doi.org/10.36721/PJPS.2026.39.11.324.1

Low-dose glucocorticoids combined with continuous blood purification in sepsis: A comparison of inflammatory factors and T lymphocyte subsets

Jianchao Li[1] and Chunhui Song[2]*

[1]Department of Emergency, Yancheng No.1 People's Hospital, Yancheng, Jiangsu, 224000, China
[2]Department of Emergency, The Affiliated Jiangning Hospitial of Nanjing Medical University, Nanjing, Jiangsu, 211100, China.

Abstract: **Background**: Sepsis is an infection-induced systemic inflammatory response syndrome with poor prognosis mainly attributed to excessive inflammation and immune dysfunction. Continuous blood purification (CBP) is a core treatment and low-dose glucocorticoids exert anti-inflammatory and immunoregulatory effects. However, whether low-dose glucocorticoids combined with early CBP is associated with more favorable inflammatory, immune and short-term clinical outcomes than CBP alone remains unclear. **Objectives**: To evaluate the association of low-dose hydrocortisone combined with early CBP, compared with CBP alone, with inflammatory factors, T lymphocyte subsets and short-term prognosis in sepsis patients. **Methods**: A total of 120 sepsis patients were included in a retrospective 1:1 matched cohort analysis, including 60 patients in the CBP-alone cohort and 60 patients in the LD-GCs + CBP cohort, as identified from routinely recorded clinical data. Inflammatory factors, T lymphocyte subsets, HLA-DR, HPA axis function and clinical outcomes were evaluated. **Results**: The LD-GCs + CBP group showed lower 28-day mortality, shorter ICU stay and lower septic shock incidence than the CBP-alone group ($P<0.05$). Proinflammatory factors were lower, anti-inflammatory IL-10 higher and immune function better preserved ($P<0.05$). After treatment, CD3+, the CD4+/CD8+ ratio and HLA-DR were significantly higher in the LD-GCs + CBP group than in the CBP-alone group ($P<0.05$), whereas sCD163 was significantly lower ($P<0.05$). **Conclusion**: Low-dose hydrocortisone combined with early CBP was associated with attenuated inflammatory responses, more favorable immune marker changes and improved short-term outcomes in this cohort, with manageable adverse events. These findings require confirmation in larger multicenter studies.

Keywords: Continuous blood purification; Inflammatory factors; Low-dose glucocorticoids; Sepsis; T lymphocyte subsets

Submitted on 25-12-2025 – Revised on 08-02-2026 – Accepted on 25-03-2026

INTRODUCTION

Sepsis is an infection-induced systemic inflammatory response syndrome, which is a major challenge in the field of critical care medicine worldwide. Its high mortality is closely related to uncontrolled inflammatory storm leading to multiple organ dysfunction and the dynamic imbalance of immune activation and immunosuppression is the core pathological and physiological characteristic of its progression (Chiu & Legrand, 2021; Njoki *et al.*, 2026). Current clinical treatments are mainly based on anti-infection, fluid resuscitation and organ support, but the precise regulation of inflammatory response is still the key bottleneck to improve the prognosis of sepsis patients (Srzic *et al.*, 2022). In recent years, low-dose glucocorticoids (LD-GCs) (e.g., hydrocortisone) have attracted extensive attention due to their anti-inflammatory and lysosomal membrane-stabilizing effects (Fujii *et al.*, 2022) and early continuous blood purification can alleviate organ damage by removing circulating inflammatory mediators (Wang *et al.*, 2021). They can inhibit the excessive release of proinflammatory factors and reduce the immune suppression caused by excessive inflammatory response. However, existing studies have mostly evaluated CBP or LD-GCs as monotherapy (Guo *et al.*, 2024; Fan *et al.*, 2024), and direct clinical comparisons of LD-GCs combined with early CBP versus CBP alone remain limited. Although adjunctive glucocorticoid therapy has been reported to improve outcomes in septic shock patients (Fujii *et al*., 2022), the optimal dosing regimen and its clinical value when combined with organ support therapies, including CBP, remain controversial.

Inflammatory factors and T lymphocyte subsets are core biomarkers for evaluating the inflammatory-immune balance in sepsis, which is the core pathophysiological driver of disease progression. Unlike previous studies that focused solely on clinical prognosis or a single treatment modality, we examined whether receipt of LD-GCs combined with early CBP was associated with lower inflammatory-marker levels, less pronounced T lymphocyte subset imbalance and more favorable short-term prognosis in sepsis patients compared with CBP alone. Accordingly, this retrospective 1:1 matched cohort analysis was conducted to compare these two treatment regimens and to provide real-world evidence for optimizing treatment strategies in patients with sepsis.

**Corresponding author:* e-mail: sch202512@163.com

MATERIALS AND METHODS

Cohort selection and matching

As this was a retrospective cohort analysis, no a priori sample-size calculation was performed. Consecutive eligible patients treated between May 2023 and May 2025 were screened from the institutional electronic medical record system, and patients receiving low-dose hydrocortisone plus CBP were matched 1:1 with patients receiving CBP alone. After matching, 60 patients were included in each group, resulting in a final analytic cohort of 120 patients.

Research participants

This was a single-center, retrospective, 1:1 matched cohort analysis conducted at the Emergency Department of the participating hospitals from May 2023 to May 2025. The study was approved by the Institutional Ethics Committee of Yancheng No.1 People's Hospital (No. 2023-014), and the requirement for written informed consent was waived because anonymized retrospective clinical data were used. Eligibility criteria were strictly defined: Inclusion criteria: (1) Aged 20-70 years old; (2) Confirmed diagnosis of sepsis in line with the Sepsis-3 diagnostic criteria (documented infection evidence + SOFA score ≥2) (Ackerman *et al.*, 2021); (3) Time from symptom onset to admission ≤24h and meeting the clinical indications for CBP treatment (AKI stage 2-3 according to KDIGO criteria, or refractory high volume load combined with severe electrolyte disorders unresponsive to 6h conservative treatment); (4) Complete baseline, treatment, laboratory and 28-day outcome data were available in the medical records. *Exclusion criteria*: (1) Severe primary immunosuppressive diseases (e.g., AIDS, systemic lupus erythematosus) or long-term use of immunosuppressants; (2) Pregnant or lactating women; (3) Terminal malignant tumors or other terminal illnesses with expected survival <28 days; (4) Active gastrointestinal or intracranial bleeding, or confirmed hypersensitivity to hydrocortisone or CBP consumables; (5) Had received CBP treatment for more than 24 h before cohort entry; (6) Severe liver failure (Child-Pugh grade C).

Cohort grouping and treatment exposure

Patients were grouped according to the treatment actually received during the index hospitalization. The CBP-alone group received early CBP plus standard treatment, whereas the LD-GCs + CBP group received low-dose hydrocortisone in addition to early CBP and standard treatment. Outcome adjudicators were not involved in treatment decisions and assessed clinical endpoints using predefined objective clinical and laboratory criteria.

Peripheral blood sampling was standardized relative to CBP filter and adsorption column changes: pre-CBP sampling was performed 30 min before CBP initiation (no filter/column replacement within 2 h prior to sampling); post-CBP sampling was completed 1 h before scheduled filter/column replacement (filter replaced every 72 h, adsorption column replaced every 24 h in this study). Online pressure monitoring was performed for the adsorption column and sampling was suspended if column pressure exceeded 300 mmHg to avoid interference from column saturation on test results. Both groups were administered broad-spectrum antibiotics (carbapenems + antimicrobial drugs for Gram-positive infections) within 1 hour after admission, with the therapy adjusted according to etiology within 48 hours. The goal of fluid resuscitation was to maintain CVP at 8-12 mmHg and $ScvO_2$ at ≥70%, with crystalloid fluids (normal saline/balanced solution) being the preferred choice. Additionally, norepinephrine was administered to maintain MAP ≥65 mmHg and vasopressin was added when indicated. On this basis, CBP was initiated within 24 hours after cohort entry, using the continuous venovenous hemodiafiltration (CVVHDF) mode (blood flow rate: 150-200 ml/min, replacement fluid: 2 L/h, dialysate: 1 L/h). The ultrafiltration rate was adjusted according to the volume status (target negative fluid balance ≤50 ml/h). Local anticoagulation with citrate was preferred (to maintain blood calcium at 1.0-1.2 mmol/L) and unfractionated heparin (to maintain APTT at 45-60 s) was used for patients with a high risk of bleeding. On this basis, patients in the LD-GCs + CBP group had additionally received intravenous hydrocortisone (HYD) 200 mg/day (50 mg every 6 h, 4 divided doses) for 7 days, followed by a 50 mg dose reduction every 2 days from day 8, with a maximum total treatment duration of 10 days. Identical CBP consumables were used for all patients in both cohorts to ensure consistency of CBP delivery: AN69ST hemofilter (Fresenius Medical Care, Germany) and polymyxin B-immobilized fiber adsorption column (Toray Medical, Japan). To quantify HYD exposure variability during tapering, plasma HYD concentrations were measured by HPLC-MS/MS at trough (30 min before dosing) and peak (1 h after dosing) at each dose adjustment. A one-compartment first-order elimination pharmacokinetic model was used to fit concentration-time curves and the coefficient of variation (CV) of AUC0-24h was calculated to assess exposure variability (CV<30% was predefined as clinically acceptable). CBP was discontinued according to predefined standardized criteria: (1) hemodynamic stability for ≥48 h, with MAP ≥70 mmHg without vasopressors; (2) recovered renal function (urine output ≥0.5 mL·kg/h for ≥24 h, serum creatinine reduced by ≥50% from baseline); (3) corrected and stable severe electrolyte/acid-base disorders; (4) occurrence of uncontrollable severe CBP-related complications.

To reduce selection bias in this retrospective cohort, propensity scores were estimated using baseline variables

available before treatment exposure, including age, sex, smoking status, drinking history, family history of disease, source of infection, baseline SOFA score and lactate level. Patients in the LD-GCs + CBP group were matched 1:1 with patients in the CBP-alone group using nearest-neighbor matching without replacement, and covariate balance after matching was assessed before outcome comparison.

Sample collection and testing

The time points for peripheral blood collection (0 h, 6 h, 24 h, 48 h, 72 h and 7 d) were selected from routinely recorded institutional monitoring time points because they corresponded to the acute pro-inflammatory phase (6 – 24 h) and compensatory anti-inflammatory phase (24 – 48 h) of sepsis immunopathology. For each time point, 3mL of peripheral venous blood was collected and centrifuged at 3000 r/min for 15 min at 4℃ to separate plasma, which was stored at -80℃ for batch detection. Plasma levels of IL-6, TNF-α, IL-10 and IL-1β were detected by enzyme-linked immunosorbent assay (ELISA) using commercial kits (R&D Systems, USA), with the intra-assay coefficient of variation (CV) <5% and inter-assay CV <8% and all operations were performed in strict accordance with the kit instructions. The following parameters were calculated using clinically commonly used simplified formulas and endogenous cytokine production, rebound phenomena and non-steady-state conditions were corrected by data screening: IL-6 clearance rate=(pre-CBP concentration - 6-hour post-CBP concentration) /pre-CBP concentration × 100%; TNF-α sieving coefficient (θ) = (post-CBP plasma concentration/filtrate concentration) × (filtrate flow rate/plasma flow rate); IL-10 adsorption rate=(initial IL-10 concentration in the adsorption column - final concentration in the adsorption column) /initial concentration in the adsorption column × 100% (only for CVVHDF mode where an adsorption column is present). Data with a sudden increase in cytokine concentration >5% at a single time point (considered as rebound or non-steady-state change) were excluded from the final statistical analysis. In addition, plasma sCD163 was detected by ELISA before and after treatment (same kit brand as above). The expression of HLA-DR on monocytes and the proportions of T lymphocyte subsets (CD3+, CD4+, CD8+) were detected by flow cytometry (BD FACSCanto II, USA) with fluorochrome-conjugated monoclonal antibodies (CD3-APC, CD4-FITC, CD8-PE, HLA-DR-PerCP, BD Biosciences, USA). A minimum of 10,000 gated events were collected for each sample and the data were analyzed using FlowJo V10 software. Cortisol (Cor), adrenocorticotropic hormone (ACTH) and dehydroepiandrosterone sulfate (DHEA-S) were determined by chemiluminescence immunoassay using an automatic biochemical analyzer (Beckman AU5800, USA) at a standardized sampling time: sampling was performed at 8:00 a.m. (the peak of the cortisol circadian rhythm) and 30 min before hydrocortisone administration (trough concentration) to avoid the interference of circadian rhythm and drug administration on detection results.

Endpoints

Primary endpoint: The 28-day all-cause mortality rate (survival status from cohort entry to day 28).

Secondary endpoints: The length of intensive care unit (ICU) stay, incidence of septic shock (sepsis with persistent hypotension requiring vasopressors to maintain MAP ≥65 mmHg and serum lactate >2 mmol/L despite adequate fluid resuscitation) and MODS (based on the SOFA score criteria, with the definition of ≥2 organ systems having a SOFA score increase of ≥2 points compared with the baseline) within 8 days, dynamic changes of inflammatory factors, the clearance efficiency of CBP-associated inflammatory mediators and the alterations in immune markers, cells and stress indices before and after treatment. An independent endpoint review committee consisting of three senior critical care physicians, none of whom had been involved in the treatment decisions, determined the occurrence of septic shock and MODS using objective clinical and laboratory data extracted from the medical records. Adverse event adjudication: An independent adverse event review panel composed of a clinical pharmacist, a senior critical care physician and a biostatistician reviewed all adverse events according to the Common Terminology Criteria for Adverse Events (CTCAE) v5.0 (Freites-Martinez *et al*., 2021), including severity grading, causality assessment and treatment-relatedness judgment.

Statistical analysis

This study used SPSS32.0 to analyze and process the data. Propensity scores were estimated using multivariable logistic regression, and 1:1 nearest-neighbor matching without replacement was performed to construct comparable treatment cohorts; covariate balance was evaluated using standardized mean differences, with values below 0.10 considered acceptable. Measurement data were presented as ($\bar{\chi}\pm s$) and underwent t-testing if normally distributed; otherwise, the M(P25, P75) was used for statistical description and the rank-sum test for analysis. The count data were shown as percentages, with comparisons made using χ^2 or Fisher's exact tests. Survival rates were calculated using the Kaplan-Meier method and compared using the Log-rank test. For the repeated measurement data of inflammatory factors and immune function markers at multiple time points, Bonferroni correction was used to adjust the P value to control the Type I error caused by multiple pairwise comparisons. FDR (False Discovery Rate) correction (q=0.05) was applied to the statistical analysis of multiple secondary endpoints to

reduce the false positive rate and all reported P values were corrected values. After matching, age, baseline SOFA score, lactate level and source of infection were included in a binary logistic regression model as a sensitivity analysis to account for residual confounding in the assessment of the primary endpoint, namely 28-day all-cause mortality. A two-tailed P<0.05 was considered statistically significant.

RESULTS

Comparison of clinical baseline data

After 1:1 matching, age, sex, family medical history, living habits, infection source, baseline SOFA score and lactate level were comparable between the two groups (all P>0.05), supporting baseline balance in the matched cohort (Table 1).

Comparative analysis of clinical outcomes

According to statistics, the length of ICU stay was shorter in the intervention group than in the control group (P<0.05). A reduced 28-day all-cause mortality rate (16.67%) and a decreased incidence of 28-day septic shock were also identified in the intervention group (both P<0.05 vs. controls). However, the incidence of MODS was similar between the groups (P>0.05) (Table 2).

Dynamic changes in inflammatory factors

The intervention group exhibited lower levels of proinflammatory factors IL-6, TNF-α and IL-1β than the control group at 6-24h (P<0.05). Additionally, the level of IL-10 in the intervention group during the 24-48 hour anti-inflammatory period was higher than that in the control group (P<0.05). IL-6, TNF-α, IL-1β and IL-10 in the intervention group recovered to normal levels at 48h, 48h, 72h and 72h, respectively (Fig. 1).

Comparison of the clearance efficiency of inflammatory mediators

Through quantitative analysis, it can be seen that the IL-6 clearance rate, TNF-α and IL-10 adsorption rate were all higher in the intervention group versus controls (P<0.05), suggesting higher inflammatory mediator clearance-related indices in the intervention group (Table 3).

Comparison of co-regulators of immunosuppression and immunoactivation

The intervention and control groups were not statistically different in pre-treatment sCD163 and HLA-DR or the number of T lymphocyte subsets (P>0.05). Following the treatment, the sCD163 was reduced in both groups, with even lower levels in the intervention group (P<0.05); CD3+, CD4+/CD8+ and HLA-DR increased from pre-treatment levels, with greater increases in the intervention group (P<0.05) (Fig. 2).

Table 1: Clinical baseline data

Group (60 cases in each group)	Age	Male/ female	Family history of disease Yes/no	Smoking Yes/no	Drinking alcohol Yes/no	Source of infection Lung/abdominal cavity/urinary system/skin or soft tissue/other	SOFA	Lactate (mmol/L)	Source of infection Lung/abdominal cavity/urinary/skin
Intervention	59.72±6.64	34/26	5/55	22/38	16/44	29/16/7/6/2	6.84±2.19	4.12±1.32	29/16/7/8
Control	59.98±6.38	38/22	6/54	20/40	12/48	28/19/5/8/0	6.60±2.01	4.05±1.11	27/19/5/9
t or $\chi 2$	0.22	0.56	0.10	0.15	0.75	2.89	0.57	0.28	0.72
P	0.823	0.456	0.752	0.702	0.388	0.576	0.57	0.78	0.87

Table 2: Clinical outcomes

Group (60 cases in each group)	Length of ICU stay (d)	All-cause mortality	Septic shock	MODS
Intervention	7.12±1.70	10 (16.67)	12 (20.00)	16 (26.27)
Control	8.22±2.42	20 (33.33)	23 (38.33)	23 (38.33)
t or χ2	2.88	4.58	4.88	1.861
P	0.005	0.032	0.027	0.173
95%CI	0.344 to 1.856	0.166 to 0.915	0.182 to 0923	0.282 to 1.256

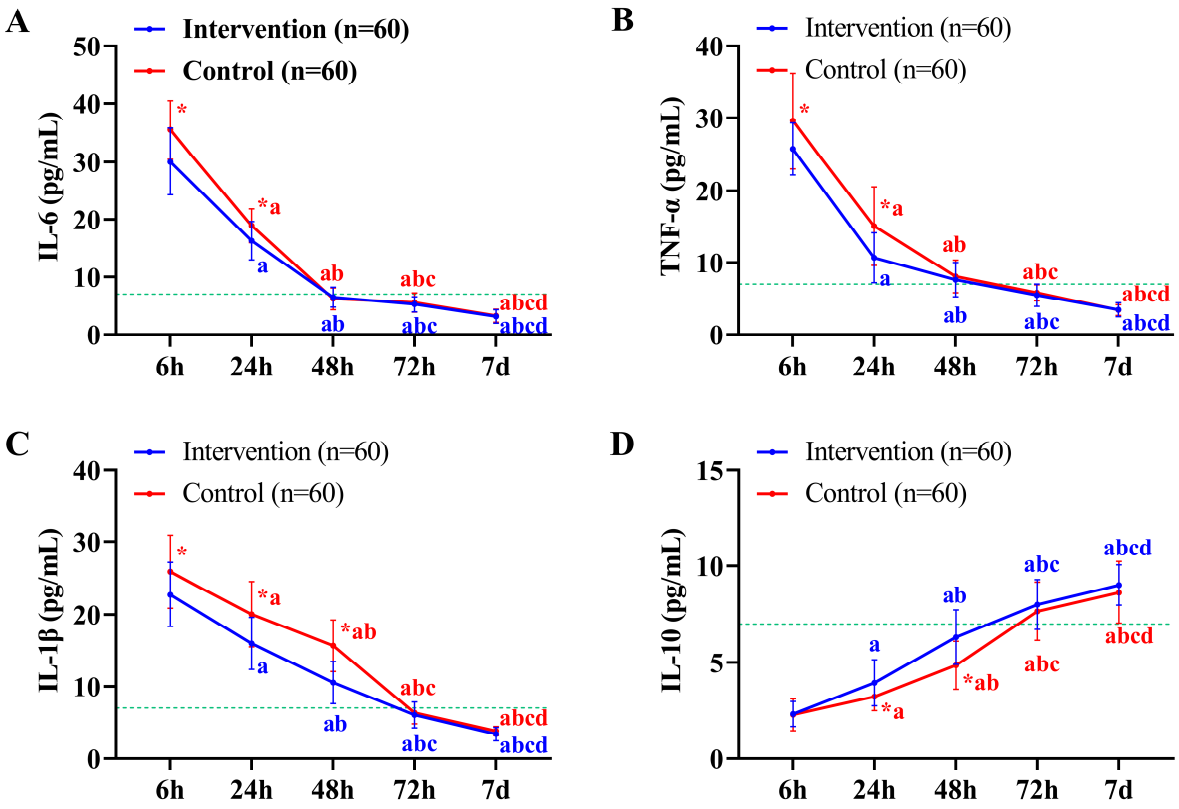

Fig. 1: Dynamic changes in inflammatory factors. (A) The change of IL-6. (A) The change of TNF-α. (A) The change of IL-1β. (A) The change of IL-10. Note: a, b, c, d and * indicate P<0.05 compared with 6h, 24h, 48h, 72h and control group, respectively. Green dashed line: reference value.

Table 3: Clearance efficiency of inflammatory mediators

Group (60 cases in each group)	IL-6 clearance rate	TNF-α	IL-10 adsorption rate
Intervention	37.68±6.99	0.74±0.08	26.70±4.94
Control	33.45±6.37	0.63±0.13	21.00±5.14
t	3.46	5.46	6.20
P	<0.001	<0.001	<0.001
95%CI	-6.649 to -1.812	-0.145 to -0.068	-7.525 to -3.879

Comparison of changes in GC -HPA axis function

Similarly, Cor, ACTH and DHEA-S were equivalent between groups before treatment (P>0.05). Both cohorts exhibited a decline in Cor post-treatment, particularly in the intervention group (P<0.05). As to ACTH and DHEA-S, their levels remained barely changed in the control group after treatment, but were decreased in the intervention group (P<0.05). All HPA axis indicators in the intervention group remained above the clinical diagnostic threshold of adrenal insufficiency (Cor> 100 nmol/L) and no clinical symptoms of adrenal insufficiency (e.g., persistent hypotension, unexplained hyponatremia, fatigue) were observed in any patient in the two groups during the follow-up period (Fig. 3).

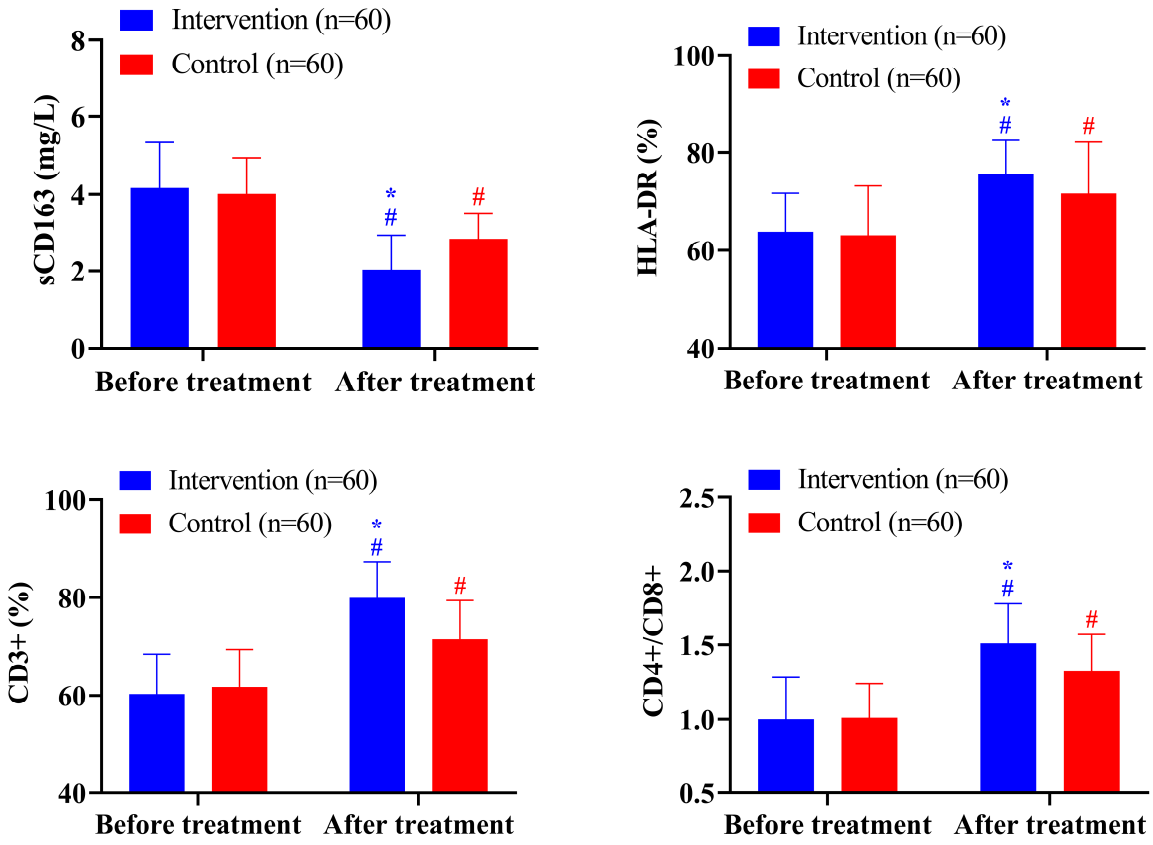

Fig. 2: Comparison of co-regulators of immunosuppression and immunoactivation. (A) Comparison of sCD163. (B) Comparison of HLA-DR. (C) Comparison of CD3+. (D) Comparison of CD4+/CD8+. Note: # and * indicate P<0.05 compared with before treatment and control group, respectively.

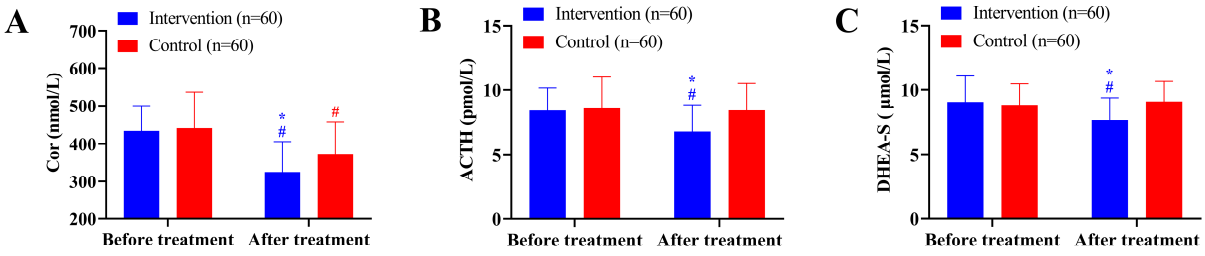

Fig. 3: Changes in GC -HPA axis function. (A) Comparison of Cor. (B) Comparison of ACTH. (C) Comparison of DHEA-S. Note: # and * indicate P<0.05 compared with before treatment and control group, respectively.

Comparison of treatment safety

A similar incidence of secondary infections, gastrointestinal bleeding and CBP catheter-related thrombosis was found between the intervention and control groups (P>0.05). However, GC-associated hyperglycemia and electrolyte acid-base disorders occurred more frequently in the intervention group (P<0.05). After insulin adjustment and potassium supplementation, the conditions were corrected (no ketoacidosis occurred) (Table 4).

DISCUSSION

This study evaluated the association of LD-GC plus early CBP with inflammatory factors, immune status and short-term prognosis in patients with sepsis. The results showed that, compared with the CBP-alone group, the LD-GCs + CBP group had a lower 28-day all-cause mortality rate, shorter ICU stay and lower incidence of septic shock.

Table 4: Adverse effects

Group (60 cases in each group)	Hormone-related hyperglycemia	Electrolyte acid-base disorder	Secondary infections	Gastrointestinal bleeding	Blood coagulation in CBP pipeline
Intervention	16 (26.27)	13 (21.67)	3 (5.00)	2 (3.33)	5 (8.33)
Control	7 (11.67)	5 (8.33)	4 (6.67)	2 (3.33)	4 (6.67)
$\chi 2$	4.36	4.18	0.16	-	0.12
P	0.037	0.041	0.697	-	0.729
95%CI	1.000 to 6.937	1.000 to 8.119	0.180 to 2.854	-	0.354 to 4.316

According to the dynamic monitoring of inflammatory factors, the levels of pro-inflammatory factors (IL-6, TNF-α and IL-1β) were lower in the LD-GCs + CBP group than in the CBP-alone group within 6-24 h, whereas the level of the anti-inflammatory factor IL-10 was higher within 24-48 h. In addition, higher IL-6 clearance rates, TNF-α sieving coefficients and IL-10 adsorption rates were observed in the LD-GCs + CBP group. Concerning immunomodulation, monocyte HLA-DR expression and T lymphocyte subset levels increased more markedly in the LD-GCs + CBP group after treatment, whereas sCD163 decreased more substantially. The analysis of the GC-HPA axis function indicated slightly reduced Cor and ACTH in the intervention group and all indicators remained above the clinical diagnostic threshold of adrenal insufficiency (Cor > 100 nmol/L) with no corresponding clinical symptoms observed. In terms of safety, the LD-GCs + CBP group had a higher incidence of hormone-related hyperglycemia and electrolyte acid-base disorders, but all cases were effectively controlled after targeted management, including insulin adjustment and electrolyte supplementation, with no severe adverse events related to the combined therapy observed.

The core finding of this study—that LD-GCs + CBP was associated with more favorable inflammatory marker profiles and better short-term clinical outcomes than CBP alone—is broadly consistent with previous studies (Fan *et al.*, 2023). However, the present retrospective cohort analysis was not designed to establish the underlying biological mechanisms. In the present study, lower IL-6 and TNF-α levels were observed in the intervention group during the 6-24h period. One possible explanation is that hydrocortisone and CBP may have affected inflammatory mediator kinetics through different pathways (Bastida *et al.*, 2025); however, this remains speculative because no mechanistic endpoints were assessed. This contrasts with the result of Tao *et al*., who found that high-dose GCs failed to improve prognosis (Tao *et al.*, 2025) and may indicate that the timing and dosing of glucocorticoid therapy deserve further investigation in future studies. In addition, IL-1β levels in the intervention group were lower than those in the control group at 6-24h and returned to the reference range by 72h. This temporal pattern suggests an association between the combined regimen and lower circulating IL-1β during the early inflammatory phase, but it does not establish a specific biological mechanism. Potential explanations may include altered cytokine production and extracorporeal removal, although these possibilities were not directly tested in the present study. The trajectory of IL-1β observed here may nonetheless be useful for hypothesis generation in future studies. Whether early changes in IL-1β could serve as a treatment-response marker or support threshold-based clinical decision-making requires validation in independent cohorts before any clinical application.

Secondly, the dynamic change in IL-10 expression in the intervention group may reflect a more balanced pattern of immune regulation rather than a persistent anti-inflammatory shift. The compensatory up-regulation of IL-10 in the late stage of SS is an important sign of immunosuppression (Zhang *et al.*, 2022). However, in this study, IL-10 in the intervention group increased moderately during the 24-48h phase and returned to normal levels by day 7. This pattern may be consistent with less pronounced immune dysregulation in the intervention group, but the present data do not demonstrate that HYD directly prevented T-cell depletion through IL-10-related pathways (Teja *et al.*, 2024). The concurrent increase in HLA-DR is in line with this interpretation, although causality cannot be inferred from the current study.

It is worth noting that changes in HPA-axis-related indices after HYD exposure were modest in magnitude in this study. Although Cor was lower in the intervention group than in the control group, it did not fall below the adrenal insufficiency threshold of 100 nmol/L (Wentworth & Siragy, 2022) and DHEA-S showed only a mild decline (20-25%). These findings differ from the more pronounced HPA-axis suppression reported with traditional high-dose GC therapy (Boretti *et al.*, 2025). However, the present data should be interpreted as observational only and do not establish a specific modulatory effect of LD-GCs + CBP on HPA-axis function. Our results simply indicate that no overt biochemical or clinical evidence of adrenal insufficiency was observed during the study period.

Furthermore, we observed higher inflammatory mediator clearance indices in the LD-GCs + CBP group than in the CBP-alone group. Prior experimental work has suggested that hydrocortisone may influence inflammatory signaling pathways such as NF-κB (Fang *et al.*, 2025), while CBP physically removes circulating mediators (Wang *et al.*, 2022). These prior observations provide possible context

for our findings, but the present study was not designed to confirm synergy between these interventions or to define the molecular pathway involved. Since NF-κB and related signaling molecules were not measured, the mechanistic basis of the observed differences remains to be clarified.

However, regional bias may be present as the samples mainly came from a single medical center, which warrants multicenter research to verify the universality of the conclusions. Furthermore, although the cohort was matched in a 1:1 ratio (60 cases/group), some subgroup analyses may have had reduced statistical power because of the limited sample size. Moreover, a 28-day follow-up is too short to evaluate long-term outcomes such as long-term quality of life and cognitive dysfunction. Given a reported one-year mortality of 40% among SS survivors (Cai *et al.*, 2025), extending the follow-up period to more than 6 months is needed in future research. Fifth, the sample size of this single-center study is relatively small, leading to underpowered statistical analysis of adverse events, especially rare adverse events. The incidence of adverse events reported in this study provides only preliminary clinical reference, and the accurate incidence and risk factors should be further verified in larger multicenter studies with standardized data collection and longer follow-up. In the future, it is necessary to combine multi-omics techniques to reveal the "drug-host-microorganism" interaction".

CONCLUSION

Compared with CBP alone, low-dose glucocorticoids combined with early CBP was associated in this study with lower pro-inflammatory cytokine levels, more favorable immune marker changes and better short-term clinical outcomes in patients with sepsis. Although the safety profile was acceptable within the observation period, these findings should be interpreted cautiously, as this single-center retrospective cohort analysis was not designed to establish mechanisms or support immediate clinical stratification. The regimen may have potential clinical value, but multicenter studies with larger samples, standardized data collection and longer follow-up are needed before firm conclusions can be drawn regarding effectiveness, safety and the most appropriate target population.

Acknowledgements
Not applicable.

Author's contributions
Jianchao Li conceived and designed the retrospective analysis and wrote the paper. Chunhui Song collected and verified the clinical data. Chunhui Song analyzed the data. Jianchao Li modified the manuscript. All authors gave final approval of the version to be published and agreed to be accountable for all aspects of the work.

Funding
No funds, grants, or other support was received.

Data availability statement
The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Ethical approval
The study was approved by the Institutional Ethics Committee of Yancheng No.1 People's Hospital (No. 2023-014), and the requirement for written informed consent was waived because anonymized retrospective clinical data were used. This study was performed in adherence with the STROBE guidelines. See supplementary file for the STROBE checklist.

Conflict of interest
The authors report no conflict of interest.

Supplementary data
https://www.pjps.pk/uploads/2026/08/SUP1786180338.pdf

REFERENCES

Ackerman MH, Ahrens T, Kelly J and Pontillo A (2021). Sepsis. *Crit Care Nurs Clin North Am*, **33**(4): 407-418.

Bastida C, Egues Lugea A, Fernandez Polo A, Becerril Moreno F, Martin Cerezuela M, Domingo Chiva E, Betancor Garcia T, Amor Garcia MA, Aquerreta Gonzalez I, Albanell-Fernandez M, Domenech Moral L, Ortiz Perez S and Cobo Sacristan S (2025). Sepsis and septic shock. *Farm Hosp.,* **50**(2): T108-T114.

Boretti FS, Harburger L, Riond B, Neubert E, Hofmann-Lehmann R, Unterer S, Dennler M and Sieber-Ruckstuhl NS (2025). Effects of long-term high-dose prednisolone in Beagle dogs on structural and functional responses of the HPA Axis. *BMC Vet Res*, **21**(1): 480.

Cai D, Zou B, Zhang Y, Chen X, Wang B and Tao Y (2025). The association between body mass index and ICU 28-day mortality rate in patients with sepsis: A retrospective observational study. *Am J Med Sci*, **370**(2): 148-154.

Chiu C and Legrand M (2021). Epidemiology of sepsis and septic shock. *Curr Opin Anaesthesiol*, **34**(2): 71-76.

Fan HP, Zhou Y, Zhou Y, Jin J and Hu TY (2023). Association between short-term systemic use of glucocorticoids and prognosis of cardiogenic shock: A retrospective analysis. *BMC Anesthesiol*, **23**(1): 169.

Fan M, Zhu S, Liu M, Cao A, Jiang F and Wang R (2024). Nursing based on humanistic care concept for continuous blood purification for patients with severe sepsis in the intensive care unit. *Altern Ther Health Med*, **30**(7): 96-102.

Fang Y, Song F, Gao C and Wang Z (2025). Hydrocortisone improves post-resuscitation myocardial dysfunction by inhibiting the NF-κB pathway. *Biochem Cell Biol*, **103**: 1-11.

Freites-Martinez A, Santana N, Arias-Santiago S and Viera A (2021). Using the common terminology criteria for adverse events (CTCAE - Version 5.0) to evaluate the severity of adverse events of anticancer therapies. CTCAE version 5.0. Evaluacion de la gravedad de los eventos adversos dermatologicos de las terapias antineoplasicas. *Actas Dermosifiliogr (Engl Ed)*, **112**(1): 90-92.

Fujii T, Salanti G, Belletti A, Bellomo R, Carr A, Furukawa TA, Luethi N, Luo Y, Putzu A, Sartini C, Tsujimoto Y, Udy AA, Yanase F and Young PJ (2022). Effect of adjunctive vitamin C, glucocorticoids and vitamin B1 on longer-term mortality in adults with sepsis or septic shock: A systematic review and a component network meta-analysis. *Intensive Care Med*, **48**(1): 16-24.

Guo C, Huang A, Yang S, Cheng W and Zhu J (2024). Analysis of the effect of continuous blood purification combined with xuebijing in the treatment of sepsis and its impact on inflammatory factors and hemodynamic indicators in patients. *Panminerva Med*. doi: 10.23736/S0031-0808.24.05058-4.

Njoki C, Angelo S, Wambui M and Riviello E (2026). Global Sepsis Epidemiology. *Clin Chest Med*, **47**(1): 17-31.

Srzic I, Nesek Adam V and Tunjic Pejak D (2022). Sepsis definition: What's new in the treatment guidelines. *Acta Clin Croat*, **61**(Suppl 1): 67-72.

Tao T, Shi Y, Ye X, Mi W and Lou J (2025). Intraoperative low-dose glucocorticoids in surgical patients with abdominal sepsis: A multicenter retrospective cohort study. *Health Sci Rep*, **8**(2): e70360.

Teja B, Berube M, Pereira TV, Law AC, Schanock C, Pang B, Wunsch H, Walkey AJ and Bosch NA (2024). Effectiveness of fludrocortisone plus hydrocortisone versus hydrocortisone alone in septic shock: A systematic review and network meta-analysis of randomized controlled trials. *Am J Respir Crit Care Med*, **209**(10): 1219-1228.

Wang L, Zhao Y, Yao S, Lou H and Zhang L (2022). Vitamin D improves the effect of glucocorticoids on attenuating lipopolysaccharide-induced IL-6 Production via TLR4/NF-kappaB pathway in human respiratory epithelial cells. *Int Arch Allergy Immunol*, **183**(9): 1017-1028.

Wang R, Lin L, Zhu Q, Niu Y, Wang M and Chen T (2021). Nursing effect of continuous blood purification therapy in treatment of severe sepsis. *Am J Transl Res*, **13**(9): 10801-10808.

Wentworth BJ and Siragy HM (2022). Adrenal Insufficiency in Cirrhosis. *J Endocr Soc*, **6**(10): bvac115.

Zhang W, Wang W, Hou W, Jiang C, Hu J, Sun L, Hu L, Wu J and Shang A (2022). The diagnostic utility of IL-10, IL-17 and PCT in patients with sepsis infection. *Front Public Health*, **10**: 923457.