Original article

Evaluation of right liver lobe size to serum albumin concentration ratio in predicting the presence of esophageal varices in cirrhotic patients taking endoscopy as gold standard

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ABSTRACT

Background: Cirrhosis with its complication is a major health concern in Pakistan. Endoscopy is an invasive and expensive modality for screening for esophageal varices which is one of the most common complication of liver cirrhosis. Research is being conducted to explore non-invasive markers that can replace this invasive technique. We aimed to evaluate the predictive value of the ratio of the size of the right lobe of liver to serum albumin concentration in prediction of the presence of esophageal varices.

Methods: It was a cross-sectional study conducted at the Medicine Department, Ghurki Trust Teaching Hospital, Lahore from January 4 till July 31. The study included 297 patients of all the genders, aged 20-70 years, diagnosed cases of liver cirrhosis for at least 6 months and having suspected esophageal varices on right liver lobe size to serum albumin ratio >4.1. All the patients were subjected to upper GI endoscopy to confirm predicted varices. Data was analyzed using SPSS 23.0. PPV of the ratio was calculated. Post-stratification chi square was used to find association (p value <0.05 as significant).

Results: The patients had a mean age of 51.5 ± 9.2 years with 180 (60.6%) male and 117 (39.4%) female patients. Diagnosis of esophageal varices was confirmed in 225 (75.8%) patients on endoscopy. There were 225 true positive and 72 false positive cases. Positive predictive value was 75.8%.

Conclusion: The positive predictive value of the ratio of the size of the right liver lobe to serum albumin was statistically significant in predicting the presence of esophageal varices on upper GI endoscopy. These findings were not dependent on the patient's age, BMI, gender, duration of disease or serum bilirubin level.

Keywords:

Cirrhosis, Esophageal Varices, Right Liver Lobe Diameter to Serum Albumin Ratio

INTRODUCTION

Liver diseases remain a major health concern in Asia-Pacific region.[1] According to the third round of 2015 Global Health Estimates (GHE) by WHO, liver diseases are responsible for more deaths in Asia-Pacific region compared to the USA and Europe. [1] The major cause of liver related deaths is cirrhosis followed by liver cancer.[1,2] The main cause of cirrhosis varies depending on the geographical area. Alcoholism, hepatitis C and non-alcoholic fatty liver disease (NAFLD) are the main causes in the West. Whereas, chronic hepatitis B is the main cause in Asia and the Pacific region. [2] In Pakistan, hepatitis C is particularly found as a major issue.[1] Environmental and/or genetic factors are also involved in the etiopathology of cirrhosis. [3]

Regardless of the nature of initial pathology, the cellular mechanisms causing hepatic cirrhosis are thought to be the same.[3] The sustained stimulation of quiescent hepatic stellate cells (HSC's) is responsible for the accumulation of collagen and extracellular matrix (ECM) components. This leads to the destruction of liver architecture and a decrease in hepatic function. [4] Cirrhosis is generally considered to be irreversible, although reversibility is shown in some studies when the causative agent is removed. The mechanism responsible for myofibroblasts inactivation is yet to be discovered. [5]

Until decompensation, most patients suffering from cirrhosis experience no symptoms. Decompensation can manifest as ascites, variceal bleeding secondary to portal hypertension, hepatic encephalopathy or spontaneous bacterial peritonitis.[6] Almost one-half of the patients suffering from cirrhosis are found to have gastroesophageal varices and the lifetime incidence is as high as 90 percent. [7] Despite the significant improvement in diagnostic and therapeutic modalities, mortality of the hemorrhage from

Conflict of interest: The authors declared no conflict of interest exists.
Citation: Zahoor S, Raza HA, Ali W, Ijaz M. Evaluation of right liver lobe size to serum albumin concentration ratio in predicting the presence of esophageal varices in cirrhotic patients taking endoscopy as gold standard. J Fatima Jinnah Med Univ. 2022; 16(3):119-123.

DOI: https://doi.org/10.37018/DGGR3020

gastroesophageal varices remains high.[8] Therefore, the important aspects of management include prevention, early identification of this serious complication and halting the disease progression and delaying decompensation along with cost effectiveness.[9]

In patients with cirrhosis, endoscopy is required for screening for the gastroesophageal varices each year.[10] Endoscopy is an invasive method that is uncomfortable and costly as well. Sedation is given to the patients that further causes complication. Recurrent Endoscopy for screening will put burden on the patient especially in developing countries and will also increase the risk for bacterial infections. Thus, there is always a need to identify non-invasive means to detect the varices. There are several noninvasive tools that have been developed to predict esophageal varices. These includes right liver lobe diameter (RLLD)/albumin ratio, albumin-bilurubin (ALBI) score, left liver lobe diameter (LLLD)/albumin ratio, and platelet count/spleen diameter (PC/SD) ratio.[11,12] A study conducted at the Medicine Department, Pakistan Atomic Energy Commission (PAEC), has established the usefulness of right liver lobe diameter (RLLD) to serum albumin (SA) ratio for this purpose in high probability patients.[7] Since the predictive values change with the prevalence of disease and there is no data available to define this relation in the local population, the present study will describe its utility and define this relation in the local community.

MATERIALS AND METHODS

It was a prospective cross sectional study conducted at the department of Medicine, Ghurki Trust Teaching Hospital, Lahore for a duration of six months from January 4 till 31, 2021. Total 297 patients were included in the study. Sample size was calculated with 95% confidence interval, 5% margin of error and PPV of 73.9%.[13]After getting permission from the ethical review board of the institution, patients were selected by non-probability technique with consecutive sampling. Patients of all the genders with an age range of 20-70 years having diagnosed CLD (Coarse Shrunken liver) on ultrasound by consultant ultrasonologist due to any cause for at least 6 months and predicted to have esophageal varices based on RLLD/SA ratio (greater than 4.1)[13] were included in the study. The ratio was calculated by taking right lobe live diameter in cm as numerator and serum albumin in mg/dl as denominator and patients having a cut off value > 4.1 were labeled to have esophageal varices. Those patients who had focal lesion on ultrasound suggestive of tumour, previously had variceal bleeding or esophageal varices on endoscopy, had been taking beta blockers for >2 weeks in the last 2 months and has also not been injected with albumin in last 1month or had undergone shunt procedure for portal hypertension as per clinical record were excluded from the study. Patients having renal disease, blood clotting disorders, HIV or critical cardiovascular disease were also omitted from the study.

Informed consent was taken from each participant. Demographics variables like age, gender etc. and history of disease duration was also noted. 5ml of blood was drawn using aseptic measures and was sent to the laboratory of the hospital for serum albumin levels and serum bilirubin levels in mg/dl. Right lobe of liver diameter was measured on ultrasound in centimeters (cm) by consultant radiologist having experience of more than 5 years in the field. 297 patients were counseled, explained the details of the study and were enrolled. They underwent endoscopy under local anesthesia of the pharynx. Protrusion of dilated veins (>50.0% of normal diameter) into the lumen of esophagus seen on the endoscope was labeled as esophageal varices (True Positive).[12,13] All the data including the demographics were noted into the attached proforma. To eliminate bias, all the laboratory investigations were acquired from the same laboratory (Hospital Lab), all the ultrasonographic measurements of the right lobe of liver were taken by the same consultant of the radiology department and all the endoscopies were performed by the same consultant of the medical department. The confounding variables were controlled by exclusion.

The data was entered and analyzed in SPSS version 23.0. Numerical variables like age, duration of disease, serum bilirubin level etc. were presented by mean ± SD. Categorical variables like gender etc. were presented as frequency and percentage. Positive predictive value was calculated and was presented as percentage. The data was stratified for BMI, age, serum bilirubin level, gender, and duration of CLD to address effect modifiers. After stratification, the chi-square test was applied upon the data with p value ≤ 0.05 as significant.

RESULTS

Total 297 patients were enrolled. Mean age was 51.5 ± 9.2 years (range: 38 to 70 years). Most common age group was 38-54 years (61.6%), then 55-70 years (38.4%). 180 (60.6%) male and 117 (39.4%) female patients were included giving a male to female

Table 1: Baseline characteristics of the study sample

Characteristics	(Mean and Frequencies) Participants (n=297)
Age (in years)	51.5±9.2
38-54 years	183 (61.6%)
55-70 years	114 (38.4%)
Gender	
Male	180 (60.6%)
Female	117 (39.4%)
BMI (Kg/m²)	26.7±3.6
20-25 Kg/m²	110 (37.0%)
25-30 Kg/m²	124 (41.8%)
30-35 Kg/m²	63 (21.2%)
Duration of Disease (months)	12.3±4.1
6-12 months	152 (51.2%)
813-19 months	145 (48.8%)
Serum Bilirubin Level (mg/dl)	3.8±1.3
1.9-4.0 mg/dl	176 (59.3%)
4.1-6.2 mg/dl	121 (40.7%)

Table 2 : Frequency of varices found on endoscopy n=297

Esophageal Varices	Frequency (n)	Percent (%)
Yes (True Positive)	225	75.8
No (False Positive)	72	24.2
Total	297	100.0
PPV = 225 x 100	225 + 72	PPV = 75.8%

ratio1.5:1. Cirrhosis had been present in the patients from 6 months to 19 months with a mean of 12.3 ± 4.1 months. The level of bilirubin in the serum ranged from 1.9 mg/dl to 6.2 mg/dl, with a mean value of 3.8 ± 1.3 mg/dl whereas the BMI of these patients varied from 20.6 kg/m2 to 33.4 kg/m2 with a mean value of 26.7 ± 3.6 kg/m2. (Table1)

Diagnosis of esophageal varices was confirmed in 225 (75.8%) patients on endoscopy. Thus there were 225 true positive and 72 false positive cases. It yielded a positive predictive value of 75.8% for RLLD/SA ratio in predicting esophageal varices in patients suffering from liver cirrhosis. (Table 2)

Similar positive predictive value was noted across various subgroups based on gender, age, BMI, serum bilirubin level and duration of disease as shown in Table 3.

DISCUSSION

The gold standard test for detecting esophageal varices is upper GI endoscopy. Being an invasive procedure, it is costly, demands expertise and is not free of complications. Studies are being conducted to look for noninvasive markers that can indicate the presence of esophageal varices. Parameters like platelet count and spleen size have been assessed. Platelet count to spleen diameter ratio is a good predictor for the assessment of severity of esophageal varices. [14] So far, no non-invasive marker for predicting the varices has been studied extensively. [15]

A recent study has established the usefulness of RLLD/SA ratio in this regard. [13] However there is no evidence available to describe the PPV of this ratio for our local population. This study was conducted with the aim to describe this relation for the local community. PPV of RLLD/SA ratio in predicting the presence of esophageal varices is 75.8% in this study. A similar value of 73.9% has been mentioned in the study by Salem and coauthors. [13] Another recent study evaluated PPV of the RLLD/ SA ratio to be 92.98% which is even more than that found in present study.

The patients had a mean age of 51 ± 9.2 years. This is in line with the mean age in other regional and international studies. [16-20] However, relatively younger age (40.4 to 45.6 years) has been reported in some studies from India, Sudan and Germany .[21] Male preponderance (1.5:1) found in this study is similar to other studies.[23,24] However female predominance (1:1.5) is reported in a local study at Dow University Hospital, Karachi. [18] The mean levels of serum bilirubin in present study is 3.8 ± 1.3mg/dl and mean value of BMI is 26.7 ± 3.6 kg/m². This is similar to the findings of Zou and co-authors. [25]

These ratios including platelet count to spleen size and RLLD/SA, though represent a promising potential path to replace the invasive procedure of endoscopy, are at present not enough to replace endoscopy. An interesting approach to these findings might be to use these parameters to assess the need of endoscopy in patients having a low probability or decreased risk of having esophageal varices. Moreover, this ratio can be used to assess the interval between endoscopies in cirrhotic patients having regular screening for esophageal varices. Thus, further work should be conducted in this path.

This study is limited by the fact that we have not categorized the patients depending upon the Child-Pugh class of cirrhosis. RLLD/SA ratio might get distorted with decreasing hepatic function .The strength of this study lies in its larger sample size of 297 and adjusted analysis which has been done to control for various confounders. In our study, even after stratifying for patients' gender, BMI, age, duration of illness and serum bilirubin level, we found the same PPV of 75.8% of RLLD/SA ratio in predicting the presence of esophageal varices among patients suffering from cirrhosis. This is the first study which reports this relation in our local population. There is still a need to stratify the patients depending upon their Child-Pugh class and to describe the positive predictive value for

Table 3: Stratification of positive predictive value across various groups

Characteristics	Diagnosis on Endoscopy		Total	PPV	p-value
	True Positive (n=225)	False Positive (n=72)			
Age groups					
38-54 years	139 (76.0%)	44 (24.0%)	183 (100%)	76.0%	0.919
55-70 years	86 (75.4%)	28 (24.6%)	114 (100%)	75.4%	
Gender					
Male	137 (76.1%)	43 (23.9%)	180 (100.0%)	76.1%	0.860
Female		88 (75.2%)	29 (24.8%)	117 (100.0%)	75.2%
BMI					
20-25 Kg/m^2	83 (75.5%)	27 (24.5%)	110 (100%)	75.5%	0.994
25-30 Kg/m^2	94 (75.8%)	30 (24.2%)	124 (100.0%)	75.8%	
30-35 Kg/m^2	48 (76.2%)	15 (23.8%)	63 (100.0%)	76.2%	
Duration of disease					
6-12 months	115 (75.7%)	37 (24.3%)	152 (100.0%)	75.7%	0.967
13-19 months	110 (75.9%)	35 (24.1%)	145 (100.0%)	75.9%	
Serum bilirubin level					
1.9-4.0 mg/dl	133 (75.6%)	43 (24.4%)	176 (100.0%)	75.6%	0.927
4.1-6.2 mg/dl	92 (76%)	29 (24%)	121 (100%)	76%	

each class separately. Such a study should definitely be conducted in future.

CONCLUSION

Ratio of right liver lobe diameter to serum albumin value carries a high positive predictive value in assessment of the presence of esophageal varices in known cases of hepatic cirrhosis. Thus, this non-invasive marker can be considered a potential replacement of upper gastrointestinal endoscopy particularly in those patients who have low probability of the presence of varices. This will make the screening process easier for patients and less burdensome for the health sector.

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