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## **Evaluation of the efficacy of convalescent plasma in moderate to severe COVID-19 during 2020-2021: a retrospective observational study**

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## **Abstract**

Convalescent plasma therapy (CPT) is one of the treatment modalities used for COVID-19. Initial smaller studies showed the usefulness of CPT in COVID-19, but larger studies showed that it is not effective. This is a retrospective observational study conducted between 1st June 2020 and 31st July 2021 at a tertiary hospital in Noida, India. Our analysis was done on 213 COVID-19 patients, comprising 170 cases who were given convalescent plasma and 43 controls who did not get CPT. Outcomes analyzed were improvement in PaO<sub>2</sub>:FiO<sub>2</sub> ratio (PFR) by day 5 of CPT, 28-day mortality, and level of inflammatory markers. Mean PFR before plasma transfusion was comparable between CPT and control groups (142.11±73.99 vs. 151.11±88.87, p=0.56). There was no significant difference in mean PFR after 5 days of CPT between cases and the control group (187.02±102.34 vs. 160.29±83.39, p=0.206). 28-day mortality was 47.05% in the CPT group and 37.20% in the control group (p=0.246). Mortality amongst the subgroup of patients on invasive mechanical ventilation was 89.74% in cases and 80% in controls (p=0.518). No significant difference was found in levels of serum ferritin, interleukin-6, and C-reactive protein between the two groups. Convalescent plasma does not have a significant effect on day 5 PFR and 28-day mortality. Our study could not find any subgroup of patients who would benefit from CPT. This study reinforces that CPT does not benefit moderate to severe patients with COVID-19.

**Key words:** convalescent plasma therapy, COVID-19, mortality, PaO<sub>2</sub>:FiO<sub>2</sub> ratio, retrospective study.

## **Introduction**

COVID-19 (Coronavirus disease-19) virus saga started off as a mere scare, but soon caused a pandemic of gigantic proportions. Even few years later it is still causing local outbreaks. World Health Organization has only recently declared that the pandemic is over. Initial days of COVID-19 were difficult with no specific treatment or vaccines. Soon many therapeutic options came up, some helped while many did not and faded away. Convalescent plasma therapy (CPT) was one such treatment modality that was studied extensively [1-6].

The SARS-CoV-2 virus belongs to the Coronaviridae family and previous reports indicated usefulness of CPT in treatment of Corona virus infections like severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) [7,8]. Hence, transfusion of convalescent plasma from individuals who had recovered from the SARS-CoV-2 infection came up as a possible treatment option.

In the initial phase of the COVID-19 pandemic, many reports indicated positive effects achieved by transfusion of convalescent plasma [1,2]. In the United States of America an Extended Access Program, outside of a controlled trial, led to CPT in over half a million patients with reduction in risk of death in non-intubated patients [3].

In India, CPT was widely used by many hospitals. Indian Council of Medical Research (ICMR) initiated a randomized control trial to evaluate use of convalescent plasma in COVID-19 patients. The study was approved by COVID-19 National ethics committee on 29<sup>th</sup> April 2020 [4]. In our hospital we used CPT for the first time on 1<sup>st</sup> July 2020. On 17<sup>th</sup> November 2020, ICMR released evidence-based advisory to address use of convalescent plasma in COVID-19 patients and also defined criteria for potential donors and recipients [9].

Later ICMR released the results of PLACID trial [open label phase II multicenter randomized controlled trial (RCT) of CPT for moderate COVID-19 adult patients] [4]. It showed that CPT did not reduce progression to severe disease or all-cause mortality, but the study did not include severe or life-threatening COVID-19 patients. Similar smaller RCTs also documented no significant benefit of CPT in hospitalized COVID-19 patients [10-13]. A randomized trial of CPT by Ling Li et al. that enrolled patients with severe and life-threatening COVID-19 was stopped early due to slow enrollment [10]. Kurtz et al. observed that in subgroup of patients of COVID-19 without moderate to severe ARDS, mortality was significantly less in convalescent plasma group [14]. Due to varied results in subgroups and limitations of the published studies, there remains uncertainty whether CPT is beneficial in specific populations of COVID-19 patients.

ICMR in its advisory on 17<sup>th</sup> May 2021 ruled against CPT for COVID-19 patients [15]. We followed the advisory and stopped advising CPT to our patients thereafter. As clinicians we

had clinical impression that CPT was useful in our patients. We hypothesized that transfusion of convalescent plasma in moderate to severe COVID-19 patients results in improvement in PaO<sub>2</sub>:FiO<sub>2</sub> ratio (PFR), reduction in mortality and improvement in inflammatory variables. The present study was therefore designed to retrospectively evaluate the above hypothesis.

## **Materials and Methods**

### ***Study design***

It is a retrospective observational study.

### ***Patient enrolment***

#### *Inclusion criteria*

1. Adult patients (>18 years) admitted to the COVID High Dependency Unit (HDU)/Intensive Care Unit (ICU) from 1<sup>st</sup> June 2020 to 31<sup>st</sup> July 2021 with COVID-19 infection. Diagnosis was based on a positive reverse transcriptase polymerase chain reaction (RT-PCR) [on nasopharyngeal/throat swabs or endotracheal (ET) aspirate or mini-bronchoalveolar lavage (BAL) fluid] or rapid antigen test (RAT) [on nasopharyngeal or throat swabs].
2. Patients who were treated with conventional oxygen therapy (COT) or high flow nasal canula (HFNC) or non-invasive ventilation (NIV) or invasive mechanical ventilation (IMV).
3. Patients who met the above two inclusion criteria and were treated with convalescent plasma at the discretion of treating team based on multiple factors including lack of improvement over 24-48 hours despite corticosteroids, severely hypoxemic patients or showing rapid deterioration of oxygenation including need for higher mode of respiratory support (HFNC/NIV/IMV).
4. Patients who met the above inclusion criteria but did not receive CPT due to lack of consent or non-availability of convalescent plasma or CPT not being part of the protocol (i.e., before the adoption of CPT for COVID-19 infections at our center or after it was removed from the ICMR advisory [14]) were taken as controls.

#### *Exclusion criteria*

1. Patients who did not require oxygen supplementation by any means.
2. Pregnant and lactating mothers.

### ***Convalescent plasma***

The convalescent plasma was either arranged from the government approved plasma banks or donor could donate the plasma at our hospital blood bank if he/she met the criteria for

donation and had sufficient antibody levels. Two units of plasma, 200ml each were transfused at 24 hours interval. The criteria used for plasma donors were as follows: 1) prior diagnosis of COVID-19 documented by a laboratory test; 2a) complete resolution of symptoms at least 28 days prior to donation or 2b) complete resolution of symptoms at least 14 days prior to donation, with two negative COVID RT-PCR reports 24 hours apart. All donor selection criteria for blood donation were followed as per Drugs and Cosmetics (second Amendment) Rules, 2020 [16]. AdviseDx SARS-CoV-2 IgM by Abbott (a chemiluminescent immunoassay) was used to check the antibody levels and a cut-off of 50AU/ml was taken.

### ***Data collection***

Data was collected retrospectively in case record forms (CRF), for the patients who were admitted between 1st June 2020 to 31<sup>st</sup> July 2021, from the hand written case records and hospital information system (HIS). Total 1533 patients were admitted during this period in our hospital's COVID-ICU and HDU; 276 patients, who met the inclusion criteria, were selected for the study. Data for 63 out of 276 cases was missing for outcome variables of PFR and mortality. So, these cases were excluded from the study. Means of available data of inflammatory markers were used to compare the two groups. All our analysis was done on the remaining 213 patients comprising of 170 cases who were given convalescent plasma and 43 controls who did not get CPT (Figure 1). Data was recorded under the following headings.

### ***Demographic data***

Age, gender, comorbidities, and blood group, APACHE- II score, SOFA score (first 24 hours)

### ***Patient's vital signs data***

It was recorded at baseline (on admission to hospital) and at zero hour (just before plasma transfusion) and daily for next 5 days. For controls, zero hour was taken as the time when CPT was advised or when the patient had clinical deterioration and would have been advised CPT if it had been standard-of-care at that time.

### ***Ventilatory/Oxygen supplementation data***

Parameters including type of ventilator support/ mode of oxygen supplementation was recorded. PaO<sub>2</sub>/FiO<sub>2</sub> ratios (PFR) were calculated at baseline, zero hour and then at 24, 48, 72, 96 and 120 hours. FiO<sub>2</sub> was calculated as per following: - Nasal prongs: 1L/min-25%, 2L/min-29%, 3L/min-33%, 4L/min-37%, 5L/min-41%, 6L/min-45%. Simple face mask:

6L/min-35%, 7L/min-41%, 8L/min-47%, 9L/min-53%, 10L/min-60%. Nonrebreather mask 15L/min: 80%. For portable BIPAP FiO<sub>2</sub> was calculated as per the oxygen flow rates [17].

#### *Plasma transfusion data*

Time and date of plasma transfusion was recorded.

#### *Medication data*

All drugs related to COVID treatment including Azithromycin, Hydroxychloroquine (HCQS), Ivermectin, Steroids, Remdesivir, Tocilizumab, were noted. These different drug treatments were adopted according to varying government policies in place at that moment.

#### *Radiologic data*

X-ray chest findings were recoded as Murray score calculated by intensivist. Computed tomogram (CT) findings were recorded as CT severity score (CTSS) as provided by the radiologist.

#### *Laboratory data*

Hemoglobin, total leukocyte count, Platelet count, blood urea nitrogen, serum creatinine, serum sodium and potassium, serum bilirubin and liver enzymes levels were recorded. Serum ferritin, IL-6, CRP, D-dimer levels were recorded before and 2 to 5 days after plasma transfusion.

#### *Adverse effects*

Any allergic reaction, hemodynamic instability, worsening of oxygenation (attributable to plasma therapy, as decided by the treating intensivist) or any other adverse clinical event within 6 hours of plasma transfusion was noted from the case records.

Being predictors and potential effect modifiers, the plasma and control groups were compared for co-morbidities, APACHE- II score, SOFA score and different drug treatments.

### **Outcome**

#### *Primary outcomes*

Improvement in the PFR by day 5 of CPT.



### *Secondary outcomes*

Mortality at 28 days of hospitalization. Patients transferred to other centers or discharged against medical advice were followed telephonically for 28-day mortality data.

Change in levels of inflammatory markers (before CPT and between 2-5 days after CPT)

### **Data analysis**

All parametric and nonparametric tests for descriptive and comparative analysis were performed using IBM-SPSS-Statistics-v.27 (2020) Software. Continuous variables were expressed as means with standard deviations. Categorical variables were expressed as frequencies with percentages. The student's t-test was performed to compare means of continuous variables. The Chi-square test was performed to compare frequencies of categorical variables. ANOVA test was used to compare means of continuous variables in more than two groups. A p-value <0.05 was considered significant.

### **Results**

Patient's demographic details are given in *Supplementary Table 1*. Study population consisted of 67.05% (114/170) males in plasma group and 72.09% (31/43) males in control group ( $p = 0.527$ ). Mean  $\pm$  SD age of patients was  $59.97 \pm 14.34$  years in CPT group and  $59.11 \pm 14.17$  years in control group ( $p = 0.728$ ). Most commonly occurring comorbidities in patients were diabetes mellitus (DM) (48.13%), hypertension (HTN) (41.78%), coronary artery disease (CAD) (8.92%) and chronic obstructive pulmonary disease (COPD) (7.04%). However, there was no significant difference between the two groups with respect to comorbidities (*Supplementary Table 1*). Baseline clinical, laboratory and radiological characteristics were similar across the two groups (*Supplementary Tables 1 and 2*). Mean  $\pm$  SD APACHE-2 score and SOFA score (first 24 hours) in the study population were  $9.85 \pm 5.81$  and  $3.07 \pm 2.05$  respectively. Mean number of days from symptoms onset to plasma transfusion was 9.95 days in our study; 64.7% of the patients received plasma within 10 days of onset of symptoms and 91.7% of the patients received plasma within 14 days of onset of symptoms. Mean  $\pm$  SD time from admission to plasma transfusion was  $4.205 \pm 2.39$  days. Mean  $\pm$  SD PFR at baseline (at the time of hospital admission) and before plasma transfusion were  $195.37 \pm 107.07$  and  $143.38 \pm 75.64$  respectively. Drug treatments between the two groups were similar except for HCQS, azithromycin and steroids (*Supplementary Table 2*). Percentage of patients on different modes of oxygen therapy (room air, COT, NIV, HFNC, IMV) at baseline was not statistically different between the two groups (*Supplementary Table 2*). Overall, 28 days-mortality in the study population was 45%. Mean  $\pm$  SD PFR at the baseline was higher in CPT group ( $199.346 \pm$

107.72) as compared to the control group ( $173.013 \pm 102.388$ ) ( $p = 0.2400$ ), while mean pre-CPT PFR (at zero hour) was lower in CPT group ( $142.11 \pm 73.99$ ) compared to control group ( $151.11 \pm 88.87$ ) ( $p = 0.56$ ), however these differences were non-significant. Figure 2 shows the trend of PFR from baseline to 5 days post CPT in cases and in controls. In CPT group, there was a small but consistent improvement in PFR till day 5. In control group after initial fall in PFR for 2 days, PFR improved at day 3 only to fall again. Although mean PFR after 5 days of CPT was higher in CPT group than that in control group ( $187.02 \pm 102.34$  versus  $160.29 \pm 83.39$ ), this difference was not statistically significant ( $p = 0.206$ ).

We analyzed the trends in PFR in patients on different modes of respiratory support (Figures 3 and 4). In the CPT group there was a gradual constant improvement in the PFR in the COT and NIV patients till day 5 after CPT, however in IMV group, after initial improvement, there was a decline after 72 hours (Figure 2). In the Control group, in contrast, there was a significant increase in PFR in IMV and NIV patients, while it decreased in COT patients.

Means of the available data for inflammatory markers were compared between the two groups (*Supplementary Table 3*). Mean  $\pm$  SD ferritin values before plasma transfusion were  $1559.79 \pm 6624.78$  in CPT group and  $1356.29 \pm 2709.17$  in control group ( $p = 0.864$ ). Mean  $\pm$  SD ferritin values after plasma transfusion in CPT and control groups were  $881.77 \pm 824.91$  and  $2961.08 \pm 7039.41$ , respectively ( $p = 0.191$ ). Similarly, mean  $\pm$  SD IL-6 values in CPT and control groups before ( $103.80 \pm 126.75$  and  $78.32 \pm 156.79$ ,  $p = 0.366$ ) and after CPT ( $192.20 \pm 827.21$  and  $807.26 \pm 2125.95$ ,  $p = 0.281$ ) was not statistically different between the two groups. There was also no significant difference in the values of CRP between the two groups (pre-plasma:  $110.27 \pm 93.50$  vs  $105.24 \pm 89.74$ ,  $p = 0.77762$  and post-plasma:  $63.71 \pm 64.60$  vs  $108.26 \pm 117.29$ ,  $p = 0.07825$ ). The frequencies of pre-CPT raised D-dimer ( $>1000$  ng/ml) [18,19] was comparable (39% vs 35%;  $p = 0.706$ ) in two groups but post CPT D-dimer was significantly more frequently (44% vs 71%;  $p = 0.026$ ) raised ( $>1000$  ng/ml) in control arm for the patients with available data (*Supplementary Table 3*).

In the CPT and control groups, the mean  $\pm$  SD length of ICU stay was  $12.16 \pm 5.11$  and  $9.76 \pm 5.89$  days respectively, however this difference was not statistically significant ( $p = 0.064$ ). Similarly, length of hospital stay was not statistically different between the CPT and control groups ( $16.11 \pm 8.06$  versus  $17.76 \pm 10.08$  days,  $p = 0.256$ ) (*Supplementary Table 3*).

Out of the total 213 patients, 96 patients died. Out of the total deaths, 80 were in CPT group (47.05%), while 16 were in the control group (37.20 %), however the difference was not statistically significant ( $p = 0.246$ ) (*Supplementary Table 3*). Mortality amongst the different blood groups in patients who received plasma was statistically similar (*Supplementary Table 4*). Mortality amongst subgroups based on mode of oxygen therapy and different age-groups

was also analyzed but the difference was not found to be statistically significant (*Supplementary Tables 5 and 6*).

None of the patients in the study group were noted to have any allergic reaction, hemodynamic instability, worsening of oxygenation (attributable to plasma therapy) or any other adverse clinical event within 6 hours of plasma transfusion.

## **Discussion and Conclusions**

There have been a number of studies of CPT from different parts of the world [20-22]. Duan et al. were the first to report benefit of CPT in a small cohort of 10 patients with improvement in all 10 patients and undetectable viral load in 7/10 patients [20]. The results from many other trials and observational studies have been mixed and many recent trials did not report benefit of convalescent plasma in COVID-19 patients [4,10,12,13]. ICMR released an evidence based advisory to address the use of convalescent plasma in COVID-19 patients on 17 Nov 2020 [9] and on 17 May 2021, ICMR delisted the use of convalescent plasma for COVID-19 from its guidelines [15]. In December 2021, WHO (World Health Organization) recommended against the use of CPT in non-severe COVID-19 patients and to use it only in context of a clinical trial in severe or critical COVID-19 patients [23].

We used CPT as part of therapeutic armamentarium for moderate to severe COVID-19 patients admitted at our center while the guidelines still advocated for it. In our retrospective study we analyzed effects of CPT on oxygenation, anti-inflammatory effects and in-hospital mortality.

In our study, convalescent plasma did not significantly improve the oxygenation status (as measured by PFR on day 5 post CPT). In the PLACID trial, the average fraction of inspired oxygen over 14 days of hospital stay did not differ between the study arms ( $\beta=-0.1$ , 95% confidence interval  $-25$  to  $2.3$ ) [4].

In our study, there was no significant effect on 28 days mortality after CPT. This lack of effect of CPT on mortality was also seen when analyzed for different age groups (*Supplementary Table 6*). PLACID study also did not find any difference in mortality between plasma and control patients (14.5% vs 13.5%; OR = 1.06, 95% CI: 0.61–1.83) [4] but had not included very severe or life threatening COVID-19 patients. RECOVERY trial too did not show any difference in 28 days mortality after CPT (24% in both convalescent plasma group and usual care group, RR 1.00, 95% CI 0.93 to 1.07, p value = 0.95) [5]. Study by S Budhiraja et. al. found 22.4% mortality in convalescent plasma group vs 18.5% mortality in best supportive care group (p = 0.125; OR = 1.27, 95% CI: 0.94–1.72) [24]. However, in their study, the mortality benefit emerged only in more critically ill patients of COVID-19 who were in ICU (25.5% vs 33.2%; p = 0.026; OR = 0.69, 95% CI: 0.50–0.96) [24]. All patients enrolled in our

study were admitted in ICU or HDU. On subgroup analyses on the basis of mode of oxygenation/ventilation, we found that there was no difference in mortality in conventional oxygen therapy (COT), non-invasive ventilation (NIV) group and invasive mechanical ventilation (IMV).

Convalescent plasma did not show any anti-inflammatory properties in our study except for D-dimer. There was no difference in levels of serum Ferritin, IL-6, and CRP between the two arms of our study. However, in our study, data for different inflammatory markers were available from the records for only 60-80% of the patients. Some other studies have associated clinical improvement with decrease in inflammatory markers titers (e.g., CRP, IL-6) after transfusion of convalescent plasma [25,26]. Our findings are similar to the findings of PLACID trial, that detected no difference in the levels of ferritin, CRP, or lactate dehydrogenase between the trial arms [4]. In our study, post CPT D-dimer was raised (>1000 ng/ml) more frequently in control arm than study arm, while pre CPT frequency of raised D-dimer was comparable in both arms. As post CPT D-dimer data is available for <50% patients in both arms, a caution is required in drawing any conclusion.

Effect of blood group on mortality has also been studied by others. Michael Zeitz et al. found that patients with blood group A had decreased risk of intubation and death relative to group O, while patients with group AB were at increased risk of both outcomes. Conversely, they found that individuals with blood group B were at higher risk of intubation but at lower risk of death, compared with group O [27]. On the other hand, in a retrospective study Agrawal et al. showed no significant association of mortality with patients' blood group [28]. In our study too, no difference was found in mortality rates among different blood groups in the convalescent plasma arm (*Supplementary Table 4*).

Transfusion of convalescent plasma did not affect the length of stay in hospital and ICU in our study. In the study by Altuntas et al., a retrospective case control study, the duration of stay in ICU was shorter in the CPT patients (9 days versus 12 days;  $p = 0.001$ ) [29]. However, they found no statistically significant difference in the mortality rate between the CPT and control groups (24.7% vs 27.7%,  $p = 0.150$ ). In CONCOR1 trial, the length of stay in ICU by day 30 was similar in convalescent plasma and control group ( $4.3 \pm 7.9$  vs  $3.7 \pm 7.1$ ,  $p = 0.22$ ) [6]. Similarly, PLACID trial [4] also did not find any decrease in total hospital stay as a result of CPT [mean 14 (interquartile range 10-19 days);  $n=227$  vs 13 (interquartile range 10-18) days;  $n=224$ ,  $p = 0.2$ ].

There are several limitations of our study. Our study is a retrospective study and much of the data was extracted from hand-written case records that were created when critical care was severely understaffed and overburdened. Further, 63 patients had incomplete clinical details

for outcome variables of PFR and mortality and had to be excluded from our analysis. Means of available data of inflammatory markers were used to compare the two groups (*Supplementary Table 3*). This could have decreased the power of the study. The number of subjects in control group were small as compared to the plasma group. This was bound to happen because all the patients who required oxygen therapy and were not improving or were deteriorating were advised CPT. During the study period, control arm consisted of patients (or surrogate) who refused consent for CPT or for whom convalescent plasma couldn't be arranged despite consent. As the control population was small, we also included patients who met the criteria for CPT but were treated before or after CPT was authorized treatment modality in India, hence CPT was not offered. During the study period, patients received different treatments for COVID-19 as per the discretion of treating intensivist (e.g., ivermectin, tocilizumab, azithromycin, hydroxy-chloroquine, steroids, remdesivir, heparins) and according to the prevailing and everchanging local guidelines. Out of different treatments given, Hydroxychloroquin, Azithromycin and steroids were significantly different between the two groups (*Supplementary Table 2*). However, most of the treatment modalities (e.g. Azithromycin, Hydroxychloroquin, Vitamin C) have shown no impact on outcome of COVID-19 patients [30-32], steroids have shown to be beneficial [33]. In our study, steroids were more frequently used in control group (*Supplementary Table 2*). Still there was no significant difference in outcome between the two groups. Mean number of days from symptoms onset to plasma transfusion was 9.95 days in our study; though it was given  $4.205 \pm 2.39$  days after admission implying late presentation. Some patients who were not hypoxemic initially but needed increasing oxygen support later in the disease course were also provided CPT at clinician's discretion. There were few patients in whom plasma therapy was advised, but there was a delay in arranging plasma. We do not have information about the antibody titers of patients at the time of CPT. Some patients may have already naturally developed adequate antibody response. We can't rule out the possibility that earlier use of CPT could have had different patient outcomes. Further, exact antibody titers in donor plasma units were not measured, rather donors were selected based on a pre-specified cut-off value. Our study shows that use of convalescent plasma did not improve PFR over 5 days after transfusion in COVID-19 patients. It did not have any significant effect on 28-day mortality. Our study could not find any subgroup of patients who would benefit from this therapy. This study reinforces the findings of previous studies that convalescent plasma therapy does not benefit moderate to severe patients with COVID-19 and that it should perhaps not be used outside the context of clinical trials. The results of the study should be interpreted with caution due to study's inherent limitations. Whether convalescent plasma would benefit other patient

groups can be evaluated in other randomized clinical trials in future. Our study was carried out when COVID-19 pandemic was a new global challenge and CPT was used in absence of definite treatment recommendations. It is not very likely the similar situation will arise again soon. Hence the results of the study may have limited generalizability.

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#### Online supplementary material

Supplementary Table 1. Demographic and baseline characteristics of study participants.

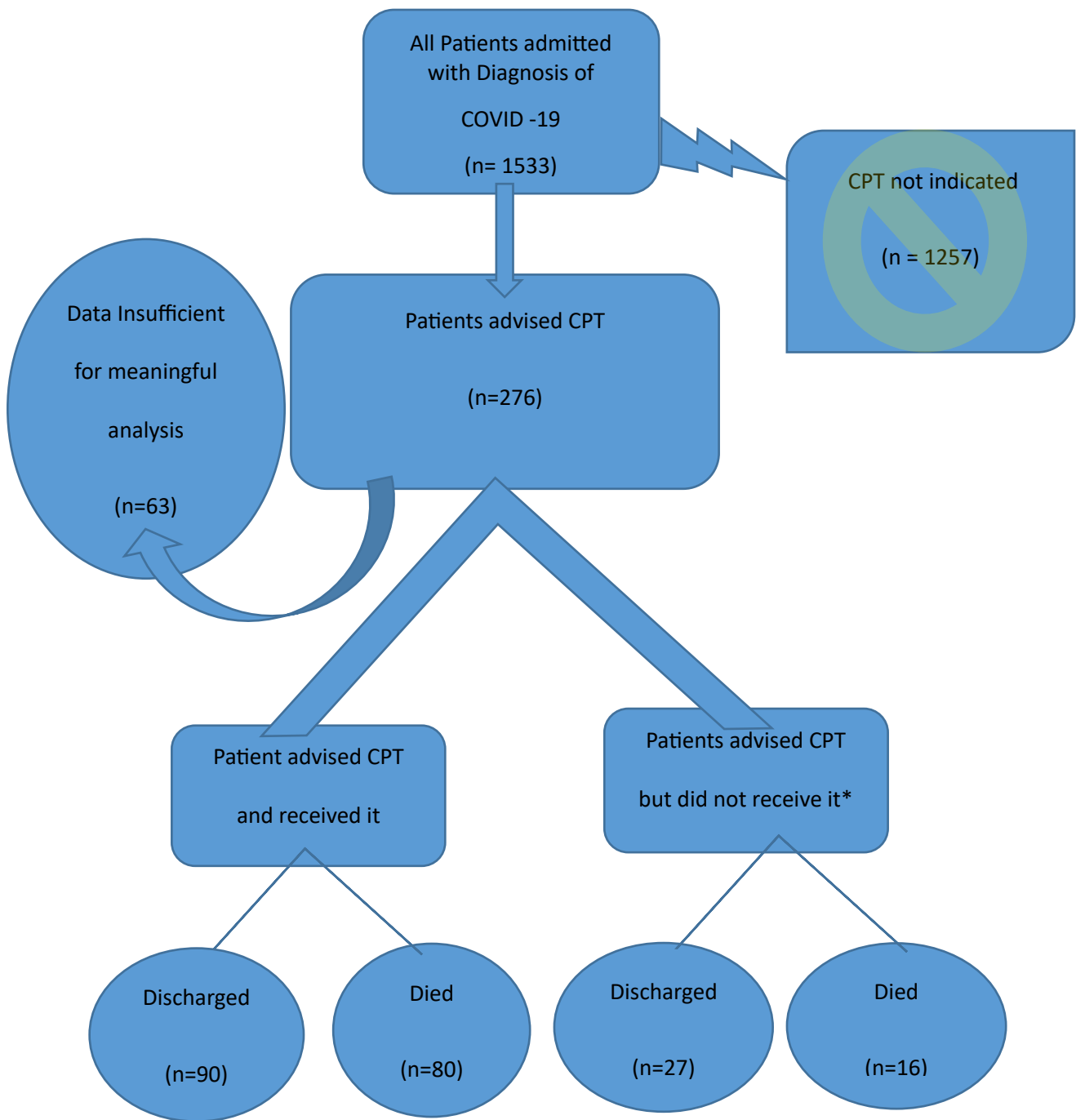
Supplementary Table 2. Clinical, laboratory and radiological findings in study population at baseline and drugs received during hospital stay.

Supplementary Table 3. Comparison of primary and secondary outcomes between convalescent plasma therapy (intervention arm) and control arm.

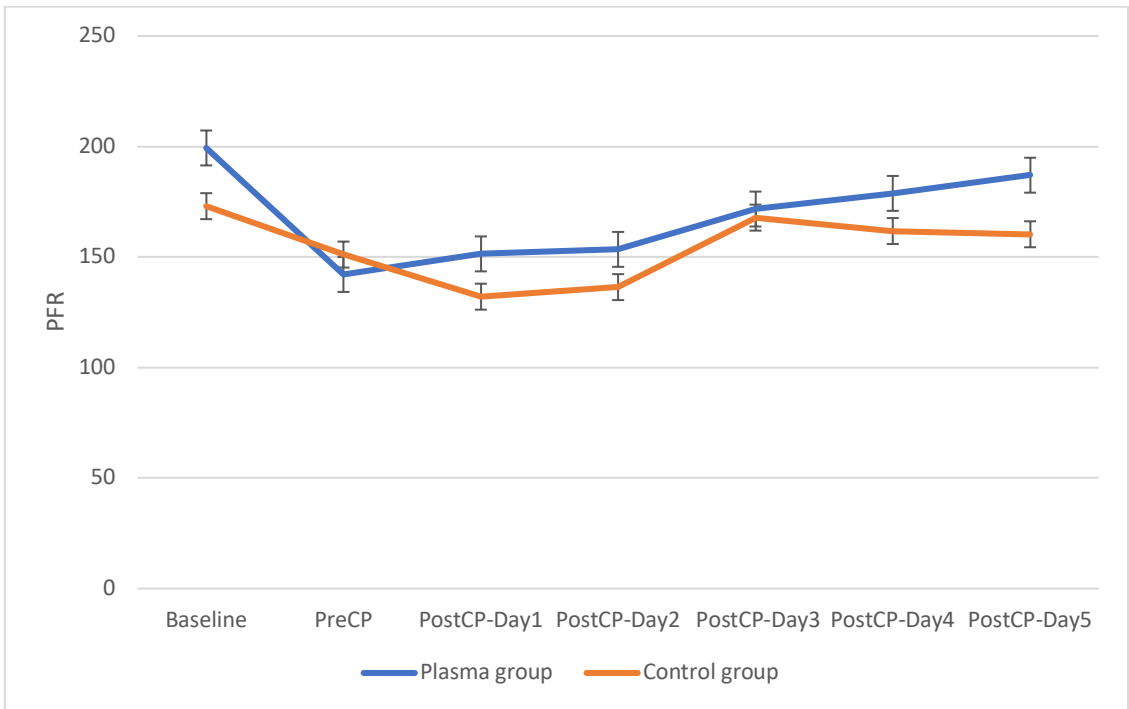
Supplementary Table 4. Comparison of mortality amongst the different blood groups in patients who received convalescent plasma.

Supplementary Table 5. Mortality in subgroups based on mode of oxygen therapy.

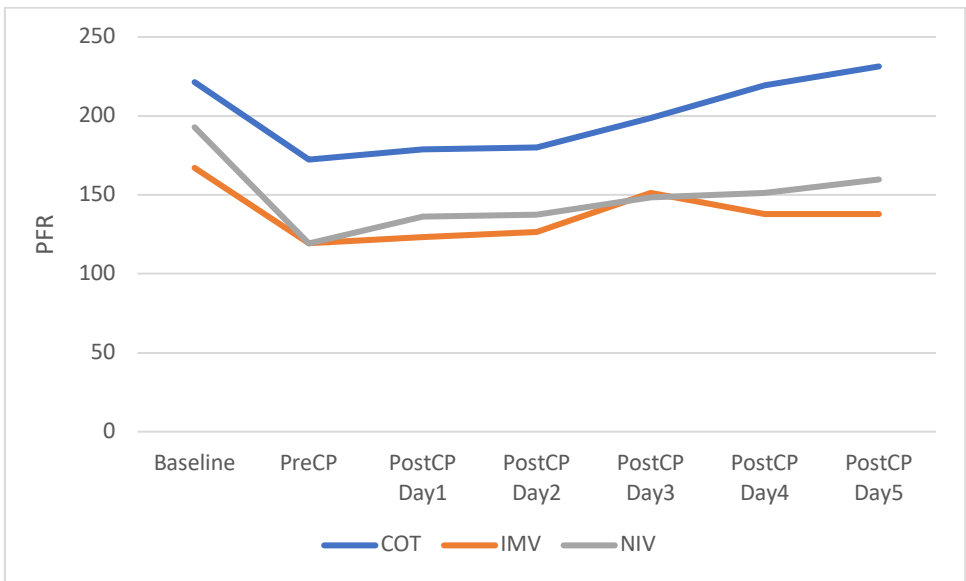
Supplementary Table 6. Mortality in age subgroups.



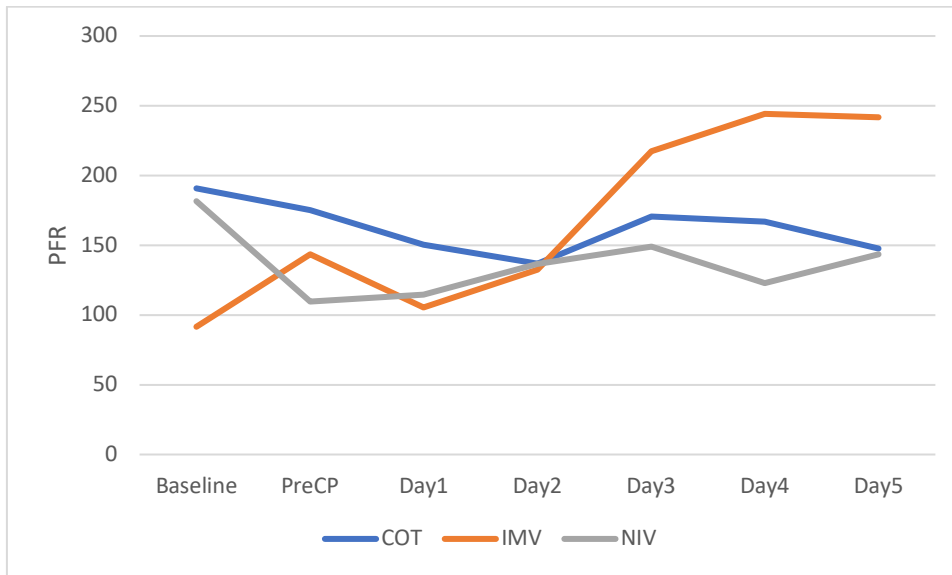
**Figure1. Study design. CPT, convalescent plasma therapy. \*Also includes the patients who would have been potential candidates of CPT, if CPT was authorized at the time of their treatment.**



**Figure 2: Trend of mean PFR (on Y axis) in CPT and control groups at different points of time (on X axis). CP, convalescent plasma; PFR, PaO<sub>2</sub>:FiO<sub>2</sub> ratio.**



**Figure 3. Trend of PFR (on Y axis) amongst Convalescent Plasma therapy patients on Invasive Mechanical ventilation (IMV), Non-invasive ventilation (NIV) and Conventional Oxygen therapy COT) at different points of time (on X axis). CP, convalescent plasma; PFR, PaO<sub>2</sub>:FiO<sub>2</sub> ratio.**



**Figure 4. Trend of PFR (on Y axis) amongst control group patients on Invasive Mechanical ventilation (IMV), Non-invasive ventilation (NIV) and Conventional Oxygen therapy (COT) at different points of time (on X axis). CP, convalescent plasma; PFR, PaO<sub>2</sub>:FiO<sub>2</sub> ratio.**