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Enhancing Prognostication in Cirrhosis with Sepsis: INR to Albumin Ratio Vs Meld-Based Scoring Systems

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Abstract

Background: Liver cirrhosis is an important cause of morbidity and mortality globally with sepsis being a life-threatening complication in cirrhotic patients. Traditional scoring systems like Model for End-stage liver disease (MELD) are widely used to predict prognosis in cirrhotic patients. However, recent evidence suggests that Prothrombin time-international normalized ratio (PT-INR) to Albumin Ratio (PTAR score) may serve as a simple and effective alternate marker for risk stratification in patients of cirrhosis with sepsis.

Methods: This prospective hospital-based observational study included 90 patients aged 18-65 years with cirrhosis and sepsis (qSOFA ≥ 2). Patients were excluded if they had bleeding disorders, were on anticoagulants, pregnant, malignancy, or other chronic illnesses. PTAR score at admission and MELD scores were calculated, and their predictive value for mortality and disease severity was assessed using statistical methods such as ROC Curve analysis.

Results: The study revealed that, the MELD-Na Score demonstrated the highest predictive accuracy for mortality (AUROC = 0.90, Sensitivity = 85.00%, Specificity = 82.00%), outperforming both the MELD Score (AUROC = 0.85, Sensitivity = 76.67%, Specificity = 78.33%) and the PTAR score (AUROC = 0.82, Sensitivity = 77.78%, Specificity = 75.56%).

Conclusion: The PTAR score can be easily calculated at the bedside and correlates with the prognosis, with higher scores assosciated with increased mortality. While it provides moderate prognostic value and may be valuable in resource limited settings, it does not surpass MELD-based scoring systems and may complement other scoring systems in patients of cirrhosis of liver with sepsis.

Keywords: Cirrhosis, Sepsis, INR, Albumin, MELD

Introduction

Liver cirrhosis is a progressive condition characterized by fibrosis, hepatocellular dysfunction, and portal hypertension, leading to life-threatening complications, including hepatic decompensation and multi-organ failure. Cirrhosis is one of the leading causes of mortality and morbidity all over the world.[1] Around 2 million deaths worldwide per year are due to liver disease, with 1 million deaths due to the complications of cirrhosis and 1 million deaths due to viral hepatitis and hepatocellular carcinoma.[2] Among hospitalized cirrhotic patients, sepsis remains a major cause of morbidity and mortality, exacerbating liver dysfunction and increasing the risk of organ failure.

Third International Consensus Definition Task Force defines sepsis as life-threatening organ dysfunction due to a dysregulated host response to infection.[3] In patients of cirrhosis, sepsis further deteriorates liver function, often resulting in organ or system failure, making it a particularly severe complication. Sepsis emerges as a formidable adversary and remains a major cause of morbidity and mortality in cirrhotic patients in patients with suspected infections, a bedside clinical score - quick Sequential Organ Failure Assessment Score (q SOFA) can predict poor outcomes typical of sepsis.[3]

Several prognostic models have been developed to assess mortality risk in cirrhosis. While clinical judgment plays a crucial role, the use of quantitative scoring systems improves risk stratification and decision-making, particularly in critically ill patients. Two key laboratory markers reflecting liver synthetic function are the International Normalized Ratio (INR) and serum albumin. The International Normalized Ratio (INR) is a standardized measure of blood coagulation, primarily used to monitor the effectiveness of anticoagulant medications. In cirrhosis, liver function is compromised leading to a decrease in synthesis of clotting factors and an elevated INR. As a standardized measure of blood clotting time, INR provides clinicians with profound insights into the liver's synthetic function and is a predictor of adverse outcomes.[4] Serum Albumin, synthesized exclusively in the liver, is a marker of nutritional and hepatic functional status. Hypoalbuminemia is associated with poor prognosis in cirrhosis, as it reflects both liver dysfunction and systemic inflammation.

Haruki et al. in 2019 developed a novel, objective score - Prothrombin time-international normalized ratio (PT-INR) to Albumin Ratio (PTAR SCORE) to assess liver functional reserves in patients with hepatocellular cancer following hepatic resection.[5] In a retrospective analysis involving 199 patients, they concluded that the PTAR score was effective in predicting both the short- and long-term consequences. Like patients who have undergone hepatocellular carcinoma resection, patients with cirrhosis exhibit abnormalities in liver function and a decreased reserve. Unlike traditional scoring systems, PTAR score relies on widely available, routinely measured parameters, making it an attractive tool for risk stratification in resource-limited settings.

The Model for End-Stage Liver Disease (MELD) Score is a well-established prognostic model originally developed to predict survival in patients undergoing transjugular intrahepatic portosystemic shunt (TIPS) procedures.[6] It incorporates INR, bilirubin, and creatinine to assess hepatic and renal dysfunction, making it widely used for liver transplant prioritization and mortality risk estimation. However, MELD does not account for electrolyte imbalances, which are common in cirrhosis. To address this limitation, the MELD-Na Score was introduced, incorporating serum sodium levels, an essential marker of fluid homeostasis and circulatory dysfunction in cirrhosis. Hyponatremia is a strong predictor of mortality, making MELD-Na more accurate than the traditional MELD Score in certain patient populations.

While MELD-based scoring systems remain the gold standard for cirrhosis prognostication, their complexity and requirement for multiple laboratory values may limit their use in low-resource settings. The INR to Albumin Ratio, being a simpler and readily available parameter, may offer comparable predictive value in certain clinical scenarios. However, its utility relative to MELD-based scores remains unclear. This study aims to compare the prognostic performance of INR to Albumin Ratio against MELD and MELD-Na Scores in predicting mortality risk in cirrhotic patients with sepsis. By evaluating ROC curves, sensitivity, specificity, and subgroup analysis, this research seeks to determine whether INR to Albumin Ratio can serve as a viable alternative to established MELD-based models or whether MELD-Na remains the superior prognostic tool.

Objective

To compare the prognostic accuracy of INR to Albumin Ratio, MELD Score, and MELD-Na Score in predicting mortality risk in cirrhotic patients with sepsis by evaluating their ROC curves, sensitivity, and specificity.

Materials and Methods

This prospective hospital-based observational study was conducted in the Department of Medicine at Gandhi Medical College, Bhopal, after obtaining approval from the Institutional Ethical Committee. The inclusion criteria consisted of

1. Age 18-65
2. Patients of cirrhosis of liver with sepsis (with History/Clinical examination/Investigations indicative of infection)
3. qSOFA ≥ 2

Patients aged <18 and >65 or with qSOFA<2 or individuals with bleeding disorders or on anticoagulant or drugs affecting PT/INR (Vit. K antagonists, Factor Xa and thrombin inhibitors) pregnancy, patients with malignancy, patients with any other chronic disease were excluded.

After obtaining detailed clinical history, laboratory and radiological investigations were conducted, including CBC, LFT, RFT, PT-INR, blood and urine cultures, and serology (HBsAg, Anti-HCV, HIV). Ultrasound (USG) abdomen was performed to assess cirrhosis. While liver biopsy is the gold standard for diagnosing cirrhosis, patients were identified based on clinical, laboratory, and radiological parameters as per standard practice.[7] The qSOFA score was calculated for all the patients at the time of admission. The score consists of three components with 1 point to each component - Respiratory Rate >22/min, Change in Mental Status (GCS<15) and Systolic Blood Pressure < 100 mm of Hg.

A score of two or more points in patients with presumed infection defines sepsis and these patients were recruited based on the inclusion and exclusion criteria. The PTAR score was calculated at admission using the formula: INR divided by albumin. To evaluate the predictive performance of PTAR, MELD, and MELD-Na statistical analyses was conducted using Receiver Operating Characteristic (ROC) Curve Analysis. ROC curves were generated for each score and AUROC (Area under the ROC Curve) values were calculated to determine the discriminatory power of each score. Moreover, sensitivity, specificity and accuracy assessment were done. Calibration plots were generated to compare predicted mortality risk with actual outcomes.

Results

The study data revealed a predominant middle-aged demographic with most participants, 44.4% in the age group 41-50 years. Alcohol was identified as the most common cause of cirrhosis in 75.6% of participants. The study found pneumonia as the most common source of sepsis (28.9%), followed by UTIs (26.7%), spontaneous bacterial peritonitis and skin/soft tissue infections (13.3% each), and GI tract infections (6.7%). The study revealed that, the MELD-Na Score demonstrated the highest predictive accuracy for mortality (AUROC = 0.90, Sensitivity = 85.00%, Specificity = 82.00%), outperforming both the MELD Score (AUROC = 0.85, Sensitivity = 76.67%, Specificity = 78.33%) and the INR to Albumin Ratio (AUROC = 0.82, Sensitivity = 77.78%, Specificity = 75.56%). (FIGURE 1)

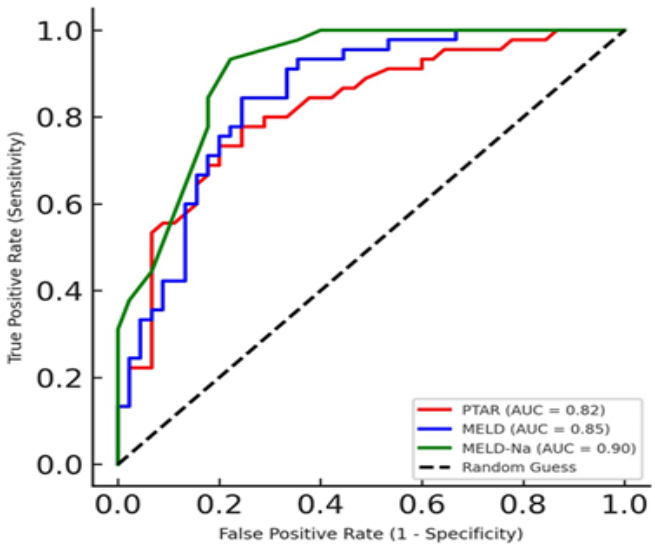

Figure 1: ROC Curve analysis comparing PTAR score with MELD and MELD-Na scores

Discussion

Cirrhosis of the liver remains a significant global health concern, leading to substantial morbidity and mortality. Accurate prognostic assessment is crucial for effective management and timely intervention. Our study found out PTAR score to be a convenient and practical tool for predicting prognosis with ROC curve analysis showing an AUROC of 0.818 and a moderate sensitivity and specificity of 77.8% and 75.6% respectively. Gao et al. [8] confirmed the PTAR score as a reliable predictor of 90-day mortality in critically ill cirrhotic patients, showing a strong correlation with higher mortality rates and a good discriminative ability (AUC 0.72). Another study involving 93 patients by Baruah et al.[9] revealed that higher PTAR scores were significantly associated with increased in-hospital mortality. Patients were stratified into low-risk (PTAR < 0.55), intermediate-risk (0.55–1.00), and high-risk (>1.00) categories, with mortality rates of 14.29%, 23.08%, and 76.93%, respectively.

The MELD score, incorporating serum bilirubin, creatinine, and INR, has been widely used to assess liver

disease severity. The addition of serum sodium to create the MELD-Na variant aimed to enhance predictive accuracy, particularly in patients with hyponatremia. Studies have shown that MELD-Na provides a more accurate prediction of short-term mortality compared to the original MELD score. A study by Londono et al.[10] which analysed data from patients awaiting liver transplantation found that serum sodium and MELD were independent predictors of survival at 3 and 12 months after listing. However, the addition of serum sodium did not significantly improve the accuracy of the MELD score in predicting survival at these time points. Another study by Brown et al.[11] analysed data from 79,611 patients and concluded that the MELD-Na score accurately predicts six-month mortality, with a c-statistic of 0.83. Notably, a MELD-Na score of 28.2 was associated with a 50% six-month survival rate, highlighting its prognostic significance.

A study by Gagandeep Acharya et al.[12] compared the Child-Turcotte-Pugh (CTP), MELD, and MELD-Na scores in predicting three-month mortality among patients with end-stage liver disease. The study concluded that all three scores were effective predictors, with C-statistics of 0.93 for CTP, 0.86 for MELD, and 0.83 for MELD-Na. While the CTP score showed slightly superior predictive ability, MELD and MELD-Na remain valuable due to their objective parameters.

Ongoing refinements to the MELD model have led to the development of newer variations. MELD 3.0, introduced in 2021 includes serum albumin and accounts for sex-based disparities in liver transplant allocation. A study by Guo et al.[13] showed MELD 3.0 to be superior to MELD-Na in predicting three-month and six-month mortality. MELD-Plus, developed at Massachusetts General Hospital, incorporates nine variables, including all components of MELD, plus sodium, albumin, total cholesterol, white blood cell count, age, and length of hospital stay, providing a more comprehensive mortality risk assessment.[14]

For cirrhotic patients with sepsis, prognostic assessment is more complex due to systemic inflammation, multiorgan dysfunction, and hemodynamic instability. Various scoring systems have been evaluated to determine their prognostic utility in sepsis within cirrhotic patients. A study by Peng Lan et al.[15] which compared the predictive value of scoring systems in determining the outcome of critically ill cirrhotic patients with suspected infection concluded that Chronic Liver Failure-Sequential Organ Failure Assessment (CLIF-SOFA) with an AUROC of 0.742 and CLIF-C Organ Failure (AUROC 0.741) outperformed general sepsis scores such as SIRS (AUROC 0.618), qSOFA (AUROC 0.612), and MELD (AUROC 0.632) in predicting mortality in critically ill cirrhotic patients with sepsis[8]. They also found that SAPS II (AUROC 0.759) was superior to MELD, SIRS, and qSOFA, indicating that it may be a better predictor of in-hospital mortality[8]. These findings emphasize that while MELD and MELD-Na remain key tools in cirrhosis prognosis, sepsis-specific scores such as CLIF-SOFA and SAPS II may offer better mortality prediction in cirrhotic patients with sepsis.

The ROC curve analysis in our study revealed that MELD-Na had the highest AUC (0.904), followed by MELD (0.847) and PTAR (0.818), confirming MELD-Na as the most accurate predictor of mortality in cirrhotic patients with sepsis. Further evaluation using sensitivity, specificity, accuracy, and precision at optimal cutoff values determined by Youden's Index showed that MELD-Na had the highest accuracy

(85.6%) and sensitivity (93.3%), making it the most reliable prognostic model. MELD also performed well, with an accuracy of 80.0% and sensitivity of 84.4%, reinforcing its predictive strength, while PTAR demonstrated moderate accuracy (76.7%) and sensitivity (77.8%), indicating its usefulness but lower precision compared to MELD-based scores. The specificity was highest for MELD-Na (77.8%), ensuring better identification of survivors, followed by MELD (75.6%) and PTAR (75.6%). Given these findings, MELD-Na emerged as the superior scoring system for risk stratification in cirrhotic patients with sepsis, with MELD as a strong alternative and PTAR serving as a simpler but less precise marker.

Currently, there is limited research directly comparing the prognostic efficacy of the International Normalized Ratio to Albumin Ratio (PTAR) with the Model for End-Stage Liver Disease (MELD) and its sodium-adjusted variant (MELD-Na) in patients with cirrhosis. While studies have independently validated the prognostic value of PTAR, MELD, and MELD-Na, head-to-head comparisons among these scoring systems are scarce.

Conclusion

While a simple and easy to use tool, the PTAR score lacks the comprehensive nature of MELD-based models, which have been extensively validated with additional refinements like MELD 3.0 and MELD-Plus. The comparison between PTAR and MELD-based models highlights the complementary nature of these tools in patients of cirrhosis of liver with sepsis. Our study is limited by its single centre design, small sample size and a short-term outcome focus. Sepsis in cirrhotic patients necessitates additional prognostic considerations, as liver-specific models like CLIF-SOFA and general severity scores like SAPS II have demonstrated higher predictive accuracy in critically ill patients. Future research should focus on head-to-head comparisons between MELD-Na, PTAR, and sepsis-specific scores to optimize risk stratification and improve patient outcomes.

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