INTRODUCTION

In China, hepatitis B virus (HBV) is the predominant cause of liver cirrhosis.\(^1\) Decompensated cirrhosis (DeCi) is a major cause of mortality in HBV patients and can be accompanied by various complications.\(^2\) Although several treatments are available, DeCi patients have a high-mortality rate.\(^2,\!^3\) An accurate and convenient predictor is therefore needed to determine the mortality risk for HBV-DeCi patients, and accordingly stratify and help improve clinical management to increase the survival rate.

Electrolyte disturbances are a serious complication in patients with advanced cirrhosis.\(^4,\!^6\) Clinicians pay most attention to serum sodium and potassium levels, compared to other electrolytes. Some previous study indicated that low sodium parallel liver disease progression and serve as an independent predictor for mortality.\(^7,\!^9\) Model for End-Stage Liver Disease (MELD)-sodium score was developed in addition to the MELD score in the light of this finding and accepted as the gold standard in determination of liver transplant need.\(^10,\!^12\) On the other hand, potassium disorder is one of the commonest electrolyte derangements and the relationship between potassium levels and poor outcomes is U-shaped.\(^13,\!^14\) Both hypokalemia and hyperkalemia are consistently linked to unfavorable outcomes.\(^15\) For instance, Uslan et al.\(^16\) found that patients with higher potassium levels had higher mortality rates in cirrhotic patients. Moreover, Wallerstedt et al.\(^17\) reported that potassium levels of ≥4.8 mmol/L died within 1 year in a cirrhotic patient with ascites. In addition, Cai and colleagues\(^18\) indicated that hyperkalemia (>5.5 mmol/L) is an independent risk factor for the 90-day mortality.
in liver failure patients. On the contrary, Kaplan et al.\(^\text{19}\) founded that hypokalemia (below 3.4 mmol/L) was a risk factor for adverse outcomes in cirrhotic patients and Gaduputi et al. showed that hypokalemia considerably prolonged hospitalization time in patients with hepatic encephalopathy.\(^\text{20}\) However, there are limited data describing the association between potassium levels and outcomes in HBV-DeCi patients. Therefore, we aim to assess the effects of serum potassium on survival in these patients.

2 | MATERIALS AND METHODS

2.1 | Patients

We continuously analyzed all 155 HBV-DeCi patients from October 2016 to December 2020 in Shengzhou People’s Hospital. This study was approved by the Institutional Ethics Committee. Eligibility criteria were all patients were hepatitis B surface antigen positive longer than 6 months and age ranging from 18 to 75, with a clinical diagnosis of liver decompensation according to the histological findings, clinical, laboratory, and imaging data, and presence of ascites, variceal bleeding, encephalopathy, hepatorenal syndrome, or any combination of these.\(^\text{21}\) Exclusion criteria included chronic liver disease (e.g., viral infection other than HBV or autoimmune hepatitis, alcoholic liver disease), and malignancy. The end-points were survival rates at days 30. Data on mortality were obtained from the medical records.

2.2 | Data collection

The patient demographics, clinical, and laboratory variables were retrospectively collected from medical records. Laboratory parameters, including alanine aminotransferase, aspartate aminotransferase, creatinine, serum potassium, serum sodium, total protein, serum albumin, total bilirubin, blood urea nitrogen (BUN), platelet count, hemoglobin, and international normalized ratio (INR). We assessed liver function using the MELD score calculated based on laboratory tests performed at admission.\(^\text{13}\)

2.3 | Statistical analysis

Continuous values were expressed as median (interquartile range) and analyzed by the Mann–Whitney U test. Categorical values were expressed as number and analyzed by Fisher’s exact test. Correlations between variables were examined by Spearman’s analysis. To identify potential correlates of poor outcomes, univariate analyses were first performed in clinical variables. A multivariate regression was subsequently performed to include variables with \(p\text{-value}<0.10\) in the univariate analysis. Finally, a stepwise selection with the same set of variables was conducted using \(p\text{-value}<0.05\) as a criterion for inclusion. The area under the receiver operating curve (AUC) was calculated to determine the prognostic accuracy of the identified variables for mortality. Statistical analyses were done using SPSS version 20.0 or MedCalc version 12.7 softwares. A \(p\text{-value}<0.05\) were considered statistically significant.

3 | RESULTS

3.1 | Study population

We reviewed data obtained from 155 HBV-DeCi patients. The main causes of admission were ascites (78.7%), hepatorenal syndrome (21.0%), variceal bleeding (16.2%), and encephalopathy (2.0%). As shown in Figure 1, serum potassium level had a positive correlation with serum creatinine, MELD score and serum BUN and a negative correlation with sodium (all \(p\text{-value}<0.05\)). In addition, the potassium levels ranged from 3.15 to 7.36 mmol/L (median: 4.38 mmol/L) in our patients at admission.

During the 30 days after admission, 20 patients died (12.9%). We divided the patients into two groups based on whether or not they survived. As shown in Table 1, there were marked differences were observed between the survivors and non-survivors for total protein, creatinine, total bilirubin, INR, MELD score, BUN, serum potassium, and serum sodium (all \(p\text{-value}<0.05\)). No difference was found in other demographic and laboratory findings (all \(p\text{-value}>0.05\)).

![Figure 1](image_url) Correlations between serum potassium and serum creatinine, serum blood urea nitrogen, serum sodium, and MELD score in HBV-DeCi patients.
3.2 | Possible prognostic factors associated with mortality

On univariate analysis, MELD score, serum potassium, BUN, serum total protein, and serum sodium were associated with poor outcomes in HBV-DeCi patients. After multivariate analysis, MELD score and potassium remained independently predictive of mortality (Table 2). The AUROCs of serum potassium and MELD score for predicting the 30-day mortality were 0.799 (95% CI, 0.728–0.859) and 0.846 (95% CI, 0.779–0.899), respectively. The cutoff values of serum potassium and MELD score were 4.7 mmol/L (sensitivity 65.0%, specificity 87.4%) and 15.8 (sensitivity 80.0%, specificity 79.3%), respectively. In the present study, serum potassium and MELD score predicted mortality with similar power ($Z=0.849$, $p=0.396$). As shown in Figure 2, the combination of potassium and MELD score, further improved the prognostic accuracy for mortality [AUC (95% CI): 0.887 (0.827–0.933)], compared to the respective AUCs of potassium ($p=0.025$) or MELD score alone ($p = 0.040$).

3.3 | Clinical and laboratory findings related to serum potassium levels

Patients were divided into two groups based on the cutoff value of serum potassium levels ($\leq$4.7 mmol/L, $n = 125$ vs. $>4.7$ mmol/L, $n = 30$). Patients with high-serum potassium were found to be associated with higher MELD score, creatinine, total bilirubin, BUN, mortality, and lower serum sodium (all $p < 0.05$) (Table 3).
DISCUSSION

Serum potassium disorders are commonly seen in patients with advanced cirrhosis. This study evaluated the prognostic role of serum potassium level in HBV-DeCi patients. The results displayed that serum potassium level were associated with adverse outcome. Furthermore, serum potassium was an independent predictor of mortality in these patients.

Currently, the MELD score has been used for predicting prognosis of patients with liver disease and determining the priority of patients for liver transplantation, but it requires complex calculation and is inconvenient for clinical practice. In the present study, we found that non-survivors had higher serum potassium levels than survivors. Moreover, serum potassium was independently associated with adverse outcomes in HBV-DeCi patients, with a similar predictive power to the MELD score. Because serum potassium is a single laboratory parameter, it is more readily available and more inexpensive to assess than the MELD score. Of note, serum potassium in combination with MELD score further improved the prognostic accuracy for poor outcomes compared to serum potassium or MELD alone.

Several conditions can disrupt potassium homeostasis during hospitalization in HBV-DeCi patients, as a result of mechanisms inherent to the disease per se and the required therapeutic interventions. First, the kidney is one of the organs that regulate blood electrolyte balance has a close relationship with electrolytes. It is well known that the renal dysfunction is one of the most common complications in DeCi patients and is linked to adverse outcomes. Our findings indicated that serum potassium had a positive correlation creatinine and BUN, which are considered indices of renal dysfunction. Recently, Chen et al. reported that higher serum potassium was associated with acute kidney injury progression and prognosis in ICU patients. Renal dysfunction may bring about serum potassium disorders, and in turn, changes in serum potassium may lead

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**TABLE 3** Clinical data according to serum potassium levels

| Serum potassium level (mmol/L) | ≤4.7, n = 125 | >4.7, n = 30 | p |
|--------------------------------|--------------|-------------|---|
| Gender (female/male)           | 23/102       | 7/23        | 0.721 |
| Age (years)                    | 53.0 (47.8–62.0) | 56.0 (45.0–60.0) | 0.937 |
| Total protein (g/L)            | 61.2 (56.6–66.5) | 59.8 (52.4–68.0) | 0.521 |
| Albumin (g/L)                  | 31.0 (26.9–34.8) | 30.9 (26.4–33.1) | 0.622 |
| Alanine aminotransferase (U/L) | 29.0 (17.0–51.0) | 32.5 (17.0–56.0) | 0.591 |
| Aspartate aminotransferase (U/L)| 44.0 (28.0–72.0) | 53.5 (29.0–91.0) | 0.264 |
| Total bilirubin (μmol/L)       | 36.0 (22.0–87.0) | 78.5 (36.0–180.0) | 0.024 |
| BUN (mmol/L)                   | 5.4 (4.1–7.2) | 7.6 (5.5–13.8) | <0.001 |
| INR                            | 1.34 (1.21–1.58) | 1.55 (1.22–1.73) | 0.198 |
| Serum creatinine (µmol/L)      | 72.0 (60.8–84.0) | 82.5 (66.0–119.0) | 0.010 |
| MELD score                     | 11.3 (6.8–14.9) | 17.4 (11.6–21.2) | <0.001 |
| Hemoglobin (g/L)               | 107.0 (88.5–120.3) | 96.0 (83.0–121.0) | 0.391 |
| Platelet (×10^9/L)             | 66.0 (39.8–96.3) | 66.5 (53.0–138.0) | 0.223 |
| Serum sodium (mmol/L)          | 140.0 (137.0–142.0) | 137.5 (134.0–140.0) | 0.002 |
| 30-day mortality (yes/no)      | 7/118        | 13/17        | <0.001 |

Note: Data are expressed as number or median (interquartile range).
Abbreviations: BUN, Blood urea nitrogen; INR, international normalized ratio; MELD, Model for End-stage Liver Disease.
to renal injury and, consequently, worse outcomes. Second, the use of potassium sparing diuretics such as spironolactone, which commonly used in the management of cirrhotic patients and may lead to high-serum potassium level. Third, cirrhotic patients are characterized by a state of secondary hyperaldosteronism. Aldosterone acts by increasing the number of open sodium channels, leading to increased sodium reabsorption and potassium secretion. In line with this hypothesis, there is the negative relationship between serum potassium and sodium in HBV-DeCi patients in our study. Although serum sodium was identified as risk factors by univariate analyses, it was failed to be an independent predictor of poor outcomes by multivariate analysis. It is may be a limited number of patients were included in the present study. We also found that the serum potassium was positively correlated with the MELD score. As expected, high-serum potassium patients presented signs of more advanced liver disease characterized by higher creatinine, higher total bilirubin, higher BUN, and higher mortality. These findings are similar to the results of studies by Uslan et al., Wallerstedt et al., and Cai et al., which suggest that the high-serum potassium has a risk factor in patients with liver diseases. However, our findings differ from those of Kaplan et al. and Gaduputi et al., which indicate that hypokalemia has association with severity of disease and prognosis in cirrhotic patients. The first reason for this discrepancy may be due to the differences in the stages of liver diseases of patients recruited. In the Kaplan et al. study, all patients had well-compensated cirrhosis; however, all patients in our study had DeCi. In the Gaduputi et al. study, they focused on in patients with hepatic encephalopathy, while only three patients with hepatic encephalopathy in our study. The second reason may be because their study population was made up liver diseases patients with variety of etiologies, while we focused on patients caused by HBV infection; different causes may be associated with different outcomes. In addition, Gundling et al. reported that cardiac arrhythmia was commonly observed in cirrhotic patients and hyperkalemia was one of the most significant precipitants causing cardiac arrhythmia. Based on these data, we hypothesize that the increase in mortality in high-serum potassium patients may be a result of electrolyte disorder’s aggravating conditions such as renal failure or increased arrhythmia frequency due to high-serum potassium level. Of course, further studies are still required to clarify underlying mechanisms for the associations of potassium imbalances with poor prognosis.

This study had limitations. First, the present study was an observational study and the retrospective study design may have led to a selection bias. Second, we did not measured other electrolyte levels (chloride, calcium, and phosphorus), which may have been helpful in establishing the mechanism underlying the present findings. Finally, serum potassium level was not monitored during the follow-up period. Further verification in a multicenter prospective study is warranted.

In conclusion, serum potassium was associated with severity of liver disease and also associated with short-term prognosis in HBV-DeCi patients. The findings will be helpful in identifying prognostic parameters that assist patient classification and adjust treatment disciplines. However, our findings need to be validated by additional studies.

CONFLICT OF INTEREST
None of the authors have any commercial or other association that might pose a conflict of interest.

DATA AVAILABILITY STATEMENT
The data are available upon reasonable request.

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