Novel Prognostic Model to Predict In-Hospital Mortality in Patients with Liver Cirrhosis

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ABSTRACT

Background: *Liver cirrhosis remains a major global health concern associated with high in-hospital mortality, especially in Southeast Asia. Existing prognostic scores, such as Child-Pugh and albumin-bilirubin scores, exhibit variable accuracy, necessitating simpler and more practical tools. This study aimed to identify independent predictors and to propose a novel prognostic model of in-hospital mortality in hospitalized cirrhosis patients.* ***Methods:*** *This retrospective cohort study included 190 patients with cirrhosis who were admitted to Adam Malik General Hospital, Medan, between 2022 and 2023. Demographic, clinical, and laboratory data were analyzed using univariate and multivariate logistic regression. A prognostic model was derived from significant variables and evaluated using the area under the receiver operating characteristic curve (AUROC) and Hosmer–Lemeshow test.* ***Results:*** *Of the 190 patients, 79 (41.6%) died during hospitalization. Independent predictors of in-hospital mortality were grade III–IV hepatic encephalopathy (odds ratio [OR] 30.12, 95% confidence interval [CI] 10.71–84.67, p<0.001), serum creatinine (ln-transformed; OR 3.23, 95% CI 1.80–5.79, p<0.001), and international normalized ratio (ln-transformed; OR 17.93, 95% CI 3.54–90.83, p<0.001). The model demonstrated excellent discrimination (AUROC 0.906) and good calibration (Hosmer–Lemeshow p = 0.587).* ***Conclusion:*** *Severe hepatic encephalopathy, renal dysfunction, and coagulopathy were the strongest predictors of in-hospital mortality among patients with cirrhosis. The model derived from these factors demonstrated reliable accuracy in this retrospective cohort and may support risk stratification in clinical practice. However, prospective multicenter studies are required to confirm the validity and clinical utility of this model before its routine application.*

Keywords: *Cirrhosis, mortality, prognostic model, hepatic encephalopathy, creatinine, international normalized ratio (INR).*

INTRODUCTION

Liver cirrhosis is the final stage of chronic liver disease, characterized by fibrosis, vascular remodeling, and progressive hepatocellular dysfunction. It is one of the leading causes of morbidity and mortality worldwide.[1,2] Liver cirrhosis accounted for approximately 1.47 million deaths globally in 2019 and 2.4% of all deaths in 2024, with mortality greatest in Southeast Asia and sub-Saharan Africa.[3,4]. Despite advances in screening, antiviral therapies, and supportive care, liver cirrhosis remains progressive and usually fatal, particularly in Asia, where the hepatitis B and C viruses are prevalent.[5,6]

Southeast Asia bears a disproportionate burden of cirrhosis, with more than 443,000 cirrhosis-related deaths annually.[4] In Indonesia, cirrhosis is often diagnosed late, usually at the decompensated stage, when complications such as ascites, variceal hemorrhage, hepatic

encephalopathy (HE), and hepatorenal syndrome occur.[7–10] Cirrhosis follows a heterogeneous clinical course. Some patients remain compensated for years, while others develop acute decompensation and life-threatening complications such as ascites, variceal hemorrhage, HE, and hepatorenal syndrome.

In patients with cirrhosis, risk stratification is crucial for guiding management, allocating resources, and prioritizing those for intensive monitoring and possibly liver transplantation. Several existing prognostic models that are commonly used, including the Child–Pugh, model for end-stage liver disease (MELD), MELD plus sodium (MELD-Na), and Albumin–Bilirubin (ALBI) scores.[11–15] While these models are useful, they also have their limitations. The Child–Pugh method involves subjective assessments; the MELD and MELD-Na methods may underestimate acute decompensation (e.g., HE), and the ALBI method was designed primarily for patients with hepatocellular carcinoma rather than cirrhosis.[12,16,17]

Given these limitations, there is an urgent need for simple, reliable, and context-appropriate prognostic tools that can be implemented in routine hospital practice, especially in Indonesia. Therefore, this study aimed to identify independent predictors of in-hospital mortality in patients with cirrhosis and propose a novel prognostic function.

METHODS

This retrospective cohort study analyzed all patients diagnosed with cirrhosis who were admitted between January 2022 and December 2023 at the Adam Malik General Hospital, a tertiary referral center in North Sumatra, Indonesia. The inclusion criteria were patients ≥ 18 years old and a confirmed diagnosis of liver cirrhosis based on clinical, laboratory, and imaging findings. All patients who were pregnant, on regular hemodialysis, on antiretroviral therapy, on immunosuppressants, had a history of liver transplantation, known to have any type of advanced-stage cancer, or had incomplete medical records were excluded from this study. This study protocol was approved by the Institutional Ethics Committee at Adam Malik General Hospital, with the need for informed consent waived due to the study's retrospective design.

The patients' demographic, clinical, and laboratory data were extracted from their hospital records. The examined variables were age, sex, comorbidities, presence of ascites, gastrointestinal bleeding, HE, leukocyte count, serum albumin, bilirubin, creatinine, international normalized ratio (INR), sodium, and prognostic scores (Child–Pugh, MELD, MELD-Na, and ALBI). The primary outcome was in-hospital mortality.

All statistical analyses were performed using SPSS (version 25; IBM Corp., Armonk, NY, USA), and $p<0.05$ was considered statistically significant. The analyses included descriptive statistics, bivariate analysis, and multivariate logistic regression with backward selection. Odds ratios (ORs) are reported with 95% confidence intervals (CIs). Model discrimination was assessed using the area under the receiver operating characteristic curve (AUROC), and model calibration was assessed using the Hosmer–Lemeshow test.[15]

RESULTS

During the study period, 190 patients with cirrhosis met the eligibility criteria, of whom 79 (41.6%) died during hospitalization. Among the patients, the mean age was 54.9 years, and most were male (76.8%). Most patients (n=130, 68.4%) had no significant comorbidities at admission. Ascites was present in all patients, reflecting that the study cohort consisted of patients with decompensated cirrhosis. Over half of the patients (n=104, 54.7%) presented with upper gastrointestinal bleeding, while 81 (42.6%) developed HE. Of those with HE, 10 (12.1%) were classified as grade I–II and 25 (30.5%) as grade III–IV (**Table 1**).

Differences in clinical characteristics were apparent between patients who survived and those who died. Severe HE (grade III–IV) was much more frequent among non-survivors, whereas mild HE was more frequent among survivors. Interestingly, gastrointestinal bleeding was slightly more common in survivors, which may reflect that bleeding episodes, although alarming, are often manageable with timely intervention.

Additionally, differences in laboratory parameters were apparent between survivors and non-survivors. Non-survivors exhibited lower serum albumin levels, higher bilirubin levels, elevated creatinine levels, and prolonged INR compared to survivors, indicating more severe hepatic failure, renal dysfunction, and coagulopathy. Hyponatremia was also more frequent among non-survivors. Leukocytosis was more common among non-survivors, possibly suggesting concomitant infection or systemic inflammation (**Table 1**).

The established prognostic tools mirrored these differences. Most deaths occurred in patients classified as Child–Pugh class C and ALBI grade 3. Median MELD and MELD-Na scores were also higher among non-survivors than among survivors, confirming their predictive utility in bivariate analysis (**Table 2**).

Table 1. Demographic Characteristic of The Study

Characteristics	Deceased (n = 79)	Alive (n = 111)	Total (n = 190)
Age (year), mean ± SD	55.73 ± 10.26	54.37 ± 9.59	54.94 ± 9.87
Gender, n (%)			
Male	64 (81)	82 (73.9)	146 (76.8)
Female	15 (19)	29 (26.1)	44 (23.2)
Comorbidity, n (%)			
Yes	22 (27.8)	38 (34.2)	60 (31.6)
No	57 (72.2)	73 (65.8)	130 (68.4)
Upper gastrointestinal bleeding, n (%)			
Yes	46 (58.2)	58 (52.3)	104 (54.7)
No	33 (41.8)	53 (47.7)	86 (45.3)
Hepatic Encephalopathy, n (%)			
Grade III-IV	51 (64.6)	7 (6.3)	58 (30.5)
Grade I-II	8 (10.1)	15 (13.5)	23 (12.1)
None	20 (25.3)	89 (80.2)	109 (57.4)
Ascites, n (%)			
Yes	79 (100)	111 (100)	190 (100)
No	0 (0)	0 (0)	0 (0)
Leukocyte count (x 10^3/µL), n (%)			
Increased	47 (59.5)	23 (20.7)	70 (36.8)
Normal	29 (36.7)	73 (65.8)	102 (53.7)
Decreased	3 (3.8)	15 (13.5)	18 (9.5)
Serum albumin (g/dL), mean ± SD	2.36 ± 0.54	2.61 ± 0.56	2.51 ± 0.56
Total bilirubin (mg/dL), median (min – max) (ln)	3.7 (0.20 – 42)	1.32 (0.22 – 14.4)	2.17 (0.20 – 42)
Serum creatinine (mg/dL), median (min – max)	2.41 (0.52 – 16.9)	1.08 (0.37 – 10.3)	1.3 (0.37 – 16.9)
INR, median (min – max) (ln)	1.65 (0.88 – 5.1)	1.35 (0.59 – 3.2)	1.45 (0.59 – 5.1)
Serum sodium (mEq/L), median (min – max)	134.81 ± 6.76	139 (112 – 158)	136.79 ± 6.97
ALBI, n (%)			
Grade 3	63 (79.7)	58 (52.3)	121 (63.7)
Grade 2	16 (20.3)	49 (44.1)	65 (34.2)
Grade 1	0 (0)	4 (3.6)	4 (2.1)
Child-Pugh, n (%)			
C	68 (86.1)	47 (42.3)	115 (60.5)
B	11 (13.9)	62 (55.9)	73 (38.4)
A	0 (0)	2 (1.8)	2 (1.1)
MELD, median (min – max) (ln)	24 (7 – 40)	13 (6 – 36)	16.5 (6 – 40)
MELD-Na, median (min – max) (ln)	23 (10 – 40)	14 (7 – 33)	17 (7 – 40)

Table 2. Bivariate Analysis of The Study

Variables	Bivariate Analysis	
	p value	OR (CI 95%)
Age (year)	0.382	1.014 (0.985 – 1.045)
Gender	0.252	0.663 (0.328 – 1.340)
Comorbidity	0.351	1.349 (0.719 – 2.530)
Variceal Bleeding	0.415	0.785 (0.439 – 1.405)
Hepatic Encephalopathy	<0.001	0.190 (0.123 – 0.292)
Leukocyte count	<0.001	0.238 (0.136 – 0.416)
Serum albumin	0.003	0.242 (0.136 – 0.749)
Total bilirubin	<0.001	2.103 (1.552 – 2.848)
Serum creatinine	<0.001	3.895 (2.406 – 6.307)
INR	<0.001	20.074 (5.731 – 70.309)
Serum sodium	0.001	0.929 (0.888 – 0.972)
ALBI	<0.001	0.282 (0.148 – 0.536)
Child-Pugh class	<0.001	0.121 (0.058 – 0.253)
MELD	<0.001	19.585 (7.957 – 48.205)
MELD-Na	<0.001	34.369 (11.540 – 102.359)

Table 3. Multivariate Analysis of The Study

Variables	Multivariate Analysis		
	Coefficient	p value	OR (CI 95%)
Hepatic Encephalopathy (Grade III-IV)	3.405	0.000	30.117 (10.712 – 84.672)
Hepatic Encephalopathy (Grade I-II)	0.469	0.430	1.599 (0.499 – 5.126)
Creatinine serum (ln)	1.172	0.000	3.228 (1.799 – 5.792)
INR (ln)	2.886	0.000	17.925 (3.537 – 90.829)
Constant	-3.215	0.000	0.040

When all variables were assessed together in a multivariate logistic regression, three remained independently associated with in-hospital mortality:

- **Severe HE (grade III–IV):** Patients in this category had an almost 30-fold increased risk of death (OR 30.12, 95% CI 10.71–84.67, p<0.001).
- **Renal dysfunction (ln-transformed creatinine):** Even modest increases in creatinine were associated with a threefold increased risk of death (OR 3.23, 95% CI 1.80–5.79, p<0.001).
- **Coagulopathy (ln-transformed INR):** A prolonged INR was associated with an almost 18-fold increased risk of death (OR 17.93, 95% CI 3.54–90.83, p<0.001).

The other variables, including serum sodium and bilirubin, were significant in the bivariate models but became non-significant after adjustment, suggesting that their effects were mediated through renal and coagulation pathways.

Based on these predictors, we derived the following new prognostic model:

$$y = -3.215 + (3.405 \times \text{HE grades III–IV}) + (1.172 \times \ln[\text{Creatinine}]) + (2.886 \times \ln[\text{INR}])$$

Note that HE grades III–IV were coded as 1 (yes) or 0 (no).

This model demonstrated excellent performance, with an AUROC of 0.906 (**Figure 1**). An AUROC of greater than 0.9 is generally regarded as outstanding, highlighting the model's strong discriminatory ability. Calibration analysis using the Hosmer–Lemeshow test (p=0.587) revealed good agreement between the predicted and observed outcomes, confirming the model's robustness.

In summary, our findings highlight that severe encephalopathy, renal impairment, and coagulopathy are the independent factors of in-hospital mortality among patients with cirrhosis. Notably, a simple combination of these three parameters yielded a prognostic model with reliable predictive accuracy, potentially offering a practical tool for clinical use.

Table 4. AUROC

Area Under Curve			
Area	SE	p value	CI 95%
0,906	0,023	0,000	0,862 – 0,951

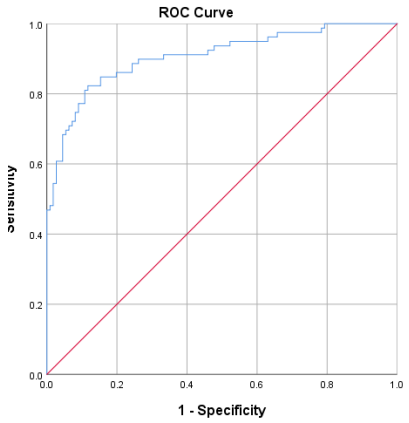

Figure 1. AUROC Graph

DISCUSSION

This study found a high in-hospital mortality rate of 41.6% among patients with cirrhosis, with severe HE, creatinine, and INR identified as independent predictors of in-hospital mortality. These findings align with those of studies conducted worldwide, emphasizing the prognostic importance of HE and renal dysfunction. Compared to cohorts in Western countries, mortality was higher in our Indonesian cohort, reflecting later presentation and limited access to advanced therapies such as transplantation. The mortality rate observed in our study is markedly higher than that reported for a similar cohort in Jakarta (12.0%) and comparable to the 90-day mortality rate (42.2%).[7,18,25] Discrepancies may reflect differences in patient characteristics and access to healthcare.[6,8]

Severe HE was the strongest predictor of in-hospital mortality, increasing the risk up to 30-fold. HE develops in 30%–45% of patients with cirrhosis and is strongly associated with short-term mortality. Bjerring et al. reported higher 90-day mortality in patients with HE grades III–IV.[19] while Bajaj et al. confirmed its prognostic significance in the North American Consortium for the Study of End-Stage Liver Disease cohort.[20,21]

Renal dysfunction, indicated by an elevation in serum creatinine, was identified as another significant predictor of in-hospital mortality. Previous studies have shown that a serum creatinine level ≥2 mg/dL predicts poor short-term survival and acute kidney injury worsens the prognosis.[22–24]

As a marker of acute liver dysfunction and coagulopathy, the INR emerges as a strong predictor of in-hospital mortality. The INR was found to be strongly and positively correlated with short-term mortality in hospitalized patients with cirrhosis in China.[26] Studies from both Ghana and Indonesia have also reported similar results.[7,18]

In our study, hyponatremia was significantly associated with in-hospital mortality in the bivariate analysis but became non-significant in the multivariate analysis. Previous studies have consistently identified sodium as a prognostic marker of in-hospital mortality, with the risk increasing by 5% for every 1 mmol/L decrease in serum sodium.[25,27] According to our findings, coagulation and renal dysfunction might have a greater impact on in-hospital mortality than sodium.

We suggest that in-hospital mortality was more strongly associated with markers of acute decompensation, such as hepatic encephalopathy and renal dysfunction, than with static composite

scores (Child–Pugh, MELD, MELD-Na, and ALBI), although these scores were also significantly associated with mortality.

Two strengths of our study are the large cohort and the creation of a straightforward prognostic model. The prognostic model was intended to provide a more detailed risk stratification for predicting short-term clinical outcomes in individual patients. However, it also had some limitations, including its retrospective single-center design and lack of long-term follow-up. Our proposed model must be validated in multicenter studies before it can be implemented more widely.

CONCLUSION

In-hospital mortality is high among patients with cirrhosis in Indonesia. Severe HE, elevated creatinine, and INR are independent predictors of in-hospital mortality. A novel prognostic model incorporating these variables demonstrated excellent predictive performance in this retrospective single-center cohort. This model offers a practical tool for in-hospital mortality risk stratification in patients with cirrhosis, particularly in settings with limited resources. Nevertheless, prospective multicenter studies are required to confirm the validity, calibration, and clinical applicability of this model before it can be implemented for routine clinical decision-making.

CONFLICT OF INTERESTS

All the authors declare that there are no conflicts of interest.

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