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Published Online: 2026 April 30 **Brief Report**

The Impact of Hemoperfusion on Clinical Outcomes in Severe COVID-19 Patients: A Retrospective Propensity Score-Matched Study

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Abstract

Background: Severe COVID-19 is frequently complicated by hyperinflammation and is associated with a high mortality rate.

Objectives: Adjunctive hemoperfusion (HP) aims to remove inflammatory mediators; however, its clinical benefits remain controversial.

Methods: This retrospective 1:1 propensity score-matched case-control study included 70 patients with severe COVID-19 who were admitted to the intensive care unit (ICU) at Dr. Gharazi Hospital, Malayer, Iran, from March 2020 to September 2022. Patients received adjunctive HP using Jafron cartridges plus standard care (n = 35) or standard care alone (n = 35).

Results: After matching, baseline characteristics were well balanced. Adjunctive hemoperfusion was associated with a significantly greater reduction in C-reactive protein (46% ± 14% vs. 18% ± 9%; P < 0.001), a greater improvement in peripheral oxygen saturation (SpO_2; +7% ± 2% vs. +2% ± 1%; P = 0.01), a shorter ICU length of stay (11.2 ± 4.1 vs. 16.5 ± 5.8 days; P = 0.03), and a lower need for mechanical ventilation (40.0% vs. 62.9%; P = 0.04). In-ICU mortality was numerically lower in the HP group (20.0% vs. 34.3%; P = 0.08) but did not reach statistical significance. No procedure-related deaths occurred.

Conclusions: In this propensity-matched cohort, adjunctive hemoperfusion was associated with attenuated systemic inflammation, improved oxygenation, a reduced need for mechanical ventilation, and a shorter ICU stay. These findings should be interpreted cautiously given the retrospective design.

Keywords: COVID-19, Hemoperfusion, Intensive Care Unit Outcomes

1. Background

A dysregulated hyperinflammatory response (cytokine storm) is common in severe COVID-19 and can result in endothelial dysfunction, acute respiratory distress syndrome, multiorgan failure, and high mortality (1-3). Despite the use of corticosteroid and antiviral therapies in some patients, those with refractory hyperinflammation generally have a poor prognosis (4, 5).

Extracorporeal blood purification, particularly hemoperfusion (HP), has been adopted as a supportive therapy to remove circulating inflammatory mediators. Several studies and meta-analyses have shown reductions in inflammatory markers with HP; however, its effects on clinical outcomes, including mortality and mechanical ventilation, have been inconsistent (6, 7). Previous studies have been conducted mainly in high-resource settings, and data from resource-limited environments remain limited.

2. Objectives

This retrospective, propensity score-matched study was designed to evaluate the associations between adjunctive hemoperfusion and inflammation, oxygenation, mechanical ventilation, intensive care unit (ICU) length of

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stay, and mortality among patients with severe COVID-19 in a resource-limited ICU in Iran.

3. Methods

3.1. Study Design and Setting

This retrospective, 1:1 propensity score-matched case-control study was conducted in the ICU of Dr. Gharazi Hospital, Malayer, Iran, from March 2020 to September 2022. The study was approved by the Ethics Committee of Hamadan University of Medical Sciences (IR.UMSHA.REC.1400.865), and informed consent was waived because of the retrospective design and the use of deidentified data.

3.2. Participants and Eligibility

A total of 142 patients with severe COVID-19 were screened. The inclusion criteria were age ≥ 18 years, a positive severe acute respiratory syndrome coronavirus 2 polymerase chain reaction result, compatible chest imaging findings, and severe disease (respiratory rate > 25/min, SpO_2 < 90% on room air, or PaO_2/FiO_2 < 200). The exclusion criteria were coagulopathy contraindicating extracorporeal therapy, hypersensitivity to cartridge materials, or substantially incomplete records. Finally, 70 patients were included after 1:1 propensity score matching (Figure 1).

3.3. Intervention

Patients in the hemoperfusion group received a median of 2 HP sessions (IQR, 1 - 3) per patient. Each session was performed on a Fresenius platform using Jafron cartridges and lasted 3 - 6 hours. The median interval from ICU admission to the first session was 38 hours (IQR, 24 - 52). Blood flow ranged from 150 to 200 mL/min, and unfractionated heparin was used for anticoagulation. Hemoperfusion was initiated when the C-reactive protein (CRP) level was > 80 mg/L or the PaO_2/FiO_2 ratio was < 150 mm Hg after routine treatment. Co-interventions were similar between the 2 groups (Table S1 in the Supplementary File).

3.4. Propensity Score Matching and Statistical Analysis

Propensity score matching was performed to balance age, sex, diabetes, hypertension, and the baseline PaO_2/FiO_2 ratio. A 1:1 nearest-neighbor matching approach with a caliper of 0.1 was used. All standardized mean differences after matching were < 0.10. Given the matched design, paired statistical tests were applied as appropriate, including the paired t test, Wilcoxon signed-rank test, and McNemar test. Logistic regression was used to obtain adjusted odds ratios. All data were analyzed using SPSS, version 26. A P value < 0.05 was considered statistically significant.

4. Results

After 1:1 propensity score matching, 35 patients were included in each group, for a total of 70 patients with severe COVID-19. Demographic and clinical characteristics were evenly distributed between the hemoperfusion and control groups (Table 1).

Adjunctive hemoperfusion was associated with a significantly greater reduction in CRP (46% ± 14% vs. 18% ± 9%; P < 0.001) and a greater improvement in SpO_2 (+7% ± 2% vs. +2% ± 1%; P = 0.01) at 48 hours (Table 2).

ICU length of stay (11.2 ± 4.1 vs. 16.5 ± 5.8 days, respectively; P = 0.03) and the use of invasive mechanical ventilation (40.0% vs. 62.9%, respectively; P = 0.04) were significantly lower in the hemoperfusion group. In-ICU mortality was numerically lower in the hemoperfusion group (20.0% vs. 34.3%; P = 0.08) but did not reach statistical significance (Table 3).

Adjusted odds ratios are presented in Table 4. The most frequent adverse events in the hemoperfusion group were transient hypotension (22.9%), electrolyte imbalance (14.3%), and chills or low-grade fever (8.6%). All events were managed with supportive care, and no procedure-related deaths occurred.

5. Discussion

This study showed that adjunctive hemoperfusion was associated with a significantly greater reduction in systemic inflammation, improved oxygenation, a shorter ICU stay, and a reduced need for mechanical ventilation among patients with critical COVID-19. In-ICU mortality was numerically lower in the hemoperfusion group than in the control group (20.0% vs. 34.3%; P = 0.08).

These results are consistent with previous studies and meta-analyses demonstrating beneficial effects of hemoperfusion on inflammatory markers and certain physiological parameters, although its effect on survival remains unclear (6, 8, 9). The timing of hemoperfusion initiation may be relevant. In this study, early

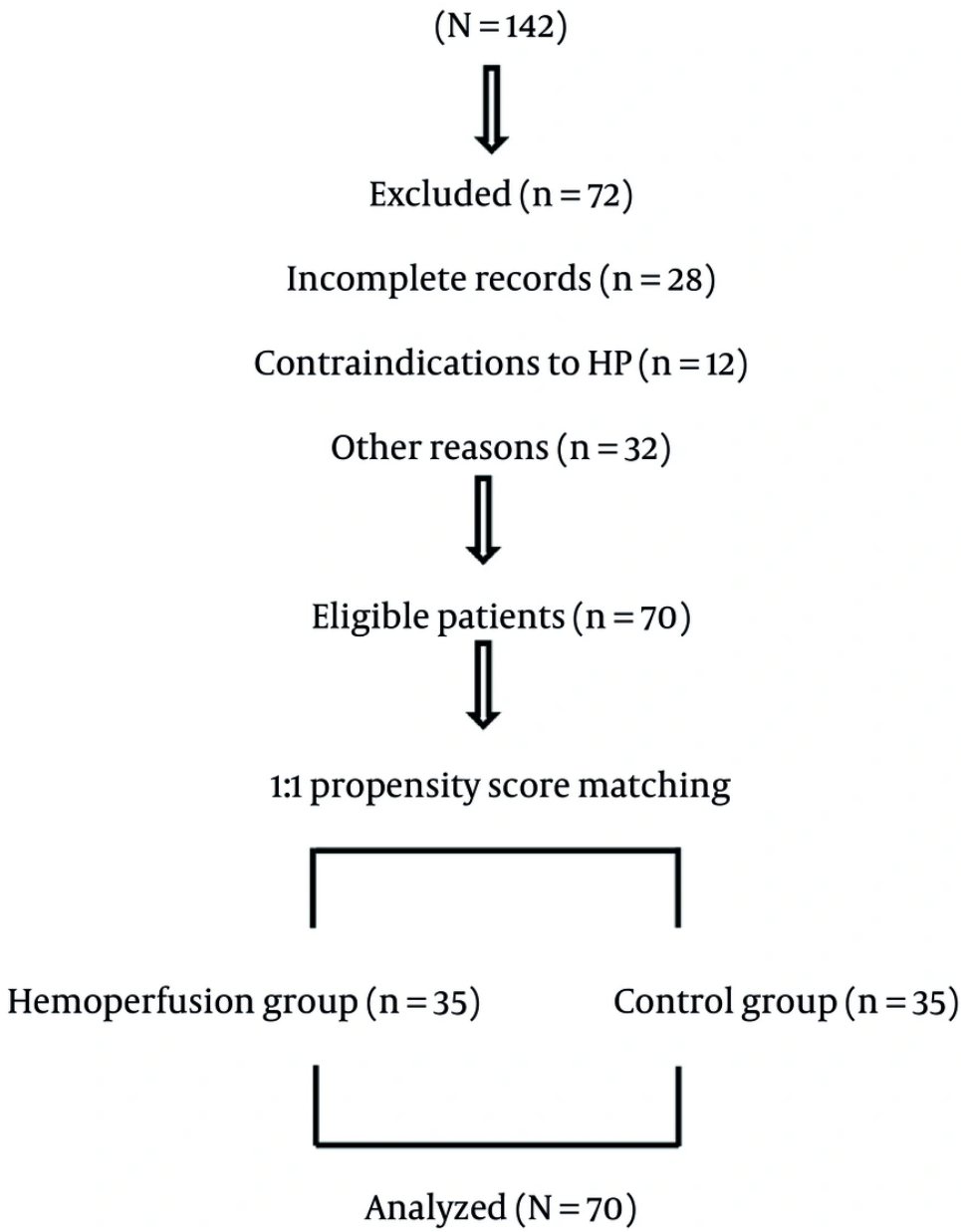

Figure 1. Flow diagram of the study participants

administration of HP within 48 hours of ICU admission was associated with improved outcomes. This finding aligns with previous reports indicating that early intervention may be more effective before irreversible organ damage occurs (10).

Patients with COVID-19 may have comorbid conditions that contribute to mortality. Other adjunctive therapies,

Table 1. Demographic and Baseline Clinical Characteristics of the Study Participants [a]

Variables	HP Group (n = 35)	Control Group (n = 35)	P-Value
Age (y)	63.4 ± 11.2	62.9 ± 10.8	0.81
Gender			0.79
Male	21 (60)	22 (63)	
Female	14 (40)	13 (37.1)	
Diabetes	14 (40)	15 (43)	0.84
Hypertension	16 (46)	17 (49)	0.77
Initial PaO_2/FiO_2 (mm Hg)	138 ± 42	141 ± 39	0.72

[a] Values are expressed as mean ± SD or No. (%).

Table 2. Changes in Inflammatory and Oxygenation Parameters Before and After the Intervention

Parameters	HP Group	Control Group	P-Value
CRP reduction [a]	46 ± 14	18 ± 9	< 0.001
Preintervention CRP (mg/L) [b]	82.4 ± 12.1	79.8 ± 13.5	0.52
Postintervention CRP (mg/L) [b]	43.2 ± 8.7	65.5 ± 11.9	< 0.001
SpO_2 improvement [a]	7 ± 2	2 ± 1	0.01

[a] Values are expressed as % ± SD.

[b] Values are expressed as mean ± SD.

Table 3. Primary Clinical Outcomes in the Hemoperfusion and Control Groups [a]

Outcome	HP Group	Control Group	P-Value
Mortality	7 (20)	12 (34.3)	0.08
ICU length of stay (d)	11.2 ± 4.1	16.5 ± 5.8	0.03
Need for mechanical ventilation	14 (40)	22 (62.9)	0.04

[a] Values are expressed as No. (%) or mean ± SD.

such as statins, have also been investigated, with inconsistent effects on outcomes (11, 12). In small hospitals and clinics with limited resources, hemoperfusion may represent a useful treatment option because more sophisticated treatment modalities are often unavailable.

Hemoperfusion may act by adsorbing circulating cytokines, including interleukin 6, tumor necrosis factor α, and interleukin 1β, thereby attenuating the cytokine storm; this mechanism is biologically plausible (13). However, the benefit may be short-lived because of cytokine rebound and cartridge variability.

5.1. Limitations

This study has several limitations. First, its single-center retrospective design may have introduced selection and information bias despite the use of propensity score matching. Second, the sample size (n = 70) was small and did not provide sufficient statistical power to detect differences in mortality. Third, cytokines such as interleukin 6 and tumor necrosis factor α were not measured serially because doing so was not logistically feasible in this resource-limited setting. Fourth, follow-up data after ICU discharge were not assessed. Finally, the number of hemoperfusion sessions was not uniform and was left to the physician's discretion. These limitations highlight the need for larger, multicenter prospective studies to validate these findings.

Table 4. Adjusted Odds Ratios for the Main Binary Clinical Outcomes

Outcome	Adjusted OR	95% CI	P-Value
Need for mechanical ventilation	0.39	0.16 - 0.94	0.036
In-ICU mortality	0.47	0.19 - 1.22	0.119

5.2. Conclusions

Adjunctive hemoperfusion was associated with improved intermediate clinical outcomes, including reduced systemic inflammation, improved oxygenation, a reduced need for mechanical ventilation, and a shorter ICU stay. In-ICU mortality was also numerically lower in the hemoperfusion group (20.0% vs. 34.3%), but the difference was not statistically significant (P = 0.08).

Hemoperfusion may be considered an adjunctive treatment in resource-limited settings, particularly when initiated early. Larger multicenter trials are needed to confirm these observations and determine its effect on survival.

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Supplementary Material

Supplementary material(s) is available here [To read supplementary materials, please refer to the journal website and open PDF/HTML].

Footnotes

AI Use Disclosure: The authors declare that no generative AI tools were used in the creation of this article.

Authors' Contribution: M. S. K. and M. R. T. conceived and designed the study and supervised the work; K. M., E. M-T., and A. R. collected the clinical data; M. S. K. and M. R. T. performed the statistical analysis; M. S. K. drafted the manuscript. All authors critically revised and approved the final manuscript and agreed to be accountable for the accuracy and integrity of the work.

Conflict of Interests Statement: The authors declare no conflicts of interest. The hemoperfusion cartridges were provided as part of routine clinical care and not sponsored by the manufacturer.

Data Availability: The data presented in this study are uploaded during submission as a supplementary file and are openly available for readers upon request.

Ethical Approval: The study was approved by the Institutional Ethics Committee of Hamadan University of Medical Sciences, Hamadan, Iran (approval code: IR.UMSHA.REC.1400.865).

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