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ORIGINAL

Evaluation of King's variceal prediction score as a marker of portal hypertension in children with chronic liver diseases

Evaluación de la puntuación de predicción de varices de King como marcador de hipertensión portal en niños con enfermedades hepáticas crónicas

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Abstract

Background: Variceal bleeding is one of the serious complications of portal hypertension due to chronic liver disease in children which can be life threatening. There is limited useful tool to selection the children with chronic liver disease who will benefit from upper endoscopy for evaluation of clinically significant varices.

Materials and Methods: This study included all Patients of either sex, aged less than 18 years old with diagnosis of chronic liver disease(CLD) independently of etiology. All cases underwent esophagogastroduodenoscopy(EGD) for evaluation of esophageal varices presented in Pediatric Gastroenterology (GI) ward in Nemazee Hospital-a referral center in south of Iran- affiliated to Shiraz University of Medical Sciences. Patient demographics, etiologies and complications of chronic liver disease with clinical, biochemical and radiological data were collected. Kings variceal prediction score index and other prediction indices were calculated.

Results: Data on 104 patients were collected;17.3% had Wilson disease and 16% had biliary atresia. Twenty seven (27%) children present with gastrointestinal bleeding and overall 62 (59.6%) had clinically significant(grade II- III) varices. Kings variceal prediction score (K-VaPS), Clinical prediction rule(CPR),Varices prediction rule(VPR), platelet count/spleen diameter ratio and platelet count/equivalent adult spleen diameter ratio had at optimal cut-off sensitivity and specificity of 51.61% and 69.05%,43.55% and 73.81%,51.61% and 73.81%,53.33% and 71.43%,51.61% and 69.05% respectively. Clinical prediction rule (CPR) had a favourable AUROC of 0.699 (0.59-0.80) compared to Kings variceal prediction score o.646 (0.53-0.75). Kings variceal prediction score cut-off of 45.8 yielded a sensitivity and specificity of 51.61% and 69.05% and a positive and negative predictive value of 71.1% and 49.15% respectively.

Conclusion: King variceal prediction score is an appropriate tool for selection of the children with chronic liver disease for surveillance and is a useful tool in the screening of clinically significant varices in the children with chronic liver disease.

Keywords: Esophageal varices, chronic liver disease, children.

Resumen

Antecedentes: La hemorragia varicosa es una de las complicaciones graves de la hipertensión portal debida a la enfermedad hepática crónica en los niños, que puede poner en peligro su vida. Existe una herramienta útil limitada para seleccionar a los niños con enfermedad hepática crónica que se beneficiarán de la endoscopia superior para la evaluación de las várices clínicamente significativas.

Materiales y métodos: Este estudio incluyó a todos los pacientes de ambos sexos, de menos de 18 años de edad, con diagnóstico de enfermedad hepática crónica (EPC), independientemente de su etiología. A todos los casos se les realizó una esofagogastroduodenoscopia (EGD) para evaluar las várices esofágicas presentadas en la sala de Gastroenterología Pediátrica (GI) del Hospital Nemazee -un centro de referencia en el sur de Irán- afiliado a la Universidad de Ciencias Médicas de Shiraz. Se recogieron los datos demográficos de los pacientes, las etiologías y las complicaciones de la enfermedad hepática crónica con datos clínicos, bioquímicos y radiológicos. Se calculó el índice de predicción de varices de Kings y otros índices de predicción.

Resultados: Se recogieron datos de 104 pacientes; el 17,3% tenía la enfermedad de Wilson y el 16% atresia biliar. Veintisiete (27%) niños presentaban hemorragia gastrointestinal y, en total, 62 (59,6%) tenían várices clínicamente significativas (grado II-III). La puntuación de predicción de varices de Kings (K-VaPS), la regla de predicción clínica (CPR), la regla de predicción de varices (VPR), la relación recuento de plaquetas/diámetro del bazo y la relación recuento de plaquetas/diámetro equivalente del bazo del adulto tuvieron una sensibilidad y especificidad óptimas del 51,61% y el 69,05%, el 43,55% y el 73,81%, el 51,61% y el 73,81%, el 53,33% y el 71,43%, el 51,61% y el 69,05%, respectivamente. La regla de predicción clínica (RPC) tuvo un AUROC favorable de 0,699 (0,59-0,80) en comparación con la puntuación de predicción de varices de Kings o,646 (0,53-0,75). La puntuación de predicción de varices de Kings de 45,8 arrojó una sensibilidad y especificidad del 51,61% y 69,05% y un valor predictivo positivo y negativo del 71,1% y 49,15% respectivamente.

Conclusión: La puntuación de predicción de varices de King es una herramienta apropiada para la selección de los niños con enfermedad hepática crónica para su vigilancia y es una herramienta útil en el cribado de varices clínicamente significativas en los niños con enfermedad hepática crónica.

Palabras clave: Várices esofágicas, enfermedad hepática crónica, niños.

Introduction

Cirrhosis is a diffuse process that histologically characterized by fibrosis and conversion of the normal liver architecture into structurally abnormal nodules, which lead to the disorganization of liver architecture[1]. The progression of liver injury to cirrhosis may occur over weeks to years, it's also relatively uncommon in pediatric age groups[2]. Cirrhosis was long thought to be irreversible and associated with limited life expectancy. Although, todays it is considered as a dynamic condition, which can be reversed if adequately treated. Studies of the natural history of cirrhosis have found that the disease tends to present with a silent clinical course, followed by the onset of liver dysfunction and portal hypertension[3].

In clinical practice severity of the disease and mortality risk is generally estimated on the basis of hypoprothrom binemia, hypoalbuminemia, MELD (Model for End-Stage Liver Disease)/PELD (Pediatric End-Stage Liver Disease) and Child-Pugh Turcotte scores and body mass index, considering this fact that low weight gain is characteristics of liver cirrhosis in infants[4]. The most common causes of cirrhosis in the first years of life are biliary atresia and genetic-metabolic diseases, whereas in older children, cirrhosis is most commonly caused by chronic viral hepatitis and autoimmune diseases[5,6].

As a result in 5-15% of cases, the condition is considered as cryptogenic. Cryptogenic cirrhosis in pediatric patients may result from the progression of fatty liver disease or from the effects of complex metabolic syndromes, such as mitochondriopathies. Chronic cholestasis, inborn errors of metabo¬lism and chronic hepatitis are the main causes of cirrhosis in the children[7].

There are many causes of portal hypertension including etiologies above the liver, within the liver, and below the liver. Suprahepatic abnormalities leading to portal hypertension include cardiac disease, hepatic vein etiology(Hepatic vein thrombosis, or Budd-Chiari syndrome), and inferior vena cava thrombosis or webs. Liver fibrosis can result from suprahepatic disease, and cirrhosis can also develop late in the disease course[8].

Development of esophageal varices is almost universal, and the statistical risk of bleeding reaches 76% at 24 years of age[9-13]. Probability of bleeding is directly correlated with the size of varices as seen on endoscopy, from the absence of bleeding episode in children without varices or with grade I varices, to 85% prevalence of bleeding in patients with grade II or III varices, as reported by Lykavieris et al.[4].

The currently accepted best available test for the diagnosis of varices is EGD. However, EGD has important limitations, including a lack of validated grading systems for variceal size and appearance, poor inter observer variation, and the requirement for significant sedation or general anesthesia when it is performed in children[14-16]. Therefore, there has been considerable effort to find a noninvasive test for esophageal varices. Preliminary data suggests that laboratory tests such as platelet count, albumin and ultrasonographic parameters such as presence of splenomegaly, spleen size z score and platelet count to spleen size ratio and the clinical prediction rule (CPR) which calculated from platelet count, spleen size z-score, and albumin concentration may be useful as first-line tools for identification of adults and pediatric patients at risk of variceal development and thus reduce the number of unnecessary EGDs[10].Kings prediction score is a useful tool in the selection of children with clinically significant varices eligible for a screening endoscopy using mentioned parameter in prediction of variceal grade[17].

Materials and methods

This study include all Patients of either sex-aged less than 18 years old with diagnosis of chronic liver disease(CLD) independently of etiology. All cases underwent EGD for evaluation of esophageal varices presented in Pediatric Gastroenterology (GI) ward in Nemazee-Hospital-a referral center in south of Iran-affiliated to Shiraz University of Medical Science. EGD indications were suspicion of portal hypertension(PHT) based on persistent splenomegaly on the background of chronic liver disease or thrombocytopenia or gastrointestinal bleeding. Patients with portal vein thrombosis (PVT) were excluded from the study considering that the disease pathophysiology is different than that of CLD and PHT. At time of endoscopy grading of esophageal varices were recorded using Kings College Hospital three-size classification. Varices were considered CSV if they were grade II and III or if variceal bleeding was present. Patients were categorised for analysis purposes into clinically significant varices(CSV)+ve and CSV-ve groups.

Clinical data collected at the time of endoscopy included patient demographics, etiology of liver disease and complications such as hepatic encephalopathy, gastrointestinal bleeding, ascites, spontaneous bacterial peritonitis and other infections.

Laboratory data included alanine aminotransferase(ALT), aspartate aminotransferase (AST), serum bilirubin, albumin, international normalized ratio(INR), haemoglobin (Hb), white cell count (WCC) and platelet count, serum creatinine, serum sodium(Na),Child-Turcotte-Pugh Classification(CHILD) score and Pediatric End-stage Liver Disease(PELD) score or Model for End-stage Liver Disease(MELD) score. All measurements were performed within 6 months of the EGD, Spleen size was measured by abdominal ultrasound. Spleen size values were expressed as spleen size z score (SSAZ).Equivalent adult

spleen size(EASS) was calculated as the mean adult spleen size(for gender) plus spleen size z score(SSAZ).

Females: 9.91(cm) + SSAZ x 1.27(cm)
Males: 11.29(cm) + SSAZ x 1.49(cm)

Kings Variceal Prediction Score(K-VaPS) index and other prediction indices such as Varices Prediction Rule(VPR),Clinical Prediction Rule(CPR), AST-platelet ratio index(APRI),platelet count/spleen diameter ratio and platelet count/equivalent adult spleen diameter ratio which considered prediction of the presence of esophageal varices were calculated.

Variceal prediction indices

Index 1- Kings Variceal Prediction Score (K-VaPS):
(3 x albumin (g/L))-(2 x Equivalent Adult Spleen Size(EASS) (cm))
Index 2- Varices Prediction Rule (VPR):
(albumin (g/dL) x platelet count (x109/L))/1000)
Index 3- Aspartate aminotransferase(AST)-platelet ratio index (APRI) :
(AST/Upper limit of normal)/platelet count (x109/L) x100)
Index 4- Clinical Prediction Rule (CPR):
((0.75x platelet count(x109/L))/(Spleen Size Z Score(SSAZ)+5))+(2.5x albumin (g/dL)
Index 5- platelet count/spleen diameter ratio:
(platelet count (x109/L))/spleen size (mm))
Index 6- equivalent adult platelet count/spleen diameter ratio:
(platelet count (x109/L))/ Equivalent Adult Spleen Size(EASS) (mm))

Statistical analyses

All statistical analysis were performed with the Statistical Pachage for Social Sciences(SPSS) version 18. Descriptive results were expressed as mean ± SD (standard deviation) or number (percentage) of patients with a condition. When appropriate, either the Student t-test was used to compare quantitative data, and the Pearson chi-square test was applied for comparison of frequency data. All tests were two tailed and p values < 0.05 were considered significant. ROC curve analysis was used to calculate diagnostic accuracy as areas under the curve (AUROC) along with 95% confidence intervals. The diagnostic accuracy [sensitivity, specificity, positive and negative predictive values (PPV and NPV)] of these variables was calculated using the best cut-off as defined by the ROC curve analysis.

Results

Baseline characteristics

One hundred and four patients were consecutively included in our study, from which 51 were male (49%). The mean age of the patients was 6.43±4.48 years. The mean duration of disease was 1.81±2.45 years. the mean Child and PELD/MELD scores were 9.39±2.89 and 19.32±16.22 respectively (**Table I**).

Table I: The mean amount of the clinical, biochemical and radiological data and different indices.

	Mean	Maximum	Minimum	St. deviation
Age (year)	6.43	18.00	0.25	4.48
Weight (Kg)	23.32	70.00	2.80	16.92
Duration (year)	1.81	16.00	0.08	2.45
Child score	9.39	15.00	5.00	2.89
PELD/MELD score	19.32	63.50	.00	16.22
Albumin	3.34	5.80	1.70	0.91
Total bilirubin	10.80	51.20	0.30	11.73
INR	2.84	14.00	1.00	2.60
AST	254.39	1770.00	12.00	325.89
ALT	184.08	3090.00	10.00	365.69
Creatinine	0.43	2.20	.10	0.30
WBC	9770.19	35400.00	1500.00	8650.00
Hb	10.01	17.20	3.60	2.46
Platelet	203250.00	1266000.00	6000.00	201772.00
Na	136.04	145.00	120.00	3.90
Spleen size (cm)	11.28	24.00	3.90	4.17
SSAZ	7.69	11.00	4.90	1.46
EASS	21.23	27.23	16.89	2.54
Index 1	57.56	133.4	5.02	27.69
Index 2	0.68	4.30	0.01	0.73
Index 3	6.22	90.30	0.12	11.95
Index 4	20.52	98.00	6.72	13.39
Index 5	2.19	26.37	0.04	3.07S
Index 6	0.947	7.44	0.02	1.00

Chronic liver disease etiologies

The most underlying chronic liver disease in this study were wilson disease (n:18),biliary atresia (n:16),cryptogenic cirrhosis (n:16),autoimmune hepatitis (n:14), tyrosinemia (n:9) and progressive familial intrahepatic cholestasis(PFIC) (n:8) (**Table II**).

Table II: The etiologies of the liver cirrhosis.

Ethiology	Number	Percent
Wilson disease	18	17.3
Biliary atresia	16	15.3
Cryptogenic Cirrhosis	16	15.3
Autoimmune hepatitis	14	13.4
Tyrosinemia	9	8.6
PFIC (progressive familial intrahepatic cholestasis)	8	7.6
GSD (glycogen storage disease)	3	2.8
INH (idiopathic neonatal hepatitis)	2	1.9
Alagille syndrome	2	1.9
Congenital hepatic fibrosis	1	0.9
Viral hepatitis	1	0.9
CF (cyctic fibrosis)	1	0.9
Other disease	13	12.5

Complications of chronic liver disease

Acute gastrointestinal bleeding was the indication of the first esophagogastroduodenoscopy(EGD) in 27 patients who presenting with hematemesis or melena. **Table III** shows the prevalence of different chronic liver disease complications. Encephalopathy was seen in 45.2% of cases as the most prevalent complication followed by ascites and GI bleeding. other complications included cyanosis, hepatorenal syndrome, hepatopulmonary

syndrome. Spontaneous bacterial peritonitis(SBP) was the least complication in our cases.

Table III: Prevalence of different complications of chronic liver disease .

Encephalopathy	45.2%
GI bleeding	26%
Ascites	37.5%
SBP	9.6%
Infection	10.6%
Other complications	26.0%

Table IV represent the relation between different complications and also sex and the EGD results. In CSV positive patients prevalence of GI bleeding was higher comparing with CSV negative cases but this relation was not statistically significant. Prevalence of other complications had an invert relation with CSV presentation in which in CSV positive cases other complications were less prevalent than those without complications, although this relation wasn't statistically significant (p>0.05).

Table IV: The relation between different complications and sex and the endoscopy results.

		CSV negative %	CSV positive %	P-value
Sex	Male Female	45.1 35.8	54.9% 64.2	0.93
Encephalopathy	No Yes	43.9 36.2	56.1 63.8	0.42
GI bleeding	No Yes	45.5 25.9	54.5 74.1	0.07
Ascites	No Yes	44.6 33.3	55.4 66.7	0.25
SBP	No Yes	41.5 30.0	58.2 70.0	0.48
Infection	No Yes	39.8 45.5	60.2 45.5	0.71
Other complications	No Yes	35.1 55.6	64.9 44.4	0.062

The relation between different criteria and the EGD results

As it showed in **table V** a subgroup analysis was carried out, evaluating the relation between different criteria that measured in our study and the EGD results. Out of 104 patients 62 (59.6%) cases were clinically significant varices (CSV) positive. By this detail that 32 cases had no varices, and prevalence of grade I, II and III varices were 10, 35 and 27; respectively. The CSV positive group had higher values of total bilirubin, INR, spleen size, Child score and PELD/MELD scores and lower platelet, albumin, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) compared to the CSV negative group. There were significant relation between presence of CSV and disease duration(p<0.001), albumin (p=0.02), serum Na level (p=0.02), platelet count(p=0.003) and spleen size (p=0.01). There was an significant relation (p<0.05) between all indices and presence of CSV except index 3 (APRI index) (**Table V**).

Table V: Baseline clinical, biochemical and radiological data and different indices according to the presence or absence of clinically significant varices(CSV).

	Endoscopy	Mean	Std. Deviation	P- value
Age	CSV negative CSV positive	6.38 6.47	5.02 4.76	0.92
Weight	CSV negative CSV positive	23.32 23.33	17.37 16.75	0.99
Duration	CSV negative CSV positive	1.01 2.35	1.22 2.89	< 0.001
Childscore	CSV negative CSV positive	8.80 9.79	2.75 2.94	0.09
PELDscore	CSV negative CSV positive	17.18 20.77	16.43 16.05	0.26
Albumin	CSV negative CSV positive	3.59 3.17	0.87 0.90	0.02
Totalbilirubin	CSV negative CSV positive	8.89 12.09	11.00 12.12	0.17
INR	CSV negative CSV positive	2.64 2.97	1.94 2.97	0.52
AST	CSV negative CSV positive	332.69 201.35	414.54 238.22	0.068
ALT	CSV negative CSV positive	214.21 163.67	297.73 406.42	0.49
Creatinine	CSV negative CSV positive	0.40 0.44	0.19 0.35	0.51
WBC	CSV negative CSV positive	10430.95 9322.58	7210.10 5409.74	0.37
Hb	CSV negative CSV positive	9.89 10.10	2.67 2.33	0.67
Platelet	CSV negative CSV positive	285095.23 147806.45	261934.53 122033.29	0.003
Na	CSV negative CSV positive	137.11 135.32	3.18 4.19	0.02
Spleen size	CSV negative CSV positive	10.10 12.08	3.35 4.49	0.01
SSAZ	CSV negative CSV positive	7.65 7.72	1.53 1.42	0.586
EASS	CSV negative CSV positive	21.28 21.19	2.41 2.64	0.87
Index 1	CSV negative CSV positive	65.32 52.64	27.61 26.75	0.012
Index 2	CSV negative CSV positive	1.00 0.47	0.95 0.42	<0.001
Index 3	CSV negative CSV positive	7.28 5.50	14.98 9.43	0.63
Index 4	CSV negative CSV positive	26.02 16.80	17.69 7.58	0.001
Index 5	CSV negative CSV positive	3.27 1.46	4.36 1.35	0.012
Index 6	CSV negative CSV positive	1.30 0.70	1.35 0.56	0.01

Variceal prediction score indices

ROC analysis For the Kings variceal prediction score index demonstrated air under ROC curve (AUROC) of 0.646 (CI 0.53-0.75) and p=0.012 with the optimal cut-off point of 45.8 and sensitivity and specificity of 51.61% and 69.05% respectively. Positive predictive value (PPV) and negative predictive value (NPV) were 71.1% and 49.15%, respectively (**Table VI, figure 1**).This yielded a

diagnostic accuracy of 64%,so it can be considered as a suitable index in prediction of CSV in the children with chronic liver disease.

Table VI: Sensitivity, specificity, negative and positive predictive value and diagnostic accuracy of six indices.

Indices	Cut of point	P- value	Diagnostic accuracy	95% CI	Specificity %	Sensitivity %	PPV %	NPV %
1	45.8	0.012	0.64	0.53-0.75	69.05	51.61	71.1	49.15
2	0.325	0.001	0.68	0.58-0.69	73.81	51.61	74.4	50.8
3	3.19	0.63	0.47	0.35-0.59	52.38	51.61	61.5	46.9
4	13.84	0.001	0.69	0.59-0.80	73.81	43.55	71.0	46.9
5	1.19	0.002	0.68	0.57-0.79	71.43	53.33	73.3	50.8
6	0.615	0.004	0.66	0.55-0.77	69.05	51.61	71.1	49.1

Based on our study result,Varices Prediction Rule(VPR) with AUROC of 0.688 and p=0.001 and sensitivity and specificity 51.61% and 73.81% respectively (**Table VI**, **figure 2**), and Clinical Prediction Rule(CPR) with AUROC of 0.699 and p=0.001 and sensitivity and specificity 43.55% and 73.81%, respectively (**Table VI, figure 3**) were efficacious at predicting the presence of clinically significant varices.

In this results there was not a statically significant relation between the AST-Platelet Ratio Index and the incidence of CSV (P= 0.633).This index also has a worthless specificity (52.38%) and sensitivity(51.61%).In prediction of CSV based on area under ROC curve which was less than 0.5, it can not be considered as a suitable index in prediction of CSV in children with chronic liver disease (**table VI, figure 4**).

Figure 1: Area under curve 0.646 of index 1 (Kings Variceal Prediction Score).

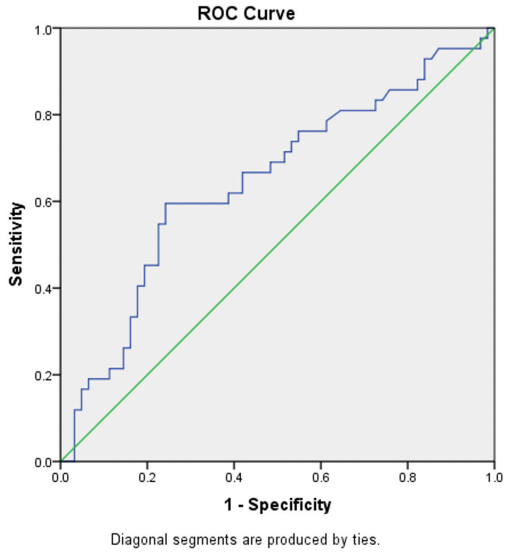


Figure 2: Area under ROC curve 0.688 of index 2 (varices prediction rule (VPR)).

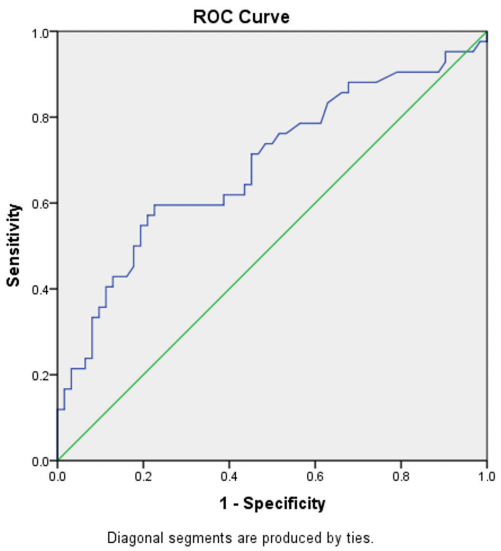


Figure 3: Area under ROC curve 0.699 of index 4 (Clinical Prediction Rule (CPR)).

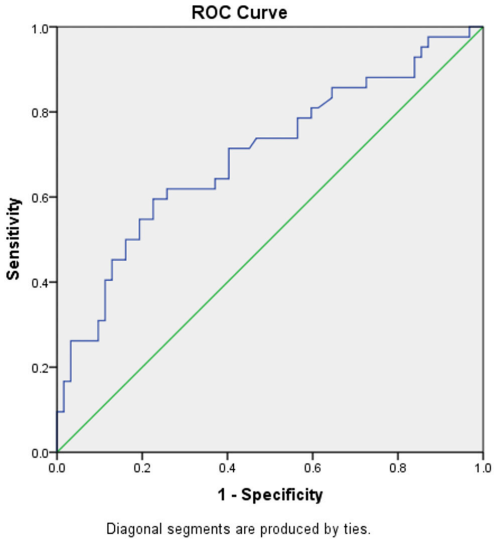
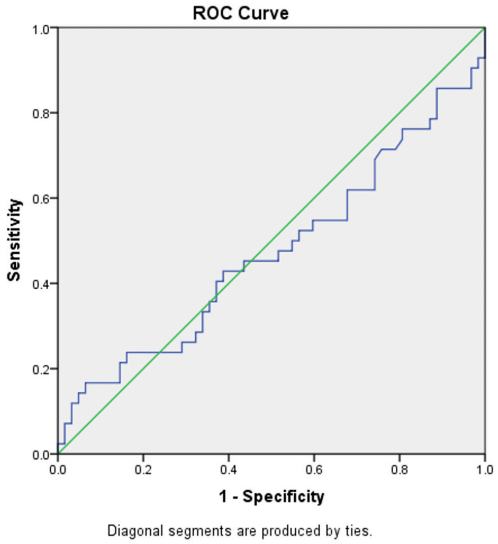


Figure 4: Area under ROC curve 0.472 of index 3 (AST-platelet ratio index (APRI)).



Other good indices for prediction of CSV were platelet count/spleen diameter ratio and platelet count/equivalent adult spleen diameter ratio with p:0.002 and p:0.004 respectively and sensitivity 53.33% and 51.61% and specificity 71.43% and 69.05% and AUROC 0.682 and 0.666, respectively (**Table VI** and **figures 5** and **6**).

Figure 5: Area under ROC curve: 0.682 of index 5 (Platelet Count/Spleen Diameter ratio).

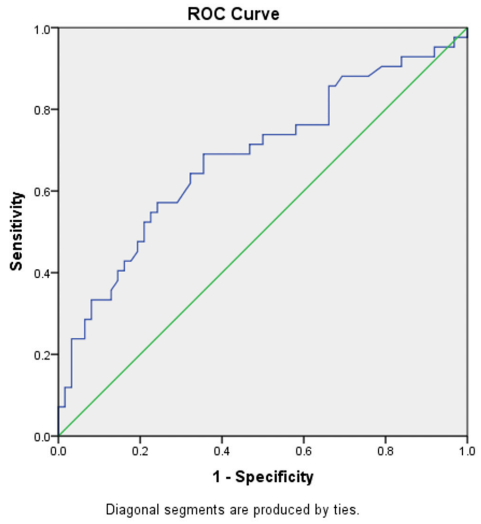
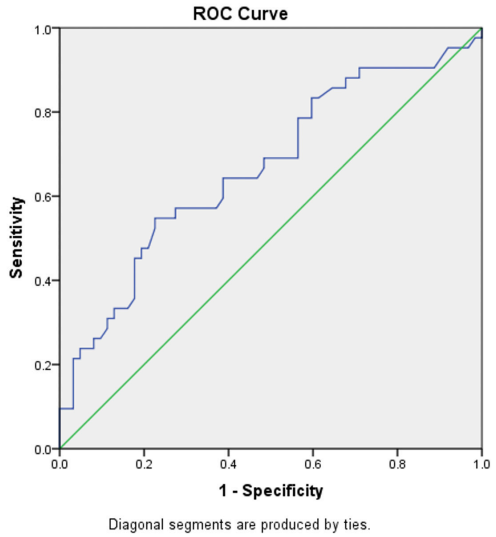


Figure 6: Area under ROC curve 0.666 of index 6(platelet count/ equivalent adult spleen diameter ratio).



Discussion

Portal hypertension is a key factor in the pathogenesis of cirrhosis outcomes. PHT is associated with development of a hyperdynamic circulation and complications such as ascitis, hepatic encephalopathy, and esophagogastric varices[12]. About 50% of patients presenting with cirrhosis are reported to have varices, 24- 80% in cases who have PHT. Development of esophageal varices may occur in up to 90% of patients with liver cirrhosis, being more common in Child-Pugh Class C patients compared to Child-Pugh Class A patients (85% versus 40%)[13]. Early diagnosis of varices before the first bleeding is essential as studies of primary prophylaxis clearly show that the risk of variceal hemorrhage can be reduced by 50% to about 15% for large esophageal varices. So early diagnosis and screening of varices should be warranted to improve the prognosis of liver cirrhosis-Considering the impact of upper GI bleeding due to esophageal varices(EV) rupture in the prognosis of cirrhotic patients, AASLD (American Association forthe Study of Liver Disease) and the Baveno Consensus suggest that every patient diagnosed with cirrhosis should be investigated for esophageal varices(EV)[14].

Endoscopy should be performed at 2-3 years intervals in the patients without varices and at 1-2 years intervals in the patients with small varices[11,12]. A generalized screening program of periodic upper gastro-esophageal endoscopy in cirrhotic patients leads to high costs, and patient compliance may become reduced. However, at a given point in time, a variable proportion of patients will not have varices. Thus, screening all cirrhotic patients with upper GI endoscopy to detect the presence of varices implies a number of unnecessary endoscopies, which increase the workload of endoscopy units. Hence, the selection of patients who may be at a higher risk of having gastro-esophageal varices would be highly beneficial and cost-effective[15].

Various non-invasive markers, such as model for end-stage liver disease (MELD), aspartate aminotransferase (AST) to alanine aminotransferase (ALT) ratio (AST/ALT), AST to platelet ratio index (APRI), platelet count to spleen diameter (PC/SD), fibrosis-4-index (FIB-4), fibrosis index (FI) and King's score, have been demonstrated as a simple, non-invasive and easier practical alternative to predict the presence of esophageal varices in cirrhotic patients[16-18].

In Eslam et al study platelet count was one of three markers that significantly predict presence of esophageal varices in cirrhotic patients[11]. The present study showed same results in which platelet count beside spleen size, serum albumin level and Na level were simple markers that had significant relation with presence of esophageal varices[11].

Giannini et al have suggested that PC/SD (platelet count/ spleen diameter ratio) could be an accurate predictor of esophageal varices in cirrhotic patients, and as the measurement of platelet and spleen size are part of the routine workup of these patients it could probably be the most cost effective non-invasive method for this[20].In our study equivalent platelet count/spleen diameter ratio amount had a significant relation with presence of clinically significant varices(CSV) in endoscopy. Considering the area under curve in ROC curve this index had good sensitivity and specificity in predicting CSV. Sanyal et al. were the first authors to raise the hypothesis that APRI

could be related to the presence of esophageal varices. They found a sensitivity of 68%, a specificity of 64%, a PPV of 51% and a NPV of 78%.We found values of 51.61%, 52.38%, 61.5% and 46.9% respectively, they proposed the cutoff point of 1.3 for APRI as a predictor of esophageal varices our cut off point for this index was 3.19[21]. Mattos et al performed a study that analysed the ability of APRI in predicting the existence of esophageal varices in a population of cirrhotic patients. APRI was not an independent factor for the prediction of esophageal varices. Its sensitivity, specificity and predictive values were insufficient for the index to be used for the screening of esophageal varices in cirrhotics[22]. Also in our study APRI index amount had not statically significant relation with the prevalence of esophageal varices with a worthless sensitivity and specificity in esophageal varices prediction.

Motto et al peformed another study to investigate the platelet count squared/spleen diameter ratio (PS/SA), as a non-invasive predictor of esophageal varices in cirrhotics. In their study PS/SA had an excellent sensitivity to predict esophageal varices, allowing almost one fourth of patients without esophageal varices to spare endoscopy[23]. Our study also showed a good sensitivity and specificity in prediction of esophageal varices. In Meyer et al study using a platelet count/spleen diameter ratio with a cut-off value of 0.909, yielded a negative predictive value of only 73% and a positive predictive value of 74%[24]. In our study the sensitivity, specificity, negative predictive value and positive predictive value was 53.33%, 71.43%, 73.30% and 50.8% respectively with a cut-off value of 1.10. In Mosqueira et al study the PC/SD ratio had a sensitivity of 40%, specificity of 75%, PPV of 82%, NPV 30%. They concluded in their study that the PC/SD ratio was not an effective diagnostic test for esophageal varices[25].

Gana et al measured the ability of clinical prediction rule (CPR) to predict the presence of esophageal varices in children. Their study showed that noninvasive tests such as CPR and platelet count can assist in triaging children for EGD to identify esophageal varices[24].In our study CPR had the most sensitivity and specificity in predicting EV comparing to other indices. In Istrd et al study variceal prediction rule(VPR), CPR and APRI considered as suitable indices in prediction of esophageal varices with area under ROC curve of 0.75, 0.73-0.80 and 0.69-0.83 respectively[24].In our study results were the same for VPR and CPR but not for APRI. Platelet count had significant relation with Prescence of esophageal varices with p-value 0.002. In Gana et al study the best noninvasive predictors of esophageal varices of any size were as follows: platelet/spleen size ratio, CPR (AUROC: 0.80), and platelet count (AUROC:0.79). The positive predictive values for the CPR and platelet count were 0.87 and 0.86, the negative predictive values were 0.64 and 0.63, the positive likelihood ratios were 3.06 and 2.76, and the negative likelihood ratios were 0.64 and 0.63, respectively. Based on positive and negative predictive values, the most accurate noninvasive tests were the CPR and platelet counts[26]. Our study showed the same result and the CPR was the most accurate noninvasive test with sensitivity, specificity, negative predictive value and positive predictive value of 43.56%, 73.81%, 71.0% and 46.9% respectively the AUROC was 0.699. The CPR or platelet count therefore may be used as noninvasive tests for esophageal varices in a clinical or research setting to triage children to undergo EGD for confirmation and grading of varices[27].

Witters et al concluded in their study that King score can facilitate the selection of children with chronic liver disease undergoing an esophagogastroduodenoscopy(EGD) for the detection of clinically significant varices in a surveillance program[17]. In Timothy et al study a King's Score of greater than or equal to 16.7 predicted cirrhosis in 34% of patients (P <0.0001) with sensitivity 86%, specificity 80% and a high negative predictive value of 96%[27]. In our study sensitivity 51.61%, specificity 69.05% and a high negative predictive value of 49.15% and positive predictive value of 71.1 with P-Value 0.012 and AUROC of 0.646. Based on our study results Kings Variceal Prediction Score amount has statistically significant relation with the incidence of CSV. This index has specificity and sensitivity based on area under ROC curve, so it can be considered as a suitable index in prediction of esophageal varices in children with chronic liver disease.

This study allowed us to prove that there is satisfactory cut-off value for Kings score to be used as a predictor of esophageal varices. A screening tool, in a context of a serious situation as the presence of esophageal varices, which is responsible for the most dramatic complication of cirrhosis, variceal bleeding, must have an excellent negative predictive value in order not to miss patients who could benefit from primary prophylaxis-The results of our study lead to the conclusion that Kings score is an appropriate substitute for endoscopy and can be used in the screening of esophageal varices among cirrhotic patients.

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Interests conflict

The researchers declare that they have no conflict of interest.

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