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# Convalescent Plasma for COVID-19- is it Time to Say Goodbye? A Single-Center, Retrospective, Observational Study from Northern India

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***Authors' contributions***

*This work was carried out in collaboration among all authors. Authors RS, MD and AB- Conceptualization, study design, data collation, analysis and writing the manuscript; RP, AB, SN, RKS, AV, DGP, TG, GA, SK, MG, SG, were involved in clinical care including ICU management; RS, MD, RY, GPT, AEB were transfusion medicine experts and contributed in CP donor selection, collection and maintaining records. All authors have seen and approved the final draft.*

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## ABSTRACT

**Background:** COVID-19 pandemic continues threatening the world with no effective treatment to tackle the menace. Till date, there is conflicting evidence on efficacy of CP in reducing COVID-19 related mortality. The objective of this study was to see disease progression and 7, 14 and 28-day mortality after CP therapy and analyze CP efficacy with/without Remdesivir.

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**Materials and Methods:** A retrospective single-centre observational study done from August 20, 2020, to 20 November 2020. Records of 294 COVID-19 patients with moderate to severe disease given CP therapy were analysed based on disease progression and length of hospital stay, further subcategorized on age, clinical profile, risk factors, ward/ICU, ventilatory support and co-administration of Remdesivir.

**Results:** Lowest 7-day mortality rate was seen within age group 20-40 years (0%) and was highest in ≥61 years (24.3%). 87 patients on ventilatory support showed higher 28day mortality (48.28%) compared to non-ventilated (10.14%), (P<0.00001). Lesser 7-day mortality was seen in early CP therapy ≤3 days of admission (P=0.01). Patients requiring ICU admission showed higher 14 and 28-day mortality compared to ward P=0.001%). Median (IQR) length of hospital stay from CP transfusion was shorter, 4 (3 to 9) days in group 2 (CP only) compared to 7 (4 to 12) days in group1 (CP+Remdesivir ).

**Conclusion:** CP therapy in ≤3 days of hospital admission in COVID-19 patients with moderate to severe infection not on ventilatory support showed reduction in mortality and length of hospital stay. Length of hospital stay was shorter in the CP-only group as compared to the CP+ Remdesivir group.

*Keywords: convalescent plasma; COVID-19; ARDS; CP therapy.*

## 1. INTRODUCTION

As the COVID-19 pandemic continues to rampage the world, returning every time with more vengeance, researchers are struggling to find an effective treatment to tackle this menace. The unpredictable disease course throws a tough challenge in deciding which patient will benefit from which investigational therapy. A large number of affected patients progress into acute respiratory distress syndrome (ARDS) about 7–10 days after onset of COVID-19 due to rapid viral replication, a stormy increase of pro-inflammatory cytokines-chemokine response, and inflammatory cell infiltrates [1]. Most promising therapeutics option considered at the very onset of the pandemic was convalescent plasma (CP) collected from a COVID-19 recovered individual and transfused into infected patients along with standard supportive care including oxygen supplementation, high dose steroids, intensive care for critically ill patients. Several retrospective observational studies in mid-2020 suggested an important role of CP for patients hospitalised with COVID-19 [2-4]. Evidences suggest that CP contains receptor binding domain-specific antibodies, which have potent antiviral activity [5,6]. Initial randomized trials on use of CP in hospitalized patients with severe COVID -19 reported weak evidence of clinical efficacy [7-9]. Observational studies, have reported more positive results and have suggested measurable surrogate virologic outcomes with good efficacy [10,11]. Though India is currently driving the largest vaccination program in the world, with 21,85,46,667 vaccine[12] doses administered, there is still a long way to go. March 2021 saw a sharp upsurge in numbers with 28,307,832 confirmed cases of which 1,793,645 are still active [12]. The second wave of COVID-19 has left healthcare overwhelmed with the exponentially growing number of patients referring to hospitals with ARDS symptoms.

The aim this study was to evaluate efficacy of CP in limiting disease progression in COVID-19 patients with moderate to severe disease. This study is unique as apart from comparisons amongst different age groups, patients with and without co-morbidities. we have tried to compare the effect of CP therapy along with Remdesvir vis-à-vis CP therapy alone on disease outcome.

## 2. MATERIALS AND METHODS

Study design: This is a single-centre retrospective observational study spanning over a period of three months, from August 20, 2020 to 20 November 2020. COVID-19 patients admitted at BLK Super Speciality Hospital with moderate to severe disease with increasing oxygen requirement non-responsive to steroids, given CP therapy were included in the study. Clinical and laboratory data was retrieved from patients' files. Total 311 admitted patients received CP during this period of which 17 patients were excluded due to unavailability of sufficient clinical data. Records of remaining 294 patients were retrieved and analysed.

All patients received treatment as per physician's discretion, institutional protocol, and/or national guidelines for management of COVID-19 issued by the government from time to time. "Drugs used included" Azithromycin, Doxycycline, Ivermectin, Remdesivir, anticoagulants, other

broadspectrum antibiotics, steroids (Methylprednisolone or Dexamethasone in equivalent doses), Tocilizumab and oxygen support along with ventilation (invasive or non-invasive) as required.

## 2.1 Donor Selection Criteria

Eligibility criteria for CP donors were per standard blood banking practices [13] and additionally:

1. Donors in the 18–60-year age group
2. Prior diagnosis of COVID-19 documented by a laboratory test
3. Complete resolution of symptoms at least 28 days before donation and within 4 months of testing positive for COVID-19 infection
4. Only males and nulliparous female donors of weight > 50 kg
5. Donors were tested for Anti-SARS-CoV-2 IgG (Spike) antibodies on VITROS-3600 chemiluminescent immunoassay (CLIA) in accordance with manufacturer instructions. Based on Current FDA guidance through the CP Emergency Use Agreement (EUA) recommending high titer CP. CP was collected from donors with IgG ≥ 9.5 S/Co [14].

## 2.2 Patient Characteristics

1. COVID-19 infection was established by real-time polymerase chain reaction test (rRT-PCR) and/or rapid antigen testing. CP therapy was administered to patients ≥18 years, with progressively increasing oxygen requirement despite use of steroids or at a high risk of progression to severe or life-threatening conditions. Patients were classified as moderate (symptomatic with $SpO_2$ 90-94%on room air and respiratory rate ≥24 breaths/minute) or severe diseases (patients with clinical signs of pneumonia, severe respiratory distress, respiratory rate >30 breaths/minute and $SpO_2$ <90% on room air) were as per Clinical Management Protocol: COVID-19-Ministry of Health and Family Welfare (MOHFW) [15].
2. Patients with history of allergic reaction to blood component transfusion were not eligible.

## 2.3 Plasma Collection

CP was obtained by apheresis using Amicus ™ (Fresenius Kabi) or Trima Accel ® (Terumo BCT, Lakewood, CO) cell separators. 400-450 ml plasma was collected from each donor and divided into two 200-225-ml aliquots and stored at less than -30˚C. Units were thawed at 37˚C for issue.

## 2.3 Plasma Transfusion

A transfusion dose was 4 to 13 ml/kg (usually 200 ml single dose) given slowly over not less than 2 hours with additional doses, if clinically justified.

## 2.4 Statistical Analysis

Descriptive statistical analysis, like percentage, median, 95% confidence interval for proportion and Interquartile range (IQR) were used. Regression analysis, Odd's ratio was done to assess categorical variables. P-value <0.05 was considered statistically significant [16].

## 2.5 Objectives

Primary objective was to see disease progression and 7, 14 and 28-day mortality after CP therapy. If severity of disease increased leading to mortality, outcome was considered to be unfavourable and if disease progression/mortality could be prevented, then outcome was favourable. Assessment of secondary outcomes was done on basis of decrease in oxygen requirement assessed by reduced ventilator support, decrease in stay in ICU/hospital, resolution of symptoms like fever, cough, and breathlessness. Patients who responded to CP therapy, but required transfusion of second aliquot after 24 hours were also included. We also analysed CP efficacy with Remdesivir administration, prior to staring Remdesivir and after Remdesivir administration.

## 3. RESULTS

A total of 294 consecutive patients who received CP therapy were included in the study. Median age of patients was 59 years (range, 18-88years) 225 were males and 69 females. 174 patients prescribed CP had moderate and 120 had

**Table1. Overall clinical outcomes according to WHO Ordinal scale for clinical improvement**

| | N (%) | Co-morbidities | N (%) | Outcome | N (%) |
|---|---|---|---|---|---|
| Moderate Disease | 174(59.2%) | Present | 120(68.9%) | Improvement seen | 93(77.5%) |
| | | | | Deteriorated | 27(22.5%) |
| | | Absent | 54(31%) | Improvement seen | 51(94.4%) |
| | | | | Deteriorated | 3(5.5%) |
| Severe Disease | 120(40.8%) | Present | 84(70%) | Improvement seen | 54(64.3%) |
| | | | | Deteriorated | 30(35.7%) |
| | | Absent | 36(30%) | Improvement seen | 33(91.6%) |
| | | | | Deteriorated | 3(8.3%) |

**Table 2. All cause crude mortality**

| | N | % |
|---|---|---|
| Total cases observed | 294 | |
| 7-day all cause crude mortality | 42 | 14.28 |
| 14 days all cause crude mortality | 57 | 19.38 |
| 28 days all cause crude mortality | 63 | 21.42 |

**Table 3. Crude Mortality (7, 14 and 28 day) of patients with IgG transfused with COVID-19 Convalescent Plasma**

| | Sample No | Events No | Estimate95 % CI | Sample No | Events No | Estimate 95% CI | Sample No | Events No | Estimate 95% CI |
|---|---|---|---|---|---|---|---|---|---|
| | 7 days Mortality | | | 14* days Mortality | | | 28** days Mortality | | |
| **Overall mortality** | | | | | | | | | |
| **Age in years** | | | | | | | | | |
| 20-40 | 48 | 0 | 0% (0 - 7.4) | 48 | 0 | 0% (0 - 7.4) | 48 | 0 | 0% (0 - 7.4) |
| 41-60 | 123 | 12 | 9.76% (5.14 - 16.42) | 123 | 15 | 12.2% (6.99 - 19.32) | 123 | 18 | 14.63% (8.91 - 22.14) |
| 61-80 | 111 | 27 | 24.32% (16.68 - 33.38) | 111 | 39 | 35.14% (26.31 - 44.77) | 111 | 39 | 35.14% (26.31 - 44.77) |
| >80 | 12 | 3 | 25% (5.49 - 57.19) | 12 | 3 | 25% (5.49 - 57.19) | 12 | 6 | 50% (21.09 - 78.91) |
| **On ventilation prior to infusion** | | | | | | | | | |

| | Sample No | Events No | Estimate95 % CI | Sample No | Events No | Estimate 95% CI | Sample No | Events No | Estimate 95% CI |
|---|---|---|---|---|---|---|---|---|---|
| Yes | 87 | 30 | 34.48% (24.61 - 45.44) | 87 | 39 | 44.83% (34.15 - 55.87) | 87 | 42 | 48.28% (37.42 - 59.25) |
| No | 207 | 12 | 5.8% (3.03 - 9.91) | 207 | 18 | 8.7% (5.23 - 13.39) | 207 | 21 | 10.14% (6.39 - 15.09) |
| **Days to transfusion from admission** | | | | | | | | | |
| ≤ 3days | 165 | 12 | 7.27% (3.81 - 12.36) | 165 | 24 | 14.55% (9.55 - 20.87) | 165 | 27 | 16.36% (11.07 - 22.91) |
| 4-6 days | 87 | 24 | 27.59% (18.54 - 38.21) | 87 | 27 | 31.03% (21.55 - 41.86) | 87 | 30 | 34.48% (24.61 - 45.44) |
| ≥7 days | 42 | 6 | 14.29% (5.43 - 58.54) | 42 | 6 | 14.29% (5.43 - 58.54) | 42 | 6 | 14.29% (5.43 - 58.54) |
| **Admitted with complications (shock, septicaemia, ARDS)** | | | | | | | | | |
| Yes | 72 | 15 | 20.83% (12.16 - 32.02) | 72 | 24 | 33.33% (22.66 - 45.43) | 72 | 27 | 37.5% (26.36 - 49.7) |
| No | 222 | 27 | 12.16% (8.17 - 17.2) | 222 | 33 | 14.86% (10.46 - 20.24) | 222 | 36 | 16.22% (11.62 - 21.74) |
| **Comorbidity** | | | | | | | | | |
| None | 96 | 9 | 9.38% (4.38 - 17.05) | 96 | 12 | 12.5% (6.63 - 20.82) | 96 | 12 | 12.5% (6.63 - 20.82) |
| ≤ 2 | 135 | 24 | 17.78% (11.74 - 25.29) | 135 | 30 | 22.22% (15.52 - 30.18) | 135 | 36 | 26.67% (19.43 - 34.96) |
| ≥ 3 | 63 | 9 | 14.29% (6.75 - 25.39) | 63 | 15 | 23.81% (13.98 - 36.21) | 63 | 15 | 23.81% (13.98 - 36.21) |
| **Remdesivir therapy along with CP Transfusion** | | | | | | | | | |
| Given ≥3 | 87 | 18 | 20.69% | 87 | 24 | 27.59% (18.54 | 87 | 24 | 27.59% (18.54 - |

| | Sample No | Events No | Estimate95 % CI | Sample No | Events No | Estimate 95% CI | Sample No | Events No | Estimate 95% CI |
|---|---|---|---|---|---|---|---|---|---|
| days before CP | | | (12.75 - 30.71) | | | - 38.21) | | | 38.21) |
| Started with CP | 135 | 12 | 8.89% (4.68 - 15.01) | 135 | 15 | 11.11% (6.35 - 17.66) | 135 | 15 | 11.11% (6.35 - 17.66) |
| Started after 1st dose CP | 21 | 3 | 14.29% (3.05 - 36.34) | 21 | 6 | 28.57% (11.28 - 52.17) | 21 | 9 | 42.86% (21.82 - 65.98) |
| **ICU/WARD (At the time of admission)** | | | | | | | | | |
| ICU | 176 | 42 | 23.86% (17.77 - 30.86) | 176 | 55 | 31.25% (24.49 - 38.66) | 176 | 59 | 33.52% (26.6 - 41.01) |
| WARD | 118 | 0 | 0% (0 - 3.08) | 118 | 2 | 1.69% (21 - 5.99) | 118 | 4 | 3.39% (0.93 - 8.45) |

** Including the 7 day mortality cases; ** including the 7 day and 14 day mortality cases*

**Table 4. Regression analysis**

| | 7 Day Mortality | | | 14 Day Mortality | | | 28 Day Mortality | | |
|---|---|---|---|---|---|---|---|---|---|
| | *B | **p | Adjusted Odds Ratio | B | p | Adjusted Odds Ratio | B | p | Adjusted Odds Ratio |
| Age | 0.030 | 0.218 | 1.031 | 0.030 | 0.183 | 1.030 | 0.047 | 0.034 | 1.048 |
| Sex (male) | 1.797 | 0.004 | 6.033 | 2.782 | 0.000 | 16.156 | 3.280 | 0.000 | 26.586 |
| Co-Morbidity (present) | -0.338 | 0.633 | 0.713 | 0.362 | 0.587 | 1.436 | 0.513 | 0.439 | 1.671 |
| Remdesivir (not taken) | | 0.431 | | | 0.237 | | | 0.036 | |
| Remdesivir (Before CP) | -0.354 | 0.545 | 0.702 | -0.664 | 0.265 | 0.515 | -1.456 | 0.021 | 0.233 |
| Remdesivir (After CP) | -0.810 | 0.200 | 0.445 | -1.073 | 0.090 | 0.342 | -1.470 | 0.020 | 0.230 |
| Ventilation (yes) | 2.008 | 0.000 | 7.448 | 2.690 | 0.000 | 14.725 | 2.940 | 0.000 | 18.920 |
| Complication (present) | 0.475 | 0.353 | 1.609 | 1.032 | 0.033 | 2.806 | 1.223 | 0.013 | 3.398 |
| CP transfused on day 4 or later | 1.194 | 0.011 | 3.301 | 0.395 | 0.387 | 1.484 | 0.433 | 0.360 | 1.542 |
| ICU/ward (ICU) | 19.266 | 0.996 | 2.33E+08 | 2.868 | 0.001 | 17.598 | 2.167 | 0.001 | 8.731 |
| Constant | -24.742 | 0.994 | 0.000 | -9.000 | 0.000 | 0.000 | -9.474 | 0.000 | 0.000 |

**unstandardized regression coefficient **p value*

**Table 5. Comparison of convalescent plasma therapy and Remdesivir with convalescent plasma therapy alone**

| Outcome | Group1 (CP+ Remdesivir) | Group 2 (CP alone) |
|---|---|---|
| N | 243 | 51 |
| Length of hospital stay | Median (IQR) | Median (IQR) |
| From admission | 11 (7 to 16) | 10 (7 to 16) |
| From CP transfusion | 7 (4 to 12) | 4 (3 to 9) |

Mortality due to COVID-19 is multifactorial, therefore, multifactor based evaluation of mortality rate was done (Table 3) comparing outcomes according to age, complications at time of admission, presence of co-morbidities (≤2 and ≥ 3), ward or ICU admission, co-administration Remdesivir and ventilator support before CP therapy. 48 patients (16.33%) were in age group of 20-40 years and had 7 day and 14-day mortality and 28-day mortality of 0%. Mortality was higher (9.76, 12.20, and 14.63%) in 41-60 years age group and highest in the ≥61 years (24.3, 34.14 and 36.5%). 87 (29.59%) patients were already on the ventilator support before receiving CP and mortality significantly high (P <0.001) across the length of hospital stay compared to those who were not on ventilator support. 165 patients received CP therapy within 3 days of admission, 87 patients received within 4-6 days and 42 patients were administered CP on or after 7 days of admission. A significant clinical improvement with a decline in oxygen requirement with lesser 7-day mortality was seen in cases who received CP therapy within 3 days of admission (P value = 0.01). People who received CP on day 4 or later were 1.5 times more likely to deteriorate than the patients who received CP in the first 3 days of admission. No statistically significant correlation was observed when patients with or without co morbidities were compared, however patients with co morbidities were more likely to deteriorate than the patients without comorbidities (Table 4).

243 patients received CP therapy along with Remdesivir, of which 87 received Remdesivir 3 or more days before CP and 7, 14, 28-day mortality was 20.69%, 27.59%, and 27.59% respectively. 135 patients received Remdesivir with CP and 7, 14, 28-day mortality was 8.89%, 11.11%, and 11.11% respectively. 21 patients received Remdesivir after CP with a 7, 14, 28day mortality of 14.29%, 28.57% and 42.86% respectively. In ICU patients 28-day mortality was high (33.52%) and mortality was lower in those in wards (3.39%).

243 patients received CP therapy plus Remdesivir (group 1) and 51 patients received CP therapy alone (group 2). Median (IQR) length of hospital stay from admission in group1 was 11(7 to 16) days and in group2 was 10 (7 to 16) days. Median (IQR) length of hospital stay from CP transfusion was shorter 4 (3 to 9) days) in group2 (CP only) compared to7 (4 to 12) days in group1 (CP + Remdesivir) (p=0.0031(Table 5).

## 4. DISCUSSION

Numerous case series and observational studies have since been published, with variable results on efficacy of CP in hospitalized patients with COVID-19 [18-24]. We, in our study, analysed the efficacy of CP based on 7, 14 and 28-day mortality and also compared disease outcomes in different age groups, time of administration, effect of existing co-morbidities and disease severity, and comparison of efficacy of CP therapy along with Remdesvir vis-à-vis CP therapy alone. These objectives were chosen as COVID-19 has caused significant mortality and it continues to thrust a substantial burden on healthcare systems. In most viral illnesses, primary immune response develops around 10 days of illness, followed by viral clearance [25]. Based on this, it was hypothesized that transfusion of CP during early stage of disease maybe be more effective.

In our study outcomes were favourable after early CP transfusion, when transfused in ≤3 days after admission, compared to ≥4 days (P=0.011) for 7-day mortality) with reduction in length of hospital stay and lower 7-day mortality in pre-critical and moderate cases. These findings are in consensus with the revised European Commission Guidelines on CP, which

recommend early transfusion of CP with high neutralizing antibody titres' [26]. Shenoy AG et al. too in their study have reported that patients with COVID-19, who received early CP therapy, had a decreased risk of death at 7 and 14-days. 7-day mortality was statistically better for CP cases (9·1%) compared to control cases (19·8%, P < 0·001) and continued at 14 days (14·8% vs. 23·6%, P = 0·01). Additionally 72 hours post CP transfusion significant number of transited from nasal cannula to room air (P = 0·02) [27]. A multicentre clinical trial done in Iran, has reported good efficacy of CP therapy in 115 patients out of 189 COVID-19 patients, in seven hospitals across Iran. All-cause mortality, total hospitalization days, and patients need for intubation between the two groups showed that 98 (98.2 %) of patients who received CP were discharged from the hospital compared to 56 (78.7 %) patients in the control group. Length of hospitalization days was significantly lower in the CP group(9.54 days) compared to control group(12.88 days) and only 7% in the CP group required intubation compared to 20 % in control group [28].

Salazar et al., in their study, have reported significant mortality reduction when CP was given within 72 hour of admission in severe and life threatening COVID-19 patients (2.7% vs 8.9%; p = 0.04; PE = 3.64, 95% CI: 1.05–12.62). They too reported that clinical improvement was less frequent in patients who received invasive ventilation at any time or were >70 years [29]. In another study, Hegerova et al., also found better disease outcomes in cases who received CP transfusion early within the first seven days of hospitalization [30]. Joyner M.J et al. in an observational study in 35,322 patients found reduced 7-day and 30-day mortality in patients who received early CP therapy. 7-day mortality rate was 8.7%[95% CI 8.3%-9.2%] in patients transfused within 3 days of diagnosis compared to 11.9%[11.4%-12.2%] in patients transfused ≥4days after diagnosis (p<0.001). Trend continued in 30-day mortality (21.6% vs. 26.7%, p<0.0001) [31]. In contrast an open-label parallel-arm phase II multicentre randomized controlled trial (PLACID Trial) conducted in India by Agarwal A. et al., done in 464 patients of moderate severity COVID-19, did not find any difference in mortality or progression to severe disease between plasma versus no plasma group (14.5% vs13.5%; OR = 1.06, 95% CI: 0.61–1.83) [32].

We found more beneficial effects of CP therapy in pre-critical, moderate to severe cases compared to critical cases on ventilator support (<0.00001). On the contrary, a multi-centre, retrospective observational study done by Budhiraja S et al. found that CP therapy significantly reduced mortality in elderly patients COVID-19 with severe disease compared to control group (25.5% vs 33.2%; p=0.026). Patients on ventilator support had lower mortality in the plasma arm (37.2% vs 49.3%; p = 0.009); especially on invasive mechanical ventilation (63.9% vs. 82.9%; p = 0.014) [33].

We observed higher mortality in severe disease (27.5%) as compared to moderate disease (17.2%). All-cause crude 7-day, 14 day and 28-day mortality, was lesser in the younger patients with least in age group 20-40 years (0%, 0%, 0%) followed by 41-60 years (9.76%, 12.20%, 14.63%) and still higher in 60- 80 years (24.32%, 35.14%, 35.14%) with maximum mortality rate in elderly, >80 years (25%, 25%,50%). Patients already on ventilator support had significantly higher mortality (<0.00001) compared to those not ventilated. 72 patients were admitted with complications like shock, septicaemia or ARDS. 7, 14, 28-day mortality rate was higher in these patients (20.83%, 33.33%, 37.50%) compared to patients admitted without complications (12.16%, 14.86%, and 16.22%) and the 14-day and 28-day mortality was statistically significant in (P= 0.03 and P= 0.01 respectively). A trend to higher 14, 28 days mortality despite CP therapy was seen with increase in number of co morbidities;, however, difference was not statistically significant. Tworek, Adam, et al. however, suggest that high-risk patients with co morbidities and severe COVID-19 symptoms benefit more with CP therapy. They found significantly lower mortality rate in plasma group versus control group (13.7% vs. 34.3 %, p = 0.001) and a significant difference in cumulative incidence of death between the two groups (p < 0.001). CP treatment was associated with lower risk of death (OR=0.25 CI95 [0.06; 0.91], p=0.041), however, no significant differences in ICU stay, ventilator time, and hospitalization time between the two groups [34].

Several case reports of successful concomitant use of Remdesivir and CP in treating patients with severe COVID-19 infections have been reported in literature [35-38]. A single clinical trial conducted in Nepal has evaluated treatment of COVID-19 in hospitalized patients with Remdesivir, CP or both. They reported a higher discharge rate of 84% for Remdesivir only recipients (N=910) compared to 39% for plasma

only recipients (N=59), and 54.4% for plasma with Remdesivir group (N=114) recipients. Difference in rates was possibly attributed to the fact that patients in the CP only and CP+ Remdesivir recipients had severe to life-threatening infections (CP 98.3%; CP+ Remdesivir 92.1%) and were admitted to the ICU (CP 91.8%; CP+ Remdesivir 94.6%) compared to Remdesivir alone recipients (57.5%,) [39]. In our study, we found that length of hospital stay was shorter in the CP only group as compared to the CP+ Remdesivir group (Table 5). According to time of administration of Remdesivir with CP, we found lesser 7, 14 and 28-day mortality in cases where Remdesivir and CP therapy was given together at same time than those who received Remdesivir before administration of CP therapy .

Recent interim recommendations issued by the AABB, who have endorsed not only safety of CP, but have also recommended use of high-titer CP as close to symptom onset as possible as the main predictors of its effectiveness. They have stated that CP is unlikely to provide benefit for patients with late-stage disease or on mechanical ventilation [40].

## 5. CONCLUSION

To conclude, early CP infusion in less than 3 days of hospital admission in younger COVID-19 patients with moderate to severe infection not on ventilator support was associated with a significant reduction in mortality and length of hospital stay compared to patients who were transfused CP later suggesting that it is too early to say bye to CP therapy and like any other therapy it should be considered. Also length of hospital stay was significantly shorter in the CP only group compared to CP+ Remdesivir group. Patients fared better when given Remdesivir along with CP therapy or earlier than CP therapy. Mortality was higher in those who received Remdesivir after CP therapy.

## CONSENT

Written informed consent was obtained from patient or legally authorized surrogate before CP transfusion.

## ETHICAL APPROVALS

Study was approved by the Institutional Ethics Committee vide IEC. no. EC/AARCE/Approval Letter/September/2020/95.

## LIMITATIONS

Clinical management of a potentially life-threatening illness with an unpredictable clinical course and concomitant use over other drugs was the main contributor to this limitation. We did not study an interaction with co-administration of other drugs and their observed effect in our patients. Nevertheless, the numerous evidences in current literature agree with our observation on efficacy of CP therapy when administered early (within 3 days of admission) in COVID-19 treatment. Also this research was done at that particular point of time when healthcare system was at the verge of crashing, may be this study and other studies reviewed could enlightens the future path as far as COVID 19 is concerned.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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