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Original Research Article

Effect of convalescent plasma therapy on mortality in patients suffering from respiratory COVID-19 infection at a dedicated COVID-19 hospital in Central India: A retrospective observational study

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Abstract

Background: Convalescent plasma therapy (CPT) can exert its therapeutic effect via antibody dependent cellular cytotoxicity, complement activation, or phagocytosis in COVID-19 patients. Use of convalescent plasma therapy has been tried but the effectiveness of using CPT is uncertain in previous studies.

Aims and objectives: To study the effect of CPT on mortality in patients suffering from respiratory COVID infection.

Materials and Methods: A retrospective observational study was performed including 390 patients with moderate to severe COVID-19 respiratory illness admitted to the District COVID-19 Hospital located at the Super Speciality Hospital of Jayaragya Groups of Hospitals Gwalior, MP during the period of 8th September to 7th Oct 2020. Patients were categorised in to two groups: Group A: COVID 19 patients receiving plasma therapy along with standard care (n=46), and Group B: COVID 19 receiving standard care but no plasma therapy (n=344)). The outcome was measured in terms of mortality.

Results: COVID-19 was more prevalent in the age group of 61-70 years (36.96%) and 51-60 years (19.57%) affecting mainly males (73.91%). Moderate COVID-19 patients had longer hospital stay (17.86±9.27 days) compared to severe patients (10.13±9.01 days) with a p-value of 0.024. Mortality was more in the severe case in Group A (85.72%) and Group B both. No significant difference was obtained in mortality rates in both the groups (p=0.228).

Conclusions: CPT does not provide any mortality benefit in patients suffering from moderate to severe respiratory COVID infection.

Keywords: Coronavirus disease 2019, Mortality, Respiratory Infection,

1. Introduction

Convalescent plasma is a source of antiviral neutralising antibodies.[1] It is found that Convalescent plasma can exert its therapeutic effect via antibody dependent cellular cytotoxicity, complement activation, or phagocytosis in COVID-19 patients. Other immune pathways, such as antibody-dependent cellular cytotoxicity, complement activation, or phagocytosis, may play a role in convalescent plasma's therapeutic impact in patients with COVID-19 disease.[2, 3]

Convalescent plasma obtained from covid-19 survivors appears to contain receptor binding domain specific antibodies with potent antiviral activity, according to evidence.[4] Efficient

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antiviral neutralising antibody titres, the best time for convalescent plasma therapy, the best time for plasma donation, and the severity class of patients that are likely to benefit from convalescent plasma are all factors to consider.

However, the evidence is lacking for its effectiveness in managing moderate to severe patients of COVID-19.[5] Hence, study aimed to evaluate the effect of convalescent plasma therapy (CPT) on mortality in patients suffering from respiratory COVID infection.

2. Materials and Methods

In this retrospective observational study, the case records of patients suffering from moderate to severe COVID respiratory illness admitted to the District Covid Hospital located at the Super speciality Hospital of Jayaragya Groups of Hospitals Gwalior, MP were studied. These patients were admitted during the period of 8th September to 7th Oct 2020.
Eligible patients for CPT were men and non-pregnant women with COVID-19 who were aged at least 18 years, were RT-PCR positive for SARS-CoV-2 and had pneumonia confirmed by chest imaging, or, had an oxygen saturation of 94% or less.
Exclusion criteria included pregnancy or breastfeeding; hepatic cirrhosis; alanine aminotransferase or aspartate aminotransferase more than five times the upper limit of normal; known severe renal impairment (estimated glomerular filtration rate <30 mL/min per 1·73 m^2) or receipt of continuous renal replacement therapy, hemodialysis, or peritoneal dialysis; the possibility of transfer to a non-study hospital within 72 h; and enrolment into an investigational treatment study for COVID-19 in the 30 days before screening.
The cases were categorised in to two groups; Group A: Cases of COVID-19 respiratory infection who received CPT along with standard care (n=46), Group B: Cases of COVID-19 respiratory infection who received standard care but no plasma therapy (n=344). The outcome was measured in terms of mortality.
Patients were further divided into moderate (patients with symptoms of dyspnea and hypoxia, presence of a fever, cough, and respiratory rate greater than or equal to 24 breaths per minute, SpO2, 90 to ≤93% in adults) and severe cases (a respiratory rate >30 breaths/minute, severe respiratory distress, or a SpO2 below 90% on room air) in both the groups. 6

All the data were analyzed using IBM SPSS ver. 20 software. Cross tabulation and frequency distribution were used to prepare the tables. Quantitative data were expressed as mean and standard deviation, whereas categorical data were expressed as a percentage. Independent sample t testwas used to compare the means, whereas the chi-square test was used to compare the percentage. The level of significance was assessed at 5%.

3. Results

Majority of the patients who were found positive for COVID-19 were aged between 61-70 years (36.96% in Group A and 57.27% in Group B). Mean age of study cohort was 56.86±7.34 years. Males were more commonly affected in both the groups (figure 1)

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Table 1: Showing age distribution between groups

Age group (years)	Group A	Group B
<40	7 (15.22)	38 (11.05)
41-50	6 (13.04)	45 (13.08)
51-60	9 (19.57)	58 (16.86)
61-70	17 (36.96)	197 (57.27)
>70	7 (15.22)	6 (1.74)
Total	46 (100)	344 (100)

Data is expressed as number of patients (percentage)

Figure 1: Showing COVID-19 prevalence by gender in both the groups

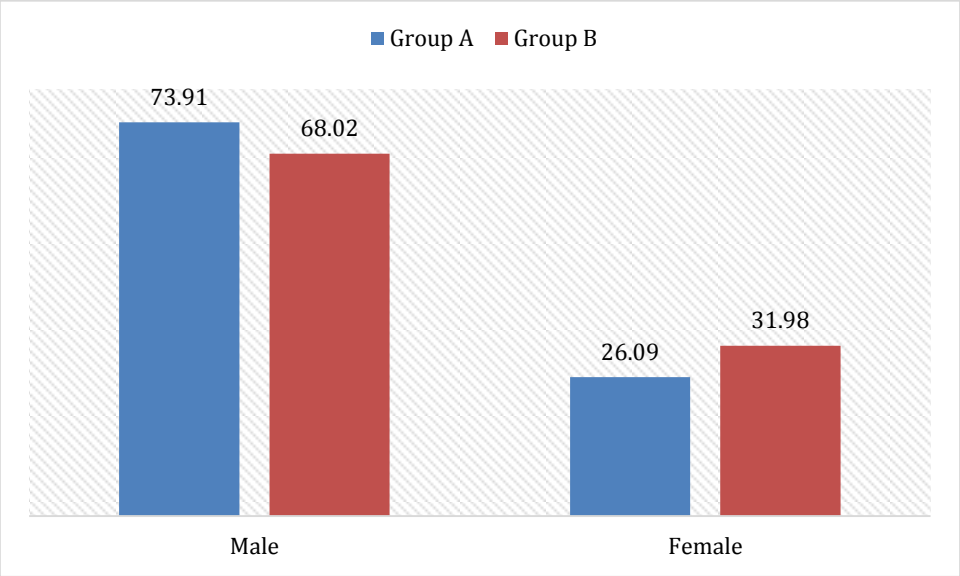

Table 2: Comparing the mean duration of hospital stay with case severity

Groups	Case severity	Mean duration (days)	Standard deviation	P-value
Group A	Moderate (n=23)	17.86	9.27	0.023
	Severe (n=23)	10.13	9.01	
Group B	Moderate (n=254)	16.67	8.76	0.022
	Severe (n=90)	12.34	8.24	

Mean duration of hospital stay was significantly higher in moderate cases compared to sever cases in group A. Similar pattern was observed in group B patients (table 2).

Table 3: Showing Mortality rates with CPT between groups

Outcome	Group A	Group B
Discharged	25 (54.34)	280 (81.40)
Died	21 (45.66)	64 (18.60)
Grand Total	46 (100)	344 (100)

Data is expressed as number of patients (percentage)

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Out of the 46 patients in Group A enrolled in the study, the majority were discharged (54.34%). Mortality was reported in 21 (45.66%) patients. The mortality rate in Group A was 45.66%.

Table 4: Association of Outcome with case severity in Group A (n=46)

Outcome	Case severity		Total	P-value
	Moderate	Severe		
Discharged	20 (80)	5 (20)	25 (100)	0.002*
Died	3 (14.28)	18 (85.72)	21 (100)	
Grand Total	23 (50)	23 (50)	46 (100.00)	

*Highly significant

Out of 21 patients who expired, most were patients with severe disease severe (85.72%), whereas 3 (14.28%) had moderate disease (p=0.002).

In Group B: A total 344 patients did not receive plasma therapy, out of them 64 died. The mortality rate among those who did not receive plasma therapy was 18.60%.

Table 5: Comparison of mortality between Group A and Group B

Plasma therapy received	Outcome		Mortality rate (%)	P value
	Survived	Died		
Yes (n=46)	25	21	45.66	0.228
No (n=344)	280	64	18.60	
Total	305	85		

No significant difference was found in the mortality rates of the two groups (p=0.228).

4. Discussion

CPT is a classic adaptive immunotherapy which has been found effective in the prevention and treatment several infectious diseases.

The FDA approved an Emergency Investigational New Drug (eIND) application for the use of convalescent plasma to treat COVID-19 patients on March 24, 2020. Plasma is the liquid component of blood that transports blood cells throughout the body. People who have recovered from COVID-19 have their plasma stored as convalescent plasma. It is then given to someone who is infected with the coronavirus. Antibodies present in convalescent plasma are thought to aid in the battle against coronavirus infection.

In present study majority of COVID-19 patients were of age between 61-70 years with mean age of 56.86±7.34 years. In line with the present study Duan et al studied 10 severe patients with COVID-19 who received plasma therapy and reported that mean age of patients with COVID-19 was 52.5 years. [7]

In the present study, out of 21 patients who expired in Group A, most of them were with severe disease patients 18 (85.72%), whereas 3 (14.28%) had moderate disease (p=0.002). This highlights higher mortality among severe COVID-19 patients. However, we did not find any significant difference in mortality among those who received the plasma therapy compared to those who did not. However, in contrast a meta-analysis including 32 studies reported significant reduction in the pooled odds of mortality in those who received CPT compared to no therapy. [8] Another recent study by Zeng et al reported plasma therapy as a

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potential therapy for severe patients with COVID-19. However, the sample size of this study was only 7. [1] Our' s is a study including 46 COVID-19 patients receiving plasma therapy.
In the Indian setup, permission for several clinical trials have been granted to Indian Council of Medical Research (ICMR) and other institutes by the Drug Controller General of India (DCGI). The first patient receiving the CPT from Delhi had shown significant improvement and ventilator support was weaned off.[2] However, outcome in only one patient cannot determine the effectiveness of the plasma therapy in the management of COVID-19 in Indian setup. The present study provides further clue on the effectiveness of CPT for managing COVID-19.
In line with present study the findings of thePLACID Trial which was a multicentre randomized phase II trial including 464 adults (≥18 years) moderately severe COVID-19 patients. Participants received two doses of 200 mL convalescent plasma, transfused 24 hours apart. Primary end point was either compositeof progression to severe disease or all-cause mortality at 28 days post-enrolment. Findings revealed that convalescent plasma was not associated with any reduction in progression to severe disease or all-cause mortality.[9] Another uncertainty was reported by a recent Cochrane review which included 20 studies. There was no benefitin improving the mortality and clinical condition in COVID-19 patients, time to death, or need for breathing support.[3] Further strengthening the present study findings, a similar study from China, which was a randomised controlled trial including 103 severe and life threatening COVID-19 patients reported no significant effect of CPT in terms of time to clinical improvement.[4] Another trial from Netherlands including 86 patients which was prematurely terminated could not find any improvement in mortality. This study also did not find any improvement in hospital stay, or disease severity at 15 days.[5]
Further, to have concrete evidence on the effectiveness of plasma therapy on mortality among COVID-19 patients requires a large randomized clinical trial.
In India, off-label use of convalescent plasma as a treatment for covid-19 is permitted. This authorization has been accompanied by dubious activities such as social media appeals for donors and the black market selling of convalescent plasma in India at exorbitant prices.[10] Furthermore, though convalescent plasma is a safe method of care when transfused in compliance with the regulations for the transfusion of blood and blood products, plasmapheresis, plasma storage, and neutralising antibody calculation are all resource-intensive procedures, with only a few institutes in India having the capacity to perform these procedures in a high-quality manner.

5. Conclusions

While convalescent plasma appeared to improve resolution of shortness of breath and fatigue in patients with moderate covid-19 and resulted in higher negative conversion of SARS-CoV-2 RNA on day 7 post-enrolment in previous studies, this did not translate into a reduction in mortality or progression to serious disease based on the present study findings and results obtained from some previous studies.It can be concluded that plasma therapy does not provide any improvement in mortality among moderate to severe patients with COVID-19 respiratory illness. The use of convalescent plasma with high neutralising antibody titres and the efficacy of convalescent plasma in neutralising antibody negative patients may be areas of future study. Finding appropriate patients as well as plasma donors would be a challenge. Furthermore, this difficulty can restrict the use of convalescent plasma to a small group of patients.

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE7, 2023

6. References

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