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Short communication

# A novel scoring system for selecting the target patients of COVID-19 convalescent plasma therapy: A hypothesis



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## ABSTRACT

The primary cause of mortality in patients of coronavirus disease 2019 (COVID-19) is the cytokine storm and not directly due to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus. Therefore, it is being stressed by transfusion medicine specialists to use COVID-19 convalescent plasma (CCP) therapy early in the course of the disease, preferably within 72 h of diagnosis. The authors herein, propose a scoring system for the rapid assessment of the patients who have tested positive for SARS-CoV-2. Therefore, a systematic approach may be followed where the patients are categorised into two groups, namely, the low-risk group [LRG; score < 5] and the high-risk group [HRG; score ≥ 5] based on this scoring system. Those classified as an HRG should be administered CCP therapy within 72 h of a confirmed diagnosis of COVID-19 to neutralise the SARS-CoV-2 virus and prevent the occurrence of the cytokine storm. This in turn could help reduce the overall mortality in the recipients.

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## 1. Introduction

With the evolving understanding of coronavirus disease 2019 (COVID-19) [1], the COVID-19 convalescent plasma (CCP) therapy has emerged as an important investigational therapy being used in the management of the same [2]. It is now well established that the mortality in COVID-19 patients is due to the SARS-CoV-2 virus-induced cytokine storm and systemic inflammatory response syndrome and not directly due to the SARS-CoV-2 virus [3]. The autopsy findings in patients with COVID-19 have confirmed the presence of cytokine release syndrome (CRS) characterized by hypercytokinemia and multi-organ damage [4]. Furthermore, there is a window of opportunity of few days between the entry of SARS-CoV-2 inside the body and the development of CRS [5]. Therefore, early CCP therapy can result in SARS-CoV-2 neutralisation and prevent the occurrence of cytokine storm [6]. However, practically it has been observed that clinicians have been using CCP even in

severe COVID-19 patients as a compassionate therapy and in whom the CRS has already occurred. Therefore, it is highly unlikely that CCP will be effective in such cases [7]. The authors have conceptualised a novel scoring system for identifying the high-risk patients who are likely to develop severe COVID-19 and remain ideal candidates for early CCP therapy. However, even before the authors could test the hypothesis, the CCP therapy was dropped from the treatment protocol for COVID-19 patients in India largely due to the unscientific and indiscriminate use of CCP in the country [8].

## 2. Proposing the hypothesis

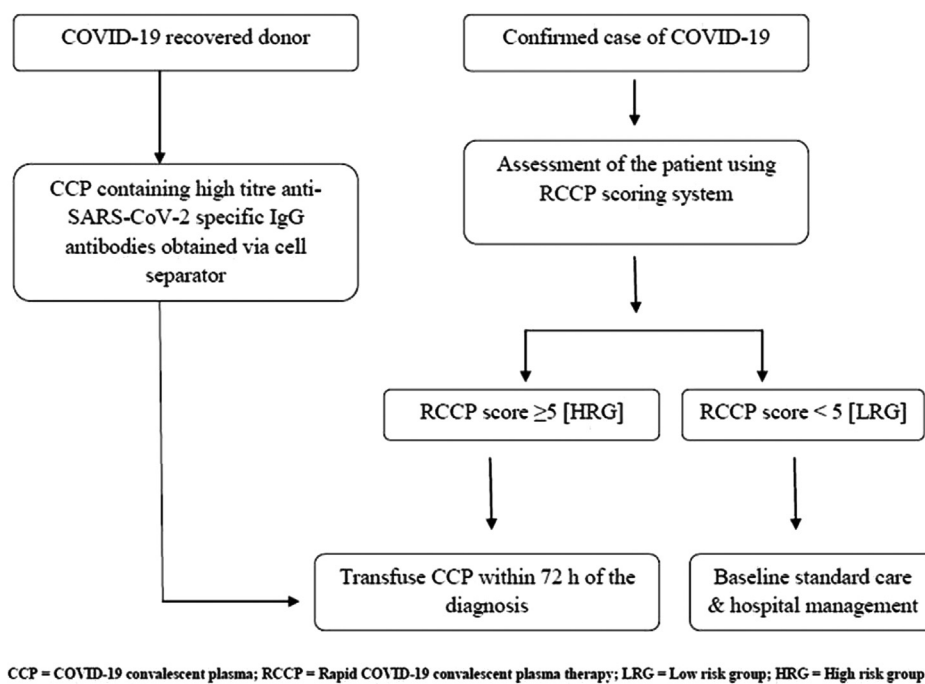
The authors herein propose a novel Rapid CCP [RCCP] scoring system for the early assessment of patients who have tested positive for SARS-CoV-2. The scoring system has a total of twelve parameters and can be used to identify those who are at a high risk of developing severe COVID-19 infection (Table 1). The parameters selected are based on the conditions which have been found to have a significant co-relation of developing severe COVID-19 infection based on the published research [9–15]. Therefore, a systematic approach may be followed and the patients can be categorised into two groups, namely, the low-risk group [LRG; score < 5] and the high-risk group [HRG; score ≥ 5] based on this scoring system

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**Table 1**  
Rapid COVID-19 convalescent plasma therapy (RCCP) scoring system.

Parameter	Score	
	0	1
Age	< 60 years	≥ 60 years
Core body temperature > 37 °C	No	Yes
Cough	No	Yes
Smoking history	No	Yes
Hypertension	No	Yes
Diabetes	No	Yes
Cardiovascular disease	No	Yes
Hematological and/or non-hematological malignancies	No	Yes
Chronic liver diseases	No	Yes
Chronic renal diseases	No	Yes
Breathlessness	No	Yes
Oxygen saturation	> 94%	≤ 94%
<b>Total score</b>		
<b>Score 0-4: No intervention [Baseline standard care &amp; hospital management]</b>		
<b>Score ≥5: Early convalescent plasma therapy preferably within 72 h</b>		



**Fig. 1.** CCP therapy using RCCP scoring system (CCP: COVID-19 convalescent plasma; RCCP: Rapid COVID-19 convalescent plasma therapy; LRG: Low-risk group; HRG: High-risk group).

(Fig. 1). Those classified as an HRG should be administered CCP therapy within 72 h of a confirmed diagnosis of COVID-19 to neutralise the SARS-CoV-2 virus and prevent the occurrence of the CRS. This in turn could help reduce the overall mortality in the recipients.

### 3. Support for the hypothesis

CCP therapy as an experimental treatment is being used as early as January 2020 [16]. Initial studies gave conflicting results about its safety and efficacy in the treatment of COVID-19. The majority of this data was either case reports or institutional experiences [17–19]. In fact, the PLACID trial [a multi centre clinical trial] from India concluded that the CCP was successfully able to neutralise the SARS-CoV-2 virus, however, it did not result in a decreased patient mortality [20]. This result could be explained by the fact that the primary cause of mortality in patients of COVID-19 is a SARS-CoV-2 virus-induced cytokine storm and not the SARS-CoV-2 virus itself. The most probable reason for the ineffectiveness of CCP therapy in reducing the patient mortality could be attributed to the transfu-

sion of CCP in patients who had already developed severe COVID-19 symptoms compounded with a CRS. Moreover, the convalescent plasma contains non-neutralising antibodies which can assist the virus to gain entry into the macrophages. The virus undergoes rapid proliferation in the macrophages, establishing a pro-inflammatory environment, resulting in the aggravation of the cytokine storm [21]. This was observed in a case report wherein, the use of the convalescent plasma therapy in a patient with Ebola virus disease resulted in acute respiratory distress syndrome (ARDS) [22]. Therefore, in patients having severe COVID-19 infection, where cytokine storm has already occurred, the use of the CCP therapy is not only unjustified rather it merits a clinical reconsideration.

If the CCP therapy is given within the first few days of the diagnosis, the passive IgG anti-SARS-CoV-2 antibodies can neutralise the virus and prevent the occurrence of this CRS in the patients. Early treatment with CCP had resulted in a better outcome in patients having severe symptoms during the 2002-04 SARS epidemic [23,24]. In a recent study, early administration of convalescent plasma (i.e. within 72 h of the onset of mild COVID-19

symptoms) resulted in the decreased progression to severe COVID-19 infection in elderly patients [25]. Similar results have been observed in another study wherein there was a decreased mortality seen in COVID-19 patients when they were administered the CCP within seven days of hospitalisation [26].

**4. Conclusion**

CCP therapy must be used judiciously in a specific patient population where it is likely to be effective. The HRG patients can be identified by using the proposed RCCP scoring system which could be easily utilised in hospital settings and or screening centres. Multicentre prospective interventional studies need to be done to be able to understand the effectiveness of CCP therapy in reducing the mortality rate when administered within the first 72 h of diagnosis especially in those susceptible to develop severe COVID-19 infection.

**Author contributions**

S.No.	Category of contribution	Author 1 Naveen Bansal	Author 2 Manish Raturi	Author 3 Yashik Bansal	Author 4 Pushpendra Singh
1.	Conceptual design	Yes	No	No	No
2.	Literature search	Yes	Yes	Yes	No
3.	Data compilation	Yes	Yes	Yes	Yes
4.	Manuscript preparation and editing	Yes	Yes	Yes	Yes
5.	Manuscript review and final approval	Yes	Yes	Yes	Yes
6.	Final guarantor of the entire manuscript	No	Yes	No	No

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**Disclosure of interest**

The authors declare that they have no competing interest.

**References**

[1] Raturi M, Kala M, Das K, Kusum A. Reviewing the ethical concerns of the convalescent plasma therapy in COVID-19. *J Lab Phys* 2021;13:91–4.

[2] Garraud O, Lacombe K, Tiberghien P. A look-back at convalescent plasma to treat COVID-19. *Transfus Apher Sci* 2021;60:103063. <http://dx.doi.org/10.1016/j.transci.2021.103063>.

[3] Mélo Silva Júnior ML, Souza LMA, Dutra REMC, Valente RGM, Melo TS. Review on therapeutic targets for COVID-19: insights from cytokine storm. *Postgrad Med J* 2020. <http://dx.doi.org/10.1136/postgradmedj-2020-138791>, postgradmedj-2020-138791 [published online ahead of print, 2020 Oct 2].

[4] Núñez-Torrón C, Ferrer-Gómez A, Moreno Moreno E, et al. Secondary haemophagocytic lymphohistiocytosis in COVID-19: correlation of the autopsy findings of bone marrow haemophagocytosis with HScore. *J Clin Pathol* 2021. <http://dx.doi.org/10.1136/jclinpath-2020-207337>, jclinpath-2020-207337 [published online ahead of print, 2021 Mar 15].

[5] Sun X, Wang T, Cai D, et al. Cytokine storm intervention in the early stages of COVID-19 pneumonia. *Cytokine Growth Factor Rev* 2020;53:38–42. <http://dx.doi.org/10.1016/j.cytogfr.2020.04.002>.

[6] Tiberghien P, Toussiot E, Richard P, Morel P, Garraud O. Commentary: Convalescent plasma to treat COVID-19: following the Argentinian lead. *Transfus Apher Sci* 2021:103161. <http://dx.doi.org/10.1016/j.transci.2021.103161> [published online ahead of print, 2021 May 23].

[7] Katz LM. (A Little) Clarity on convalescent plasma for Covid-19. *N Engl J Med* 2021;384:666–8. <http://dx.doi.org/10.1056/NEJMe2035678>.

[8] Bansal N, Raturi M, Bansal Y. Covid-19 convalescent plasma therapy: analyzing factors that led to its failure in India. *Transfus Clin Biol* 2021. <http://dx.doi.org/10.1016/j.traci.2021.05.009>. S1246-7820(21)00080-X [published online ahead of print, 2021 June 5].

[9] Motta LP, Silva PPF, Borguezan BM, et al. An emergency system for monitoring pulse oximetry, peak expiratory flow, and body temperature of patients with COVID-19 at home: Development and preliminary application. *PLoS One* 2021;16. <http://dx.doi.org/10.1371/journal.pone.0247635>, e0247635. Published 2021 Mar 26.

[10] Du RH, Liang LR, Yang CQ, et al. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. *Eur Respir J* 2020;55:2000524. <http://dx.doi.org/10.1183/13993003.00524-2020>. Published 2020 May 7 [published correction appears in *Eur Respir J* 2020;56(3)].

[11] de Almeida-Pititto B, Dualib PM, Zajdenverg L, et al. Severity and mortality of COVID 19 in patients with diabetes, hypertension and cardiovascular disease: a meta-analysis. *Diabetol Metab Syndr* 2020;12:75. <http://dx.doi.org/10.1186/s13098-020-00586-4>. Published 2020 Aug 31.

[12] Bonanad C, García-Blas S, Tarazona-Santabalbina F, et al. The Effect of age on mortality in patients with Covid-19: a meta-analysis with 611,583 subjects. *J Am Med Dir Assoc* 2020;21:915–8. <http://dx.doi.org/10.1016/j.jamda.2020.05.045>.

[13] Hosseinzadeh R, Goharri MASB, Bahardoust M, et al. Should all patients with hypertension be worried about developing severe coronavirus disease 2019 (COVID-19)? *Clin Hypertens* 2021;27:3. <http://dx.doi.org/10.1186/s40885-021-00161-7>. Published 2021 Jan 15.

[14] Xie J, Covassin N, Fan Z, et al. Association between hypoxemia and mortality in patients with COVID-19. *Mayo Clin Proc* 2020;95:1138–47. <http://dx.doi.org/10.1016/j.mayocp.2020.04.006>.

[15] Gülsen A, Yigitbas BA, Uslu B, Drömann D, Kilinc O. The effect of smoking on COVID-19 symptom severity: systematic review and meta-analysis. *Pulm Med* 2020;2020. <http://dx.doi.org/10.1155/2020/7590207>, 7590207, published 2020 Sep 8.

[16] Shen C, Wang Z, Zhao F, et al. Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. *JAMA* 2020;323:1582–9. <http://dx.doi.org/10.1001/jama.2020.4783>.

[17] Zeng QL, Yu ZJ, Gou JJ, et al. Effect of convalescent plasma therapy on viral shedding and survival in patients with coronavirus disease 2019. *J Infect Dis* 2020;222:38–43. <http://dx.doi.org/10.1093/infdis/jiaa228>.

[18] Ye M, Fu D, Ren Y, et al. Treatment with convalescent plasma for COVID-19 patients in Wuhan, China. *J Med Virol* 2020;92:1890–901. <http://dx.doi.org/10.1002/jmv.25882>.

[19] Zhang L, Pang R, Xue X, Bao J, Ye S, Dai Y, et al. Anti SARS-CoV-2 virus antibody levels in convalescent plasma of six donors who have recovered from COVID-19. *Aging (Albany NY)* 2020;12:6536–42. <http://dx.doi.org/10.18632/aging.103102>.

[20] Agarwal A, Mukherjee A, Kumar G, et al. Convalescent plasma in the management of moderate covid-19 in adults in India: open label phase II multicenter randomised controlled trial (PLACID Trial). *BMJ* 2020;371. <http://dx.doi.org/10.1136/bmj.m3939>, m3939. Published 2020 Oct 22 [published correction appears in *BMJ* 2020;371:m4232].

[21] Channappanavar R, Fehr AR, Vijay R, et al. Dysregulated type I Interferon and inflammatory monocyte-macrophage responses cause lethal pneumonia in SARS-CoV-infected mice. *Cell Host Microbe* 2016;19:181–93. <http://dx.doi.org/10.1016/j.chom.2016.01.007>.

[22] Mora-Rillo M, Arsuaga M, Ramírez-Olivencia G, et al. Acute respiratory distress syndrome after convalescent plasma use: treatment of a patient with Ebola virus disease contracted in Madrid, Spain. *Lancet Respir Med* 2015;3:554–62. [http://dx.doi.org/10.1016/S2213-2600\(15\)00180-0](http://dx.doi.org/10.1016/S2213-2600(15)00180-0).

[23] Cheng Y, Wong R, Soo YOY, et al. Use of convalescent plasma therapy in SARS patients in Hong Kong. *Eur J Clin Microbiol Infect Dis* 2005;24:44–6. <http://dx.doi.org/10.1007/s10096-004-1271-9>.

[24] Soo YO, Cheng Y, Wong R, et al. Retrospective comparison of convalescent plasma with continuing high-dose methylprednisolone treatment in SARS patients. *Clin Microbiol Infect* 2004;10:676–8. <http://dx.doi.org/10.1111/j.1469-0691.2004.00956.x>.

[25] Libster R, Pérez Marc G, Wappner D, et al. Early high-titer plasma therapy to prevent severe covid-19 in older adults. *N Engl J Med* 2021;384:610–8. <http://dx.doi.org/10.1056/NEJMoa2033700>.

[26] Hegerova L, Gooley TA, Sweerus KA, et al. Use of convalescent plasma in hospitalized patients with COVID-19: case series. *Blood* 2020;136:759–62. <http://dx.doi.org/10.1182/blood.202006964>.