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Research article

# D-dimer-to-platelet count ratio as a novel indicator for predicting prognosis in HBV-related decompensated cirrhosis

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ABSTRACT

*Background:* Hepatitis B virus-related decompensated cirrhosis (HBV-DC) is a critical illness with a low survival rate. Timely identification of prognostic indicators is crucial for risk stratification and personalized management of patients. The present study aimed to investigate the potential of the D-dimer-to-platelet count ratio (DPR) as a prognostic indicator for HBV-DC.

*Methods:* A retrospective review of medical records was conducted for 164 patients diagnosed with HBV-DC. Baseline clinical and laboratory characteristics were extracted for analysis. The endpoint was 30-day mortality. Disease severity was assessed by the Model for End-stage Liver Disease (MELD) score. A multivariate logistic regression model and receiver operating characteristic curve analysis (ROC) were used to evaluate the predictive value of DPR for mortality.

*Results:* During the 30-day follow-up period, 30 (18.3%) patients died. Non-survivors exhibited significantly higher DPR values than survivors, and a high DPR had a strong association with increased mortality. Importantly, DPR was identified as an independent risk factor for mortality in HBV-DC patients after adjustments for confounding factors (Odds ratio = 1.017; 95% Confidence interval, 1.006–1.029; $p = 0.003$). The cut-off value of DPR as a predictor of mortality was>57.6 (sensitivity = 57%, specificity = 86%, $p < 0.001$). The area under ROC curve for DPR for 30-day mortality was 0.762, comparable to the MELD score ($p = 0.100$). Furthermore, the combined use of DPR and MELD score further increased the area under the ROC curve to 0.897.

*Conclusion:* Elevated DPR was demonstrated to have a correlation with unfavorable outcomes in HBV-DC patients, suggesting its potential utility as an effective biomarker for assessment of prognosis in these patients.

## 1. Introduction

Hepatitis B virus (HBV) infection is a major global health issue, affecting almost 240 million people worldwide [1,2]. Decompensated cirrhosis (DC) is a prominent source of morbidity and mortality among the severe consequences associated with chronic HBV infection [3]. A previous study found that the 5-year survival rate for patients with decompensated cirrhosis was approximately 14%, compared with 84% for patients with compensated cirrhosis [4]. The best opportunity for survival and improved quality of life in

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**Abbreviations**

| | |
|---|---|
| AUCs | Areas under the curve |
| CI | Confidence interval |
| DC | Decompensated cirrhosis |
| DPR | D-dimer-to-platelet count ratio |
| HBV | Hepatitis B virus |
| INR | International normalized ratio |
| MELD score | Model for End-stage liver disease score |
| ROC | Receiver operating characteristic |

patients with HBV-related decompensated cirrhosis (HBV-DC) remains liver transplantation. However, the lack of available donor livers and the high cost of treatment restrict its practical applicability, preventing many patients from receiving this life-saving procedure. Hence, it is crucial to promptly discover biomarkers capable of accurately predicting the prognosis of HBV-DC patients, to enable timely intervention, optimize treatment strategies, and improve patient outcomes.

D-dimer is a breakdown product of cross-linked fibrin that can serve as a marker for the activation of both coagulation and fibrinolysis processes. Increased D-dimer levels have been detected in various severe disorders, and this elevation was linked with poor outcomes in severely ill patients [5,6]. According to recent research, a poor prognosis can also be predicted by increased D-dimer levels in patients with liver disorders [7–9]. Meanwhile, platelet count is a common laboratory indicator with important roles in hemostasis and thrombosis. Decreased platelet count was associated with systemic inflammation and high mortality in patients within the intensive care unit [10]. Decreased platelet count can also reflect the extent of liver fibrosis and is recognized as a key player in the pathogenesis and progression of liver diseases [11,12]. For example, in patients with end-stage liver disease, platelet count was associated with hypersplenism and decreased thrombopoietin synthesis [13]. Furthermore, platelets produce abundant growth factors, such as serotonin [14], that act as important promoters of liver regeneration. Therefore, thrombocytopenia may contribute to insufficient liver regeneration. Thus, it can be hypothesized that combined assessment of D-dimer and platelet count may serve as a reliable and practical prognostic indicator for certain clinical conditions. Notably, a recent study demonstrated the usefulness of the D-dimer-to-platelet count ratio (DPR) in distinguishing preeclampsia from normal pregnancy and gestational hypertension [15]. However, no studies have explored the relationship between DPR and prognosis in HBV-DC patients. Therefore, we conducted an observational study to investigate whether DPR can be utilized as a potential marker for predicting 30-day mortality in these patients.

## 2. Materials and methods

### 2.1. Patients

The study included 214 HBV-DC patients who were admitted to our hospital between May 2021 and January 2023. DC was diagnosed when cirrhotic patients experienced any of the following complications: ascites, encephalopathy, hepatorenal syndrome, or variceal hemorrhage [16]. Fifty patients were excluded for various reasons, including age >80 years (n = 6), alcoholic liver disease (n = 12), autoimmune hepatitis (n = 6), other viral infections (n = 13), malignant tumors (n = 5), hematological disease (n = 3), or incomplete clinical data (n = 5). Finally, a total of 164 patients were enrolled. In our cohort, 134 patients were receiving antiviral therapy (Lamivudine, Entecavir, or Tenofovir); 87 of them started antiviral therapy before admission, and 47 had started after admission. Only 30 patients did not receive any antiviral therapy throughout the clinical course due to economic or other reasons. None of the patients underwent liver transplantation during the study period. The endpoint was the survival rate at 30 days. This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki (7th revision, 2013). Approval for the study was obtained from the Ethics Committee of Shengzhou People's Hospital in China (approval number: 2021 [17]). Due to the retrospective nature of the study, the necessity of obtaining informed consent from patients was waived.

### 2.2. Baseline data collection

Demographic data and laboratory measurements were collected. DPR was calculated by dividing the D-dimer level by the platelet count. Survival was recorded at 30 days after admission. Hepatic function was assessed by calculating the Model for End-Stage Liver Disease (MELD) score using the following formula [18]: 3.8 ln (total bilirubin, mg/dL) + 11.2 ln (INR) + 9.6 ln (creatinine, mg/dL) + 6.4, where INR is the international normalized ratio.

### 2.3. Statistical analysis

Categorical variables were reported as number, and statistical analyses were conducted using the $\chi^2$ test. Continuous variables were presented as median (P25–P75), and comparisons were made using the Mann–Whitney *U* test. Factors that exhibited potential associations with poor outcomes in the univariable analyses were included in the multivariate binary regression analysis. To assess the predictive value of these factors for mortality and compare the differences in their performance, we generated receiver-operator

characteristic (ROC) curves and calculated the area under the curve (AUC) values. Statistical analyses were conducted using SPSS version 21 and MedCalc 12.7.0. Statistical significance was set at $p < 0.05$.

## 3. Results

### 3.1. Baseline characteristics

The present retrospective analysis involved 164 patients with HBV-DC. The median age was 50 years and 136 (83%) patients were male. Among these 164 cases with clinical decompensation, ascites was observed in 136 cases (83%), variceal bleeding occurred in 55 cases (34%), hepatorenal syndrome manifested in 30 cases (18%), and hepatic encephalopathy was present in 4 cases (2%). Thirty-two patients (20%) had more than one feature of decompensation on admission. The DPR ranged from 9.9 to 54.2 (median: 24.3).

During the 30-day period following admission, a total of 30 patients (18.3%) died. The causes of death were as follows: hepatic failure in 10 patients, upper gastrointestinal bleeding in 15 patients, hepatic encephalopathy in two patients, and hepatorenal syndrome in three patients. Based on their survival outcomes, we divided the patients into two groups. As shown in Table 1, the non-survivors exhibited higher MELD scores, D-dimer levels, DPR values, total bilirubin levels, creatinine levels, and INR values than the survivors. Conversely, the non-survivors had lower albumin levels than the survivors. Although the non-survivors had slightly lower platelet counts than the survivors, the difference did not reach statistical significance. No significant differences were observed in the demographic characteristics and other laboratory findings.

### 3.2. Factors associated with mortality

To identify prognostic factors, we conducted both univariate and multivariate analyses. The univariate analyses revealed that higher MELD score, elevated D-dimer level, increased DPR, and decreased albumin level were significantly associated with mortality in HBV-DC patients. In the multivariate analysis, MELD score and DPR retained their status as independent predictors of mortality (Table 2). The predictive abilities of DPR and MELD score for mortality were assessed by ROC curve analyses. The cut-off value for MELD score was determined to be 18.4, with sensitivity of 83% and specificity of 69%, while the cut-off value for DPR was determined to be 57.6, with sensitivity of 57% and specificity of 86%. Furthermore, for DPR, the accuracy was 0.715, the precision was 0.800, and the F1 score was 0.667. The AUC values for DPR and MELD score for predicting mortality did not differ significantly (0.762 vs. 0.850; $p = 0.100$). When DPR and MELD score were analyzed in combination, the AUC was 0.897, which was slightly higher than the AUC value for MELD score ($p = 0.068$) and significantly higher than the AUC for DPR ($p = 0.001$) (Fig. 1).

### 3.3. DPR-related clinical and laboratory results

The patients were categorized into two groups according to the cut-off value for DPR ($\leq$57.6, n = 128 vs. >57.6, n = 36). Patients with elevated DPR demonstrated significant associations with higher MELD scores, INR values, D-dimer levels, and mortality rates, as well as lower albumin levels and platelet counts (Table 3).

## 4. Discussion

HBV-DC is a life-threatening syndrome, but accurate prediction of its clinical outcomes remains challenging. The widely used MELD scoring system incorporates three laboratory variables (total bilirubin, INR, and creatinine) to predict patient outcomes. However, the MELD score cannot effectively predict an unfavorable prognosis in approximately 15%–20% of patients [19] because it

**Table 1**
Clinical characteristics of the patients at baseline.

| | All patients (n = 164) | Survivors (n = 134) | Non-Survivors (n = 30) | *P* |
|---|---|---|---|---|
| Gender (female/male) | 28/136 | 20/114 | 8/22 | 0.196 |
| Age (years) | 50.0 (43.0–59.0) | 50.0 (42.0–59.0) | 52.0 (44.0–59.0) | 0.352 |
| Total protein (g/L) | 58.6 (53.8–62.9) | 58.9 (54.3–62.9) | 58.5 (52.7–63.0) | 0.461 |
| Albumin (g/L) | 30.0 (27.5–33.6) | 30.3 (28.0–34.1) | 29.0 (26.2–31.2) | 0.024 |
| Alanine aminotransferase (U/L) | 69.5 (30.0–212.5) | 68.0 (29.0–182.0) | 71.0 (40.0–246.0) | 0.146 |
| Aspartate aminotransferase (U/L) | 73.0 (41.5–151.5) | 72.5 (41.0–125.0) | 126.0 (70.0–184.0) | 0.053 |
| Serum creatinine (μmol/L) | 66.0 (57.5–79.0) | 65.0 (57.0–75.0) | 84.5 (58.0–120.0) | 0.017 |
| Total bilirubin (μmol/L) | 166.1 (141.5–338.8) | 139.1 (36.0–332.9) | 280.2 (131.0–485.5) | 0.002 |
| INR | 1.52 (1.29–1.84) | 1.45 (1.26–1.73) | 1.99 (1.66–2.54) | <0.001 |
| D-dimer (μg/L FEU) | 2123.0 (886.5–3729.5) | 1738.5(795.0–2925.0) | 3910.0 (2325.0–6912.0) | 0.001 |
| Platelet ( $\times 10^9$/L) | 83.5 (54.5–115.0) | 84.0 (55.0–122.0) | 70.5 (52.0–108.0) | 0.243 |
| DPR | 24.3 (9.9–54.2) | 19.3 (7.9–44.3) | 61.9 (25.2–103.7) | <0.001 |
| MELD score | 16.8 (11.2–21.2) | 14.7 (10.1–19.9) | 23.3 (18.7–25.7) | <0.001 |
| HBV-DNA ($\log_{10}$IU/mL) | 5.3 (4.0–6.9) | 4.9 (3.8–6.8) | 5.5 (4.1–7.7) | 0.256 |

Data are expressed as number or median (P25–P75).
Abbreviations: INR, international normalized ratio; DPR, D-dimer-to-platelet count ratio; MELD, Model for End-stage Liver Disease.

**Table 2**
Results of the univariate and multivariate logistic regression analyses to identify predictive factors for mortality in HBV-DC patients.

| | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| | Odds ratio | 95% CI | *P* | Odds ratio | 95% CI | *P* |
| Age (years) | 1.021 | 0.987-1.057 | 0.224 | | | |
| Albumin (g/L) | 0.900 | 0.823-0.984 | 0.020 | | | |
| D-dimer (μg/L FEU) | 1.001 | 1.000–1.001 | <0.001 | | | |
| PLT ( × $10^9$/L) | 0.994 | 0.985-1.002 | 0.116 | | | |
| DPR | 1.018 | 1.009-1.027 | <0.001 | 1.017 | 1.006-1.029 | 0.003 |
| MELD score | 1.3347 | 1.198-1.515 | <0.001 | 1.396 | 1.210-1.611 | 0.001 |

Abbreviations: DPR, D-dimer-to-platelet count ratio; MELD, Model for End-stage Liver Disease.

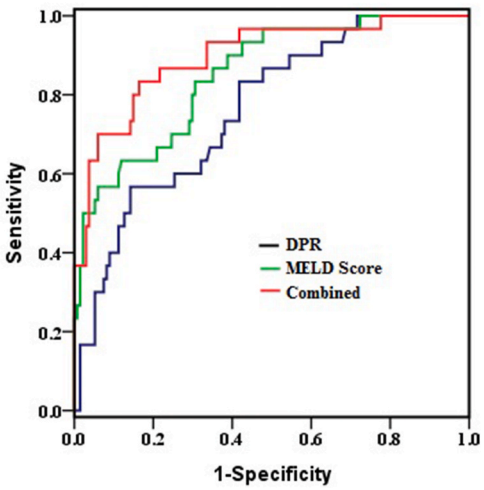


**Fig. 1.** Receiver operating characteristic curve analyses for MELD score, DPR, and combination of MELD score and DPR for prediction of mortality in HBV-DC patients.

**Table 3**
Clinical data according to the cut-off value for DPR.

| | High group (DPR >57.6, n = 36) | Low group (DPR ≤57.6, n = 128) | *P* |
|---|---|---|---|
| Gender (female/male) | 7/29 | 21/107 | 0.859 |
| Age (years) | 49.0 (44.0–59.0) | 50.0 (42.5–59.0) | 0.773 |
| Total protein (g/L) | 58.6 (53.7–63.2) | 58.7 (53.9–62.9) | 0.841 |
| Albumin (g/L) | 28.7 (25.5–31.0) | 31.1 (28.1–34.1) | 0.004 |
| Alanine aminotransferase (U/L) | 39.3 (25.0–129.5) | 82.0 (30.5–222.5) | 0.053 |
| Aspartate aminotransferase (U/L) | 71.5 (38.0–141.5) | 73.5 (46.0–151.5) | 0.477 |
| INR | 1.75 (1.57–2.19) | 1.46 (1.24–1.75) | <0.001 |
| Serum creatinine (μmol/L) | 61.5 (53.0–87.0) | 66.0 (58.0–78.5) | 0.370 |
| Total bilirubin (μmol/L) | 135.5(69.5–342.2) | 188.4 (37.5–338.8) | 0.725 |
| D-dimer (μg/L FEU) | 4305.0 (3686.5–6734.0) | 1460.5 (730.0–2588.0) | <0.001 |
| Platelet ( × $10^9$/L) | 45.0 (31.5–63.0) | 93.5 (66.0–128.5) | <0.001 |
| MELD score | 18.4 (14.4–24.0) | 15.6(10.5–20.8) | 0.029 |
| 30-day mortality (yes/no) | 17/19 | 13/115 | <0.001 |
| HBV-DNA ($log_{10}$IU/mL) | 5.3 (4.0–7.2) | 5.1 (4.1–6.6) | 0.342 |

Data are expressed as number or median (P25–P75).
Abbreviations: DPR, D-dimer-to-platelet count ratio; INR, international normalized ratio; MELD, Model for End-Stage Liver Disease.

does not consider crucial factors such as hepatic encephalopathy, inflammation, and variceal bleeding, which can significantly impact patient prognosis. In the present study, we investigated the potential of DPR for predicting prognosis in HBV-DC patients. We found that the non-survivors exhibited higher DPR values than the survivors. DPR was also identified as a novel predictor of 30-day outcomes in HBV-DC patients, and its AUC of 0.762 was only slightly lower than the AUC for MELD score. Moreover, DPR is easily calculated from patients' laboratory test results without any need for additional tests or expenses. The combined use of DPR and MELD score further increased the AUC to 0.897. Previous studies identified age [20], total bilirubin level [21], neutrophil-to-lymphocyte ratio [22], and INR-to-albumin ratio [17] as factors associated with poorer survival in patients with cirrhosis. Our findings complement

existing research by identifying high DPR as an additional prognostic factor for HBV-DC.

Several factors may contribute to an explanation for the correlation between DPR and prognosis in HBV-DC patients. Regarding the first component of DPR, D-dimer was clearly higher in non-survivors than in survivors. In the context of cirrhosis, elevated D-dimer levels indicate an increase in fibrinolytic activity and impaired hemostasis. These changes can be attributed to a combination of factors, such as decreased synthesis of coagulation factors and impaired clearance due to liver damage, as well as increased fibrin degradation. Furthermore, cirrhosis is recognized as a multisystem disorder, and systemic inflammation plays a crucial role in its progression [23]. There is compelling evidence for a close interaction between inflammation and coagulation. Inflammation triggers coagulation, while coagulation significantly impacts inflammatory activity [24]. Several studies have demonstrated that elevated D-dimer levels not only indicate underlying hypercoagulability but also suggest the presence of an inflammatory process [25–28]. The activation of both coagulation and inflammation can lead to the formation of microvascular clots, which may contribute to the increased plasma D-dimer levels. Excessive fibrin degradation can result in thrombosis and endothelial dysfunction, thereby contributing to the poor prognosis of HBV-DC.

Regarding the second component of DPR, platelet counts were slightly lower in non-survivors than in survivors. Chronic HBV infection often leads to a low platelet count, and severe thrombocytopenia can result in fatal hemorrhage. Thrombocytopenia is commonly caused by a combination of factors, including decreased platelet production, accelerated platelet destruction or turnover, and increased platelet consumption by the spleen [29]. Emerging evidence has highlighted a crucial role of platelets in the development of liver diseases. For example, platelet count was shown to be correlated with the extent of liver fibrosis and display an inverse correlation with outcomes in cirrhotic patients [30–32]. Platelets were also found to exert protective effects on the liver and stimulate liver regeneration [33]. Moreover, a recent study found that the development of thrombocytopenia in patients with acute liver failure was associated with the development of multi-organ system failure and unfavorable prognosis. The researchers speculated that inflammation-induced activation of platelets, yielding microparticles, may result in clearance of platelet remnants and subsequent thrombocytopenia [34]. Meanwhile, in decompensated cirrhosis, several complications, such as infections and acute kidney injuries, can impact platelets and hemostasis, and potentially lead to adverse outcomes. In the present study, 106 of the 164 patients (65%) had thrombocytopenia (platelet count $<100 \times 10^9$/L). Our findings indicate that the high DPR values in the non-survivors can be attributed to increased D-dimer levels and slightly decreased platelet counts. However, the multivariate analysis indicated that neither D-dimer level nor platelet count could predict mortality. The present study identified a significant association between elevated DPR and increased in-hospital mortality. This finding suggests that elevated DPR may be indicative of the complex interplay between coagulation dysregulation, inflammatory response, liver dysfunction, and fibrosis in HBV-DC. As a result, we propose that DPR has the potential to serve as a valuable prognostic indicator for patients with HBV-DC. However, further research is needed to clarify the underlying mechanisms contributing to the association between DPR and prognosis in HBV-DC patients. A more comprehensive understanding of these mechanisms will be useful for the development of precise interventions, leading to enhanced management strategies and improved outcomes for patients with HBV-DC.

We acknowledge that our study has several limitations. First, it was a retrospective study conducted at a single center, and thus there is a potential for selection bias. Second, the sample size was relatively small. Third, we were unable to evaluate other inflammatory markers, such as C-reactive protein, which could aid in understanding the possible mechanisms. Fourth, the analysis did not include a validation cohort. Finally, the follow-up duration was 30 days due to economic or other reasons, and the predictive performance for the long-term prognosis remains unclear. Consequently, further prospective studies involving multiple centers with a longer duration of follow-up are necessary to validate the prognostic value of DPR in HBV-DC.

## 5. Conclusion

The present study has demonstrated that DPR is a non-invasive and easily accessible prognostic biomarker for HBV-DC patients. DPR may provide useful information that can enhance traditional methods of monitoring the disease status in these patients. Nevertheless, further research is needed to validate and strengthen the present findings, ensuring the broader applicability and reliability of DPR as a prognostic indicator in HBV-DC patients.

## Data availability statement

The data that has been used is confidential.

## CRediT authorship contribution statement

**Xia He:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation. **QiuMing Ding:** Formal analysis, Data curation.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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