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Letter to Editor

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Fluid-sparing hyperoncotic albumin in severe dengue: A retrospective case series

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The global incidence of dengue continues to escalate, posing a significant public health burden, particularly in Southeast Asia[1]. While the majority of patients recover, a subset progresses to dengue shock syndrome (DSS), characterized by profound vascular permeability, hemoconcentration, and hypovolemic shock. The cornerstone of DSS management is timely fluid resuscitation to maintain effective intravascular volume. Current international and national guidelines, including those from the World Health Organization and the Ministry of Health of Vietnam, recommend a stepwise approach starting with crystalloids, followed by synthetic colloids like Hydroxyethyl Starch (HES) for refractory shock[2,3]. In this conventional algorithm, human albumin is typically reserved as rescue therapy for cases resistant to synthetic colloids or complicated by severe hepatic dysfunction[3].

However, aggressive fluid resuscitation is a double-edged sword. Accumulating evidence suggests that fluid overload is strongly associated with respiratory failure, prolonged intensive care unit (ICU) stays, and increased mortality in severe dengue[4,5]. Synthetic colloids, while effective for volume expansion, have dose-limiting toxicities and may exacerbate cumulative fluid positivity[4,5]. Furthermore, hypoalbuminemia has been identified as an independent predictor of dengue severity and shock[1,6]. In patients with severe plasma leakage, rapid albumin depletion further depletes oncotic pressure, creating a vicious cycle of extravasation that isotonic fluids may fail to reverse efficiently[7]. Hyperoncotic albumin (20%-25%), with its superior ability to restore oncotic pressure and recruit interstitial fluid, offers a theoretical advantage for fluid-sparing resuscitation[8].

Despite this, clinical data comparing early albumin monotherapy versus the standard stepwise HES-to-albumin protocol remains scarce[7,9]. To address this gap, we conducted a retrospective analysis of clinical data from patients with DSS treated at our center. Specifically, we aimed to characterize a distinct phenotype of patients presenting with severe hemoconcentration and hypoalbuminemia, and to evaluate whether early administration of 20%-25% hyperoncotic albumin provides a fluid-sparing benefit and accelerates shock reversal.

A retrospective case series study was conducted at our intensive care unit (ICU) in Vietnam. The study population comprised consecutive adult patients (≥18 years old) admitted with a diagnosis of DSS between January 2022 and December 2025. Patients were included if they met the Ministry of Health criteria for DSS, were confirmed by dengue NS1 antigen or IgM rapid tests, and presented with concurrent hypoalbuminemia (serum albumin <35 g/L)[3]. Shock was defined as severe plasma leakage with hemodynamic instability (narrow pulse pressure ≤20 mmHg, systolic blood pressure <90 mmHg, or clinical hypoperfusion). Patients with an undocumented time of shock onset were excluded.

Electronic medical records were screened using ICD-10 codes, and two independent researchers confirmed eligibility. Data encompassing baseline demographics, hemodynamic parameters, laboratory findings, and resuscitation details were extracted. Patients were categorized according to three resuscitation strategies: (1) crystalloid-only; (2) early adjunct albumin (crystalloids+20%-25% albumin); and (3) rescue albumin (crystalloids+6% HES+20%-

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Table 1. Baseline characteristics, fluid resuscitation strategies, and clinical outcomes in patients with dengue shock

Characteristics	Total cohort (*n*=9)	Crystalloid-only (*n*=3)	Crystalloids+Albumin (*n*=2)	Crystalloids+HES+Albumin (*n*=4)
Demographics				
Age, median (IQR), years	33.0 (24.0-42.5)	33.0 (25.5-38.5)	44.5 (37.0-52.0)	29.5 (24.0-36.0)
Sex: Female, *n* (%)	7 (77.8%)	3 (100.0%)	1 (50.0%)	3 (75.0%)
BMI, kg/m^2	22.7 (21.3-23.7)	22.8 (21.8-23.1)	25.5 (21.8-29.1)	22.4 (19.4-23.3)
Day of illness at shock	5 (5-6)	5 (5-6)	5.5 (5-6)	5 (5-5.5)
Clinical & Laboratory				
Heart rate, beats/min	90 (79-103)	94 (90-110)	91 (72-110)	88 (78-93)
Systolic blood pressure, mmHg	100 (87.5-110)	90 (85-110)	90 (70-110)	100 (95-105)
Pulse pressure, mmHg	20 (20-30)	30 (25-32.5)	25 (20-30)	20 (17.5-22.5)
Hematocrit, %	48.9 (39.2-52.6)	45.0 (41.9-49.3)	43.6 (38.2-48.9)	50.8 (44.9-57.5)
Platelet count, 10^9/L	29 (14.5-40)	32 (30.5-34.5)	9.5 (9-10)	31.5 (19.5-52)
Serum albumin, g/L	26 (24.5-30)	32 (29.5-33)	25.5 (25-26)	24.5 (23-26.5)
Peak AST, U/L	524 (116.5-1 742)	625 (453.5-1 663.5)	4 111 (524-7 698)	116.5 (100.5-452.5)
Outcomes				
Shock reversal time, hours	7.0 (5.8-15.8)	6.1 (5.7-6.4)	6.3 (5.6-7.0)	15.8 (10.2-19.4)
Total 24-hour fluid volume, mL/kg	116.9 (100.7-157.8)	116.9 (105.4-120.4)	109.2 (107.5-110.9)	157.8 (112.6-172.3)
24-hour fluid balance, mL/kg	65.3 (52.6-90.3)	61.0 (59.2-66.5)	31.9 (-1.5-65.3)	87.0 (56.7-120.6)
ICU length of stay, hours	46.2 (37.0-52.4)	44.3 (40.2-45.2)	41.6 (35.5-47.8)	52.4 (42.9-58.6)
Hospital length of stay, days	6.5 (5.7-7.5)	5.6 (5.6-6.8)	9.3 (6.0-12.6)	6.6 (6.1-6.9)
Survival rate, *n* (%)	9 (100.0%)	3 (100.0%)	2 (100.0%)	4 (100.0%)
Mechanical ventilation, *n* (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

BMI: Body mass index; AST: Aspartate aminotransferase; ICU: Intensive care unit.

25% albumin). Administration of 6% HES 130/0.4 was strictly in accordance with national guidelines for refractory DSS[3].

Shock reversal time was defined as the duration (in hours) from the initiation of active resuscitation to sustained hemodynamic stability (systolic blood pressure 90 mmHg, MAP ⩾65 mmHg, pulse pressure >20 mmHg, HR <110 bpm) for at least 6 hours, alongside the cessation of active resuscitation. Total 24-hour fluid volume included all intake within the first 24 hours of shock onset, standardized to adjusted body weight (mL/kg) to prevent iatrogenic fluid overload[3]. Data analysis was performed using Python version 3.14. Due to the small sample size (*n*=9), descriptive statistics [medians with interquartile ranges (IQR) and frequencies] were utilized without formal inferential testing.

During the 4-year study period from January 2022 to December 2025, a total of 9 patients with DSS meeting the inclusion criteria were analyzed. The baseline characteristics of the study cohort are summarized in Table 1. The median age was 33 years, with a predominance of females. At the onset of shock, patients presented with marked hemoconcentration (median HCT: 48.9%) and hypoalbuminemia (median serum albumin: 26 g/L).

Observationally, when comparing the combined albumin-treated patients (*n*=6) to those resuscitated with crystalloids only (*n*=3), patients requiring albumin presented with a lower median baseline serum albumin concentration (25 *vs*. 32 g/L) (Figure 1A). Other baseline clinical parameters, such as age, BMI, and initial HCT levels, appeared broadly comparable between the two groups.

Interestingly, although patients in the crystalloid-plus-albumin group had the shortest median ICU length of stay (41.6 hours), they had the longest median total hospital stay (9.3 days). This discrepancy was primarily driven by an outlier in this group who developed severe dengue hepatitis with markedly elevated liver enzymes (peak AST: 7 698 U/L; peak ALT: 1 323 U/L), necessitating prolonged ward observation. Additionally, this was the only patient in our cohort who developed mild respiratory compromise (SpO_2 dropping to 92% on room air), which was adequately managed with 2 L/min of supplemental oxygen *via* nasal cannula. Notably, lung auscultation revealed no crackles, indicating the absence of overt alveolar pulmonary edema.

Regarding safety and overall prognosis, the survival rate for the entire study cohort was 100% (9/9 patients). Despite the aforementioned case of transient hypoxemia, no patients progressed to severe respiratory failure necessitating mechanical ventilation, and no allergic or anaphylactic reactions were recorded across all three groups.

Clinical outcomes across the three fluid resuscitation strategies are detailed in Table 1 and Figure 1B. Observationally, descriptive trends in the primary outcome (shock reversal time) varied across the groups. Notably, patients who required albumin as rescue therapy following initial resuscitation with crystalloids and HES experienced the longest median shock reversal time (15.8 hours). Regarding the secondary outcome (total 24-hour fluid volume), we observed a similar clinical trend toward higher median fluid requirements in this rescue albumin group compared to the crystalloid-only and crystalloid-plus-albumin groups.

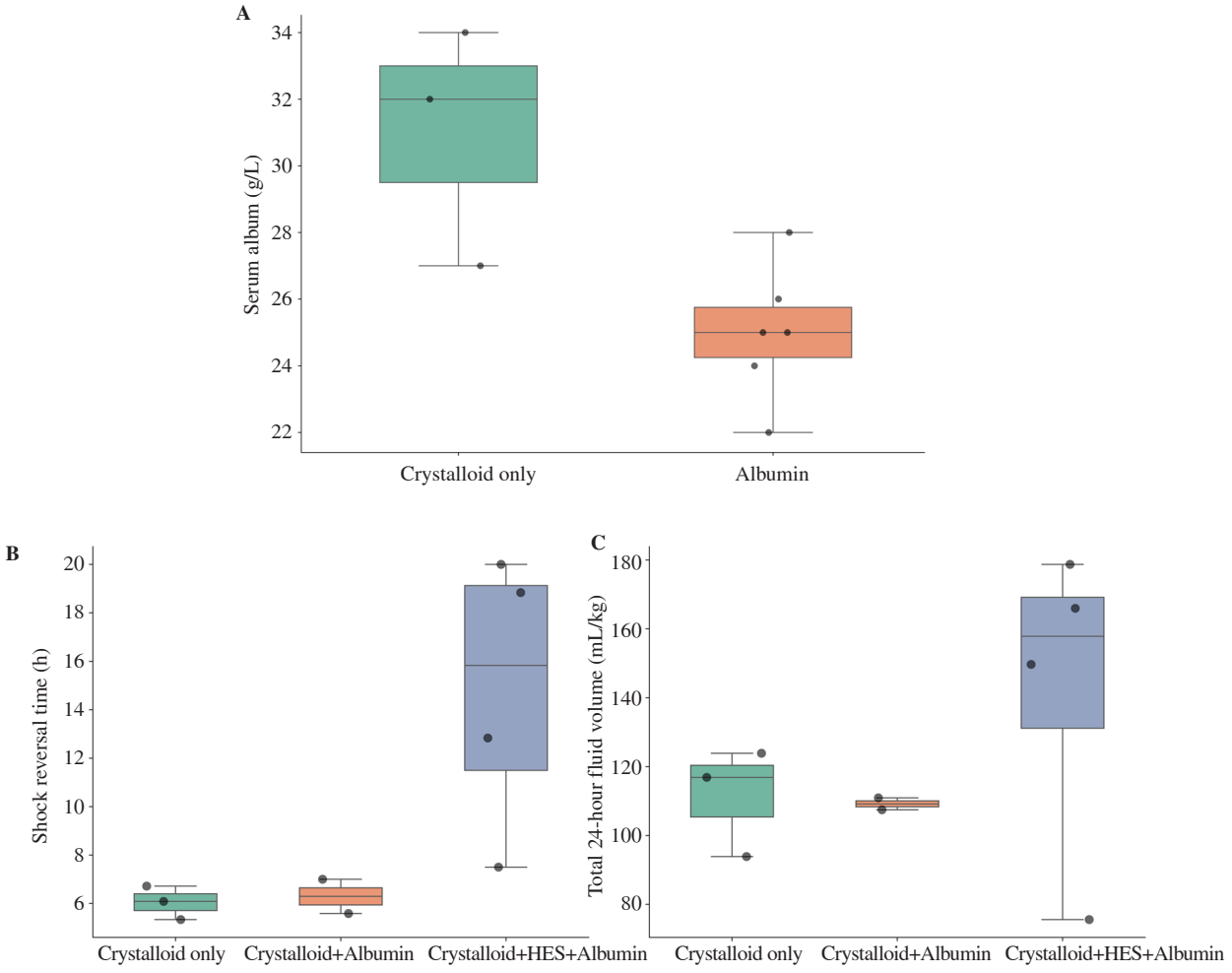

Figure 1. Baseline serum albumin levels and clinical outcomes across fluid resuscitation strategies. (A) Baseline serum albumin levels in the crystalloid-only and albumin-treated groups. (B) Shock reversal time (primary outcome) across the three fluid resuscitation strategies. (C) Total 24-hour fluid volume (secondary outcome) across the three fluid resuscitation strategies. Data are presented as box plots with overlaid individual data points. The horizontal line within each box represents the median, and the box spans the interquartile range (IQR).

Interestingly, the individual data points in Figure 1C reveal that the patient with the absolute lowest 24-hour total fluid volume (75.55 mL/kg) actually belonged to the rescue albumin group.

For the six patients who received 20%-25% hyperoncotic albumin, the median total administered dose within the first 24 hours was 0.41 g/kg (IQR: 0.40-0.45 g/kg), ranging from 0.35 to 0.83 g/kg depending on individual hemodynamic responses, and infused over 3 to 6 hours.

Our analysis of severe DSS complicated by hypoalbuminemia yielded three pivotal clinical findings. First, albumin replacement was clinically targeted toward patients with significantly more profound baseline hypoalbuminemia, reflecting deliberate real-world prioritization. The female predominance (77.8%) observed aligns with recent systematic reviews identifying female sex as a significant predictor for progression to severe dengue[6].

Second, the integration of 20%-25% hyperoncotic albumin—either as an early adjunct or as rescue therapy—was associated with the restoration and maintenance of hemodynamic stability. Patients receiving early adjunct albumin achieved rapid shock reversal (6.3 hours), consistent with recent clinical trials demonstrating that early albumin supplementation expedites stabilization and restores endothelial integrity[7,9]. By rapidly restoring intravascular oncotic pressure, hyperoncotic albumin effectively counteracts vascular leakage. Conversely, the prolonged shock reversal time in the rescue albumin group (15.8 hours) reflects the profound intrinsic severity of refractory shock, as these patients had reached the therapeutic ceiling for synthetic colloids. Sustained stability was ultimately achieved only after the introduction of hyperoncotic albumin, highlighting its critical role as a rescue intervention.

Third, our clinical observations strongly support the fluid-sparing

hypothesis in severe DSS. While crystalloids transiently expand the intravascular space before leaking into the interstitium, hyperoncotic albumin exerts a potent colloid osmotic pressure that actively draws interstitial fluid back into the circulation[8]. This mechanism is corroborated by Kaur *et al*., who demonstrated that early 25% albumin in refractory severe dengue significantly reduces cumulative fluid overload[7]. Clinically, a modest median albumin dose (0.41 g/kg) was sufficient to restore effective circulating volume and break the cycle of continuous synthetic fluid administration. Notably, one refractory patient demonstrated an abrupt cessation of fluid requirements post-albumin, ultimately recording the lowest 24-hour fluid volume (75.55 mL/kg) in the entire study.

The clinical imperative of this fluid-sparing capability cannot be overstated. Excessive cumulative fluid infusion and a high synthetic colloid-to-crystalloid ratio are established independent predictors of severe respiratory failure necessitating mechanical ventilation[4,5]. By curbing the need for repeated crystalloid boluses and optimizing the 24-hour net fluid balance, targeted albumin administration effectively protects patients from massive third-space accumulation and iatrogenic overload. While early albumin administration expedited ICU discharge, total hospital stay was occasionally prolonged by intrinsic viral organ involvement, such as acute hepatic impairment, rather than by hemodynamic failure alone.

Coupled with a 100% survival rate and the absence of anaphylactoid reactions or iatrogenic pulmonary edema, our data suggest a favorable safety profile. Given the frequent global shortages of preferred synthetic colloids and the well-documented nephrotoxic risks of 6% HES 130/0.4, the early administration of 20%-25% hyperoncotic albumin represents a potentially safer and more physiologically rational alternative.

We acknowledge several limitations, primarily the retrospective, single-center design and the small sample size (n=9), which preclude formal inferential statistics. Consequently, these findings should be interpreted cautiously as descriptive and hypothesis-generating observations. Nevertheless, the meticulous documentation of clinical trajectories and strict adherence to standardized protocols provide valuable real-world insights.

In conclusion, our pilot study suggests that 20%-25% hyperoncotic albumin is a feasible, safe, and potentially beneficial intervention for severe DSS complicated by hypoalbuminemia. Whether utilized as an early adjunct or a rescue therapy, targeted albumin administration effectively restored circulating volume. Furthermore, its distinct fluid-sparing properties help optimize net fluid balance and mitigate the life-threatening risks of fluid overload. These preliminary findings strongly advocate for future large-scale, randomized controlled trials to systematically validate its efficacy and standardize treatment protocols in severe dengue management.

Conflict of interest statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical approval and institutional review board approval

The study protocol was reviewed and approved by the Institutional Review Board (Ethics Committee) of Xuyen A General Hospital (Approval Number: 15/2026/QD-BVXA, dated February 2, 2026). The study was conducted in accordance with the Declaration of Helsinki.

Consent to participate

Patient consent was waived by the Institutional Review Board due to the retrospective, observational nature of this study. All patient data were fully anonymized and de-identified prior to analysis to ensure strict confidentiality.

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Data availability statement

The datasets generated and analyzed during the current study are not publicly available to protect patient confidentiality but are available from the corresponding author on reasonable request.

Declaration of generative AI and AI–assisted technologies in the writing process

During the preparation of this work, the author used Google Gemini to translate parts of the initial draft from Vietnamese to English and to polish the academic language to meet publication standards. After using this tool/service, the author thoroughly reviewed and edited the content as needed and takes full responsibility for the accuracy, integrity, and originality of the final publication.

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Author contributions' statement

QL: Conceptualization, methodology, data curation, formal analysis, writing-original draft, writing-review & editing. HT: Data curation, validation, writing-review & editing. NV: Investigation, resources, validation.

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