# Correlation of Child-Pugh Classification with Esophageal Varices in Patients with Liver Cirrhosis

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**ABSTRACT**

**Introduction:** The severity of the chronic liver disease can be assessed by several non-invasive methods one of them includes scoring system like Child-Pugh classification. **Aims:** The objective of this study was to assess the correlation of Child Pugh class with esophageal varices in patients with liver cirrhosis. **Methods**: This was a cross-sectional hospital-based study of 406 patients with liver cirrhosis. Demographic and relevant clinical data were collected using a standardized questionnaire. Abdominal ultrasound, liver function test, full blood count, viral markers were done for all patients. All patients underwent upper gastrointestinal endoscopy to screen for varices and if found were categorized as small and large. **Results:** A total of 406 patients with a mean age of 48 ± 11 years were evaluated. There were 72.4% and 27.6% men and women respectively. Variceal screening by upper gastrointestinal endoscopy revealed esophageal varices in 90.1% patients. By Child-Pugh Classification, 60 (14.8%) patients were in class A, 156 (38.4%) in class B and 190 (46.8%) in class C. Among patients with Child class A, 29 (48.3%) had varices. Similarly, 147 (94.2%) and 190 (100%) of Child class B & C had varices respectively. Odds of presence of esophageal varix were 9 times higher for patients with Child-Pugh Classification B and C compared to class A. **Conclusion**: Most patients with cirrhosis present late and with advanced stage in this referral center. Most have esophageal varices on their first screening endoscopy. Child-Pugh classification is a reliable measure of stratifying variceal risk in chronic liver disease patients.

***Keywords:*** Child pugh classification, Esophageal varices, Liver disease

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## INTRODUCTION

Cirrhosis, which is defined as the histological development of regenerative nodules surrounded by fibrous bands can lead to portal hypertension (PHTN).[1] The formation of venous collaterals in an attempt to decompress the portal venous systemcan lead to generation of varices and variceal bleed which contribute to the morbidity and mortality of the disease. Small varices can progress to large varices at a rate of 10% annually.[2] Annual risk of variceal bleeding among small and large varices is 5% and 15% respectively.[3] The six-week mortality rate with index variceal bleeding is approximately 20%.[4] Given the high prevalence of varices and the significant mortality rate associated with variceal hemorrhage, early diagnosis of varices is of paramount importance in the management and in the prevention of liver-related morbidity and mortality. Child-Pugh classification (CPC) and Model for End-stage Liver Disease (MELD) are the commonly used models to stratify risk in cirrhotic patients. The Child-Pugh score is described in Table I. Patients with a score of 5 or 6 denotes CPC-A i.e., well-compensated, those with a score of 7 to 9 denote CPC-B i.e., significant functional compromise, and those with a score greater than 10 denote CPC-C i.e., decompensated cirrhosis. Child-Pugh class is also associated with the increased likelihood of developing complications. As an example, prevalence of varices in CPC- A, B and C is 42.7%, 70.7% and 75.5% respectively.[5,6] The aim of the current study is to determine the severity of cirrhosis on the basis of CPC and its correlation with esophageal varices.

## METHODS

From a prospectively collected database, we analyzed the data of 406 consecutive patients with chronic liver disease (CLD) of liver unit, Bir Hospital from March to June 2019. The study participants were recruited for the original study after

obtaining their informed consent and the study was approved by the institutional review board and ethics committee.[7] CLD was diagnosed on the basis of history, clinical examination, laboratory parameters, and ultrasound findings. Ultrasound findings suggestive of CLD/cirrhosis[8] were noted. Those included nodular surface or irregular margin of liver with dull edge, coarse echo texture and increase portal vein diameter ≥ 12 mm. Patient unwilling to give consent, or with ongoing comorbid conditions like acute exacerbation of chronic obstructive pulmonary disease/asthma, myocardial infarction (within six months) and patients on the ventilator were excluded. Patients having Hepatocellular carcinoma, portal vein or splenic vein thrombosis, Severe alcoholic hepatitis, acute on chronic liver failure, non-cirrhotic portal hypertension, and CLD of unknown etiology/mixed etiology were excluded. Patients on beta-blockers, non-steroidal anti-inflammatory drugs, proton pump inhibitors, and active bleeding were also excluded.

All the patients underwent upper GI endoscopy (Fujinon EPX 2500). The presence of esophageal varices (EV) was noted and graded as small varices (straight, <5 mm) and large EV (tortuous >5 mm) as per the American Association for the Study of Liver Disease Guidelines.[9]

### Stratifying liver disease severity

Complete blood count, renal function test, liver function test, abdominal ultrasonography, prothrombin time, International Normalized ratio (INR) level data were collected. The severity of liver disease was assessed by Child-Pugh class.[10]

| Parameter | Points Assigned | | |
|---|---|---|---|
| | 1 | 2 | 3 |
| **Ascites** | Absent | Slight | Moderate |
| **Bilirubin** | <2 mg/dL | 2 to 3 mg/dL | >3 mg/dL |
| **Albumin** | >3.5 g/dL | 2.8 to 3.5 g/dL | <2.8 g/dL |
| **INR** | <1.7 | 1.7 to 2.3 | >2.3 |
| **Encephalopathy** | None | Grade 1 to 2 | Grade 3 to 4 |

A total Child-Pugh score of 5 to 6 is considered Child-Pugh class A (well-compensated disease); 7 to 9 is CPC-B (significant functional compromise); and 10 to 15 is CPC-C (decompensated disease)

***Table I: Child Pugh Classification***

Continuous variables were expressed as mean (±SD) and categorical variables as numbers and percentage. Continuous variables were compared by using Student T-test or Mann Whitney as relevant and categorical variables by chi-square test or Fischer's exact test as relevant. Pearson's correlation coefficient assessed bivariate correlation. Statistical Package for the Social Sciences (SPSS) version 25 was used for statistical analysis. A two-sided p-value of <0.05 was considered significant.

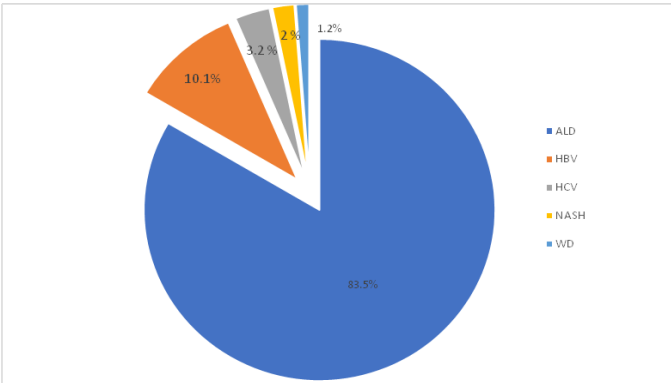
## RESULTS

A total of 406 CLD patients were enrolled for the study. Mean age was 48 ± 11 years with 294 (72.4%) male and 112 (27.6%) females. Patient demographics are listed in Table II

| | All (n=406) | Patients With esophageal Varices n=366 | Patients Without esophageal Varices n=40 |
|---|---|---|---|
| Age, years | 48.5 ±11.1 | 48.78 ±11.17 | 46.35 ±10.37 |
| **Sex** | | | |
| Male | 294 (72.4%) | 267 (90.8%) | 27 (9.2 %) |
| Female | 112 (27.6%) | 99 (88.4%) | 13 (11.6%) |
| **Clinical findings [n (%)]** | | | |
| Ascites | | | |
| None | 68 (16.7%) | 39 (57.4%) | 29 (42.6%) |
| Mild | 111 (27.3%) | 100 (90.1%) | 11 (9.9%) |
| Mod-Severe | 227 (55.9%) | 227 (100%) | 0 (0.0%) |
| **Laboratory findings [mean ±SD]** | | | |
| Hemoglobin (gm/dl) | 9.62 ±1.77 | 9.62 ±1.77 | 10.5 ±2.01 |
| Albumin (gm/dl) | 2.9 ±0.6 | 2.82 ±0.55 | 3.64 ±0.54 |
| Platelet (x103/µL) | 124 ±42 | 117 ±35 | 184 ±46 |
| Bilirubin (mg/dl) | 4.36 ±5.25 | 4.61 ±5.2 | 4.61 ±5.2 |
| AST, IU/L | 126 ±111 | 123 ±97 | 155 ±195 |
| ALT, IU/L | 64 ±121 | 57 ±78 | 125 ±302 |
| INR | 1.57 ±0.43 | 1.6 ±0.44 | 1.32 ±0.22 |
| Creatinine (mg/dl) | 1.05 ±0.58 | 1.06 ±0.60 | 0.9 ±0.3 |

***Table II: Profile of study population***

The etiology of CLD was alcohol-related (ALD) in 339 (83.5%) patients. Chronic HBV and HCV-related liver disease was found in 41 (10.1%) & 13 (3.2%) of patients. 8 (2%) patients were found to be probable NASH related and 5 (1.2%) patients had Wilson disease. Figure 1.

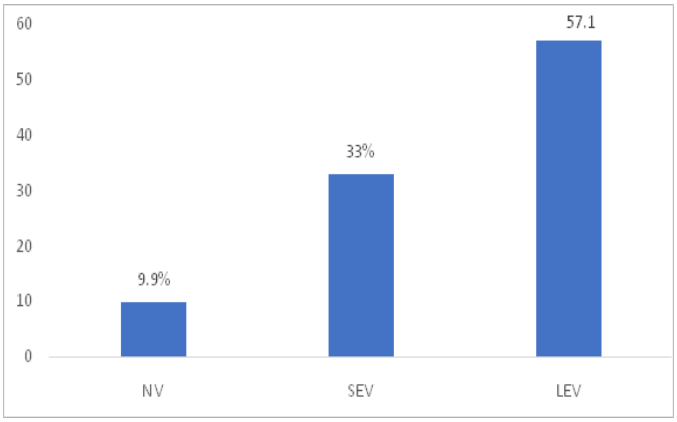



ALD; alcohol-related liver disease, HBV; chronic hepatitis B related, HCV; chronic hepatitis C related, NASH; probable non-alcoholic steatohepatitis, WD; Wilson disease

***Figure 1: Chronic liver diseases according to etiology***

### Profile of variceal Assessment

Three hundred sixty-six patients (90.1%) had esophageal varices and 40 (9.9%) had no varices. Among all patients, 134 (33%) had small and 232 (57.1%) had large esophageal varices. Figure 2.




NV; no varices, SEV; small esophageal varices, LEV; large esophageal varices

***Figure 2: Assessment of esophageal varices after endoscopy***

### Liver disease severity assessment

Severity of liver disease was assessed by Child-Pugh classification. Based on Child-Pugh score, 60 (14.8%) patients were in CPC-A, 156 (38.4%) in CPC-B and 190 (46.8%) in CPC-C at presentation. Table III. Among patients with CPC-A, 29 (48.3%) had varices. Similarly, 147 (94.2%) and 190 (100%) of CPC-B & C had varices respectively. Table IV.

| CP Score | N (%) |
|---|---|
| <7 | 60 (14.8%) |
| 7-9 | 156 (38.4%) |
| ≥10 | 190 (46.8%) |
| Total | 406 (100%) |

***Table III: Severity of liver disease by CP Score***

| | EGD Findings | | Total |
|---|---|---|---|
| | Without varices | With varices | |
| CPC- A | 31 (51.7%) | 29 (48.3%) | 60 |
| CPC- B | 9 (5.8%) | 147 (94.2%) | 156 |
| CPC- C | 0 | 190 (100%) | 190 |
| Total | 40 (9.9%) | 366 (90.1%) | 406 |

Pearson's Chi-square test p-value of 0.0001 (<0.05) shows that there is association between these two variables

***Table IV: CP class and Upper GI endoscopy Crosstabulation***

Crosstabulation Child Pugh and varices shows that there is association (p-value of 0.0001 (<0.05) between these two variables. Multivariate logistic regression analysis confirms that odds of presence of esophageal varix is 6.1 times higher for patients with ascites compared to patients without ascites controlling for other variables and 9.41 time higher for patients with CPC-B and C compared to the patient's CPC-A score controlling for other variables in the model. Table V

| | Unadjusted (bi-variate) model | | | Adjusted (multivariate) model | | |
|---|---|---|---|---|---|---|
| Variable | OR | SE | p-value | AOR | SE | p-value |
| Age | 1.020 | 0.015 | 0.190 | 1.029 | 0.026 | 0.302 |
| **Sex** | | | | | | |
| Female | Reference | | | | | |
| Male | 1.299 | 0.358 | 0.465 | Dropped as p-value>0.25 | | |
| **Ascites Categories** | | | | | | |
| None | Reference | | | | | |
| Mild+Severe | 22.105 | 0.393 | <0.0001 | 6.101 | 0.650 | 0.006 |
| **CPS Categories** | | | | | | |
| Class A | Reference | | | | | |
| Class B+C | 40.027 | 0.425 | <0.0001 | 9.408 | 0.713 | 0.002 |
| HB | 0.711 | 0.105 | 0.001 | 0.890 | 0.157 | 0.459 |
| PLT | 1.000 | 0.000 | <0.0001 | 1.000 | 0.000 | <0.0001 |
| AST | 0.998 | 0.001 | 0.102 | Dropped as VIF > 2 | | |
| ALT | 0.998 | 0.001 | 0.011 | 0.998 | 0.002 | 0.184 |
| INR | 11.377 | 0.624 | <0.0001 | 0.561 | 0.984 | 0.542 |
| Bilirubin | 1.297 | 0.099 | 0.009 | 1.022 | 0.075 | 0.768 |
| Creatinine | 2.269 | 0.444 | 0.065 | 1.760 | 0.769 | 0.444 |

***Table V: Bivariate and multivariate logistic regression result***

Note: Variables with p-value>0.25 in the unadjusted model as it can no longer considered clinically significant and variables with variance inflation factor >2 were dropped from the adjusted model as it confirms the confounding effect. OR = Odds ratio, SE=Standard error, AOR=Adjusted odds ratio, VIF = Variance inflation factor

## DISCUSSION

Cirrhosis is a leading cause of mortality and morbidity across the world. It ranks as 11$^{th}$ leading cause of death and 15$^{th}$ leading cause of morbidity, that accounts for 2.2% of deaths and 1.5% of disability-adjusted life years worldwide in 2016.[11] Based on data of Global burden of Disease study, the age-standardized incidence rate of CLD was 20.7 per 100000 in 2015, a 13% increase from 2000. The estimated incidence in Southeast Asia is 23.6 per 100000.[12] Historically, Alcohol and chronic viral infections accounted for major causes of CLD, however NAFLD is on the rise changing the trend globally. Globally, 1.5 billion peoples had CLD in 2017, among which the most common cause was NAFLD (60%), HBV (29%), HCV (9 %) and ALD (2 %).[13]

Multiple recent developments have reshaped the epidemiology of CLD. Vaccination campaigns, obesity epidemic, metabolic syndrome, improved HCV treatment are one of the few examples that could have been the factors. It should be understood that precise estimate of ALD is difficult to determine as the diagnosis relies on patient's self-report of alcohol intake, unlike condition of viral hepatitis, which can be determined based on lab testing. In summary, the three most

common causes of CLD in Nepal can be attributed to alcohol, chronic viral infection like HBV & HCV and NAFLD-related.

Assessment of severity of liver disease is best done by liver biopsy. However, in recent era, non-invasive methods are also proven to be a reliable measure. These includes Liver Elastography (e.g., Fibroscan), scoring systems like AST/platelet ratio (APRI), Hepascore model, MELD and CPC are among the few. In this study we have assessed the severity in terms of Child-Pugh class. An important parameter of CPC is "Ascites". Ascites is also a marker of decompensation and thus reflects the onset of progression towards end-stage liver disease. In this study, 16.7% had no ascites, 27.3% had mild (grade-1) and 55.9% had mod-severe (grade2-3) ascites. Upon Bivariant analysis, the adjusted model confirms that odds of presence of esophageal varix is 6.1 times higher for patients with ascites compared to patients without ascites.

In this study, all 406 patients underwent variceal screening by upper GI endoscopy. Among which 90.1% had esophageal varices. Among patients with varices, 33% had small and 57.1% had large esophageal varices. Study by Shrestha et al[14] reported varices of 95 %, whereas varices were present in 57.3% and 57.5% in study of Chaudhary et al[15] and Bhattarai et al[16] respectively. Further subtyping of varices cannot be compared because of the use of different grading system. Based on CPC score, 14.8% patients were in class A, 38.4% in class B and 46.8% in class C in this study. Among patients with Child class A, 48.3% had varices. Similarly, 94.2% and 100% of Child class B & C had varices respectively. Crosstabulation Child Pugh class and varices shows that there is an association (p-value of 0.0001 (<0.05) between these two variables. Multivariant logistic regression analysis confirms that odds of presence of esophageal varix is 9.41 times higher for patients with CPC-B and C compared to the patient with CPC-A. Bhattarai et al[16] study showed a similar result. In their study, CPC- A, B & C had 16.6%, 19.1% and 79.9% varices respectively and this difference in detection of varices in different CPC grades was statistically significant (P <0.05). Similar was the findings from the study by Shrestha et al[14] that shows the correlation between higher grades of varices with higher Child Pugh score (CPC- B and C).

## LIMITATIONS

This study is not without limitations. First, CLD was diagnosed based on clinical, laboratory and radiologic examinations. Histological diagnosis and severity assessment was not done. Secondly, since this study was conducted at a single, tertiary referral center with convenient sampling, thus the result might not be generalized. Most patients with end stage liver disease are more likely to get recruited. Thus, there are chances of selection bias. A community-based study could eliminate this error but it would be expensive and time consuming. Thirdly, another parameter "Hepatic encephalopathy (HE)" was taken into consideration. Patients with mild – moderate HE was admitted and managed and thereafter endoscopy was done. However, patients with severe HE whose altered mental status couldn't be reverted despite adequate management were excluded from the study as endoscopic assessment was out of the question. Finally, apart from esophageal varices, gastric varices and portal hypertensive gastropathy were not taken into consideration.

## CONCLUSION

In terms of severity of CLD, as measured by Child-Pugh classification score, higher the Child-Pugh class, greater the proportion of occurrence of varices is present.

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Conflict of Interest: None.

## REFERENCES

1. Schuppan D and Afdhal NH. Liver Cirrhosis. Lancet. 2008;371(9615):838–51. PMID: 18328931 DOI: 10.1016/S0140-6736(08)60383-9

2. Merli M, Nicolini G, Angeloni S, Rinaldi V, De Santis A, Merkel C, Attili AF, Riggio O. Incidence and natural history of small esophageal varices in cirrhotic patients. J Hepatol. 2003;38:266-72. PMID: 12586291 DOI: 10.1016/s0168-8278(02)00420-8

3. North Italian Endoscopic Club for the Study and Treatment of Esophageal Varices. Prediction of the first variceal hemorrhage in patients with cirrhosis of the liver and esophageal varices. A prospective multicenter study. N Engl J Med 1988;319:983-89. PMID: 3262200 DOI: 10.1056/NEJM198810133191505

4. Amitrano L, Guardascione MA, Manguso F, Bennato R, Bove A, DeNucci C, Lombardi G, Martino R, Menchise A, Orsini L, Picascia S, Riccio E. The effectiveness of current acute variceal bleed treatments in unselected cirrhotic patients: refining short-term prognosis and risk factors. Am J Gastroenterol. 2012;107:1872-8. PMID: 23007003 DOI: 10.1038/ajg.2012.313

5. Kovalak M, Lake J, Mattek N, Eisen G, Lieberman D, Zaman A. Endoscopic screening for varices in cirrhotic patients: data from a national endoscopic database. Gastrointest Endosc. 2007;65:82-8. PMID: 17185084 DOI: 10.1016/j.gie.2006.08.023

6. D'Amico G, Pagliaro L, Bosch J. The treatment of portal hypertension: a meta-analytic review. Hepatology. 1995;22:332-54. PMID: 7601427 DOI: 10.1002/hep.1840220145

7. Tiwari P S, Kc S, Sharma D, et al. Prevalence of Portal Hypertensive Gastropathy in Chronic Liver Disease and Correlation with the Severity of Liver disease. Cureus. 2019;11(8):e5454. PMID: 31641555 PMCID: PMC6802813 DOI 10.7759/cureus.5454

8. Procopet B and Berzigotti A. Diagnosis of cirrhosis and portal hypertension; imaging, non-invasive markers of fibrosis and liver biopsy. Gastroenterology report 2017;5(2):79-89.PMID: 28533906 DOI: 10.1093/gastro/gox012

9. Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W, Practice Guidelines Committee of the American Association for the Study of Liver Diseases; Practice Parameters Committee of the American College of Gastroenterology: Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. Hepatology. 2007;46:922-38. PMID: 17879356 DOI: 10.1002/hep.21907

10. Child CG and Turcotte JG: Surgery and Portal Hypertension. The Liver and Portal Hypertension. In: Child, C.G (ed): Saunders, Philadelphia; 1964. 50-64.

11. Global Health Estimates. Geneva: World Health Organization; 2016 Available at: https://www.who.int/healthinfo/global_burden_disease/estimates/en/. Accessed February 2, 2022.

12. Wong M.C.S, Huang J.L.W, George J, et al. The changing epidemiology of liver diseases in the Asia-Pacific region. Nat Rev Gastroenterol Hepatol. 2019;16: 57-73. PMID: 30158570 DOI: 10.1038/s41575-018-0055-0

13. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392:1789-1858. PMID: 28919117 PMCID: PMC5605509DOI: 10.1016/S0140-6736(18)32279-7

14. Shrestha A, Khadka D, Shrestha R. Correlation of Grading of Esophageal Varices with Child Turcotte Pugh Class in Patients of Liver Cirrhosis. JNGMC. 2018;16(2):50-3. DOI:10.3126/jngmc.v16i2.24879

15. Chaudhary S. Clinical Profile and Upper Gastrointestinal Endoscopic Findings of Patients Presenting with Liver Cirrhosis with Portal Hypertension. JKHAS. 2020; 3(1):7. DOI: 10.3126/jkahs.v3i1.27780

16. Bhattarai S, Gyawali M, Dewan KR, Shrestha G. Demographic and Clinical Profile in Patients with Liver Cirrhosis in a Tertiary Care Hospital in Central Nepal. J Nepal Med Assoc. 2017;56(208):401-6. PMID: 29453469