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Effect of Plasma Exchange on Hepatitis B-Related Acute-On-Chronic Liver Failure: A Cross-Sectional Study

Lu Wang | Lu Song | Jie Yang

Clinical Laboratory, The People's Hospital of Danyang, Danyang Hospital Affiliated to Nantong University, Danyang, Jiangsu, China

Correspondence: Jie Yang (yctcyangjie@163.com)

Received: 19 March 2024 | **Revised:** 28 March 2025 | **Accepted:** 3 April 2025

Funding: The authors received no specific funding for this work.

Keywords: acute-on-chronic liver failure | albumin-bilirubin score | blood ammonia | hepatitis B virus | plasma exchange

ABSTRACT

Background: To evaluate the effect of plasma exchange (PE) on the prognosis of patients with hepatitis B virus-related acute-on-chronic liver failure (HBV-ACLF).

Methods: The basic information (gender, age, blood type), the frequency and dosage of PE, the changes of indicators before and after PE, the adverse reactions related to PE and the prognosis of patients with HBV-ACLF who received PE in our hospital from April 2018 to December 2021 were retrospectively analyzed.

Results: 197 patients with HBV-ACLF who underwent PE were included in the analysis. Multivariate analysis shows that blood ammonia, ALBI, bacterial infection rate, HBV-DNA load, MELD score, etc., are independent risk factors affecting the efficacy of PE treatment in HBV-ACLF patients before and after PE treatment.

Conclusion: There are many factors influencing the efficacy of plasma exchange in patients with HBV-ACLF. Compared to other factors, high blood ammonia levels and high ALBI are the independent risk factors for poor short-term efficacy of plasma exchange.

1 | Introduction

Acute-on-chronic liver failure (ACLF) is caused by chronic liver disease [1]. The clinical symptoms mainly include acute jaundice deepening, coagulation dysfunction, etc., and the patient's condition is generally severe [2, 3]. Compared to other major infectious diseases, hepatitis B virus infection and liver disease receive less attention from the global health community [4, 5]. Data are scarce due to a lack of HBV surveillance and limited access to laboratories. Transfusion transmission, perinatal mother-to-child transmission and drug user network transmission have not been completely interrupted. Unlike HIV, there is no population-based HBV testing. The public health response to hepatitis B virus is inadequate and there is political inertia in fighting hepatitis B virus infection [6].

In China, ACLF caused by hepatitis B virus (HBV) is more common [7]. Liver transplantation is currently considered one of the effective treatments for ACLF patients who are poorly treated with drugs, but is limited by organ shortages. Artificial liver support systems have been used for the past three decades. The artificial liver support system (ALSS) has been developed to remove toxins and improve liver regeneration, especially in plasma exchange (PE) mode, which can improve the short-term

Abbreviations: ACLF, acute-on-chronic liver failure; ALBI, albumin-bilirubin score; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; HBV, hepatitis B virus; HBV-ACLF, hepatitis B virus-related acute-on-chronic liver failure; INR, international ratio; L, lymphocytes; MELD, end-stage liver disease model score.; N, neutrophils; NLR, neutrophil/lymphocyte ratio; PE, plasma exchange; PT, prothrombin time; PTA, prothrombin activity; RDW, red blood cell distribution width; SCR, serum creatinine; TBIL, total bilirubin; WBC, white blood cell; γ-GGT, γ-glutamine.

prognosis of ACLF patients. ALSS, including PE, can provide survival benefits for specific subgroups of ACLF patients [8, 9]. PE is currently listed as one of the treatment options for patients with liver failure in several guidelines. PE is a safe, reliable and well-tolerated treatment [10], but there are still some studies that believe that its long-term prognosis for ACLF patients is limited [11].

At present, plasma exchange is a commonly used treatment method, but this method is prone to adverse transfusion reactions [12]. Predicting the therapeutic effect of plasma exchange surgery through relevant indicators is beneficial for improving patient prognosis. Clinical practice has found that after plasma exchange therapy, the total bilirubin (TBIL) in patients' plasma will decrease, and there will be a redistribution of bilirubin outside the blood vessels, but there is also a chance of rebound. TBIL levels can predict the prognosis of patients.

The MELD score includes three objective variables: TBIL, serum creatinine, and standard internationalization ratio. Studies have shown [10] that the MELD score can predict the survival of ACLF patients. High blood ammonia levels can directly induce liver injury and affect immune function. According to the study [13], high blood ammonia is an independent risk factor for poor prognosis in patients with liver cirrhosis. In HBV-ACLF, this relationship needs to be further explored. The albumin-bilirubin score (ALBI) has only two objective indicators, which can avoid the evaluation of liver function due to ascites and hepatic encephalopathy [14–16].

Many studies have found that there is an inflammatory reaction involved in the pathogenesis of HBV-ACLF, and the aggravation of the inflammatory reaction will also affect the changes of peripheral blood cell parameters, for example, the survival of red blood cells is affected, so that a large number of red blood cells are in an immature state, and a large volume of red blood cells enter the circulation to increase the red cell distribution width (RDW).

In addition, the levels of white blood cells, neutrophils, lymphocytes, and platelets can reflect the degree of inflammatory response. Based on extensive research on systemic inflammatory response, RDW, Neutrophil to lymphocyte ratio (NLR) and other blood routine parameters are widely used in the evaluation of disease prognosis. There have also been many studies on NLR in liver diseases, but the results are inconsistent.

Based on the above research background, this study conducted a comprehensive analysis to evaluate and explore the relationship between baseline blood ammonia, ALBI and the efficacy of plasma exchange in patients with HBV-ACLF, so as to provide a basis for clinical practice.

2 | Data and Methods

2.1 | Research Object

Relevant information of 197 HBV-ACLF patients treated with PE in our hospital from June 2018 to December 2021 was retrospectively analyzed. we consulted and followed the "*Guidelines for reporting of statistics for clinical research in urology*" [17].

Inclusion criteria: (1) the age of patients ranged from 19 to 65 years old; (2) ACLF diagnostic criteria: ACLF is defined by the Asia Pacific Association for Study of the Liver ACLF Research Consortium (AARC) as jaundice (total bilirubin ≥ 5 mg/dL (85 μmol/L)), coagulation dysfunction (INR ≥ 1.5 or prothrombin activity $< 40\%$), and ascites, encephalopathy, or both within 4 weeks. (3) The duration of serum HBsAg positive was ≥ 6 months; (4) All patients were treated with artificial liver and plasma exchange in our hospital; (5) The patient's data are complete.

Exclusion criteria: (1) the patient had developed disseminated intravascular coagulation; (2) The patient developed circulatory and respiratory failure; (3) Patients with liver cancer or cancer in other parts; (4) Patients with HIV infection; (5) The patients were complicated with severe heart failure, atrial fibrillation, myocardial infarction, cerebrovascular disease and other major diseases; (6) The patient was complicated with other types of hepatitis virus infection.

2.2 | Treatment Methods

The recommended exchange volume for full volume PE is 1.0–1.3 plasma volumes, which can be estimated using the following formula: plasma volume = patient body mass (kg) × 70 × [(1.0 hematocrit) × 0.91].

Membrane PE uses a plasma separator to separate a portion of the whole blood extracted from the body and discard it. At the same time, various components that penetrate the membrane pores dissolved in the plasma are discarded, while blood cells and platelets that cannot pass through the membrane pores are retained. Then, an equal amount of replacement solution is mixed with blood cells and transfused back into the body. If a plasma component separator is used with a lower membrane pore size and protein screening coefficient than the plasma separator, SPE can be performed. This mode can retain more medium and large molecular substances in the patient's plasma, such as coagulation factors and globulin. Membrane PE parameter setting: blood flow velocity of 80–150 mL/min; Separation ratio of 20%–30%; The plasma separation rate should be 20–30 mL/min, and the exchange rate should be consistent with the plasma separation rate.

Centrifugal PE uses a centrifuge to centrifuge whole blood at a certain speed, separating plasma and blood cells. Part of the plasma is discarded, and then mixed with an equal amount of displacement solution and blood cells before being transfused back into the body. Centrifugal PE parameter setting: blood flow velocity of 30–80 mL/min; Plasma separation rate of 15–30 mL/min; The sum of the displacement fluid velocity and anticoagulant velocity is generally equal to the plasma separation velocity to maintain liquid equilibrium.

The exchange fluids used for PE mainly include fresh frozen plasma, albumin solution, and other plasma substitutes. Different replacement fluids should be selected according to the

specific situation of the patient. For example, when the patient's PTA is normal or the decrease is not significant, partial albumin solution can be used instead of fresh frozen plasma; When the PTA of the patient decreases significantly and the available fresh frozen plasma is insufficient, plasma substitutes can be used first, followed by fresh frozen plasma. The amount of plasma substitutes should not exceed one-fourth of the total exchange volume. Attention should be paid to setting the plasma separation ratio based on the characteristics of different plasma separators/plasma component separators and the patient's hematocrit, to avoid membrane rupture or excessive blood concentration caused by a plasma separation ratio higher than the upper limit of the plasma separator, which can lead to red blood cell damage and pipeline blockage. The treatment frequency of PE should be tailored to the specific condition of the patient, taking into account factors such as the distribution volume of pathogenic mediators in the body, the half-life of pathogenic mediators, and the severity of the primary disease (such as baseline levels and rebound amplitude of serum bilirubin in patients with liver failure) [18].

After evaluating the patient, we implemented the following treatments: Lamivudine was used for anti-hepatitis B virus treatment; reduced glutathione was used in liver protection therapy.

Plasma exchange therapy: Establishing a blood pathway through femoral vein catheterization, Jinbao Prismaflex blood filter was used to implement plasma exchange therapy. The vascular access of the patient was temporary indwelling of double-lumen catheter through the internal jugular vein or femoral vein to establish cardiopulmonary bypass. During PE, heparin-free protocol was adopted and before treatment, heparin physiological saline was used to fully pre flush, and physiological saline was regularly used to flush the tube during the treatment process. Blood flow was controlled at 150 mL/min, and plasma infusion rate was controlled at 18 mL/min. The average PE time was 2 h. The dose of fresh plasma each time was 2000 ~ 3000 mL, and the interval between two plasma exchanges was 2 ~ 3 days. The vital signs of the patients were closely monitored during the treatment. The PE speed of abnormal patients was slowed down or stopped immediately, and 10% calcium gluconate injection and dexamethasone were given for anti-allergic treatment.

2.3 | Observation Indexes and Detection Methods

The data collected included the patient's gender, age, blood type, the number of PE, the index prognosis (improvement, death) within 24 h before PE (hereinafter referred to as before PE) and within 24 h after the last PE (hereinafter referred to as after PE). Among them, the short-term efficacy of PE in the treatment of HBV-ACLF was considered to be good if it survived 90 days after the first PE, while the short-term efficacy of PE in the treatment of HBV-ACLF was considered to be poor if it died within 90 days after the first PE.

The baseline blood ammonia, ALBI, HBV-DNA load, alanine aminotransferase (ALT), aspartate aminotransferase (AST), TBIL, γ-glutamine (γ-GGT), Cystatin C, serum creatinine (SCR), blood urea nitrogen (BUN), potassium ion, sodium ion, prothrombin time (PT), standardized International ratio (INR), prothrombin activity (PTA), and white blood cell (WBC), neutrophils (n), lymphocytes (L), monocytes, and end-stage liver disease model score (MELD) before treatment were compared between the two groups, improvement (hereinafter referred to as effective; 132 cases) and death (hereinafter referred to as ineffective; 65 cases).

Fasting venous blood 3 mL was collected before and after PE treatment, centrifuged for 15 min (3000 RPM), and serum was collected for test. The levels of AST, ALB, TBIL, γ-GGT, SCR, Cystatin C, potassium ion and sodium ion were detected by Hitachi 008AS biochemical analyzer. Venous blood 4 mL was collected with anticoagulant tube; and Pt, INR, and PTA levels were detected by the Sismecon CS-5100 Automatic Coagulation Analyzer; The levels of WBC, N, L and monocytes were measured by Mind 6800 automatic blood analyzer. Venous blood 3 mL was collected from the two groups, and the blood ammonia concentration was detected by the American Johnson VITR 5600 automatic biochemical analyzer and dry chemistry method. The level of HBV-DNA was detected by abi7500 fluorescent quantitative PCR. $\mathrm{MELD} = 9.6 \times \ln(\mathrm{Scr\ mg/dL}) + 3.8 \times \ln(\mathrm{TBIL\ mg/dL}) + 11.2 \times \ln(\mathrm{INR}) + 6.4$. $\mathrm{ALBI} = 0.66 \times \log 10\,[\mathrm{TBIL}\ (\mu\mathrm{mol/L})] - 0.085\,[\mathrm{ALB}\ (\mathrm{g/L})]$.

2.4 | Statistical Methods

The data were processed by SPSS 21.0. The normal distribution of count data such as blood ammonia, ALBI, HBV-DNA load, TBIL, Cystatin C, Scr, BUN, Pt, INR, WBC, N, l, monocytes and MELD scores collected in this study were statistically described by $\bar{\chi} \pm s$ method. The comparative hypothesis test between the two groups of measurement data was conducted by independent sample *t*-test; count data (gender, liver cirrhosis, bacterial infection, liver ascites, etc.) were described by the number of cases (percentage), and the comparison of non-grade count data between groups was analyzed by χ^2 test; logistic regression model was used for multivariate analysis; $p < 0.05$ shows that the statistical difference is significant.

2.5 | Ethics Approval Statement

After examination, the article written by Wang Lu from Clinical Laboratory: Effect of plasma exchange on hepatitis B-related acute-on-chronic liver failure: A cross-sectional study, which was reviewed by Medical Ethics Committee of Danyang People's Hospital, and meets ethical requirements, agreed to submit the article for publication, ethics number 20240417.

The participant's consent statement is not applicable because it does not involve a statement of consent from the participants.

3 | Results

3.1 | Comparison of General Clinical Data Between the Two Groups

From April 2018 to December 2021, our hospital admitted a total of 197 HBV-ACLF patients treated with PE. Including 130

males and 67 females; The average age is (50 ± 10) years old. The blood type distribution includes 61 cases of type A, 73 cases of type B, 52 cases of type O, and 11 cases of type AB; The median number of PE was 2 (1, 11) times, and the median total plasma dose was 3800 (1,200; 20,000) mL.

There was no significant difference in age, BMI, gender, liver cirrhosis, liver ascites between the effective group and the ineffective group ($p > 0.05$); The bacterial infection rate and hepatic encephalopathy rate in the ineffective group were significantly higher than those in the effective group ($p < 0.05$) (Table 1).

3.2 | Comparison of Blood Ammonia, ALBI and Other Indicators Between the Two Groups

There was no significant difference in serum ALT, AST, potassium ion, sodium ion and γ-GGT levels between the effective group and the ineffective group ($p > 0.05$); The scores of blood ammonia, ALBI, HBV-DNA load, TBIL, Cystatin C, SCR, bun, Pt, INR, WBC, N, L, monocytes and MELD in the ineffective group were higher than those in the effective group, while PTA in the ineffective group was lower than that in the effective group, the difference was statistically significant ($p < 0.05$) (Table 2).

3.3 | Multivariate Analysis of Poor Effect of Plasma Exchange in Patients With HBV-ACLF

The logistic regression model was established by taking the statistically significant single factor analysis of whether it was complicated with bacterial infection, whether it was complicated with hepatic encephalopathy, blood ammonia, ALBI, HBV-DNA load, TBIL, Cystatin C, SCR, BUN, Pt, INR, WBC, N, L, monocytes, MELD score and PTA as independent variables and the treatment effect of patients as dependent variable.

The results showed that bacterial infection, hepatic encephalopathy, increased blood ammonia, increased ALBI, increased HBV-DNA load, increased TBIL, increased cystatin C, increased Pt, increased INR, increased MELD score and decreased PTA were the independent risk factors of poor effect of plasma exchange in patients with HBV-ACLF ($p < 0.05$) (Table 3).

3.4 | Adverse Reactions

Comparing the PE related adverse reactions between the effective and ineffective groups of patients, it was found that in the effective group ($n = 132$), there were 5 cases of allergic reactions, 10 cases of electrolyte disorders, 0 cases of hypotensive reactions, and 2 cases of catheter coagulation; Among the ineffective group ($n = 65$) patients, there were 6 cases of allergic reactions, 9 cases of electrolyte disorders, 1 case of hypotension reaction, and 1 case of catheter coagulation; There was no statistically significant difference ($p > 0.05$) between the two groups of patients in terms of adverse reactions such as allergic reactions, electrolyte imbalances, hypotensive reactions, and catheter coagulation (Table 4).

TABLE 1 | Comparison of general clinical data between the two groups ($\bar{x} \pm s$).

Group	*n*	Age	BMI (kg/m^2)	gender (%)		Liver cirrhosis (%)	Bacterial infection (%)	Hepatic ascites (%)	Hepatic encephalopathy (%)
				male	female				
effective group	132	46.92 ± 8.50	23.90 ± 2.00	90 (68.18)	42 (31.82)	98 (74.24)	68 (51.52)	74 (56.06)	14 (10.61)
ineffective group	65	48.44 ± 8.22	24.17 ± 1.86	40 (61.54)	25 (38.46)	52 (80.00)	45 (69.23)	43 (66.15)	28 (43.08)
t/χ^2		−1.193	−0.911	0.856		0.759	5.589	1.840	27.375
p		0.234	0.363	0.355		0.373	0.018	0.175	< 0.001

TABLE 2 | Comparison of blood ammonia, ALBI and other indicators between the two groups.

Group	*n*	Blood ammonia (μmol/L)	ALBI	HBV-DNA load (10^7IU/mL)	ALT (U/L)	AST (U/L)	TBIL (μmol/L)
effective group	132	98.41 ± 22.74	−0.88 ± 0.23	1.65 ± 0.73	248.1 ± 43.8	237.6 ± 43.2	241.8 ± 51.6
ineffective group	65	165.90 ± 43.78	−0.62 ± 0.17	1.90 ± 0.84	259.3 ± 49.2	247.3 ± 50.5	347.1 ± 64.4
t		−14.254	8.087	−2.149	−1.619	−1.400	−12.382
p		< 0.001	< 0.001	0.033	0.107	0.163	< 0.001
group	*n*	γ-GGT (U/L)	Cystatin C (mg/L)	Scr (μmol/L)	BUN (mmol/L)	potassium ion (mmol/L)	sodium ion (mmol/L)
effective group	132	82.91 ± 14.66	1.28 ± 0.46	86.59 ± 9.20	7.50 ± 1.83	3.95 ± 0.26	136.94 ± 3.81
ineffective group	65	85.04 ± 18.24	1.45 ± 0.44	94.02 ± 11.55	8.20 ± 1.77	4.01 ± 0.28	135.77 ± 4.20
t		−0.883	−2.474	−4.888	−2.552	−1.485	1.959
p		0.378	0.014	< 0.001	0.011	0.139	0.052
group	*n*	INR	PTA (%)	WBC ($\times10^9$/L)	N ($\times10^9$/L)	L ($\times10^9$/L)	monocyte ($\times10^9$/L)
effective group	132	2.11 ± 0.40	38.57 ± 9.50	9.40 ± 2.41	4.39 ± 1.95	1.03 ± 0.30	0.59 ± 0.16
ineffective group	65	2.46 ± 0.52	33.78 ± 8.47	13.26 ± 2.81	6.43 ± 2.13	0.86 ± 0.27	0.80 ± 0.21
t		−5.214	3.446	−9.997	−6.695	3.862	−7.787
p		< 0.001	0.001	< 0.001	< 0.001	< 0.001	< 0.001

Abbreviations: γ-GGT, γ-glutamine; ACLF, acute-on-chronic liver failure; ALBI, albumin bilirubin score; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; HBV, hepatitis B virus; HBV-ACLF, HBV-related acute on chronic liver failure; INR, standardized international ratio; L, lymphocytes; MELD, end-stage liver disease model score; N, neutrophils; NLR, neutrophil/lymphocyte ratio; PT, prothrombin time; PTA, prothrombin activity; RDW, red blood cell distribution width; Scr, cystatin C; TBIL, total bilirubin; WBC, white blood cell.

TABLE 3 | Multivariate analysis of poor effect of plasma exchange in patients with HBV-ACLF.

Index	□β	SE	Walds	*p*	OR	95%CI	
Bacterial infection	0.601	0.287	4.385	0.046	1.824	1.039	3.201
Hepatic encephalopathy	0.772	0.328	5.540	0.018	2.164	1.138	4.116
Blood ammonia	0.498	0.226	4.856	0.039	1.645	1.057	2.562
ALBI	0.517	0.276	3.509	0.087	1.677	0.976	2.880
HBV-DNA load	0.663	0.301	4.852	0.040	1.941	1.076	3.501
TBIL	0.717	0.334	4.608	0.041	2.048	1.064	3.942
Cystatin C	0.633	0.265	5.706	0.014	1.883	1.120	3.166
Scr	0.281	0.255	1.214	0.396	1.324	0.803	2.183
BUN	0.472	0.281	2.821	0.107	1.603	0.924	2.781
PT	0.659	0.311	4.490	0.045	1.933	1.051	3.556
INR	0.487	0.196	6.174	0.003	1.627	1.108	2.390
PTA	−0.654	0.301	4.721	0.040	0.520	0.288	0.938
WBC	0.701	0.474	2.187	0.241	2.016	0.796	5.104
N	0.548	0.411	1.778	0.226	1.730	0.773	3.871
L	0.524	0.326	2.584	0.184	1.689	0.891	3.199
Monocyte	0.276	0.208	1.761	0.225	1.318	0.877	1.981
MELD score	0.741	0.301	6.060	0.005	2.098	1.163	3.785
Constant term	0.901	0.322	7.830	< 0.001	2.462	1.310	4.628

Abbreviations: γ-GGT, γ-glutamine; ACLF, acute-on-chronic liver failure; ALBI, albumin bilirubin score; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; HBV, hepatitis B virus; HBV-ACLF, HBV-related acute on chronic liver failure; INR, standardized International ratio; L, lymphocytes; MELD, end-stage liver disease model score; N, neutrophils; NLR, neutrophil/lymphocyte ratio; PT, prothrombin time; PTA, prothrombin activity; RDW, red blood cell distribution width; Scr, cystatin C; TBIL, total bilirubin; WBC, white blood cell.

TABLE 4 | Comparison of adverse reactions between effective and ineffective groups of patients.

	Effective group ($n = 132$)	Ineffective group ($n = 65$)	*p*
Allergic reaction	5	6	1.000
Electrolyte disturbance	10	9	1.000
Hypotensive response	0	1	1.000
Pipeline coagulation	1	1	1.000

4 | Discussion

According to research [19], the core pathogenesis of HBV-ACLF is inflammation and immunity. Its prognosis is related to factors such as infection, cytokine release, oxidative stress, and immune dysfunction. Plasma exchange can effectively treat HBV-ACLF patients. This method can remove harmful substances formed by liver cell necrosis such as bilirubin and inflammatory factors from the body's plasma, and then introduce beneficial substances such as coagulation factors and electrolytes into the blood to improve the microenvironment and prolong patient survival. This study will explore the factors that affect the effectiveness of plasma exchange, to provide a basis for clinical practice.

The results of this study showed that the bacterial infection rate and hepatic encephalopathy rate in the ineffective group were significantly higher than those in the effective group, and the difference was statistically significant ($p < 0.05$). A higher rate of bacterial infection and hepatic encephalopathy before treatment may affect the effectiveness of treatment. The occurrence of bacterial infection and hepatic encephalopathy can exacerbate the disorder of the body's immune system, leading to the formation of an endotoxin environment. The accumulation of harmful and toxic substances also exacerbates liver damage, affecting the effectiveness of treatment. The high replication of HBV and the extensive expression of its protein antigens can lead to extensive hepatocyte necrosis, which is one of the main pathways for the pathogenesis of HBV-ACLF. Inhibiting HBV-DNA replication is a therapeutic approach, and this study also found that increased HBV-DNA load is an independent risk factor for poor plasma exchange efficacy in HBV-ACLF patients ($p < 0.05$). Elevated HBV-DNA load can increase liver inflammation and damage, inhibit liver function recovery, and have a certain impact on prognosis.

The results of this study showed that the scores of ALBI, TBIL, and MELD in the ineffective group were higher than those in the effective group. The PTA of the ineffective group was lower than that of the effective group, and the difference

was statistically significant ($p < 0.05$). ALBI score is mainly composed of Alb and TBIL, which has the advantages of few indicators, good objectivity and few influencing factors, and has been widely used in predicting the prognosis of patients with liver disease. Some studies pointed out that [20] the ALBI score can be used as a predictor of the short-term mortality of hepatitis B-related acute/chronic liver failure, and a similar conclusion was reached in this study. Previous studies have shown that the higher the MELD score, the higher the mortality. This score has predictive value in many patients with liver disease. This study found that after plasma exchange treatment, the serum TBIL of patients with effective treatment decreased. The decrease of its level represents the increase of the degree of abnormal liver function, which can predict the poor prognosis in the short term. The change of TBIL level before and after plasma exchange has a certain predictive value for the prognosis of ACLF. According to the above research results, it can provide guidance for the treatment strategy of patients and improve the prognosis of patients.

The results of this study showed that the blood ammonia level in the ineffective group was higher than that in the effective group, and the increase of blood ammonia was an independent risk factor for the poor effect of plasma exchange in patients with HBV-ACLF. According to some studies [21], the increase of blood ammonia level is the core link of the incidence of liver cirrhosis-related complications, and is positively correlated with the degree of liver damage. This study found that high blood ammonia also affected the effect of plasma exchange. Animal experimental study found that: hyperammonemia can further induce liver injury, damage neutrophil function, and also cause adverse effects on other organs. Combined with the results of this study, it is suggested that blood ammonia may be a potential biomarker and therapeutic target of HBV-ACLF. Dynamic observation of blood ammonia level will help to predict the therapeutic effect.

In HBV-ACLF patients, excessive inflammatory response may lead to pathological immunity. Many studies have shown that RDW, INR, WBC, N, L, and the level of monocytes can reflect changes in the body's inflammatory response, and the above indicators are related to the prognosis of liver disease patients. This experiment analyzed the inflammation model mentioned above, and the results showed that the RDW of the ineffective group INR, WBC, N, L, the level of monocytes was higher in the effective group of patients. Moreover, an increase in INR is an independent risk factor for poor plasma exchange outcomes in HBV-ACLF patients ($p < 0.05$). Studies have shown that a decrease in the levels of N, L, and monocytes can also lead to a reduction in the body's nutritional status and immune function [18]. The level of NLR plays an important role in predicting the prognosis of acute coronary syndrome and malignant tumors. In recent years, its level can also predict the poor prognosis of patients with hepatitis and cirrhosis [22]. It is generally believed that an increase in NLR levels indicates a greater degree of inflammatory response in the body. The results of this study found that the NLR level was higher in the ineffective group, and its elevated level was an independent risk factor for the prognosis of HBV-ACLF plasma exchange, consistent with previous research results [23].

Cystatin C is an indicator reflecting impaired glomerular filtration function. The results of this study showed that the levels of cystatin C in the ineffective group were higher than those in the effective group, and the increased levels were an independent risk factor for poor plasma exchange results. Due to the frequent renal dysfunction in HBV-ACLF patients, the level of cystatin C increases with the worsening of liver disease [24]. Before and after plasma exchange treatment, the effective group of patients showed a significant decrease in cystatin C levels, suggesting that plasma exchange improved the degree of liver inflammation and necrosis, indirectly improving kidney function. However, there was no significant difference in Scr and BUN levels between the two groups, indicating that their relationship with plasma exchange efficacy was not significant, and it may also be related to the small sample size.

The results of this study showed that the PT of the ineffective group was higher than that of the effective group, and the PTA of the ineffective group was lower than that of the level effective group, with statistical significance. Plasma exchange eliminates toxic substances that damage liver function in the body and supplements plasma proteins and coagulation factors, improving the body's coagulation function. Changes in PT and PTA levels can reflect coagulation function and evaluate treatment efficacy. Regarding the use of heparin in PE, due to varying degrees of coagulation dysfunction in patients with liver failure, the dosage of heparin should be adjusted and individualized based on the patient's coagulation status. The overall principle is to use the smallest possible heparin dosage while ensuring smooth treatment. Suitable for patients with no clear active bleeding or low risk of bleeding or in a hypercoagulable state of blood. For patients with a history of heparin allergy, previous diagnosis of heparin-induced thrombocytopenia, and current clear active bleeding, heparin anticoagulation is not recommended.

HBV-ACLF has a high mortality rate, and the effect of plasma exchange has attracted clinical attention. Anticipating problems that may arise during treatment before or during treatment is important for developing treatment plans and allocating medical resources. For example, the PE treatment of liver failure patients requires a large amount of plasma, especially in the case of repeated PE, which puts great pressure on the guarantee and distribution of blood products. The efficacy analysis of plasma exchange during the waiting period for liver transplantation in HBV-ACLF patients is of great significance for the rational allocation and use of plasma resources.

This study uses the degree of improvement in indicators to predict the prognosis of HBV-ACLF patients, which will provide directional guidance for clinical treatment. However, this study also has certain limitations: (1) This study is a retrospective study, and some patients have been lost to follow-up, which may cause statistical research results to be biased. When relying on medical records or archives, there may be input errors, subjective descriptions, and differences in diagnostic criteria among different implementers. Due to the retrospective study being based on existing hospital records, patients who did not seek medical treatment in a timely manner may have been missed, resulting in the sample being unable to represent the target population. In subsequent research, missing values

should be promptly addressed to improve data quality. Cross-validation information such as electronic medical records, laboratory records, and follow-up phone calls should be combined to emphasize correlation rather than causality in the conclusions and avoid overinterpretation. Can be combined with other research designs, such as prospective cohorts and RCTs. (2) This study is only a single-center study and is limited to patients in the local area. It cannot be applied to areas with different medical levels. The operating personnel in the same center may cause systematic bias in the results, and the equipment and evaluation tools may also introduce systematic bias. Moreover, the sample size is small, which may lead to insufficient statistical power and increase the risk of accidental errors. Further prospective studies with multiple centers and large samples are needed to validate this result.

In summary, there are many factors that affect the effectiveness of plasma exchange in HBV-ACLF patients, and high blood ammonia levels and ALBI are independent risk factors for poor short-term efficacy of plasma exchange therapy.

Author Contributions

Lu Wang: methodology, writing – original draft. **Lu Song:** methodology. **Jie Yang:** methodology, writing – original draft, writing – review and editing.

Acknowledgments

The authors have nothing to report.

Ethics Statement

After examination, the article written by Wang Lu from Clinical Laboratory of the People's Hospital of Danyang: Relationship and significance of serum ammonia, RDW, ALBI with the efficacy and prognosis of plasma exchange in patients with HBV-ACLF, which was reviewed by the hospital ethics committee and met the ethical requirements, agreed to submit the article for publication, ethics number 20240417.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Transparency Statement

The lead author Jie Yang affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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