III and IV respectively (p <0.002),(AUC=0.688, 0.764, 0.795, 0.849) with a cut-off value of (784.37, 640.27, 597.50,462.00) in grades I, II, III and IV respectively.

Conclusion:

ThePC/SD ratio could be considered a non-invasive method of choice for screening OVs, sparing EGD for patients in need of intervention.

Keywords:

Esophagogastroduodenoscopy - oesophageal varices – cirrhotic patients - platelet count/ spleen diameter ratio.

Introduction

Liver cirrhosis is a common consequence of the long clinical course of all chronic liver diseases and is characterized by tissue fibrosis and the conversion of normal liver architecture into structurally abnormal

nodules that eventually produce portal hypertension and liver cell failure [(1)]. Portal hypertension commonly accompanies the presence of liver cirrhosis, and the development of esophageal varices (OVs) is one of the major complications of portal hypertension[(2)]. The prevalence of OVs in patients with liver cirrhosis may range from 60% to 80% and the reported mortality from variceal bleeding ranges from 17% to 57%[(3)].

Fibrosis describes the encapsulation or replacement of injured hepatic tissue by a collagenous scar [(4)]. Liver Fibrosis progresses at variable rates depending on the cause of liver disease, environmental factors, and host factors [(5)]. While cirrhosis is an advanced stage of liver fibrosis and is accompanied by distortion of the hepatic vasculature. The resultant vascular distortion leads to the shunting of the portal and arterial blood supply directly into the hepatic outflow (central veins), compromising the exchange between hepatic sinusoids and the adjacent hepatocytes[(6)].Moreover, liver cirrhosis is the major risk factor for the development of hepatocellular carcinoma (HCC), as more than 80% of HCCs develop on a fibrotic or cirrhotic background[(7)].

Esophagogastroduodenoscopy (EGD) is the gold standard for the detection and grading of PH-related complications such as GOVs, ectopic varices (EcV), and PHG as previously mentioned, and is used also for therapeutic intervention[(8)].

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During liver cirrhosis, splenomegaly and hypersplenism are relatively sub-fatal complications in the absence of bleeding varices. Splenic enlargement is one of the most palpable abnormalities accompanying liver cirrhosis and frequently occurs in parallel with hypersplenism, which is thought to be a major cause [(9)].

Thrombocytopenia is a frequent complication in patients with cirrhosis. As many as 84% of patients with cirrhosis have thrombocytopenia, and it is an independent variable indicative of advanced disease and poor prognosis[(10)].

AIM OF THE WORK

So, this study aimed to evaluate the value of platelet count/spleen diameter ratio as a non-invasive parameter to predict the presence of oesophageal varices in cirrhotic patients.

PATIENTS AND METHODS

The present study is a cross-sectional study conducted on a total of one hundred patients diagnosed to have liver cirrhosis of different causes. The patients were recruited between" February 2021 to August 2021" from the outpatient clinic and internal ward of the Gastroenterology and Hepatology Unit, at Tanta University Hospitals.

Inclusion criteria: Adult patients (more than 18 years) with cirrhotic liver whatever the etiology and divided into 2 groups (**group A: 63** cirrhotic patients with oesophageal varices and**group B: 37** cirrhotic patients without varices).

We excluded patients less than 18 years, patients withactive upper GIT bleeding, patients withhepatic encephalopathy, patients are known to have OVs with previous endoscopy (either underwent band ligation or sclerotherapy), patients with a history of partial splenic embolization or splenectomy, patients with HCC, patients have TIPS, patients with PV thrombosis confirmed by US and color doppler study, patients with a history of any liver surgery, and patients on NSBBs.

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This study is in agreement with the ethical guidelines of the Declaration of Helsinki and it follows the ethical standards of the Tanta faculty of medicine approval code (34408/1/21) all patients were aware of the steps, and goal of the study, and they were included after obtaining written informed consent from them.

Methods:

All patients in this study were subjected to full history taking and full clinical examination. Whole blood samples were collected from all patients.

Routine Laboratory tests were done such as **CBC, Liver function profile,INR,and renal function tests**

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Pelvic-Abdominal ultrasonography and upper GIT endoscopy.

- Esophageal varices were graded as I-IV, using the Paquet grading system[(11)].

•**Grade 0:** No varices.

•**Grade I:** Varices, disappearing with air insufflation.

•**Grade II:** Larger, clearly visible, usually straight varices, not disappearing with air insufflation.

•**Grade III:** More prominent varices, locally coil-shaped and partly occupying the lumen.

•**Grade IV:** Tortuous, sometimes grape-like varices occupying the esophageal lumen.

- **Assessment Child-Pugh score:**Child A= 5-6 points, Child B= 7-9 points, Child C= 10-15 points[(12)].

- **MELD score (Model for End Stage Liver Disease):** The original MELD score is calculated using the following formula: MELD Score = 9.57 x Log_e (creatinine mg/dL) + 3.78 x Log_e(bilirubin mg/dL) + 11.2 x Log_e(INR) + 6.431[13].

- **The FIB-4 index:** [age (years) × AST (U/L) / platelet (PLT) (109/L) × √ALT(U/L)][14].

- **Aspartate-aminotransferase-to-platelet-ratio index (APRI):** [(AST/upper limit of the normal AST range) X 100]/Platelet Count[15].

- **Aspartate aminotransferase-to-alanine aminotransferase (AST-to-ALT) ratio (AAR)[16].**

- **Specific investigations:**

Platelet-count-to-spleen-diameter (PC/SD) ratio=Platelet count(mm3)/maximum bipolar diameter of the spleen(mm)[17].

Statistical analysis of the data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using numbers and percentages. The Kolmogorov-Smirnov test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, and standard deviation. The significance of the obtained results was judged at the 5% level. The following tests were used: **Chi-square test:** for categorical variables, to compare between different groups. **Fisher's Exact or Monte Carlo correction:** correction for chi-square when more than 20% of the cells have an expected count of less than 5. **Standard student "t-test": a** test of the significance of the difference between two means. **F-test (ANOVA):**for normally distributed quantitative variables, to compare between more than two groups and Post-Hoc test (Tukey) for pairwise comparisons. **ROC-curve:** Receiver Operating Characteristic curve analysis. **Regression analysis:** by binary logistic regression models.

RESULTS

Laboratory and clinical investigations were shown in **tables (1, 2).**

Table (1): The clinicopathologic characteristics of patients.

Groups / Variables	Group A (n= 63)	Group B (n= 37)	P-Value
Age (years)	56.37± 9.91	54.6 ± 6.35	0.34[(a)]
Sex **Male** **Female**	29 (46.03%) 34 (53.97%)	15 (40.54%) 22 (59.46%)	0.89(b)
HCV	51 (81%)	32 (86.5%)	0.477(b)
HBV	2 (3.2%)	1 (2.7%)	1.00(c)
NAFLD	2 (3.2%)	2 (5.4%)	0.658(c)
Mixed Bilharzial and HCV	6 (9.5%)	1 (2.7%)	0.812(c)
Autoimmune hepatitis (AIH)	2 (3.2%)	1 (2.7%)	0.651(c)
Ascites clinically	36 (57.14%)	9 (24.32%)	0.001[*(b)]
Palpable liver	0 (0%)	1 (2.7%)	0.370[(c)]
Palpable spleen	31 (49.2%)	16 (43.24%)	0.564[(b)]
Jaundice	23 (36.5%)	5 (13.51%)	0.013[*(b)]
LL edema	36 (57.14%)	0 (0%)	0.000[*(b)]

Group A: cirrhotic patients with esophageal varices, **Group B:** cirrhotic patients with no varices, **(a):** student t-test, **(b):** Chi-square test, **(c):** Fisher's Exact test, *Statistically significant at $p \leq 0.05$

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Table (2): The clinicopathologic characteristics of patients.

Groups / Variables	Group A (n= 63)	Group B (n= 37)	P-Value
Hb (g/dl)	9.22 ± 1.67	11.50 ± 1.65	0.000 *[(a)]
TLC /(mm3)	4309.52 ± 1553.42	4913.51 ± 1622.78	0.067[(a)]
PLT /(mm3)	100349.21 ± 35349.94	183348.35 ± 45931.14	0.000 *[(a)]
AST (U/L)	35.57 ± 13.78	33.43 ± 10.51	0.385[(a)]
ALT (U/L)	31.73 ± 13.48	31.35 ± 7.54	0.857[(a)]
T. Bilirubin (mg/dl)	2.40 ± 1.15	1.56 ± 0.87	0.000 *[(a)]
S. Albumin (g/dl)	2.81± 0.62	3.65 ± 0.51	0.000 *[(a)]
INR	1.58 ± 0.25	1.18 ± 0.22	0.000 *[(a)]
Ascites U/S **No** **Mild** **Moderate** **Marked**	 15 (23.8%) 15 (23.8%) 26 (41.3%) 7 (11.1%)	 24 (64.9%) 2 (5.4%) 11 (29.7%) 0 (0%)	0.000 *[(b)]
PV diameter (mm)	15.88 ± 1.45	11.95 ± 2.03	0.000 *[(a)]
Spleen diameter (mm)	168.84± 20.63	139.03 ± 19.08	0.000 *[(a)]
Child			
A **B** **C**	19 (30.2%) 26 (41.3%) 18 (28.5%)	24 (64.8%) 11 (29.7%) 2 (5.4%)	0.000 *[(b)]
MELD	16.21 ± 4.42	9.47 ± 4.12	0.000 *[(a)]
APRI	0.99 ± 0.66	0.50 ± 0.31	0.000 *[(a)]
AST/ALT	1.17 ±0.339	1.07±0.287	0.115[(a)]
FIB-4	3.85 ± 2.12	2.00 ± 1.47	0.000 *[(a)]
PC/SD	681.83± 341.00	1370.36 ± 452.61	0.010 *[(a)]

Group A: cirrhotic patients with esophageal varices, **Group B:** cirrhotic patients with no varices, **(a):** student t-test, **(b):** Chi-square test, **(c):** Fisher's Exact test, *Statistically significant at $p \leq 0.05$

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Comment [E10]: Child-Pugh score

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Table (3): Relation between esophageal varices grades andPC/SD in group A (n= 63)

PC/SD	OVs				P value
	I (n= 24)	II (n= 23)	III (n= 13)	IV (n= 3)	
Min. – Max.	280.00 – 1855.56	221.05–1133.33	103.13–781.25	421.05– 464.71	
Mean ± SD	882.59± 390.43	603.33 ± 266.99	503.76± 190.80	439.69 ± 22.51	
P1		0.014*	0.004*	0.095	0.002*
P2			0.784	0.819	
P3				0.988	

F: F for ANOVA test, P1 II: Group1 versus group 2, P1 III: Group1 versus group 3, P1 IV: Group1 versus group 4, P2 III: Group2 versus group 3, P2 IV: Group2 versus group 4, P3 IV: Group 3 versus group 4, P: Probability value for comparing the studied groups *: Statistically significant at $p \leq 0.05$

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Table (4): Correlation between PC/SDand different cirrhotic markers

	PC/SD			
	Group A		Group B	
	r	p-value	r	p-value
Child score	-0.547	0.000*	-0.262	0.117
MELD	-0.488	0.000*	0.075	0.657
AST/ALT	0.108	0.399	0.150	0.377
FIB4	-0.682	0.009*	0.047	0.781
APRI	-0.689	0.000*	-0.005	0.978

r: Pearson coefficient, P:Probability value for comparing the studied groups, *: Statistically significant at $p \leq 0.05$

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Table (5):Probability value for sensitivity and specificity

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	AUC	P	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
MELD	0.861	0.000*	0.783 – 0.939	13.69	74.60	91.90	94.0	68.0
APRI	0.766	0.000*	0.671 – 0.862	0.77	61.90	94.60	95.10	59.30
FIB4	0.810	0.000*	0.723 – 0.898	2.09	77.60	81.10	87.50	68.20
AST/ALT	0.647	0.014*	0.539 - 0.755	1.06	61.90	59.90	72.20	47.80

AUC: Area Under a Curve **P:** Probability value for comparing the studied groups' **CI:** Confidence Intervals
NPV: Negative predictive value **PPV:** Positive predictive value ***:** Statistically significant at $p \leq 0.05$

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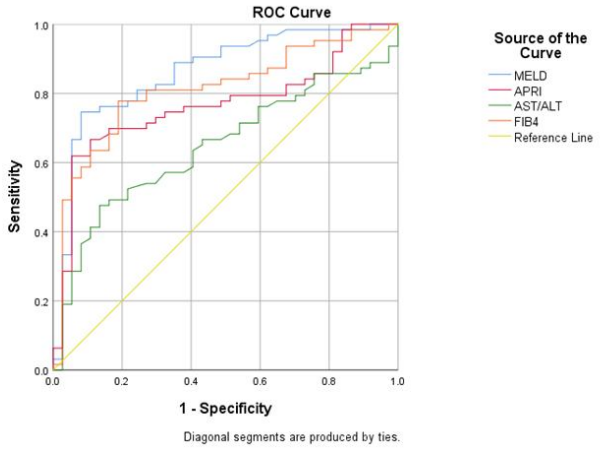

Figure (1): ROC curve for different liver cirrhosis scores to discriminate group A from group B

Table (6):Probability value for Sensitivity and specificity

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	AUC	p	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
PC/SD	0.897	0.000*	0.838– 0.957	987.28	83.80	81.0	72.10	89.50

AUC: Area Under a Curve **P:** Probability value for comparing the studied groups **CI:** Confidence Intervals
NPV: Negative predictive value **PPV:** Positive predictive value ***:** Statistically significant at $p \leq 0.05$

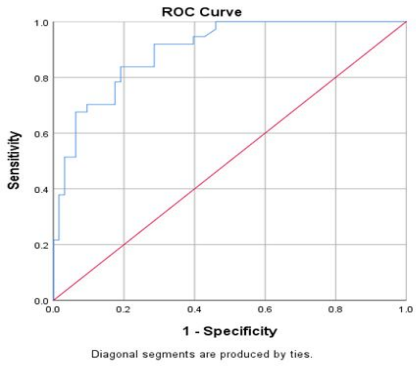

Figure (2): ROC curve for PC/SD to discriminate group A from group B

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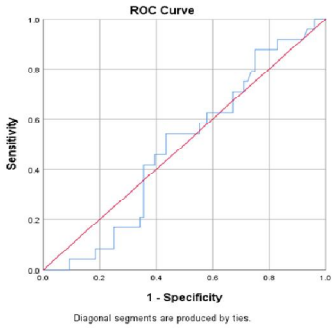
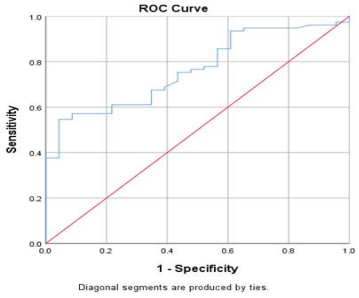
Table (7):Probability value for gradation

PC/SD	AUC	p	95% C. I	Cut off	Sensitivity	Specificity	PPV	NPV
grade I	0.688	0.859	0.616- 0.752	784.37	65.3	61.7	61.4	39.8
grade II	0.764	0.000*	0.667 - 0.862	640.27	68.8	60.9	85.5	36.8
grade III	0.795	0.001*	0.704 - 0.887	597.50	71.3	69.2	93.9	26.5
grade IV	0.849	0.040*	0.776 - 0.922	462.00	82.5	66.7	98.8	10.5

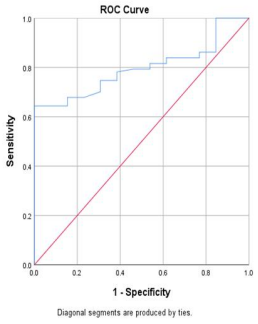
AUC: Area Under a Curve **P:** Probability value for comparing the studied group's **CI:** Confidence Intervals
NPV: Negative predictive value **PPV:** Positive predictive value ***:** Statistically significant at $p \leq 0.05$



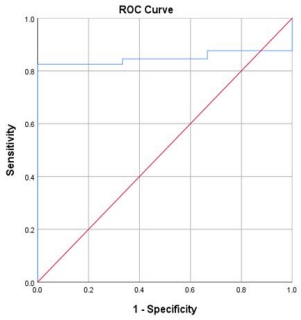
a): ROC curve for PC/SD in grade I OVs.



b) ROC curve of PC/SD in grade II OVs.



c) ROC curve of PC/SD in grade III OVs



d) ROC curve of PC/SD in grade IV OVs.

Figure 3 (a-d): Receiver operating characteristic (ROC) curves analysis ofPC/SD to discriminate between different grades of esophageal varices

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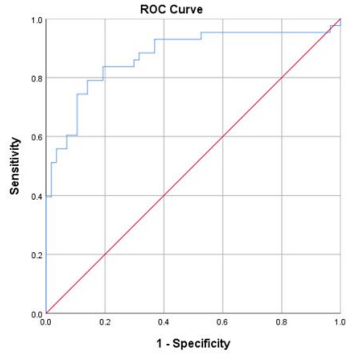
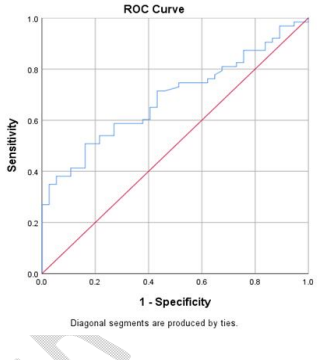
Table (8):Probability value for PC/PD

PC/SD	AUC	p	95% C. I	Cut off	Sensitivity	Specificity	PPV	NPV
CHILD A score	0.874	0.000*	0.798 - 0.949	1013.16	92.3	77.0	78.4	80.2
CHILD B score	0.686	0.002*	0.584 - 0.788	656.72	71.4	56.8	73.8	53.8
CHILD C score	0.801	0.000*	0.716 - 0.886	530.49	81.3	60.0	89.0	44.4

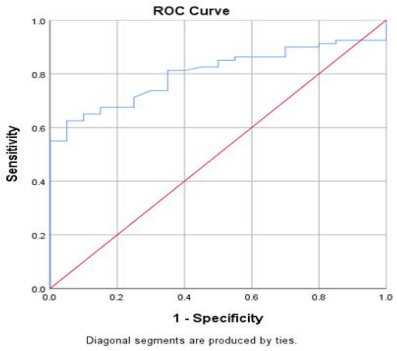
AUC: Area Under a Curve **P:** Probability value for comparing the studied groups **CI:** Confidence Intervals
NPV: Negative predictive value **PPV:** Positive predictive value ***:** Statistically significant at $p \leq 0.05$



a) ROC curve for PC/SD to CHILD A



b) ROC curve for PC/SD to CHILD B



c) ROC curve for PC/SD to CHILD C

Figure 4 (a-c): Receiver operating characteristic (ROC) curves analysis of PC/SD to discriminate between different grades of CHILD- Pugh score

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Table (9): Predictors of esophageal varices in binary logistic regression analysis:

Binary logistic regression		
	OR (95% CI)	**P value**
PC/SD	210.72 (9.86-4498.74)	0.001*
CHILD	1.91 (1.11– 3.30)	0.020*
MELD	3.58 (1.55 – 6.75)	0.001*
APRI	11.95 (0.52– 273.36)	0.120
FIB-4	0.81(0.32 – 2.05)	0.669
AST/ALT	0.42(0.03-5.68)	0.520

P: Probability value for comparing the studied groups, **OR:** odds ratio, **CI:** Confidence Intervals, ***:** Statistically significant at $p \leq 0.05$

DISCUSSION

Variceal bleeding is the one of most dramatic complications of cirrhosis, with a mortality rate of up to 20% in six weeks [(18)]. That is why it is mandatory to offer prophylactic measures against variceal rupture for patients at high risk for the first bleeding. To identify those patients at higher risk, it is traditionally recommended that every patient undergoes upper gastrointestinal endoscopy at the time of the diagnosis of cirrhosis. Although, patients with cirrhosis must have clinically significant portal hypertension before they develop ~~oesophageal varices (~~OVs), and while varices are present in around 70% of Child-Pugh B or C patients, they are present only in approximately 40% of Child-Pugh A patients[(19)].

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Bearing this in mind, it is obvious that a significant part of patients with a new diagnosis of cirrhosis will undergo endoscopy unnecessarily. This became even more important in recent years when cirrhosis is diagnosed earlier because of the availability of non-invasive methods for its diagnosis[(20)]. Moreover, endoscopy is an invasive procedure, associated with some risks (yet quite low), patient discomfort, and high costs.[(21)].

So,our study aimed to evaluate platelet count/spleen diameter ratio as a non-invasive predictor of esophageal varices in cirrhotic patients. This parameter was chosen as it allows us to identify the degree of thrombocytopenia which is most likely related to hypersplenism. In clinical practice, the measure of spleen diameter and platelet count is easily obtainable during routine ultrasonography and serum examination, respectively.

As regards age and gender of this study, there was no statistically significant difference. This result came in agreement with **(ElDesoky et al., 2022)** who documented no correlation between either age or gender and the presence of varices in cirrhotic patients[22].
In contrast to the study done by **(Yogananda et al., 2020)** among 50 patients with liver cirrhosis, 37 (74 %) had varices. Males predominance was noted [42 (84 %)][23].

In the present study, HCV infection was the most common cause of liver cirrhosis in the studied patients. This came in agreement with **(Mohamoud et al., 2013),** who reported that Egypt is enduring a large HCV disease burden, and is likely to be the most affected nation worldwide by this infection[24].

According to the clinical data in the present study, ascites, lower limb edema, and jaundice were prominent in group A (cirrhotic with varices) with statistical significance. This came in agreement with **(Lee et al., 2021)** who documented that jaundice was predominant in patients with varices[25].Also, this result agreed with that of **(Nouh et al., 2020)** who found that there was a significant statistical difference among studied groups regarding signs suggestive of hepatic decompensation such as jaundice, ascites, and lower limb edema. Patients with chronic liver disease (CLD) in group I with gastroesophageal and/or fundal varices had a higher incidence of these signs in comparison with patients with CLD without varices in group II[26].**Tsaknakis et al.(2018)** also reported that cirrhotic cases with varices had a significant increase in ascites[27].

Hemoglobin levels were significantly lower in cirrhotic patients with esophageal varices than in those without varices, this came in agreement with **(Gunda et al., 2019)** who documented a statistically significant relationship between lower HB levels and varices presence[28].But the study done by **(Sarangapani et al., 2010) and (Kumar et al., 2020)** found no statistically significant difference as regards HB levels between patients with large varices and those without varices[11, 29].

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There was no significance in white blood cell count (WBC) between patients with varices and without varices, this came in agreement with the study done by **(Elatty et al., 2019)**[30]**.** But in disagreement, the study done by **(Mahmood et al., 2019)** documented a statistically significant relationship between low WBC and varices presence[31].

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In the present study, platelet count was significantly lower in patients with varices than those without varices. Our results were also in agreement with the results reported by **(Abe et al., 2019)** who reported platelet count to be an excellent parameter for detecting esophageal varices in patients with liver cirrhosis

and portal hypertension. In addition, significant splenomegaly with low platelet count is considered a surrogate marker for portal hypertension[32].

This is also can be explained by **(Scharf et al., 2021)** who found that thrombocytopenia is one of the portal hypertension complications and caused mainly by splenic sequestration as a complication of portal hypertension-induced splenomegaly[33].

In the present study, there was no statistically significant difference between groups as regards alanine transaminase (ALT), and aspartate transaminase (AST). This came in agreement with **(Hajiani et al.,2020)**, who documented that no significant difference was observed as regards the mean values of liver enzymes between patients with esophageal varices and those without esophageal varices[34].

Serum albumin was statistically significantly lower in group A than in group B this result is in agreement with **(Elatty et al., 2019)** as serum albumin in a patient with varices had a mean value of (3.29±0.39) while those without varices had a mean value of (3.84±0.42) and serum albumin less than 3.65g/dl is significant in prediction of esophageal varices[30].

In the current study, total bilirubin was found to be higher in patients with varices than in patients without varices with statistical significance. This came in agreement with **(Pasha et al., 2020)** who documented that a high total bilirubin level was found with varices presence[35]. On the other hand, **(Abdallah et al., 2021)** showed no association between bilirubin level with esophageal varices ~~(with a P-value of 0.174)~~[36].

As regards the international normalized ratio (INR), it was higher in patients with varices (mean= 1.58±0.25) than without varices (mean= 1.18±0.22) ~~with statistical significance~~($p < 0.05$).This can be explained by **(Bates et al., 2020)** who found that elevated INR in cirrhotic patients can be explained by the reduction of the nutritional status and impairment of fat-soluble vitamins absorption (A, D, E, K) resulting from poor appetite associated with cholestasis and portal hypertensive gastropathy. As a result, patients with cirrhosis and portal hypertension have reduced levels of vitamin K–dependent coagulation factors (II, VII, IX, and X)[37].This finding is against that found by **(Chandail et al., 2017)**who studied non-invasive markers for the prediction of OVs including INR, and found no significant difference in INR for the prediction of small or large OVs[38].

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~~Statistical analysis of~~ultrasonographic findings of the studied groups revealed that there was a high~~statistically significant difference~~(P-~~value~~ < 0.000) ~~regarding~~ mean values of spleen diameter, portal vein diameter, and ascites between both groups A and B. This came in agreement with the study of **(Faheem et al.,2022)** who found that portal vein diameter and spleen diameter which are indirect predictors of portal hemodynamics can be used effectively as a screening test without subjecting patients to ~~esophagogastroduodenoscopy~~[39].

The studies done by **(Gunarathne et al., 2020 and Yoshida et al., 2021)** documented that, splanchnic vessels vasodilatation is promoted by local over-production of vasodilators, along with intrinsic vascular hypo-contractility allowing increased blood flow through the splanchnic vessels. So, splenomegaly in portal hypertension appears initially as venous congestion and structural hyperplasia with pooling of the blood and finally as an overflow related to the hyperdynamic circulation associated with portal hypertension[40, 41].

In the present study, ascites were predominant in cases with varices (63.33%) when compared to cases without varices (33.33%).

These results were in agreement with **(Nouh et al., 2022)** who reported that; ascites were significantly increased in cases with varices when compared to cases without varices (p-~~value~~= 0.008), and spleen size was significantly higher in cases with varices than those without (p-~~value~~<0.001)[42].

~~There was a statistically significant difference between both studied groups regarding~~Child score which was higher in patients with esophageal varices than those without esophageal varices. A similar finding was reported by **(Elsalakawy et al., 2020)** that showed a statistically significant difference between Child-Pugh classes as in class A,91.7% showed no varices, Whereas, in class B, 41.9% showed grade II esophageal varices. In contrast, patients in class C showed grade IV in 57.8%[43]. The variceal presence correlates with the severity of liver disease as stated by **(Kumar et al., 2020)**[11].

Results of the present study revealed that the platelets count/spleen diameter (PC/SD) ratio was lower in group A (patients with varices) than in group B (patients without varices) (681.83±341.00 VS 1370.36±452.61) with sensitivity and specificity in prediction of OVs (83.80% and 81.0% respectively), PPV 72.10%, NPV 89.50%, and proportion of AUC 89.7% at cut-off value (987.28). These results were in agreement with **(Musa et al., 2021)** who found that the cut-off point of (909) had 82.5% sensitivity and 92.6% specificity for the prediction of the presence of OVs, PPV86.3%, NPV90.4% and they also found that ~~there was~~ a direct correlation between low platelet count/spleen diameter ratio and the grade of OVs with a high statistical significance (p-~~value~~0.00001)[44]. Also, the study done by **(Kothari et al., 2019)**

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found that for the prediction of esophageal varices, thePC/SD ratio was significant and showed an area under the curve of 65.6% at a cut-off of <997[45].

The high diagnostic accuracy of thePC/SD ratio for varices can be explained as follows: varices and hypersplenism are the results of portal hypertension. The platelet count can be influenced by many factors in cirrhotic patients other than hypersplenism. The decrease in thrombopoietin production may be the reason. Thrombopoietin is mainly produced by hepatocytes and the quantity can be largely reduced when the hepatocytes are damaged. In addition, the shortened platelet mean lifetime and myelotoxic effects of alcohol or hepatitis viruses lead to thrombocytopenia. Splenomegaly is the clinical manifestation of hypersplenism. Thus, a combined index of platelet count and spleen diameter has much more relevance with portal hypertension and varices than the sole decreased platelet count[46].

In the present study, a significant stepwise progressive decrease in PC/SD ratio was recorded through the increasing grades of esophageal varices mean ± SD (882.59±390.43) (603.33±266.99) (503.76± 190.80) (439.69±22.51) for grade I, II, III and IV respectively (p-~~value~~<0.002), (AUROC= 0.688, 0.764, 0.795, 0.849) with a cut-off value of (784.37, 640.27, 597.50, 462.00) in grade I, II, III and IV respectively. These results agreed with ~~the results of the study done by~~**(Nouh et al., 2022)** who found that the mean ±SD of PC/SD ratio was(725.6 ± 273.5) (567.9 ± 280.2) (347.8 ± 162.6) (293.8 ± 91.8) in grades I, II, III and IV respectively as well (p-~~value~~< 0.001)[42].
In contrast, ~~the results of the study done by~~**(Yogananda et al; 2020)** concluded that thePC/SD ratio might not be accurate enough in predicting the presence of oesophageal varices. The evidence is not sufficient enough to replace endoscopy as a screening tool for oesophageal varices in all patients with portal hypertension. It is a useful tool for predicting the presence of oesophageal varices in patients with portal hypertension non-invasively when endoscopy facilities are unavailable[23] but this study was done only on 50 patients and only 37 patients had OVs, so this shortage in the number of cases limits its significance.

Also, **(Barrera et al., 2009)** concluded that the PC/SD ratio was significantly associated with high-risk esophageal varices (HREV), but with suboptimal sensitivity and specificity. Therefore, the results of this study do not support the routine clinical use of thePC/SD ratio for screening HREV[47]. The drawback of this study was due to it was only done on 67 patients for the detection of HREV as focusing on patients with large OVs, would miss an important subset of patients requiring medical treatment.

However, in this study the distribution of the study population was homogeneous and representative of the population of cirrhotic patients seen in clinical practice, thus biases caused by the selection of subgroups

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of patients were avoided. Diagnosis and classification of OVs were made in the same endoscopy center using a single classification (Paquet classification) and done by the same experienced operator. We focused on the presence of any OVs grade rather than on the presence of large OVs as this is the first step in the diagnostic/prognostic workup of the patients and allows decision-making processes (surveillance, repeat endoscopy at predetermined intervals, start therapy) while focusing on patients with large OVs would only miss an important subset of patients requiring medical counseling. Moreover, analysis of the presence/absence of OVs prevents misinterpretation of data and allows generalization of the results.

The variabilities in the cut-off value of PC/SD ratio measurement between different studies may be due to equipment-related, intra-observer, and inter-observer variability or according to the etiology of liver disease. In this study, we tried to decrease the effect of these variabilities through the measurement of the maximum spleen diameter of all patients by a single highly-trained physician at the same time of the day before lunchtime, and by using a highly equipped instrument done by a single expert. Also, OVs detection is done by a single expert with the same highly equipped endoscopy. Also, the main etiological factor for liver cirrhosis in the present study was HCV infection.

In the present study, we found a significant correlation between thePC/SD ratio and Child classification, MELD, FIB-4 score, and APRI score, indicating that thePC/SD ratio is correlated to the severity of liver function decompensation in patients with cirrhosis. This also agreed with **(Kothari et al., 2019)** who found a significant correlation between the PC/SD ratio with the size of OVs, and the Child-Turcotte-Pugh classification[45].

Comment [E54]: Child-Pugh score

There are some limitations in our study; the limited number of patients and a single-center study might affect results. The study participants were cirrhotic patients with different etiologies of decompensated liver cirrhosis.

CONCLUSION

PC/SD ratio is statistically significantly lower in cirrhoticpatients with OVs. It is a good indicator in predicting the development and the degree of esophageal varices. It also correlates with the severity of liver cirrhosis assessed by Child classification, FIB-4 score, and APRI score.

Comment [E55]: Child-Pugh score

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