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REPLY TO THE LETTER TO THE EDITOR

Reply to the Letter to the Editor: "Albumin in hepatic encephalopathy: Evidence, prioritization, and the affordability gap in decompensated cirrhosis"

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To the Editor,

We thank the authors of the letter entitled "Albumin in Hepatic Encephalopathy: Evidence, Prioritization, and the Affordability Gap in Decompensated Cirrhosis" for their interest in our recent systematic review and meta-analysis and for their thoughtful comments.

We agree that the role of albumin in cirrhosis has evolved substantially beyond its traditional use as a plasma expander. As emphasized in our review, the rationale for albumin administration in hepatic encephalopathy (HE) is not limited to ammonia metabolism but also includes its antioxidant, immunomodulatory, and endothelial-stabilizing properties, which may influence several pathways involved in the pathogenesis of HE.[1,2]

The authors appropriately emphasize the challenge of prioritizing albumin use in patients with decompensated cirrhosis, who frequently present with multiple concurrent complications. We agree that, in real-world practice, particularly in resource-limited settings, clinicians may face difficult decisions regarding albumin allocation. However, it is important to note that our study was designed to evaluate the efficacy and safety of albumin in patients with HE rather than to compare or rank albumin-supported indications. Therefore, questions regarding prioritization among competing clinical scenarios remain beyond the scope of the available randomized evidence included in our analysis.

We also concur that the findings should not be interpreted as definitive evidence supporting universal albumin administration for all patients with HE. As discussed in our manuscript, the trial sequential analysis demonstrated that although the mortality benefit crossed the boundary for statistical significance, the required information size was not reached, indicating that additional adequately powered randomized trials are necessary before definitive conclusions can be established.[3]

Furthermore, we agree that future investigations should focus on identifying the patient populations most likely to benefit from albumin therapy. Factors such as HE severity, baseline serum albumin concentration, systemic inflammation, renal dysfunction, infection status, and concomitant cirrhosis-related complications may all influence treatment response. Similarly, the incorporation of clinically relevant outcomes, such as hospitalization, readmission rates, adverse pulmonary events, and cost-effectiveness analyses, would provide valuable information for clinical decision-making.[3]

Finally, we appreciate the authors' emphasis on affordability and accessibility. These considerations are particularly relevant in low- and middle-income countries and deserve greater attention in future clinical trials and health policy discussions.

We thank the authors for their insightful comments and welcome further research aimed at refining the role of albumin therapy in hepatic encephalopathy and identifying the clinical settings in which its use provides the greatest benefit.

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