MEDICAL CHANNEL

Original Article

GRADES OF ESOPHAGEAL VARICES IN RELATION TO CHILD TURCOT PUGH CLASSES OF LIVER CIRRHOSIS

1. SHAIKH KHALID MUHAMMAD
2. BASHIR AHMED SHAIKH
3. KOURO MAL GURBAKSHANI
4. AZIZULLAH JALBANI

(1) ***Consultant Physician,*** Chandka Medical College & Hospital Larkana.
(2) ***Associate Professor of Medicine,*** Chandka Medical College & Hospital Larkana.
(3) ***Assistant Professor of Medicine,*** Chandka Medical College & Hospital Larkana.
(4) ***Associate Professor of Medicine,*** Chandka Medical College & Hospital Larkana.

Correspondence:
Dr. Shaikh Khalid Muhammad
M.B, B.S, FCPS (MEDICINE)
Consultant Physician
E-mail:
sheikhkhalid_doctor@hotmail.com
Cell. No: + 92 333 2619052

ABSTRACT

Objectives: To determine the frequency and assess the relation of grade of esophageal varices to Child Turcot Pugh (CTP) classes of liver cirrhosis.

Methodology: This two year study was started in January 2010 at department of medicine, C.M.C Larkana, after taking informed written consent from the participants. 739 known patients of liver cirrhosis underwent endoscopy to assess the grades of esophageal varices. CTP classes were assigned to all patients based on clinical examination and blood analysis. Data was analyzed using SPSS 19. Chi square test was applied to assess the significance of variables of CTP and classes of CTP in patients with and without varices. P value less than 0.05 was taken as statistically significant.

Results: Varices was documented in 389 (52.6%) patients. 58 (7.8%) had grade 1, 45 (6.1%) had grade 2, 162 had (21.9%) grade 3 and 124 (16.7%) grade 4 varices. Most of the patients (n=212, 54.5%) with varices were in CTP class C ($p < 0.001$) with odds of 8.78 (95% CI: 6.01 – 12.83). Patients with varices had statistically significant ($p < 0.001$) low albumin (< 2.8 g/dl), elevated INR (> 2.2) and bilirubin (> 3 mg/dl) with odds of 4.70 (95% CI: 3.08 – 7.17), 16.89 (95% CI: 10.97 – 25.99) and 1.87 (95% CI: 1.34 – 2.60) respectively.

Conclusion: Esophageal varices was documented in 52.6% cirrhotic patients and most of them were in CTP class C. Patients with varices tend to advanced liver disease as compared to cirrhotic patients not having varices.

Key Words: Esophageal Varices, Grades, Child Turcot Pugh, Class.

INTRODUCTION

Cirrhosis of liver is an irreversible disorder associated is very high mortality and morbidity. Patients with liver cirrhosis ultimately develop complications; amongst them portal hypertension is one of the major complication manifested as esophageal varices. Esophageal varices (EV) are dilated, tortuous and fragile vessels that connect portal venous with systemic venous circulation and located in sub mucosa of lower esophagus. At the time of diagnosis 30% of cirrhotic patients have EV that increase to 90%, after 10 years.[1-3]

Varices strongly correlated with deteriorating hepatic function. In Child Turcot Pugh (CTP) class A, 40% cirrhotic harbors varices, which reach to 85% in CTP class C. Approximately 30% of cirrhotic will bleed in first year after diagnosis and mortality of single episode depend on severity of liver disease. Some 10% cirrhotic in CTP class A and 70% in CTP class C die due to bleeding. The risk of variceal bleeding is also related to the size of esophageal varices, with large esophageal varices (LEV) being at a greater risk due to a higher variceal wall tension in LEV. Thus, annual incidence of gastrointestinal bleeding is only 1-2% in patients without varices, 5% in those with small esophageal varices and 15-20% in patients with LEV.[1,3,4]

Upper GI endoscopy is gold standard investigation for diagnosis of esophageal varices. Recently, Fourth Baveno International Consensus Workshop on Portal hypertension

recommended that all cirrhotic patients should be screened for varices at diagnosis. In compensated cirrhosis if no varices are detected, next review should be 2 – 3 years later. If small varices detected, repeat endoscopy should be done at 1 – 2 years. In patients with decompensated cirrhosis, follow should be yearly. The main aim of this surveillance endoscopy is to prevent bleeding from varices to improve survival of by therapeutic or endoscopic intervention.[1-3]

Certain biochemical, clinical and radiological parameters alone or together have good predictive power for non-invasively assessing the risk of bleeding from varices. Child-Pugh scoring, a combination of different clinical and biochemical parameters is one of the various predictive factors of esophageal varices. It consists of serum albumin, serum bilirubin, prothrombin time, ascites and hepatic encephalopathy. Child classes are rapid and easy method to predict not only the prognosis, but also determine the risk of variceal hemorrhage.[4]

Upper GI endoscopy is investigation of choice for diagnosis of esophageal varices. However, this approach has three limitations. Firstly, it is an invasive. Secondly, cost effectiveness of this approach is questionable procedure and thirdly, endoscopy is not available everywhere particularly in remote areas. This study will enable us to detect high risk patient for esophageal varices through clinical and biochemical parameters to carry out upper gastrointestinal endoscopy in selected patients. It may be more cost effective to routinely screen patient at high risk for the presence of varices so as to reduce the increasing burden and procedure cost of endoscopy unit.[5]

METHODOLOGY

Design: This was a hospital based cross-sectional study.
Duration: Two years from January 2010 till December 2011.
Setting: The patients were enrolled from wards of medicine department and weekly hepatology clinic of Medicine Department, Chandka Medical College (C.M.C), Larkana.
Sampling Technique: Purposive sampling.
Inclusion Criteria: All known patients of liver cirrhosis of either sex admitted in medical wards or visiting hepatology clinic of C.M.C Larkana for evaluation and management of cirrhosis of liver were enrolled.

Exclusion Criteria: following were the excluding parameters

- Patients younger than 15 years and older than 75 years.
- Past history of bleeding per mouth.

TABLE NO:1.
DEMOGRAPHIC PROFILE OF 739 CIRRHOTIC PATIENTS EVALUATED FOR ESOPHAGEAL VARICES

CHARACTERISTICS	NUMBER	PERCENTAGE
AGE		
M EAN ± SD **RANGE (Max – Min)**	**45.81 ± 15.13 years** **55 (74 – 19)**	
AGE CATEGORY		
15 – 29 years	163	22.1 %
30 – 44 years	125	16.9 %
45 – 59 years	296	40.1 %
60 – 74 years	155	21.0 %
GENDER		
MALE	481	65.1 %
FEMALE	258	34.9 %
CHILD TURCOT PUGH (CTP) SCORE & CLASS **M EAN ± SD**	**7.88 ± 2.37**	
CTP CLASS A	266	36.0 %
CTP CLASS B	225	30.4 %
CTP CLASS C	248	33.6 %
INDICATION OF ENDOSCOPY		
HEMATEMESIS	158	21.4 %
MALENA	186	25.2 %
SURVELLANCE	238	32.2 %
ANEMIA	157	21.2 %
GRADES OF VARICES		
GRADE 1	58	7.8 %
GRADE 2	45	6.1 %
GRADE 3	162	21.9 %
GRADE 4	124	16.7 %
NONE	350	47.4 %

TABLE NO:2.
DETAILS OF CHILD TURCOT PUGH VARIABLES IN 739 LIVER CIRRHOSIS PATIENTS

CHARACTERISTICS	NUMBER	PERCENTAGE
SERUM ALBUMIN (ALB)		
Mean ±SD	**3.38 ±0.77 g/dl**	
ALB > 3.5 g/dl	376	50.9 %
ALB 2.8 – 3.5 g/dl	206	27.9 %
ALB < 2.8 g/dl	157	21.2 %
SERUM BILIRUBIN (BILI)		
Mean ±SD	**2.06 ±0.89 mg/dl**	
BILI < 2 mg/dl	319	43.2 %
BILI 2 – 3 mg/dl	225	30.4 %
BILI > 3 mg/dl	195	26.4 %
INTERNATIONAL NORMALIZED RATIO (INR)		
Mean ±SD	**1.70 ±0.52**	
INR < 1.7	399	54.0 %
INR 1.7 – 2.2	153	20.7 %
INR > 2.2	187	25.3 %
HEPATIC ENCEPHALOPATHY (HE)		
HE GRADE 1	62	8.40 %
HE GRADE 2	200	27.1 %
HE GRADE 3	98	13.3 %
HE GRADE 4	29	3.90 %
NONE	350	47.4 %
ASCITES		
NONE	111	15.0 %
MILD – MODERATE	469	63.5 %
SEVERE – RESISTANT	159	21.5 %

- Patients already on nitrate or propranolol or received endoscopic intervention for variceal hemorrhage.
- Previous interventions for portal hypertension as TIPSS or Shunts.
- Ultrasonography proven Hepato Cellular Carcinoma or Alpha Feto Protein ? 10 times the normal limit.
- Haemodynamically unstable patients.
- Patients with advanced chronic disorders as COPD, CCF and hematological disorders.
- Patients with medical contraindications to upper gastrointestinal endoscopy like shock, atlanto-axial subluxation, any coagulation disorder.

Data Collection: Informed written consent was taken from each case to draw blood sample, undergo ultrasonological evaluation and endoscopic examination. Detailed history and examination of all patients was carried out to assess the grades of hepatic encephalopathy and ascites. Blood samples were taken and sent to central laboratory C.M.C Larkana for detection of serum bilirubin (normal value 0.2 – 1 milligram per deciliter (mg/dL), serum albumin (normal value 3.5 – 7.5 gram per deciliter (g/dL) and international normalized ratio (INR).

Endoscopic evaluation of all patients was done by a gastroenterologist having 10 year experience in endoscopy and were graded as,

- Grade 1: Varix is flush with the wall of the esophagus.
- Grade 2: Protrusion of the varix but not more than half way to the lumen center
- Grade 3: Protrusion more than halfway to the center.
- Grade 4: The varices are so large that they meet at the midline.

A separate Performa was filled for each patient entered into the study to record the data of these investigations and demography. All investigations were performed at the laboratory of CMC teaching hospital.

Data Analysis: The collected data was transferred to and analyzed using SPSS version 19. Means and SD (standard deviation) of numeric response variables as age, serum bilirubin, serum albumin, and INR were calculated. Frequencies and percentages were calculated for categorical response variables such as age (15 – 29 years, 30 – 44 years, 45 – 59 years, 60 – 74 years), gender, CTP classes (A, B & C), hepatic encephalopathy (grade 1, grade 2, grade 3, grade 4), serum bilirubin (<2 mg/dl, 2 – 3 mg/dl, > 3 mg/dl), serum albumin (>3.5 g/dl, 2.8 – 3.5 g/dl, < 2.8 g/dl) and INR (< 1.7, 1.7 – 2.2, > 2.2). CTP classes and CTP variables were compared in patients with and without varices by Chi-square test where applicable. Odd ratios (OR) and 95% Confidence Interval (CI)

TABLE NO:3.
SIGNIFICANSE OF CHILD TURCOT PUGH VARIABLES, AGE AND GENDER IN LIVER CIRRHOSIS PATIENTS WITH AND WITHOUT VARICES

VARIABLES	VARICES (N=389)	NO VARICES (N=350)	P value**	ODD RATIOS OR (95% CI)
AGE				
Mean ±SD	50.33 ± 15.19yrs	40.78 ± 13.41yrs	< 0.001*	NA
15 – 29 years	58 (14.9%)	105 (30.0%)	< 0.001*	0.40 (0.28 – 0.58)
30 – 44 years	41 (10.5%)	84 (24.0%)	< 0.001*	0.37 (0.24 – 0.56)
45 – 59 years	168 (43.2%)	128 (36.6%)	< 0.067	1.31 (0.98 – 1.77)
60 – 74 years	122 (31.4%)	33 (9.40%)	< 0.001*	4.38 (2.89 – 6.66)+
GENDER				
MALE	269 (69.2%)	212 (60.6%)	< 0.015*	1.45 (1.07 – 1.97)+
FEMALE	120 (30.8%)	138 (39.4%)		
SERUM ALBUMIN (ALB)				
Mean ±SD	2.98 ± 0.64 g/dl	3.83 ± 0.65 g/dl	< 0.001*	NA
ALB > 3.5 g/dl	129 (33.2%)	247 (70.6%)	< 0.001*	0.20 (0.15 – 0.28)
ALB 2.8 – 3.5 g/dl	135 (34.7%)	71 (20.3%)	< 0.001*	2.08 (1.49 – 2.91)+
ALB < 2.8 g/dl	125 (32.1%)	32 (9.10%)	< 0.001*	4.70 (3.08 – 7.17)+
SERUM BILIRUBIN (BILI)				
Mean ±SD	2.19 ±0.99 mg/dl	1.96 ±0.77 mg/dl	< 0.063	NA
BILI < 2 mg/dl	147(37.8%)	163 (46.6%)	< 0.016*	0.69 (0.52 – 0.93)
BILI 2 – 3 mg/dl	112 (28.8%)	113 (32.3%)	< 0.303	0.84 (0.62 – 1.16)
BILI > 3 mg/dl	130 (33.4%)	74 (21.1%)	< 0.001*	1.87 (1.34 – 2.60)+
INTERNATIONAL NORMALIZED RATIO (INR)				
Mean ±SD	1.98 ±0.47	1.39 ±0.39	< 0.001*	NA
INR < 1.7	88 (22.6%)	246 (70.3%)	< 0.001*	0.12 (0.08 – 0.17)
INR 1.7 – 2.2	67 (17.2%)	75 (21.4%)	< 0.147	0.76 (0.52 – 1.10)
INR > 2.2	235 (60.4%)	29 (8.30%)	< 0.001*	16.89 (10.97 – 25.99)+
HEPATIC ENCEPHALOPATHY (HE)				
HE GRADE 1	30 (7.70%)	32 (9.10%)	< 0.484	0.83 (0.49 – 1.39)
HE GRADE 2	16 (4.10%)	184 (52.6%)	< 0.001*	0.03 (0.02 – 0.06)
HE GRADE 3	47 (12.1%)	51 (14.6%)	< 0.319	0.80 (0.52 – 1.23)
HE GRADE 4	29 (7.50%)	00 (0.00%)	< 0.001*	1.97 (1.83 – 2.12)+
ASCITES				
PRESENT	322 (82.8%)	306 (87.4%)	< 0.077	0.69 (0.45 – 1.04)

**Chi – square test (2-sided significance)
*Statistically significant p values (<0.05)
+Significant and high odd ratios
NA. Not Applicable

were calculated. Probability value (p-value) of less than 0.05 (<0.05) was considered to be statistically significant

RESULTS:

A total of 739 patients were studied with mean age of 45.81 ± 15.13 years and 481 (65.1%) male. Varices were documented in 52.6% patients. Grade 1 varices was documented in 58 (7.8%), grade 2 varices in 45 (6.1%), grade 3 varices in 162 (21.9%) and grade 4 varices in 124 (16.7%) participants. 248 (33.6%) patients were in CTP class C, 225 (30.4%) in CTP class B and 266 (36.0%) in CTP class A. Their demography is outlined in table 1. The details of CTP variables are outlined in table 2.

INR > 2.2 was seen in 235 (60.4%) patients with varices (p < 0.001) as compared to 29 (8.3%) cirrhotic patients without varices, with odds of 16.89 (95% CI: 10.97 – 25.99). Serum albumin < 2.8 mg/dl was seen in 125 (32.1%) patients with varices (p < 0.001) as compared to 32 (9.1%) cirrhotic patients without varices, with odds of 4.70 (95% CI: 3.08 – 7.17). Serum bilirubin > 3 mg/dl was seen in 130 (33.4%) patients with varices (p < 0.001) as compared to 74 (21.1%) cirrhotic patients without varices, with odds of 1.87 (95% CI: 1.34 – 2.60). (Table 3)

Mean CTP score (p < 0.001) in patients with varices was 9.20

TABLE NO 4:
RELATION OF ESOPHAGEAL VARICES IN CHILD TURCOT PUGH (CTP) CLASSES OF CIRRHOSIS OF LIVER

CTP CLASS	VARICES	NO VARICES	P value**	ODD RATIOS OR (95% CI)
ALL PATIENTS				
M EAN ± SD	9.20 ± 1.93	6.42 ± 1.91	< 0.001*	2.53 (2.22 – 2.83)+
CTP CLASS A	30 (7.70%)	236 (67.4%)	< 0.001*	0.04 (0.02 – 0.06)
CTP CLASS B	147 (37.8%)	72 (20.6%)	< 0.001*	2.34 (1.68 – 3.26)+
CTP CLASS C	212 (54.5%)	42 (12.0%)	< 0.001*	8.78 (6.01 – 12.83)+
PATIENTS WITH GRADE 1 VARICES				
CTP CLASS A	10 (17.2%)	256 (37.6%)	< 0.002*	0.34 (0.17 – 0.69)
CTP CLASS B	8 (13.8%)	211 (31.0%)	< 0.006*	0.35 (0.16 – 0.76)
CTP CLASS C	40 (69.0%)	209 (30.7%)	< 0.001*	5.01 (2.81 – 8.96)+
PATIENTS WITH GRADE 2 VARICES				
CTP CLASS A	0 (0.00%)	266 (38.3%)	< 0.001*	1.10 (1.07 – 1.13)+
CTP CLASS B	10 (22.2%)	209 (30.1%)	< 0.261	0.66 (0.32 – 1.36)
CTP CLASS C	35 (77.8%)	214 (30.8%)	< 0.001*	7.85 (3.81 – 16.14)+
PATIENTS WITH GRADE 3 VARICES				
CTP CLASS A	8 (4.90%)	258 (44.7%)	< 0.001*	0.06 (0.03 – 0.13)
CTP CLASS B	64 (39.5%)	155 (26.9%)	< 0.002*	1.77 (1.23 – 2.56)+
CTP CLASS C	90 (55.5%)	159 (27.6%)	< 0.001*	3.28 (2.29 – 4.70)+
PATIENTS WITH GRADE 4 VARICES				
CTP CLASS A	12 (9.70%)	254 (41.3%)	< 0.001*	0.15 (0.08 – 0.28)
CTP CLASS B	65 (52.4%)	154 (25.0%)	< 0.001*	3.29 (2.21 – 4.90)+
CTP CLASS C	90 (55.5%)	159 (27.6%)	< 0.001*	3.28 (2.29 – 4.70)+

**Chi – square test (2-sided significance)
*Statistically significant p values (<0.05)
+Significant and high odd ratios
NA. Not Applicable

± 1.93 as compared to 6.42 ± 1.91 with odds of 2.53 (95% CI: 2.22 – 2.83). Most of the patients with varices were in CTP class C ($p < 0.001$) with odds of 8.78 (95% CI: 6.01 – 12.83), as compared to patients without varices, who tend to be in CTP class A ($p < 0.001$). The relation of grades of varices to CTP classes is detailed in table 4.

DISCUSSION:

Upper gastrointestinal (GI) bleed is a devasting complication of cirrhosis of liver. Many factors contribute to severity of bleed and prognosis. Some scoring systems have been developed to predict the prognosis of upper GI bleed, but the single most important factor predicting survival in variceal bleed is liver functional status. Patients with advanced liver disease tend to have worse prognosis. Possible reasons can be coagulopathy due to decrease synthesis or activation of coagulation factors, increase fragility of gut mucosa due to congestive gastropathy, vitamin K deficiency, high portal pressure and increasing size (grades) of esophageal varices. Child Turcot Pugh (CTP) scoring system is a non invasive method of predicting the prognosis of cirrhosis. Greater the score, poor is the hepatic functional status, greater the chances of bleed from esophageal varices and greater is the mortality.[,]

So, our study aimed to document the presence of varices in different CTP classes. We documented that patients with varices had advanced liver disease as compared to cirrhotic patients without varices. Most of the patient with varices were in CTP class C ($p < 0.001$) and (OR: 8.78 (95% CI: 6.01 – 12.83)). The mean CTP score of patients with varices was 9.20 ± 1.93 as compared to 6.42 ± 1.91in cirrhotics without varices.

Giannini EG et al., reported that prevalence of varices increased with detoriating hepatic function. Esophageal varices was documented in 78.1% cirrhotic in CTP class C, as compared to 34.2% in CTP class A. CTP class C has a sensitivity and negative predictive value for esophageal varices of 100%, but sensitivity and positive predictive values is 37.1% and 89.3%. The same findings were also endorsed by Madhotra R et al. Distribution of esophageal varices in CTP classes reported by him was 35%, 60% and 69 % in child class A, B, and C respectively.[,]

The results of our study are consistent with studies performed elsewhere. The major limitation of our study was that we did not search for gastric or ectopic varices. If we would have searched for them, the incidence of varices might have been much higher. Another limitation of study was generalization of our study. Our study may be representative of rural and poor areas of Pakistan, but the trend in urban areas is somewhat different. In rural areas, health facilities are limited and patient seeks medical advice when

disease is advanced. So, our data may be representative of rural areas of Pakistan, but not urban.

CONCLUSIONS & RECOMMENDATIONS

From the above discussion based on international data, we can conclude and recommended that,

1. Esophageal varices are commonly detected in patients with advanced liver disease.
2. Due to lack of endoscopy centre in rural areas and poverty, it may be more practical and economically feasible to refer all patients with Child Turcot Pugh class C to tertiary care centers, as chances of detecting varices is high and mortality is increased.
3. It may also be possible to start patient beta – blocker as primary prophylaxis in patients with CTP class C.
4. We recommend that multicentre and large scale trial should be conducted, so that we can establish local guidelines for general practitioners regarding managing cirrhotic patients at high risk of bleeding esophageal varices in the absence of endoscopy.

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