

Splenoportal-Index – A diagnostic Tool for the Non-Invasive Detection of Esophageal Varices

Splenoportal-
Index Diagnostic
Tool for
Esophageal
Varices

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ABSTRACT

Objective: The objective of the study entail to establish an evidence in Pakistani population regarding splenoportal-index as a diagnostic tool for the non-invasive detection of esophageal varices; a cost-effective and useful tool to screen patients in advance who are at high risk to bleed.

Study Design: Prospective cross-sectional study.

Place and Duration of Study: This study was conducted at the University Tertiary-care Hospital; conducted from December-2019 to June-2020.

Materials and Methods: Eighty (N=80) male and female subjects (30-80 years) were selected in the study based upon clinical and laboratory evidence of liver-cirrhosis. Ethical approval for the study has been taken. Endoscopy was performed in Department of Medicine. Ethical issues were considered and complied. Splenic-index results found by ultrasonography and portal-vein velocity were correlatively compared with the outcomes of endoscopy. True positive, true negative, false positive, false negative patients were segregated. Data was analyzed by SPSS-20 by keeping p-value <0.05; a significant.

Results: Male: Female ratio was 53(66%):27(34%). Subjects positive on Ultrasonography = 61 (76.25%) and positive on Endoscopy = 62 (77.50%) significantly correlated (p=0.001). Test sensitivity (92%); specificity (78%); positive-predictive-value (93%); negative-predictive-value (74%); accuracy (89%); false-positive-rate (22%) and false-negative-rate (8.0%).

Conclusion: Ultrasonography is significantly accurate non-invasive; cost-effective and useful tool for the identification of varices of esophagus in patients suffering from liver-cirrhosis.

Key Words: Cirrhosis of liver; Varices; Esophageal varices; Ultrasound/Ultrasonography; Upper gastrointestinal endoscopy.

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INTRODUCTION

Splenoportal-index is a valuable non-invasive and low cost tool for identification of the varices in esophagus in patients of liver-cirrhosis.¹

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In the last stage of liver-cirrhotic patients; deterioration of normal liver tissue causes the maximum fibrosis.² Patients who do not develop complications like; bleeding due to varices in the esophagus, ascitic fluid in abdomen, spontaneous bacterial peritonitis (SBP), hepato-cellular carcinoma, hepatic-renal syndrome are classified as compensated cirrhosis.² Unfortunately; prognosis is poor in the patients of liver-cirrhosis if they have esophageal varices (EV) compare to those who do not possess varices in esophagus. It is reported that median survival time for the compensated and decompensated liver-cirrhotic patient were 115 months and 55 months respectively.³

Patients of liver-cirrhosis had considerably higher rate of variceal bleeding; particularly those, who have the first acute episode of upper gastrointestinal bleeding in one year.⁴ Therefore; due to clinical significance and for the future management, it is imperative to assess liver-cirrhosis patients for portal-hypertension. Duplex ultrasound is a useful modality in out-patient clinics to assess the portal-hypertension.⁵ According to published literature; diminution in portal-vein velocity is linked

with progression of portal-hypertension and higher risk of bleeding from varices of esophagus.⁶

In order to diagnose varices in esophagus; Esophagogastroduodenoscopy (EGD) is a gold standard with high sensitivity and specificity. However; its invasiveness, conscious sedation and fairly high cost are demerits.⁷ Splenoportal-index is a recent parameter and emerged as a more acceptable tool among medical professionals; calculated by two parameters i.e. length of spleen and velocity of portal-vein.⁸ High acceptability of splenoportal-index method is due to its non-invasive nature and cost-effectiveness.

Most of the data regarding splenoportal-index are published from the patients of developed countries. Therefore; the main aim of current study was to establish valid evidence in Pakistani population regarding splenoportal-index as a diagnostic tool for the non-invasive detection of EV. To validate⁹ splenoportal-index; accuracy, specificity, sensitivity, positive-predictive-value (PPV), negative-predictive-value (NPV) false-positive-rate, false-negative-rate were determined in Pakistani population.

MATERIALS AND METHODS

Study Design and Settings: A cross-sectional observational study was conducted in the University Tertiary-Care Hospital of Karachi. The duration of the study was December-2019 to June-2020. Eighty (N=80) male and female subjects (30-80 years) were selected in the study based upon clinical and laboratory evidence of liver-cirrhosis.

Approval from Ethics Committee: Ethical Review Committee of Hamdard College of Medicine and Dentistry approved the study. (Reference number HCM&D/307/2019).

Male:Female ratio: 53(66%) Male and 27(34%) Female. Mean age; 55 years.

Sample Size and Technique: Sample size was determined by convenience sampling technique.¹⁰ Minimum sample size of the study was 80 patients.

Inclusion Criteria: Patients with clinical and laboratory evidence of liver-cirrhosis.

Exclusion Criteria: Patients with hematemesis due to non-hepatic cause e.g. peptic-ulcer; gastric-carcinoma, Mallory-Weiss-tear, bleeding tendencies due to abnormalities in blood coagulation, EV due to non-cirrhotic cause e.g. Budd-Chiari syndrome,

Schistosomiasis and patients already undergone variceal band ligation or sclerotherapy.

Data Collection Procedure: Endoscopy was performed in the Department of Medicine, University Tertiary-care hospital. Before initiating the study, each patient signed the written informed consent. According to Declaration of Helsinki;¹¹ the data confidentiality was ensure by all researchers. Outcomes of Ultrasonography and Endoscopy regarding splenic-index and portal-vein velocity were compared correlatively.

Assessment of Data: Analysis of collected was done by 2x2 contingency table. Positive findings on Endoscopy and Ultrasonography were considered as true-positive, false-positive cases were considered those; who have positive findings on Ultrasonography and negative findings on Endoscopy, similarly; false-negative cases were considered those; who have negative findings on Ultrasonography and positive findings on Endoscopy. True-negative were those cases; have negative findings on both Ultrasonography and Endoscopy.

Assessments of portal-vein were done by portal-vein diameter, phases in respiration, direction of flow and portal-vein velocity. Mean of portal-vein velocity (PVV) was recorded in centimeter-per-second; device was used to calculate time arranged velocity of flow in 2 to 3 cardiac-cycles, splenic-index (SI) was calculated; SI is the calculation of spleen size in cm² by sonography; it is based on the maximum transverse and longitudinal measurements. Following formula was employed for the determination of splenoportal-index:-

$$SPI \text{ (Splenoportal-Index)} = SI \text{ (Splenic-index)} / PVV$$
 SPI of 3.50 cm/s was taken into consideration for the cut-off value; because SPI value more than 3.0 has better predictability of EV.¹² To validate⁹ splenoportal-index; accuracy, specificity, sensitivity, PPV, NPV, false-positive-rate, false-negative-rate were determined in Pakistani population by a software; named SPSS version 22 (Statistical Package for Social Sciences).

RESULTS

Validity parameters of diagnostic test reveal high accuracy; sensitivity; specificity. Total predictive value (TPV), PPV, and NPV are further validating test. Low false-positive-rate (FPR) and false-negative-rate (FNR) increases the reliance of test. (Table No. 1)

Table No. 1: Validity Parameters of Diagnostic Test

Variables	Accuracy	Sensitivity	Specificity	TPV ^a	PPV ^b	NPV ^c	FPR ^d	FNR ^e
Overall	89%	92%	78%	89%	93%	74%	22%	8%
Male	87%	90%	31%	87%	92%	71%	23%	10%
Female	93%	95%	80%	93%	95%	80%	20%	5%

Total-Predictive-Value; ^a Positive-Predictive-Value; ^c Negative-Predictive-Value; ^d False-Positive-Rate; ^e False-Negative-Rate

Real time scan captures of a patient with liver-cirrhosis; measurement of splenic-index (Figure No. 1) and reduced velocity of portal-vein. (Figure No. 2).

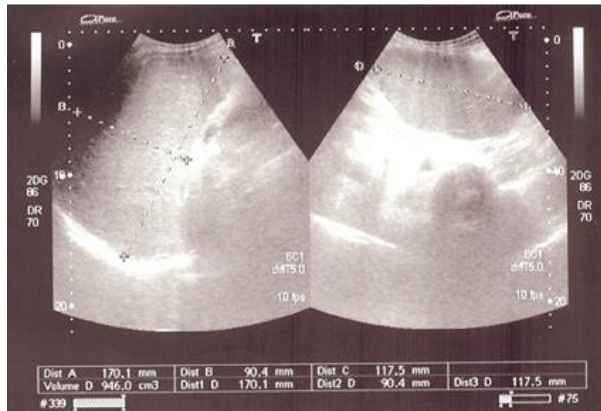


Figure No. 1: Real time scan capture of a patient with splenic (measurement) index 17.1cm x 11.7cm in cirrhosis of Liver.

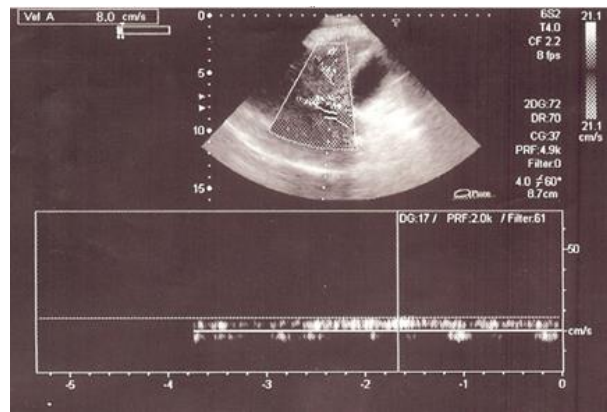


Figure No. 2: Real time scan capture; markedly reduced velocity of portal-vein depicting 8.0cm/sec in a patient with liver-cirrhosis

Significant correlation noted in between Endoscopy and Ultrasonography findings in whole population, males and in females (Table No. 2).

Table No. 2: Comparison for findings of Ultrasonography and Endoscopy

Population	Ultrasound	Endoscopy Findings		Total	Significance
		Endoscopy +ve	Endoscopy -ve		
Overall	Ultrasound +ve	57 (True +ve)	4 (False +ve)	61	p=0.001 ^a
	Ultrasound -ve	5 (False -ve)	14 (True -ve)	19	
	Total	62	18	80	
Male	Ultrasound +ve	36 (True +ve)	3 (False +ve)	39	p=0.001 ^a
	Ultrasound -ve	4 (False -ve)	10 (True -ve)	14	
	Total	40	13	53	
Female	Ultrasound +ve	21 (True +ve)	1 (False +ve)	22	p=0.0088 ^a
	Ultrasound -ve	1 (False -ve)	4 (True -ve)	5	
	Total	22	5	27	

^a p-value is significant at <0.05

DISCUSSION

It is a bleak reality that bleeding from EV carries a considerable risk of mortality. Therefore, in the patients of liver-cirrhosis; it is considered a serious complication. Portal-hypertension in the patients of liver-cirrhosis is due to development of anomaly in liver vasculature. Diagnostic value is high of non-invasive methods in the patients of liver-cirrhosis, who developed EV.¹³ In clinical practice; most of the patients of liver-cirrhosis are advised for endoscopy to determine the risk of bleeding from EV.¹⁴ According to one study; Doppler-ultrasound technique is a reliable tool to evaluate portal-vein hemodynamics; which include flow and pressure in portal-vein.¹⁵ The another study mentioned that platelet count was also a good marker for the diagnosis of EV in the patients of liver-cirrhosis; in addition, some more markers which require further validations in predicting EV included; bilirubinemia, fibrotest and splenomegaly.¹⁶ Current study also validated non-invasive diagnostic tool for early detection of EV by cut-off value of splenoportal-index; accuracy, specificity, sensitivity,

PPV, NPV, FPR, FNR were determined in Pakistani population.⁹ Sensitivity (92% v/s 79.40%⁴), specificity (78% v/s 72%⁴), PPV (93% v/s 81.80%⁴), NPV (74% v/s 68.80%⁴) and accuracy (89% v/s 76.50%⁴) of current study (Table 1) is much higher compared to another study conducted in SIUT (Sind Institute of Urology and Transplantation).⁴ Based upon statistical non-parametric test; significant correlation noted in between Endoscopy and Ultrasonography findings in whole population, male and in female (Table 2); which further proves that Ultrasonography a non-invasive diagnostic tool is not less than endoscopy in terms of accuracy.

The results of current study in Pakistani population suffering from liver-cirrhosis reveals that splenic-index and mean portal-vein velocity are helpful indicators for predicting EV; hence, splenoportal-index might also be dependable tool in further confirming EV. Similarly; Shehata et al. reported that P²/M.S-index = (Platelet count)²/ (%Monocyte fraction X % Segmented Neutrophil fraction) is also another method, which is non-invasive and used in patients of liver-cirrhosis for the diagnosis of EV.¹⁷ Correlation was reported in

between the risk of bleeding and size of varices (Grade 1 – 3); wale-mark presence and the decompensated cirrhosis; due to this reason conference on portal-hypertension conducted by American Association for the study of Liver Diseases and the Baveno VI consensus recommended; all patients diagnosed with liver-cirrhosis should have endoscopy to determine the presence of varices.¹⁸ Conference further recommended that grade of varices should also be determined in these patients and if varices are not present in the first procedure of endoscopy; the procedure of endoscopy should be repeated once in a year in decompensated cirrhosis and every two or three years in subjects with compensated cirrhosis.¹⁸

Grades of EV can also be estimated based upon upper gastro-intestinal endoscopy. According to Paquet's recommendation; Grade 0-I are categorized as No or Mild/Small EV (Group-A); Grade II-III are categorized as Moderate to Severe EV (Group-B).¹⁸ Significant ($p=0.029$) correlation was reported in between index for portal-hypertension and EV by upper gastro-intestinal endoscopy.¹⁸

Recent studies and reviews have shown that there is possibility to identify patients of liver-cirrhosis with portal-hypertension by non-invasive diagnostic tools. However; these tools have merits and demerits. A more advanced non-invasive technique; MRE (Magnetic Resonance Elastography) provides images of liver to identify nodular pathology on the surface of liver.^{18, 19} It is expected that CT (Computed Tomography) and/or MRI (Magnetic Resonance Imaging) will further improve compliance and acceptability in patients and clinicians due to their non-invasiveness.²⁰ Clinically it is useful to identify patients in advance of upper gastro-intestinal bleeding (UGIB) with high risk of esophageal variceal hemorrhages.^{18, 19} Bogdan P. et al.²⁰ also proposed that Ultrasonography hold useful value in indicating worsening of portal-hypertension; progressive changes in circulation of portal system and gradual increase in spleen size; all these changes are linked with the development of varices.²⁰ Therefore; Doppler-ultrasound can be a useful tool. Similarly; Bintintan A. et al. also reported that Doppler indexes can be used to diagnose EV in the patients of liver-cirrhosis.¹²

In current study; SPI of 3.50 cm/s was taken into consideration for the cut-off value; because SPI value more than 3.0 has better predictability of EV.¹² Ritwik C. et al. also concluded that SPI constitute reliable, accurate and sensitive tool in predicting EV.¹⁵ Another researcher and clinician found that SPI contributes significantly ($p=0.002$) as an independent predictor of fibrosis in liver.²¹ Kim MY. et al. suggested that Hepatic Vein-Portal Gradient (HV-PG) is linked with advancement of liver-cirrhosis; risk of bleeding from EV and development of ascites.²² There are some other non-invasive methods used for predicting the

probability of bleeding from EV; these include genetic and serum markers e.g. vascular endothelial growth factor (VEGF) and haplotypes (HO-1); because if HO-1 is absent; it predict low risk of bleeding from EV.^{23, 24}

CONCLUSION

Non-invasive parameters can help in early evaluation of clinical status of liver-cirrhosis patients. Due to non-invasiveness; these tools will decrease financial cost, reduce work-load on endoscopy units, increase patient compliance and acceptance. Endoscopy procedures should only limit to the subjects who have a high risk of having varices in esophagus.

Author's Contribution:

Concept & Design of Study: Ajmaal Jami
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 Final Approval of version: Ajmaal Jami

Conflict of Interest: The study has no conflict of interest to declare by any author.

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