

LETTER TO THE EDITOR

Albumin in hepatic encephalopathy: Evidence, prioritization, and the affordability gap in decompensated cirrhosis

✉ Mohammad Saquib Alam¹, ✉ Nagma Khatoon²

1: Department of Medicine, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India

2: Department of Obstetrics and Gynecology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India

To the Editor,

We read with great interest the systematic review and meta-analysis by Covre Coan et al.^[1] evaluating intravenous albumin in patients with hepatic encephalopathy (HE). The authors included four randomized controlled trials involving 306 patients and reported that albumin was associated with improved HE recovery and reduced mortality, without a significant increase in adverse events.^[1] Importantly, their trial sequential analysis showed that although the mortality signal crossed the boundary for benefit, the required information size was not reached, indicating that the evidence remains promising rather than definitive.^[1]

This review contributes to a growing shift in how albumin is conceptualized in decompensated cirrhosis. Traditionally, albumin has been used primarily as a plasma expander, particularly after large-volume paracentesis, in spontaneous bacterial peritonitis (SBP), and in hepatorenal syndrome-acute kidney injury (HRS-AKI). However, contemporary data emphasize that albumin also has antioxidant, scavenging, endothelial-stabilizing, and immunomodulatory properties.^[2,3] These non-oncotic effects are biologically relevant in HE, where ammonia toxicity, systemic inflammation, oxidative stress, endothelial dysfunction, and circulatory impairment may interact to produce neurocognitive deterioration.^[1,4]

Nevertheless, the clinical question is no longer simply whether albumin can help in HE. A more difficult bedside question is how HE should be prioritized among competing albumin indications in patients with decompensated cirrhosis. Many such patients present simultaneously with tense ascites, spontaneous bacterial peritonitis, renal dysfunction, hyponatremia, and HE. In well-resourced systems, practice recommendations may be interpreted as additive. In resource-limited settings, however, albumin availability and affordability often force clinicians to prioritize.

Current practice guidance supports albumin for large-volume paracentesis, SBP, and AKI/HRS-related scenarios, while discouraging its routine use in uncomplicated ascites.^[3] The AGA update also emphasizes careful assessment of volume status, especially during HRS-AKI therapy, because excessive albumin may contribute to pulmonary edema or respiratory complications.^[3] Similarly, broader reviews conclude that albumin has established roles in large-volume paracentesis, SBP, AKI, and HRS, while its use in HE, long-term ascites management, hyponatremia, extraperitoneal infections, and acute-on-chronic liver failure remains an area of ongoing evaluation.^[4]

In this context, the findings of Covre Coan et al.^[1] should be interpreted as a call for better stratification rather than immediate universalization. Albumin use for HE may be most defensible when HE occurs alongside other albumin-supported indications, such as SBP, AKI/HRS, marked circulatory dysfunction, or severe systemic inflammation. By contrast, isolated HE without renal dysfunction, infection, or other established indications may require more cautious use until larger, adequately powered trials confirm its benefit and identify the patients most likely to respond.

Future trials of albumin in HE should therefore move beyond binary efficacy endpoints. They should incorporate HE severity, the presence of AKI or infection, baseline serum albumin levels, inflammatory markers, volume status, the total albumin dose received, adverse pulmonary events, length of hospitalization, readmissions, and cost-effectiveness. In low- and middle-income settings, patient-level affordability and drug availability should also be assessed. A treatment that is cost-effective at the health-system level may still be unaffordable at the bedside when patients pay out of pocket.

Covre Coan et al.^[1] have provided a timely synthesis supporting the use of albumin as a promising adjunct in HE. We agree that albumin

How to cite this article: Alam MS, Khatoon N. Albumin in hepatic encephalopathy: Evidence, prioritization, and the affordability gap in decompensated cirrhosis. *Hepatology Forum* 2026; 7(3):306–307.

Received: June 02, 2026; **Accepted:** July 05, 2026; **Available Online:** July 23, 2026

Corresponding author: Mohammad Saquib Alam; Department of Medicine, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India; **E-mail:** msalam109@myamu.ac.in



This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

deserves further investigation in this setting. However, its expanding indications in cirrhosis make prioritization increasingly important. The future of albumin therapy should define not only where it works but also where it is most necessary, safest, and most feasible to deliver.

Conflict of Interest: The authors declare no conflict of interest.

Financial Disclosure: No funding was received for this work.

Use of Artificial Intelligence: During the preparation of this manuscript, the authors used OpenAI's ChatGPT for language editing and structural refinement. The authors reviewed and approved the final content.

Author Contributions: Concept – MSA, NK; Design – MSA; Writing – MSA, NK; Critical Review – MSA, NK.

Peer-review: Externally peer-reviewed.

References

1. Covre Coan AC, do Livramento Junior VA, Prata AA, Milioli NJ, Correa TL, Martins OC, et al. Use of albumin in patients with hepatic encephalopathy: A systematic review and meta-analysis of randomized controlled studies with trial sequential analysis. *Hepatol Forum* 2026;7(1):4-13. [\[CrossRef\]](#)
2. Bernardi M, Angeli P, Claria J, Moreau R, Gines P, Jalan R, et al. Albumin in decompensated cirrhosis: new concepts and perspectives. *Gut* 2020;69(6):1127-1138. [\[CrossRef\]](#)
3. Garcia-Tsao G, Abraldes JG, Rich NE, Wong VW. AGA clinical practice update on the use of vasoactive drugs and intravenous albumin in cirrhosis: Expert review. *Gastroenterology* 2024;166(1):202-210. [\[CrossRef\]](#)
4. de Mattos ÂZ, Simonetto DA, Terra C, Farias AQ, Bittencourt PL, Pase THS, et al. Albumin administration in patients with cirrhosis: Current role and novel perspectives. *World J Gastroenterol* 2022;28(33):4773-4786. [\[CrossRef\]](#)