ORIGINAL ARTICLE

Portal vein diameter and spleen size as non-invasive predictors of esophageal varices in patients with viral cirrhosis

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Abstract

Objective: To determine the frequency of esophageal varices in patients with cirrhosis and to evaluate the diagnostic value of mean spleen size and portal vein diameter for non-invasive detection of esophageal varices.

Material and Methhods: This cross-sectional study was conducted at Medical Unit-I, Dr. Ruth K. M. Pfau Civil Hospital, Karachi from July 2016 to January 2017. A total of 200-patients with established cirrhosis were included. The severity of cirrohosis was classified according to Child-Pugh classification. Ultrasound was done to assess portal vein diameter and splenic measurements. Definitive diagnosis of esophageal varices was done on endoscopy. Data were entered and analyzed in SPSS version 21. Descriptive statistics and Chi-square test were applied. P-value ≤0.05 was taken as significant.

Results: There were 132 (66%) males and 68 (34%) females. Out of 200-patients,155 (77.5%) were found to have esophageal varices on endoscopy. Overall, mean spleen size was 14.93 ± 2.99 cm and mean portal vein diameter, 1.23 ± 0.25 cm. Significant association of esophageal varices was observed with age (p<0.001), duration of cirrhosis (p=0.010), Child-Pugh class (p=0.039) and etiology of liver cirrhosis (p<0.001) while no significant association was observed with gender (p=0.411), BMI (p=0.300), residence (p=0.252), socio-economic status (p=0.262) and smoking (p=0.359). Statistically significant differences were found in mean spleen size (p<0.001) and portal vein diameter(p<0.001) among patients with or without esophageal varices.

Conclusion: In conclusion, spleen size and portal vein diameter may be used as reliable non-invasive predictors for the presence of esophageal varices among cirrhotic patients in resource-constrained setting.

Received
date: 11th January, 2019
Accepted
date:19th October, 2019

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Keywords: Esophageal varices, cirrhosis, spleen size, portal vein diameter, Child-Pugh classification, cirrhosis of liver

Introduction:

Cirrhosis is end-stage liver disease resulting from many causes, which in turn results in disruption of normal liver architecture. Cirrhosis results from necrosis of liver cells followed by fibrosis and nodule formation. Clinically, most patients are asymptomatic or have mild fatigue, and liver synthetic function is usually preserved. Others present with advanced liver disease complicated by variceal bleeding, ascites, coagulopathy, or encephalopathy.[1-4]

WHO has estimated that cirrhosis is responsible for 1.1% of all deaths worldwide. Cirrhosis is 10th most common cause of death in USA.[3] In cirrhotic patients, development of portal hypertension leads to ascites and its complications, such as spontaneous bacterial peritonitis and esophageal varices.[4]

In portal hypertension, if pressure rises above 20 mmHg, collaterals develop. Portal hypertension is caused by a combination of two simultaneously occurring hemodynamic processes:

(1) increased intrahepatic resistance to the passage of blood flow through the liver, and (2) increased splanchnic blood flow. Portal hypertension is directly responsible for variceal hemorrhage and ascites. Variceal hemorrhage is an immediate life-threatening complication with a 20–30% mortality.[5]

The chronic liver disease (CLD) is a common public health problem in South Asia. Increasing prevalence needs to be evaluated and updated from time to time for Hepatitis-B and C, as progressively more and more people are being affected by this dangerous disease.[6,7] In an area based study, 31% of the cases had hepatitis-B core antibodies and 4.3% had hepatitis-B surface antigen (HBsAg) positivity.[7] The burden of HCV-associated CLD in Pakistan has also increased and additional current data shows about 60-70% of patients with CLD to be positive for anti-HCV antibodies.[7]

Patients with CLD eventually progress to cirrhosis of liver and its associated problems like portal hypertension.[8,9] Development of esophageal varices (EVs) is one of the major complications of portal hypertension.[8,10] In the cirrhotic patients, chronic upper gastrointestinal (GI) bleeding is common because of portal hypertension seen in about 30% to 40% of cases.[11]

Esophageal varices were detected in 36 (76.6%) of cases in the study by Prihartini et al.[12] In this study, portal vein diameter of 1.15 cm (75% sensitivity; 54.5% specificity) and an antero-posterior splenic measurement of 10.3 cm (83.3% sensitivity; 63.6% specificity) were predictive factors for EVs in patients with liver cirrhosis. Degree of EVs in 36 study subjects was 1st degree EVs in 10 subjects (27.8%), 2nd degree in 23 subjects (63.9%), and 3rd degree in 3 subjects (8.3%).[12]

Gastroesophageal varices are present in almost half of patients with cirrhosis at the time of diagnosis.[14,15] Esophageal variceal bleeding is a potentially deadly complication in patients with liver cirrhosis with varying degrees of prevalence. As stated previously, the study conducted by the Prihartini et al. showed the prevalence of EVs to be 76.6%,[12] while Engy et al. found a prevalence of EVs of 91.7%.[13]

This study is an exploratory study to determine the role of non-invasive tests in predicting the presence of EVs in patients with viral cirrhosis in Pakistan. There are very few studies on this topic in Pakistan and this will add to the evidence base. If proved useful, this will be very cost-effective approach, as it involves using only the ultrasound technique which is easily available both in remote rural and urban areas of Pakistan.

This study is aimed to identify simple, non-invasive parameters, i.e. portal vein diameter and spleen size to predict the presence or absence of EVs, as non-invasive assessment of EVs may improve the management of patients with cirrhosis and decrease both the medical and financial burden related to screening.

Material and Methods:
This cross-sectional study was conducted at Medical Unit-I, Dr. Ruth K. M. Pfau Civil Hospital, Karachi from July 2016 to January 2017. The inclusion criteria were patients with cirrhosis of any duration, of any gender, with age ranging from 25 to 60 years and without history of upper GI hemorrhage. The exclusion criteria were; patients with previous history of variceal bleeding confirmed through the medical record, patients already being treated with medicines, patients receiving medicines as prophylactic measure for variceal bleeding, patients who underwent sclerotherapy or band ligation, patients suffering from hepatocellular carcinoma confirmed by CT scan, patients with previous history of porto-systemic anastomosis or portal vein thrombosis and ascites because of etiologies other than cirrhosis and patients refusing to participate in the study. Written informed consent was obtained from all patients for inclusion in the study. The study was conducted according to the ethical principles set by declaration of Helsinki.

All demographic details, including name, age and gender as well as clinical and laboratory

Table 1: *The baseline demographic and clinical variables of the study patients (n=200)*

Variables	Frequency	Percent
Age groups:		
≤ 50 years	75	37.5%
>50 years	125	62.5%
Gender:		
Male	132	66.0%
Female	68	34.0%
Body mass index:		
Normal	8	4.0%
Obese	192	96.0%
Duration of cirrhosis:		
≤ 7 years	104	52.0%
>7 years	96	48.0%
Residence:		
Urban	114	57.0%
Rural	86	43.0%
Smoking:		
Yes	108	54.0%
No	92	46.0%
Socio-economic status:		
Low	38	19.0%
Middle	115	57.5%
High	47	23.5%
Child-Pugh Class:		
A	122	61.0%
B	58	29.0%
C	20	10.0%
Etiology of liver cirrhosis:		
Hepatitis B	72	36.0%
Hepatitis C	78	39.0%
Hepatitis B+C	50	25.0%

Table 2: *Frequency distribution of different variables (n=200)*

Variables	Frequency	Percent
Esophageal varices		
Present	155	77.5%
Absent	45	22.5%
Grades of Esophageal varices		
Grade-I	32	20.6%
Grade-II	55	35.5%
Grade-III	48	31.0%
Grade-IV	20	12.9%

data were collected. All consecutive patients who fulfilled the inclusion criteria were included in study. Hepatitis-B and C were diagnosed by the standard laboratory methods or already diagnosed cases but who were treatment-native were also included in the study.

After enrollment of patients, ultrasound examination was performed to assess portal vein diameter and antero-posterior splenic measurements by an experienced sonologist with experience of more than 3-years. The subjects were classified according to Child-Pugh classification. EVs were assessed through the endoscopy as per standard guidelines.[16]

Data were entered and analyzed through SPSS-version 21. Mean and standard deviation (SD) were used for quantitative variables, i.e. age, body mass index (BMI), duration of cirrhosis, spleen size, portal vein diameter while frequency and percentages were used for qualitative variables, i.e. gender, Child-Pugh class, etiology of liver cirrhosis, smoking status, residence, socio-economic status and EVs and grades of EVs.

EVs were stratified for age, gender, residence, BMI, duration of cirrhosis, Child-Pugh class, etiology of liver cirrhosis, smoking status, and socio-economic status. Post-stratification chi-square test was applied for qualitative outcome (EVs) and independent t-test was applied to compare spleen size and portal vein diameter in patients with and without varices by taking p-value ≤0.05 as significant.

Results:

A total of 200-adult patients with established cirrhosis of liver and belonging to either gender were included and analyzed in this study. The results showed that there were 132 (66%) males and 68 (34%) female patients. The overall mean age of study subjects was 52.26 ± 6.65 years.

The overall mean weight of study subjects was 81.14 ± 5.44 Kg and mean height was 1.63 ± 0.10 m. The overall mean BMI of study subjects was 30.77 ± 3.32 kg/m^2. The overall mean duration of cirrhosis was 7.39 ± 1.41 years. Out of 200 study subjects, 57% were from urban areas. Most of the study subjects (57.5%) were from middle class of society. Among 200 study subjects, 54% patients were smokers. Results of Child-Pugh classification showed that class-A was 61%, class-B was 29% and class-C was 10%, as shown in table-1. Hepatitis-B was found positive in 36% study subjects while hepatitis-C in 39% subjects, and 25% were found positive forboth Hepatitis-B and C.

In our study, 155 (77.5%) study subjects were diagnosed with EVs. The mean spleen size was 14.93 ± 2.99 cm and mean portal vein diameter-was 1.23 ± 0.25 cm. Most common grade of EVs was grade-II. Statistically significant differences were found in mean spleen size (p<0.001) and portal vein diameter (p<0.001) among those with EVs vs. those without EVs.

The results showed that there was significant association of EVs with age (p<0.001), duration of cirrhosis (p=0.010), Child-Pugh class (p=0.039) and etiology of liver cirrhosis (p<0.001) while no significant association was observed with gender (p=0.411), BMI (p=0.300), residence (p=0.252), socio-economic status (p=0.262) and smoking (p=0.359).

Discussion:

EVs develop as a consequence of portal hypertension in patients with CLD and are present in approximately 50% of patients with cirrhosis of the liver. The grade of EVs often correlates with the severity of the liver disease. While approximately 85% of individuals with Child-Pugh class-C cirrhosis have varices, they are present in only 45% of those with Child-Pugh class-A cirrhosis.[16]

The rate of development of new varices and increase in grades of varices is 8% per year; the former is largely predicted by a hepatic venous pressure gradient (HVPG) exceeding 10 mmHg[17] and the latter by the presence of decompensated cirrhosis, alcohol etiology and red wale signs.[18]

Large size varices, the presence of red color signs, severe liver disease and portal pressure greater than 12 mmHg[19] predict greater risk of bleeding. Mortality rate of an episode of EVs bleeding is approximately 20% at six weeks.[20-21]

Several studies in the past have shown independent parameters like splenomegaly, ascites, spider naevi, Child-Pugh's class, platelet count, prothrombin time/activity, portal vein diameter, platelet count/-spleen diameter ratio, serum albumin, and serum bilirubins significant predictors for the presence of EVs.[22-24]

Giannini et al[1] proposed the platelet count-spleen diameter ratio of ≤ 909, as an accurate non-invasive marker for the presence of EVs. This was further validated in a multicenter trial.[2] A study by Agha et al[3] from Pakistan, made identical observations in the same subset of patients. Sen et al. found the platelet count-spleen diameter ratio of ≤ 650 as a sensitive non-invasive marker in HCV- related cirrhosis.[4]

In one study Child-Pugh class-B and C, low platelet count and spleen diameter emerged as significant predictors for the presence of large EVs. Of these variables, Child-Pugh class-B and C missed less than 10% of patients with large varices and saved one endoscopy procedure for every six procedures performed. 4 out of 42 patients in Child-Pugh class-A had large varices. All the four patients had either a platelet count of < 90,000/μl or spleen bipolar diameter >160 mm.[5]

Studies on non-endoscopic assessment for the presence and grades of varices from neighbouring country are few. Amarapurkar et al[22] reported that splenomegaly alone was a significant predictor for the development of large EVs. Sharma et al, in a prospective study, observed that splenomegaly and platelet count were independent predictors for the presence of large varices.[6]

The American Association for the Study of Liver Disease (AASLD) and the Baveno IV Consensus Conference on portal hypertension recommended that all cirrhotic patients should be screened for the presence of EVs when liver cirrhosis is diagnosed.[17] However, subjecting all patients with cirrhosis to screening endoscopy may not be cost-effective.[18]

A more affordable approach for screening would be possible if patients at low or high risk of having EVs could be identified from easily obtainable clinical variables. Investigators have attempted to identify characteristics that non-invasively predict the presence of varices. These studies have shown that bio-chemical, clinical and ultrasonographic parameters alone or in variable combination have good predictive

power for non-invasively assessing the presence of EVs.[17, 18]

Conclusion:

The measurement of portal vein diameter and spleen size using ultrasonography is easily achievable, reproducible and non-invasive technique and can be routinely performed on patients with cirrhosis. The portal vein diameter (>13mm) and spleen size >15 cm on ultrasonography are an independent non-invasive predictor of presence of esophageal varices (EVs) in patients with cirrhosis with portal hypertension.

Conflict of interest: None

Funding source: None

Role and contribution of authors:

Dr. Rakesh Panjwani, collected the data, references and did the initial writeup.

Dr. Wish Lal Sunder, collected the referenes and helped in interpretation of data.

Dr. Pawan Kumar, critically review the article and made final changes

Dr. Waqas Hussain, collected the references and helped in discussion and result writing

Dr. Vijay Kumar, collected the data and helped in introduction writing.

Dr. Sundeep Kumar, collected the references and helped in methodology writing.

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