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A prospective study on COVID-19 convalescent plasma donor (CCP) recruitment strategies in a resource constrained blood centre

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Background and Objectives The COVID-19 pandemic has spread across 87 million people with more than 1·8 million deaths in the world. As there is no definite treatment modality, the use of convalescent plasma has become increasingly popular worldwide. This study aimed to identify an appropriate strategy of donor recruitment and to evaluate the appropriateness of pre-set plasma donation guidelines.

Material and Methods In this prospective study conducted from May to September 2020, the donors were recruited under the following two circumstances: Group I, patients in the post–COVID-19 follow-up in the clinic, and Group II, patients recovered from COVID-19 recruited through mass and electronic media. A pre-set donor selection criteria and laboratory investigation was designed according to national and international guidelines. Approximately 500 ml of COVID-19 convalescent plasma (CCP) was collected from recovered individuals in each group by two different cell separators. The overall donor's attendance rate, deferral rate, adverse events and donor compliance was analysed and compared between the two groups.

Results There was a significant difference in attendance in relation to registration between the groups ($P < 0.0001$). Donor deferral was significantly higher in group II compared with group I. The single most frequent cause of donor deferral was low antibody index ($P = 0.0001$). The total donor adverse event rate in CCP donation was significantly lower compared with routine plateletpheresis procedures. The donor's compliance to blood centre's protocol was satisfactory in both the groups.

Conclusion Recruitment of patients in the post–COVID-19 follow-up in the clinic was more effective than the general recruitment through mass and electronic media for convalescence plasma donation in a resource-constrained blood centre.

Key words: convalescent plasma, donor recruitment, plasmapheresis.

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Introduction

Coronavirus disease, 2019, now renamed as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) disease has emerged as a global pandemic since 2019 year-end.

World Health Organization (WHO) had first declared this outbreak as a public health emergency of international concern and subsequently a worldwide pandemic.

Presently, the approach to coronavirus disease 2019 is mostly preventive and supportive [1–4]. All treatments directly targeting the virus and the inflammatory response elicited by the virus remain investigational. Due to the lack of evidence of effective treatment modalities for COVID-19 or effective vaccines, classical and historical interventions have emerged as options for the control of the disease. Historically, convalescent plasma has proven effectiveness against various infectious diseases including influenza, zumin virus and severe acute respiratory syndrome. Initial data supporting the COVID-19 convalescent plasma (CCP) transfusion included three case series from China, enrolling 5, 10 and 6 patients, and it was hypothesized that use of CCP in the early phase of the disease may reduce morbidity and mortality [5–8].

Thereafter, various trials on CCP transfusion have been conducted in various parts of the world, including India. Indian Council of Medical Research (ICMR) approved its first open labelled phase II PLACID trial in 22nd April [9]. Due to increasing demand for plasma therapy, on 1 July 2020, the Drug Controller General of India (DCGI), the regulatory body, issued an official letter related to the off-label use of CCP in moderate ARDS due to COVID-19 as a part of expanded access programme (EAP) [10].

The implementation of donor recruitment strategies to maintain a convalescent plasma repository in a tertiary care COVID-19 hospital is always challenging. The scenario was further worsened by the stringent lockdown, with public transport restriction, which prevented donor visit to blood centres. The literature evidence of appropriate donor recruitment strategies in such scenarios of pandemic is limited.

Aims

- Identify and implement an appropriate CCP donor recruitment strategy by analysing its performance through voluntary participation in a resource-constrained setting.
- A preliminary evaluation of the appropriateness of pre-set plasma donation guidelines in terms of donor attendance, deferral and incidence of adverse reactions.
- Assessment of the compliance of blood centre in terms of provision of appropriate information, counselling, medical examination, laboratory investigation and plasmapheresis procedure to the donors, based on the feedback from the donors.

Materials and methods

This prospective study was conducted at the blood centre of a 1000-bed tertiary care COVID-19 hospital of a Medical College, from 9 May 2020 to 30 September 2020. This study was approved by the institutional ethical committee.

In this study, the donors were recruited under two circumstances:

- Group I, patients in the post–COVID-19 follow-up in the clinic
- Group II, patients recovered from COVID-19, belonging to the COVID-19 Care Network (CCN), recruited through electronic and mass media.

A medical expert from the blood centre was appointed at the post–COVID-19 follow-up clinic to interact with group I donors on a regular basis. He/she interacted with the prospective donors and shared information about convalescent plasma (CP) donation. He/she also explained CCP donor selection guidelines and criteria to the treating physicians actively involved in the management of COVID-19. The suitable volunteers were identified and registered. The prospective donors were provided with round transportation from their residence to the blood centre and vice versa both on the day of medical screening and blood sampling as well as plasmapheresis procedure.

The Group II donors were recruited through newspapers-electronic media campaign, with constant support from local volunteers from COVID-19-care network (CCN), volunteers from different sections of the society, who had been cured of COVID-19 disease and appointed by the local government authority. A liaison personal was designated from the blood centre who coordinated the programme by scheduling the pre-donation counselling, screening, examination and the plasmapheresis procedure. The donors were requested to make the transport and travel arrangements to the blood centre, which were reimbursed by the blood centre.

The donors of both the groups were required to visit the blood centre on two occasions. First visit included medical examination and collection of blood samples for laboratory testing. The second visit included the scheduled plasmapheresis procedure. In both the groups, informed consent (separate for both the groups) was taken after the individual donors were explained of the whole process and the plasmapheresis procedure.

Donor inclusion criteria

Recovered COVID-19 male patients and nulliparous females (at 28 days convalescence period from last PCR negative / discharge/ fitness certificate), aged 18–55 years,

with body weight >55 kg, haemoglobin / haematocrit >12·5/38%, platelet count>150 000/μl, normal plasma albumin level and serum protein level above 6 gm/dl in case of repeat plasma donation, along with a good peripheral venous access was considered eligible [11].

Donor exclusion criteria

The donors having any other co-morbid conditions such as cancer, chronic kidney disease, chronic infectious diseases, hypertension with systemic organ failure, persons on chronic steroid regime, diabetes mellitus with multisystem involvement, abnormally high plasma albumin level and all deferral criteria as per Drugs and Cosmetics Act and its amendments were considered ineligible [12].

Sample collection and laboratory investigations

The volunteers who complied with the inclusion criteria were subjected to laboratory investigations for complete blood count, ABO-Rh type and screen, liver function tests (LFT), routine serological tests of transfusion transmissible infections (TTI) by ELISA and individual donor nucleic acid tests (ID-NAT) for HIV, hepatitis B and hepatitis C. An approximately 15 ml of whole blood was aseptically collected from the ante-cubital vein in 4 EDTA vials (3 ml each) and 1 clotted vial (3 ml). The donors' samples which qualified all these preliminary tests were further subjected to anti-Spike protein (S) IgG estimation using ErbaLisa COVID-19 IgG ELISA kit (Cat. IME000136) as per manufacturer's protocol. Antibody index Ratio ≥1·1 was interpreted as positive [13]. Donors having positive Antibody Index Ratio were further subjected to SARS-CoV-2 surrogate virus neutralization assay using GeneScript SARS-CoV-2 Surrogate Virus Neutralization kit (Cat no-L00847) [14]. Assay results were interpreted as inhibition rate of assay reaction which was calculated as: Inhibition = {1−(O.D value of sample/O.D value of negative control)}× 100. Inhibition values ≥20% signified positive detection of neutralizing antibodies [15]. Such donors were considered appropriate for plasmapheresis procedure.

Suitability of cell separator according to the donors' physical features

Selection of cell separator [MCS+ (Hemonetics, Braintree, MA, USA) / Trima Accel (Terumo BCT, Lakewood, CA, USA) / Spectra Optia (Terumo BCT)] for individual donor was done according to their physical examination and peripheral venous accessibility. The donors with relatively difficult venous access and higher body weight were selected for Hemonetics MCS+. Donors with prominent venous access and lower body weight were suited for

Trima Accel / Spectra Optia. In each setting, 500 ml of plasma collection was targeted. All the procedures were performed under the supervision of a senior personnel to provide appropriate donor care.

Assessment of donors' feedback and the compliance of the blood centre

Every donor was followed up for 24 h post-donation and requested to reply to the feedback form with leading questions (Fig. 1):

- Availability of adequate information and counselling related to plasmapheresis procedure.
- Adequacy of the participant information form and the explanation of informed consent.
- Experience related to blood collection for laboratory investigation.
- Comfort and care during plasmapheresis procedure
- Their most common de-motivating factor related to plasma donation:
  a. fear of re-infection
  b. travel constraints
  c. work pressure
  d. discouragement from the family or peers
  e. any other significant factor

Figure 1 demonstrates the workflow of our study protocol.

Analysis of results

The implementation of an appropriate strategy to donor recruitment was analysed by comparing the number of donors who registered against the actual number of donors who attended the blood centre for medical screening in group I and group II. The adequacy of the plasma donor selection guidelines was observed by the overall donor deferral rate and the donor adverse reaction rate. The reasons for donor deferral in both the groups were analysed. The donor adverse reaction rate was also compared with the adverse reaction rate observed in routine plateletpheresis which had similar donor selection guidelines, except the antibody response.

The donors' feedback response was considered to be the indicator of the blood centre's compliance to the recruitment, selection and work process.

The statistical analysis of the parametric variables was performed by one-tailed Fischer's test, using GraphPad PRISM 9 software. $P < 0.05$ is considered as significant.

Results

In group I, a total of 62 out of 150 registered participants joined the medical examination (attendance rate: 41·3%).
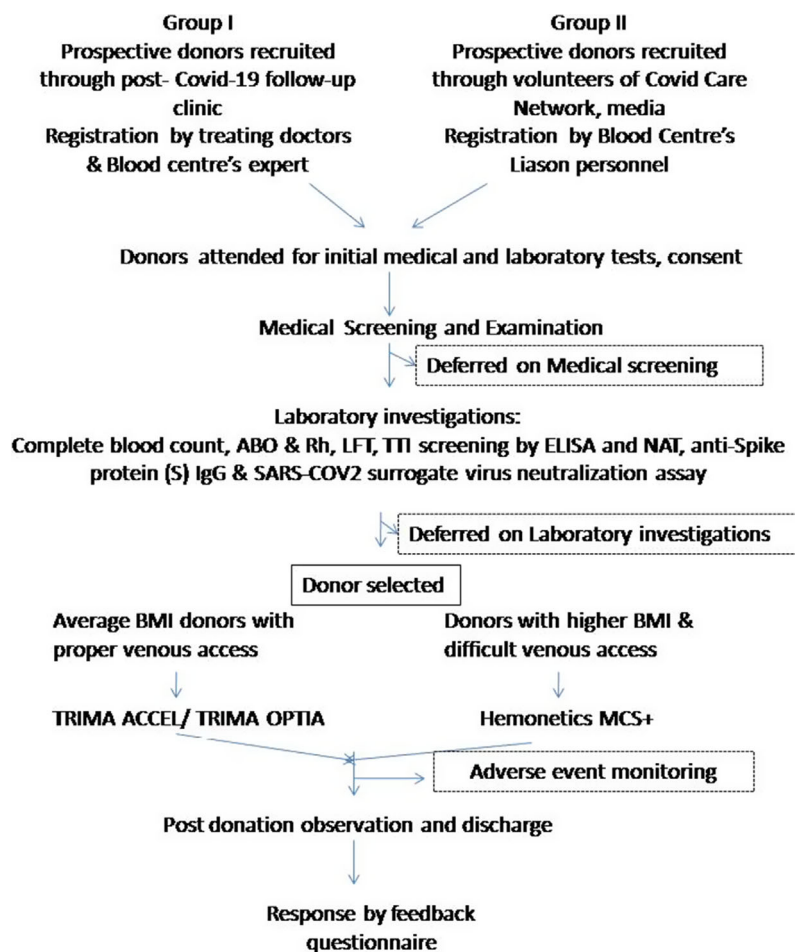
Fig. 1 Workflow of study protocol.

In Group II, after an initial coordination with 550 persons by phone, mail or social media, only 8·5% (47/550) replied by visiting the blood centre. There was a significant difference in the attendance rate of registered donors between Group I and Group II ($P < 0.0001$).

Table 1 shows the profile and the baseline analysis and the profile of the CCP donors in both the groups.

After the initial screening, 15 out of 62 donors (24·19%) were deferred in Group I. Likewise, 20 out of 47 donors (42·55%) were deferred after the initial screening in Group II. There was a significant difference in donor deferral rate between both the groups, with a higher deferral rate in Group II ($P < 0.034$).

The most frequent single cause of donor deferral was low antibody index ($P = 0.0001$). No correlation was observed between donor deferral and mode of treatment (i.e. whether hospitalized or home quarantined). The overall analysis of donor deferral in both the groups is given in Table 2.

Adverse events and outcomes

A total of 6 adverse reactions were observed in 73 plasmapheresis procedures in both the groups. In Group I, 37 procedures were performed in MCS+ and 9 in Trima Accel / Spectra Optia, with a total of 46 plasmapheresis. In group II, altogether 27 plasmapheresis were performed where 14 procedures used MCS+ and 13, Trima Accel / Spectra Optia. The overall donor adverse event rate of 8·22% (6/ 73) in convalescent plasma donation was significantly lower than the overall donor adverse event rate of 19·43% (61/314) in routine plateletpheresis procedures in our department ($P < 0.0133$) in the period January 2017–July 2018 [16]. There were no major events, and all recovered with rest and assurance. Commonly observed adverse events were hematoma and vasovagal reactions. Table 3 provides the details of 73 plasmapheresis procedures in both the groups.

–>A baseline analysis and distribution of the CCP donor's profile in both the groups

Parameters		Group I	Group II
Total no. of donors		62	47
Age	Mean ± SD	31·02 ± 9·05	35·10 ± 9·82
	<29 years	36 (58·06%)	17 (36·17%)
	30-39 years	13 (20·97%)	17 (36·17%)
	40-49 years	9 (14·52%)	8 (17·02%)
	>50 years	4 (6·45%)	5 (10·64%)
Sex	Male	43 (69·35%)	40 (85·10%)
	Female	19 (30·64%)	7 (14·89%)
Hospital admission/ home isolation	Hospital admission	15 (24·19%)	21 (44·68%)
	Home isolation	47 (75·81%)	26 (55·32%)
Blood group	A+	13 (20·97%)	9 (19·15%)
	B+	32 (51·61%)	20 (42·55%)
	AB+	2 (3·23%)	2 (4·25%)
	O+	12 (19·35%)	12 (25·53%)
	A negative	1 (1·61%)	0
	B negative	0	2 (4·25%)
	AB negative	0	1 (2·13%)
	O negative	2 (3·23%)	1(2·13%)

Table 2 The overall analysis of donor deferral in both the groups

Parameters analysed on donor deferral			GROUP I 62	GROUP II 47
Total no. of deferred			15 (24·19%)	20 (42·55%)
Causes of deferral	Non-reactive to S1RBD of SARS-CoV-2 by ELISA		7 (11·29%)	12 (25·53%)
	Low haemoglobin		2 (3·22%)	1 (2·12%)
	Low haemoglobin + low platelet		1 (1·61%)	0
	Poor venous access		1 (1·61%)	1 (2·12%)
	Serology	HBsAg	2 (3·22%)	0
		HCV	0	1 (2·12%)
		HIV	0	0
	Co morbidity		0	3 (6·38%)
	Self-deferral due to medical emergency		2 (3·22%)	2 (4·26%)
Age	Mean ± SD		27·06 ± 7·23	37·25 ± 10·27
	≤29 years		10 (16·13%)	5 (10·64%)
	30-39 years		4 (6·45%)	9 (19·15%)
	40-49 years		0	3 (6·38%)
	≥50 years		1 (1·61%)	3 (6·38%)
Hospital admission/ home isolation	Hospital admission		5 (33·33%)	10 (21·28%)
	Home isolation		10 (66·67%)	10 (21·28%)

Assessment of the donor's compliance based on the feedback related to the blood centre's methodology

Results of the assessment of the donor's compliance based on a feedback related to the blood centre's methodology are shown in Table 4.

Discussion

The studies on the role of CCP in the treatment of mild to moderate ARDS in COVID-19 have shown encouraging results [17]. However, in developing countries, it is challenging to formulate strategies of plasma donor recruitment, set up guidelines for donor selection and carry out

Table 3 Procedure details of plasmapheresis in both groups

Parameters		Group I	Group II
Total no. of procedures		46	27
Machine	MCS+	37	14
	TRIMA/ SPECTRA OPTIA	9	13
Mean plasma volume processed	1662·37 ML	1780·22 ML	
Mean ACD used	170·68 ML	170·07 ML	
Convalescence period of donation	Mean ± SD	37·34 ± 10·39	37·07 ± 9·52
	≤28 days	5	6
	29–35 days	14	6
	36–42 days	15	7
	43–49days	6	7
	≥50 days	6	1
Adverse event observed	5	1	

Table 4 Assessment of the donor's compliance by feedback

Donor's feedback regarding blood centre's methodology	Group I ($n = 62$)	Group II ($n = 47$)
Adequacy of Participant's information form	100%	100%
Informed consent	100%	100%
Comfort and care during procedure	100%	100%
Major demotivational factors		
Fear of re-infection	0	10·6% (5)
Work pressure	4·83% ($n = 3$)	23·4% ($n = 11$)
Peer/family discouragement	3·22% ($n = 2$)	17·02% ($n = 8$)
Travel Constraints	0	21·27% ($n = 10$)

It was observed that there was a significant difference in the demotivational factors faced between Group I and Group II (P value < 0·00001).

plasmapheresis to maintain a constant convalescent plasma inventory [18].

In our study, the medical screening attendance rate of donors in group I, registered in the post–COVID-19 OPD (group I), was significantly higher compared with those in group II, who were randomly recruited through mass media, social media or COVID-19 care network. This might be due to the more generalized approach, resulting in inadequate counselling and education of donors in group II, compared with group I donors, who received a more targeted approach. Thus, adequate counselling and education of donors as well as of the treating physicians were considered essential for the implementation of an appropriate CCP donor recruitment strategy. Further, affected by the lockdown, the difficulty in self arrangement of transportation by the donors was another important reason affecting attendance.

An evaluation of the appropriateness of pre-set plasma donation guidelines was done in terms of donor selection, deferral and incidence of adverse reactions. A significant difference was observed between group I and group II in terms of donor deferral rate. Random recruitment without an opportunity to provide appropriate education and fact clarification in group II may have contributed for this difference. The most frequent cause of donor deferral was low antibody index. Thus, correct timing of donor screening and selection is important to reduce donor deferral due to the falling antibody titre, and consequently improve donor recruit [11]. The stringent donor selection and the wide range of laboratory tests may also have increased donor deferral rate. Hence, the laboratory investigations and donor selection guidelines must be set addressing its appropriateness and the financial feasibility in a resource poor setting, where the programme will be run.

The incidence of adverse events in CCP plasmapheresis procedures was significantly lower compared with that in routine apheresis donations in our centre [16]. Apheresis procedures require especial skills for the execution, as well as a constant supervision; otherwise, may lead to complications or adverse donor reactions. In the present study, all the procedures were supervised

by senior skilled medical professionals, which may be the reason of the significantly low incidence of adverse events in both the groups, with both the machines. We could not compare our results with others, because presently there is minimal evidence in the literature related to the deferral rate and adverse events in CCP donation in.

Blood donor comfort and compliance are essential to motivate, recruit and retain donors in any kind of voluntary programme [19, 20]. In the present study, we confirmed that the donor care comfort could be fully achieved, and the donor consent form was appropriate. However, factors like fear of re-infection, work pressure, discouragement by peers or family played a major role as factors to de-motivate donors in group II. This further confirmed the importance of implementing a well-organized targeted intervention strategy to achieve successful CCP donor recruitment, under the situation of a pandemic. It may also serve as the basis when implementing strategies for plasma donor recruitment in the future, when other challenging pandemics may occur.

A short study period and the low sample size were the limitations of the present study.

Conclusion

The implementation of CCP—programme needs adequate resources to make it viable. Countries with limited resources need to plan a cost-effective strategy to mobilize and appropriately use them. The present study has shown the effective plasma donor recruitment by medical doctors at the post–COVID-19 clinic.

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Conflict of interests

The authors declare no conflict of interests.

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