

Original Research Article

Study of the correlation of oesophageal varices with portal vein diameter and ratio of platelet count to splenic diameter and their comparative evaluation in liver cirrhosis

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ABSTRACT

Background: The aim of the study was to determine the correlation of oesophageal varices (OV) with portal vein diameter and the platelet count to splenic diameter ratio and their comparative evaluation in patients of liver cirrhosis.

Methods: The present study consisted of 50 patients diagnosed with liver cirrhosis. Necessary investigations were performed in all the patients including Upper gastrointestinal (GI) endoscopy. Platelet count/spleen diameter ratio, spleen diameter and portal vein diameter were calculated for all patients and the presence and grading of OV was then comparatively evaluated. The results were systematically recorded and statistically analysed.

Results: The mean age of patients was 49.82 ± 10.23 years. 78% of patients presented with OV. The portal vein diameter, platelet count, spleen diameter and platelet count/spleen diameter ratio were significantly increased in patients with OV than those without OV ($p < 0.0001$). Highly significant positive correlation between portal vein diameter, spleen diameter and grading of OV was seen. Platelet count/spleen diameter ratio and platelet count was significantly decreased as the grade of OV increased in the patients. There was statistically, a highly significant negative correlation between them.

Conclusions: The non-invasive parameters used to detect presence of OV in liver cirrhosis were portal vein diameter and platelet count/spleen diameter ratio. Though, both seemed to be effective in predicting OV, platelet count/spleen diameter ratio proved to be slightly more significant when compared to the other.

Keywords: Oesophageal varices, Portal vein diameter, Platelet count, Spleen diameter and platelet count/spleen diameter ratio

INTRODUCTION

Portal hypertension commonly accompanies the 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%.^{2,3} 30% of these patients usually have at least one bleeding episode because of rupture of a varix.

The risk of the bleeding from the varices is 25-35% with majority of the initial bleeding occurring within the first year of the varices detection.⁴ Gastroesophageal area is the main site of formation of varices.⁵ OV are formed when the hepatic venous pressure gradient (HVPG) exceeds 10 mm of Hg.⁶ It usually occurs in the lower 2 to 3 cm of the oesophagus.⁷ The prevalence of the oesophageal varices in patients with liver cirrhosis may range from 60 to 80% and the reported mortality from various variceal bleeding ranges from 17 to 57%.^{1,3,8} Thus, the prevention of the

variceal bleeding is an important goal in the management of the patients with liver cirrhosis.

The gold standard for diagnosis of OV is upper gastrointestinal endoscopy.⁹ However, it is invasive and is not cost effective. Thus, various attempts are being made to identify the variables that can non-invasively predict the presence of the OV. These studies include biochemical, clinical, ultrasound parameters, transient elastography, computed tomography (CT) scanning and video capsule endoscopy.¹⁰ Overall, these studies included the parameters related directly or indirectly to the portal hypertension such as splenomegaly and decreased platelet count for the prediction of OV.

The present study was conducted to determine the correlation of OV with portal vein diameter (PVD) and platelet count/spleen diameter (PC/SD) ratio and their comparative evaluation in patients of liver cirrhosis.

METHODS

This observational prospective study consisted of 50 patients of either sex and of age 18 years and above, diagnosed with liver cirrhosis attending outpatient department (OPD)/admitted in various wards of Guru Nanak Dev Hospital attached to Government Medical College, Amritsar. The study was conducted over a period of 13 months from July 2019 to August 2020. Written and informed consent was taken from every patient. The study was conducted after approval from institutional thesis and ethical committee.

Inclusion criteria

Patients of age 18 years and above, and patients diagnosed with liver cirrhosis were included in the study.

Exclusion criteria

Patients with any co-existing condition that could influence the liver and/or spleen size and platelet count and patients in whom endoscopy was contraindicated were excluded from the study - patients with: upper gastrointestinal bleed due to other causes; who previously had undergone injection sclerotherapy, band ligation or surgery for OVs (TIPS etc.); hepatocellular carcinoma; primary hematological disorders; portal vein thrombosis; coexistent illness or infection that could influence the liver and spleen size; human immunodeficiency virus (HIV) infection; renal disease; pulmonary disease; and severe or unstable cardiovascular disease.

Necessary laboratory investigations, abdominal ultrasound was performed in all the patients with the measurement of the bipolar spleen diameter (SD) and portal vein diameter (PDV). Upper gastrointestinal (GI) endoscopy was performed in every patient for the detection and grading of OVs using Pentax endoscope. Grading of OVs was done as follows - grade 0: no varices, grade I: small and straight

varices at the level of mucosa, grade II: varices <5 mm, tortuous and occupying less than one third of the oesophageal lumen, grade III: varices >5 mm and occupying more than one third of the oesophageal lumen, and grade IV: varices occupying more than two third of the oesophageal lumen.^{7,9}

PC/SD ratio, SD and PVD were calculated for all the patients. PVD and PC/SD ratio was calculated and the presence and grading of OV was then comparatively evaluated. The results were systematically recorded and statistically analysed.

Statistical analysis was performed by IBM-compatible statistical package for the social sciences (SPSS) version 23.0.

RESULTS

In the present study maximum patients were males. The mean age of patients was 49.82±10.23 years. 78% of patients presented with OV on upper gastrointestinal endoscopy. Table 1 showcases mean value of various non-invasive parameters. Table 2 shows that PVD, platelet count (PC), SD and PC/SD ratio was significantly increased in patients with OV than those without OV (p<0.0001). Table 3 shows statistically highly significant positive correlation between PVD, SD and grading of OV. PC/SD ratio and PC was significantly decreased as the grade of OV increased in the patients. There was statistically, a highly significant negative correlation between them.

The main clinical characteristics of these patients are presented in Table 1.

Table 1 shows that 88% of the study population were males and OV were present in 78% of the study population, it also depicts the mean value of all the parameters used in the study.

Table 1: Clinical characteristics of the study population.

| Clinical characteristics | Frequency |
|--|---|
| Total patients (n) | 50 |
| Mean age (years) | 49.82±10.23, minimum age: 28, maximum age: 76 |
| Gender distribution (n; %) | Male: 44 (88%) female: 6 (12%) |
| Oesophageal varices (n %) | Present: 39 (78%), absent: 11 (22%) |
| Mean portal vein diameter (mm) | 14.2±2.87 |
| Mean platelet count (n/mm³) | 128160.0±39625.96 |
| Mean spleen diameter (mm) | 135.88±19.16 |
| Mean platelet count/spleen diameter ratio (mean±SD) | 848.35±348.81 |

Table 2 compares the mean values and range of all the parameters between those with and those without OV.

Table 3 shows that mean portal vein diameter in patients with grade 0, grade I, grade II, grade III and grade IV OV was 10.96±1.03 mm, 12.52±1.39 mm, 13.54±1.94 mm, 15.43±1.70 mm and 17.69±1.72 mm respectively. Portal vein diameter was significantly increased as the grade of OV increased in the patients. There was a statistically highly significant positive correlation between portal vein diameter and grading of OV ($r_s=0.634$, $p<0.001$).

Table 4 shows that mean PC/SD ratio in patients with grade 0, grade I, grade II, grade III and grade IV OV was 1485.35±179.32, 1112.11±162.83, 968.97±182.46, 806.09±842.69 and 638.06±147.77 respectively. PC/SD ratio was significantly decreased as the grade of OV increased in the patients. There was a statistically highly significant negative correlation between PC/SD ratio and grading of OV ($r=-0.707$, $p<0.001$).

Table 5 depicts the comparison between PVD and PC/SD ratio regarding their sensitivity, specificity, positive predictive value, negative predictive value and accuracy in predicting OV.

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of

PC/SD ratio in prediction of OV was 97.44%, 90.91%, 97.44%, 90.91% and 96% respectively at the best cut-off value of 1251.75 as calculated by applying ROC curve (Figure 2) and area under curve (AUC) was 0.965.

Figure 3 depicts the comparison between PVD and PC/SD ratio regarding their sensitivity, specificity and accuracy in predicting OV.

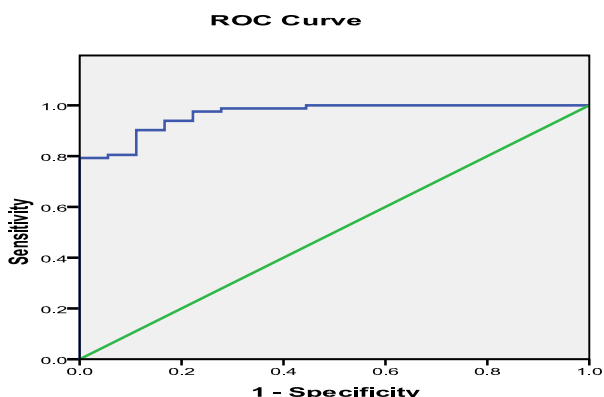


Figure 1: Receiver operating characteristic (ROC) curve for evaluation of OV with PVD as diagnostic parameter for the presence of OV.

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of PVD in prediction of OV was 87.18%, 90.91%, 97.14%, 66.67% and 88.00% respectively at the best cut-off value of 12.4 as calculated by applying ROC curve (Figure 1) and area under curve (AUC) was 0.942.

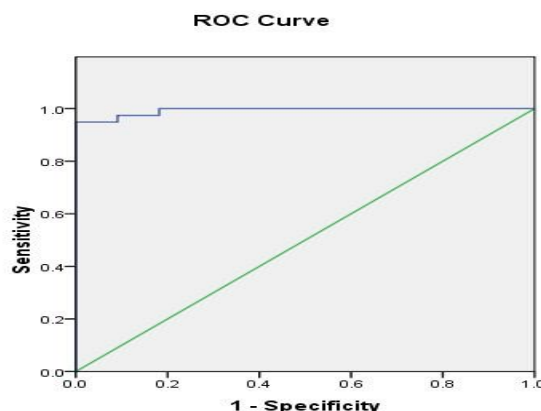


Figure 2: Receiver operating characteristic (ROC) curve for evaluation of OV with ratio of PC/SD as diagnostic parameter for the presence of OV.

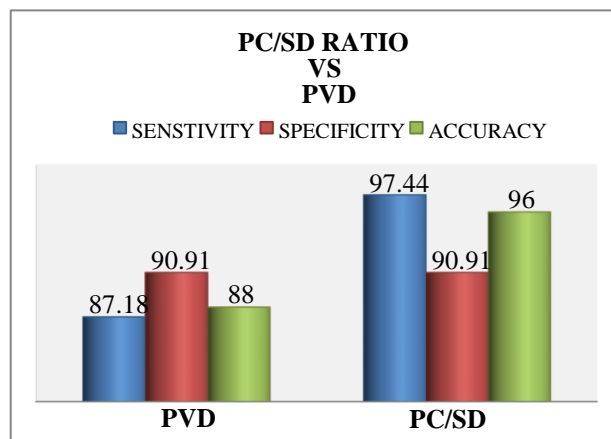


Figure 3: Comparison between sensitivity, specificity and accuracy of PVD and PC/SD ratio in prediction of OV.

Table 2: Various non-invasive parameters in correlation to presence or absence of OV.

| Oesophageal varices | Present | | Absent | | P value |
|-------------------------------------|--------------|-------------------|---------------|--------------------|--------------|
| Comparative parameters | Range | Mean±SD | Range | Mean±SD | |
| Portal vein diameter (mm) | 10.4-20.2 | 15.11±2.87 | 9.6-13 | 10.96±3.03 | <0.0001 (HS) |
| Platelet count (N/mm ³) | 52000-178000 | 115538.46±3109.45 | 120000-220000 | 172909.09±31640.02 | <0.0001 (HS) |

Continued.

| Oesophageal varices | Present | | Absent | | P value |
|--------------------------------------|-------------|---------------|-----------|----------------|--------------|
| Comparative parameters | Range | Mean±SD | Range | Mean±SD | |
| Spleen diameter (mm) | 90-180 | 137.56±18.47 | 92.4-143 | 116.49±17.75 | 0.0005* (HS) |
| Platelet count/spleen diameter ratio | 325-1266.67 | 848.35±238.35 | 1220-1700 | 1485.35±179.32 | 0.0005* (HS) |

p<0.05=significant, **p<0.001=highly significant, p>0.05=non-significant

Table 3: Portal vein diameter in correlation to grading of OV.

| Grade of OV | N | Portal vein diameter (mm) | | P value | r _s |
|-------------|----|---------------------------|------------|---------------|----------------|
| | | Range | Mean±SD | | |
| Grade 0 | 11 | 9.6-13 | 10.96±1.03 | <0.0001* (HS) | 0.634 |
| Grade I | 7 | 10.4-14 | 12.52±1.39 | | |
| Grade II | 9 | 14-15.3 | 13.54±1.94 | | |
| Grade III | 12 | 15.4-17 | 15.43±1.70 | | |
| Grade IV | 11 | 17.9-20.2 | 17.69±1.72 | | |
| Total | 50 | 9.6-20.2 | 14.2±2.87 | | |

p<0.05 is considered as significant; HS: highly significant; r_s: Spearman's correlation

Table 4: Platelet count/spleen diameter ratio in correlation to grading of OV.

| Grade of OV | N | Platelet count/spleen diameter ratio | | P value | r _s |
|-------------|----|--------------------------------------|----------------|---------------|----------------|
| | | Range | Mean±SD | | |
| Grade 0 | 11 | 1220-1700 | 1485.35±179.32 | <0.0001* (HS) | -0.707 |
| Grade I | 7 | 844.44-1266.67 | 1112.11±162.83 | | |
| Grade II | 9 | 620.69-984.84 | 968.97±182.46 | | |
| Grade III | 12 | 513.15-1111.11 | 806.09±842.69 | | |
| Grade IV | 11 | 325-842.69 | 638.06±147.77 | | |
| Total | 50 | 325-1700 | 848.35±348.81 | | |

p<0.05 is considered as significant; HS: highly significant; r_s: Spearman's correlation

Table 5: Comparison between sensitivity, specificity and accuracy of PVD and PC/SD ratio in prediction of OV.

| Parameter | AUC | Cut off value | Sensitivity (%) | Specificity (%) | Positive predictive value (%) | Negative predictive value (%) | Accuracy (%) |
|-------------|-------|---------------|-----------------|-----------------|-------------------------------|-------------------------------|--------------|
| PVD | 0.942 | 12.4 | 87.18 | 90.91 | 97.14 | 66.67 | 88.00 |
| PC/SD ratio | 0.965 | 1251.75 | 97.44 | 90.91 | 97.44 | 90.91 | 96.00 |

DISCUSSION

Out of total 50 patients included in the study; OV were seen in 78% of patients on upper GI endoscopy. Patients without OV were considered as grade 0 and patients with OV were further classified according to grading of OV on endoscopy into grade I, II, III and IV. In the present study, 11 (22%) patients without OV were classified as grade 0 and remaining 39 (78%) patients with OV were further classified as grade I OV in 7 (14%) patients, grade II in 9 (18%) patients, grade III in 12 (24%) patients and grade IV in 11 (14%) patients.

In similarity to our study, Abu El Makarem et al in their study reported 74.9% prevalence of OVs, Rina Mohanty et al reported 68% prevalence of OV, Chalasani et al in their study found OV in 70% cases while Zaman et al found in 68% cases.¹¹⁻¹⁴ This high prevalence of OV on endoscopy

may be due to the delay in seeking treatment after signs and symptoms of portal hypertension have developed.

Portal vein diameter

In the present study, PVD ranged from 9.6-20.2 mm with mean value of 14.2±2.87 mm. Mean PVD in patients with OV was 15.11±2.87 mm and in those without OV was 10.96±3.03 mm. PVD was significantly increased in patients with OV than those without OV (p<0.0001). In accordance with our study, Mohanty et al also reported a mean PVD of 13.46±0.98 mm in the group with OV, which was significantly higher in comparison to the group without OV with 10.91±0.65 mm.¹² In a study by Bhattarai et al and Sreenath et al significant association was seen between OV and PVD.^{15,16} Makarem et al also reported that PVD was higher in cirrhotic patients with OVs, but this correlation failed to reach statistical significance.¹¹

However, on contrary Savith et al in their study reported no significant correlation between PVD and the presence and severity of varices.¹⁷

Platelet count

In the present study, PC ranged from 52000-220000/mm³ with mean value of 128160±39625.96/mm³. Mean PC in patients with OV was 115538.46±3109.45/mm³ and in those without OV was 172909.09±31640.02/mm³. PC was significantly decreased in patients with OV than those without OV (p<0.0001). PC was significantly decreased as the grade of OV increased in the patients. There was a statistically highly significant negative correlation between PC and grading of OV (r=-0.566, p<0.001).

In similarity, Mohanty et al reported a mean PC in the group with varices was 1,17,000±21,000/ul, while that of the group without OV was 1,70,000±30,000/ul.¹² Even Fook-Hong et al reported a mean value of PC 110,000±52,000/ml among those with OV and 160,000±90,000/ml in the group without OV.¹⁸ This thrombocytopenia can be explained due to changes in the microcirculation and hypersplenism which is in relation to portal hypertension along with lesser amount of thrombopoietin synthesis in liver.

From a clinical point of view, 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. Indeed, the use of the PC/SD ratio bypasses this possible drawback since it normalizes platelet count to splenic sequestration.

Spleen diameter

In the present study, SD in total patients ranged from 90-180 mm with mean value of 135.88±19.16 mm. Mean SD in patients with OV was 137.56±18.47 mm and in those without OV was 116.49±17.75 mm. SD was significantly increased in patients with OV than those without OV (p<0.0005*). SD was significantly increased as the grade of OV increased in the patients. There was a statistically significant positive correlation between SD and grading of OV (r=0.403, p=0.001).

Sreenath et al reported that mean spleen size for the population of high-grade varices was 13.5 cm and that of low grade or no varices was 12.1 cm, which was also statistically significant (p<0.0001).¹⁶ Mohanty et al reported that cephalocaudal splenic measurement in group with OV was 14.7±0.82 cm, while in the group without OV was 12.2±1.01 cm.¹² Fook-Hong et al reported cephalocaudal splenic measurement of 11.7±3.2 cm in the group with OV, and 10.2±2.8 cm in the group without OV.¹⁸ Schepi et al observed a mean splenic measurement of 16.3±2.7 cm in the group with OV, and 13.9±2.5 cm in the group without OV.¹⁹ Bhattarai et al observed that patients without varices had average spleen size of

12.67±2.35 cm and those with varices had 15.367±1.210 cm.¹⁵

Platelet count/spleen diameter ratio

In the present study, PC/SD ratio in total of 50 patients ranged from 325-1700 with mean value of 848.35±348.81. Mean PC/SD ratio in patients with OV was 848.35±238.35 and in those without OV was 1485.35±179.32. PC/SD ratio was significantly decreased in patients with OV than those without OV (p<0.001*). PC/SD ratio was significantly decreased as the grade of OV increased in the patients. There was a statistically highly significant negative correlation between PC/SD ratio and grading of OV (r=-0.707, p<0.001). Sreenath et al reported that mean PC/SD ratio for the population of high-grade varices was 654.46 and that of low grade or no varices was 1290.67.¹⁶ It also showed statistically significant difference in two groups with p<0.0001.

Sensitivity, specificity and cut off value

In the present study, the best cut-off value of PVD was 12.4 (sensitivity=87.18%, specificity=90.91%) as calculated by applying ROC curve (Figure 1) and AUC was 0.942. In the present study, the best cut-off value for portal vein diameter was 1251.75 (sensitivity =97.44, specificity=90.91%) as calculated by applying ROC curve (Figure 2) and AUC was 0.965.

Bhattarai et al reported the best cut off of PVD for prediction of OV was >12.25 mm (sensitivity=92.72%, specificity=90%), Shanker et al, reported PVD>12.20 mm, value similar to ours, as a predictor of OV with sensitivity of 80 % and specificity of 80%.^{15,20} Cherian et al and Prihatini et al found PVD of 13 mm and 15 mm respectively to be predictive for variceal detection in cirrhotic patients.^{21,22} Schepis et al have proposed that PVD>13 mm was an independent risk factor for the presence of varices.¹⁹ Thomopoulos et al reported that PVD for development of gastroOV was 13.5 mm.²³

Sreenath et al had set the cut off value for PC/SD ratio at 728.2 in cirrhotic patients, such that the presence of high-grade OV can be predicted if the ratio is less than 728.2 with a sensitivity-71.43%, specificity-87.50%, PV-83.33%, NPV-77.78%, positive likelihood ratio-5.71 and negative likelihood ratio-0.33.¹⁶

In yet another study by Giannini et al, who used a cut off value of 909 and AUC of ROC curve of 0.981, corresponded to positive and negative predictive values of 95.6% and 100% respectively, for the presence of varices.²⁴ The same ratio has also been examined by Legasto et al, Agha et al and Baig et al in their studies with different populations, thus generating consistent results suggesting that the ratio is generalizable.²⁵⁻²⁷

The area was less for PVD; hence, it is considered less significant when compared to PC/SD. In similarity,

Sreenath et al also reported that area under curve was significant for PC/SD ratio (0.845) and for PVD (0.623).¹⁶

We recognize the limitations of the present study. The most important of them being that sample size though adequate for detection of endoscopic lesions, was inadequate for the subgroup analysis. The present study was a single center study and hence not reflects the wider population.

CONCLUSION

The non-invasive parameters used to detect presence of OV in liver cirrhosis were PVD and PC/SD ratio. Though, both these methods seemed to be effectively and significantly helpful in predicting OV, but PC/SD ratio proved to be slightly more significant and an independent predictor of presence of OV when compared to the other. Furthermore, PC/SD ratio can be easily calculated and may help to reduce the financial burdens of endoscopy units, particularly in developing countries. However, further large multicentric studies on these parameters are needed to validate our findings.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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