Tzu Chi Medical Journal 2024; 36 (1): 92-97

Original Article

Effect of hypoalbuminemia on mortality in cirrhotic patients with spontaneous bacterial peritonitis

*Tsung-Hsing Hung[a,b], Ping-Hung Ko[a], Chih-Ying Wang[c], Chih-Chun Tsai[d], Hsing-Feng Lee[a,b]**

[a]Division of Gastroenterology, Department of Medicine, Dalin Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Chiayi, Taiwan, [b]School of Medicine, Tzu Chi University, Hualien, Taiwan, [c]Department of Medical Research, Dalin Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Chiayi, Taiwan, [d]Department of Mathematics, Tamkang University, New Taipei, Taiwan

Submission : 25-Aug-2023
Revision : 06-Sep-2023
Acceptance : 04-Oct-2023
Web Publication : 13-Dec-2023

Abstract

Objectives: The impact of hypoalbuminemia on the short-term and long-term mortality of cirrhotic patients with spontaneous bacterial peritonitis (SBP), both with and without renal function impairment, remains insufficiently elucidated based on population-based data. **Materials and Methods:** We retrieved data from Taiwan's National Health Insurance Database encompassing 14,583 hospitalized patients diagnosed with both cirrhosis and SBP during the period from January 1, 2010, to December 31, 2013. Prognostic factors influencing 30-day and 3-year survival were computed. Furthermore, the impact of hypoalbuminemia on the mortality rate among SBP patients, with or without concurrent renal function impairment, was also assessed. **Results:** The 30-day mortality rates for patients with SBP, comparing those with hypoalbuminemia and those without, were 18.3% and 29.4%, respectively ($P < 0.001$). Similarly, the 3-year mortality rates for SBP patients with hypoalbuminemia and those without were 73.7% and 85.8%, respectively ($P < 0.001$). Cox proportional hazard regression analysis, adjusted for patients' gender, age, and comorbid conditions, substantiated that individuals with hypoalbuminemia exhibit an inferior 30-day survival (hazard ratio [HR]: 1.62, 95% confidence interval [CI]: 1.51–1.74, $P < 0.001$) and reduced 3-year survival (HR: 1.57, 95% CI: 1.50–1.63, $P < 0.001$) in comparison to those lacking hypoalbuminemia. Among SBP patients with renal function impairment, those presenting hypoalbuminemia also experienced diminished 30-day survival (HR: 1.81, 95% CI 1.57–2.07, $P < 0.001$) as well as reduced 3-year survival (HR: 1.70, 95% CI 1.54–1.87, $P < 0.001$). Likewise, in SBP patients without renal function impairment, the presence of hypoalbuminemia was associated with poorer 30-day survival (HR: 1.54, 95% CI 1.42–1.67, $P < 0.001$) and 3-year survival (HR: 1.53, 95% CI 1.46–1.60, $P < 0.001$). **Conclusion:** Among cirrhotic patients with SBP, the presence of hypoalbuminemia predicts inferior short-term and long-term outcomes, regardless of renal function.

Keywords: *Cirrhosis, Hypoalbuminemia, Mortality, Spontaneous bacterial peritonitis*

Introduction

Liver cirrhosis (LC) typically arises as a consequence of chronic infection with hepatitis B, chronic hepatitis C, and/or alcoholism [1]. LC often progresses to conditions such as hepatocellular carcinoma (HCC) or severe complications including spontaneous bacterial peritonitis (SBP), esophageal variceal bleeding (EBV), and hepatic encephalopathy (HE) [2]. The incidence of SBP in cirrhotic patients is approximately 10% [3]. The diagnosis of SBP is established by the presence of an absolute polymorphonuclear leukocyte count of >250 cells/mm^3 in the ascites fluid. Therefore, SBP predominantly manifests in cirrhotic patients exhibiting ascites.

Albumin is produced by the liver [4]. Hence, in cases of LC, particularly in its advanced stages, compromised albumin synthesis ensues. Hypoalbuminemia is frequently observed in cirrhotic patients who also present with ascites. Notably, the occurrence of hypoalbuminemia has recently emerged as a significant factor in individuals with SBP [5,6]. Nevertheless, there exists a dearth of population-based data to elucidate the precise impact of hypoalbuminemia on the

***Address for correspondence:** Dr. Hsing-Feng Lee, Division of Gastroenterology, Department of Medicine, Dalin Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, 2, Minsheng Road, Dalin, Chiayi, Taiwan.
E-mail: hflee1979@hotmail.com

How to cite this article: Hung TH, Ko PH, Wang CY, Tsai CC, Lee HF. Effect of hypoalbuminemia on mortality in cirrhotic patients with spontaneous bacterial peritonitis. Tzu Chi Med J 2024;36(1):92-7.

Access this article online

Quick Response Code:

Website: www.tcmjmed.com

DOI: 10.4103/tcmj.tcmj_211_23

prognosis of individuals with SBP. Furthermore, the influence of hypoalbuminemia on the mortality of SBP patients, both with and without concurrent renal function impairment, remains to be thoroughly assessed. As far as our knowledge extends, there is a lack of adequate population-based studies aimed at evaluating the prognosis of cirrhotic patients afflicted with both SBP and hypoalbuminemia, and the extent of hypoalbuminemia's effect on the mortality rate of SBP patients with or without renal function impairment remains uncharted territory. Utilizing an extensive nationwide population-based dataset from Taiwan, our objective is to ascertain the near-term and extended prognostic implications for cirrhotic patients affected by SBP and concurrent hypoalbuminemia. In addition, we seek to elucidate the impact of hypoalbuminemia on the mortality rate among SBP patients, regardless of the presence or absence of renal function impairment.

Materials and Methods

Database and ethical statement

Taiwan's National Health Insurance (NHI) system has been in operation for over two decades, offering coverage to over 99% of the population and ensuring equitable health care access for all. Comprehensive medical services for illnesses, injuries, and childbirth are available to individuals holding an NHI card when seeking treatment at medical facilities. The Taiwan NHI Research Database (NHIRD) meticulously archives all medical records, encompassing data such as International Classification of Diseases, 9th or 10th Revision, Clinical Modification (ICD-9-CM or ICD-10-CM) codes, prescribed medications, hospitalization expenses, and duration of hospital stays. The Taiwan NHIRD has emerged as a pivotal resource, facilitating a multitude of research endeavors [7,8].

The Buddhist Tzu Chi Medical Foundation (TCMF-A 109-01) and the Institutional Review Board of the Buddhist Dalin Tzu Chi Hospital (IRB B10403026) granted approval for the implementation of this study. Given that all data within the NHIRD has undergone de-identification, the review committee exempted us from the requirement of obtaining informed consent from the patients.

Study sample

The database was queried for patients discharged between January 1, 2010, and December 31, 2013, with a primary or secondary diagnosis of cirrhosis (ICD-9-CM code 571.5 or 571.2). These specific ICD-9 codes have been employed in previous studies to identify cirrhosis patients in Taiwan. Subsequently, within this cohort, individuals with SBP were identified using ICD-9-CM codes 567.2, 567.8, or 567.9. If a patient experienced multiple hospitalizations for SBP within the study period, only the initial episode was considered for analysis. In this study, the definition of hypoalbuminemia is based on the application for health insurance-covered albumin medication, rather than using ICD-9 coding. This choice was made because relying on ICD-9 coding to determine the presence of hypoalbuminemia can be relatively inaccurate, and it cannot be assumed that every physician has the same definition of hypoalbuminemia. According to the NHI Administration's (NHIA) principles for providing albumin medication, one of the criteria is that patients with cirrhosis who also have ascites, and whose blood albumin levels are <2.5 mg/dL. Since all the patients in our study had SBP, by definition, they all had ascites. Therefore, when these patients applied for health insurance coverage for albumin medication, their blood albumin levels should all be <2.5 mg/dL. Hence, in our study, we defined hypoalbuminemia as <2.5 mg/dL based on this fact. On the other hand, because albumin is a relatively expensive medication in Taiwan, most hospitals require clinical physicians to provide confirmation when prescribing albumin. Therefore, we believe that those classified as having hypoalbuminemia in our study would indeed have blood albumin levels below 2.5 mg/dL. In clinical practice, administering albumin infusion to cirrhotic patients with hypoalbuminemia and ascites has shown to alleviate edema and assist in ascites control. To ascertain the 30-day mortality rates of the enrolled patients, a Taiwanese National Mortality Database was consulted. The considered comorbid conditions encompassed alcoholism (ICD-9-CM codes 291, 303, 305.00–305.03, 571.0–571.3), HCC (ICD-9-CM code 155.0), HE (ICD-9-CM code 572.2), renal function impairment (ICD-9-CM codes 584, 585, 586, 572.4, or other procedure codes relevant to renal failure), ascites (ICD-9-CM code 789.5 or procedure code 54.91), and EVB (ICD-9-CM codes 456.0, 456.20). The individuals were categorized into three groups based on socioeconomic status (SES): low SES, medium SES, and high SES. In this study, low SES was defined as a monthly income of less than New Taiwan Dollar (NTD $20,000) (approximately US$556). Medium SES was defined as a monthly income ranging from NTD $20,001 to $40,000 (approximately US$556 to $1111). High SES was defined as a monthly income exceeding NTD $40,001 (approximately US$1111).

To assess the impact of hypoalbuminemia on the mortality rate among SBP patients, considering the presence or absence of renal function impairment, a subgroup analysis was conducted. The 30-day and 3-year mortality rates were computed for patients with hypoalbuminemia, both with and without concurrent renal function impairment. In addition, hazard ratios (HRs) were determined for these respective subgroup cohorts.

Statistical analyses

We performed statistical analyses using the SPSS Statistical Package version 22.0 for Windows, developed by IBM Corp (Armonk, NY, USA). Categorical variables were compared using the Chi-square test, while continuous variables were analyzed using Student's *t*-test. To assess the comorbid factors associated with LC, we employed a proportional hazards Cox regression model for survival analysis. The outcomes were presented as HRs along with their corresponding 95% confidence intervals (CIs). P <0.05 was considered statistically significant in our study. This significance level was chosen for all analyses.

Results

We gathered data from Taiwan's NHIRD, encompassing 14,583 patients diagnosed with both cirrhosis and SBP who were admitted to hospitals between January 1, 2010, and

December 31, 2013. The fundamental data are detailed in Table 1. In general, among cirrhotic patients with SBP, the mortality rates within 30 days and over a span of 3 years were 21.9% and 77.7%, respectively.

The 30-day mortality rates for SBP patients with and without hypoalbuminemia were 18.3% and 29.4%, respectively ($P < 0.001$). Correspondingly, the 3-year mortality rates for SBP patients with and without hypoalbuminemia were 73.7% and 85.8%, respectively ($P < 0.001$). Following adjustment for patient gender, age, and comorbid conditions using the Cox proportional hazard regression model, several variables were identified as increasing the risk of 30-day mortality in cirrhotic patients with SBP. These included older age (HR: 1.02, 95% CI 1.01–1.02, $P < 0.001$), male gender (HR: 1.10, 95% CI 1.02–1.20, $P = 0.016$), EVB (HR: 1.23, 95% CI 1.06–1.43, $P = 0.006$), HCC (HR: 1.91, 95% CI 1.77–2.05, $P < 0.001$), HE (HR: 1.42, 95% CI 1.30–1.55, $P < 0.001$), hypoalbuminemia (HR: 1.62, 95% CI 1.51–1.74, $P < 0.001$), impaired renal function (HR: 2.44, 95% CI 2.25–2.64, $P < 0.001$), and nonalcoholic-related cirrhosis (HR: 1.12, 95% CI 1.02–1.24, $P = 0.025$).

Table 1: Demographic characteristics of cirrhotic patients with spontaneous bacterial peritonitis (*n*=14,583)

	n (%)
Age (years)	59.54±14.08
Male	10,474 (71.8)
EVB	859 (5.9)
HCC	4246 (29.1)
HE	2268 (15.6)
Hypoalbuminemia	4776 (32.8)
RFI	2037 (14.0)
Nonalcoholic-related cirrhosis	10,813 (74.1)
Socioeconomic status	
Low	8483 (58.2)
Medium	5409 (37.1)
High	691 (4.7)

EVB: Esophageal variceal bleeding, HCC: Hepatocellular carcinoma, HE: Hepatic encephalopathy, RFI: Renal failure impairment

Patients with hypoalbuminemia also exhibited decreased 3-year survival rates (HR: 1.57, 95% CI 1.50–1.63, $P < 0.001$), as depicted in Table 2. The Kaplan–Meier survival curve is presented in Figure 1. The main findings of this study remain consistent regardless of whether the patients have hepatitis B virus (HBV)- or hepatitis C virus (HCV)-related cirrhosis. In SBP patients with HBV, the presence of hypoalbuminemia was associated with poorer 30-day survival (HR: 1.57, 95% CI 1.39–1.77, $P < 0.001$) and 3-year survival (HR: 1.49, 95% CI 1.39–1.59, $P < 0.001$). In SBP patients with HCV, the presence of hypoalbuminemia was also associated with poorer 30-day survival (HR: 1.48, 95% CI 1.31–1.68, $P < 0.001$) and 3-year survival (HR: 1.52, 95% CI 1.38–1.67, $P < 0.001$).

In the subgroup analysis of SBP patients, the 30-day mortality rates for patients with renal function impairment,

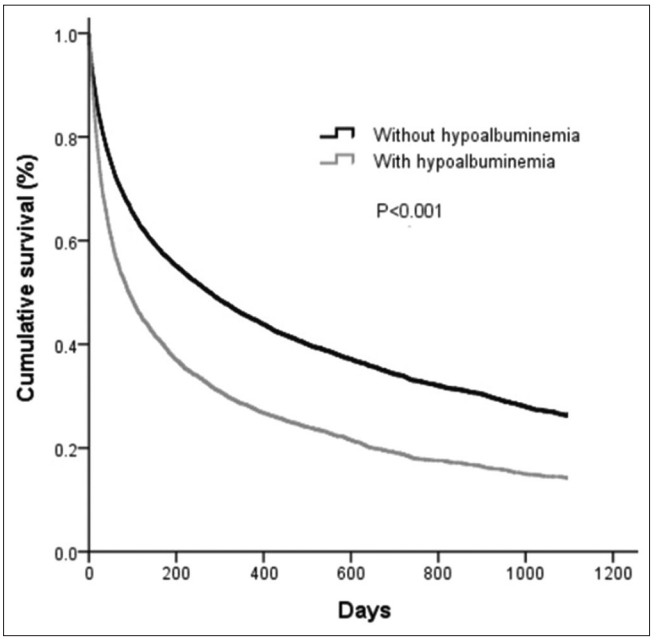

Figure 1: Kaplan–Meier survival analysis curves of 3-year mortality in cirrhotic patients with spontaneous bacterial peritonitis, by the presence of hypoalbuminemia

Table 2: Adjusted hazard ratios of the risk factors for 30-day and 3-year mortality in cirrhotic patients with spontaneous bacterial peritonitis

Variable	30-day			3-year		
	HR	95% CI	*P*	HR	95% CI	*P*
Age	1.02	1.01–1.02	<0.001	1.02	1.01–1.02	<0.001
Male	1.10	1.01–1.19	0.022	1.05	1.01–1.10	0.026
EVB	1.23	1.06–1.43	0.006	1.14	1.04–1.24	0.003
HCC	1.90	1.77–2.05	<0.001	2.13	2.04–2.22	<0.001
HE	1.42	1.30–1.55	<0.001	1.42	1.35–1.50	<0.001
Hypoalbuminemia	1.62	1.51–1.73	<0.001	1.57	1.50–1.63	<0.001
RFI	2.44	2.25–2.64	<0.001	1.75	1.66–1.85	<0.001
Nonalcoholic-related cirrhosis	1.12	1.01–1.24	0.027	1.04	0.98–1.09	0.195
Socioeconomic status						
Low			0.011			0.680
Medium	1.12	1.04–1.10	0.003	1.02	0.98–1.06	0.380
High	1.06	0.89–1.25	0.517	1.01	0.92–1.11	0.862

HR: Hazard ratio, CI: Confidence interval, EVB: Esophageal variceal bleeding, HCC: Hepatocellular carcinoma, HE: Hepatic encephalopathy, RFI: Renal function impairment

with and without hypoalbuminemia, were 51.6% and 32.0%, respectively ($P < 0.001$). Correspondingly, the 3-year mortality rates for patients with renal function impairment, with and without hypoalbuminemia, were 94.1% and 85.2%, respectively ($P < 0.001$). Moreover, the 30-day mortality rates for patients without renal function impairment, with and without hypoalbuminemia, were 24.8% and 16.3%, respectively ($P < 0.001$). The corresponding 3-year mortality rates for patients without renal function impairment, with and without hypoalbuminemia, were 84.1% and 72.1%, respectively ($P < 0.001$).

We calculated adjusted HRs for 30-day and 3-year mortality in cirrhotic patients with SBP, considering the presence or absence of renal function impairment. These results are summarized in Tables 3 and 4. Among SBP patients with renal function impairment, those with hypoalbuminemia experienced poorer 30-day (HR: 1.81, 95% CI 1.57–2.07, $P < 0.001$) and 3-year survival (HR: 1.70, 95% CI 1.54–1.87, $P < 0.001$) compared to those without hypoalbuminemia. Similarly, among SBP patients without renal function impairment, those with hypoalbuminemia displayed diminished 30-day (HR: 1.54, 95% CI 1.42–1.67, $P < 0.001$) and 3-year survival (HR: 1.53, 95% CI 1.46–1.60, $P < 0.001$) relative to those without hypoalbuminemia. The survival curves for these patient subgroups are presented in Figure 2. In SBP patients, the presence of hypoalbuminemia resulted in a poorer prognosis, irrespective of renal function.

Discussion

This study underscores the significance of hypoalbuminemia as a crucial prognostic indicator in cirrhotic patients afflicted with SBP, influencing both near-term and prolonged mortality outcomes. Remarkably, this association holds true irrespective of the degree of renal function. Consequently, in clinical settings, health-care practitioners must be vigilant to the heightened risk among SBP patients, particularly those with hypoalbuminemia, even when their renal function appears relatively sound.

Albumin is produced by the liver [4]. However, the concentration of albumin in the bloodstream is influenced by multiple factors, including the rate of catabolism, synthesis, clearance, and distribution [9-11]. Hypoalbuminemia may also serve as an indicator of diminished liver reserve. Impaired liver reserve is closely linked to elevated mortality rates in cirrhotic patients afflicted with SBP. Consequently, the association between hypoalbuminemia and unfavorable near-term and extended outcomes among SBP patients is to be expected.

Table 3: Adjusted hazard ratios of the risk factors for 30-day and 3-year mortality in cirrhotic patients with renal function impairment and spontaneous bacterial peritonitis

Variable	30-day			3-year		
	HR	95% CI	*P*	HR	95% CI	*P*
Age	1.01	1.00–1.01	0.129	1.01	1.01–1.02	<0.001
Male	1.15	0.98–1.36	0.095	1.10	0.98–1.22	0.112
EVB	1.40	0.94–2.07	0.095	1.30	0.97–1.75	0.084
HCC	1.85	1.59–2.15	<0.001	1.80	1.61–2.01	<0.001
HE	1.25	1.02–1.53	0.028	1.28	1.10–1.48	0.001
Hypoalbuminemia	1.79	1.56–2.06	<0.001	1.69	1.53–1.87	<0.001
Nonalcoholic-related cirrhosis	0.99	0.81–1.21	0.915	1.04	0.90–1.20	0.641
Socioeconomic status						
Low			0.215			0.378
Medium	1.11	0.96–1.29	0.144	1.07	0.97–1.19	0.182
High	0.89	0.64–1.24	0.500	0.98	0.78–1.23	0.874

HR: Hazard ratio, CI: Confidence interval, EVB: Esophageal variceal bleeding, HCC: Hepatocellular carcinoma, HE: Hepatic encephalopathy

Table 4: Adjusted hazard ratios of the risk factor for 30-day and 3-year mortality in cirrhotic patients with spontaneous bacterial peritonitis but no renal function impairment

Variable	30-day			3-year		
	HR	95% CI	*P*	HR	95% CI	*P*
Age	1.02	1.02–1.02	<0.001	1.02	1.01–1.02	<0.001
Male	1.08	0.99–1.19	0.092	1.05	1.00–1.10	0.074
EVB	1.22	1.04–1.43	0.017	1.12	1.03–1.23	0.010
HCC	1.90	1.75–2.07	<0.001	2.19	2.09–2.29	<0.001
HE	1.47	1.33–1.62	<0.001	1.45	1.37–1.54	<0.001
Hypoalbuminemia	1.54	1.42–1.67	<0.001	1.53	1.46–1.60	<0.001
Nonalcoholic-related cirrhosis	1.16	1.03–1.30	0.014	1.04	0.98–1.10	0.247
Socioeconomic status						
Low			0.022			0.915
Medium	1.12	1.03–1.22	0.009	1.01	0.96–1.05	0.757
High	1.15	0.94–1.40	0.184	1.02	0.92–1.13	0.738

HR: Hazard ratio, CI: Confidence interval, EVB: Esophageal variceal bleeding, HCC: Hepatocellular carcinoma, HE: Hepatic encephalopathy

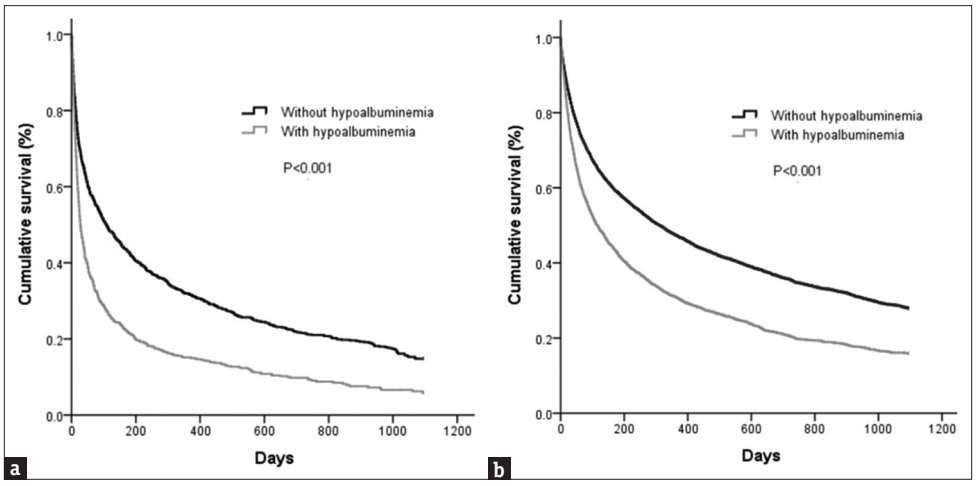

Figure 2: Kaplan–Meier survival analysis curves of 3-year mortality in cirrhotic patients with spontaneous bacterial peritonitis, by the presence of hypoalbuminemia, and (a) with or (b) without renal function impairment

Moreover, instances of inflammation, stemming from factors such as infection, trauma, or surgical procedures, have been demonstrated to reduce the synthesis of albumin [12].

Several possible reasons contribute to explaining why hypoalbuminemia increases the risk of mortality in SBP patients. First, the quantity of albumin in the blood to some extent reflects liver function. In other words, patients with low albumin levels partly indicate liver dysfunction. This can explain the increased mortality rate among such patients. Second, albumin plays a role in maintaining blood volume and fluid balance within the body. Hypoalbuminemia can lead to the accumulation of fluid in the abdominal cavity, causing ascites in patients with cirrhosis, which increases the risk of infection. These factors may exacerbate the symptoms of SBP, further increasing the mortality rate. Finally, studies support the role of albumin in the treatment of SBP, especially in patients with impaired kidney function [13]. In addition, in decompensated cirrhotic patients, albumin therapy has been shown to reduce systemic inflammation and cardiocirculatory dysfunction [14]. All of these factors indicate that higher blood albumin levels contribute to improved survival in such patients.

Hypoalbuminemia has been extensively documented as an adverse prognostic factor in various medical conditions [15-19]. For instance, Viasus *et al*. emphasized the significance of serum albumin levels within 24 h of admission as a crucial prognostic indicator for individuals diagnosed with community-acquired pneumonia [15]. Hypoalbuminemia is also recognized as an indicator of an unfavorable prognosis in patients with severe sepsis [20]. Hence, it comes as no surprise that the combination of SBP infection and hypoalbuminemia is associated with an unfavorable prognosis. The heightened mortality risk observed in SBP patients with hypoalbuminemia underscores the potential advantages of proactive albumin administration for such individuals. Prior research has demonstrated that supplementing with albumin can lead to reduced mortality rates and a decreased incidence of acute kidney injury (AKI) in SBP patients [21,22]. In a particular study, the implementation of a targeted albumin order set for high-risk SBP patients resulted in a significant reduction in both mortality rates and the occurrence of AKI [21]. Our study findings are consistent with these observations. Impaired renal function continues to be a pivotal prognostic factor in SBP patients. Our study's Cox regression analysis revealed that hypoalbuminemia, irrespective of renal function, emerged as a significant prognostic indicator for both short-term and long-term outcomes in SBP patients.

Hypoalbuminemia unveils several noteworthy clinical aspects in cirrhotic patients. Individuals with hypoalbuminemia not only exhibit reduced oncotic pressure, potentially leading to the development of ascites or edema but they also commonly experience malnutrition. It is unsurprising that these conditions can contribute to unfavorable prognoses in such patients. Another significant revelation is that hypoalbuminemia often signals inadequate liver reserve. In clinical practice, while albumin infusion may be beneficial for high-risk SBP patients, it might not solely enhance liver reserve. Our study's outcomes align with these established observations. In this study, the utilization of a National Population-based Dataset unveiled that individuals with SBP and hypoalbuminemia experience inferior near-term and extended outcomes compared to those without hypoalbuminemia. While prior research has indicated that albumin infusion is advantageous for SBP patients with AKI, it is evident that the unfavorable short-and long-term outcomes of SBP patients with hypoalbuminemia persist due to compromised liver reserve.

The primary limitation of this present study pertained to the unavailability of precise serum albumin level data within the dataset. Nevertheless, under Taiwan's NHI, albumin is typically administered when the serum albumin level falls below 2.5 g/dL in cirrhotic patients with ascites. Owing to the absence of laboratory information in this claims-based dataset, pivotal indicators of LC severity, such as the Child–Pugh score or Mayo Clinic model for end-stage liver disease, could not be ascertained. However, variables pertaining to liver reserves, such as variceal bleeding, HE, or HCC, were included for analysis. In addition, it is conceivable that transient and mild renal function impairment might not have

been adequately documented in discharge records. On the other hand, in this study, renal dysfunction was determined using ICD-9 coding, and we were unable to obtain precise data. This, of course, is a limitation of our study. Nonetheless, given the potentially reduced clinical significance of mild and transient renal function impairment, our study demonstrated consistently poor survival outcomes among all SBP patients with hypoalbuminemia, irrespective of renal function. Consequently, we maintain that the absence of laboratory data, such as creatinine levels, did not significantly impact the findings of our study. Indeed, in spite of that, we will still need real-world data in the future to validate our research. Finally, due to the limitation of reporting a maximum of five diagnoses to the NHIA, certain systemic disorders may not have been among the top five diagnoses, which could potentially result in inaccuracies.

Conclusion

In summary, within the context of cirrhotic patients with SBP, the existence of hypoalbuminemia serves as an indicator of adverse near-term and extended prognoses, irrespective of renal function. Acknowledgment of this circumstance can facilitate improved clinical management of these patients and stimulate further investigation into the significance of hypoalbuminemia in the context of cirrhotic patients with SBP.

Data availability statement

The data that support the findings of this study are available from NHIRD in Taiwan but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are, however, available from the authors upon reasonable request and with permission of NHIRD.

Acknowledgment

This study is based on data from the Taiwan NHIRD provided by the Bureau of NHI, Department of Health, which is managed by the National Health Research Institutes. The interpretation and conclusions contained herein do not represent those of the Bureau of NHI, Department of Health, or National Health Research Institutes.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Ginès P, Krag A, Abraldes JG, Solà E, Fabrellas N, Kamath PS. Liver cirrhosis. Lancet 2021;398:1359-76.
2. Poordad FF. Presentation and complications associated with cirrhosis of the liver. Curr Med Res Opin 2015;31:925-37.
3. Borzio M, Salerno F, Piantoni L, Cazzaniga M, Angeli P, Bissoli F, et al. Bacterial infection in patients with advanced cirrhosis: A multicentre prospective study. Dig Liver Dis 2001;33:41-8.
4. Doweiko JP, Nompleggi DJ. The role of albumin in human physiology and pathophysiology, part III: Albumin and disease states. JPEN J Parenter Enteral Nutr 1991;15:476-83.
5. Abdel-Razik A, Abdelsalam M, Gad DF, Abdelwahab A, Tawfik M, Elzehery R, et al. Recurrence of spontaneous bacterial peritonitis in cirrhosis: Novel predictors. Eur J Gastroenterol Hepatol 2020;32:718-26.
6. Garioud A, Cadranel JF, Pauwels A, Nousbaum JB, Thévenot T, Dao T, et al. Albumin use in patients with cirrhosis in France: Results of the "ALBU-LIVE" survey: A case for better EASL guidelines diffusion and/or revision. J Clin Gastroenterol 2017;51:831-8.
7. Hung TH, Tsai CC, Lee HF. The role of hepatic reserve in the mortality of cirrhotic patients with small hepatocellular carcinoma receiving radiofrequency ablation. Medicine (Baltimore) 2022;101:e30918.
8. Hung TH, Tseng CW, Tsai CC, Lee HF. Prognosis of hypoglycemia episode in cirrhotic patients during hospitalization. BMC Gastroenterol 2021;21:319.
9. Don BR, Kaysen G. Serum albumin: Relationship to inflammation and nutrition. Semin Dial 2004;17:432-7.
10. Fuhrman MP, Charney P, Mueller CM. Hepatic proteins and nutrition assessment. J Am Diet Assoc 2004;104:1258-64.
11. De Feo P, Lucidi P. Liver protein synthesis in physiology and in disease states. Curr Opin Clin Nutr Metab Care 2002;5:47-50.
12. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. N Engl J Med 1999;340:448-54.
13. Dever JB, Sheikh MY. Review article: Spontaneous bacterial peritonitis – Bacteriology, diagnosis, treatment, risk factors and prevention. Aliment Pharmacol Ther 2015;41:1116-31.
14. Fernández J, Clària J, Amorós A, Aguilar F, Castro M, Casulleras M, et al. Effects of albumin treatment on systemic and portal hemodynamics and systemic inflammation in patients with decompensated cirrhosis. Gastroenterology 2019;157:149-62.
15. Viasus D, Garcia-Vidal C, Simonetti A, Manresa F, Dorca J, Gudiol F, et al. Prognostic value of serum albumin levels in hospitalized adults with community-acquired pneumonia. J Infect 2013;66:415-23.
16. Horwich TB, Kalantar-Zadeh K, MacLellan RW, Fonarow GC. Albumin levels predict survival in patients with systolic heart failure. Am Heart J 2008;155:883-9.
17. Sullivan DH, Roberson PK, Bopp MM. Hypoalbuminemia 3 months after hospital discharge: Significance for long-term survival. J Am Geriatr Soc 2005;53:1222-6.
18. Chen C, Zhang Y, Zhao X, Tao M, Yan W, Fu Y. Hypoalbuminemia – An indicator of the severity and prognosis of COVID-19 patients: A multicentre retrospective analysis. Infect Drug Resist 2021;14:3699-710.
19. Kinugasa Y, Kato M, Sugihara S, Hirai M, Kotani K, Ishida K, et al. A simple risk score to predict in-hospital death of elderly patients with acute decompensated heart failure – Hypoalbuminemia as an additional prognostic factor. Circ J 2009;73:2276-81.
20. Yin M, Si L, Qin W, Li C, Zhang J, Yang H, et al. Predictive value of serum albumin level for the prognosis of severe sepsis without exogenous human albumin administration: A prospective cohort study. J Intensive Care Med 2018;33:687-94.
21. Aithal GP, Palaniyappan N, China L, Härmälä S, Macken L, Ryan JM, et al. Guidelines on the management of ascites in cirrhosis. Gut 2021;70:9-29.
22. Ebied AM, Rattanasuwan T, Chen Y, Khoury AP. Albumin utilization in spontaneous bacterial peritonitis. J Pharm Pract 2022;35:546-50.