ORIGINAL ARTICLE

CLINICAL EFFICACY OF CONVALESCENT PLASMA TREARMENT IN COVID-19 PATIENTS

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ABSTRACT

Background: Recent incidences of severe respiratory infection worldwide are diagnosed as Coronavirus primarily. A viral strain designated as SARS-CoV-2 is responsible for this havoc.
Objective: To determine the effectiveness and safety of the convalescent plasma (CP) treatment in confirmed cases of COVID-19.
Methodology: This was an experimental trial of confirmed cases of COVID-19, admitted in Lahore General Hospital, Lahore, Pakistan. The duration of these trials were six months from April - August 2021.
Results: This study was done on 20 confirmed cases of COVID-19. Out of total, 90% Participants were male and 10 % were female, 70% patients were having no comorbidities, while 10% were Diabetic, 5% Asthmatic and 10% with Hypertension. Results analyzed statistically by applying Pearson correlation to find out extract efficacy of convalescent plasma therapy (CP). Among total, 80% of the patients had shown complete recovery, while two patients died during this trial. Further sampling could not do as WHO did not recommend Plasma Therapy after that.
Conclusion: Convalescent plasma (CP) proved to be an effective and safe therapy for confirmed cases of COVID-19
Keywords: COVID-19, Convalescent plasma (CP) therapy, Symptoms, critically ill.

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INTRODUCTION

COVID-19 has proven to be a great threat to the life of humans since its emergence in 2019. The World Health Organization (WHO) characterized this disease as pandemic in 2020 and devised strategies to confront it. Currently, there is no gold standard treatment for SARS-CoV-2[1]. The clinical representation of this virus varies from mild flu to severe respiratory distress along with loss of olfaction and gustation.it may leads to death so require immediate and intensive care[2].

672 million cases to date have been clocked in globally and the associated death rate with these reported cases were 6.85 million[3]. In Pakistan 1.58 million COVID-19 cases were reported and out of these 30,640 (2%) were deceased[4]. Regarding the treatment, several investigational antiviral agents were currently being evaluated[5]. No approved antiviral agent has been reported to irradicate novel corona virus till date, even lopinavir–ritonavir, and remdesivir have not been approved to be effective in severe COVID-19 cases[6].

For the patients presented with the symptoms of severe influenza, a new therapy called convalescent plasma therapy was introduced. According to previous studies this therapy reduced mortality and improved viral

clearance[7]. Convalescent plasma therapy has also been proven to decrease the severity of respiratory distress and reduced the mortality rate[8]. However, peer-reviewed data is not sufficient to tag this mode of treatment as gold standard. Since no study has reported the clinical benefits. Therefore, this experimental study was planned to evaluate the effectiveness of convalescent plasma treatment in COVID-19 cases in Pakistan.

METHODS

This was an experimental trial and it was executed during April-August 2021. Total 20 confirmed cases of COVID-19 participated in that trial in Lahore General Hospital, Lahore, Pakistan. These patients were treated with convalescent plasma (CP). The Ethical Review Committee of affiliated institute had granted the ethical approval (ANDC/RAC/21/35/06). Each Patient had given the consent by signing the consent Performa willingly. The inclusive criteria were the confirmed cases infected by SARS-CoV-2. All COVID-19 safety protocols were acquired and all guidelines of WHO were followed for the participants as well as for the staff. Real time RT-PCR (Quant Studio 5, the latest version of REAL TIME PCR) was used for Amplification to detect the virus through nasal swabs. Predesigned primers and probes were used and conditions for the amplifications were 50°C for 15 min, 95°C for 3 min, followed by 45 cycles of 95°C for 15 s and 60°C for 30s. For collecting epidemiological, laboratory, clinical and radiological findings, standardized data collection forms were used[9]. All patients were divided in to four groups designated as mild, moderate, severe and critically ill.

In this study 20 donors were included for convalescent plasma (CP) therapy of COVID-19 confirmed cases in population of Lahore, Pakistan. Donors that were recovered from COVID-19 and having high antibody titer were included. It was confirmed that no symptom persisted at the time of blood donation. Donors were also negative for all other viral markers. Donors that have low titer level or having any symptom were excluded from this study. Donors having any allergic reaction and pregnant females or lactating mothers were also excluded from this study.

All participants were tested for ABO compatibility testing, viral markers screening including hepatitis A, E, B, C, HIV and syphilis. The plasma was collected from only those individuals who tested negative by using the automated plasmapheresis machine (XJ-II Haier Biomedical, China.), under technical supervision. 250ml to 500ml plasma was collected. All laboratory protocols were strictly followed by the treating physician for the convalescent plasma storage and transfer to the patients. This plasma was then administered to the COVID-19 patients enrolled in the trial.

Categorical variables were expressed as number (%). Statistical analyses were done using The Statistical Product and Service Solution (SPSS) 24 software (IBM Corp., Armonk, NY, USA), and a p-value <0.05 was statistically significant.

RESULTS

In the present study twenty confirmed cases of COVID-19 were included and divided on the basis of severity of disease into mild, moderate, severe, critically ill patients. (Table. 1).

Table 1: Severity of disease in COVID-19 patients.

Severity of Disease	Frequency	Valid %	Cumulative %
Mild	10	50	50
Moderate	4	20	70
Severe	3	15	85
Critically ill	3	15	100
Total	20		100

The mean age of the patients was 47 years with standard deviation (+/_15.42).

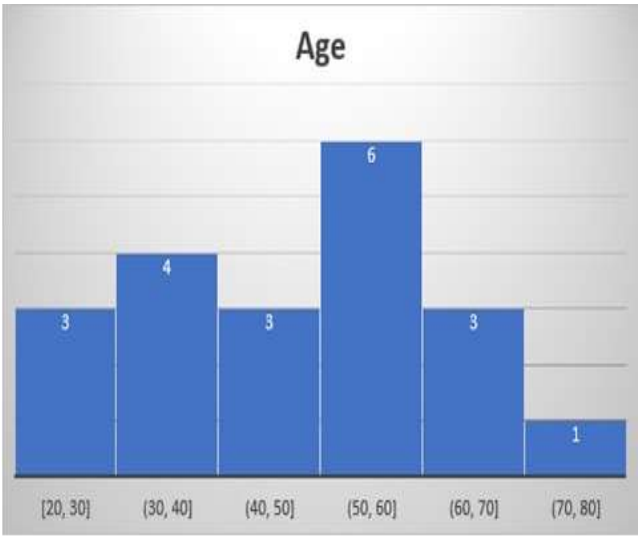

Fig 1: Age groups with incidence of COVID-19.

The male patients accounted for 90% while there were 10 % female participants. 70% patients had no underlying co morbid condition. Diabetes Mellitus (10%), Asthma (5%), Hypertension and Diabetes (10%) and Hypertension and Asthma in (5%) (Table.2).

This table is representing the Co-Morbidity of Patients as Diabetes Mellitus, Asthma, and Hypertension.

Table 2: Co-Morbid conditions in COVID-19 patients.

Co-Morbidity	Frequency	Valid percent	Cumulative percent
Nil	14	70	70
Diabetes Mellitus	2	10	80
Asthma	1	5	85
Hypertension and Diabetes	2	10	95
Hypertension and Asthma	1	5	100
Total	20		100

Serum LDH (lactate dehydrogenase) levels were raised enormously. 40% of participants had (501-1000 IU/L), 35% of participants had (1001-1500 IU/L), 10% of participant had (1501-2000 IU/L), 10% of participants had (200-500 IU/L), and 5% of participants had (2001-2500 IU/L). (Fig. 2)

Table 3: Correlations among different parameters in COVID-19 patients

		Age	Gender	Severity of Disease	Co-Morbidity	Serum LDH Level	Improvement by Plasma	Plasma Quantity
Age	Pearson Correlation	1	.173	-.023	.484*	.178	.189	.345
	Sig. (2-tailed)		.466	.923	.030	.452	.424	.161
	N	20	20	20	20	20	20	18
Gender	Pearson Correlation	.173	1	.612**	.609**	-.206	.885**	.c
	Sig. (2-tailed)	.466		.004	.004	.383	.000	0.000
	N	20	20	20	20	20	20	18
Severity of Disease	Pearson Correlation	-.023	.612**	1	.136	.028	.650**	-.348
	Sig. (2-tailed)	.923	.004		.567	.908	.002	.157
	N	20	20	20	20	20	20	18
Co-Morbidity	Pearson Correlation	.484*	.609**	.136	1	-.251	.475*	-.310
	Sig. (2-tailed)	.030	.004	.567		.286	.034	.210
	N	20	20	20	20	20	20	18
Serum LDH Level	Pearson Correlation	.178	-.206	.028	-.251	1	-.048	.207
	Sig. (2-tailed)	.452	.383	.908	.286		.840	.410
	N	20	20	20	20	20	20	18
Improvement by Plasma	Pearson Correlation	.189	.885**	.650**	.475*	-.048	1	-.219
	Sig. (2-tailed)	.424	.000	.002	.034	.840		.382
	N	20	20	20	20	20	20	18
Plasma Quantity	Pearson Correlation	.345	.c	-.348	-.310	.207	-.219	1
	Sig. (2-tailed)	.161	0.000	.157	.210	.410	.382	
	N	18	18	18	18	18	18	18

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

c. Cannot be computed because at least one of the variables is constant.

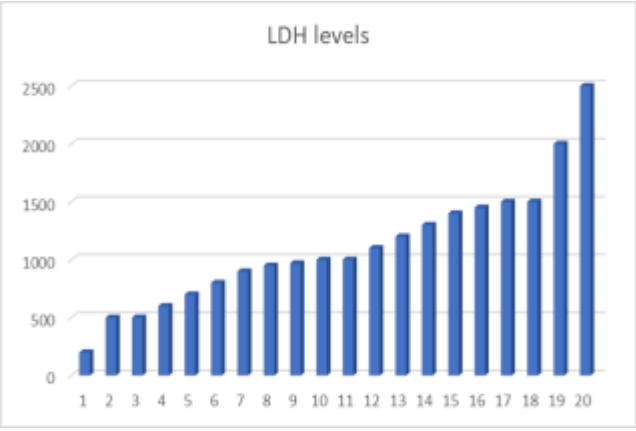

Fig 2: LDH levels (IU/L) in COVID-19 patients.

After giving convalescent plasma therapy there were improvement of symptoms and laboratory parameters of sixteen patients. Two patients expired during this duration which were previously diagnosed as critically ill. The LDH (median> 1000U/L vs 245 U/L) improved markedly. No adverse effects were observed after convalescent plasma therapy

DISCUSSION

The prime goal for prophylaxis as well as treatment of any viral infection especially COVID-19 is the provision of immediate passive immunity. As no Vaccine was available at that time so the primary goal was to save Human lives. An experimental trial with convalescent plasma (CP) treatment was performed on

COVID-19 cases. The results depicted that CP therapy is a safe and effective treatment for COVID-19 patients. It was revealed that treatment with Convalescent plasma therapy had led to complete recovery of sixteen patients that was clearly manifested in their physical as well as clinical findings. However, two of the critically ill patients could not be saved with this therapy. As the table 2 described that male patient accounted for 90% while there were 10 % female participants. 70% patients had no underlying co morbid condition. Diabetes Mellitus (10%), Asthma (5%), Hypertension and Diabetes (10%) and Hypertension and Asthma in (5%). We found out the correlations among different parameters in COVID-19 patients. The analysis done and found that Correlation significant at the 0.05 level (2-tailed).

Whereas other Correlation is significant at the 0.01 level (2-tailed).

So, it is strongly recommended that Convalescent Plasma therapy is safe and gave us encouraging results, although study done on small number of samples.

While (Hu et al, 2020) performed a retrospective analysis on seven patients infected with COVID-19, it was found that the convalescent plasma therapy was proved to be effective and safe treatment for COVID-19 cases that was in accordance to our results[10].

Whereas, Wood et al, 2021 analyzed 12 studies on efficacy of convalescent plasma therapy and found encouraging results considering transfusion volume, and administration timing. These results supported the findings of the present study[11]. The results of another study, by Hung et al, in 2011, identified that plasma treatment played a significant role in increasing the rate of recovery of H1N1 infected patients. It was found that the serum cytokine response increased significantly with significant decrease in respiratory tract viral load and risk of mortality[8].

It was concluded from one of the studies that early intervention with convalescent plasma infusion is necessary to get optimal results. Plasma therapy becomes less effective once patients has started producing antibodies or developing end organ damage[12]. This may be due to the reason that donor neutralizing antibodies initiate a fatal cascade against virus in the recipient. This observation is supported by our study in which it was found that two out of twenty patients died as they were critically ill and end organ damage had been started. Another important aspect is to minimize the viral load until it becomes negative, as in the current study the viral load of the most of the patients decreased with one pint of infusion while two of the patients had been infused with two pints of CP to get a negative result. Correlation was significant at 0.05 levels (2 tailed). Dillner and Ursing 2021 suggested the similar strategy that the infected patients should be treated with CP until the eradication of SARS-CoV-2 in the serum[13].

Although it was suggested for Cohort study but WHO banned Convalescent Plasma Therapy after that so broad-spectrum study was not done.

The strengths were the demographic evaluation of local community and every patient was observed till recovery or otherwise. The limitations were a short sample size from only one hospital. The control group was not established due to the need to save lives.

CONCLUSION

COVID-19 pandemic has marked clinical implications and unfortunately very lethal outcome but the convalescent plasma therapy has proved its effectiveness and safety if there would be an early intervention. More clinical trials are required to get a gold standard treatment for this pandemic.

Limitations and strength: The limitations were a short sample size from only one hospital. The control group was not established due to the need to save lives. The strengths were the demographic evaluation of local community and every patient was observed till recovery or otherwise.

Declaration of Conflicting Interests: None.

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ETHICAL APPROVAL

The study was approved by the Institutional Review Board of Postgraduate Medical Institute, Ameer ud Din Medical College & Lahore General Hospital, Lahore, vide AMC/PGMI/LGH/Article/ Research No. 568 Dated 21.12.2022

REFERENCES

1. WHO-nCoV-Clinical-2020.2-rus.pdf [Internet]. [cited 2022 Nov 11]. Available from: https://apps.who.int/iris/bitstream/handle/10665/330854/WHO-nCoV-Clinical-2020.2-rus.pdf
2. Rubi G, Ilyas MS, Ilyas T, Adil M, Ul M, Zia Q, et al. Clinical features of patients infected with novel corona virus (COVID 19) in Lahore, Pakistan. IJSAR 2021; 8(1):10-19
3. Coronavirus disease (COVID-19) – World Health Organization [Internet]. [cited 2022 Nov 23]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019
4. Pakistan: WHO Coronavirus Disease (COVID-19) Dashboard with Vaccination Data [Internet]. [cited 2023 Feb 9]. Available from: https://covid19.who.int

5. Milloy MJ, Wood E. Withdrawal from methadone in US prisons: cruel and unusual? The Lancet. 2015;386(9991):316–318.
6. Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G, et al. A Trial of Lopinavir–Ritonavir in Adults Hospitalized with Severe Covid-19. N Engl J Med. 2020;382(19):1787–99.
7. Wang Y, Huo P, Dai R, Lv X, Yuan S, Zhang Y, et al. Convalescent plasma may be a possible treatment for COVID-19: A systematic review. Int Immunopharmacol. 2021;91:107262.
8. Hung IF, To KK, Lee CK, Lee KL, Chan K, Yan WW, et al. Convalescent Plasma Treatment Reduced Mortality in Patients With Severe Pandemic Influenza A (H1N1) 2009 Virus Infection. Clin Infect Dis. 2011;52(4):447–456.
9. World Health Organization. World Health Organization coronavirus disease 2019 (COVID-19) situation report. Geneva Switz World Health Organ. 2020; [Internet]. [cited 2023 Feb 9]. Available from:https://www.who.int/emergencies/diseases/novel-coronavirus-2019?adgroupsurvey={adgroupsurvey}&gclid=CjwKCAiAmJGgBhAZEiwA1JZoltSfrB-PYsNnQbtGvth3mBwbm-56gHesJ0WfhkOdP2LRF-5WBxi5sxoCt5wQAvD_BwE
10. Hu X, Hu C, Jiang D, Zuo Q, Li Y, Wang Y, et al. Effectiveness of Convalescent Plasma Therapy for COVID-19 Patients in Hunan, China. Dose-Response. 2020 ;18(4):1559325820979921.
11. Wood EM, Estcourt LJ, McQuilten ZK. How should we use convalescent plasma therapies for the management of COVID-19? Blood. 2021;137(12):1573–1581.
12. Wendel S, Land K, Devine DV, Daly J, Bazin R, Tiberghien P, et al. Lessons learned in the collection of convalescent plasma during the COVID-19 pandemic. Vox Sang. 2021;116(8):872–879.
13. Dillner J, Ursing J. Convalescent plasma for treatment of COVID-19: study protocol for an open randomised controlled trial in Sweden. BMJ Open. 2021;11(12):e048337.

AUTHOR'S CONTRIBUTION:

GR: Drafting and writing of the manuscript, data collection,

MSI, AF, FS: analysis and result interpretation, theme generation

ZJ: development of the study protocol