Original Article

Effects of Plasma Therapy on Laboratory Factors and Clinical Improvement of COVID-19 Patients

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ABSTRACT

Objectives: Over 50 million confirmed cases and 1.5 million fatalities worldwide have been linked to the COVID-19 pandemic. Researchers have used convalescent plasma (CP) from recovered patients, which includes neutralizing antibodies, to develop therapeutics for virus neutralization and prevention. This study assessed the effectiveness of CP using several clinical and laboratory variables.

Methods: The intervention group received two doses of CP on the day of hospitalization, while the control group received standard care. Clinical and analytical data were documented and evaluated before plasma therapy and on the third and fifth days after therapy. The results were measured in the patient's blood using the ELISA method.

Results: The present study showed that the ICU hospitalization times for the control and CP groups were similar, with a slightly lower mortality rate in the CP group (6.2% vs. 8.2%, $p > 0.05$). There was no significant association between COVID-19 and clinical factors such as blood pressure, heart rate (HR), respiration rate (RR), and temperature. The blood serum urea, serum LDH, ALT, PTT, PLT, and IL-6 were significantly higher in the CP group than in the control group ($p < 0.05$). Our results indicated that there was no difference in blood pH, PO_2, HCO_3, ESR, WBC counts, serum troponin, Na, AST, CRP, D-dimer, and PT between patients in the CP and control groups.

Conclusion: Overall, in certain instances, CP therapy may help individuals with COVID-19 recover. In general, additional research is required to determine the efficacy of plasma treatment in COVID-19 patient care.

Keywords: COVID-19; Plasma Therapy; Clinical Improvement; Laboratory Factors

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Introduction

The coronavirus disease 2019 (COVID-19) pandemic has been the biggest global health crisis in recent years. Infections caused by a highly contagious virus have led to many deaths (1). By October 2020, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) had caused over 41 million confirmed cases of COVID-19, including about one million deaths worldwide (2). Over 700,000 confirmed cases of COVID-19 and 40,000 deaths have been reported in Iran (3). The most common symptoms of COVID-19 are fever, cough, fatigue, and myalgia. However, the disease sometimes progresses, and patients experience dyspnea, respiratory dysfunction, shock, heart disease, hypertension, and multiple organ damage, which may ultimately lead to death (4). Age, obesity, a weakened immune system, and underlying diseases such as diabetes are known risk factors associated with disease severity (5). As the SARS-CoV-2 virus first emerged at the end of 2019, there has not been an effective therapeutic option for COVID-19. COVID-19 convalescent plasma (CP) has been authorized for off-label emergency use and phase III studies, and researchers are attempting to create medicines. SARS-CoV-2 spike protein-neutralizing antibodies have been found in CP from recuperating patients, which may help COVID-19 patients who are critically ill by neutralizing the virus and stopping its reproduction (6-8). CP is beneficial in treating Middle East respiratory syndrome, influenza A (H1N1), avian influenza (H5N1), and Ebola (9-13). A recently published Mayo Clinic observational study of 20,000 patients with CP revealed a favorable safety pattern (14). According to Cheng et al., 80 SARS sufferers who received CP had a lower mortality rate than the total rate of fatalities. Furthermore, they found promising results in individuals treated with CP during the SARS outbreak in 2003. They also discovered that out of 80 patients, those who received CP within two weeks of symptom onset fared better than those who received CP later (15). By delivering passive neutralizing antibodies during the first viremia phase, CP can reduce SARS-CoV-2 replication and treat the condition without a permanent cure. However, there are differences in antibody concentrations and specificities among recovered individuals who may become donors with CP (16, 17). Therefore, this study aimed to evaluate the effect of CP on clinical and laboratory factors in patients with COVID-19 in Isfahan.

Materials and Methods

This descriptive clinical trial study was performed on patients with COVID-19 hospitalized (n= 194) in the Al-Zahra and Milad hospitals, from the first of April to the end of July 2021 in Isfahan, Iran. Patients were included according to the WHO Guidance, which defined severe COVID-19 as any of the two criteria out of five as follows: ventilated patient within 24 hours, oxygen saturation in the resting state level less than 90% in the resting state, respiratory rate ≥30 beats/min, partial pressure of oxygen/fractional inspired oxygen ratio (PaO_2)/(FiO2) ≤300 mmHg, and lung infiltrates ≥50% within 24–48 hours.

The inclusion criteria for plasma recipients were clinical manifestations of COVID-19 confirmed by real-time reverse transcriptase-polymerase chain reaction (RT-PCR), absolute lymphocyte count $>1\times10^9$ /L, clinically serious respiratory problems, and O_2>90. Exclusion criteria were blood group incompatibility, history of coagulopathy, renal failure, renal replacement therapy (RRT), allergy to plasma, pregnancy, viral hepatitis, cirrhosis, cancer, uncontrolled hypertension, heart and liver disorders, diabetes, disagreement of the patients in the project, lactation, and septic shock. According to the Iran Blood Transfusion Organization guidelines, the inclusion criteria for plasma donors were recovery from COVID-19 and normal laboratory test results. The Medical University of Isfahan Ethics Committee approved the present study (ethics code: IR.MUI.MED.REC.1399.1085 and Scientific code: 199601).

Intervention

Patients in the intervention and control groups were categorized into pre-intervention and post-intervention groups. Patients in the intervention group (n=97) received two doses of 220-280 ml of CP on the first day of hospitalization, along with standard care, whereas the control group (n=97) received only standard care. The standard of care was based on the treatment guidelines for the management of COVID-19, which were set by the World Health Organization and the Ministry of Health of Iran. Supportive protocols were used in some patients. The main drugs used included remdesivir, dexamethasone, and other drugs such as pantoprazole, famotidine, lomefloxacin, prednisolone, heparin, ceftriaxone, montelukast, atorvastatin, and insulin were also used in some patients. Depending on the patient's condition, several of the aforementioned items were used simultaneously in the care of patients. The CP used in this study was prepared according to the SOPs of the Iran Blood Transfusion Organization in the Isfahan Blood Transfusion Center and was obtained from Isfahan blood transfusion at the request of the attending physician and through the blood bank laboratory of Al-Zahra and Milad Hospital. Melting and injection of convalescent plasma were also performed according to international standards. Patients underwent plasma therapy according to the consent form.

Clinical and Laboratory parameters

Clinical and laboratory parameters were recorded

and tested in three stages as follows: before receiving plasma, on the third and fifth days after plasma therapy. Outcomes included time to improvement in clinical parameters such as the number of days to normalization of body temperature (<37°C), oxygen saturation (>94% on room air), radiological improvement on CT lung scan, and the concentration of inflammatory factors (ESR, CRP, and IL-6), coagulation factors (PT and PTT), D-dimer, troponin, and lymphocyte count on different days pre-and post-treatment. A total of 5 cc of patient blood was collected for biomarker measurements at the baseline of the intervention.

Available commercial kits were used to determine the following tests: serum creatinine; BUN; LDH; AST; ALT; ALP and CRP concentrations (Pars Azmun, Tehran, Iran). Serum IL-6 levels were quantified using an available ELISA kit (Monobind, Lake Forest, California USA).

Statistical analysis

The independent t-test and chi-square test were used to compare the related characteristics between the two groups at baseline. Statistical analyses of data were performed using SPSS version 22.0 (Statistical Product and Service Solutions, Chicago, IL, USA). Statistical significance was set at $p \leq 0.05$.

Results

Study Population

A total of 194 patients were enrolled in the present study. They were assigned to either the CP group (n=97, pre- and post-intervention) or the control group (n=97, pre- and post-intervention). The mean age was 53.9 ± 13.38 years in the control group and 63.35 ± 14.11 years in the CP group, respectively. In the control group, 47 (48.3%) were men, and in the CP group, 29 (40.2%) were men, indicating a slightly higher percentage of men than women in both groups (Table 1) (Figure 1).

The hospitalization times in the ICU for patients in the control and CP groups were the same. The mortality

Table 1: Information on age and gender of treatment (CP) and control groups

Variables	CP group (n = 97)	Control group (n = 97)	P-value
Age (mean ± SD)	63.35 ± 14.11	53.9 ± 13.38	0.41
Gender (female)	29 (29.8%)	47 (48.3%)	0.095

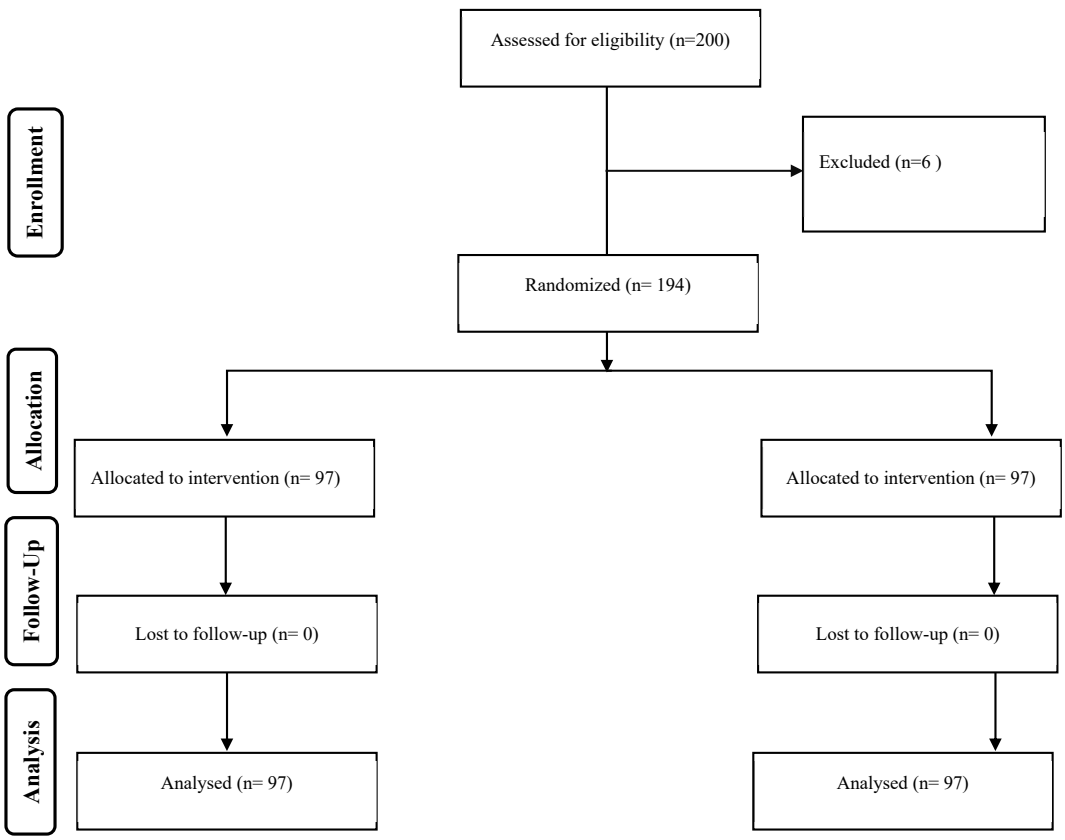

Figure 1: Summary of patient flow diagram

rate in the CP group was slightly lower than that in the control group, but this was not significant (6.2% vs. 8.2%, p >0.05) (Table 2).

In addition, there was no significant association between COVID-19 and clinical factors such as blood pressure, heart rate (HR), respiration rate (RR), and temperature. Except for the satO2% of the patients in the CP group, which was significantly reduced (p<0.05), no significant change was observed in the other parameters of the CP group compared to the control group (Table 3).

As shown in Tables 4, 5, 6, and 7, the serum LDH, serum urea, ALT, PTT, PLT, and IL-6 levels were significantly higher in the CP group than in the control group (p <0.05). In contrast, the PO2, K, Cr, ALP, and Lymph were lower than those in the control group. Our results indicated that there was no difference in blood

Table 2: Primary outcomes of treatment (CP) and control groups

Variables	CP group (n = 97)	Control group (n = 97)	P-value
Days of hospitalization (mean (min-max))	8.87 (3-13)	8.77 (4-12)	0.44
Days of ICU admission (mean (min-max))	7.36(3-12)	7.06(2-12)	0.7
Number of deaths	8 (3.2%)	6 (6.2%)	0. 21

Table 3: Comparison of the clinical parameters between and control and treatment (CP) groups

Variable	Control group (Mean± SD)	CP group (Mean ± SD)	p-value
Systolic Blood pressure (mmHg)			
SPB at baseline	119.91 ± 16.06	125.36 ± 14.41	0.10
SBP on day 3	113.66 ± 20.61	120.55 ± 14.13	0.55
SBP on day 5	114.01 ± 13.27	120.91 ± 16.40	0.45
SBP change (Between baseline and day 5)	-5.89	-4.45	
Diastolic blood pressure (DBP) (mmHg)			
DBP at baseline	73.86 ± 10.1	77.24 ± 10.07	0.64
DBP on day 3	80.68 ± 9.48	73.75± 10.41	0. 18
DBP on day 5	72.61 ± 9.19	73.29 ± 11.53	0.74
DBP change (Between baseline and day 5)	-1.25	-3.95	
Heart rate (HR)(beats/minute)			
HR at baseline	75.71 ± 21.99	78.58 ± 20.86	0.21
HR on day 3	71.01 ± 20.88	77.51 ± 19.28	0.2
HR on day 5	70.17± 21.84	75.62 ± 19.09	0.11
HR change (Between baseline and day 5)	-5.54	-2.96	
Respiration rate (RR)(breaths/minute)			
RR at baseline	26.87 ± 18.55	23.41 ± 15.62	0.07
RR on day 3	26.82 ± 18.64	25.35 ± 21.83	0.73
RR on day 5	27.34 ± 19.77	23.16 ± 15.76	0.03
RR change (Between baseline and day 5)	0.47	-0.25	
Temperature (T)(^{0}C)			
T at baseline	36.89 ± 0.60	36.95 ± 0.65	0.93
T in day 3	36.75 ± 4.6	36.75 ± 0.68	0.98
T in day 5	36.98 ± 1.12	36.64 ± 0.64	0.15
T change (Between baseline and day 5)	0.09	-0.31	
O2 saturation (SatO2) (%)			
SatO2 at baseline	88.78 ± 5.48	76.46 ± 18.26	0.00
SatO2 on day 3	88.38 ± 5.96	78.7 ± 13.77	0.00
SatO2 on day 5	89.11 ± 6.25	83.05 ± 14.51	0.00
SatO2 change (Between baseline and day 5)	0.33	6.59	
Blood pH (mmHg)			
pH at baseline	7.34 ± 0.07	7.40 ± 0.057	0.17
pH on day 3	7.3 ± 0.53	7.41 ± 0.07	0.66
pH on day 5	7.36 ± 0.15	7.37 ± 0.06	0.35
pH change (Between baseline and day 5)	0.02	-0.03	
Blood HCO3(mEq/l)			
HCO3 at baseline	23.28 ± 6.57	30.53 ± 9.2	0.00
HCO3 on day 3	25.87 ± 7.45	30.53 ± 9.2	0.00
HCO3 on day 5	26.63 ± 7.34	30.75 ± 9.97	0.08
HCO3 change (Between baseline and day 5)	3.35	0.22	
Pressure of O2 (PO2) (mmHg)			
PO2 at baseline	48.4 ± 20.04	41.41 ± 16.99	0.00
PO2 on day 3	51.63 ± 20.62	43.16 ± 9.36	0.00
PO2 on day 5	51.67 ± 19.48	50.3± 24.23	0.04
PO2 change (Between baseline and day 5)	3.27	9.16	

Table 4: Comparison of kidney-related factors (urea, creatinine, sodium and potassium) between control and CP treatment groups.

Variable	Control group (Mean ± SD)	CP group (Mean ± SD)	p-value
Serum urea (Ur)(mg/dl)			
Ur at baseline	46.76 ± 34.56	43.31 ± 26.6	0.069
Ur in day 3	54.8 ± 38.77	57.74 ± 38.86	0.32
Ur in day 5	53.08 ± 32.86	64.34 ± 32.95	0.00
Ur change (Between baseline and day 5)	6.32	21.03	
Serum creatinine (Cr) (mg/dl)			
Cr at baseline	1.79 ± 2.5	1.16± 0.32	0.00
Cr in day 3	1.52 ± 1.41	1.16 ± 0.87	0.00
Cr in day 5	1.38 ± 1.41	1.07 ± 0.4	0.01
Cr change (Between baseline and day 5)	-0.41	-0.09	
Serum sodium (Na)(mEq/l)			
Na at baseline	138.14 ± 3.95	137.34 ± 4.04	0.76
Na in day 3	138.6 ± 5.42	138.72 ± 4.7	0.39
Na in day 5	139.35 ± 3.83	139.37 ± 4.64	0.68
Na change (Between baseline and day 5)	1.21	2.03	
Serum potassium (K) (mEq/l)			
K at baseline	4.45 ± 0.66	4.18 ± 0.56	0.05
K on day 3	4.54 ± 0.51	4.09 ± 0.62	0.00
K on day 5	4.42 ± 0.67	3.96 ± 0.54	0.00
K change (Between baseline and day 5)	-0.03	-0.22	

Table 5: Comparison of factors related to liver and heart (LDH, ALT, AST, ALP and troponin) between control and CP treatment groups.

Variable	Control group (Mean ± SD)	CP group (Mean ± SD)	p-value
Serum LDH(IU/L)			
LDH at baseline	666.11 ± 291.31	654.86 ± 289.44	0.64
LDH on day 3	607.62 ± 235.65	641.58 ± 332.12	0.02
LDH on day 5	562.59 ± 233.22	626.61 ± 344.03	0.009
LDH change (Between baseline and day 5)	-103	-28.25	
Serum ALT(IU/L)			
ALT at baseline	53.34 ± 47.83	51.71 ± 29.19	0.27
ALT on day 3	41.94 ± 31.77	47.98 ± 33.03	0.08
ALT on day 5	37.69 ± 27.29	45.87 ± 28.10	0.00
ALT change (Between baseline and day 5)	-15.65	-5.84	
Serum AST(IU/L)			
AST at baseline	63.13 ± 59.19	58.42 ± 36.3	0.2
AST on day 3	57.17 ± 38.59	67.04 ± 39.72	0.05
AST on day 5	65.07 ± 39.17	69.2 ± 42.76	0.97
AST change (Between baseline and day 5)	1.94	10.8	
Serum ALP(IU/L)			
ALP at baseline	209.87 ± 232.21	203.67 ± 93.85	0.2
ALP on day 3	195.86 ± 257.82	182.69 ± 16.58	0.05
ALP on day 5	207.32 ± 247.48	185.92 ± 82.52	0.00
ALP change (Between baseline and day 5)	-2.55	-17.75	
Serum troponin (Trop)(ng/L)			
Trop at baseline	18.25 ± 56.28	14.97 ± 66.1	0.78
Trop on day 3	22.3 ± 33.24	10.99 ± 17.99	0.01
Trop on day 5	9.6 ± 13.29	6.34 ± 11.93	0.72
Trop change (Between baseline and day 5)	-8.65	-5.59	

pH, PO2, HCO3, ESR, WBC counts, serum troponin, Na, AST, CRP, D-dimer, and PT between patients in the CP and control groups (Tables 4-7).

Discussion

The COVID-19 outbreak has brought convalescent plasma (CP) treatment back into the spotlight. The Food and Drug Administration has recently asserted that administering and researching innovative CP medications may have a clinical impact on COVID-19 during public health emergencies (18, 19). Although convalescent plasma has received considerable interest in the treatment of patients with COVID-19, there is still no conclusive proof of its effectiveness (20). Therefore, this study was designed to assess the efficacy of CP on clinical and laboratory factors in patients with COVID-19.

The present study showed that patients in the control and CP groups spent approximately the same amount of time

Table 6: Comparison of factors related to inflammation (CRP, IL-6, ESR, WBC and Lymphocyte count) between control and CP treatment groups.

Variable	Control group (Mean ± SD)	CP group (Mean ± SD)	p-value
Serum CRP (mg/dl)			
CRP at baseline	61.73 ± 37.85	51.98 ± 21.74	0.00
CRP in day 3	44.21 ± 35.03	41.15 ± 24.23	0.02
CRP in day 5	22.83 ± 31.93	23.13 ± 22.19	0.5
CRP change (Between baseline and day 5)	-38.9	-28.85	
Serum IL6 (pg/mL)			
IL6 at baseline	28.82 ± 35.36	41.37 ± 27.27	0.00
IL6 on day 3	19.8 ± 20.99	35.41 ± 19.73	0.00
IL6 on day 5	13.08 ± 21.78	30.48 ± 28.04	0.00
IL6 change (Between baseline and day 5)	-15.74	-10.89	
Serum ESR (mm/hr)			
ESR at baseline	43.27± 25.13	51.41 ± 44.94	0.00
ESR on day 3	42.9 ± 24.09	45.86 ± 23.79	0.66
ESR on day 5	34.13 ± 21.97	33.52 ± 21.36	0.3
ESR change (Between baseline and day 5)	-9.14	-17.9	
WBC count (in 1µL)			
WBC at baseline	8683.57 ± 4567.99	8858.63 ± 441.68	0.6
WBC on day 3	9699.06 ± 4185.4	10267.13 ± 4821.04	0.01
WBC on day 5	10103.29 ± 4033.67	10102.23 ± 3225.9	0.3
WBC change (Between baseline and day 5)	-7673.28	1243.6	
Lymphocyte count (Lymph) (in 1µL)			
Lymph at baseline	1221.09 ± 1267.34	896.35 ± 437.59	0.00
Lymph on day 3	1223.7 ± 869.10	760.27 ± 513.099	0.00
Lymph on day 5	1364.32 ± 883.83	753.71 ± 486.37	0.00
Lymph change (Between baseline and day 5)	143.23	-142.64	

Table 7: Comparison of thrombosis related factors (Platelet, PT, PTT and D-dimer) between control and CP treatment groups.

Variable	Control group (Mean ± SD)	CP group (Mean ± SD)	p-value
Platelet count (PLT)(10^3/µl)			
PLT at baseline	178.41 ± 55.67	228.6 ± 85.28	0.00
PLT on day 3	204.6 ± 73.74	258.44 ± 95.59	0.00
PLT on day 5	226.42 ± 76.81	267.96 ± 111.61	0.00
PLT change (Between baseline and day 5)	48.01	39.36	
Prothrombin Time (PT)(Sec)			
PT at baseline	13.17 ± 1.89	14.49 ± 4.06	0.2
PT on day 3	13.57 ± 7.34	13.85 ± 5.39	0.5
PT on day 5	12.7 ± 1.9	13.71 ± 5.62	0.25
PT change (Between baseline and day 5)	-0.47	-0.78	
Partial Thromboplastin Time (PTT)(Sec)			
PTT at baseline	30.85 ± 13.42	36.51 ± 8.55	0.00
PTT in day 3	29.99 ± 9.47	33.13 ± 9.02	0.00
PTT in day 5	29.55±5.31	31.91±7.87	0.01
PTT change (Between baseline and day 5)	-1.3	-4.6	
Serum D-dimer (µg/L)			
D-dimer at baseline	1592.51 ± 1239.23	749.96 ± 889.58	0.00
D-dimer on day 3	1401.16 ± 974.26	1257.26 ± 1265.4	0.00
D-dimer on day 5	1372.63 ± 979.52	1234.81 ± 1334.65	0.07
D-dimer change (Between baseline and day 5)	-219.88	484.85	

in the hospital and the ICU. In the CP group, the mortality rate was somewhat, albeit not significantly, reduced. Clinical variables were not significantly correlated with COVID-19. Since the onset of symptoms, early transfusion of CP into patients with severe COVID-19 has been associated with a lower death rate compared to other standard treatments, but some claimed that it had no statistically significant impact on death rates (7, 21-26).

In agreement with this, CP use during the SARS-CoV-2 epidemic was reported in a study of five patients with COVID-19 who received CP. Three patients were extubated, 60% left the hospital, and the other two remained stable after 37 days (27). According to another study, patients with CP had a mortality rate of 23% and a discharge rate of 77.8% (28). In this context, it was discovered that the clinical signs were alleviated, and neutralizing antibody levels rose quickly in five cases

within 3 days after transfusing CP. C-reactive protein and lymphocyte counts, among other metrics, have also improved (29).

In a case report experiment, Zhang et al. observed that all four severely sick patients who received CP between days 11 and 18 after admission recovered (30). Additionally, according to another study, CP did not achieve the predetermined effectiveness goals; however, high-titer CP may have helped COVID-19 hospitalized patients early in the pandemic when other therapies were not being used, indicating a heterogeneous therapeutic impact over time (31). Given the findings of Gharbharan et al., no significant differences were found between the two groups in terms of reducing illness severity within 15 days or death incidence (23).

In addition, in a controlled experiment, giving older persons with SARS-CoV-2 infection high-titer convalescent plasma within 72 hours of the onset of moderate symptoms slowed the disease's development to a more serious disease. In this regard, they found that this straightforward and affordable action might lessen the strain on the healthcare system and even save lives. Therefore, they stated that until vaccinations are readily available, early injections of convalescent plasma can offer at-risk patients an alternative to wellness (32).

Another group illustrated that the developmental period was shorter in the CP-treated group, but the difference was not statistically significant. In addition, compared to the control group, more than half of the patients in the CP-treated group showed recovery (33). Another research team found that the mortality rate was marginally lower in the CP-treated group than in the control group. It is stated that there was not a statistically significant correlation between CP and the amount of time spent in the hospital (34).

These inconsistencies between our outcomes and previous investigations may result from variations in the amount of anti-COVID-19 antibodies, the dosage of injected CP to patients, the frequency and timing of administration, the number of patients under study, and deviations in age and sex.

In line with the findings of our experiment, in a randomized controlled trial, the percentage of patients released from the hospital within 28 days had no discernible effect on allocation to convalescent plasma (35). The use of convalescent plasma therapy combined with conventional treatment, as opposed to conventional therapy, independently did not produce a statistically significant difference in the duration of clinical recovery within 28 days in patients with severe COVID-19 (33). In addition, the combined administration of CP therapy and normal care did not substantially increase mortality or clinical recovery within 28 days according to a randomized experiment by Li et al. Furthermore, after CP therapy in patients with severe COVID-19, researchers compared the CFR in these patients with that in a control group of 11 critically ill patients. They found no statistically significant changes in COVID-19 patients who did not receive CP (36).

In the present study, in comparison to the control group, HCO3, ESR, PLT, serum LDH, ALT, AST, D-dimer, and IL-6 levels in the CP group were considerably higher. Moreover, in a carefully monitored trial, the IL-6, IL-10, IP-10, fatty acid, and glycerophospholipid levels were higher in individuals with severe COVID-19, according to their results. Increased IgG, IgA, and anti-S1-SARS-CoV-2 antibodies, and a temporary change in the cytokine profile were caused by COVID-19 CP. Activated, effector, and effector memory CD4+ and naïve B cells and IL-6/IFN- and IL-6/IL-10 proportions were reduced in plasma recipients (37).

In general, it should be considered that transfusion-related acute lung injury (TRALI), hemolysis, and allergic and anaphylactic responses are possible side effects of plasma transfusion. Owing to donor screening and testing, microbial transfer rates are minimal in wealthy nations. Pathogen reduction processes can be used in single-unit parts or plasma pools to lower the risk of viral transmission and coagulation factors. Certain products, such as intravenous immunoglobulin and coagulation factors, have particular side effects. The pool of plasma units and subsequent production dilutes the low prion infectivity in an infected person's blood (38).

Moreover, screening, authorizing, gathering, and monitoring donors, as well as having access to suitable assay facilities, are administrative and technical challenges when managing convalescent plasma (CP) transfusion in underdeveloped nations. Systemic and transfusion-specific challenges, such as donor recruiting and collection capacities and ineffective healthcare systems, constrain CP therapy (CPT) utilization. Donors must adhere to strict guidelines, such as passing a SARS-CoV-2 test and being clear of COVID-19 symptoms (39). The absence of neutralization antibodies in donor plasma, which lasts for weeks to months, might impede the generation of CP for treating patients. The timing of administration matters when using CPT since there is no set transfusion dosage and large infusion volumes are needed. It could be challenging to treat a large number of infected individuals if there is a significant difference between recovered and current cases. The generation of antibodies may be lowered by viral alterations, especially those involving coronaviruses (40-43). The scientific community is deeply concerned about CPT's effectiveness in combating new SARS-CoV-2 variants because the virus has undergone several modifications since its first emergence in 2019. Patients undergoing CPT should be closely monitored to ensure there are no unanticipated adverse effects and to evaluate the practicality and potential hazards of CPT in the field (39).

Conclusion

Overall, it is not possible to draw a firm conclusion regarding the value of plasma therapy in the management of COVID-19 patients because of the conflicting results between the parameters of our study and those of earlier studies; therefore, additional research should be conducted to generate solid conclusions.

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Conflict of interests

None.

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