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Assessing the impetus and impediments to donate coronavirus disease-2019 convalescent plasma: A survey study from a tertiary care Indian blood center

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Abstract:

BACKGROUND: Amidst the raging coronavirus disease-2019 (COVID-19 pandemic), COVID-19 convalescent plasma (CCP) therapy emerged as an important experimental therapy. The majority of the research studies have focused on determining the safety and efficacy of CCP in the management of COVID-19 and little attention has been paid to the source of CCP, i.e., the CCP donor recruitment. The main challenge at our blood center was maintaining high spirits and continuous motivation among the volunteers to keep donating CCP. With this background, our primary aim was to observe the impetus and impediments of potential CCP donors among the SARS-CoV-2 recovered individuals.

MATERIALS AND METHODS: All the potential CCP donors who met the inclusion criteria were telerecruited, i.e., contacted telephonically by trained personnel of the blood center. Donors were informed about CCP and its harvest procedure. Subsequently, donors were presented with 10 statements to assess the potential impetus (motivators) and impediments (barriers) toward donating CCP. In addition, SARS-CoV-2 IgG antibody titers were performed using chemiluminescence assay in donors who passed the predonation screening.

RESULTS: Based on their medical records, a total of 96 potential CCP donors were contacted telephonically for inclusion in the study. Among these 68.75% (n = 66/96) individuals expressed their willingness to donate CCP. "Altruism from adversity" was the most common motivational factor among voluntary donors (47.8%), whereas kinship was the strongest motivational factor among replacement donors (40%). Logistical reasons such as their distance from the blood center (33.3%) were the most common reason for not donating CCP. About 21.2% (n = 18/66) of the donors were deferred due to absent or low levels of anti-SARS-CoV-2 IgG antibodies.

CONCLUSIONS: Motivation factors such as "altruism from adversity" are more common in CCP donation. At the same time, most of the impediments to CCP donation were similar to those of the routine apheresis procedure. Knowledge of these motivators and barriers should form the cornerstone of plasma therapy-based donation program in any future pandemic.

Keywords:

Anti-SARS-CoV-2 antibodies, blood center, convalescent plasma donor, COVID-19 pandemic, donor deferral, plasmapheresis, seroprevalence rates

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Introduction

Coronavirus disease-2019 (COVID-19) Caused by severe acute respiratory

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syndrome coronavirus-2 (SARS-CoV-2) spread at a very rapid rate worldwide.^[1] COVID-19 was subsequently declared a global pandemic by the World Health Organization on March 11, 2020.^[2] Published literature mentions the potential benefits of convalescent plasma therapy in the H1N1 influenza pandemic, SARS-CoV-1, and middle east respiratory syndrome-CoV epidemics.^[3] This led the medical fraternity to use COVID-19 convalescent plasma (CCP) therapy in COVID-19 disease as an experimental therapy.^[4] The CCP therapy is based on the principle that the plasma of blood donors recovered from COVID-19 infection contains neutralizing antibodies against SARS-CoV-2 which may help neutralizing the virus in patients with COVID-19.^[5] In fact, in India, CCP therapy was recommended for off-label use in July 2020, based on the presence of IgG antibodies against SARS-CoV-2.^[6] This led to a sudden escalation in the demand for CCP across the country.^[7] Although the focus of research has been on establishing the efficacy of CCP as one of the management strategies for COVID-19, little attention has been given to the source of CCP, i.e., the CCP donors. Our blood center had a functional apheresis facility at the time of beginning of the COVID-19 pandemic, helping us to start providing CCP therapy on an immediate basis. Consequently, the biggest challenge for us was to telerecruit potential CCP donors from the limited population of COVID-19 recovered patients who were willing to come to our hospital-based blood center for the harvest. Furthermore, reticence to donate blood is a well-known fact among the eligible donor population.^[8] Furthermore, understanding the various motivators and barriers to CCP donation is an important part to ensure adequate availability of the CCP inventory not just for the present but for any potential future pandemics as well. With this background, we aimed to understand various impetus and impediments for CCP harvest among our donor population.

Materials and Methods

Study design, definitions, and procedures

The present study was a survey study conducted from September 2020 to May 2021 at the Department of Immunohematology and Blood Transfusion supporting a 1200 bedded tertiary care academic hospital. A list of laboratory-confirmed COVID-19 recovered individuals who were successfully treated and discharged from our hospital was compiled categorically from the data obtained through their medical records.

Individuals who met the following criteria were included in the study: (i) age between 18 and 65 years; (ii) more than 21 days since recovery from COVID-19. Multiparous women were excluded from the study as CCP collected from them could lead to transfusion-related acute lung injury. All the potential donors who met the inclusion criteria were telerecruited, i.e., contacted telephonically by trained personnel of the blood center. Donors were first asked if they were aware of CCP therapy to assess their level of awareness. Then they were informed about CCP and its harvest procedure. Subsequently, the donors who were willing to donate CCP were presented with four statements to assess the motivation factors [Table 1]. Similarly, the donors who refused to donate to CCP were asked about the reason for their unwillingness to assess the impediments (barriers) for CCP donation. The demographic details of the donors were extracted from the electronic medical records available in the hospital information system (HIS, Akhil Diagnostics Pvt Ltd, New Delhi, India). The predonation screening of all potential donors who reported to the blood center for CCP donation was carried out using the standard donor questionnaire as per the Drugs and Cosmetics Act, Government of India.^[9] SARS-CoV-2 IgG antibody titers were measured using a chemiluminescence assay (Vitros ECi, Ortho Clinical Diagnostics, New Jersey, USA) in donors who passed the predonation screening. A signal-to-cutoff value (S/CoV) of \geq 9.5 was considered a high/acceptable titer.^[10] Antibody screening was performed to identify the presence of any irregular red cell alloantibodies. Few donors were recruited by relatives of the patients. They were also subjected to the same recruitment process as aforementioned. The sample size was determined assuming 80% awareness about CCP donation among the eligible population with a confidence interval of 95% and 5% degree of error.

Donors were classified using the following definitions:

Voluntary donors: These were nonremunerated donors who donated for random patients at their free will.

Replacement donors: These were friends or relatives of a patient who donated for a specific patient.

All the data were entered into a spreadsheet and verified by two authors independently.

Ethical considerations

The study was based on the ethical guidelines as given

Table	1:	Questions	asked	from	donors	and	their
corres	pc	onding mot	ivators				

Questions asked from donors	Corresponding motivator
I feel grateful that I survived COVID-19	Altruism from adversity
Donating plasma to my fellow countrymen is my duty	Moral and civic duty
Donating plasma for my family or friend will help them fight COVID-19	Kinship
I don't think others might not donate plasma after recovery from COVID 19	Signaling reluctant altruism
COVID 19=Coronavirus disease 2019	

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in the 1964 "Declaration of Helsinki." Further, the study was approved both by the ethics and the scientific research committee of our institute.

Statistical analysis

Simple descriptive statistics were expressed as mean \pm standard deviation (SD; range) and quantitative data were expressed as number with percentage (%). The categorical data were compared using Chi-square test. The two-tailed *t*-test was used to compare paired data and a *P* < 0.05 was considered statistically significant. Data were analyzed using SPSS software version 20 (IBM Inc., Armonk, NY, USA).

Results

Donor demographics

Based on their medical records, a total of 96 potential CCP donors were contacted telephonically for inclusion in the study. Among these 68.75% (n = 66/96) individuals

expressed their willingness to donate [Figure 1]. A total 16.6% (n = 16/96) potential donors could not be contacted, as they had provided incorrect contact details, whereas 14.5% (n = 14/96) potential donors expressed their unwillingness to donate plasma. About 93.7% (n = 75/80) of the potential CCP donors contacted had already heard about CCP. As per the demographic details of the donors, out of the total of 66 potential willing CCP donors, 46 (69.6%) were voluntary donors, whereas 20 (30.3%) were replacement donors. The majority of the donors were O blood type (33.3%). Overall the male:female ratio of all the 66 donors was 8.4:1. Their mean age (\pm SD; range) was 32.8 (\pm 8.8; 19–62) years. None of the donors were positive for red cell alloantibodies.

Impetus/motivators

A total of four statements were presented to the 66 potential donors who expressed their willingness to donate to assess the motivation factors. Based



Figure 1: Process flowchart of telerecruitment for COVID-19 convalescent plasma donation

on the response, donors were categorized into four categories [Table 2]. "Altruism from adversity" was the most common motivational factor among voluntary donors (47.8%) and it was significantly higher among the voluntary donors as compared to replacement donors (47.8% vs. 20%; P < 0.05). Kinship was the strongest motivational factor among replacement donors (40%).

Impediments/barriers

Out of 96 donors contacted by telephone, 14 (14.6%) of the potential CCP donors expressed their unwillingness to donate plasma. In addition, four of the 66 individuals who had initially agreed to donate CCP, expressed their unwillingness just before the planned harvest procedure. A total of six statements were presented to these 18 potential donors to assess the barriers to CCP donation [Table 3]. Logistical reasons, such as their distance from the blood center and lack of sufficient funds to travel to the blood center were the most common reason for not donating CCP among 33.3% (n = 6/18). Fear of health issues as a result of the procedure (27.7%), not feeling well (16.6%), apprehension that the donated CCP may be sold (16.6%), and fear of reinfection with COVID-19 (5.5%), were the other reasons given by the donors to express their unwillingness to donate. All these impediments negatively impacted our CCP inventory.

Donor deferral

All 66 donors were screened as per the donor screening criteria established in the Drugs and Cosmetics Act, 2020 amendment, Government of India.^[9] Among these, 7.5% (n = 5/66) of the donors were deferred due to the absence of COVID-19 antibodies, whereas 13.6% (n = 9/66) donors were deferred

Table 2: Moti	vation factors	for core	onavirus
disease-2019	convalescent	plasma	donation

Motivator	Voluntary donors (<i>n</i> =46), <i>n</i> (%)	Replacement donors (<i>n</i> =20), <i>n</i> (%)	P *
Altruism from adversity	22 (47.8)	4 (20)	0.000029
Moral and civic duty	10 (21.7)	3 (15)	0.20
Signaling reluctant altruism	14 (30.4)	5 (25)	0.42
Kinship	0	8 (40)	-

*P<0.05=Significant

Table 3: Impediments/barriers for coronavirusdisease-2019 convalescent plasma donation

Impediment/barrier	Total respondents (<i>n</i> =18), <i>n</i> (%)
Logistic reasons	6 (33.3)
Fear of health issues as a result of procedure	5 (27.7)
Not feeling well	3 (16.6)
Donated blood might be sold	3 (16.6)
Fear of reinfection	1 (5.5)
Family pressure	0

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due to low SARS-CoV-2 IgG antibody titers. The S/CoV (signal-to-cutoff value) of anti-SARS-CoV-2 IgG antibodies among the accepted blood donors (n = 48) was 19.5 (±9.94; 9.5–47.3) as against 3.2 (±2.6; 0.01–8.05) in the deferred (n = 18) cohort (two-tailed P < 0.0001).

Discussion

In the absence of any definitive treatment for COVID-19, CCP emerged as an important experimental therapy as early as February 2020.^[5] Clinical trials were initiated in different parts of the world to test the effectiveness and safety of CCP.^[11] Authorization for the emergency use of CCP was granted by various regulatory authorities in different parts of the world.^[12] However, the availability and recruitment of CCP donors emerged as a major challenge for blood transfusion services, which were already affected due to the restrictions imposed as a result of the COVID-19 outbreak.^[8]

Understanding the various motivators and barriers to CCP donation is an important part of ensuring adequate CCP availability during the present or any future pandemic. In the present study, 93.7% of the potential CCP donors contacted had already heard about CCP. Awareness about blood donation is an important component of a successful blood donation program.^[13] The awareness levels were far higher as compared to a study by Masser et al. in which only 45% of the donors had heard about convalescent plasma.^[8] This can be attributed to media campaigns by the government of India mainly through television and social media. The appeal for blood donation through the media is in itself a motivational factor for 69.4% of the donors in a study by Mohammed and Essel.^[13] Furthermore, during the initial phase of COVID-19, due to the complete lockdown in India, people were more likely to watch television and use social media, which could have been attributed to the high level of awareness among potential CCP donors.

We studied the motivation factors among voluntary and replacement donors separately. Among the voluntary donors, "altruism from adversity" was the strongest motivator. This is in agreement with the findings of the study by Masser *et al.*,^[8] in which "altruism from adversity" was the strongest motivator among CCP donors. Vollhardt and Staub have suggested that adversity results in the development of inclusive altruism in an individual.^[14] Similarly, the phenomenon of voluntary reciprocal altruism, which has been effectively used to encourage organ donation,^[15] can also be utilized as a donor motivation strategy for CCP donors. As suggested by Masser *et al.*, invoking the abovementioned feelings can be an efficient tool to promote the CCP recruitment drive.^[8]

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Interestingly, we found that "signaling reluctant altruism" and "kinship" were the strongest motivator factor among replacement CCP donors. The results are in agreement with a study by Evans and Ferguson, in which reluctant altruism was found to have a positive association with routine whole blood donation behavior.^[16] Similar findings were seen in a study by Mohammed and Essel, in which the authors found that 90.3% of the donors were motivated to donate blood when their friend or relative was in need of blood.^[13] Nowak has also suggested that individuals are more likely to show preferential cooperation for their relatives.^[17] Although this can be considered a form of "impure altruism," perhaps interaction with such donors during their time at the blood center can help develop "pure altruism" in their minds for future.

Moral and civic duty was another motivator for CCP donation, both among voluntary and replacement donors. Awareness campaigns for dissemination should be designed to invoke these feelings in the potential CCP donors. Furthermore, while moral and civic duty, signaling reluctant altruism are common motivators seen among routine blood donors as well as CCP donors, "altruism from adversity" is more of a motivator factor for CCP donors. This becomes increasingly more important because the individual's tendency for CCP donation is likely to evolve with time.^[18]

In the present study, all potential donors were contacted telephonically during the CCP donor recruitment drive. Out of the 96 donors contacted, 16 donors (16.7%) had documented an incorrect phone number. In another study by Dhiman *et al.* done in New Delhi, India, 25.3% of the potential donors had provided incorrect contact details.^[19] This emphasizes that the demographic data collected from donors should be strengthened by the medical registration departments of the hospitals, especially in India.

A total of 18 donors (18.75%) expressed their unwillingness to donate plasma. Among the various factors, logistical reason (33.3%) was the most common reason for not donating CCP. In the study by Dhiman et al., 21.7% of potential donors were lost because they were out of town.^[19] Similar findings were observed in a study by Wong et al. done on plasma donors during the H1N1 pandemic.^[20] The percentage of potential donors lost for this reason is too high. Moreover, the blood banking system in India is decentralized. This highlights the importance of creating an online donor pool registry, so that blood centers can contact nearby potential donors. One such facility such as the "e-RaktKosh" application, which is an online centralized blood bank information system, is already available in India, and therefore, such donor pool data can be easily captured.^[21]

Fear of health issues as a result of procedure (27.7%) was the second-most common reported barrier for CCP donation. In a study by Sahu et al.,^[22] fear of procedure was present among 15% of the potential CCP donors. Interestingly, the respondents in that study were health-care workers; therefore, the fear of procedure is likely to be higher in the general population. Bagot *et al.* found that fear of health issues as a result of apheresis procedure was a cause of deterrent among 25% of the respondents.^[23] In the study by Dhiman et al., fear of procedure was observed among 21.5% of the respondents as a deterrent to CCP donation. This impediment can be overcome simply by dissemination of the information, education, and communication (IEC) material among the potential donors explaining in detail and in an easy language about what the donors should expect during an apheresis procedure.^[24]

Finally, the absence or low level of anti-SARS-CoV-2 IgG antibodies is a major cause of CCP donor deferral among otherwise healthy donors. In the present study, 21.2% (n = 18/66) of the donors were deferred due to absent or low levels of anti-SARS-CoV-2 IgG antibodies. Similar results were seen in studies by Dhiman et al.^[19] and Izak et al.,^[25] in which 15.4% and 27.8% of the donors were deferred due to absent or low levels of anti-SARS-CoV-2 IgG antibodies. Blood centers should ensure that anti-SARS-CoV-2 IgG antibody levels are done in all donors before CCP donation. In fact, CCP harvest without testing for anti-SARS-CoV-2 IgG antibodies was one of the major documented causes of the failure of CCP therapy in India.^[26] However, having equipment and trained workforce for performing anti-SARS-CoV-2 IgG antibody levels remains a challenge for resource-constrained countries like India.

Conclusions

Motivation factors such as "altruism from adversity" are more common in CCP donation. At the same time, most of the deterrents to CCP donation were similar to those of routine apheresis procedures. Knowledge of these motivators and barriers should form the cornerstone for a successful plasma therapy-based donation program in any future pandemic.

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Conflicts of interest

There are no conflicts of interest.

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