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COMPARISON OF MEAN PLATELETS COUNT/ SPLEEN LENGTH RATIO AND PORTAL VEIN DIAMETER AMONG DIFFERENT GRADES OF ESOPHAGEAL VARICES: CROSS SECTIONAL STUDY

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Abstract

Background and aims: Cirrhotic patients frequently undergo screening endoscopy for the presence of oesophageal varices (OV). In the future, this social and medical burden will increase due to the greater number of patients with chronic liver disease and their improved survival. Researches showed that the use of the platelet count/spleen diameter ratio and portal vein diameyter for the noninvasive assessment of EV seems to fulfill these requirements and is based on pathophysiological criteria as well.In this study, our aims were to determine the correlation of OV with portal vein diameter (PVD) and platelet count/spleen diameter (PC/SL) ratio and their comparative evaluation in patients of liver cirrhosis.

Methods: The cross sectional study was conducted in the department of medicine, SNMC and MDM Hospital, Jodhpur on 60 patients of liver cirrhosis. Then the patients were classified into two groups, those having esophageal varices and those without esophageal varices. Portal vein diameter‘ and platelet count to spleen length ratio‘ were compared between these two groups to obtain conclusions

Results: There were significant difference in term of portal vein diameter, platelet count, spleen length, and PC/SL ratio in patients with esophageal varices and patients without esophageal varices. Use of the PC/SL ratio along with thrombocytopenia, splenomegaly and increased portal vein diameter will help create a lower-cost and more effective method to identify esophageal varices in patients with portal hypertension. The PC/SL ratio cannot substitute for upper gastrointestinal endoscopy in the scrutiny of esophageal varices. When compared with other noninvasive predictor tools, the PC/SL ratio is elegant, simple, and inexpensive. With some minor modifications, it may become a helpful tool to limit the number of endoscopies to be performed in patients for primary prophylaxis of variceal bleeding in portal hypertension.

Keywords: oesophageal varices, liver cirrhosis, platelet count, spleen diameter, endoscopy

BACKGROUND-

Portal hypertension commonly accompanies the presence of liver cirrhosis, and the development of oesophageal varices (OV) is one of the major complications of portal hypertension.[1] The prevalence of OV in patients with liver cirrhosis may range from 60% to 80%, and the reported mortality from variceal bleeding ranges from 17% to 57%.[2–5] It is noteworthy however that variceal haemorrhage is not confined

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to patients with large OV although they are more likely to bleed from ruptured varices than patients with small OV.

The 1996 the American Association for the Study of Liver Disease single topic symposium stated that cirrhotic patients should be screened for the presence of OV when portal hypertension is diagnosed.[6] Recently, the Baveno III Consensus Conference on portal hypertension recommended that all cirrhotic patients should be screened for the presence of OV when liver cirrhosis is diagnosed.[7] Other authors have suggested repeating endoscopy at 2–3 year intervals in patients without varices and at 1–2 year intervals in patients with small varices so as to evaluate the development or progression of this feature.[8,9]

In order to reduce the increasing burden that endoscopy units will have to bear, some studies have attempted to identify characteristics that non-invasively predict the presence of any OV or of large OV. These studies have shown that biochemical, clinical, and ultrasonographic parameters alone or together have good predictive power for non-invasively assessing the presence of OV.[10–23] Overall, the most common result of these studies was that parameters directly or indirectly linked to portal hypertension, such as splenomegaly and decreased platelet count, were predictors of the presence of OV. However, in patients with chronic liver disease the presence of decreased platelet count may depend on several factors other than portal hypertension, such as shortened platelet mean lifetime, decreased thrombopoietin production, or myelotoxic effects of alcohol or hepatitis viruses.[24] On the other hand, the presence of splenomegaly in cirrhotic patients is likely the result of vascular disturbances that are mainly related to portal hypertension.[25] With this in mind, in this study we used the platelet count/spleen diameter ratio as a parameter linking thrombocytopenia to spleen size in order to introduce a variable that takes into consideration the decrease in platelet count which most likely depends on hypersplenism caused by portal hypertension.

MATERIALS AND METHODS

STUDY SETTING:

The study was conducted in the department of medicine, SNMC and MDM Hospital, Jodhpur.

STUDY DESIGN:

Observational Cross-sectional study

SAMPLE SIZE

Sample size was calculated using software(biosoft.hacettepe.edu) at alpha error 0.05 study power 80%. Assuming area under the curve for ratio of platelet count/ splenic length for detecting esophageal varices and allocation ratio of 2.

Sample size was calculated to be a minimum of 12 cases which was increase to 60 cases of cirrhosis.

INCLUSION CRIETERIA

- All patients with age >18yrs with USG confirmed diagnosis of cirrhosis of liver of any aetiology.

EXCLUSION CRIETERIA

- Portal hypertension due to extrahepatic portal vein obstruction on USG
- Patients with splenomegaly due to any cause other than portal hypertension due to cirrhosis

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- Patients who have undergone TIPS (Trans-jugular Intrahepatic Portosystemic Shunt)
- Patients on antiplatelet drugs for atleast 1 month
- Patients on prophylactic therapy with non-selective Beta blockers for variceal bleed 1 month
- Patients with intra-abdominal mass lesion.
- Patients with known case of coagulopathy.
- Patients with known case of hepatocellular carcinoma or secondaries in the liver
- Patients with illnesses accompanied by fever with hepatosplenomegaly.

METHODOLOGY

A brief history and clinical examination of all patients were done.History included:

Jaundice, Abdominal distention, Fever, Abdominal pain, Hematemesis / Melaena, Altered sleep, Altered sensorium, Drug intake, Alcohol consumption, Decreased appetite/ Weight loss, Blood transfusion in past and other relevant history

Physical Examination:

Through physical examination was done for every patient which included; Body temperature, Respiratory rate, Neurological status (asterixis, personality changes), Cardiac status (heart rate, blood pressure), signs of liver cell failure, Bleeding manifestation, Per-abdominal examination for organomegaly and to assess the presence of fluid.

Then all patients underwent routine investigations which included Complete blood count, Haematocritm, Random blood sugar, Electrocardiography, coagulation profile, Serum electrolytes, Kidney function test, Liver function test,Viral Markers- HbsAg, Anti HCV antibody, Blood culture sensitivity, urine culture sensitivity, urine routineChest X Ray PA view. Platelet count was assessed by HARIBA MEDICAL PENTRA XLR® Counter. After routine investigations patients were subjected to USG abdomen.

USG abdomen was be done after 6 hrs of fasting by a radiologist by PHILIPSHD11XE® Machine using convex 2-5 MHz probe.

In USG, patients was assessed for signs of portal hypertension like

1.Ascites

2.Splenomegaly (spleen length)3.Portal vein diameter

Spleen was assessed by a curvilinear transducer of frequency 2-5 MHz in the coronal plane in the posterior aspect and cephalocaudal length was noted with patient in supine position. spleen length >13cm is considered as splenomegaly (normal 10-11cm)

Portal vein diameter was measured where PV crosses the inferior vena cava anteriorly and in quiet respiration (Normal value 6.4-12.1 mm and never >13 mm in normal individuals) .

Patients were assessed for Liver surface nodularity & Overall course and heterogeneous echotexture of the liver to confirm the diagnosis of cirrhosis.

Then all patients were subjected to upper GI endoscopy to see the presence of varices UGI ENDOSCOPY was be done by a single endoscopist by OLYMPUS GIF-H170VIDEO ENDOSCOPE® and varices were noted and were classified according toBeppu classification.

Then the patients were classified into two groups, those having esophageal varices and those without esophageal varices. Portal vein diameter‘ and platelet count to spleen length ratio‘ were compared between these two groups to obtain conclusions.

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S.N	ESOPHAGEAL VARICES PRESENCE	ESOPHAGEAL VARICES ABSENT	P-VALUE
PLATELET COUNT /SPLEENLENGHT			
PORTAL VEIN DIAMETER			
MALE			
FEMALE			

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Table 1.Oesophageal Varices profile of Patients

Oesophageal varices	Present	Absent
Cases	40	20
%	66.67	33.33

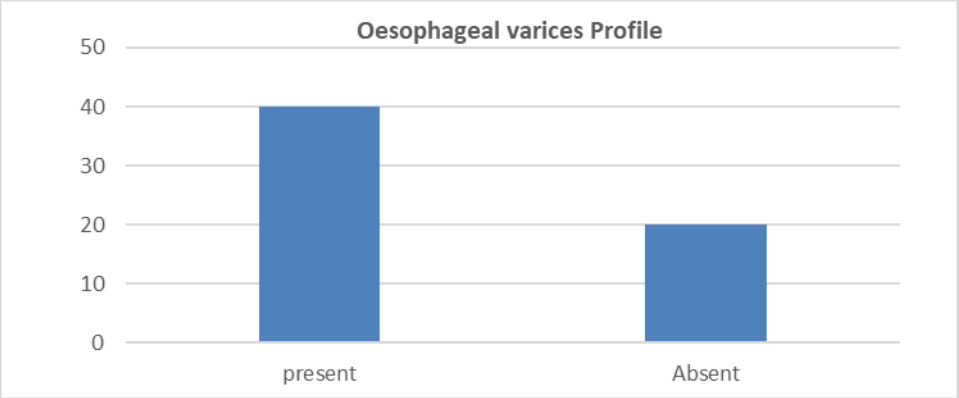

Table 4.Oesophageal Grades Profile

Oesophageal Grades	Cases	%
Absent	20	33.34
Grade I	9	15
Grade II	13	21.67
Grade III	11	18.33
Grade IV	7	11.67
Total	60	100

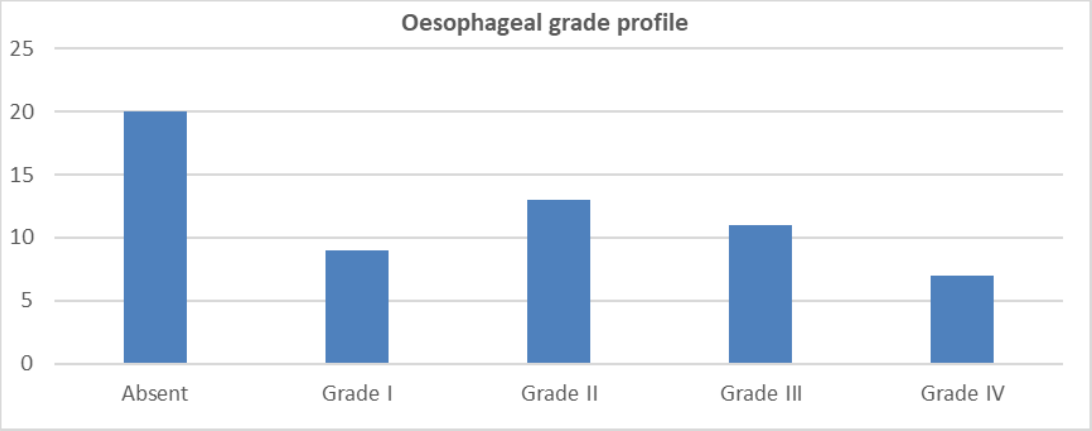

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Table 2.Age Profile of Patients

Age	Mean	SD	Median	Q1	Q3
Years	51.23	7.26	50.5	46	57

Table 3.Gender based profile of patients as per the presence and absence ofOesophageal Varices

Parameter		Oesophageal Varices						P Value
		Absent		Present		Total		
		No.	%	No.	%	No.	%	
Gender	Female	4	44.4%	5	55.6%	9	15.0%	.464
	Male	16	31.4%	35	68.6%	51	85.0%	
	Total	20	33.3%	40	66.7%	60	100.0%	

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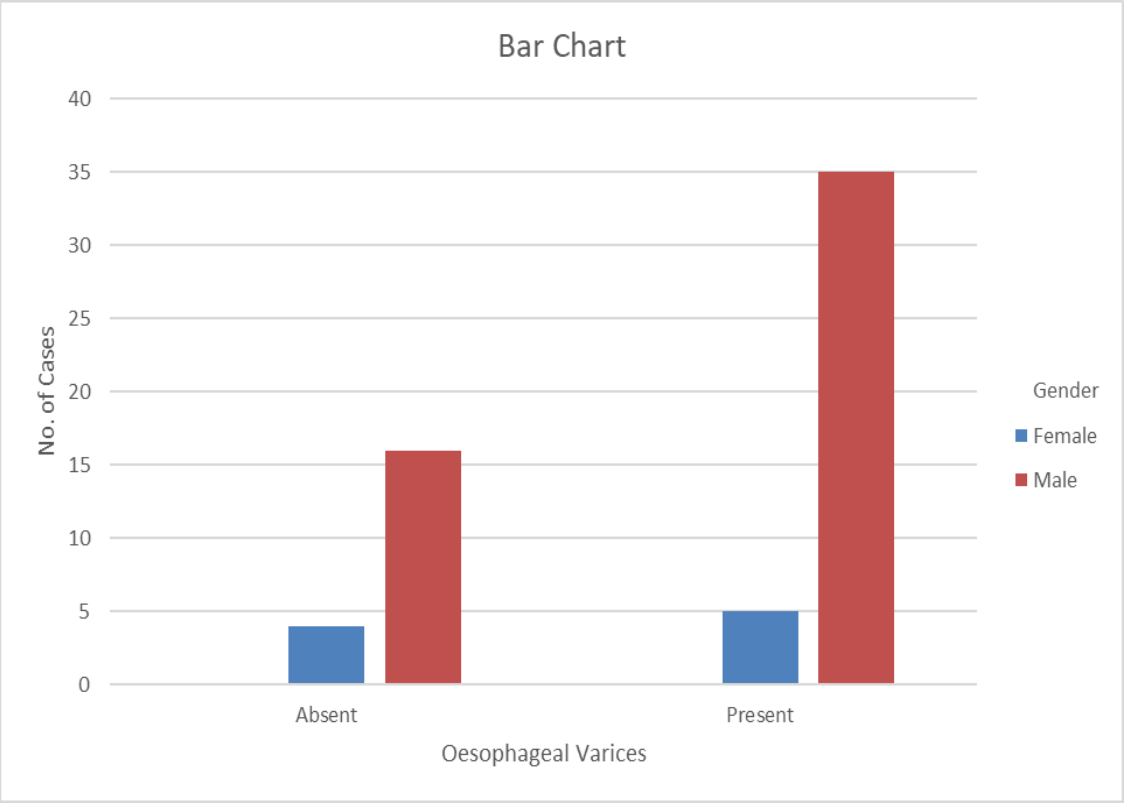

Table 4 Etiological profile as per Oesophageal Varices presence and absence

Parameters		Oesophageal Varices						P Value
		Absent		Present		Total		
		No.	%	No.	%	No.	%	
Etiology	Alcoholic	11	35.5%	20	64.5%	31	51.7%	.200
	Auto-immune	3	50.0%	3	50.0%	6	10.0%	
	Hepatitis B	2	16.7%	10	83.3%	12	20.0%	
	Hepatitis C	0	0.0%	3	100.0%	3	5.0%	
	NAFLD	4	66.7%	2	33.3%	6	10.0%	
	Wilson disease	0	0.0%	2	100.0%	2	3.3%	
	Total	20	33.3%	40	66.7%	60	100.0%	

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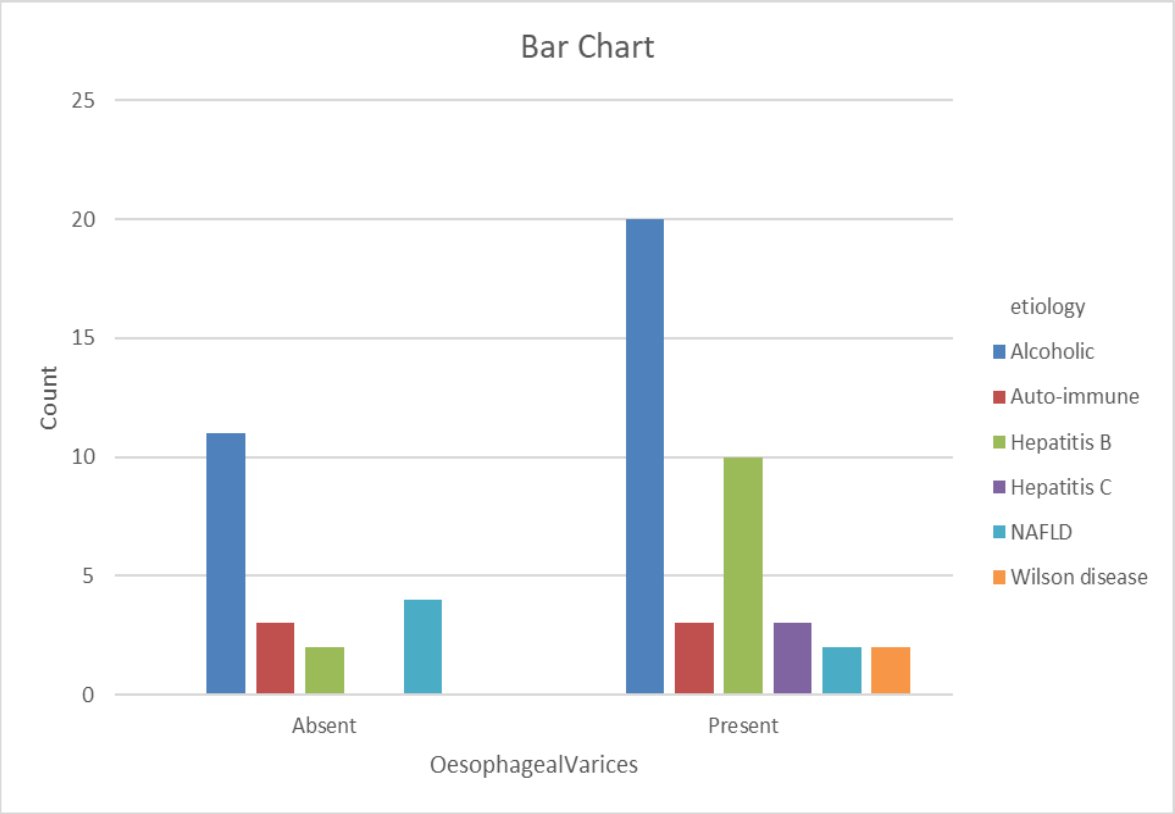

Table 5. Pairwise Comparisons of Platelet Count for Oesophageal Grades

Sample 1-Sample 2	P Value
4-3	.157
4-2	.033
4-1	.000
4-0(absent)	.000
3-2	.445
3-1	.012
3-0(absent)	.000
2-1	.061
2-0(absent)	.002
1-0(absent)	.453

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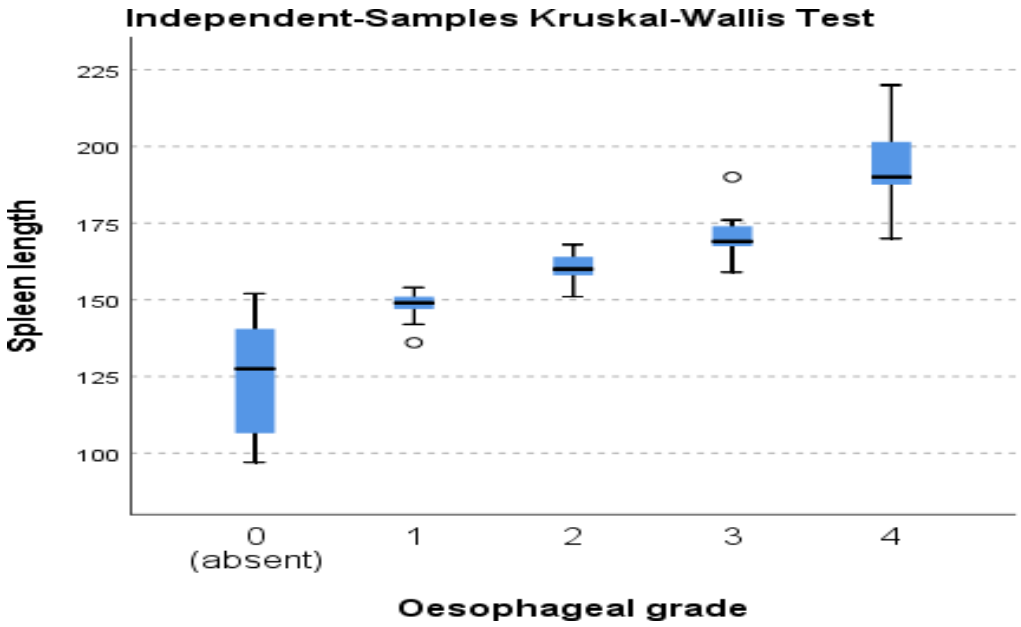

Table 6.Pairwise Comparisons of Spleen Length for Oesophageal grade

Sample 1-Sample 2	P Value
0(absent)-1	.083
0(absent)-2	.000
0(absent)-3	.000
0(absent)-4	.000
1-2	.091
1-3	.003
1-4	.000
2-3	.138
2-4	.018
3-4	.298

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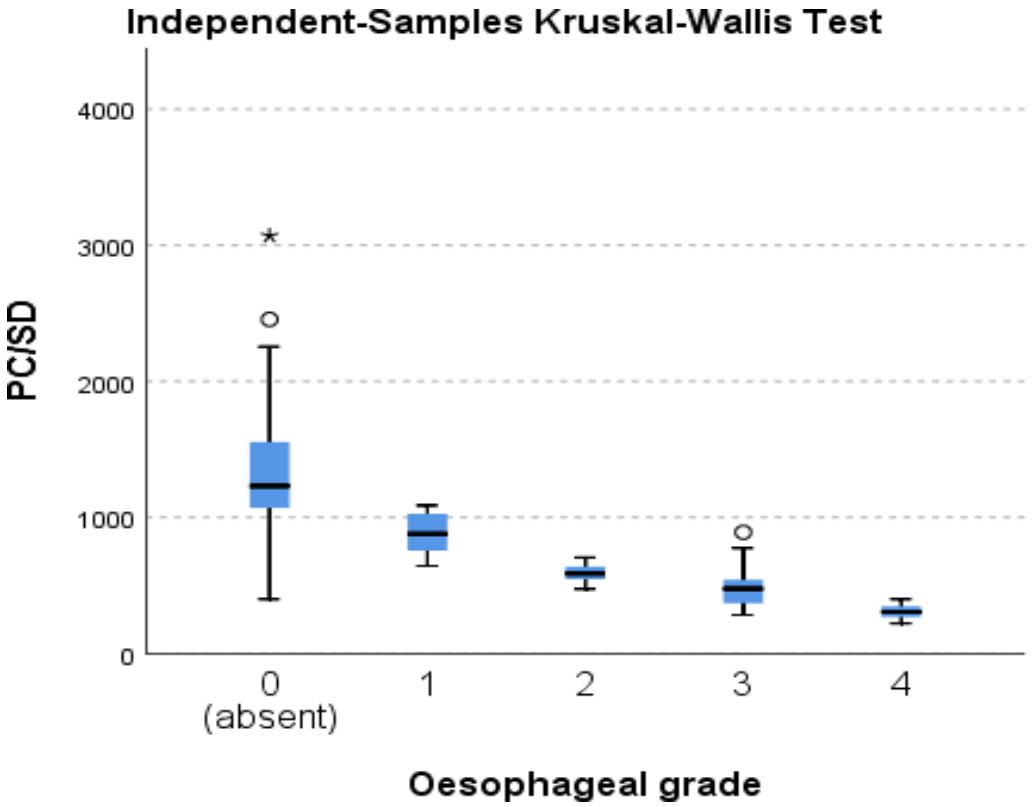

Table 7.Pairwise Comparisons of PC/SL ratio for Oesophageal grade

Sample 1-Sample 2	P Value
4-3	.172
4-2	.018
4-1	.000
4-0(absent)	.000
3-2	.277
3-1	.009
3-0(absent)	.000
2-1	.089
2-0(absent)	.000
1-0(absent)	.200

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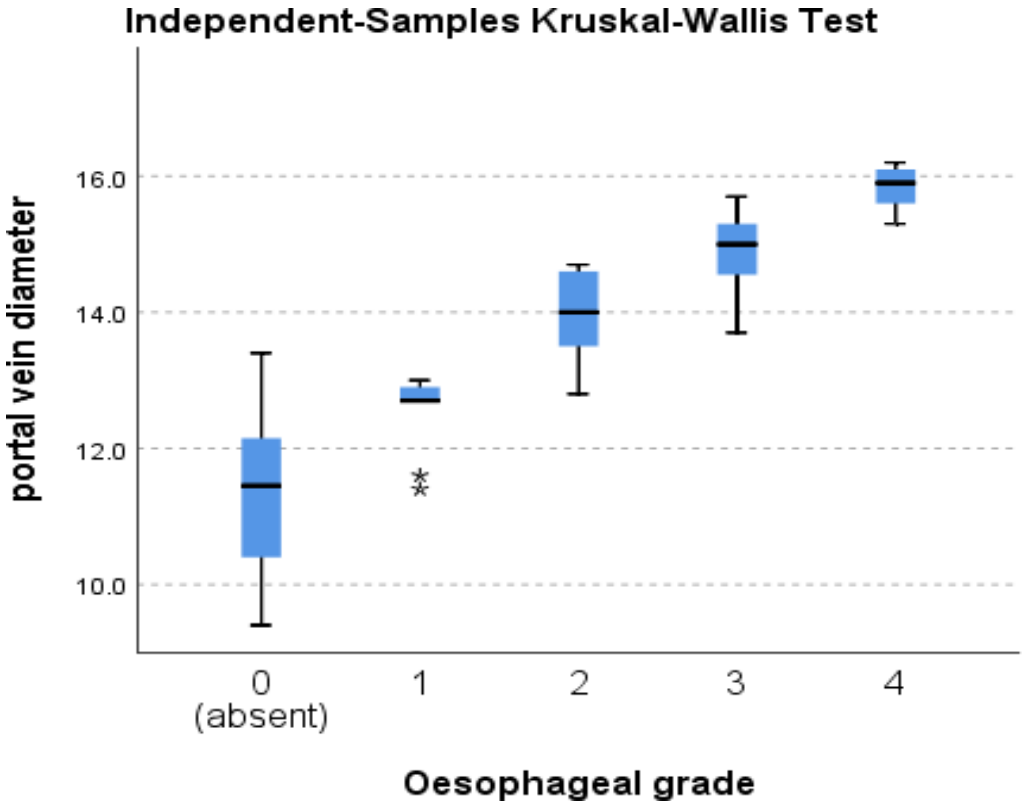

Table 8.Pairwise Comparisons of PVD for Oesophageal grades

Sample 1-Sample 2	P Value
0(absent)-1	.184
0(absent)-2	.000
0(absent)-3	.000
0(absent)-4	.000
1-2	.048
1-3	.002
1-4	.000
2-3	.172
2-4	.018
3-4	.255

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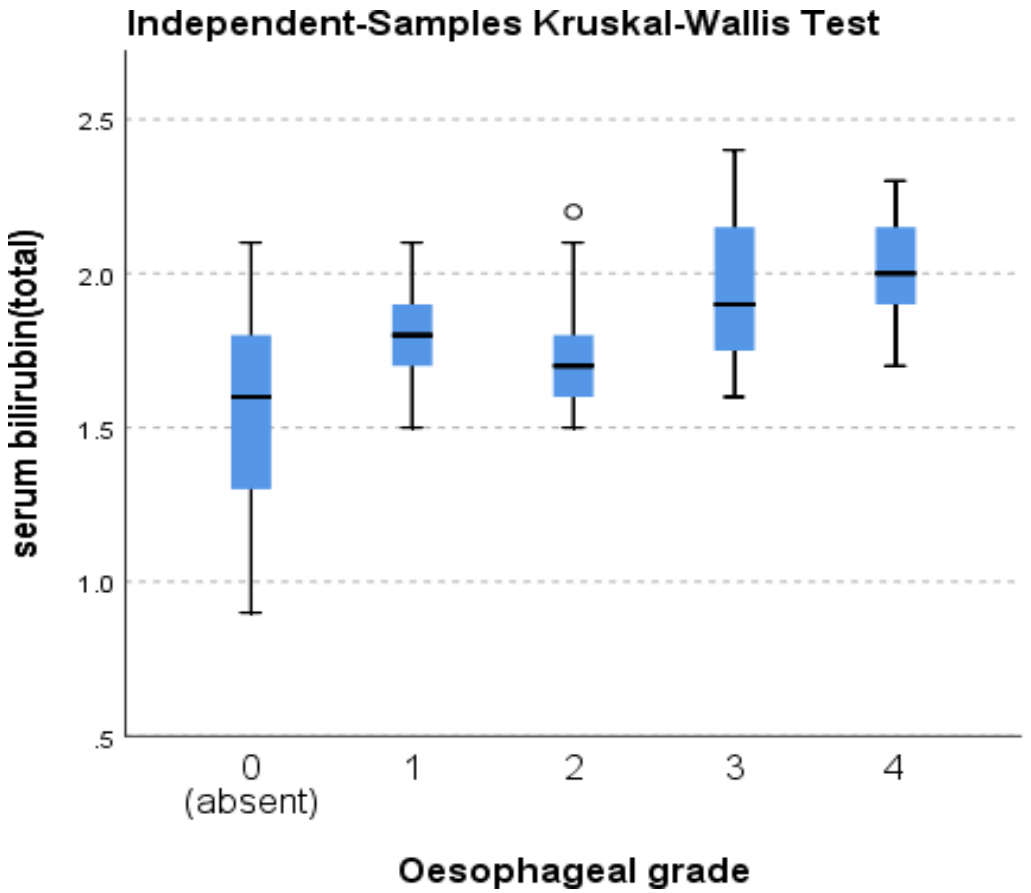

Table 9.Pairwise Comparisons of Serum Bilirubin for Oesophageal grade

Sample 1-Sample 2	P Value
0(absent)-2	.119
0(absent)-1	.067
0(absent)-3	.002
0(absent)-4	.001
2-1	.677
2-3	.121
2-4	.044
1-3	.312
1-4	.129
3-4	.520

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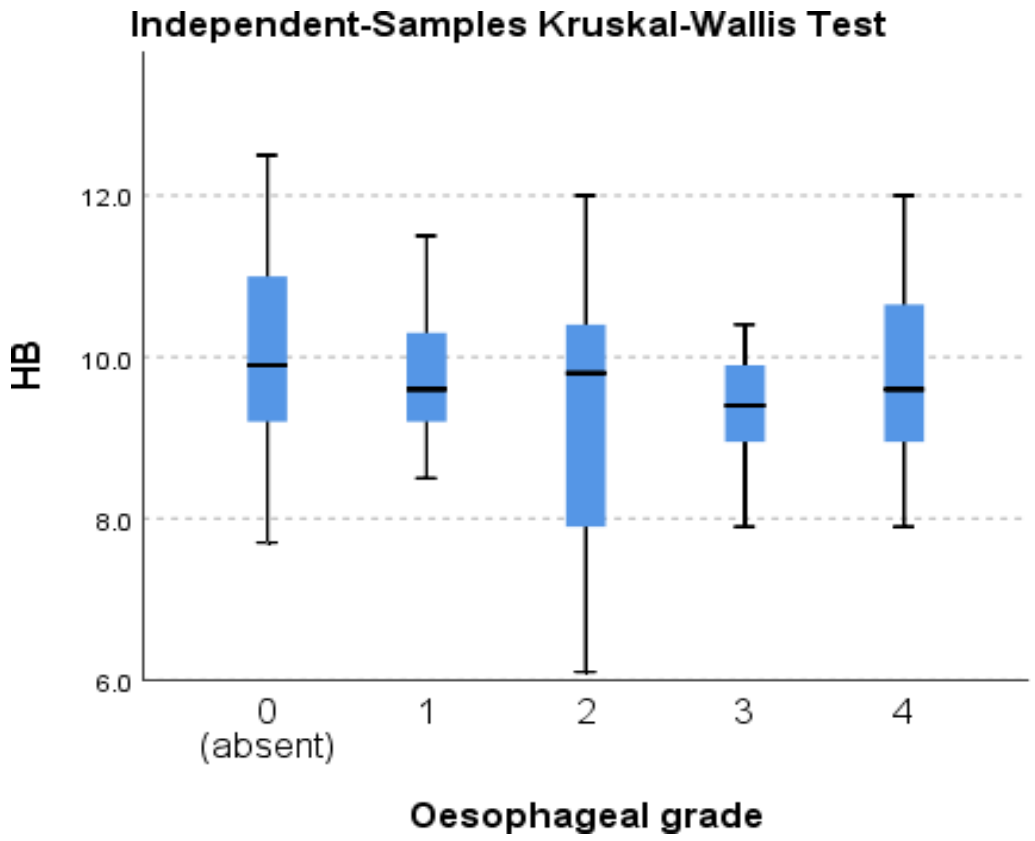

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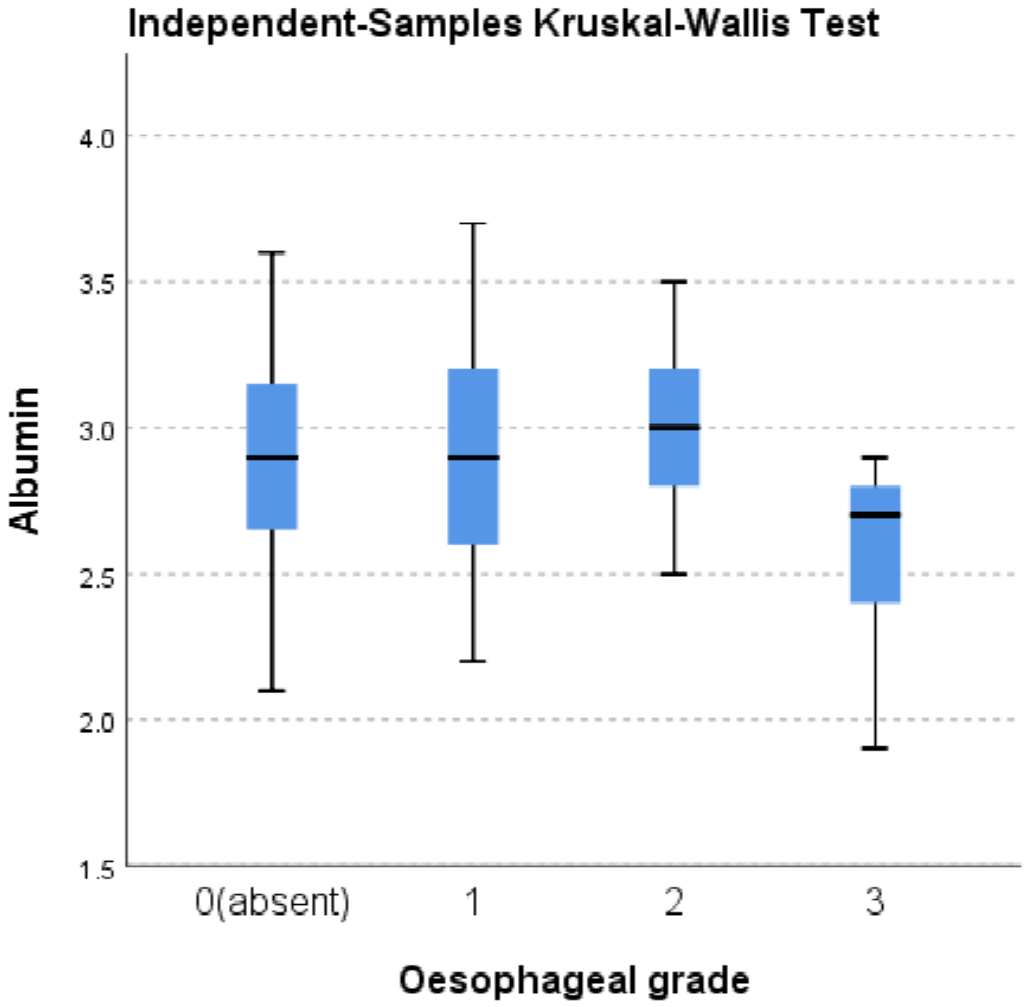

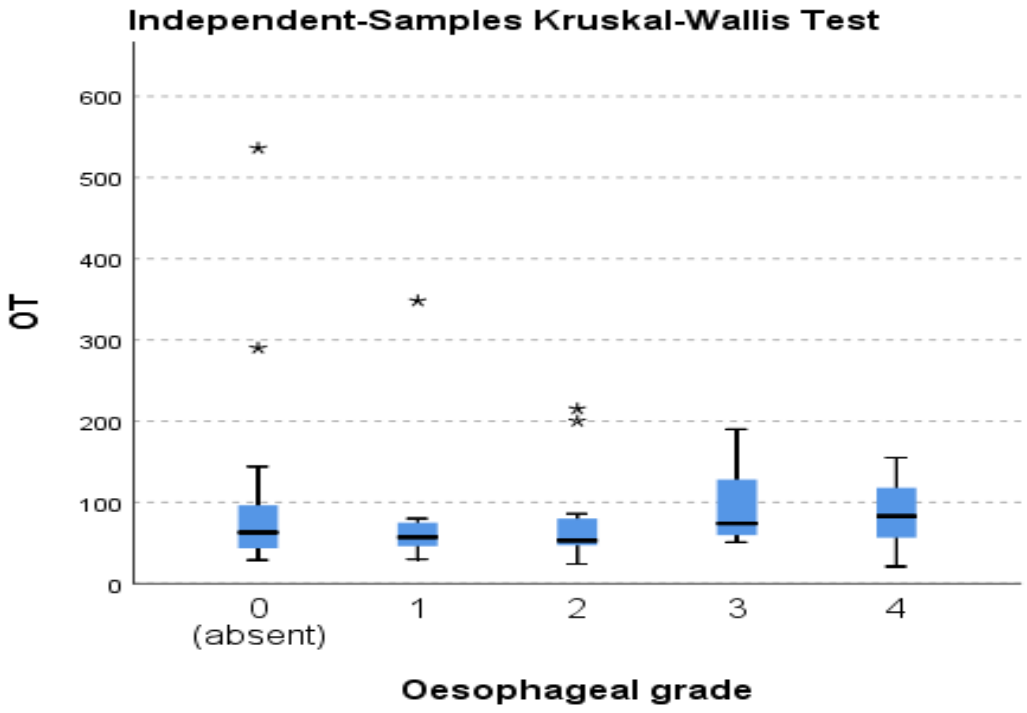

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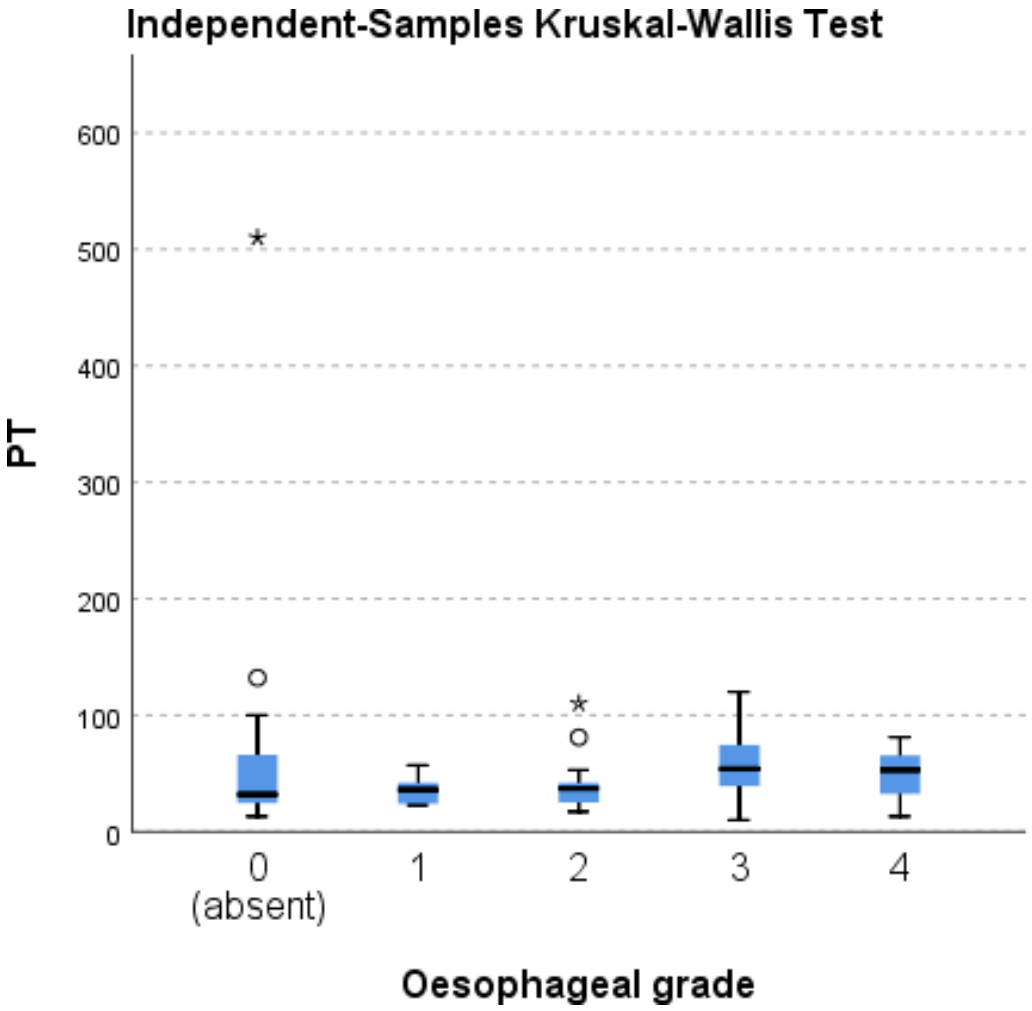

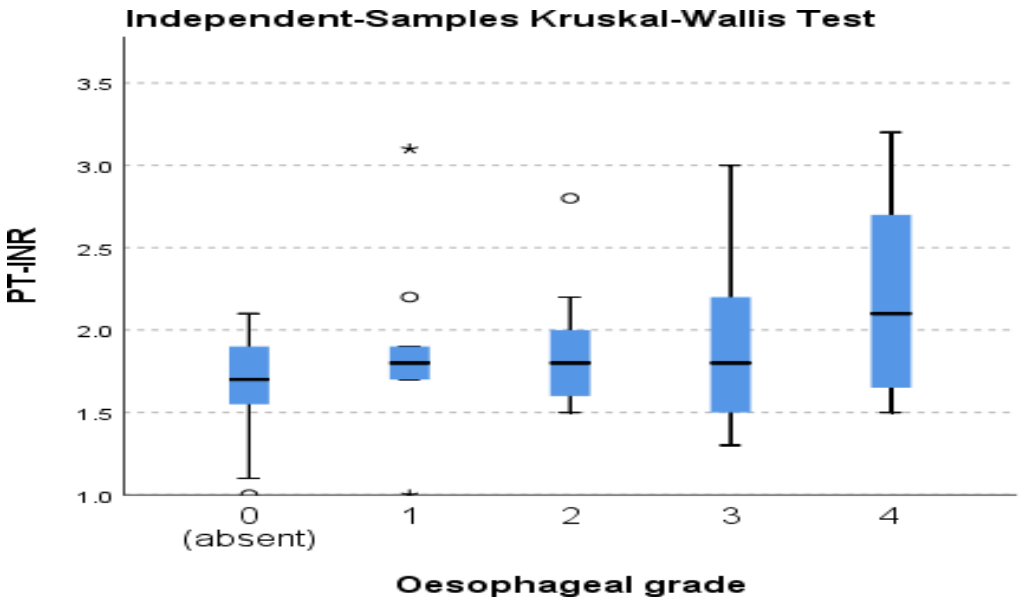

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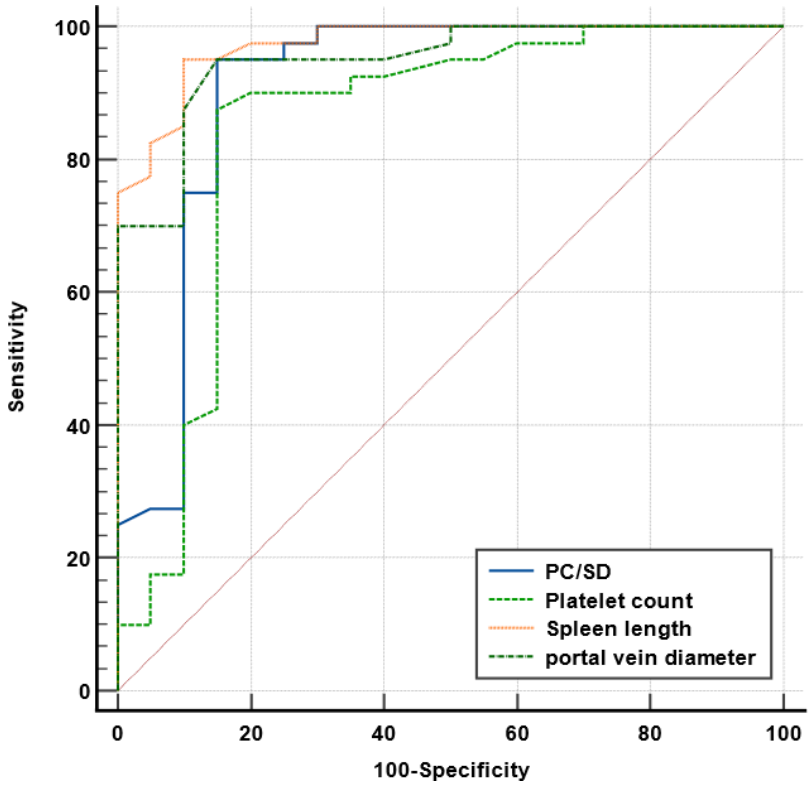
Table 10.Comparison between sensitivity, specificity, and accuracy of Portal Vein Diameter, PC/SL ratio, Platelet Count and Spleen Length in prediction of OV

Parameter	AUC	Cut off value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Portal Vein Diameter	.949	12.45	95	85	92.68	89.47	91.67
PC/SL ratio	.908	>1045.50	95	80	90.48	88.89	90.00
Platelet Count	.847	<137	87.5	85	92.11	77.27	86.67
Spleen length	.973	>145	95	90	95.00	90.00	93.33



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DISCUSSION-

Relatively few studies have been performed in past to formally assess the correlation between platelet count, spleen length, Portal vein diameter and platelet count to spleen length ratio in patients of Chronic liver disease to predict presence of Oesophageal varices in tertiary care center. The present study was conducted on 60 Chronic liver disease patients admitted or visited OPD in SN Medical College and attached hospitals, Jodhpur .

Chronic liver disease patients are increasing day by day so number of patients undergoing screening for the presence of Oesophageal varices is likely going to increasein the near future and Upper Gastrointestinal Endoscopy is expensive and requires much expertise, the need of the hour is development of non-invasive, inexpensive and easily available test for screening presence of Oesophageal varices.

The mean age of the study population in our study is 51.23±7.26 years and on the basis of gender 51/60(85%) belonged to male category and 9/60 belonged to the female gender. The gender difference in our study could be explained on the fact that alcohol habits are more prevalent in males as compared to females and Alcoholic liver disease is one ofthe important cause of Chronic liver disease .

On analyzing the aetiological profile we found that alcohol was the most common cause of Chronic liver disease. The other important cause of Chronic liver disease found in our study was auto immune, Hepatitis B, Hepatitis C and NAFLD which is comparable withresults of Alejandro González-Ojeda et al (2014) (25) study in which they found that alcohol was the most common cause of Chronic liver disease.

We found significant association between serum bilirubin and presence or absence of esophageal varices(1.5±0.3 mg/dl in no esophageal group versus 1.9±0.2 mg/dl).At the same time, we did not find any association between parameters of age, Hemoglobin, SGOT, SGPT , serum albumin and PT-INR with presence of esophageal varices. Similarly Nayak et al.(2016) (26) did not find any association between parameters of age, SGOT, SGPT or Serum albumin and presence of varices which is consistent with our results. However Nayak et al.(2016) in their study found significant linear association between INR and serum bilirubin with esophageal varices which is not consistent with ourresults.

The inconsistency in relation of INR and bilirubin with varices in the two studies could be explained on the basis of differences in sample size, severity of the disease and differences in comorbidity of the participants.

The mean±SD of Portal vein diameter in our study was 13.26±1.79, the mean±SD of Platelet count(PC) in our study was 116.53 ±52.66(10^3mm/dl) ,the mean±SD of spleen length(SL) in our study was 152±26.62 mm and the mean ±SD of PC/SL ratio of our study group was 847.93±561.23.We found statistically significant difference in terms of Portal vein diameter(PVD), Platelet countPC) ,spleen length(SL), and SL/PC ratio between Oesophageal variceal group versus no Oesophageal group.

In our study the mean Portal vein diameter in patients without esophageal varices was 11.39±1.12 mm (range-9.40-13.40) whereas the mean Portal vein diameter in patients

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with oesophageal varices was 14.20±1.26 (range-11.40-16.20) and further it varied significantly with Oesophageal varices grades and application of t test showed that this difference was statistically significant i.e. meanPortal vein diameter(PVD) increased in presence of Oesophageal varices and increases proportionately with increase in Oesophageal varices grades.

In our study the mean Platelet count in patients with Oesophageal varices was 93.98±30.39 (10^3mm/dl) (range-42-164) whereas the mean Platelet count in patients without Oesophageal varices was 161.65 ±58.47 (10^3mm/dl) (range 56-310) .Further it also decreases in a linear pattern as grade of Oesophageal varices increases and application of t test showed that this difference was statistically significant i.e. mean platelet count decreased in presence of esophageal varices and lower platelet are associated with higher grades .

Nayak et al.(2016) (26) in their study also found that platelet count decreased significantly inpresence of esophageal varices and decreased further in a linear pattern with increased EV grades which is consistent with our results

Waqas Wahid Baig et al (2008) (27) in their study found significant differences on platelet count parameter between patients with esophageal varices and without esophageal varices and varied with EV grade which is consistent with our results. They found that platelet count decreased significantly in presence of esophageal varices and lowestplatelet count seen in highest grade of EV which is consistent with our results.

In our study the mean spleen diameter in patients without esophageal length was 123.80±18.04 mm whereas the mean spleen length in patients with esophageal varices was 166.10±17.43 mm and it increased significantly in a linear fashion as grade of EV inceased and application of t test showed that this difference was statistically significant i.e. spleen length increased significantly in presence of esophageal varices and increasesproportionately with increase in EV grades.

Nayak et al.(2016) in their study also found significant differences on spleen diameter parameter between patients with esophageal varices and without esophageal varices , They found that spleen length increased significantly in presence of esophageal varices which is consistent with our results.

Waqas Wahid Baig et al (2008) in their study found significant differences on spleen diameter parameter between patients with esophageal varices and without esophageal varices , They found that spleen length increased significantly in presence of esophagealvarices and grade which is consistent with our results

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In our study the PC/SL in patients without esophageal length was 1377 ± 648.86 whereas the mean PC/SL in patients with esophageal varices was 583.40± 228.09 and application of t test showed that this difference was statistically significant i.e. PC/SL decreased in presence of esophageal varices and decreased PC/SL is proportionate to

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grade of EV.

E Giannini et al (2003) in their study found significant differences on PC/SL parameter between patients with esophageal varices and without esophageal varices , they found that .PC/SL decreased in presence of esophageal varices and decreased PC/SL is proportionate to grade of EV which is consistent with our results.

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Pascal JP et al (1989) (29) in their study found that platelet count and spleen diameter correlates with presence of EV which is consistent with our results.

Our results had been supported by studies of Schepis F et al (2001), Zein CO et al (2004), Zimbwa TA et al (2004) (30) and Andrew K Burroughs who found significant association between platelet count,spleen diameter and presence of esophageal varices.

When we analyze our data taking cut off point for PC/SL > 1045.50 we found that sensitivity and specificity of PC/SL for prediction of EV was 95% and 80% respectively. In study of Baig et al. the sensitivity and specificity of PC/SL for prediction of EV was 80% and 90% respectively at cut off point of 909 which is comparable to our results. In study of Giannini et al (2003) the sensitivity and specificity of PC/SL for prediction of EV was 100% and 93% respectively at cut off point of 909 which is comparable to our results. In study of Alejandro González-Ojeda (2014) the sensitivity and specificity of PC/SLfor prediction of EV was 84% and 70% respectively at cut off point of 884 which was lower than our results.

The variation in sensitivity and specificity in various studies could be explained on basisof differences in cut-off values for PC/SL for predicting EV which may depend on racialfactors and genetic factors. In our study Portal Vein Diametr at cut-off of 12.45 mm, sensitivity and specificity of PVD for prediction of EV was 95% and 85% respectively. In our study Platelet count at cut-off of 137 (10^3mm/dl) sensitivity and specificity of Platelet count for prediction of EV was 87.5% and 85% respectively.In our study spleen length at cut-off of 14.5 cm sensitivity and specificity of spleen length for prediction of EV was 95% and 90% respectively.

In study of Giannini et al (2003) (28) spleen length at cut-off of 14.5 cm sensitivity and specificity of spleen length for prediction of EV was 95% and 90% respectively. While evaluating we must consider that platelet count may decrease for several reasons in patients with chronic liver disease. Thus the use of platelet count alone as a non- invasive predictor of OV can be misleading and cannot be solely attributed to portal hypertension. This drawback can be overcome by use of use of the platelet count/spleen diameter ratio since it normalizes platelet count to splenic sequestration and reflect thrombocytopenia caused by portal hypertension.

However researches revealed that the presence of a decreased platelet count in patients with chronic liver disease may depend on several factors other than portal hypertension, such as shortened mean platelet lifespan, decreased thrombopoietin production or myelotoxic effects of alcohol or hepatitis viruses [24]. The presence of splenomegaly in

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cirrhotic patients is likely the result of vascular disturbances that are mainly related to portal hypertension.

While evaluating we must consider that platelet count may decrease for several reasons in patients with chronic liver disease. Thus the use of platelet count alone as a non-invasive predictor of OV can be misleading and cannot be solely attributed to portal hypertension. This drawback can be overcome by use of use of the platelet count/spleen diameter ratiosince it normalizes platelet count to splenic sequestration and reflect thrombocytopenia caused by portal hypertension.

CONCLUSION

There were significant difference in term of portal vein diameter, platelet count, spleen length, and PC/SL ratio in patients with esophageal varices and patients without esophageal varices. Use of the PC/SL ratio along with thrombocytopenia, splenomegaly and increased portal vein diameter will help create a lower-cost and more effective method to identify esophageal varices in patients with portal hypertension. The PC/SL ratio cannot substitute for upper gastrointestinal endoscopy in the scrutiny of esophageal varices. When compared with other noninvasive predictor tools, the PC/SL ratio is elegant, simple, and inexpensive. With some minor modifications, it may become a helpful tool to limit the number of endoscopies to be performed in patients for primary prophylaxis of variceal bleeding in portal hypertension.

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