**Original Article**

# Study of Complications of Cirrhosis and their Impact on Survival

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## Abstract

**Introduction:** Cirrhosis of liver is a dreaded disease when decompensated shortens survival. Various complications of cirrhosis adversely affect survival. In the scenario where liver transplantation can offer a definitive cure, prognostication of patients with liver cirrhosis has become an issue of important concern as it can prioritize the patients on waiting list for liver transplant and can ensure proper allocation of donor livers.

**Purpose:** To study the incidence of various complications in patients with cirrhosis and to correlate these complications with the outcome of these patients in terms of mortality.

**Methods:** A total of 96 cirrhotic patients admitted to the Department of Medicine Services, NSCB Medical College, Jabalpur, India, during 2015-2016 were studied. Diagnosis of cirrhosis was based on clinical, biochemical, and ultrasonographic findings. Various complications were assessed and patients were prognosticated using model for end-stage liver disease (MELD) and Child-Turcotte-Pugh (CTP) score. They were then followed up after 3 months and their outcomes were assessed in terms of survival versus mortality.

**Results:** The mean age of patients of cirrhosis was 48 ± 8 years. The male: female ratio was 4:1. Alcoholic cirrhosis predominated constituting about 60.4% of our study population followed by those with hepatitis B virus-induced cirrhosis (19.8%) and hepatitis C virus-related cirrhosis (4.2%). Among complications, ascites was most common (all cases) followed in order of frequency by anemia > thrombocytopenia > hepatic encephalopathy > coagulopathy > hepatorenal syndrome (HRS) > hyponatremia > variceal bleeding. The complications that could be attributed to mortality included HE, HRS, spontaneous bacterial peritonitis, coagulopathy, variceal bleeding, and hyponatremia. All cases (14%) who died belonged to child's C category. Those patients who died had a higher CTP and MELD scores than those who survived.

**Conclusion:** Most complications of cirrhosis had high mortality. Those patients who had high CTP and MELD prognostication score had high chances of mortality.

**Key words:** Cirrhosis, Complications, Mortality

## INTRODUCTION

Cirrhosis has become one of the leading causes of death worldwide with alcohol abuse contributing to the most common inciting etiology in developed countries and viral hepatitis contributing to the vast majority of cases in developing countries. Following the global trend, in our country, also, liver cirrhosis has become a major cause of mortality owing to the large number of cases of viral hepatitis and heavy alcohol consumption.

In this scenario where liver transplantation can offer a definitive cure, prognostication of patients with liver cirrhosis has become an issue of important concern as it can prioritize the patients on waiting list for liver transplant and can ensure proper allocation of donor livers. For about 3 decades, Child-Turcotte-Pugh (CTP) score has been the reference for assessing the prognosis of cirrhotic patients based on its prediction of 1-year survival. Because of its several limitations, model for end-stage liver disease (MELD) score has recently emerged as a modern alternative to CTP

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score for effectively predicting 3-month mortality. However, these days, new modified MELD scores such as MELD-Na and delta MELD have been developed and validated. Other scores that can predict mortality in patients with liver disease include chronic liver failure-sequential organ failure assessment score and Acute Physiology and Chronic Health Evaluation II score.

The main concern of our study was to study the incidence of various complications in patients with cirrhosis and to correlate these complications with the outcome of these patients in terms of mortality versus survival. The study also aims to prognosticate patients with cirrhosis based on MELD and CTP scores and also to compare the predictive efficacy of these scores in predicting the 3-month mortality.

## METHODS

This was a longitudinal prospective study conducted on 96 patients with cirrhosis (diagnosed on the basis of clinical, biochemical, and radiological findings) and who were admitted in various wards and intensive care unit under the Department of Medicine, NSCB Medical College, Jabalpur, India, during a study period of March 1st, 2015, to August 31st, 2016. Cirrhotic patients with significant comorbidities were excluded from the study.

A relevant medical history was taken along with proper clinical examination to look for any stigmata of liver failure. Routine laboratory parameters were studied. Radiological investigations were done including ultrasound of abdomen with Doppler and computed tomography abdomen (whenever necessary). Upper gastrointestinal endoscopy was also performed as per the guidelines.

These patients were then evaluated for various complications such as ascites, spontaneous bacterial peritonitis (SBP), hepatorenal syndrome (HRS), hepatic encephalopathy (HE), coagulopathy, variceal bleeding, and hyponatremia; their CTP and MELD scores were calculated at the time of admission and after 3 months. Their outcomes were assessed in terms of survival versus mortality. Furthermore, correlations were made between various complications present with the outcome of the patients. All the patients were categorized as per Child's Criteria (Table 1) and MELD. MELD score was calculated on the basis of the formula: $(9.57 \times \log \text{creatinine}) + (3.78 \times \log \text{bilirubin}) + (11.2 \times \log \text{INR}) + 6.43$ (constant for liver disease etiology).

The probability level of <0.05 was set for statistical significance. SPSS 10 (SPSS Inc., Chicago, IL, USA) was used for statistical computations. Ethical Committee of the Institute approved the study.

## RESULTS

The mean age of patients of cirrhosis was $48 \pm 8$ years. The male:female ratio was 4:1. Etiology wise, alcoholic cirrhosis predominated constituting about 60.4% of our study population followed by those with hepatitis B virus (HBV)-induced cirrhosis (19.8%) and hepatitis C virus (HCV)-related cirrhosis (4.2%). The complications of cirrhosis are described in Table 2.

On prognostication of these cases using CTP scoring, it was seen that majority of these cases, i.e., about 52.1% ($n = 50$), belonged to the category C and the rest 47.9% ($n = 46$) belonged to category B; none of them belonged to category A. At 3 months, it was found that all the cases who died belonged to category C which constituted about 28% of the total cases which originally belonged to category C. Category B had no mortality; at 3 months, there was reduction in the number of cases from 46 to 35 which implied that 9 cases of 46 cases deteriorated to category C. None of the cases improved to category A.

The presence of variceal bleed, hyponatremia, HRS, SBP, INR >2, and HE were associated with increased mortality. Anemia and thrombocytopenia were not associated with increased mortality. The mean CTP and MELD scores of cirrhotics were significantly higher in those who died than those who survived (Table 3).

### Table 1: CTP criteria for categorizing disease severity in cirrhotic patients

| Parameter | 1 point | 2 points | 3 points |
|---|---|---|---|
| Serum bilirubin (mg/dL) | 2.0 | 2.0-3.0 | >3.0 |
| Serum albumin (g/dL) | >3.5 | 3.0-3.5 | <3.0 |
| Prothrombin time (sec prolonged) | 0-4 | 4-6 | >6 |
| Ascites | None | Easily controlled | Poorly controlled |
| Hepatic encephalopathy | None | Minimal | Advanced |

CTP: Child-Turcott-Pugh

### Table 2: Complications of cirrhosis

| Complications | Number of cases | Wise distribution (%) |
|---|---|---|
| Anemia | 70 | 72.9 |
| Thrombocytopenia | 69 | 71.9 |
| Ascites | 96 | 100 |
| Variceal bleeding | 20 | 20.8 |
| Hepatic encephalopathy | 28 | 29.16 |
| Spontaneous bacterial peritonitis | 14 | 14.6 |
| Hepato-renal syndrome | 25 | 26 |
| Coagulopathy | 26 | 27.1 |
| Hyponatremia | 23 | 24 |

**Table 3: Mean MELD and CTP among dead and survivors**

| Prognostic scores | At admission | | At 3 months |
|---|---|---|---|
| | Dead | Survivors | |
| MELD±SD | 30.2±5.2 | 12.83±3.2 | 16.1±5.1 |
| CTP±SD | 13.93±1.3 | 9.68±1.8 | 9.89±1.5 |

CTP: Child-Turcott-Pugh, MELD: Model for end-stage liver disease, SD: Standard deviation

## DISCUSSION

The mean age of patients of cirrhosis was 48 ± 8 years. The male:female ratio was 4:1. Mean age of our cirrhotic patients was similar to that noted by Kudva in Malaysia.[1] In another study by Baijal et al., the mean age of the patients was 46.42 years, and the male:female ratio was 5:1.[2]

Etiology wise, alcoholic cirrhosis predominated about 60.4% (n = 58) followed by those with HBV-induced cirrhosis about 19.8% (n = 19). Patients with HCV-induced cirrhosis constituted 4.2% (n = 4). In 15 cases (15.6%), no cause could be ascertained. In a study at KEM Hospital, Mumbai, the authors reported that among 72 patients of cirrhosis, etiology of cirrhosis was alcoholism in 37 cases, hepatitis B in 25 cases, and hepatitis C in 10 cases.[3] In the study at GB Pant Hospital, New Delhi, the authors observed that among 176 cases of cirrhosis, 104 were related to viral etiology, 40 with alcoholic liver disease, 26 cryptogenic, and 6 with miscellaneous causes.[4]

Among the complications, ascites was found to be present in 100% of the cases taken (n = 96), meaning that ascites was the most common presenting complaint followed in order of frequency by anemia - 72.9% (n = 70), thrombocytopenia - 71.9% (n = 69), HE - 29% (n = 28), coagulopathy - 27% (n = 26), HRS - 26% (n = 25), hyponatremia - 24% (n = 23), and variceal bleeding - 20.8% (n = 20). In the Goteborg University study, ascites was most common complication in 61% followed by upper gastrointestinal bleeding in 55% and hepatocellular carcinoma in 11%.[5]

On prognostication of these cases using CTP scoring, it was found that about majority of these cases, i.e., about 52.1% (n = 50), belonged to the category C and the rest 47.9% (n = 46) belonged to category B while none of them belonged to category A.

At the end of 3 months, it was found that all the cases who died belonged to category C which constituted about 28% of the total cases which originally belonged to category C. Category B had no mortality, while at the end of 3 months, it was found that there was a reduction in the number of cases from 46 to 35 which implied that about 9 cases out

of 46 deteriorated to category C while the rest remained in the same category. This indirectly implied that liver transplantation is the only definitive cure in cirrhosis and that medical therapy has limited role in decompensated cirrhosis.

Consistent with CTP scoring, the progression of MELD scoring over 3 months also implied the need for liver transplantation in cirrhosis to prevent any clinical deterioration. Those who died had higher CTP and MELD scores than those who survived.

In an article by Attia et al., to study the performance of CTP versus MELD for predicting survival in a retrospective cohort of 172 African cirrhotic patients, by univariate analysis, the following parameters have been found to significantly influence mortality which includes age >48 years ($P < 0.023$), male gender, ($P < 0.003$), CTP score Stage C ($P < 0.016$), MELD >21 ($P < 0.03$). The cutoff value above which maximum mortality was found to occur was 10 for CTP score and 21 for MELD score. AUROC was also significantly more for MELD as compared to CTP at 3 months.[6]

In a case–control study published in NIH public access, 41 cases were identified who died from liver-related causes with a MELD <20 within 3 months while waiting for liver transplant. In univariate analyses, variceal bleed (odds ratio [OR] 5.6, $P = 0.003$), albumin (OR 0.5, $P = 0.041$), increasing cirrhosis stage ($P = 0.003$) and reaching stage 2, 3, or 4 cirrhosis versus lower stages (OR 3.6, $P = 0.048$; OR 7.4, $P < 0.001$; OR 4.1, $P = 0.008$; respectively), sodium < 135 (OR 3.4, $P = 0.006$), and HE (OR 2.3, $P = 0.082$) were associated with liver-related death. In a multivariable model including cirrhosis stage, albumin, sodium, and HE, increasing cirrhosis stage ($P = 0.010$) was independently associated with liver-related death.[7]

## CONCLUSION

Etiology wise, alcoholic cirrhosis predominated over other groups while HBV-induced cirrhosis occupied the second position. Complications wise, ascites was the most common complication as well as the most complaint common presenting complaint followed in order of frequency by thrombocytopenia > HE > coagulopathy > HRS > hyponatremia > variceal bleeding. On prognostication using CTP scoring at the time of admission, majority of the cases had decompensation. Irrespective of their prognostic category, i.e., whether CTP or MELD, at 3-month follow-up, all of the cases were either found to remain in their same prognostic category or deteriorate down to lower down prognostic categories carrying poorer outcome despite giving medical treatment which necessitated the need of liver transplantation as a definitive cure for these patients.

Maximum mortality was observed in child's C category. A major limitation of our study was a small sample size an inability to have a histological diagnosis. Since the facility for liver transplantation was not available in our hospital and majority of patients belong to low socioeconomic status, even after identifying patients belonging to poor prognostic category, definitive cure treatment in the form of liver transplantation could not be offered to these patients.

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