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RESEARCH ARTICLE

Convalescent plasma operations during the COVID-19 pandemic: The Turkish Red Crescent's experience

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ABSTRACT

After COVID-19 was first observed in Wuhan at the end of 2019, it spread all over the world and became a pandemic which has yet to end. The United States Food and Drug Administration (FDA) suggested that convalescent plasma obtained from individuals who've recovered from COVID-19 might be helpful in treating COVID-19 infections, and this treatment has started to be applied in various countries. Convalescent plasma started to be used in Turkey to treat COVID-19 as per a decision of the Ministry of Health. The Turkish Red Crescent has been placed in charge of the convalescent plasma supply. In this scope, objectives for recruiting convalescent plasma donors have been set in motion. The supply of convalescent plasma required for COVID -19 treatment has been conducted in three main stages: managing the course of operations, determining donor selection criteria, and recruiting donors. For the course of operations, convalescent plasma donation centers have been founded, and a national reference guide has been prepared about convalescent plasma donations in addition to documents for providing standard practices in line with this guide. Convalescent plasma donor selection criteria have been defined, followed by convalescent plasma donor recruitment strategies. This study summarizes the Turkish Red Crescent's experiences and the strategies used to encourage individuals to donate convalescent plasma.

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COVID-19 is a disease associated with the SARS-CoV-2 virus that originated in Wuhan, China in 2019 and became a pandemic affecting the whole world. The disease spreads rapidly with no specific cure yet to be found. Regardless of the reason, using the plasma received from the blood of noninfected and infected but recovered ones is considered the precursor of immune response; it has been a method known since 1890 and implemented by the medical community in epidemics such as SARS, MERS, Ebola, and avian influenza, which had taken hold of the world in the past (Ko et al., 2018; Zhang et al., 2005; Zhou et al., 2007; World Health Organization [WHO], 2021).

In this process, the FDA (2021) has recommended convalescent plasma therapy, using plasma obtained from the blood of people who've recovered from COVID-19. Convalescent plasma therapy has been implemented in many countries. In Turkey, the Ministry of Health made the decision on April 1, 2020 that convalescent plasma treatment would be one of the treatments for COVID-19 patients. The Ministry of Health authorized the Turkish Red Crescent (TRC) to be in charge of the blood plasma supply, and it currently meets 90% of the blood needs of the country. TRC has combined its experience with innovative technologies and approaches by carrying out the Safe Blood Provision Program with the aim of increasing society's sensitivity and being a sustainable model for the provision of safe blood since 2005 (TRC, 2018). In this direction, convalescent plasma donor acquisition studies have been initiated by taking the number of cases in Turkey into consideration so as to meet the plasma demands used in treating COVID-19 (Ministry of Health, 2021).

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This study was planned with the aims of analyzing the strategies to be implemented during convalescent plasma donor acquisition activities, investigating the successful impact of the implemented strategies, and sharing TRC's corporate experiences.

Materials and Methods

The first COVID-19 case in Turkey was diagnosed on March 11, 2020, after which it started to spread. Overall, 375,367 laboratory-confirmed patients with COVID-19 have been reported by the Ministry of Health from March 11 to October 31, 2020; 14,124 of these reported cases represent the number of intensive care patients (Ministry of Health, 2021). With the start of confirmed COVID-19 cases in Turkey, the Blood Crises Commission was created under the Turkish Red Crescent Directorate General of Blood Services to protect the health of staff and donors, to meet the blood needs of the country during the pandemic, and to swiftly commence convalescent plasma donor acquisition studies.

Operational Process

On April 6, 2020, 12 convalescent plasma donation centers were established to cover 18 Regional Blood Centers throughout the country. While establishing these donation centers, particular importance was given to the population and geographical location of cities, as well as to cities with high numbers of patients. The number of convalescent plasma donation centers increased gradually as the number of recovering patients increased. The first donation was received on April 7, 2020 within the framework of the internationally recognized convalescent plasma donation adoption practices.

The Ministry of Health designed a national guide (COVID-19 Immune-Convalescence-Plasma Provision and Clinical Use Guide) regarding convalescent plasma on April 13, 2020. This guide addresses the criteria on how to collect convalescent plasma donations and use it clinically. Documents to be used within the Turkish Red Crescent Blood Service Units were prepared to ensure a standard implementation in line with this guide. Forms were also designed to be able to determine donor eligibility for convalescent plasma donation (Ministry of Health, 2021).

Software has been developed to share between Ministry of Health and Turkish Red Crescent the lists of recovering patients who will be able to donate convalescent plasma. This software keeps track of the identity, contact information, and COVID-19 diagnosis test details of the applicant donors, and call groups made interviews with the donors to assess their eligibility. Meanwhile, an online appointment system was developed for call groups to contact convalescent plasma donor applicants and to provide appointments those deemed eligible. Table 1 summarizes the convalescent plasma donor acquisition strategies.

Table 1
Convalescent Plasma Donor Acquisition Process

Convalescent Plasma Donor Acquisition Strategies	Justification for the Implementation of Strategies
Call Groups Formation	Call groups composed of blood donor acquisition staff were created to invite patients diagnosed with and recovered from COVID-19 for the convalescent plasma donation.
Social Media Study	To ensure correct and reliable information is communicated regarding convalescent plasma donation and convalescent plasma demands, instant follow-ups were made and notifications on the convalescent plasma donation were quickly answered. Meanwhile, the requests of people who reported their convalescent plasma needs were swiftly met, and applicants synchronously declared through their social media accounts that they wanted to make a donation were directed to the relevant convalescent plasma centers.
Community-Wide Information Works	External visual designs of the vehicles to be used within the scope of convalescent plasma donation were prepared. Convalescent plasma donors were transported using these vehicles. Banners and leaflets were prepared to inform donors, particularly in regard to convalescent plasma donation. A page special to the convalescent plasma as part of this project was also created on the website. 3 Introductory films were recorded and allowed to be published on national channels and through social media accounts. Posts with the same content were created and shared concurrently through the digital media channels.
Inviting Applicant Donors by SMS for Convalescent Plasma Donation	Blood donations decreasing because of COVID-19 infection showed more decreases due to the curfews during the pandemic period. Therefore, special exemptions were included in the curfew notices for blood and convalescent plasma donors to be able to go to donation centers without being subject to the restrictions.

Qualification Criteria for Convalescent Plasma Donor and Collection

To be a convalescent plasma donor, a person first needs to meet the adopted criteria for whole blood donation. Convalescent plasma donations from women who are/have been pregnant (childbearing, miscarriage, abortion) and people who have had previous blood transfusions are not accepted, as human leukocyte antigen (HLA) antibody screenings have to be performed for them. HLA antibodies are not examined in the routine practices of the Turkish Red Crescent blood banking activities (Ministry of Health, 2021).

According to the national guide, the COVID-19 infection diagnosis must be made through laboratory test results (a positive PCR test conducted through the nasopharyngeal swab sample or a positive serologic test for SARS-CoV-2 antibodies) and the resolution of symptoms (e.g., coughing, fever, shortness of breath, weakness). At least 14 days must have passed since recovery with at least two PCR test results (one of the tests must have been performed within the last 48 hours). In case 28 days have passed since clinical recovery, a negative PCR test is not required (Ministry of Health, 2021).

Convalescent plasma donation is received at least 14 days and at most three months after recovery. The date of the first donation is accepted as the starting date. A maximum of three donations can be received in 1 month with intervals of at least 10 days. A donor can donate convalescent plasma at most eight times in three months. A maximum of 1800 ml of plasma can be collected from a donor in one month (Ministry of Health, 2021).

TRC has decided that the SARS-Cov-2 IgG Assay should be performed for all collected convalescent plasma in consideration of the recommendations given in the guide. As part of this, a special laboratory protocol was assigned on April 22, 2020 for the SARS-COV-2 IgG Assay study. All convalescent plasma with a positive test result are put into service. Convalescent plasma donations from IgG-negative donors were not reaccepted.

If the collected convalescent plasma will be used without being frozen, the national guide recommends that the pathogen inactivation procedure should be performed within six hours (Ministry of Health, 2021). When considering the logistic facilities, this procedure is seen able to be performed within the given period, and pathogen inactivation procedures began being implemented on May 15, 2020 in two metropolises where the number of COVID-19 cases were high. Documents to be used within the Blood Service Units have been prepared to allow for standard implementation.

Convalescent plasma components and all relevant procedural steps are quickly integrated into the Blood Banking Information Management System. The documents required for the staff to use the system easily have been prepared.

The relevant documents the General Directorate of Public Health published as part of the guide regarding COVID-19 were updated to protect the safety of donors and staff. Steps to be taken in addition to the routine measures are listed in these documents.

Placards published by the Ministry of Health related to the use of personal protective equipment were prepared at all blood donation centers and mobile teams and distributed to all blood donation points. Information placards related to mask use and hand hygiene were also provided. Having hand disinfectants in all areas was made compulsory, as well as ensuring that the same individuals work with each other by forming staff teams as much as possible to prevent the risk of cross-infection contact. Donation sites were reorganized in a way to ensure physical distance to increase the safety of donors and staff, and each donor was required to wear a mask in the donation site. The areas for blood donors and convalescent plasma donors were kept separate from one another at the blood service units. Separate staff were assigned for blood donations and for convalescent plasma donations; staff who were ill were allowed to not work and directed to a physician.

Results

23,749 units of convalescent plasma donation were collected from 18,383 donors between April 15 and October 31, 2020 (see Table 2). Of the convalescent plasma donors, 94% (17,362) are male while 6% (1,021) are female. When examining donors' age distribution, donors between 26-35 ages rank first, making up 34% (4,017) of donors, followed by the 36-45 age group at 31% (3,649), the 46-55 age group at 16% (1,871), the 18-25 age group at 16% (1,855), and the 56-61 age group at 3% (318). Of the convalescent plasma donors, 52% had made blood donations previously to TRC. When examining donors' educational status, high-school graduates rank first at 31% (3,656), followed by those with a bachelor's degree at 27% (3,213), primary school graduates at 14% (1,606), middle school graduates at 12% (1,398), those with an associate degree at 10% (1,169), those with a master's degree at 4% (520), and those with a doctoral degree at 1% (97).

Table 2
Periodic Distribution of Convalescent Plasma Donors, Donations, and Plasma Donations; Rate of Increase in the Number of Donations

Period	Number of Donations	Number of Donors	Number of First-Time Plasma Donors	Number of 2-Time Plasma Donors	Number of 3-Time Plasma Donors	Number of Donors 4+-time Plasma Donors	Number of People Called	Increase Rate in Number of Donation
April 15-May 01, 2020	577	455	210	131	112	2	17,667	
April 01-June 01, 2020	2,812	2,033	1,262	399	365	7	55,838	287%
April 01-July 01, 2020	4,320	2,990	1,918	562	490	20	71,935	-33%
April 01-August 01, 2020	5,540	3,860	2,486	747	574	53	95,065	-19%
April 01-September 01, 2020	7,862	5,807	3,916	1,075	682	134	129,876	90%
April 01-October 01, 2020	14,925	11,710	8,576	1,877	992	265	192,605	204%
April 01-November 01, 2020	23,749	18,383	13,368	2,906	1,313	796	343,793	25%

Table 2 presents the percentage variations regarding the monthly rate of increases in numbers of donors and donations provided cumulatively due to repeat donations. The rate of increase in the number of donations has been calculated by considering the monthly number of convalescent plasma donation numbers, which is not cumulative. The rate of increase was found by subtracting the number of donations in one month from the number of donations in the subsequent month divided by the number of donations in that month. Table 2 shows the rate of increase from April 15 to November 1, 2020 in convalescent plasma donation numbers for successive months. Because convalescent plasma donation activities started in April 2020 and no convalescent plasma was donated in the previous month of March, the rate of increase between these two months has not been calculated. The highest rate of increase was seen in May at 287% in the first period of pandemic, followed by September (204%) and August (90%).

Tables 3 and 4 show the reasons for rejecting donors and for becoming disqualified for donation, respectively. The highest number of ineligible donors was observed in May (35,603), followed by September (26,036) and October (23,465). The numbers for unwilling donors and unreached donors increased over time. The main reason for being disqualified for donation is the ineligibility of donors due to the criteria for convalescent plasma donation (45.8%). The second reason is becoming ineligible in terms of blood donor selection criteria, (38.45%). The third reason involves donor-related issues such as a negative past donation experience (15.8%).

Table 3
Reasons Why Donors Refused/Were Rejected When Called for Convalescent Plasma Donation

Month	Number of Ineligible Donors	Number of Donors Unwilling to Donate	Number of Unreachable Donors*	Absence of a Convalescent plasma Donation Center in Donor's City
April	15,034	577	978	122
May	35,603	1,413	2,276	289
June	14,060	1,017	1,352	343
July	15,390	2,426	2,826	496
August	17,694	3,169	5,677	744
September	26,036	5,052	9,348	2,131
October	23,465	6,641	7,312	1,568

*unreachable due to wrong phone number or unanswered call

Table 4
Reasons for Being Disqualified for Donation

Reasons for Being Disqualified for Donation	Number of Donors	Rate of Reasons for Being Unqualified (%)
Reasons Related to the Donor	**17,125**	**15.8**
Not Doctor Approved	291	1.7
Negative Donation Experience	919	5.0
Will Make Donation at the Hospital	15,953	93.2
Ineligibility due to convalescent plasma donation criteria	**49,591**	**45.8**
Pregnancy/Miscarriage History	386	1
Blood Transfusion History	635	1
Negative Antibody Test Result	554	1
Absence of Positive Antibody Test Result	990	2
3-Month Period Expiration	47,026	95
Ineligibility for Blood Donation Criteria as per the National Guide	**41,666**	**38.4**
Not Able to Make Donation Due to Final Rejection	2,808	7
Chronic Disease	8,120	19
Not Feeling Well	8,250	20
Rejection Reasons through Donor Inquiry Form	22,488	54
Total	**108,382**	**100.0**

In convalescent plasma donor recruitment efforts, communication activities have been carried out through digital media. When analyzing the number of views of posts made between January and October 2020 from the official Twitter account of the TRC Directorate General of Blood Services, the first convalescent plasma donor post on April 7, 2020 ranks first, the live broadcast on April 18, 2020 in which the questions related to the convalescent plasma were answered ranks second, and the video of convalescent plasma donation from a football technical director of one of the three biggest teams in the Turkish football league ranks third.

While only one unit of convalescent plasma was donated when plasma donation started on April 7, 2020, nine units of plasma were collected on April 10. A live stream on the official TRC YouTube channel was ran to inform about convalescent plasma donation on April 18, 2020. The number of donated plasma units was 19 on April 18 and increased to 47 only two days after the live stream. The number of donated convalescent plasma units was 42 on May 26. When the video from the coach of one of the three big teams active in Turkey's football league invited people to donate and had a massive number of supporters, the number of donated convalescent plasma units grew to 99 units on May 27 and increased to 102 the following day.

Discussion

The experience of the Turkish Red Crescent shows that meticulous follow-up of the strategies determined in encouraging patients diagnosed with and recovering from COVID-19 through treatment to make donations and its use of strong communication methods in motivating donors have played an important role in acquiring donors.

The demographic data from the convalescent plasma donors show males to have higher donor rates than females. This was observed to result from the inclusion criteria that women donors should not have any history of childbearing or pregnancy in order to donate convalescent plasma. When evaluating the strategies created as part of the convalescent plasma donor acquisition process and the related practices and findings, donor acquisition was seen to have been ensured and the number of donations to have increased through the efforts of the call groups that had been formed at the 27 convalescent plasma centers established with the participation of 18 regional blood centers and with the aim of establishing one-on-one communication with applicant donors and inviting them to donate their convalescent plasma.

During the acquisition efforts initiated in April, an increasing trend in the number of donors and donations was observed in April and May due to the call groups' initial efforts, the initiation of the online appointment system and convalescent plasma donor acquisition practices, the start of online education and working in shifts, the implementation of curfew measures, the promotion of plasma donations through messages, and the contact made with 100% of the recovered patients.

When analyzing plasma donation numbers and the rates of increase in the number of donations, a decrease in donation percentages was observed in July and August; this is thought to be related to the start of the normalization period. In these months, 66% of recovering patients were called for donations. However, through the effect of ineligible and unwilling donors, the numbers of donations and donors decreased, as shown in Table 2. In September and October, the increase in the number of cases and recovering patients in Turkey as well as the changes in the convalescent plasma treatment protocols clinics implemented led to an increase in the number of both donors and donations. Although 19% of the recovering patients in October were contacted due to the revisions in the Ministry of Health's COVID-19 Immune (Convalescence) Plasma Supply and Use Guide (Ministry of Health,2020) a need-oriented increase in the number of convalescent plasma donation centers and having plasma donors' transportation and food service costs covered saw the highest number of plasma donation appointments-8822 plasma donations- in the pandemic period be reached in October (Table 2).

When analyzing the communication efforts carried out with the applicant donors and patients' relatives in Turkey with the start of the period of convalescent plasma donation acquisitions in April 2020, an increase in the number of views on TRC's official social media accounts was observed. The first convalescent plasma donation in Turkey was announced to the public through social media accounts. The most important reasons for the increase in the number of views in April, May, and June were the live broadcast on plasma acquisition and use through TRC's official YouTube channel and the call for the convalescent plasma donation announced by the technical director of a top-three football team in the Turkish league with a large supporter mass who had been diagnosed with and recovered from COVID-19.

The number of plasma donations was seen to increase from 46 to 102 units following this announcement. These data show how high the awareness of applicant donors and the society had been raised through the behaviors that set an example in society and the invitations/calls made by notable people. At the same time, digital media has been indicated as one of the most powerful communication methods for reaching the awareness that needed to be created in the target population within the scope of corporate activities.

While the convalescent plasma donor acquisition process was being conducted, an invitation SMS was sent to applicant donors able to donate where they would be exempted from the curfews implemented as part of the COVID-19 epidemic throughout the country so they could donate. Apart from this, informational SMSs about the appointments created through the online appointment system were also sent to the eligible convalescent plasma donors. The numeric data regarding how many donations were realization from the sent SMSs were not analyzed. However, regarding the blood donation activities carried out by the Turkish Red Crescent, the fact that 36% of the total blood donation in 2019 and 49% of the total blood donation collected in the first 6 months of 2020 were collected from donors who had received an SMS suggests that the sent SMSs were valuable in influencing the increase in donation numbers. From this point on, SMSs sent within the scope of convalescent plasma donations are suggested to possibly also be effective in acquiring convalescent plasma donations; however, this could not be analyzed numerically in terms of how many donations had been achieved through SMSs.

As a result of the experience of the Turkish Red Crescent within the scope of the blood donor acquisition activities that have been conducted since 2005, strategies for acquiring convalescent plasma donors were quickly formed at the start of the pandemic in Turkey. In unexpected situations, the process has been proven to be best manageable by communicating quickly with both internal and external stakeholders.

Ethical approval

All patients involved in this study provided informed consent. The study protocol was approved by the Turkish Red Crescent Ethical Committee (2020/02).

Authors' contribution
All authors contributed equally to this manuscript.

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