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Comparative Study of Treatment of HBV ACLF Patients by Tenofovir without Albumin Infusion and Tenofovir with Albumin Infusion

***Dr. Sharker Mohammad Shahadat Hossain[1], Prof. Dr. Salimur Rahman[2], Mariam Akter[3]**

[1]Assistant Professor, Department of Hepatology, Kurmitola General Hospital, Dhaka, Bangladesh
[2]Professor, Department of Hepatology, Anwer Khan Modern Medical College Hospital, Dhaka, Bangladesh
[3]Research Assistant, Department of Hepatology, Dr. Amanat Khan Hospital, Dhaka, Bangladesh
Corresponding Author: Dr. Sharker Mohammad Shahadat Hossain, Assistant Professor, Department of Hepatology, Kurmitola General Hospital, Dhaka, Bangladesh

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KEYWORDS

HBV-ACLF, Tenofovir, Albumin Infusion, Liver Failure, Survival, MELD Score, CTP Score.

ABSTRACT:

Background: ACLF is an acute hepatic insult manifesting as jaundice, complicated within 4 weeks by clinical ascites and/or encephalopathy in a patient with previously diagnosed or undiagnosed chronic liver disease/cirrhosis and is associated with a high 28-day mortality (ranging from 30% to 70). The aim of this study was to compare treatment of HBV ACLF patients by antiviral tenofovir without albumin therapy and tenofovir with albumin infusion.

Methods: This prospective comparative study was conducted at the Department of Hepatology, Kurmitola General Hospital, Dhaka, Bangladesh, from July 2022 to June 2024. A total of 32 patients aged over 18 years with HBV-ACLF were enrolled and randomized into two groups: tenofovir with albumin infusion (n = 16) and tenofovir without albumin infusion (n = 16). Patients were followed for 90 days. Key clinical parameters including Child-Turcotte-Pugh (CTP) score, MELD score, serum albumin, and survival outcomes were assessed at baseline and during follow-up.

Results: The group receiving albumin demonstrated significantly better outcomes. At day 90, survival was 81.2% in the albumin group vs. 43.7% in the non-albumin group (p = 0.018). Mean CTP scores decreased to 5.8 vs. 9.3, and MELD scores to 9.3 vs. 17, respectively. Serum albumin levels were significantly higher in the albumin group (3.5 vs. 3.0 mg/dL, p = 0.023).

Conclusion: Adjunctive albumin infusion with tenofovir significantly improves liver function and survival in HBV-ACLF patients, suggesting a potential role in standard care protocols.

Introduction

Acute-on-chronic liver failure (ACLF) is a distinct clinical entity characterized by acute hepatic decompensation in patients with pre-existing chronic liver disease, accompanied by high short-term mortality [1]. The syndrome is marked by systemic inflammation, multi-organ dysfunction and rapid deterioration of liver function. In Asia, hepatitis B virus (HBV) is one of the leading etiologies of ACLF, with HBV-associated ACLF (HBV-ACLF) accounting for a significant proportion of liver-related morbidity and mortality [2]. Despite its clinical importance, there remains no universally effective standard treatment for HBV-ACLF beyond supportive care and antiviral therapy [3].

Tenofovir disoproxil fumarate (TDF), a potent nucleotide reverse transcriptase inhibitor, is widely used as first-line therapy in chronic hepatitis B. Its role in HBV-ACLF is critical, as early viral suppression can potentially mitigate hepatic injury and improve clinical outcomes [4]. Several studies have shown that prompt initiation of antiviral therapy in HBV-ACLF patients is associated with improved survival. However, the inflammatory milieu and circulatory dysfunction seen in ACLF often limit the effectiveness of antivirals alone, leading researchers to explore adjunctive therapies [5].

One such adjunct is human albumin, a plasma protein with multifaceted roles in maintaining oncotic pressure, binding toxins, modulating immune responses and improving circulatory function [6, 7]. Albumin has been increasingly recognized not just as a volume expander but as a disease-modifying agent in decompensated liver disease [8]. The use of albumin infusion has shown promising results in conditions such as spontaneous bacterial peritonitis, hepatorenal syndrome and in the

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prevention of paracentesis-induced circulatory dysfunction. In ACLF, albumin may help attenuate systemic inflammation, stabilize hemodynamics and improve organ perfusion—factors crucial for recovery [9].
Despite its theoretical benefits, the evidence supporting routine use of albumin in HBV-ACLF remains limited and inconclusive [10]. Furthermore, there is a paucity of data from resource-constrained settings like Bangladesh, where the burden of HBV-related liver failure is high but access to advanced therapies like liver transplantation is restricted. In such settings, optimizing medical management—including cost-effective and evidence-based use of antivirals and adjunctive therapies—is of paramount importance [11].
This study was designed to compare the clinical outcomes of HBV-ACLF patients treated with tenofovir alone versus those treated with tenofovir in combination with albumin infusion. By analyzing survival rates and key liver function parameters over a 90-day follow-up period, we aim to evaluate the potential added benefit of albumin therapy in improving short-term prognosis. The findings may help guide treatment strategies in HBV-ACLF, particularly in settings with limited access to liver transplantation.

Methodology & Materials

This prospective comparative study was conducted at the Department of Hepatology, Kurmitola General Hospital, Dhaka, Bangladesh, from July 2022 to June 2024. A total of 32 patients aged over 18 years, of both sexes, diagnosed with hepatitis B virus-associated acute-on-chronic liver failure (HBV-ACLF) were enrolled. The diagnosis of ACLF was established based on clinical features, biochemical parameters such as elevated bilirubin and INR and virological confirmation of HBV infection. All patients had HBV as the cause of both chronic liver disease and the acute hepatic insult. Patients with co-infections (e.g., HCV, HDV, HIV), hepatocellular carcinoma, or significant extrahepatic comorbidities were excluded from the study.
Participants were randomized into two equal groups. One group (n=16) received oral tenofovir disoproxil fumarate 300 mg once daily without albumin infusion, while the other group (n=16) received tenofovir at the same dose along with intravenous human albumin infusion (20 grams daily for 7 days). Both groups received standard supportive care including nutritional support, fluid management and treatment for complications as per clinical need. Patients were followed for at least 3 months.
Clinical and biochemical parameters, including serum albumin, total bilirubin, INR, serum creatinine, MELD score and Child-Turcotte-Pugh (CTP) score, were assessed at baseline and on days 7, 14 and 90. HBV DNA levels were measured at baseline and at 90 days. The primary endpoint was survival at 90 days and secondary outcomes included improvement in liver function markers. Statistical analysis was performed using SPSS version 25.0 and a p-value < 0.05 was considered statistically significant.

Results

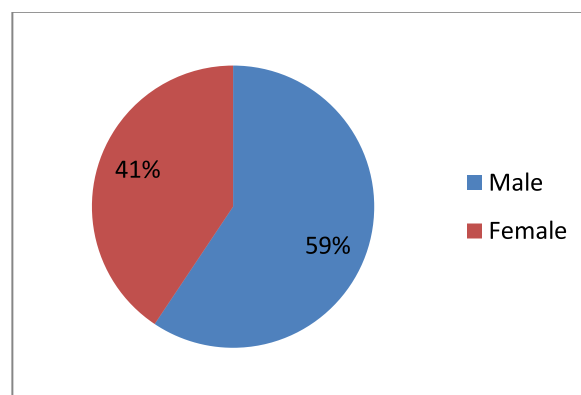

Figure 1: Gender Distribution of our Study Participants (N = 32)

Figure 1 illustrates the gender distribution of the study participants (N = 32). Out of the total patients enrolled, 19 (59%) were male and 13 (41%) were female.

Table 1: Mean Child-Turcotte-Pugh (CTP) Scores over Time

Time Point	Tenofovir with albumin	Tenofovir without albumin
Pretreatment	12.1	12
1st Follow-up (7 days)	10.4	11.9
2nd Follow-up (14 days)	9.6	11.3
3rd Follow-up (90 days)	5.8	9.3

Table 1 presents the mean CTP scores at different time points among HBV-ACLF patients treated with tenofovir alone and tenofovir in combination with albumin infusion. At baseline (pretreatment), the CTP scores were comparable between the two groups—12.1 in the tenofovir with albumin group and 12.0 in the tenofovir without albumin group. Over time, patients receiving albumin demonstrated a more pronounced improvement in liver function, as reflected by a greater reduction in CTP scores. By day 90, the mean CTP score in the albumin group had decreased to 5.8, compared to 9.3 in the non-albumin group, indicating a significant clinical

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improvement associated with adjunctive albumin therapy.

Table 2: Survival Outcomes

Group	Survived (n, %)	Died (n, %)	Total (n)
Tenofovir with albumin	13 (81.2%)	3 (18.8%)	16
Tenofovir without albumin	7 (43.7%)	9 (56.3%)	16

Table 2 compares the 90-day survival outcomes between the two treatment groups. In the group receiving tenofovir with albumin infusion, 13 out of 16 patients (81.2%) survived, while 3 patients (18.8%) died. In contrast, the tenofovir without albumin group had a lower survival rate, with only 7 patients (43.7%) surviving and 9 patients (56.3%) succumbing to the illness.

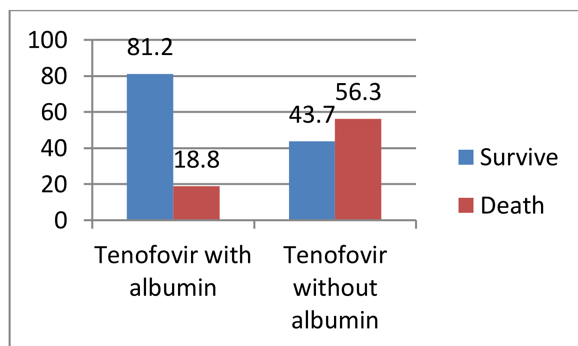

Figure 2: Clinical Outcomes by Treatment Group

Figure 2 illustrates the clinical outcomes at 90 days among HBV-ACLF patients treated with tenofovir alone versus tenofovir with albumin infusion. The survival rate was significantly higher in the group receiving albumin (81.2%) compared to the group without albumin (43.7%), while the mortality rate was lower (18.8% vs. 56.3%, respectively). The difference in survival between the two groups was statistically significant (p = 0.018), indicating a potential therapeutic benefit of albumin infusion in this population.

Table 3: Comparison of Mean Serum Albumin Levels between Tenofovir with albumin and Tenofovir without albumin

Time Point	Tenofovir with albumin (Mean ± SD, mg/dL)	Tenofovir without albumin (Mean ± SD, mg/dL)	P value
Pretreatment	2.2	2.3	0.612
1st Follow-up (7 days)	2.7	2.5	0.425
2nd Follow-up (14 days)	2.8	2.5	0.301
3rd Follow-up (90 days)	3.5	3	0.023

Table 3 presents the mean serum albumin levels (mg/dL) at baseline and during follow-up in HBV-ACLF patients treated with tenofovir with and without albumin infusion. At pretreatment, serum albumin levels were similar between the two groups (2.2 vs. 2.3 mg/dL; p = 0.612). Although no statistically significant differences were observed at day 7 (p = 0.425) or day 14 (p = 0.301), a significant increase in serum albumin was noted at day 90 in the group receiving albumin infusion (3.5 vs. 3.0 mg/dL; p = 0.023).

Table 4: Comparison of MELD Scores between Tenofovir with albumin and Tenofovir without albumin

Time Point	Tenofovir with albumin (Mean)	Tenofovir without albumin (Mean)
Pretreatment	25	26.5
1st Follow-up (7 days)	23.3	25.9
2nd Follow-up (14 days)	22.5	24.7
3rd Follow-up (90 days)	9.3	17

Table 4 summarizes the changes in Model for End-Stage Liver Disease (MELD) scores over time in patients treated with tenofovir with or without albumin infusion. At baseline, the MELD scores were comparable between the two groups (25 vs. 26.5). During follow-up, both groups showed gradual improvement; however, the reduction was more pronounced in the tenofovir with albumin group. By day 90, the mean MELD score had decreased to 9.3 in the albumin group, compared to 17 in the non-albumin group, indicating a greater improvement in liver function among patients receiving adjunctive albumin therapy.

Discussion

In this prospective comparative study, we evaluated the impact of albumin infusion in addition to tenofovir disoproxil fumarate (TDF) on clinical outcomes in patients with HBV-associated acute-on-chronic liver failure (HBV-ACLF). Our results demonstrated that the

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combination of tenofovir with albumin led to significantly better improvement in liver function parameters and survival outcomes compared to tenofovir alone. Specifically, 90-day survival was 81.2% in the albumin group compared to 43.7% in the non-albumin group ($p = 0.018$), accompanied by greater reductions in CTP and MELD scores and improved serum albumin levels.

The survival benefit observed in our albumin group is consistent with the established understanding of albumin's multifunctional role beyond plasma volume expansion. In decompensated cirrhosis and ACLF, albumin modulates systemic inflammation, stabilizes endothelial function and improves organ perfusion, which can contribute to better clinical outcomes [12]. Piano et al., reviewed multiple mechanisms by which albumin exerts these protective effects in ACLF, supporting our findings that adjunctive albumin therapy may have disease-modifying potential [12].

Our study's results are in line with several previous investigations on the efficacy of tenofovir in HBV-ACLF. Garg et al., showed that tenofovir significantly improves survival in patients with spontaneous HBV reactivation presenting as ACLF, highlighting the importance of early viral suppression [13]. Similar survival benefits have been reported in Bangladeshi cohorts treated with tenofovir, underscoring its role as a potent antiviral agent in HBV-ACLF management [14, 15].

In terms of liver function recovery, our findings demonstrated a more substantial reduction in both MELD and CTP scores in the albumin group over the 90-day period. Li et al. and Zhang et al., have similarly reported that patients treated with tenofovir-based regimens showed significant improvements in liver function markers, further validating tenofovir's hepatoprotective role in ACLF settings [16, 17].

The observed increase in serum albumin levels in the albumin group (from 2.2 to 3.5 mg/dL by day 90) is expected given the direct supplementation; however, the clinical significance lies in its association with improved prognosis. Caraceni and Bernardi have previously emphasized that higher serum albumin levels are linked with better outcomes in decompensated liver disease, reinforcing our conclusion that maintaining albumin levels may be a key therapeutic strategy [12].

Our study also contributes to the ongoing debate about optimal supportive strategies for HBV-ACLF in resource-limited settings like Bangladesh. With liver transplantation often unavailable, maximizing medical therapy is crucial. The study by Hossain et al., similarly emphasized the role of accessible antivirals like tenofovir and their impact on outcomes in such settings [15].

Although previous research has raised concerns about potential nephrotoxicity associated with tenofovir in ACLF patients, no acute kidney injury was observed in our cohort, consistent with findings by Zhang et al., who noted that the risk of nephrotoxicity may be mitigated by careful patient monitoring and co-management strategies [18].

Our findings are also supported by Liu et al., who proposed an advanced therapeutic framework for HBV-ACLF that includes antivirals, anti-inflammatory strategies and adjunctive therapies like albumin to address the multifactorial pathophysiology of the disease [19]. The integration of antiviral and supportive care, as implemented in our study, reflects this comprehensive management model.

The beneficial impact of albumin infusion observed in our study aligns with a growing body of evidence supporting its multifactorial role in decompensated liver disease. Beyond volume expansion, albumin exerts significant non-oncotic functions including anti-inflammatory, antioxidant, and endothelial-stabilizing properties, which are crucial in managing ACLF. Wong et al., emphasized that albumin improves immune modulation and detoxification in cirrhotic patients, helping counteract systemic inflammation and circulatory dysfunction [20]. Similarly, Lee highlighted that albumin infusion in end-stage liver disease improves renal function, reduces spontaneous bacterial peritonitis, and enhances survival—effects particularly relevant to HBV-ACLF [21]. These pleiotropic benefits may explain the improved MELD, CTP scores, and survival outcomes seen in our albumin group.

Historical and regional perspectives also support albumin's therapeutic value. Gines and Arroyo advocated for albumin in managing hepatorenal syndrome and ascites [22]. Henriksen and Schmidt & Ring-Larsen emphasized albumin's clinical utility in decompensated liver disease despite economic concerns [23, 24]. Rena and Wibawa further demonstrated improved circulatory and biochemical profiles following albumin infusion. These findings collectively support our results [25].

Limitations of the study

Despite the promising results, our study has limitations. The sample size was relatively small and the follow-up period was limited to 90 days. Additionally, although our

findings showed statistical significance, larger multicenter studies are needed to confirm the long-term efficacy and safety of albumin infusion in this patient population. Cost-effectiveness and risk-benefit analysis of routine albumin use should also be considered in future research.

Conclusion

In conclusion, this study provides evidence that the addition of albumin infusion to tenofovir therapy significantly improves survival and liver function in patients with HBV-ACLF. These findings support the role of albumin as a beneficial adjunct in the management of HBV-ACLF and underscore the need for further large-scale trials to establish optimized treatment protocols.

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Conflicts of interest

There are no conflicts of interest.

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