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# Comparison of the Effects of Plasmapheresis, Hemoperfusion, and Convalescent Plasma Therapy on Inflammatory Factors in COVID-19 Patients

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## Abstract

**Background:** Since the emergence of coronavirus disease 2019 (COVID-19), the treatment protocols are continuously updated, based on the evidence gathered all around the world and reported to the World Health Organization. Like many other emerging infectious diseases, using convalescent plasma from those recovered from the disease was a preliminary treatment approach that showed partial effectiveness for severe COVID-19 patients. Besides, blood filtration strategies, such as hemoperfusion and plasmapheresis, are employed to lessen the load of inflammatory molecules. However, few studies compared their effects to conclude which treatment might be more efficacious for COVID-19 patients. We compared the effects of plasmapheresis or plasma exchange, convalescent plasma therapy, and hemoperfusion on O2 saturation and inflammatory factors in COVID-19 patients.

**Methods:** In this retrospective study, 50 COVID-19 patients received standard treatments based the international guidelines. Patients were divided into 4 groups: hemoperfusion, plasmapheresis, plasma therapy, and control. The control group received only the standard treatments. The mortality rate, $O_2$ saturation, and laboratory factors were compared between the 4 groups.

**Results:** We found a significant decrease in the C-reactive protein level following hemoperfusion (32.75 ± 23.76 vs 13 ± 7.54 mg/dL; $p$ = 0.032) but not plasmapheresis and plasma therapy. Besides, serum levels of lactate dehydrogenase ($p$ = 0.327, 0.136, 0.550, for hemoperfusion, plasmapheresis, and plasma therapy, respectively) and other inflammatory molecules did not significantly change following treatments. There is also no significant difference in the mortality rate between the treatment groups ($p$ = 0.353).

**Conclusion:** It seems that hemoperfusion, plasmapheresis, and plasma therapy did not have considerable effects on decreasing the inflammation and mortality rate compared with standard treatment.

**Keywords:** COVID-19, Plasmapheresis, Hemoperfusion, Convalescent Plasma

***Conflicts of Interest:*** *None declared*
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## Introduction

At the end of 2019, a new coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-COV2) led to an outbreak of a severe respiratory illness in Wuhan, China (1). The World Health Organization (WHO)

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***↑What is "already known" in this topic:***
Since the emergence of COVID-19, convalescent plasma therapy, hemoperfusion, and plasmapheresis have been employed to lessen the inflammatory burden and improve patients. However, few studies compared their effects to conclude which treatment might be more efficacious for COVID-19 patients.

***→What this article adds:***
We compared the effects of plasmapheresis or plasma exchange, convalescent plasma therapy, and hemoperfusion on $O_2$ saturation and inflammatory factors in COVID-19 patients. It seems that hemoperfusion, plasmapheresis, and plasma therapy did not have considerable effects on decreasing the inflammation and mortality rate compared with standard treatment.

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called the disease “coronavirus disease 2019” or “COVID-19” for short (2). COVID-19 is spread by droplets (1). For the last 2 years, it has become a global pandemic that has caused a major crisis around the world, thus the WHO declared a global crisis (3).

According to the latest statistics of the WHO, as of August 1, 2022, the number of confirmed cases of this disease includes 579,092,623 people globally, of whom 6,407,556 people have died due to this disease (4). In Iran, so far (August 5, 2022), the coronavirus epidemic has infected 7,418,615 people and killed 142,209 people (5). Approximately 20% of patients with severe respiratory complications need to be hospitalized in specialized wards, and 60% of them suffer from severe tissue damage following cytokine storm (1, 6).

Despite numerous treatment approaches that have been tried so far, no exclusive treatment is approved for COVID-19. The proposed treatments mainly include antiviral agents, antibiotics, anticoagulants, corticosteroids, and several medications, such as antipyretics and analgesics to manage the symptoms (7). Noteworthy, COVID-19 treatment protocols are continuously updated based on the evidence gathered all around the world and reported to the WHO.

Like many other emerging infectious diseases, using convalescent plasma (CP) from those recovered from the disease was a preliminary treatment approach that showed partial effectiveness for severe COVID-19 patients (6-13). Following more evidence on COVID-19, it has been clear that severe COVID-19 is a phase of hyperinflammation with significant increases in the inflammatory cytokines and molecules known as “cytokine storm” or “cytokine release syndrome” (14). Therefore, the blood filtration strategies, such as hemoperfusion (6, 11, 15), plasmapheresis (13, 16), and plasma exchange (9, 10, 12, 17), are employed to lessen the load of inflammatory molecules.

Since inflammatory mediators and cytokines increase in COVID-19, plasmapheresis and plasma exchange can decrease inflammatory cytokines and consequently increase $O_2$ saturation in patients, leading to less need for patient intubation (9-12, 17). Besides, convalescent plasma therapy (CPT) could provide anti-SARS-CoV2 neutralizing antibodies, which can bind to the virus and prevent more attachments to the lung cells (12, 18). Each of the mentioned modalities showed promising results in reducing the inflammatory burden and management of COVID-19 (6-13, 15-18). However, few studies compared their effects to conclude which treatment might be more efficacious for COVID-19 patients.

Therefore, it is necessary to conduct further studies on their effectiveness and side effects (6-13, 15-19). The present study aimed to compare the effects of plasmapheresis or plasma exchange, CPT, and hemoperfusion on $O_2$ saturation and inflammatory factors in COVID-19 patients.

## Methods

### Patients

The study was ethically approved by the local ethics committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.REC.1399.10). Given the study’s retrospective nature, all the procedures performed were part of routine care. This research was conducted on 50 COVID-19 patients referred to Taleghani hospital, Tehran, Iran, between February and August 2020. The inclusion criteria were as follows: (1) positive COVID-19 quantitative reverse-transcriptase polymerase chain reaction (qRT- PCR) test; (2) COVID-19 manifestations in the lung CT scan; (3) undergoing hemoperfusion, plasmapheresis, or CPT; (4) age over 18. The exclusion criteria were as follows: (1) pregnancy or lactation; (2) immunoglobulin allergy; (3) IgA deficiency; (4) preexisting comorbidity that could increase the risk of thrombosis; (5) life expectancy less than 24 hours; (6) disseminated intravascular coagulation; (7) severe septic shock; (8) $PaO_2/FiO_2$ of less than 100; (9) severe congestive heart failure; (10) detection of high titer of S protein-RBD-specific (receptor binding domain) IgG antibody (≥1: 640); and (11) other contraindications as determined by the patient's physicians. All patients signed informed consent, and the project was ethically approved by the ethics committee of Shahid Beheshti University of Medical Sciences, Tehran, Iran.

### Treatment

Patients were divided into 4 categories of control (standard treatment only), plasmapheresis, CPT, and hemoperfusion to evaluate their effects on $O_2$ saturation of patients, mortality rate, duration of hospitalization, and inflammatory factors. Besides the aforementioned therapies, all patients received standard national COVID-19 treatment protocol as the main treatment. All patients received intravenous remdesivir 200 mg loading dose for the first time followed by 100 mg daily, intravenous dexamethasone 8 mg bidaily, and oral pantoprazole 40 mg daily. The antiviral, antibiotic, and anti-inflammatory drugs had no statistically significant differences between the 3 groups.

### Hemoperfusion

At the time of hemoperfusion, any complications will be monitored and recorded. The cartridge used for this treatment was Cytosorb cartridge – 300. The recommended dose is 1 to 3 cartridges during the first 48 to 72 hours, according to the cartridge saturation by cytokines and other inflammatory mediators. The approximate use time of each Cytosorb-300 cartridge is 24 hours. Due to increased coagulation in COVID-19 patients, significant amounts of heparin are required at a minimum dose of 10 units per kg of body weight per hour. The recommended dose of heparin is 50 to 70 units/kg at first and then 15 to 20 units/kg per hour following treatment every 6 hours. Due to the need for adequate blood flow, the arterial pump rate should be set at least 150 mL per minute. The levels of platelet, albumin, calcium, PTT, and activated clotting time were monitored, and it was tried to keep PTT for 80 to120 seconds and ACT for 2 to 3 minutes.

### Plasmapheresis

Plasmapheresis was performed by exchanging plasma with the combination of ABO-matched fresh frozen plas-



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ma (FFP), 5% human albumin (Biotest), and 0.9% saline. Therefore, it could be called plasma exchange. Patients received 1 to 3 rounds of plasma exchange. Each round comprised 5 units (1 L) FFP, 250 mL albumin 5%, and 750-mL saline. The plasma exchange was conducted using the apheresis system (MCS 3P, Haemonetics).

### Convalescent Plasma Therapy

For CPT, the plasma of persons recovered from COVID-19 was used based on the previously published protocol (12). Donors were double-checked for negative results of the qRT-PCR test for SARS-CoV-2. They were also negative for HIV, hepatitis B and C, cytomegalovirus, herpes simplex viruses, Epstein-Barr virus, and other infectious agents. The donated plasma was checked for SARS-CoV-2 specific IgG and IgM using an ELISA kit (PishtazTeb). Those with 1:10 and lower IgM and 1:1000 and higher IgG were selected for plasma donation. The transfusion dose was 4 to 13 mL/kg. The compatibility of CP with patients' blood cells was checked by matching the ABO blood group and cross-matching the donors' plasma with patients' blood cells. The amount of administered CPT was 10 mL for the first 15 minutes and then raised to 100 mL per hour with close monitoring.

### Outcome Measures

The clinical and laboratory data of patients, including $O_2$ saturation, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), platelet (PLT), hemoglobin (Hb), hematocrit (HCT), lactate dehydrogenase (LDH), albumin (Alb), red blood cells (RBC), white blood cells (WBC), creatinine (Cr), blood urea nitrogen (BUN), sodium (Na), magnesium (Mg), calcium (Ca), alkaline phosphatase (ALP), and international normalized ratio (INR) of coagulation time of patients were evaluated before and after the treatment.

### Statistical Analysis

The statistical analyses included both intergroups and before/after comparisons. All analyses were performed using SPSS Version 25 (SPSS Inc). Kruskal-Wallis and Mann-Whitney tests were used for quantitative variables. Fisher and chi-square tests were used for qualitative variables. Significance level for performed tests was set at 0.05.

## Results

### Descriptive Data

Among 50 COVID-19 patients included in the study, 21 patients with a mean age of 65.61 ± 13.69 years were in the control group and received standard treatment. Ten patients with a mean age of 49.2 ± 17.27 years were in the hemoperfusion group, where they underwent hemoperfusion. Thirteen and 6 patients with a mean age of 54.76 ± 16.2 and 62 ± 18.44 years were also in plasmapheresis and plasma therapy groups, respectively. The descriptive data of each group is depicted in Table 1. There was no difference between age, gender, total death events, underlying disease, and hospitalization period between groups (Table 1). The underlying diseases included hypertension, cardiovascular disease, diabetes, cancers, hyperlipoproteinemia, hepatitis, fatty liver, and hypo/hyperthyroidism. Table 2 demonstrates the effects of age, gender, underlying disease, and hospitalization period on death in total patients. As shown, no significant association was found between the mentioned variables and death events.

### Clinical and Laboratory Findings

The mean value of laboratory markers and $O_2$ saturation of patients in each group are listed in Table 3. Besides, these values in each group were compared with the control group to find differences. The mean levels of Hb in the hemoperfusion (mean,12.57 ± 1.39; $p = 0.003$) and plasmapheresis (mean,11.89 ± 2.38; $p = 0.033$) groups are significantly higher than the control group (mean, 10.42 ± 1.66). The mean MCV level in the hemoperfusion group was significantly lower than that of the control group (mean, 79.76 ± 5.37 vs 84.35 ± 9.33; $p = 0.032$). The HCT level of patients who underwent hemoperfusion is significantly higher than control patients (mean, 37.24 ± 3.44 vs 33.57 ± 8.33; $p = 0.012$). The mean LDH levels of patients who underwent hemoperfusion (mean, 1,119.12 ± 343.2; $p = 0.001$) or plasma therapy (mean, 1,132.86 ± 445.43; $p = 0.032$) were significantly higher than control patients (mean, 777.13 ± 253.77). The mean INR of patients who

*Table 1.* Comparing the demographic data of patients between groups

| variable | All (n=50) | Control (n=21) | Hemoperfusion (n=10) | Plasmapheresis (n=13) | CPT (n=6) | *p* |
|---|---|---|---|---|---|---|
| Age, mean±SD, years | 59.08±16.57 | 65.61±13.69 | 49.2±17.27 | 54.76±16.2 | 62±18.44 | 0.113 |
| Male Gender n(%) | 35 (67.3) | 9 (42.9) | 10 (90.9) | 10 (76.9) | 6 (67.3) | 0.414 |
| Death events, n(%) | 25 (48.1) | 7 (35) | 7 (58.3) | 6 (46.2) | 5 (71.4) | 0.353 |
| Underlying disease n(%) | 34 (64.2) | 15 (71.4) | 5 (41.7) | 8 (61.5) | 6 (85.7) | 0.225 |
| Hospitalization period (Days) | 15.30±12.14 | 13.5±10.16 | 17.08±9.2 | 14±13.68 | 19.85±18.74 | 0.400 |

CPT: Convalescent plasma therapy

*Table 2.* Effects of age, gender, underlying disease, and hospitalization period on the mortality rate

| variable | Total (n=50), n (%) | Death events, n (%) | | *p* |
|---|---|---|---|---|
| | | Yes (n=25) | No (n=26) | |
| Age, mean±SD, years | 59.08±16.57 | 62.82±15.63 | 56.42±17.06 | 0.179 |
| Male Gender | 35(67.3) | 18(72) | 16(61.5) | 0.555 |
| Underlying disease n(%) | 34(64.2) | 18(72) | 16(59.3) | 0.390 |
| Hospitalization period (Days) | 15.30±12.14 | 17.04±16.04 | 13.7±6.78 | 0.826 |



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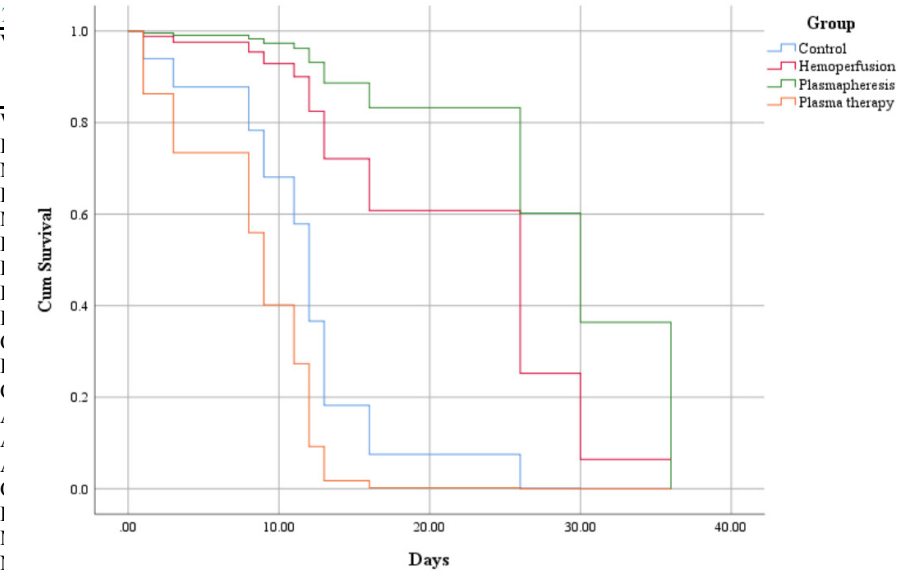


*Fig. 1.* Survival Function of Unadjusted model

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| $O_2$ sat | 83.83±8.47 | 85.43±8.94 | 84.98±4.76 | 1.000 | 82.75±13.55 | 0.606 | 73.83±18.14 | 0.317 | 0.628 | 0.799 |
| ALB | 3.71±0.56 | 3.29±.31 | 3.23±0.00 | 0.827 | 4.22±0.33 | 0.008* | 4.14±0.47 | 0.042* | 0.311 | 0.024* |

The significant values are marked with asterisks.
CPT. Convalescent plasma therapy; WBC. White blood cell; LYM. Lymphocyte; Neu. Neutrophil; Hb. hemoglobin; MCV. Mean corpuscular volume; HCT. Hematocrit; PLT. Platelet; LDH. Lactate dehydrogenase; ESR. Erythrocyte sedimentation rate; CRP. C-reactive protein; BUN. Blood urea nitrogen; Cr. Creatinine; AST. Aspartate aminotransferase; ALT. Alanine aminotransferase; ALP. Alkaline phosphatase; Ca. Calcium; PH. Phosphate; Mg. Magnesium; Na. Sodium; K. Potassium; PT. Prothrombin time; INR. International normalized ratio of coagulation time; PTT. Partial thromboplastin time; $O_2$ sat. Oxygen saturation; ALB. Albumin.

underwent plasma therapy was significantly higher than control patients (mean, 2.21 ± 1.69 vs 1.38 ± 0.68; $p$ = 0.021). Finally, the mean level of albumin in plasmapheresis (mean, 4.22 ± 0.33; $p$ = 0.008) and plasma therapy (mean, 4.14 ± 0.47; $p$ = 0.042) groups were significantly higher than the control group (3.29 ± 0.31).

The mean levels of laboratory markers were also compared between the 3 treated groups. As shown in Table 3, the mean levels of lymphocyte count, Hb, HCT, LDH, INR, and albumin have significant differences between the three groups ($p$ = 0.040, 0.013, 0.045, 0.004,0.036, and 0.024, respectively).

### Survival Analysis

Table 4 shows the effects of clinical and laboratory markers and treatments on patients' survival with or without modifying the effects of covariates such as age and gender. It is shown that no laboratory marker or treatment significantly affects the risk of mortality. However, as shown in Figure 1, patients who underwent plasmapheresis or hemoperfusion have better overall survival than those in control or plasma therapy groups.

### Before/After Analysis

In the next step, we compared the mean levels of laboratory markers before and after the treatment in each group (Table 5). In the control group, the data of the admission day and discharge day were considered before and after treatment, respectively. In the control group, mean levels of Hb (11.05 ± 1.61 vs 9.53 ± 2.32; $p$ = 0.009), MCV (86.62 ± 10.01 vs 84.34 ± 9.61; $p$ = 0.003), HCT (34.04 ± 3.89 vs 29.11 ± 5.78; $p$ = 0.004), and CRP (37.66 ± 62.4 vs 24.74 ± 43.46; $p$ = 0.046) were significantly decreased,

*Table 4.* Effects of laboratory markers and treatments in patients' survival

| variable | Adjusted HR | 95% CI | $p$ | Unadjusted HR | 95% CI | $p$ |
|---|---|---|---|---|---|---|
| $O_2$ sat | 0.097 | (0.004,2.35) | 0.152 | 0.91 | (0.81,1.01) | 0.098 |
| ALP | 0.41 | (0.143,1.19) | 0.102 | 0.98 | (0.97,1.00) | 0.090 |
| ALT | 0.30 | (0.077,1.23) | 0.096 | 1.00 | (0.96,1.03) | 0.880 |
| CRP | 0.57 | (0.167,1.95) | 0.372 | 0.99 | (0.95,1.04) | 0.900 |
| ESR | 0.65 | (0.185,2.33) | 0.517 | 0.94 | (0.88,1.01) | 0.130 |
| LDH | 1.14 | (0.96,1.35) | 0.128 | 1.00 | (0.99,1.004) | 0.300 |
| Group | | | | | | |
| Group (Hemoperfusion) | inf | (0.00,inf) | 0.09 | 0.192 | (0.01,2.36) | 0.192 |
| Group (Plasmapheresis) | 0.00 | (0.00,inf) | 0.571 | 0.07 | (0.001,3.57) | 0.071 |
| Group (CPT) | inf | (0.00,inf) | 0.096 | 2.37 | (0.028,200.34) | 0.914 |

HR. Hazard ratio; CI. Confidence interval; $O_2$ sat. Oxygen saturation; ALP. Alkaline phosphatase; ALT. Alanine aminotransferase; CRP. C-reactive protein; ESR. Erythrocyte sedimentation rate; LDH. Lactate dehydrogenase; CPT. Convalescent plasma therapy.

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while the mean BUN (18.36 ± 8.68 vs 31.36 ± 20.81; $p$ = 0.010) level was considerably increased after treatment. In the hemoperfusion group, the mean levels of lymphocyte count (13 ± 6.83 vs 8.49 ± 4.59; $p$ = 0.042), Hb (13.31 ± 1.34 vs 11.82 ± 2.25; $p$ = 0.037), MCV (83.15 ± 4.25 vs 81.46 ± 4.55; $p$ = 0.001), HCT (39.26 ± 3.65 vs 35.62 ± 4.22; $p$ = 0.008), CRP (32.75 ± 23.76 vs 13 ± 7.54; $p$ = 0.032), Cr (1.17 ± 0.289 vs 0.96 ± 0.16, $p$ = 0.003), and Mg (2.07 ± 0.13 vs 1.91 ± 0.28; $p$ = 0.042) were significantly diminished following the treatment. In the plasmapheresis group, the mean levels of WBC (6.66 ± 3.36 vs 9.81 ± 3.93; $p$ = 005) was significantly increased, while the Hb levels (12.25 ± 1.1 vs 11.19 ± 1.82; $p$ = 0.021) had a significant fall after treatment. Finally, the mean levels of Hb (11.64 ± 0.89 vs 9.74 ± 1.76; $p$ = 0.005) and HCT (34.55 ± 3.44 vs 29.4 ± 4.21; $p$ = 0.001) were significantly decreased after treatment in the plasma therapy group.

## Discussion

With the advent of COVID-19, efforts to decrease the complications and mortality rate started. The primary approach in confronting hyperinflammation is to prevent the unbridled increase of inflammatory mediators using immunosuppressors (20). In severe cases in which inflammatory mediators are already excessive, they should be filtered using plasma exchange modalities (10, 12). In COVID-19, numerous reports showed the safety and partial efficacy of hemoperfusion, plasmapheresis, and CPT in decreasing patients' complications and mortality (7-9, 16-18). Several groups in Iran, including ours, have published reports suggesting that the plasmapheresis and CPT might decrease inflammatory markers leading to patients' recovery and discharge (6, 10-13, 15).

We have shown in a case report that plasma exchange followed by CPT increased the oxygen saturation and decreased the body temperature and laboratory factors, including CRP, LDH, CPK, AST, BUN bilirubin, D-dimer, interleukin-6, and CD4+/CD8+ T cell ratio (12). Despite numerous reports on the safety and efficacy of plasma exchange therapies, there are not enough studies comparing their effects to conclude which treatment might be more efficacious for COVID-19 patients. The present study compared the effects of plasmapheresis or plasma exchange, CPT, and hemoperfusion on $O_2$ saturation and inflammatory factors in COVID-19 patients. We found that the Hb levels in control patients who received standard treatment were lower than the normal range and continued to decrease even after standard treatment. Although patients who underwent hemoperfusion, plasmapheresis, and plasma therapy showed higher Hb levels than controls, none of the treatments could increase the Hb levels. Instead, all patients experienced lower Hb levels following treatment.

Besides, MCV and HCT indices in the control group were lower than those in hemoperfusion, which were in the normal range. The lower levels of blood indices, such as Hb, HCT, and MCV, might be due to the changes in plasma levels following plasma exchange treatments. Similar studies have shown a fall in blood indices, such as Hbs and HCT, following plasma exchange (21, 22). Though, contradictory findings have also been reported (22).

Plasmapheresis and plasma therapy showed normal albumin level, which was higher than the control group. The reason for differences in albumin levels stems from the difference between the control and other groups before

*Table 5.* Comparing the laboratory markers and $O_2$ saturation before and after the treatments

| Variable | Control | | | Hemoperfusion | | | Plasmapheresis | | | CPT | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Before mean±SD | After mean±SD | *p* | Before mean±SD | After mean±SD | *p* | Before mean±SD | After mean±SD | *p* | Before mean±SD | After mean±SD | *p* |
| WBC | 9.34±7.41 | 7.85±3.53 | 0.371 | 7.32±4.93 | 496.09±482.17 | 0.333 | 6.66±3.36 | 9.81±3.93 | 0.005* | 7.84±3.86 | 10.47±5.08 | 0.320 |
| LYM | 10.95±3.72 | 14.52±9.84 | 0.183 | 13±6.83 | 8.49±4.59 | 0.042* | 15.63±5.11 | 12.3±7.49 | 0.225 | 11.28±4.6 | 10.14±5.01 | 0.541 |
| Seg | 75.88±24.31 | 71.29±27.2 | 0.604 | 82±8.43 | 85.05±6.28 | 0.246 | 79.9±5.72 | 81.76±8.15 | 0.531 | 84.14±4.63 | 83.85±5.08 | 0.907 |
| Hb | 11.05±1.61 | 9.53±2.32 | 0.009* | 13.31±1.34 | 11.82±2.25 | 0.037* | 12.25±1.1 | 11.19±1.82 | 0.021* | 11.64±0.89 | 9.74±1.76 | 0.005* |
| MCV | 86.62±10.01 | 84.34±9.61 | 0.003* | 83.15±4.25 | 81.46±4.55 | 0.001* | 83.96±7.9 | 80.57±17.37 | 0.424 | 86.08±4.19 | 86.04±3.31 | 0.951 |
| HCT | 34.04±3.89 | 29.11±5.78 | 0.004* | 39.26±3.65 | 35.62±4.22 | 0.008* | 62.93±95.9 | 33.63±5.07 | 0.288 | 34.55±3.44 | 29.4±4.21 | 0.001* |
| PLT | 188.47±64.72 | 171.52±101.09 | 0.366 | 153±43.82 | 188.75±89.74 | 0.266 | 169.84±64.49 | 194.69±78.67 | 0.313 | 164.57±46.35 | 152±60.94 | 0.695 |
| LDH | 848.78±347.28 | 682.52±335.58 | 0.095 | 883.36±591.64 | 1081.63±437.01 | 0.327 | 726.6±296.06 | 1017.4±582.97 | 0.136 | 934.13±585.74 | 1228.14±836.53 | 0.550 |
| ESR | 25.33±20.77 | 23.66±20.62 | 0.748 | 36.08±26.43 | 38.75±28.13 | 0.799 | 31.81±16.35 | 27.09±17.4 | 0.461 | 49.42±18.64 | 43.71±39.08 | 0.779 |
| CRP | 37.66±62.4 | 24.74±43.46 | 0.046* | 32.75±23.76 | 13±7.54 | 0.032* | 28.81±19.33 | 27.36±22.82 | 0.849 | 36.52±26.66 | 20.81±16.09 | 0.306 |
| BUN | 18.36±8.68 | 31.36±20.81 | 0.010* | 21.83±10.46 | 17.41±8.15 | 0.208 | 19.61±9.44 | 28.46±21.72 | 0.119 | 20.28±16.51 | 21.57±9.69 | 0.821 |
| Cr | 1.42±1.27 | 1.54±1.25 | 0.338 | 1.17±0.289 | 0.96±0.16 | 0.003* | 1.05±0.17 | 1.31±0.78 | 0.219 | 1.08±0.42 | 1.05±0.28 | 0.846 |
| AST | 57.11±30.64 | 63.16±40.11 | 0.568 | 49.9±12.03 | 57.63±18.19 | 0.346 | 66.41±44.18 | 60.75±38.96 | 0.449 | 57.71±27.02 | 50.14±30.2 | 0.175 |
| ALT | 98.56±135.44 | 86.5±126.45 | 0.347 | 47.3±26.97 | 68.2±50.49 | 0.246 | 56.33±30.94 | 66.41±42.48 | 0.247 | 71.14±53.94 | 72.71±56.96 | 0.717 |
| ALP | 355.88±312.2 | 257.16±173.56 | 0.151 | 191.63±63.15 | 202±66.57 | 0.524 | 207.15±57.61 | 182.61±78.65 | 0.166 | 248.83±121.15 | 256.33±115.38 | 0.178 |
| Ca | 9.29±0.62 | 9.35±0.8 | 0.524 | 9.43±0.71 | 33.38±71.48 | 0.344 | 9.25±0.78 | 9.23±0.69 | 0.888 | 9.23±0.67 | 9.26±0.72 | 0.893 |
| Ph | 4.13±1.45 | 4.11±1.36 | 0.901 | 4.1±1.96 | 4.46±1.66 | 0.722 | 3.78±1.03 | 4.11±0.87 | 0.437 | 3.96±0.57 | 4.05±0.81 | 0.846 |
| Mg | 1.97±0.36 | 2±0.31 | 0.651 | 2.07±0.13 | 1.91±0.28 | 0.042* | 1.99±0.27 | 2.04±0.15 | 0.410 | 2.01±0.35 | 1.95±0.22 | 0.655 |
| Na | 139.42±4.36 | 140.47±2.71 | 0.387 | 141.1±3.31 | 140.4±2.27 | 0.601 | 233.61±341.15 | 141.23±2.71 | 0.348 | 142.28±7.27 | 140±4.16 | 0.567 |
| K | 4.26±0.64 | 4.23±0.44 | 0.797 | 4.22±0.42 | 4.14±0.34 | 0.710 | 4.13±0.43 | 4.15±0.68 | 0.942 | 4.38±0.6 | 3.92±0.28 | 0.125 |
| PT | 13.14±1.15 | 13.78±1.87 | 0.196 | 12.8±0.81 | 19.02±16.39 | 0.244 | 12.78±0.69 | 12.71±0.75 | 0.529 | 13.86±0.96 | 15.1±2.56 | 0.235 |
| INR | 1.16±0.182 | 1.23±0.252 | 0.272 | 2.26±3.89 | 1.31±0.32 | 0.428 | 1.1±0.09 | 1.13±0.17 | 0.491 | 1.28±0.14 | 5.92±10.81 | 0.347 |
| PTT | 36.88±5.6 | 39.05±11.81 | 0.518 | 31.58±6.2 | 33.25±14.68 | 0.686 | 30.94±9.61 | 29.35±8.88 | 0.089 | 35.33±4.88 | 36.66±8.33 | 0.785 |
| $O_2$ sat | 75.96±22.47 | 87.28±10.94 | 0.430 | 85.85±8.91 | 87.28±9.67 | 0.726 | 90.33±5.5 | 64.66±49.07 | 0.424 | 50±62.22 | 62.5±3.53 | 0.833 |
| ALB | 3.15±0.36 | 3.07±0.66 | 0.786 | 4.1±0 | 2.7±0 | - | - | - | - | 4.4±0 | 4.4±0 | - |

The significant values are marked with asterisks.

WBC. White blood cell; LYM. Lymphocyte; Neu. Neutrophil; Hb. hemoglobin; MCV. Mean corpuscular volume; HCT. Hematocrit; PLT. Platelet; LDH. Lactate dehydrogenase; ESR. Erythrocyte sedimentation rate; CRP. C-reactive protein; BUN. Blood urea nitrogen; Cr. Creatinine; AST. Aspartate aminotransferase; ALT. Alanine aminotransferase; ALP. Alkaline phosphatase; Ca. Calcium; PH. Phosphate; Mg. Magnesium; Na. Sodium; K. Potassium; PT. Prothrombin time; INR. International normalized ratio of coagulation time; PTT. Partial thromboplastin time; O2 sat. Oxygen saturation; ALB. Albumin; CPT. Convalescent plasma therapy

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starting the treatment. It has also been reported that the serum albumin is significantly increased following plasma exchange (21). However, it has been observed that the LDH levels of patients who underwent hemoperfusion or plasma therapy were significantly higher than control patients. Surprisingly, it has been observed that the plasma exchange treatments could not decrease the LDH levels. LDH is commonly reported to fall following plasma exchange treatments (12, 13). The controversial finding seen in our study might stem from the fact that the patients in the control group had a better prognosis and fewer complications than those who underwent plasma exchange modalities. Hence, these patients were in the middle of a hyperinflammatory response course, and it took more time to alleviate their inflammatory responses (23).

On the other hand, CRP showed a decrease following treatment, especially in the control and hemoperfusion groups. It might indicate that the CRP is faster than LDH to increase or decrease after inflammation (23). Accordingly, CRP is an acute inflammation marker that starts rising within the first 6 to 8 hours of inflammation (24). Besides, it has been known that CRP quickly decreases after reducing inflammation (23, 25). However, LDH is a general indicator of acute or chronic tissue damage (24). We found that BUN was significantly increased in the control treatment so that it surpassed the normal range.

It seems that hemoperfusion was more able among plasma exchange therapies to mitigate the inflammatory markers. This finding is confirmed by the results of survival analysis, showing that the patients in hemoperfusion and plasmapheresis groups had better survival than those in the control and plasma therapy groups. One could ask why the plasma exchange treatments could not significantly affect the patients' outcomes compared with the control group. As mentioned earlier, the patients in the control group had moderate COVID-19, while those who received plasma exchange treatments had the severe form. Ergo, comparing outcomes among 3 plasma exchanged groups is more reliable than comparing them with the control group.

In the field of plasma-mediated therapy of COVID-19, numerous case reports, case series, and uncontrolled studies showed a relative improvement in the clinical outcomes following treatment (7, 8, 12, 26). However, controlled studies in this era are still scarce. Recently, a placebo-controlled trial on 333 patients showed no significant differences in the clinical outcomes and mortality rate between COVID-19 patients who received CP and those who received a placebo (27). This study confirmed our findings that the majority of laboratory markers in our groups were not significantly different. In another clinical trial, it has been indicated that the CPT in patients within 1 week after the symptom onset could not prevent disease progression (28).

Although the inflammatory cytokines and mediators, such as interleukin (IL)-1, IL-6, IL-8, tumor necrosis factor (TNF)-α, and interferon (IFN)-γ, are reduced by performing the above treatments (6, 29), the possibility of reduced concentrations of anti-SARS-CoV2 antibodies (IgG, IgM, and IgA) (6) and other therapeutic medications is a disadvantage of exchange/filtration strategies. Besides, the concern of transfusion-related complications might be a challenge in CPT (7).

## Conclusion

Overall, our findings showed that plasma exchange therapeutics have relatively positive roles in decreasing inflammation. However, we agree with recent studies in doubting the significant benefits of plasma exchange therapeutics in considerably decreasing the mortality rate. More controlled multiarm studies are required to compare the different types of plasma exchange therapeutics and determine their mere effects.

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### *Ethical Approval*

This study was ethically approved by the local Ethics Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.REC.1399.10). Given the study's retrospective nature, all the procedures performed were part of routine care.

### *Authors Contributions*

S.S.A, AH., and F.S.M: conception and design, H.M., K.N., and S.P.: acquisition of data, or analysis and interpretation of data. SH.A., K.H, and M.H.G: drafting the article or revising it critically for important intellectual content. All authors approved the final version to be submitted for publication.

### *Conflict of Interests*

The authors declare that they have no competing interests.

## References

1. Khorramdelazad H, Kazemi MH, Najafi A, Keykhaee M, Emameh RZ, Falak R. Immunopathological similarities between COVID-19 and influenza: Investigating the consequences of Co-infection. Microb Pathog. 2021;152:104554.
2. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382(18):1708-20.
3. Kazemi MH, Dehaghi BK, Roshandel E, Bonakchi H, Parkhideh S, Mehdizadeh M, et al. Association of HScore Parameters with Severe COVID-19: A Systematic Review and Meta-Analysis. Iran J Med Sci. 2021;46(5):322.
4. Statistics GC-. WHO Coronavirus (COVID-19) Dashboard [Available from: https://covid19.who.int.
5. Statistics IC-. WHO COVID-19 statistics (Islamic Republic of Iran) [Available from: https://covid19.who.int/region/emro/country/ir.
6. Vardanjani AE, Moayedi S, Golitaleb M. COVID-19 pandemic hemoperfusion therapy versus plasma exchange therapy in intensive care. Iran J Allergy Asthma Immunol. 2020:7-9.
7. Li L, Zhang W, Hu Y, Tong X, Zheng S, Yang J, et al. Effect of convalescent plasma therapy on time to clinical improvement in patients with severe and life-threatening COVID-19: a randomized clinical trial. JAMA. 2020;324(5):460-70.
8. Franchini M, Marano G, Velati C, Pati I, Pupella S, Liumbruno GM.



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[ DOI: 10.47176/mjiri.36.142 ]

Operational protocol for donation of anti-COVID-19 convalescent plasma in Italy. Vox Sang. 2020.
9. Zhang L, Zhai H, Ma S, Chen J, Gao Y. Efficacy of therapeutic plasma exchange in severe COVID-19 patients. Br J Haematol. 2020.
10. Tabibi S, Tabibi T, Conic RR, Banisaeed N, Streiff MB. Therapeutic plasma exchange: a potential management strategy for critically ill COVID-19 patients. J Intensive Care Med. 2020;35(9):827-35.
11. Vardanjani AE, Ronco C, Rafiei H, Golitaleb M, Pishvaei MH, Mohammadi M. Early hemoperfusion for cytokine removal may contribute to prevention of intubation in patients infected with COVID-19. Blood Purif. 2021;50(2):257-60.
12. Roshandel E, Sankanian G, Salimi M, Jalili A, Salari S, Sadeghi A, et al. Plasma exchange followed by convalescent plasma transfusion in COVID-19 patients. Transfusion and Apheresis Science. 2021:103141.
13. Hashemian SM, Shafigh N, Afzal G, Jamaati H, Tabarsi P, Marjani M, et al. Plasmapheresis reduces cytokine and immune cell levels in COVID-19 patients with acute respiratory distress syndrome (ARDS). Pulmonology. 2020.
14. Khorramdelazad H, Kazemi MH, Azimi M, Aghamajidi A, Mehrabadi AZ, Shahba F, et al. Type-I interferons in the immunopathogenesis and treatment of Coronavirus disease 2019. Eur J Pharmacol. 2022:175051.
15. Mousavi-Roknabadi RS, Haddad F, Fazlzadeh A, Kheirabadi D, Dehghan H, Rezaeisadrabadi M. Investigation of plasma exchange and hemoperfusion effects and complications for the treatment of patients with severe COVID-19 (SARS-CoV-2) disease: A systematic scoping review. J Med Virol. 2021;93(10):5742-55.
16. Balagholi S, Dabbaghi R, Eshghi P, Mousavi SA, Heshmati F, Mohammadi S. Potential of therapeutic plasmapheresis in treatment of COVID-19 patients: Immunopathogenesis and coagulopathy. Transfus Apher Sci. 2020:102993.
17. Keith P, Day M, Choe C, Perkins L, Moyer L, Hays E, et al. The successful use of therapeutic plasma exchange for severe COVID-19 acute respiratory distress syndrome with multiple organ failure. SAGE Open Med Case Rep. 2020;8:2050313X20933473.
18. Lung T, Kazatchkine MD, Risch L, Risch M, Nydegger UE. A consideration of convalescent plasma and plasma derivatives in the care of Severely-ill patients with COVID-19. Transfus Apher Sci. 2020:102936.
19. Bakhshaei P, Kazemi MH, Golara M, Abdolmaleki S, Khosravi-Eghbal R, Khoshnoodi J, et al. Investigation of the cellular immune response to recombinant fragments of filamentous hemagglutinin and pertactin of Bordetella pertussis in BALB/c mice. J Interferon Cytokine Res. 2018;38(4):161-70.
20. Mirtaleb MS, Mirtaleb AH, Nosrati H, Heshmatnia J, Falak R, Emameh RZ. Potential therapeutic agents to COVID-19: An update review on antiviral therapy, immunotherapy, and cell therapy. Biomed Pharmacother. 2021:111518.
21. Patale D, Bajpai M, Maiwall R, Kumar G. Hemodynamic stability in liver failure patients undergoing therapeutic plasma exchange. J Clin Apher. 2020;35(2):86-93.
22. Deng J, Zhou F, Wong CY, Huang E, Zheng E. Efficacy of therapeutic plasma exchange for treatment of autoimmune hemolytic anemia: a systematic review and meta-analysis of randomized controlled trials. J Clin Apher. 2020;35(4):294-306.
23. Petel D, Winters N, Gore GC, Papenburg J, Beltempo M, Lacroix J, et al. Use of C-reactive protein to tailor antibiotic use: a systematic review and meta-analysis. BMJ Open. 2018;8(12):e022133.
24. Poggiali E, Zaino D, Immovilli P, Rovero L, Losi G, Dacrema A, et al. Lactate dehydrogenase and C-reactive protein as predictors of respiratory failure in CoVID-19 patients. Clin Chim Acta. 2020;509:135-8.
25. Pepys MB, Hirschfield GM. C-reactive protein: a critical update. The J Clin Investig. 2003;111(12):1805-12.
26. Hegerova L, Gooley TA, Sweerus KA, Maree C, Bailey N, Bailey M, et al. Use of convalescent plasma in hospitalized patients with COVID-19: case series. Blood. 2020;136(6):759-62.
27. Simonovich VA, Burgos Pratx LD, Scibona P, Beruto MV, Vallone MG, Vázquez C, et al. A randomized trial of convalescent plasma in Covid-19 severe pneumonia. N Engl J Med. 2021;384(7):619-29.
28. Korley FK, Durkalski-Mauldin V, Yeatts SD, Schulman K, Davenport RD, Dumont LJ, et al. Early convalescent plasma for high-risk outpatients with Covid-19. N Engl J Med. 2021.
29. Faqihi F, Alharthy A, Alodat M, Asad D, Aletreby W, Kutsogiannis DJ, et al. A pilot study of therapeutic plasma exchange for serious SARS CoV-2 disease (COVID-19): a structured summary of a randomized controlled trial study protocol. Trials. 2020;21:1-3.

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