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Prediction of Aspartate Aminotransferase to Platelet Ratio Index with Size of Esophageal Varices in Liver Cirrhosis

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ABSTRACT

Background: Liver cirrhosis is one of the major causes of morbidity and mortality. The threatening complication of Liver cirrhosis is variceal bleeding. Early diagnosis and initiation of therapy can reduce mortality associated with variceal bleeding. This study is designed to predict the esophageal varices by non-invasive method using aspartate aminotransferase to platelet count ratio index (APRI).

Methods: A total of 100 patients were studied between March 2016 and February 2017 with the diagnosis of Liver cirrhosis admitted at Bir Hospital fulfilling the inclusion and exclusion criteria. Ethical approval was obtained from Institutional review board of National Academy of Medical Sciences.

Results: Out of one hundred patients, 80 were males and 20 females. On endoscopy, small varices were present in 28 (28%) patients and large varices in 51(51%) patients. APRI with a cutoff value of 0.908 has sensitivity of 87.3% and specificity of 71.4%, positive predictive value of 92% and negative predictive value of 60% (p=0.001) for the detection of varices.

Conclusions: Aspartate aminotransferase to platelet count ratio index can be a useful tool to indirectly predict esophageal varices in a patient with Liver Cirrhosis.

Keywords: Aminotransferase; aminotransferase to platelet ratio index APRI; esophageal varices; liver cirrhosis; platelet count.

INTRODUCTION

Aspartate to platelet count ratio index (APRI) was proposed as an easily determined and accurate noninvasive marker of liver fibrosis.[1,2] Using optimized cut-off values, it has been shown that significant fibrosis may be accurately predicted in 51% of significant fibrosis and 81% of patients in cirrhosis with chronic Hepatitis C Virus (HCV) infection and its usefulness is also proven in other etiologies of liver diseases.[3] However, APRI index was first described for the prediction of fibrosis in patients with HCV infection.[1]

In order to spare patients from the invasive procedures like UGI endoscopy as well to reduce the cost, discomfort, and risk related the endoscopy there has been effort to find the non-invasive tools to screen esophageal varices. Since portal hypertension leads to esophageal varices and is a major complication of liver fibrosis. It remains unclear whether serum liver fibrosis markers can be useful for screening the presence of esophageal varices as there are conflicting evidences for the use of APRI in predicting esophageal varices.[4-6]

In this context, we aimed to assess the non-invasive markers (APRI) in predicting the presence of esophageal varices in patients with liver cirrhosis.

METHODS

This is a cross sectional study which was carried out at National Academy of Medical Sciences, Bir Hospital, Kathmandu, Nepal. The study was conducted in March 2016 and completed in February 2017 after 100 consecutive samples were collected for analysis.

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Patient aged between 18 and 70 years without variceal bleeding were enrolled in the study. The diagnosis of Liver cirrhosis was based on clinical symptoms, laboratory parameters, imaging modalities and histopathology whenever available.[7] The exclusion criteria were as follows: previous variceal bleed; patients on beta blockers for prophylaxis for variceal bleed, history of hepatocellular carcinoma (HCC), portal or splenic vein thrombosis, any infections that could affect AST and or Platetelet.

The degree of esophageal varices was classified according to American Association for the study of liver diseases (AASLD) guidelines.[8] Patients admitted to ward (Department of Medicine, Liver unit or Gastroenterology unit) of Bir Hospital with a clinical diagnosis of Liver Cirrhosis were included. Clinical examination and investigations including USG abdomen, Platelet count, Serum bilirubin, Aspartate aminotransferase, Alkaline phosphatase, prothrombin time/ international normalized ratio (PT/INR), serum total protein and albumin were performed. Child-Turcotte-Pugh (CTP) score was calculated.

Upper gastrointestinal (UGI) endoscopy findings were evaluated for presence and degree of esophageal varices. The FUJINON endoscopy (video processor, EPX-4450HD) was performed by an expert GI endoscopist. The degree of esophageal varices was classified according to AASLD guideline as small varices: <5 mm and large varices: ≥5 mm.[8]

The sample size was calculated using the following formula:

$N = Z^2P(1-P)/D^2$ where, N is the required sample size, Z is the level of confidence (for 95% level of confidence, Z=1.96), D is the precision or maximum tolerable error as a percentage 20% of Prevalence (P)[9], which was taken as 50. The sample size with above formula was calculated to be N = 96.04.

APRI = (AST elevation/platelet count) x 100

The APRI index was calculated using the Aspartate aminotrasferase (AST) elevation (which is the AST level divided by the upper limit of normal [ULN] for the lab) and the platelet count per mm^3divided by 1000.[10]

Cut off value of APRI for prediction of presence of esophageal varices was determined by using receiver operating characteristics procedure (ROC curve) as 0.908. Patients with Index lower than this were not supposed to have esophageal varices.

Statistical analysis was performed using SPSS (Statistical Package for Social Sciences) version 23. Continuous parameters were expressed as mean and standard deviation (SD). These were analyzed using Chi square test. Means between various esophageal varices groups were analyzed by ANOVA (Analysis of Variance) test. Sensitivity, specificity, positive predictive value, negative predictive values were determined for APRI cut off of 0.908. P-value of less than 0.05 was considered significant. Ninety five percent confidence intervals (CI) were used in all analyses.

RESULTS

In this study total of 100 patients with Liver Cirrhosis were enrolled, from which eighty 80 (80%) were male and twenty 20 (20%) were females. The mean age of patients with cirrhosis was 50.26 ±11.54 years. The most common etiology of Liver Cirrhosis was alcoholic liver disease 72 (72%) followed by chronic hepatitis B infection 14 (14%), chronic hepatitis C infection 11 (11%) and others (3%). Abdominal distention (86%) and jaundice (63%) were the common presenting complaints. A baseline characteristic of the study population is shown in table 1.

Table 1. Baseline characteristics of the study population with Liver cirrhosis who underwent UGI endoscopy.

Parameters	n (%)	Mean ± SD
Age (years)		50.26 ±11.54
Sex		
Male	80 (80)	
Female	20 (20)	
Etiology		
Alcohol	72 (72)	
Chronic hepatitis B	14 (14)	
Chronic hepatitis C	11(11)	
Others	3 (3)	
Esophageal Varices		
Present	79 (79)	
Absent	21 (21)	
Lab		
Platelet count		125.23 ± 8.46
Total Bilirubin		3.30 ± 3.8
Direct Bilirubun		2.15 ± 3.56
Albumin		2.70 ± 0.68
AST		103.21 ±63.31
Child-Turcotte-Pugh class (CTP)		
A	8 (8)	
B	22 (22)	
C	70 (70)	

Of these 100 patients, 79 (79%) had esophageal varices (28 classified as small, 51 as large). There was no varices detected with APRI score of below 0.8, 28 % small varices were detected with APRI (0.8 to 1.3), and 51 % had large varices APRI (≥1.3). Also, patients with presence of esophageal varices had mean APRI of 2.166 ±1.823 vs 0.8 ± 0.57 without varices. (p=0.001, CI 95%) as shown in table 2a and 2b.

Table 2a: Relation of grade of esophageal varices with Aspartate to platelet ratio index (APRI)

Esophageal varices	Number of Patients	Mean APRI	Standard deviation	p value
None	21	0.81	0.57	0.001
Small	28	1.3	0.85	
Large	51	2.6	2.04	

Table 2 b: Correlation of presence of esophageal varices with APRI.

Esophageal varices	Number of Patients	Mean APRI	Standard deviation	p value
Absent	21	0.811	0.575	0.001
Present	79	2.166	1.823	

Using the cutoff value of 0.908 for prediction of esophageal varices, APRI has sensitivity of 87.3% and specificity of 71.4%, positive predictive value of 92% and negative predictive value of 60% (p=0.001).

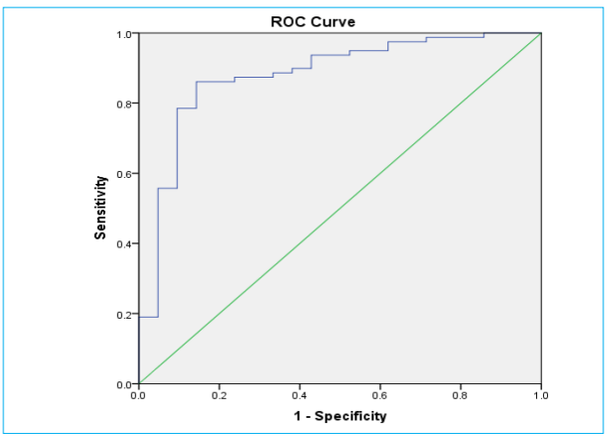

Figure 1: Receiver operating characteristic curve (ROC) for APRI

Area under the receiver operating characteristics procedure (ROC curve) for accurately predicting esophageal varices is 0.879 [95% CI (0.792-0.967)]

DISCUSSION

Our study has demonstrated a significant difference in patients with varices as compared to patients without varices with regards to APRI (AST to platelet ratio index). Our study also showed that majority of patient (51%) had large esophageal varices reflecting higher number (70%) of patients presented in Child-Turcotte-Pugh (CTP)-C stage of liver cirrhosis. Similar to our study, Park et al in a study of 614 Liver Cirrhotic patients also observed a correlation of APRI index with presence of esophageal varicecs ($p<0.05$) in univariate analysis but not in the multivariate.[11]

Likewise, Tafarel et al, Sanyal et al, and de Mattos et al also revealed a correlation of APRI index with the presence of esophageal varices. [2,6,12]

Unlike our study, Sanyal et al had both groups of patients including liver fibrosis and also cirrhosis and their observation was among the initial studies showing promising correlation of APRI with detection of esophageal varices. Sebastian et al observed a strong correlation between APRI index in the presence of esophageal varices (APRI = 1.4, sensitivity 54%, specificity 69%).[13] Suprianto et al observed that APRI score of < 0.5, 0.5-1.5 and 1.5 were observed in 21.81%, 41.81% and 36.36% subjects with esophageal varices respectively and showed a correlation between APRI index and the grade of esophageal varices in patients with liver cirrhosis (p = 0.011).[5] In our study, there was no varices detected with APRI score of <0.8, but there were 28 % who had small varices observed with APRI index between 0.8 and 1.3 and 51 % patents actually had large varices with APRI > 1.3. This shows that lower APRI of below 0.8 in our study may be better correlated in excluding esophageal varices especially in our population.

Comparing between our study and another study by Singh et al; there was not much difference in mean APRI index for the detection of esophageal varices. Mean APRI index of 2.166 ±1.823 was observed in our study whereas mean APRI index of 2.34±1.28 was also observed in Singh et al study for the detection of esophageal varices.[14]

In our study, area under the receiver operating characteristics curve (AUROC curve) of APRI for accurately predicting esophageal varices in patients with liver cirrhosis was 0.87 with APRI cut off of 0.908 which has a sensitivity of 87.3% and specificity of 71.4%, positive predictive value of 92% and negative predictive value of 60% (p=0.001, CI=95%).

Wang et al reported that lower APRI cut off (0.77)

predicted the esophageal varices with a sensitivity of 71%.[15] de Matos et al used a different APRI cut off index of 1.3 to predict the presence of esophageal varices, which showed a sensitivity of 64.7 %.[6] Regardless of higher cut off as compared to Wang et al study; we observed a higher sensitivity. These variations in predicting esophageal varices with different cut off of APRI index in several studies may be explained by different population group and also a number of etiologies of liver cirrhosis.

Further studies of APRI index with a definite cut-off value in a large population may be more informative.

CONCLUSIONS

The APRI index is an important diagnostic tool to predict esophageal varices in patients with liver cirrhosis in resource limited setting like ours where endoscopic facilities are not widely available.

REFERENCES

1. Wai CT, Greenson JK, Fontana RJ, Kalbfleisch JD, Marrero JA, Conjeevaram HS, et al. A simple noninvasive index can predict both significant fibrosis and cirrhosis in patients with chronic hepatitis C. Hepatology. 2003; 38(2):518-26.[FullText]
2. Sanyal AJ, Fontana RJ, Di Bisceglie AM, Everhert JE, Doherty Mc, Everson GT, et al. The prevalence and risk factor associated with esophageal varices in subject with hepatitis C and advanced fibrosis. Gastrointest Endosc 2006;64:855-64.[PubMed]
3. Soresi M, Giannitrapani L, Cervello M, Licata A, Montalto G. Non invasive tools for the diagnosis of liver cirrhosis. World J Gastroenterol. 2014;20(48):18131-50. [FullText]
4. Voutilainen S, Kivisaari R, Lohi J, Jalanko H, Pakarinen MP. A Prospective Comparison of Noninvasive Methods in the Assessment of Liver Fibrosis and Esophageal Varices in Pediatric Chronic Liver Diseases. Journal of clinical gastroenterology. 2016. [PubMed] [DOI]
5. Supriyanto I, Suyata S, Rasyad SB, Bakry F. Correlation between Aspartate Aminotransferase to Platelet Ratio Index Score and the Degree of Esophageal Varices with Liver Cirrhosis. The Indonesian Journal of Gastroenterology, Hepatology, and Digestive Endoscopy. 2012;13(3):141-4. [DOI]
6. de Mattos ÂZ, de Mattos AA, Daros LF, Musskopf MI. Aspartate aminotransferase to-platelet ratio index (APRI) for the non-invasive prediction of esophageal varices. Ann Hepatol. 2013;12(5):810-4.[PubMed]
7. Harbin WP, Robert NJ, Ferrucci Jr J. Diagnosis of cirrhosis based on regional changes in hepatic morphology: a radiological and pathological analysis. Radiology. 1980;135(2):273-83. [PubMed]
8. Retrieved from https://www.aasld.org/publications/practice-guidelines-0
9. Loaeza-del-Castillo A, Paz-Pineda F, Oviedo-Cardenas E. AST to platelet ratio index (APRI) for the noninvasive evaluation of liver fibrosis. Ann Hepatol. 2008 Oct-Dec;7(4):350-7.[PubMed]
10. D'Amico, G. and Luca, A. Natural history (Clinical-haemodynamic correlations. Prediction of the risk of bleeding) . Baillieres Clin Gastroenterol. 1997; 11: 243–256. [PubMed]
11. Park J, Kwon H, Cho J, Oh J, Lee S, Han S, et al. Is the spleen stiffness value acquired, using acoustic radiation force impulse (ARFI) technology, predictive of the presence of esophageal varices in patients with cirrhosis of various etiologies? Medical ultrasonography. 2016;18(1):11-7. [PubMed] [Crossref]
12. Tafarel JR, Tolentino LHL, Correa LM, Bonilha DR, Piauilino P, Martins FP, et al. Prediction of esophageal varices in hepatic cirrhosis by noninvasive markers. Eur J Gastroenterol Hepatol. 2011;23(9):754-8.[PubMed]
13. Sebastiani G, Tempesta D, Fattovich G, Castera L, Halfon P, Bourliere M, et al. Prediction of oesophageal varices in hepatic cirrhosis by simple serum non-invasive markers: results of a multicenter, large-scale study. Journal of hepatology. 2010;53(4):630-8. [PubMed]
14. Chandail VS, Kotwal SK, Koul S, Gupta R, Mahajan A. Non-invasive markers for prediction of varices in patients with portal hypertension. International Journal of Research in Medical Sciences. 2017;5(3):1007-10.[FullText][DOI]
15. Wang JH, Chuah SK, Lu SN, Hung CH, Chen CH, Kee KM et al. Transient elastography and simple blood markers in the diagnosis if esophageal varices for compensated patients with hepatitis B virus-related cirrhosis. J Gastroenterol Hepatol. 2012;27:1213-8.[PubMed] |[DOI]