

Original Research Article

Investigation of hesitancy to donate plasma among COVID-19 survivors in Goa: an online survey

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ABSTRACT

Background: The ongoing COVID-19 pandemic led to surge in mortality. In the absence of definitive treatment, convalescent plasma therapy was accepted as a modality to treat COVID-19 patients. There exists hesitancy with regards to COVID-19 convalescent plasma donation. The objective of this study is to find the deterrents to CCP donation.

Methods: An online survey was conducted by snowball technique. The study participants were COVID-19 survivors. They were asked to express their willingness to donate CCP. The reasons for not donating CCP were recorded. The data was analyzed using R-program. The adjusted and unadjusted Odds ratios were calculated to find the predictors of willingness to donate CCP.

Results: 110 study participants responded to the survey. 49.1% of the responders were willing to donate plasma. The top three deterrents of CCP donation were ill health (27.6%; 95% CI, 18.28%-39.27%), ineligibility (10.5%; 95% CI, 4.98%-20.21%), not recovered completely (6.58%; 95% CI, 2.45%-15.34%). The female gender, older age, being symptomatic, unaware of government incentives, tested by RAT, and unaware of CPT were associated with lower odds of donating CCP.

Conclusions: Ill health, ineligibility, and perceived incomplete recovery were the major deterrents of CCP donation. Being female, older age, being symptomatic, unaware of government incentives, tested by RAT, and unaware of CPT were associated with lower willingness to donate CCP. There is a need to develop interventions to target these factors to improve CCP donation whenever it is indicated.

Keywords: COVID-19, SARS-CoV-2, Convalescent plasma therapy, Deterrents, COVID-19 plasma donation

INTRODUCTION

Convalescent plasma therapy (CPT) has been used for almost a century to treat various infectious diseases. Emil von Behring was awarded Nobel prize for the discovery of serotherapy for diphtheria in 1901.¹ During Spanish flu of 1918, serotherapy was found to decrease mortality among its recipients.² Coronavirus disease 2019 (COVID-19) convalescent plasma (CCP) is plasma derived from COVID-19 survivors, which contains neutralizing antibodies against severe acute respiratory syndrome

coronavirus-2 (SARS-CoV-2).³ CCP having specific neutralizing antibodies and immune-modulators could save the life of the COVID-19 affected patients.⁴ On August 23, 2020 the United States food and drug administration (US FDA) issued an emergency use authorization (EUA) for CCP as a potential treatment for COVID-19.⁵ The ongoing mayhem caused by the COVID-19 pandemic led to adoption of this therapy in the absence of definitive treatment and vaccination. EUA granted by US FDA was revised on February 4, 2021. As

per US FDA, the CCP must have a high antibody titer to be an effective against neutralizing the virus.⁶

Shen et al treated five critically ill COVID-19 patients with CCP and they all improved.⁷ Karbiener et al concluded that selecting older donors immediately after convalescing with moderate to severe disease might yield high titer CCP.⁸ A recent RCT on the CPT for Severe COVID-19 from New York found no improvement in the 28 days clinical status, however they noticed reduction in the mortality in the CPT group.⁹ Simonovich et al did not find significant difference in the clinical or mortality among the plasma arm when compared to the placebo in a RCT.¹⁰

The ministry of health and family welfare, Government of India recommended CPT as an investigational and off-label use for the treatment of moderate to severe COVID-19 disease.¹¹ The all India institute of medical sciences Indian council of medical research (AIIMS-ICMR) COVID-19 management protocol algorithm included CPT as a treatment modality till May 16, 2021.¹² The Government of Goa inducted CPT as a treatment modality on the August 3, 2020.¹³ The need for the CCP has been increasing with rising COVID-19 related mortality, however the donors are reluctant to donate CCP.¹⁴ A CCP donation program cannot succeed without comprehending the deterrents to it. Addressing the deterrents may help to augment CCP donation. There is limited information on what deters the COVID-19 recovered individuals from becoming a plasma donor. This study aims to understand the reasons behind this hesitancy among the COVID-19 survivors to become a CCP donor. The study findings will help the local health authorities to enhance recruitment of CCP donors by addressing the barriers to CCP donation.

METHODS

An online questionnaire was generated by using Google Form and was circulated among the moderate to severe COVID-19 convalescing patients through snow-ball technique.¹⁵ The first part of the form included a written consent which would open the rest of the questions once positive consent was provided by the study participant. Since this was an online survey, in person consenting process could not be completed. The second and third author contacted the COVID-19 survivors and obtained their verbal consent over phone before emailing or sending it by medium acceptable to the study participants. The data captured was converted into comma separated file (.csv) and analyzed using R-program (3.6.2 version).¹⁶ The sample size was calculated by using the nMaster software (1.0) developed by Christian Medical College, Vellore.¹⁷ A total of 110 subjects participated in the study.

The descriptive analysis in the form of proportions along with 95% confidence intervals were calculated by using the R-program. Simple and multiple logistic regression

analysis were used to identify the predictors for willingness to become a prospective CCP donor. The model used for the simple regression is as follows:

$$\ln(\text{odds of willing to be a donor}) = \beta_0 + \beta_i \times x_i$$

Where, “ln” is log odds of willingness to become a prospective CPP donor, which is a binary variable with responses of “yes=1” and “no=0.” β_0 is the intercept and β_i is the slope (coefficient) for any given variable (x_i). Similarly, the model used for the multiple regressions was as follows:

$$\ln(\text{odds of willing to be a donor}) = \beta_0 + \beta_1 \times x_1 + \dots + \beta_p \times x_p$$

The log odds for willingness to donate CCP were obtained for each variable after adjusting for multiple predictors. After exponentiating the coefficient, we obtained the adjusted and unadjusted odds ratios of willingness to be a CCP donor for each predictor. The crude and adjusted odds ratios (OR) along with 95% confidence intervals (CI) and p-values are presented in a tabular form.

RESULTS

A total of 62,304 SARS-CoV-2 positive cases were detected in Goa at the time of the data collection. 201 of these cases were contacted. Out of which only 116 responded. A total of 110 patients consented to participate in the study while six did not consent. Following is the analysis of 110 participants. The mean age of the study participants was 43.7 ± 17.5 years, ranging from 18 to 81 years. The median age of males was higher than the female participants (Figure 1).

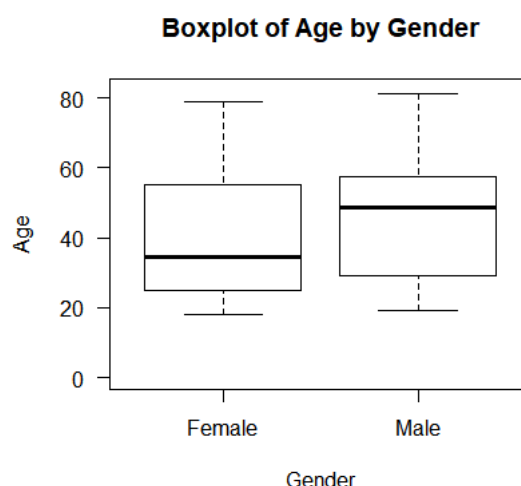


Figure 1: Boxplot of age by gender.

The males were 47.3% and females were 52.7%. About 12% of the study participants were doctors by occupation.

Only 76.4% were symptomatic, rest were asymptomatic. Out of the total SARS-CoV-2 positive participants, 45.5% were detected by reverse transcriptase polymerase chain

reaction (RTPCR) test, 35.5% by rapid antigen test (RAT), 7.3% Truenat™ test and rest were unaware of type of test performed (Table1).¹⁸

Table 1: The prevalence of variables among the study population.

Variable	Responses	Percentage	95% CI	P value
Heard of plasma therapy	Yes	96.4	90.4-98.8	2.2e-16
	No	3.6	1.2 - 9.6	2.2e-16
Have donated plasma	Yes	4.5	1.7 - 10.8	2.2e-16
	No	95.5	89.2 - 98.3	2.2e-16
Willing to donate plasma	Yes	49.1	39.5 - 58.7	0.924
	No	50.9	41.3 -60.5	0.924
How does plasma therapy helpful	Saves life of more than one COVID-19 patient	52.7	43.0 - 62.2	0.6336
	Saves life of one COVID-19 patient	20.9	13.9 - 29.9	1.892e-09
	Not aware	22.7	15.5 - 31.9	1.85e-8
	Does not help	3.6	1.2 - 9.6	2.2e-16
Heard of Government incentives for plasma donors	Yes	15.5	9.5-23.9	8.617e-13
	No	84.5	76.1 - 90.5	8.617e-13

Table 2: The univariate and multivariate regression analysis of willing to donate plasma.

Variable		Univariate analysis (OR, 95% CI)	P value	Multivariate analysis (OR, 95% CI)	P value
Age (years)		0.98 (0.96,1 .0)	0.0587	0.98 (0.95, 1.0)	0.147
Sex	Female	Ref		Ref	
	Male	0.93 (0.44, 1.96)	0.84	0.90 (0.38, 2.16)	0.819
Symptoms experienced	Experienced	Ref		Ref	
	Not experienced	0.69 (0.28, 1.69)	0.43	0.74 (0.23, 2.29)	0.603
Severity of disease	Mild	Ref		Ref	
	Moderate	0.66 (0.23, 1.79)	0.415	0.74 (0.23, 2.29)	0.604
	Severe	0.60 (0.08, 3.82)	0.589	0.88 (0.09,7.50)	0.902
Kind of test	Rapid antigen test	Ref		Ref	
	RTPCR	0.95 (0.4, 2.2)	0.904	0.98 (0.39, 2.42)	0.963
	Truenat™	1.58 (0.34, 8.59)	0.564	1.6 (0.30,9.68)	0.584
Heard of plasma therapy	No	Ref		Ref	
	Yes	0.96 (0.11, 8.27)	0.97	0.65 (0.06, 6.63)	0.709
Have donated Plasma	Yes	4.4 (0.62, 87.62)	0.192	2.6 (0.32, 53.75)	0.428
	No	Ref		Ref	
Heard of Government incentives for plasma donors	Yes	1.2 (0.42, 3.46)	0.730	1.06 (0.33, 3.39)	0.918
	No	Ref		Ref	

Ref= reference value.

Only 4.5% of the study participants had donated plasma, whereas 95.5% had not donated it. Only 49.1% of the study participants were willing to donate plasma. The deterrents of becoming a CCP donor were categorized into seven categories as given in the Table 3. Ill health

was the major reason for not becoming a CCP donor (27.6%). The second important reason for not willing to donate was ineligibility to donate (10.5%). The third common reason for not being able to donate was incomplete recovery from COVID-19 (6.58%). The other

reasons comprised of, fear of procedure (5.26%), fear of reinfection (3.95%), uncertainty of the usefulness of CPT (3.95%), and others (includes out of station, will decide later, and not answered).

The following were the reasons as per the verbatim of the participants. One participant said, "There is no clarity due to lack of research." Another said, "Scared to visit Goa medical college in view of rising cases." "Anxiety about

plasma donation and lack of evidence about plasma in treatment of COVID" said another participant. "Since I am not within the age group who can donate plasma, my age is 69 years" said another participant. Another said, "News stating plasma donation doesn't help." "I'm feeling very weak due to COVID-19" lamented one participant. "I am ready to donate but my hemoglobin is always less" said another, while another one said, "I feel it is not effective."

Table 3: Deterrent of becoming a plasma donor.

Codes	Deterrents	Frequency	Percentage	95% CI	P value
A	Do not fulfill donor requirements	8	10.5	4.98, 20.21	0.00000000001308
B	Ill Health	21	27.6	18.28, 39.27	0.0001535
C	Uncertainty over effectiveness of plasma	3	3.95	1.03, 11.88	0.00000000000002476
D	Not fully recovered	5	6.58	2.45, 15.34	0.00000000000008918
E	Fear of reinfection	3	3.95	1.03, 11.88	0.00000000000002476
F	Fear of procedure	4	5.26	1.70, 13.64	0.000000000000015250
G	Others	32	42.11	31.05, 53.97	0.207
	Total	76	100.0		

Multiple responses are added.

A total of 52.7% of the participants correctly said that one plasma donation can help two recipients. Others said following, around 20.9% participants believed that it saves life of one person, 3.6% opined that it does not help, and 22.7% did not know the benefits of plasma therapy. Almost 25% of the participants were approached by some health care worker for CCP donation, while 60.9% said that they were not approached. They said that Doctors (15.4%), Nurses (10.9%), and Health care workers (10%) workers approached them for plasma donation. About 84.5% participants were not aware of any incentives provided to plasma donors by the local government. Out of the 15.5% who had heard about the incentives correctly identified free treatment for the family members in the local Medical College hospital and executive health check-ups for the donors as the incentive for plasma donation by the Government.^{19,20} Most of the respondents said that there has to be more awareness to facilitate the plasma donation. More than half of the study participants correctly identified Goa medical college as the facility for plasma donation (49.1%). Only 71.8% respondents were aware that free transport was made available for travelling to plasma donation facility.

The univariate and multivariate analysis are presented in the Table2. The outcome of interest for the logistic regression was willingness to donate plasma. The unadjusted ORs are presented as follows. The unadjusted odds ratios were less than one for most of the variables except for Truenat™ testing, have donated plasma, and heard of government incentives. The OR of willingness to donate plasma for female individuals was 0.93 [95% CI,

0.44-1.96] as compared to males. In other words, females had 7% (i.e., $1-0.93=0.07$) lower odds of willingness to donate plasma as compared to males. The higher age group individuals had 2% lower odds of willingness to donate plasma as compared to lower age group individuals (OR 0.98; 95% CI, 0.96-1.0) who differ by one year. Those individuals who had symptoms had 31% lower odds of willingness to donate as compared to those who were asymptomatic (OR 0.69; 95% CI, 0.28-1.69). The individuals with mild disease had 34% and 40% lower odds of willingness to donate compared to those who had moderate (OR 0.66; 95% CI, 0.23-1.79) and severe diseases (OR 0.60; 95% CI, 0.08-3.82), respectively.

The individuals who had done RTPCR had 5% lower odds of willingness to donate compared to individuals who had done RAT (OR 0.95; 95% CI, 0.4-2.2). The OR of willingness to donate plasma was 1.58 (95% CI, 0.34-8.59) in individuals who were tested by Truenat™ as compared to individuals who had tested by RAT. Individuals who had not heard of plasma therapy had 4% lower odds of willingness to donate compared to individuals who had heard of plasma therapy (OR 0.96; 95% CI, 0.11-8.27). The OR of willingness to donate plasma was 1.2 (95% CI, 0.42-3.46) among those who have heard of government incentives as compared to individuals who were not aware of government incentives.

The multivariate analysis also did not show significant results. The adjusted ORs are presented as follows. The adjusted odds ratios were less than one except for

Truenat™ testing, have donated plasma, and heard of government incentives. The females had 10% lower adjusted odds of willingness to donate plasma when compared to males (OR 0.90; 95% CI, 0.38-2.16) after adjusting for other predictors. The symptomatic individuals had 26% lower adjusted odds of willingness to donate plasma as compared to asymptomatic individuals (OR 0.74; 95% CI, 0.23-2.29). The individuals with moderate disease had 26% lower adjusted odds of willingness (OR 0.74; 95% CI, 0.23-2.29) to donate as compared to mild disease after adjusting for other predictors. Similarly, individuals with severe disease had 12% lower adjusted odds of willingness to donate plasma (OR 0.88; 95% CI, 0.09-7.50) as compared to mild disease. The individuals who were tested with RAT had 2% lower adjusted odds of willingness to donate (OR 0.98; 95% CI, 0.39-2.42) as compared to individuals who had done RTPCR test. Similarly, adjusted odds ratio of willingness to donate plasma among individuals who had tested by using Truenat™ was 1.6 (95% CI, 0.30-9.68) as compared to the individuals tested by RAT. The adjusted odds ratio of willingness to donate plasma among those who had heard of government incentives was 1.06 (95% CI, 0.33- 3.39) as compared to those who have not heard of government incentives.

DISCUSSION

In a country like India, blood donation is met with a very poor response, and therefore motivating recuperating COVID-19 survivors to donate CCP is a great challenge. To increase the number of CCP donors in the state of Goa, we needed to understand the barriers for plasma donation. The awareness about CCP donation was higher in the state of Goa (96.4%) as compared to findings of Masser et al who reported that only 34.3% had heard of CCP.²¹ In spite of having such high level of awareness, the percentage of COVID-19 plasma donors was very less (4.5%), Masser et al found that only one study participant had donated plasma.²¹ Among those who had not donated plasma, the willingness to donate plasma was 49.1%, which is lower than reported by Dhiman et al (72.8%).²² Around 10.5% of the study population thought that they were ineligible for CCP donation, which is consistent with the findings of Masser et al who found that 9.9% of the study participants believed that they were ineligible for CCP donation.²¹ The most profound reasons for not willing to donate CCP were; skepticism about effectiveness of CPT, fear of reinfection, anxiety associated with plasma donation, not fulfilling the eligibility criteria. The study findings are consistent with the findings of Mahapatra et al reported that 31% donors who came for CCP donation changed their mind due to doubts, fears, apprehensions of getting infected.²³ Masser et al concluded that the fears were negatively associated with plasma donation.²¹ There were other reasons such as the media news about the ineffectiveness of the convalescent plasma therapy, not fully recovered from COVID-19, low hemoglobin level. There is a greater

need to address some of the misconceptions surrounding the CCP donations. For this purpose, the success stories of COVID-19 patients who benefitted from CPT should be widely circulated in the print and electronic media. The medical doctors could be invited to advocate the donations by addressing the concerns of the CCP donors to allay their fears. The Odisha government initiated a plasma donation drive wherein they circulated frequently asked questions on the plasma donation in all districts via print and multi-media. With the help of administration and political leaders they motivated the COVID-19 survivors to donate CCP. The municipal administration tracked the discharged COVID-19 survivors and contacted them over telephone. Many donors were convinced about the donation when they came to know that the CCP collected from them could save two lives.²³

There is a need to focus on creating awareness of CCP donation among the most eligible group of individuals who have survived the dreaded COVID-19 disease. The study findings suggest that the mere existence of knowledge of need to donate convalescent plasma will not be sufficient to motivate a CCP donor. The studies also suggest that the individual beliefs about plasma donation and COVID-19 pandemic has an impact on the willingness to become a donor.²¹ There were many individuals who were afraid of reinfection, such individuals need an assurance of safety of their health while they choose to be a CCP donor. The blood banks are usually less crowded and relatively safe places. There is also a need to create awareness with regards to plasma apheresis so that peoples' misconceptions and fears could be taken care. Mahapatra et al also reported that the COVID-19 surviving Government staff volunteered to be CCP donors. They were hailed as COVID-19 warriors. All CCP donors were presented with a certificate of appreciation which was signed by the highest State authority. Sriram Chandra Bhanja medical college and Hospital collected highest number of CCP donations. They continued to provide the CCP free of charge to government and private health care facility even in the absence of replacement donor.²³

The study suggests that as age advances the willingness to donate plasma reduces. The reason for such phenomenon is that the 20% of the study group was comprised of the elderly age group. Similarly, the female gender was associated with lower odds of willingness to donate plasma as compared to the male gender. The female population expressed more fear about the plasma donation as compared to the male gender. After accounting for the other predictors, the odds of willingness to donate further reduced by 3% in women as compared to men. The symptomatic individuals had lower odds of donating plasma as compared to those who did not experience any symptoms. The odds of willing to donate the plasma were further reduced by 5% after adjusting for the other predictors among individuals who experienced symptoms as compared to individuals who did not experience the symptoms. The most probable

reason for this finding is that the symptomatic would require more time to recover as compared to asymptomatic individuals. Similarly, the perceived moderate to severe forms of the disease was associated with the lower odds of willingness to be a donor. The odds of willingness to donate among the moderate and severe disease improved after adjusting for the other predictors. The moderate to severe individuals would require more time to get back to normalcy as compared to milder form of COVID-19. Voluntary reciprocal altruism was an important motivator among the UK study participants. This characteristic could be tapped to motivate the potential donors to donate CCP.²¹

The individuals who had tested through RTPCR had lower odds of being donors as compared to those who had done Truenat™ testing. Those who had done Truenat™ had 58% higher odds to be a plasma donor as compared to RAT tested individuals. The odds of willingness increased to 60% after controlling for other predictors. The severe diseased individuals were sent for the RTPCR testing as compared to the mild to moderate disease. Hence, Truenat™ tested individuals felt more energetic to go for plasma donation. The odds of willingness to donate plasma were 20% higher among the individuals who had heard of the incentives provided by the government. The odds of willingness among the individuals who had heard of government incentives reduced after adjusting for other variables. Incentives given by the government must have had a positive impact on the willingness to be a plasma donor. The Government of Goa had made the transport available to visit the CCP donation centre, yet many were unaware of this facility. There is a need to publicize this information to the COVID-19 survivors. This study has following limitations. The first limitation is that the study analyses the intentions and not actual practice of CCP donation. The intentions are indirect predictors of actual behavior. Those who were willing might change their thoughts and may not donate and vice-versa. The second limitation is the small sample size. The actual calculated sample size was four hundred. Although the authors tried their best to reach out to as many COVID-19 survivors as possible however many of them did not respond. The Third limitation is that the snowball sampling techniques is inherently non-probability based sampling technique. Since only selected members had an opportunity to be part of the study, this could affect the generalizability of the research findings.

CONCLUSION

To conclude, the willingness to donate CCP was just close to 50%. Many personal perspectives were negatively impacting the decision to become a plasma donor. The recruiting agencies must address these concerns so that people could take informed decision to donate CCP. Being female, older age, being symptomatic, unaware of government incentives, tested by RAT, and unaware of CPT were associated with lower willingness to donate CCP. The study proves that the younger age

group, male gender, and milder form of the disease are better predictors of the willingness of the COVID-19 convalescent plasma donation. The Government incentives have helped to improve the possibility of plasma donation. The second wave has had a greater impact on the younger individuals and therefore an appeal to this section of the population will be helpful to increase the recruitment of eligible COVID-19 convalescent plasma donors.

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