Validation Study of the Cirrhosis Acute Gastrointestinal Bleeding Score as Predictor Mortality in Patients with Liver Cirrhosis and Upper Gastrointestinal Bleeding

I Ketut Mariadi,**, Harris Hardian***, Ajib Zaim Alamsyah**, Ni Luh Putu Yunia Dewi**, Putu Itta Sandi Lesmana Dewi**, Ni Nyoman Gita Kharisma Dewi**, Kadek Mercu Narapati Pamungkas**, Gde Somayana*,**, Komang Agus Wira Nugraha*,**, Dwijo Anargha Sindhughosa*,**, Mohamad Fadli bin Abd Rahman*****

* Division of Gastroenterology and Hepatology, Department of Internal Medicine, Faculty of Medicine, Udayana University/Ngoerah Hospital, Denpasar, Bali, Indonesia
**Centre Research for Alimentary and Hepatobiliary System (CRABS), Denpasar, Bali, Indonesia
*** Department of Internal Medicine, Faculty of Medicine, Udayana University/Ngoerah Hospital, Denpasar, Bali, Indonesia
**** Department of Gastroenterology and Hepatology, Island Hospital, George Town, Penang, Malaysia

Corresponding author:
I Ketut Mariadi. Division of Gastroenterology and Hepatology, Department of Internal Medicine, Faculty of Medicine, Udayana University/Ngoerah Hospital. Jl. Diponegoro, Bali Indonesia 80113. E-mail: mariadi@unud.ac.id. Phone (0361) 227911.

ABSTRACT

Background: *The Cirrhosis Acute Gastrointestinal Bleeding (CAGIB) score was developed as a mortality predictor by integrating a range of clinical and laboratory parameters. This research seeks to validate the efficacy of the CAGIB score in predicting in-hospital mortality among cirrhotic patients experiencing upper gastrointestinal bleeding (UGIB) at Ngoerah Hospital.*

Methods: *This study is a prospective observational study employing a validation test approach. A total of 161 patients diagnosed with liver cirrhosis and upper gastrointestinal bleeding (UGIB) at Ngoerah Hospital were enrolled. Receiver Operating Characteristic (ROC) analysis was utilized to evaluate the prognostic capability of the CAGIB score in predicting mortality and to identify the optimal cutoff point. Validation was conducted by assessing the CAGIB score's sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV).*

Results: *The analysis of the CAGIB score as a predictor of mortality yielded an area under the curve (AUC) value of 0.83, with the optimal cutoff point determined at ≥ -4.66, based on the point farthest from the diagonal line on the ROC curve. The 95% Confidence Interval (CI) ranged from 0.777 to 0.897. Validation testing of the CAGIB score as a predictor of in-hospital mortality demonstrated a sensitivity of 80.8%, specificity of 70.5%, PPV of 69.4%, and NPV of 81.6%.*

Conclusion: *The CAGIB score has been demonstrated to serve as a valid predictor of mortality, exhibiting commendable sensitivity and specificity, along with satisfactory positive and negative predictive values. The optimal cutoff points appropriately reflect the demographic and clinical characteristics of the cirrhosis patient population with UGIB at Ngoerah Hospital.*

Keywords: *Gastrointestinal Hemorrhage, Liver Cirrhosis, Predictive Value, Prognosis, Risk Assessment*

ABSTRAK

Latar Belakang: *Skor Cirrhosis Acute Gastrointestinal Bleeding (CAGIB) dikembangkan sebagai prediktor mortalitas dengan menggabungkan berbagai parameter klinis dan laboratorium. Penelitian ini bertujuan untuk memvalidasi skor CAGIB dalam memprediksi mortalitas selama perawatan inap pada pasien sirosis hepatis dengan perdarahan saluran cerna bagian atas di RS Ngoerah.*

Metode: *Penelitian ini merupakan penelitian observasional prospektif dengan metode uji validasi. Sebanyak 161 pasien sirosis hati dan perdarahan saluran cerna bagian atas di RS Ngoerah direkrut. Analisis Receiver Operating Characteristic (ROC) digunakan untuk menilai kemampuan skor CAGIB dalam memprediksi mortalitas dan menentukan titik potong yang optimal. Validasi dilakukan melalui sensitivitas, spesifisitas, akurasi, nilai prediksi positif (NPP), dan nilai prediksi negatif (NPN) skor CAGIB.*

Hasil: *Analisis skor CAGIB sebagai prediktor mortalitas menghasilkan nilai area under curve (AUC) sebesar 0,83 dengan titik potong optimal ditetapkan pada ≥ -4,65 berdasarkan titik terjauh dari garis diagonal pada kurva ROC. Rentang interval kepercayaan (CI) 95% adalah 0,777 sampai 0,897. Uji validasi skor CAGIB sebagai prediktor mortalitas di rumah sakit menunjukkan sensitivitas 80,8%, spesifisitas 70,5%, nilai NPP 69,4%, dan nilai NPN 81,6%.*

Kesimpulan: *Skor CAGIB terbukti sebagai prediktor mortalitas yang valid dengan sensitivitas dan spesifisitas yang baik, serta nilai NNP dan NPN yang baik, dimana titik potong terbaik mencerminkan karakteristik populasi pasien sirosis dengan perdarahan saluran cerna bagian atas di RS Ngoerah.*

Kata Kunci: *Nilai prediktif, Penilaian risiko, Perdarahan saluran cerna atas, Prognosis, Sirosis hati*

INTRODUCTION

Upper gastrointestinal bleeding (UGIB) resulting from the rupture of gastro-oesophageal varices constitutes the most prevalent cause of UGIB, with an incidence rate reaching 85% among patients with liver cirrhosis. It represents a medical emergency and is regarded as a life-threatening complication of liver cirrhosis.[1] Hospital care reports a mortality rate of approximately 23.5% in cirrhosis patients presenting with UGIB.[2] Early risk stratification in these cases is crucial for guiding clinical decision-making, resource allocation, and providing prognostic information to families. Several scoring systems have been developed to predict outcomes in UGIB (e.g., Rockall, Glasgow-Blatchford, AIMS65) and in cirrhosis (e.g., Child-Turcotte-Pugh [CTP], Model for End-Stage Liver Disease (MELD). However, these tools were not specifically designed for patients presenting with both conditions concurrently, which limits their accuracy and clinical utility in this particular context.[3,4] Consequently, newer, more targeted tools have been developed, such as the Cirrhosis Acute Gastrointestinal Bleeding (CAGIB) score.[5]

The CAGIB score employs straightforward clinical and laboratory variables to forecast in-hospital mortality among patients with cirrhosis experiencing upper gastrointestinal bleeding (UGIB). It has been documented to exhibit superior predictive accuracy for inpatient mortality when compared to the Child-Pugh (CTP), Model for End-Stage Liver Disease (MELD), and neutrophil-lymphocyte ratio (NLR) scores. Furthermore, the parameters included in the CAGIB score depend on more basic variables, such as a history of diabetes mellitus (DM), hepatocellular carcinoma (HCC), as well as serum bilirubin, alanine aminotransferase (ALT), albumin, and creatinine levels. Although the CAGIB scoring system has demonstrated ease of use and practical applicability, it was developed and validated within a Chinese population, where the predominant cause of cirrhosis is non-alcoholic metabolic disease.

Conversely, the primary cause of cirrhosis in Indonesia is hepatitis infection, highlighting notable epidemiological differences between the two regions. Furthermore, mortality rates from cirrhosis-related complications vary, with a reported death rate of 9.6 per 100,000 population in China compared to 25 per 100,000 in Southeast Asia. Meanwhile, gastrointestinal bleeding leads to hospitalization of a substantial number of cirrhosis patients at Ngoerah Hospital. Consequently, a more comprehensive assessment is elucidatwarranted to determine the stratification of mortality among cirrhosis patients experiencing gastrointestinal bleeding.

To date, no validation tests of the CAGIB score have been conducted within the Indonesian population or the Southeast Asia region. Consequently, researchers are interested in performing a validation study of this scoring system within the Indonesian population, particularly at Ngoerah Hospital, to provide a pertinent

tool for enhancing mortality risk stratification and guiding evidence-based clinical management in this demographic.

METHODS

This study is a prospective observational cohort study conducted to validate the CAGIB score for predicting in-hospital mortality among patients with liver cirrhosis presenting with upper gastrointestinal bleeding (UGIB) at Ngoerah Hospital, Denpasar, Indonesia. Ethical approval was obtained from the Institutional Review Board of the Faculty of Medicine, Udayana University (No. 2058/UN14.2.2.VII.14/LT/2024). The study utilizes data derived from patient medical records during the specified period, with assessments based on the CAGIB score criteria in patients diagnosed with liver cirrhosis and UGIB.

The etiology of UGIB was variceal bleeding, including oesophageal and gastric varices, confirmed via endoscopy. The management protocol for all patients adhered to standardized procedures, including resuscitation, administration of vasoactive agents, prophylactic antibiotics, and endoscopic interventions as indicated. Demographic, clinical, and laboratory data, such as serum bilirubin, ALT, albumin, creatinine, history of diabetes mellitus (DM), and hepatocellular carcinoma (HCC), were extracted from medical records to facilitate CAGIB score calculations. Mortality status (alive or deceased) was documented at discharge.

The research was conducted at Ngoerah Hospital, with data collected from a total of 161 patients who were consecutively enrolled and admitted between December 2024 and April 2025. The minimum sample size was calculated using a diagnostic sensitivity estimation formula, assuming a sensitivity of 80%, a mortality rate of 20%, and a margin of error of 5%. Samples were selected via consecutive sampling from hospitalized patients who met the inclusion criteria and did not meet any of the exclusion criteria.

The inclusion criteria comprised patients aged over 18 years with liver cirrhosis and upper gastrointestinal bleeding (confirmed via endoscopy and clinical presentation) who received treatment at Ngoerah Hospital. The exclusion criteria included lower gastrointestinal bleeding, history of liver transplantation, renal replacement therapy, acute-on-chronic liver failure (ACLF), active infection, and hepatic encephalopathy. Patients with ACLF, active infection, and hepatic encephalopathy were excluded because these conditions independently impact short-term prognosis and could confound the predictive accuracy of the CAGIB score. Excluding these conditions was intended to ensure a more homogeneous study population for proper score validation.

Data analysis was conducted utilizing SPSS 25.0. Descriptive statistics were employed to characterize the study subjects. Validity assessments were carried out to evaluate sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy, each accompanied by 95% confidence intervals (CI). Receiver Operating Characteristic (ROC) analysis was implemented to appraise the predictive capability and to establish the optimal cutoff point of the CAGIB score for mortality, with an area under the curve (AUC) of ≥0.7 deemed to indicate strong predictive performance.

RESULTS

Sample Characteristics

A total of 161 patients with liver cirrhosis and UGIB were included. The basic demographic and clinical characteristics of the research subjects can be seen in **Table 1.** The study population was predominantly composed of patients in advanced stages of liver disease, as captured by the CTP class. A substantial proportion of patients also had significant comorbidities, including DM and HCC. More than half of the patients (52.8%) had a CAGIB score in the high category (≥−4.6646).

Table 1. Sample characteristics

Variable	Sample (n=161)
Age (years)	56 (48 – 63)
Gender	
Male, n(%)	111 (68.94%)
Female, n(%)	50 (31.06%)
Hemoglobin (g/dL)	7.9 (6.5 – 9.3)
Etiology	
Alcohol	1 (0.62%)
Hepatitis B	73 (45.34%)
Hepatitis C	40 (24.84%)
Unknown	47 (29.2%)
CTP Class	
A	26 (16.15%)
B	62 (38.51%)
C	73 (45.34%)
Cause of Death	
Liver failure	41 (56.16%)
Massive bleeding	13 (17.80%)
Infection	17 (23.28%)
Cardiovascular	2 (2.7%)
CAGIB score parameters	
Diabetes mellitus	
Yes	122 (75.78%)
No	39 (24.22%)

Variable	Sample (n=161)
Hepatocellular carcinoma	
Yes	38 (23.6%)
No	123 (76.4%)
Albumin (g/dL)	2.5 (2.1–3.0)
ALT (IU/L)	34 (21–68)
Bilirubin (mg/dL)	2.8 (1.4–6.5)
Creatinine (mg/dL)	1.1 (0.8–1.6)
CAGIB Score	−4.1 (−5.8 to −2.3)
Yes (≥ -4,6646)	85 (52.8%)
No (< -4,6646)	76 (47.2%)
Mortality Status	
Yes	73 (54.66%)
No	88 (45.34%)

CTP=Child–Turcotte–Pugh, CAGIB=The Cirrhosis Acute Gastrointestinal Bleeding, ALT= Alanin Aminotransferase

CAGIB Score Cutoff Point as a Mortality Predictor

The evaluation of the CAGIB score as a prognostic indicator for mortality resulted in an Area Under the Curve (AUC) of 0.83. The most appropriate cutoff value, identified as the point maximally distant from the diagonal on the Receiver Operating Characteristic (ROC) curve, was established at ≥ -4.66, as outlined in **Table 2**. Analysis of area under ROC showed that the curve deviates from the diagonal line, indicating reliable separation between survivors and non-survivors, as shown in **Figure 1**.

Table 2. ROC Analysis

ROC Area (95% CI)	Cut Off	Sensitivity	Specificity	LR+	LR-
0.8373 (0.777-0.897)	≥ -4.66	80.8%	70.5%	2.45	0.28

ROC=Receiver Operating Characteristic, LR=Likelihood Ratio

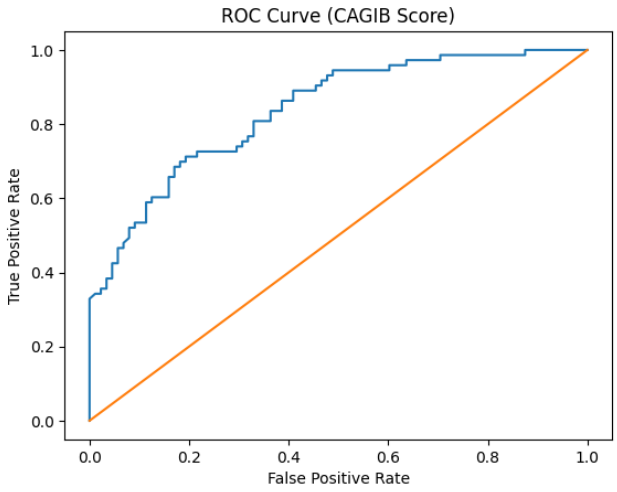

Figure 1. Receiver Operating Characteristic (ROC) Curve of the CAGIB Score (AUC = 0.83, 95% CI 0.777–0.897) for Predicting In-Hospital Mortality

Comparison of CAGIB, CTP, and MELD Score

Comparison analysis of CAGIB, CTP, and MELD score was conducted in 106 patients, due to uncomplete data which need to be included in the calculation of CTP and MELD score. The CAGIB score demonstrates better discriminatory performance compared to CTP and MELD, as shown in **Figure 2.**

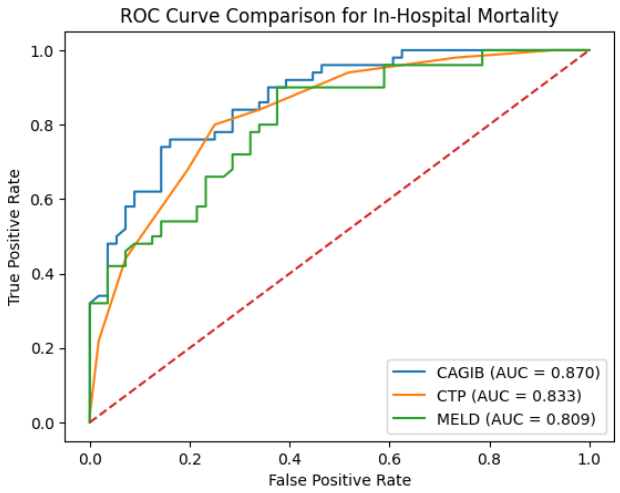

Figure 2. Comparison of CAGIB, CTP, and MELD score in predicting in-hospital mortality

CAGIB Score Validation Test

The validation assessment of the CAGIB score as a predictor for inpatient mortality, utilizing a 2x2 contingency table as illustrated in **Table 3,** indicated a sensitivity of 80.8%, a specificity of 70.5%, a positive predictive value (PPV) of 69.4%, and a negative predictive value (NPV) of 81.6%.

Table 3. Results of CAGIB Score Analysis with Mortality Status

		Mortality		Total
		Yes	No	
CAGIB Score	≥ -4.6646	59	26	85
	< -4.6646	14	62	76
Total		73	88	161

CAGIB= The Cirrhosis Acute Gastrointestinal Bleeding

CAGIB Score Calibration and Overall Accuracy

The calibration and overall predictive performance of the CAGIB score for inpatient mortality were evaluated using a 2x2 contingency matrix. Calibration was assessed by comparing observed mortality rates across CAGIB score categories. Patients with scores greater than or equal to –4.6646 exhibited an observed mortality rate of 69.4%, while those with scores below –4.6646 had a mortality rate of 18.4%. The CAGIB score demonstrated a sensitivity of 80.8% and a specificity of 70.5%, indicating a balanced

ability to correctly identify both patients who died and those who survived. The positive predictive value (64.9%) showed that a substantial proportion of patients classified as high risk experienced mortality. In contrast, the negative predictive value (81.6%) confirmed that most patients categorized as low risk survived. Calculation of overall accuracy using the standard formula (TP+TN)/TP+TN+FP+FN) yielded an accuracy 75.2%, reflecting a robust overall classification performance.

$$\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN}$$

$$= \frac{59 + 62}{59 + 62 + 26 + 14} = 0.752$$

DISCUSSION

The mean age of patients within this study was 55.11 years, with a predominance of males, consistent with research indicating that the incidence of liver cirrhosis is higher in males than in females.[8] Furthermore, the male subset was also reported to have a greater incidence of decompensation and complications compared to females.[9] signifyAdditionally, the mean hemoglobin level was 8.17 g/dL, indicating moderate-to-severe anemia, a common finding among cirrhotic patients presenting with upper gastrointestinal bleeding (UGIB). Similarly, Zhao et al. documented a mean hemoglobin level of 8.2 g/dL among 376 cirrhotic patients with UGIB.[10] Bai et al. (2019) reported a lower mean hemoglobin level of 7.6 g/dL in a cohort of 865 comparable patients.[5] Moreover, Kumar and Sibia (2015) observed that hemoglobin levels below 8.02 g/dL were associated with increased inpatient mortality, and current guidelines recommend restrictive transfusion strategies targeting levels of 7–8 g/dL.[11,12]

Concerning the severity of cirrhosis, the majority of patients were classified as CTP class C (45.34%), followed by class B (38.51%) and class A (16.15%). A comprehensive literature review involving 1,010 patients with liver cirrhosis in Indonesia revealed that the most common CTP category among these patients was class C. Conversely, a cohort study conducted in China reported a different distribution, with the predominant classification as CTP class B (54.1%), followed by class A (29.6%) and class C (16.4%). This variation likely reflects differences in referral patterns and disease burden at presentation. Furthermore, regarding etiology, hepatitis B virus (HBV) infection remains the most prevalent cause (45.34%), followed by hepatitis C virus (HCV) infection (24.84%). Only one case (0.62%) was attributed to alcoholic liver disease.

These findings are consistent with those reported in China, where HBV was the leading cause of cirrhosis, followed by HCV infection and alcoholic liver disease. These studies reinforce the conclusion that HBV and HCV infections remain the leading causes of liver cirrhosis.[10,14] In contrast, alcoholic liver disease was the predominant cause in South Korean cohorts,[15] underscoring the regional variability in cirrhosis etiology. A study in Indonesia also identified viral hepatitis, particularly HBV, as the most common aetiology of cirrhosis in their study population. This aligns with the 2015 report from the Asian Pacific Association for the Study of the Liver, which noted that the Asia-Pacific region has a medium to high prevalence of HBV infection and accounts for 50% of the global hepatitis B burden.[16]

The inpatient mortality rate in this study was 45.34%, significantly higher than the rates documented in certain other studies. Lazar et al. reported a mortality rate of 18.44% among 115 patients within a Romanian cohort.[17] Conversely, Zhao et al. documented a lower inpatient mortality rate of 6.6% among 347 cirrhotic patients presenting with UGIB in China.[10] The elevated mortality rate observed in this study may be ascribed to the setting at Ngoerah Hospital, a tertiary referral center that manages patients with more advanced disease and complications.

The CAGIB score, which incorporates DM, HCC, and laboratory markers such as albumin, ALT, bilirubin, and creatinine, was evaluated in Indonesian patients with cirrhosis experiencing upper gastrointestinal bleeding (UGIB). It was observed that 24.22% of the subjects had diabetes mellitus (DM), and 23.6% had hepatocellular carcinoma (HCC). The mean albumin level was 2.64 g/dL, the mean total bilirubin level was 4.9 mg/dL, the mean ALT level was 59.91 U/L, and the mean serum creatinine level was 1.46 mg/dL. This study marks the initial validation of the CAGIB score within an Indonesian population. The analysis resulted in an area under the curve (AUC) of 0.83, with an optimal cutoff point of ≥ -4.66 (95% confidence interval: 0.777–0.897). These findings indicate that the CAGIB score demonstrates strong performance in predicting inpatient mortality among cirrhotic patients with UGIB in this population. The identified cutoff aligns with the original threshold (≥ -4.6646) proposed in previous studies, thereby supporting the

clinical applicability of the CAGIB score within the Indonesian healthcare setting.

The mean CAGIB score observed in this study was -3.856. A total of 85 patients (52.8%) exhibited a score of ≥ -4.6646, which was correlated with increased inpatient mortality, whereas 76 patients (47.2%) had a score of < -4.6646. In comparison, Zhao et al. documented a lower mean CAGIB score of -5.6 among 376 patients in China. Given that a higher CAGIB score is associated with an elevated risk of mortality in cirrhotic patients experiencing UGIB, this data may contribute to an explanation of the higher mortality rate observed in the current study.

This study demonstrates that the CAGIB score is a reliable predictor of inpatient mortality among patients with liver cirrhosis and upper gastrointestinal bleeding (UGIB), exhibiting a sensitivity of 80.8% and a specificity of 70.5%. The overall accuracy of the score was 75.2%, signifying that the majority of outcomes were accurately identified. The high sensitivity indicates that most patients who succumbed had scores exceeding the cutoff point, whereas the commendable specificity suggests that the majority of survivors scored below this threshold. These findings are consistent with those of Bai et al., who reported an area under the receiver operating characteristic curve (AUC) of 0.714 (95% confidence interval: 0.682–0.746, p = 0.0006) in their validation cohort.

In comparison, the CTP, MELD, MELD-Na, and NLR scores exhibited Area Under the Curve (AUC) values of 0.693 (95% Confidence Interval [CI]: 0.659–0.725), 0.662 (95% CI: 0.627–0.695), 0.660 (95% CI: 0.626–0.694), and 0.538 (95% CI: 0.503–0.574), respectively, for the purpose of predicting in-hospital mortality among cirrhotic patients with gastrointestinal bleeding. A significant statistical difference was identified between the CAGIB score and NLR (p = 0.0165), whereas no such difference was observed when compared with the CTP, MELD, or MELD-Na scores. Our findings are further corroborated by Bai et al. (2025), who reported an AUC of 0.801 for the CAGIB score in predicting in-hospital mortality within their validation cohort. The performance of the CAGIB score did not differ significantly from that of the CTP score (AUC = 0.809, p = 0.801), MELD-Na (AUC = 0.803, p = 0.960), MELD 3.0 (AUC = 0.813, p = 0.667), the D'Amico model (AUC = 0.851, p = 0.05), or the Augustin score (AUC = 0.830, p = 0.213).

Recently, a comprehensive prospective international multicenter study further validated the CAGIB score in a cohort of 2,467 cirrhotic patients presenting with acute gastrointestinal bleeding. In the training cohort of this study, the CAGIB score alone achieved an Area Under the Curve (AUC) of 0.789 in predicting in-hospital mortality, while a machine-learning adaptation of its components reached an AUC of as high as 0.986.[18.] Additionally, the CAGIB score demonstrated a very good Negative Predictive Value (NPV) of 81.6% and a commendable Positive Predictive Value (PPV) of 69.4%. According to Monaghan et al. (2021), high NPV and PPV values are of significant clinical importance, reflecting the score's practical applicability in forecasting patient outcomes. Specifically, patients with CAGIB scores above the established cutoff are more likely to experience mortality during hospitalization. In contrast, those with scores below the cutoff are more likely to survive the hospitalization period.

In addition to its strong statistical performance, the CAGIB score also has significant clinical implications in the management of cirrhotic patients with upper gastrointestinal bleeding. Early identification of high-risk patients (CAGIB ≥ –4.66) can aid triage decisions, including prioritizing care in intensive ward, due to some predictors like renal impairment, HCC, or multiorgan failure. This score also has the potential to assist in determining transfusion strategies and the urgency of endoscopic procedures. High-risk patients can be prioritized for early endoscopy and intensive hemodynamic monitoring.[20]

CONCLUSION

The CAGIB score is a validated scoring system employed as a predictive tool for mortality in the management of patients with liver cirrhosis complicated by upper gastrointestinal bleeding (UGIB) at Ngoerah Hospital. This score demonstrates excellent sensitivity, good specificity, and reliable negative and positive predictive values (NPV and PPV) in forecasting mortality among this patient cohort. The optimal cutoff value identified in this study aligns with the initial threshold of the CAGIB score, indicating similarity in population characteristics at Ngoerah Hospital. To enhance the applicability and robustness of this scoring system, future prospective, multicenter research is essential to validate its effectiveness across a broader Indonesian population and to evaluate its influence on clinical outcomes for a wider patient demographic.

LIMITATION

This study presents several limitations. It was conducted at a single tertiary referral center, where patients with cirrhosis generally exhibit more advanced disease, thereby restricting the applicability of the findings to primary or secondary healthcare environments. Furthermore, the sample size was relatively limited and was collected through consecutive sampling over a specified period. As a result, variations in patient characteristics may not have been fully captured, potentially affecting the stability and accuracy of the score estimates. Additionally, formal calibration metrics, such as the Hosmer–Lemeshow test and calibration plot, were not utilized, due to the categorical nature of the score and the limited sample size. Moreover, comparative analysis with CTP and MELD scores was conducted only in patients with complete laboratory data, which may introduce selection bias. This limitation could affect the robustness of the comparative results. Future multicenter studies with larger populations are needed to further validate these findings.

CONFLICT OF INTEREST

The authors declare that there are no competing interests concerning the publication of this manuscript.

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AUTHOR CONTRIBUTIONS

IKM and GS conceptualized the study and supervised the research process. HH conducted the data analysis. AZA finalized and refined the manuscript. NLPYD and PISLD designed the study methodology. NNGKD and KMNP contributed to data processing and manuscript drafting. DAS, KAWN, and MFAR reviewed, evaluated, and validated the work. All authors contributed to manuscript development and approved the final version.

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DATA AVAILABILITY

The supporting dataset utilized in this study is available from the corresponding author upon reasonable request. Public dissemination of the raw clinical data is restricted due to ethical considerations aimed at safeguarding patient confidentiality.

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