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Original article

Constraints and challenges in convalescent plasma collection amidst the Covid 19 pandemic- strategies and recommendations to overcome these

S. Mahapatra [a,*], S. Pati [b]

[a] C/O- Mr NK Mishra, N-1/256, Nayapalli, IRC Village, 751015 Bhubaneswar, Odisha, India
[b] Regional Medical research Centre, Chandrasekharpur, 751023 Bhubaneswar, Odisha, India

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ABSTRACT

Background. – COVID 19 is an acute respiratory disease caused by infection by the virus SARS-COV-2 and has been declared as a pandemic whose specific treatment is still not established. One of the options in the treatment is Convalescent plasma (CP) therapy when there is presence of required amount of neutralizing antibodies in the plasma of recovered COVID patients. Our objective was to analyze the challenges and the constraints encountered in motivation of COVID 19 recovered persons to come for the screening procedures and to convince the selected persons to come for Plasma donation voluntarily.
Material & methods. – The present retrospective observational study was conducted for a period of five and half months. Out of 1515 number of persons contacted telephonically for Plasma donation, 1291 persons came for screening of whom 1028 persons were eligible for donation, 263 cases were deferred and 966 persons finally donated.
Results. – Maximum number of acceptance cases were from males-(98.7%). Of the accepted cases, (41.73%) were from the 18-30 years' age group. 33.94% were from blood group 'O' Rh D positive giving maximum contribution from any blood group. 38.3% of the accepted cases had resolution of all COVID symptoms within time period of 28-40 days. Maximum number of accepted individuals (39.75%) had suffered from multiple symptoms followed by 39.02% of asymptomatic persons. Highest number of Plasma donation was contributed by Odisha Government Police personnel (51.56%).
Discussion. – In this global ongoing pandemic, the "Fear Factor of contracting the disease" has acted as a major challenge in motivating and convincing a COVID recovered patient for plasma donation. The challenge before the medical professionals was to motivate, educate and convince the potential donors and the society about the likely benefits of convalescent plasma. This could be finally overcome with the help of positive orientation through social and conventional media as well as mass appeal from government side on the benefits of plasma therapy in saving lives in the present pandemic.

1. Introduction

COVID 19 is an acute respiratory disease caused by infection by the virus SARS-COV-2 which was first detected in Wuhan (China) in December 2019. WHO declared the COVID-19 outbreak a Public Health Emergency of International Concern on January 30, 2020 and classified the disease as a pandemic on March 11, 2020. The protection from COVID-19 infection is yet to be directly correlated with levels of circulating antibodies against SARS-CoV-2 [1]. Convalescent Plasma (CP) is the liquid constituent of Blood which is collected from people who have recovered from COVID-19 infection. This plasma contains antibodies that can neutralize SARS-CoV-2 and thus improve disease course in patients with COVID-19 infection before the maturation of a patient's own humoral response [2,3].

In the past, convalescent plasma transfusion was used to treat a variety of infectious diseases, including influenza, Argentine haemorrhagic fever and SARS 10 [4–6]. Still, the effectiveness of CP in treating other infectious diseases, such as Ebola, remains inconclusive [7]. Since COVID-19 convalescent plasma (CP) was approved by the USFDA as an experimental treatment for patients with COVID-19, facilities have been set up for collecting CP throughout the US. In

* Corresponding author.
E-mail addresses: doctorsmita@rediffmail.com, dr.smitamahapatra@gmail.com (S. Mahapatra), drsamghamita12@gmail.com (S. Pati).

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India, permission to conduct a Clinical Trial of Convalescent Plasma for COVID-19 patients was given by the Drugs Controller General of India in early April 2020. Later, Government of India on 25.6.2020 and Director General of Health Services on 01.7.2020 laid down circulars to use CP as an off label drug [8,9]. Basing on the above circulars, the Govt of Odisha decided to start Convalescent Plasma Therapy in the Sate as an off label drug.

The aim and objective of the present study was to analyze the challenges and the constraints encountered during the motivation of COVID 19 recovered persons through counselling to come for the screening procedures to donate CP and to convince the selected persons to come for Plasma donation voluntarily.

2. Materials and methods

2.1. Study designs

The present observational retrospective study was conducted for a period of five and half months from July 15 2020 to December 31st 2020 in the Department of Transfusion Medicine, Sriram Chandra Bhanja (SCB) Medical College & Hospital, Cuttack, Odisha, India.

2.2. Registry set-up

A State registry was set-up in the Plasma Bank for the maintenance of data and public registry was set up by the Govt. of Odisha for enrolment of interested persons to donate CP voluntarily. After looking into factors like age, symptoms, date of discharge, and eligibility criteria, 1515 number of COVID recovered persons were contacted telephonically. The rationale behind plasma collection, procedure in detail, expected or likely time to be taken, various tests to be carried out and risks of the procedure, etc., were explained to each provisional Donor.

2.3. Logistics and services to motivate voluntary plasma donation

To motivate voluntary plasma donation, the Govt of Odisha decided to provide free accommodation, food and travel to the persons coming from other districts of Odisha to Cuttack. On reaching the Plasma Bank, they were screened and those who qualified were requested to donate their CP. Out of 1515 persons contacted, 1291 number of person came forward for screening, 1028 were accepted while 966 finally donated. Certificates of appreciation on behalf of Govt of Odisha was distributed to all those who donated their plasma.

Inclusion criteria for Donor selection:

- Prior diagnosis of COVID-19 documented by a laboratory test (RTPCR);
- Complete resolution of symptoms for COVID-19 before 28 days prior to donation;
- Donors with Haemoglobin >12.5 g/dl, platelet count > 1,50,000 per microliter of blood and Total Leukocyte Count within normal limits were accepted;
- Donors negative for screening for HIV, HBV and HCV by Enzyme linked Immunosorbent (ELISA), Nucleic acid amplification(NAT), syphilis and malaria by rapid tests were included;
- Donors with total serum protein > 6gm/dl were accepted;
- All the Plasma Donors were screened for SARS-COV2-IgG antibody and those with IgG antibody of 2 IgG Index (1:80 titer of neutralizing antibodies) estimated by Electrochemiluminescence immunoassay (ECLIA) technology (Abbott Architect i2000SR) were allowed to donate.

Exclusion criteria for Donor selection:

- Those who have uncontrolled diabetes or hypertension;
- Women, who have ever been pregnant;
- A cancer survivor or any patient with Chronic kidney/heart/lung/liver disease;
- Neutralizing antibody titer for IgG of < 1:80.

2.4. Informed Consent Process

CP was collected from individuals who gave written consent to donate. The consent was taken after informing the Donors in person regarding the procedural time taken, the amount to be collected (which will be divided into two aliquots) and the utility of the plasma collected for two COVID 19 patients. This was preceded by thorough counselling sessions, telephonic as well as one-on-one. All the connected papers related to Donor consent were kept on record.

2.5. Collection

Convalescent Plasma was collected by Plasmapheresis procedure (Trima Acele machine) which ranged from 400 ml to maximum up to 500 ml which was divided into two aliquots each with 200 to 250 ml of Plasma. It was independent of the donor size and weight.

This was as per the guidelines laid down on 17.4.2020 by the Directorate General Health Services, Central Drugs Standard Control Organization, Govt of India, which stated volume of CP collected will not exceed 500 ml per sitting (as per Drugs and Cosmetics (Second Amendment) Rules, 2020).

The Plasma units were stored at −30 °C in the Deep Freezer and were issued after thawing at 37°c and cross- matching.

Outcome: 1028 number of individuals were accepted of whom 966 number of persons donated CP & each unit was aliquot into two units to be issued to two patients. CP collected from Donors tested with SARS-COV2- neutralizing antibody titer of more than 1:80 were issued soon (starting from few hours to maximum one week from day of collection) after the collection due to the heavy demand of the same. CP were issued without any charge for COVID patients admitted in the 29 number of designated COVID Hospitals in the State of Odisha.

3. Results

Out of 1515 number of persons contacted telephonically, consisting of 1485 number of males and 30 number of females, 1291 persons came for screening from which 1028 persons were accepted for donation. But, only 966 persons donated and 62 persons did not donate out of whom, 31 (50%) avoided telephonic calls when contacted, 19 persons (31%) came for donation, but did not finally donate because of last-minute doubts, internal fears and apprehensions of getting infected again. The persons who came for screening included 1274 number of males and 17 number of females.

1015 and 13 cases of Convalescent Plasma were finally accepted from males & females respectively. Deferral from males and females were 259 and 4 respectively. From the age group 18-30 years, the highest acceptance and deferral cases were 429 and 142 respectively. Similarly, the lowest acceptance and deferral cases were 30 &10 and they were from the 51-60 years' age group (Table 1).

Maximum acceptance of 239 was from group of persons whose screening was done in the time period of 28-40 days after complete resolution of symptoms. Deferral of 148 persons in screening was

Table 1
Number of persons contacted, screened, accepted, deferred and donated as per the gender and age groups.

Number of persons approached	Number of Donors screened	Number of Donors accepted	Number of Donors deferred	Number of Donors donated Plasma
1515	1285	1028 (1015 males 13 females) (18-30 years-429 31-40 years-405 41-50 years-164 51-60 years-30)	263 (259 males 4 females) (18-30 years-142 31-40 years-85 41-50 years-26 51-60 years-10)	966

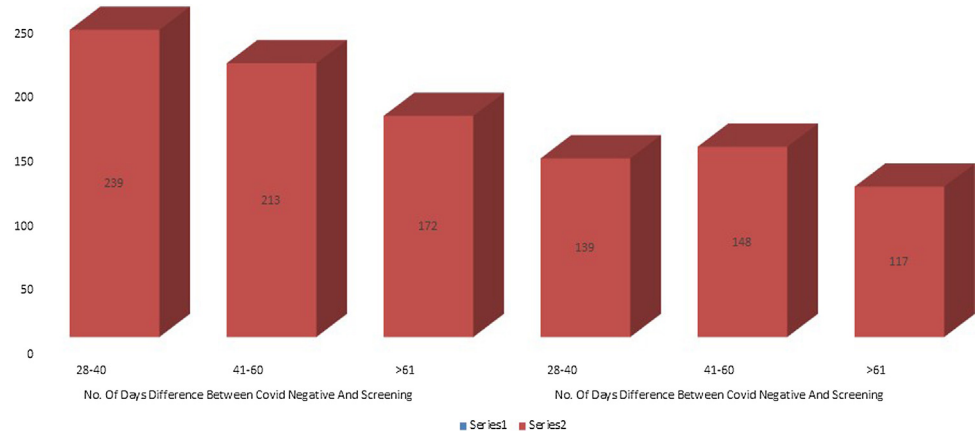

Fig. 1. Number of plasma donors accepted and deferred as per the time period of between complete resolution of symptoms and screening.

highest in the case of time interval of 41-60 days after resolution of symptoms. (Fig. 1).

Maximum number of accepted individuals (384) had suffered from multiple symptoms like fever, cold, loss of smell, loss of taste, headache, body ache etc. followed by 377 asymptomatic persons. 80 persons had suffered only with fever, 70 only with cold, 26 with only headache, 18 with cough only and 11 had only body ache (Fig. 2).

Maximum number of persons (176) deferred had low neutralizing antibody titer followed by 22 number of deferral cases due to high hematocrit count, 13 with poor venous status, 11 due to uncontrolled diabetes, 9 for low platelet count and 8 each for positive hepatitis B, Syphilis, low body weight, venous access problem (Fig. 3).

Highest number of Plasma donation was contributed by Police personnel (499) followed by general public (318), Odisha Government Fire Services Jawans (100), Doctors (27), NDRF (National Disaster Response Force) Jawans (20) and important political personalities (2).

4. Discussion

There are only a few available antiviral treatments, which have limited efficacy on COVID-19 at present. Plasma therapy trials conducted globally have given positive interim results. COVID-19 cases have also shown improvement to a certain degree after CP therapy in China [10]. Mayo Clinic plasma therapy trial reported that the early timing of plasma transfusions in a cohort of 35,322 patients was associated with lower mortality [11]. In India, the results of the PLACID Trial indicate that there is no difference in the 28-day mortality or progression to severe COVID-1, across the trial arms [12].

According to Olivier Garraud, convalescent plasma therapy remains a solid option to treat COVID patients, though this option falls into a portfolio of many other therapeutic approaches and does not provide complete cure [13]. Early administration of high-titer convalescent plasma against SARS-CoV-2 to mildly ill infected older adults reduced the progression of Covid-19 [14]. In all studies the highlight has been on the patients' outcome. But, the real challenge in Plasma Therapy studies lies in the collection of CP from the recovered patients.

In our present study, out of 1515 number of persons contacted telephonically only 966 persons donated and 62 persons did not donate out of whom, 31 (50%) avoided telephonic calls when contacted, 19 persons (31%) came for donation, but did not finally donate because of last-minute doubts, internal fears which refer to apprehensions and self- conjectures of the Donors mostly based on hearsay and unfounded accounts from friends and relatives. These included fears of weakness, loss of immunity and reinfection. 12 persons (19%) could not donate as they were suffering from other minor medical ailments when they came for donation after few days of screening.

Maximum number of Donor acceptance as well as deferral were from males and from the age group of 18-30 years. This may be due to the fact that as only nulliparous lady can donate Plasma, so maximum contribution was from the males. The acceptance was highest when the screening was done within 28- 40 days after complete resolution of the disease and the deferral was highest when the screening was done at a later period of 41-60 days after the complete resolution. Deferral rate was highest with neutralizing antibody screening as we had strictly taken the cut-off of neutralizing antibody for a Donor to become eligible for Plasma donation as 1:80 [15]. A research on SARS demonstrated that the specific IgG began to increase around week 3 after onset, and peaked at week 12 [16]. So, screening done before this period results in comparatively lesser deferral rate than when done at a later period. Still, the biggest challenge for the Plasma donation is to get a suitable donor with accepted neutralizing antibody titer.

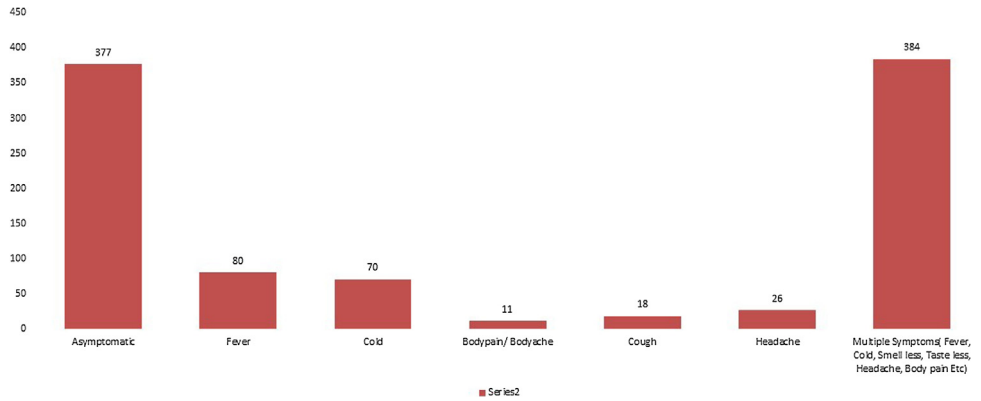

Fig. 2. Number of donors having symptoms and with no symptoms.

Maximum acceptance rate was found in persons who had suffered from multiple symptoms followed by persons who were asymptomatic while suffering from COVID infections. This may be due to the fact that even a symptomatic person can develop adequate SARS-COV2-IgG antibodies in response to the infection and can be a potential Plasma donor. Even with free accommodation, food and travel facilities given for the Plasma donors, maximum contribution for donation was from police person which was followed by the general public who required a lot of efforts to be motivated and recruited. The above facilities given aided in handling Donors from far-off areas and a logistics exercise to avoid any inconvenience to prospective Donors.

During COVID pandemic, to counsel recently recovered patients before discharge to donate in future was a difficult task & from the list of the discharged patients, many were in the exclusion criteria. From the remaining cured persons, very few consented to come forward and donate. One specific reason mentioned by some eligible donors was the fear of contracting the disease again if they visit a Medical establishment, even if it may be a Plasma Bank. In some of our prospective plasma donors, even when the donor was willing, the family was instrumental in denying consent. Hence, the emotional quotient also played a big role. Thus, it was slightly easier to get Donors from a single public organization like Odisha Government Police who supported us.

We started a Plasma donation drive where the frequently asked questions(FAQ) on Plasma donation were circulated across all districts in the State of Odisha through newspapers, television and social media. The administration and local politicians were instrumental in motivating the people to save lives by Plasma donation. The Municipal Corporations or District Administrations, as applicable, tracked the list of discharged persons, took consent from them telephonically and the list was shared with the Plasma Bank.

When these persons were contacted telephonically to come for screening, many of them did not turn up due to internal fear of contracting the disease again. A few individuals, out of those persons who were selected after screening, refused to come giving plea of some problems or avoided the phone calls may due to some fear factor or unwillingness of the family members. The persons who donated were motivated and convinced that the plasma collected from them is going to save two lives of serious COVID patients. The Donors got certificates of appreciation from us signed by the highest State authorities for their noble gesture. Certificates of appreciation was an encouragement to the Donors and served as a souvenir/memory for the Donor.

A dedicated counsellor in our Plasma Bank gave maximum efforts for the motivation and recruitment of donors in our case. The media, both print and digital, also played a positive role in this matter. Odisha State Govt. gave inputs for some positive stories on plasma donations in both print and digital media. Posters and video clips for appeal were designed and circulated on Twitter and Facebook (both in the English and local languages). Public servants

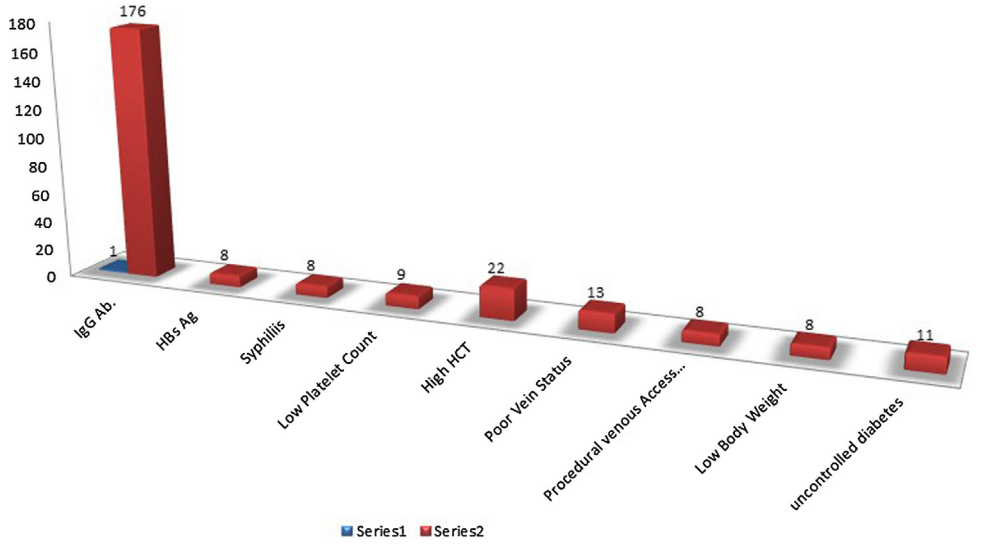

Fig. 3. Number and reasons of deferral.

led by example. There is an altruistic atmosphere whereby public servants in the line of duty have been hailed as COVID warriors and real heroes in society. They were also easier to reach, in groups, and approachable through their command structure.

Plasma donations at our centre was purely voluntarily and without any incentives given to the Donors or any harassment given to the relatives of the COVID patients to arrange for a plasma donor. Due to this ethical practice, persisting efforts from our end and support from the State Govt, we got one of the highest number of Plasma donations in the country, as a single medical institute. A great game changer in this entire exercise was that the Govt made availability of Plasma units free of any charges to all COVID 19 patients admitted in the dedicated COVID hospitals in the State of Odisha. Convalescent Plasma was also made available without exchange for the COVID patients requiring the same.

5. Conclusions

Blood donation is inherently an altruistic act and in normal times, donors are healthy individuals who volunteer to donate. Donor Altruism is a larger subject which was aimed at by Government as one of the factors for Donor motivation. In a global ongoing pandemic, the "Fear Factor of contracting the disease" acts as a major challenge to motivate and convince a COVID recovered patient for plasma donation. But, with the help of targetted publicity on the benefits of plasma donation which can save two precious lives with a single donation, we can increase the plasma donation drive. The challenge is to motivate, convince, educate the potential donors and society about the likely benefits of COVID convalescent plasma. This can be overcome with the help of positive orientation on the benefits of plasma therapy in managing the pandemic.

The medical professionals should take the support of the Administration by convincing the administration on the efficacy of the Convalescent Plasma Therapy. Support of the Civil Administration at District/Municipal levels can go a long way in making this exercise successful. In the case of the Govt of Odisha, it was the zeal at the highest levels to make Plasma Donation a community-led movement, free from political competition, that helped this idea to become widely accepted all across the State.

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Ethical approval

The study protocol was approved at the stage of conception and initiation by Expert Committee, Health & Family Welfare Department, Govt. of Odisha, India.

Disclosure of interest

The authors declare that they have no competing interest.

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