Original Article

Prediction Of Oesophageal Varices In Cirrhotic Patients By Prothrombin Time As A Non-invasive Marker

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Objective: The objective of the study was to determine the diagnostic accuracy of prothrombin time for the non invasive diagnosis of esophageal varices keeping upper gastrointestinal endoscopy as Gold Standard.

Methods: The study was conducted in Medical unit 4, Services Hospital Lahore over a period of 6 months. It is a cross-sectional study

Results: In our study, 43.5%(n=87) were between 12-30 years and 56.5%(n=113) were between 31-60 years, mean±sd was calculated as 39.90±12.29 years, 43.5%(n=87) were male and 56.5%(n=113) were females, frequency of esophageal varices keeping upper gastrointestinal endoscopy as gold standard was recorded in 57%(n=114) while 43%(n=86) had no findings of the morbidity, diagnostic accuracy of prothrombin time for the non-invasive diagnosis of esophageal varices keeping upper gastrointestinal endoscopy as gold standard 53%(n=106) true positive, 2%(n=4) false positive, 4%(n=8) false negative and 41%(n=82) as true negative. Whereas specificity, sensitivity, positive predictive value, negative predictive value and diagnostic accuracy was calculated as 92.98%, 95.35%, 96.36%, 91.11%, and 94% respectively.

Conclusion: We concluded that the predictive value of prothrombin time for presence of oesophageeal varices is a higher and it is a useful non-invasive diagnostic modality.

Keywords: Esophageal varices, non-invasive diagnosis, prothrombin time, diagnostic accuracy

Introduction

Cirrhosis is the end stage of every chronic liver disease, resulting in formation of fibrous tissue, disorganization of liver architecture, and nodule formation, which interferes with liver function and results in portal hypertension.[1]

Liver damage from chronic liver can disturb balance between clotting and fibrinolysis. The causes are multiple: quantitative and qualitative platelet defects; decrease production of coagulation factors and inhibitor of coagulation; vitamin K deficiency; synthesis of abnormal clotting factors; decreased clearance of activated factors; hyperfibrinolysis and disseminated intravascular coagulation.[2]These coagulation abnormalities can predispose patients from minor localized bleeding to massive life threatening haemorrhage or thrombus formation.[3]

Oesophageal varices are present at diagnosis in approximately 50% of cirrhotic patients, being more common in Child-Pugh class C. The greatest bleeding risk is seen in large varices classified as being >5mm diameter and is also influenced by liver disease severity as assessed by Child-Pugh score, and by the presence of red wale markings on varices at endoscopy. Therefore, these factors should also be taken into consideration to classify "high-risk varices.[4]

Variceal hemorrhage is a leading cause of morbidity and Mortality in cirrhosis.[5] Therefore, it is recommended that patients with cirrhosis should undergo endoscopic screening for Esophageal Varices (EV) at the time of diagnosis.[6]

In this study, the non invasive marker prothrombin time will be correlated with presence of oesophageal varices in patients with liver cirrhosis as compared to Upper gastrointestinal endoscopy which is Gold Standard. This study didn't evaluate the direct correlation between Prothrombin time and presence of oesophageal varices.[10]

The available data shows variations in results[10,11] so I want to study so that if significant results come then interventions can be made to diagnose varices noninvasively and to assess the predictive value of prothrombin time for presence of oesophageeal varices. Thus we can prevent life threatening variceal bleeding. This will also prove a diagnostic tool for stratification of patients regarding the presence of varices.

Methods

The study was conducted in Medical unit 4, SHL.200 patients was sample size keeping sensitivity 60.4%

diagnosis of oesophageal varices with 95% confidence interval and 10% margin of error with prevalence of varices 50.8%[7,9] by taking endoscopy as gold standard. It was non probability consecutive sampling.It is a cross-sectional study and of chronic liver disease showing coarse liver eco. Patients of 12 60 years of age and both genders. Patients presenting with variceal bleed. Patients taking non selective beta blockers and/or nitrat and patients who have received any therapeutic intervention for their varices like banding or injection sclerotherap. Patients who refuse to undergo upper gastrointestinal Endoscopy were included. 200 Patients with coarse liver ecotexture on abdominal ultrasound were selected from emergency department of SIMS/SHL and Prothrombin time was determined by using blood sample of patient by emergency laboratory, SHL. After taking informed consent these patients were booked for diagnostic upper gastrointestinal endoscopy at a later date. Upper gastrointestinal endoscopy was performed in these selected patients and presence or absence of oesophageal varices was documented. All those patients who did not fulfill inclusion criteria were rejected so that bias could be controlled.

Data analysis:

Data was entered and analyzed using SPSS 15. Quantitative variables like age were expressed by using mean±SD. Qualitative variables like gender, presence or absence of varices and prothrombin time was expressed using frequency and percentages. A 2x2 contingency table was generated to evaluate sensitivity, specificity, PPV, NPV and accuracy of prothrombin time in the prediction of oesophageal varices by taking endoscopy as gold standard.

Results

A total of 200 cases fulfilling the inclusion/exclusion criteria were enrolled to determine the diagnostic accuracy of prothrombin time for the non invasive diagnosis of esophageal varices keeping upper gastrointestinal endoscopy as Gold Standard.

Age distribution of the patients was done which shows that 43.5%(n=87) were between 12-30 years and 56.5%(n=113) were between 31-60 years, mean±sd was calculated as 39.90±12.29 years. **Table No. 1.**Gender distribution of the patients was done which shows that 43.5%(n=87) were male and 56.5%(n=113) were females. **Table No. 2**

Frequency of esophageal varices keeping upper gastrointestinal endoscopy as gold standard was recorded in 57%(n=114) while 43%(n=86) had no findings of the morbidity. **Table No. 3** Diagnostic accuracy of prothrombin time for the non-invasive diagnosis of esophageal varices keeping upper gastrointestinal endoscopy as gold standard 53%(n=106) true positive, 2%(n=4) false positive, 4%(n=8) false negative and 41%(n=82) as true

Table-1: Distribution of patients by age (n=200).

Age (Years)	No. Of Patients	Percentage
12-30	87	43.5
31-60	113	56.5
Total	200	100
Mean±sD	39.90±12.29	

Table-2: Distribution of patients by gender (n=200).

Age (Years)	No. Of Patients	Percentage
Male	87	43.5
Female	113	56.5
Total	200	100

Table-3: Frequency of esophageal varices keeping upper gastrointestinal endoscopy as gold standard (n=200).

Esophageal varices	No. Of Patients	Percentage
Yes	114	57
No	86	43
Total	200	100

Table-4: Diagnostic accuracy of prothrombin time for the non invasive diagnosis of esophageal varices keeping upper gastrointestinal endoscopy as gold standard

Prothrombin Time	Upper gastrointestinal endoscopy Positive	Negative	Total
Positive	True positive (a)	False positive (b)	a+b
	106 (53%)	4 (2%)	110 (55%)
Negative	False negative (c)	True negative (d)	c+d
	8 (4%)	82 (41%)	90 (45%)
Total	a+c 114 (57%)	a+c 86 (43%)	200 (100%)

Sensitivity = 92.98%
Specificity = 95.35%

Negative. Whereas specificity, sensitivity, positive predictive value, negative predictive value and diagnostic accuracy was calculated as 92.98%, 95.35%, 96.36%, 91.11%, and 94% respectively. **Table No. 4**

Discussion

Variceal hemorrhage is a leading cause of morbidity and mortality in cirrhosis.[11] Primary prophylaxis with nonselective beta blockers and endoscopic band ligation may reduce the risk of variceal bleeding.[12] Therefore, it is recommended that patients with cirrhosis should undergo endoscopic screening for esophageal varices (EV) at the time of diagnosis.[13] If no varices are observed on initial endoscopy in patients with compensated cirrhosis, endoscopy should be repeated in 3 years; in decompensated cirrhotic patients, it should be repeated annually.[14] As a result of the cost and invasive nature of endoscopic screening, there is interest in developing a noninvasive predictor of the presence and development of varices that would decrease the number of endoscopies performed.[11] Predicting the presence of esophageal varices by non-invasive means would restrict the performance of endoscopy to those patients with a high probability of having varices.

In our study, the non invasive marker prothrombin time was correlated with presence of oesophageal varices as compared to Upper gastrointestinal endoscopy which is Gold Standard to determine that if significant results come then interventions can be made to diagnose varices noninvasively and to assess the predictive value of prothrombin time for presence of oesophageeal varices.

In our study, 43.5%(n=87) were between 12-30 years and 56.5%(n=113) were between 31-60 years, mean±sd was calculated as 39.90±12.29 years, 43.5%(n=87) were male and 56.5%(n=113) were females, frequency of esophageal varices keeping upper gastrointestinal endoscopy as gold standard was recorded in 57%(n=114) while 43%(n=86) had no findings of the morbidity, diagnostic accuracy of prothrombin time for the non-invasive diagnosis of esophageal varices keeping upper gastrointestinal endoscopy as gold standard 53%(n=106) true positive, 2%(n=4) false positive, 4%(n=8) false negative and 41%(n=82) as true negative. Whereas specificity, sensitivity, positive predictive value, negative predictive value and diagnostic accuracy was calculated as 92.98%, 95.35%, 96.36%, 91.11%, and 94% respectively.

Our findings are in agreement with a study showed Sensitivity of 60.4% and Specificity of 91.7%8 though sensitivity in our study was higher than this study but specificity was closely related to our study, our findings are in contrast with a study showing that prothrombin time was found to have Sensitivity of 61.8% and Specificity of 81.8% in a study done in china.[7] Wan-dong Hong and others revealed that a tree model that was consisted of spleen width, portal vein diameter and prothrombin time was developed by classification and regression tree analysis achieved a diagnostic accuracy of 84% for prediction of large esophageal varices.

Pilette C and co-authors studied the diagnostic accuracy of non-endoscopic means for the diagnosis of esophageal varices and recorded that prothrombin index, diagnosis of large esophageal varices (grades 2±3): diagnostic accuracy was globally 71%, and 72% with 3 variables: platelet count, prothrombin index, spider naevi and concluded that using a few non-endoscopic criteria, esophageal varices can be correctly diagnosed in 81% of patients with chronic liver disease and in 71% of patients with cirrhosis. These results show that the non-invasive screening of patients who are candidates for the primary prevention of variceal bleeding is possible, but should be improved before being used in a clinical setting.

However, considering the abvoe facts, we are of the view that significant accuracy emphases that interventions can be made to diagnose varices noninvasively and the predictive value of prothrombin time for presence of oesophageeal varices is a useful diagnostic modality. Thus we may prevent life threatening variceal bleeding. It also proves to be a diagnostic tool for stratification of patients regarding the presence of varices. However, these findigns are primary in our local setup, further trials should be done to authenticate our findings.

Conclusion

We concluded that the predictive value of prothrombin time for presence of oesophageeal varices is a higher and it is a useful non-invasive diagnostic modality.

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Answer Picture Quiz

"butterfly glioma"

Typical appearances of a butterfly glioma, with little possible differences.