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REVIEW ARTICLE

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Covid-19 Pandemic and Its Impact on Blood Transfusion Services in India

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ABSTRACT

The COVID-19 patient counts rapidly increasing in the whole world as well as in India and as per WHO report on 06 July 2021 with total 183,934,913 confirmed cases and 3,985,022 confirmed deaths. To prevent community spread, Government of India has announced nationwide lockdown which also affect the blood transfusion services and many small-scale lockdowns was announced by state government and local authority. SARS-CoV-2 pandemic is having an impact on blood supply. In order to maintain the chain of blood transfusion services (i.e., from the collection of blood to the transfusion of patients) in this outbreak is a big challenge. It is also important to know that how much we have learnt from the past pandemics and what extent we are prepared for the current pandemic. The major challenge for blood transfusion services are donor recruitment and safety of blood donors, blood bank staff as well as transfusion recipients. Blood transfusion services playing a vital role in the management of COVID -19 patients. In this review article we will discuss the challenges of blood transfusion services, our experience in the management of these challenges and role of convalescent plasma therapy in the management of COVID- 19 patients.

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Introduction

Corona virus pandemic started from Wuhan, China in December 2019 as a cluster of SARSs like cases majority of whom were exposed to Huanan seafood market [1]. The disease started in China but rapidly spread to various other countries due to easy person to person transmission and absence of herd immunity and was characterized as Pandemic by WHO on 11 March 2020 [2]. The virus responsible for the pandemic has been named SARS-CoV-2 as it shares 80 % similarity with SARS-CoV that was responsible for 2002-2003 Pandemic. The current outbreak of infections with SARS-CoV-2 is termed Coronavirus Disease 2019 (COVID-19) [3]. The novel virus is enveloped, single stranded, positive sense RNA virus with spike like structures on its surface and belongs to beta corona viridae family [4, 5]. Due to its rapidly spreading nature and cases climbing higher, various countries enacted measures to contain its spread. Common symptoms developed in COVID-19 infected patients are fever (98.6%), fatigue (69.6%), and dry cough (59.4%), dyspnea (43%) and asymptomatic (3%). Some studies also suggested that, in contrast to SARS, COVID-19 patients might be infectious during an asymptomatic incubation period [6, 7]. Although corona viruses usually infect the upper or lower respiratory tract, shedding of virus in plasma or serum is not very uncommon. There is a theoretical risk of transmission of corona viruses through blood and/or blood components. Young patients with no fever and asymptomatic carriers have been identified in China, which increase the possibility that a COVID-19 patient or virus carrier could donate blood. The rate of infectivity of patients who are in the incubation period remains uncertain [8]. To prevent COVID-19 spread many measures have been taken by various agencies at global as well as national level. One such measure was complete nationwide lockdown announced in India from 25 March 2020 in first wave and there was curfew in many cities and states to break the transmission chain during the second wave. The blood transfusion service which is a critical part of daily health care system faced a large blow due to this emerging pandemic as well as nationwide lockdown and curfews. In order to maintain the chain of blood transfusion services i.e., from collection to supply of blood in this outbreak, all that we need to know is what are the strategies to be applied, how to be prepared, how to prevent the loss of healthy donor pool so as to maintain sufficient blood stock and how to prevent its transmission by transfusion so as to supply safe blood and also at the same time protecting our staff and donors from such a contagious disease.

Epidemiology

A cluster of atypical pneumonia like cases of unknown etiology appeared in Wuhan, China in December 2019 which were epidemiologically linked to seafood whole sale market also called wet market. The cases were reported to WHO on 31 December 2019. The WHO reported that environmental samples taken from the wet market have come out to be positive for the COVID-19, but

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specific animal association has not been identified [9]. The novel corona virus was identified from the culture of bronchoalveolar lavage fluid and with use of RT-PCR for genome sequencing [10]. Due to its similarity with bat corona virus, it was inferred that bats are the primary source with yet to be known intermediate host. On7 January 2020 the novel virus was named SARS-CoV-2 and the outbreak was declared a Public Health Emergency of International Concern (PHEIC) by WHO on 30 January 2020 [11].

The new cases continued to occur and soon the disease was exported to other countries by the infected international travelers. WHO published the first Strategic Response and Preparedness Plan on 3 February 2020 [12]. On 11 March 2020 WHO declared COVID-19 as pandemic and the situation became alarming.

India reported its first confirmed case on 30 January 2020 in Kerala and since then the number has been swelling in India as well as in other countries involving both the general population as well as health care workers. As of now total 183,934,913 confirmed cases and 3,985,022 confirmed deaths and a total of 2,989,925,974 vaccine doses have been administered as per WHO report on 06 July 2021.

Past Pandemics and Lessons Learnt

In year 2002, there was a SARS pandemic caused by novel Corona virus named SARS-CoV. The disease originated from Guangdong, China and soon spread to other countries due to its highly contagious nature [13]. The mode of transmission was droplets or fomites [14]. Due to its nature of transmission various cities of different countries were put under lockdown to limit its spread. The lockdown affected various sectors of life and health care system including blood transfusion services. There was decline by one- tenth in daily collection of blood in Beijing, China due to non-availability of donors [15].

In 2012, there was another corona virus outbreak that started in Arabian Peninsula when a person from Jeddah, Kingdom of Saudi Arabia (KSA) presented with pneumonia like illness and was named Middle East Respiratory Syndrome (MERS). The virus identified was a corona virus (MERS-CoV). MERS-CoV belonged to C β-Corona virus lineage while as earlier SARS-CoV belonged to B β-Corona virus. There was human to human transmission of the virus through close contact via larger droplets [16]. In response to the pandemic, blood transfusion services (BTS) from various countries developed various criteria to prevent its spread like introduction of deferral period of 28 days for blood donors returning from the Arabian Peninsula and neighboring countries in 2013 [17].

In view of various periodic influenza pandemics, Zimrin AB et al. published a review article where they highlighted the blood bank crisis that can occur during the height of pandemics. Decrease in donor pool, shortage of staff and depletion of consumables like panels of reagent RBCs for blood grouping and antibody screening will lead to more manual work in time of manpower crisis in addition to blood stock crisis [18].

Challenges in Current Pandemics and Our Preparedness (Fig. 1)

Donor Recruitment, Safety and Its Management

For every blood transfusion service, the fundamental segment is constituted by healthy donor flock. In India, there is a need of 85 donations per 1000 eligible people. However, in 2018 India reported 12•4 million donations, equivalent to 31 per 1000 eligible people. Therefore, in a total need of 52•5 million units of blood products there is an unmet need of 40•9 million donations [19]. So, in an already 'unmet need' state, the pandemic like situation can have a dreadful impact and this calls for the first challenge for the blood banks out of many. The reasons for less collection are clear. The two most important reasons being fear of contracting the infection among donors by visiting high risk areas like hospitals or blood banks and second being the inability to reach to the blood collection center due to restrictions imposed by administration in view of evolving public health situation. Others can be the presence of infection itself among various donor population groups. This challenge can be retorted if appropriate measures are implicated reason wise. To combat the fear among the donors, donor confidence is gained by assuring them of proper precautionary measures being followed at blood collection center like regular sanitization of donor couches after every donation, disinfection of other contacting surfaces, proper social distancing and donation through prior appointments to allow them to come in staggered manner and also to reduce their waiting time in the center to maintain donor safety and staff safety. In India many blood banks are still dependent on the replacement donations [20]. To allow replacement as well as voluntary donors to reach the blood donation center, they were provided with valid lockdown passes or vehicles should be arranged for their hassle-free travel amid lockdown. Following these measures, the Blood Banks in Madhya Pradesh ,Karnataka and many other states in the country, setup the helpline numbers where the donors shall register themselves for blood donation and the blood bank will provide pick up and drop facility to such donors free of cost. Donors are provided with special certificates for honoring them to provide immeasurable support in the time of crisis. A post donation experience from such donors is collected and a discussion with donors is done to know the fear of donor and other donor issues and such a knowledge is be translated into guidance. Creating public awareness about the need of blood by those who are transfusion dependent like thalassemia patients, cancer patients, patients on dialysis and assuring them of implementing infection prevention and control measures and making them clear that COVID-19 is not transmitted by blood donation can help to increase the blood collection by recruiting more donors [21]. This is achieved by repeatedly spreading messages on national media and social media platforms and involving ministers and other personalities from fame world. As maintaining adequate blood supply is critical, national blood transfusion council (NBTC) under Ministry of Health and Family Welfare (MOHFW) advised to organize in house and outreach voluntary blood donation camps however only after following proper precautionary measures. The presence of infection among the donors can pose a threat to the other donors, staff and there is theoretical risk to recipient also. To maintain safety, a temporary deferral period of 28 days was recommended by NBTC India for donors with history of travel from a country with community transmission of COVID-19 or with history of contact with suspected/confirmed case of COVID-19. For confirmed case, the temporary deferral period of 28 days was recommended after complete recovery from the disease including radiological and virological clearance. As per the NBTC guidelines, donors should be advised to report back to the blood bank within 14 days of post donation if he/she suffers from illness that is suspected of

COVID-19, or becomes a confirmed case of COVID-19 or his/her close contact is confirmed case of COVID-19. Blood unit collected from such donor should be discarded and reported to Hemovigilance Program of India (HvPI) [22]. As vaccination drive began in India , the post vaccination deferral of 14 days was recommended by NBTC India. Iran is among the worst affected countries by COVID-19. The Iranian Blood Transfusion Organization (IBTO) adopted various measures to fight the crisis. They developed the online portal that showed the blood unit inventory of all centers in real time setting. This allowed to loan out the units from centers with maximum stock to others in need and highlighted the importance of communication among blood centers. In addition to this, short videos regarding preparation of the donation center were made and posted on their website to gain public confidence and the working hours were increased to allow more collection [23].

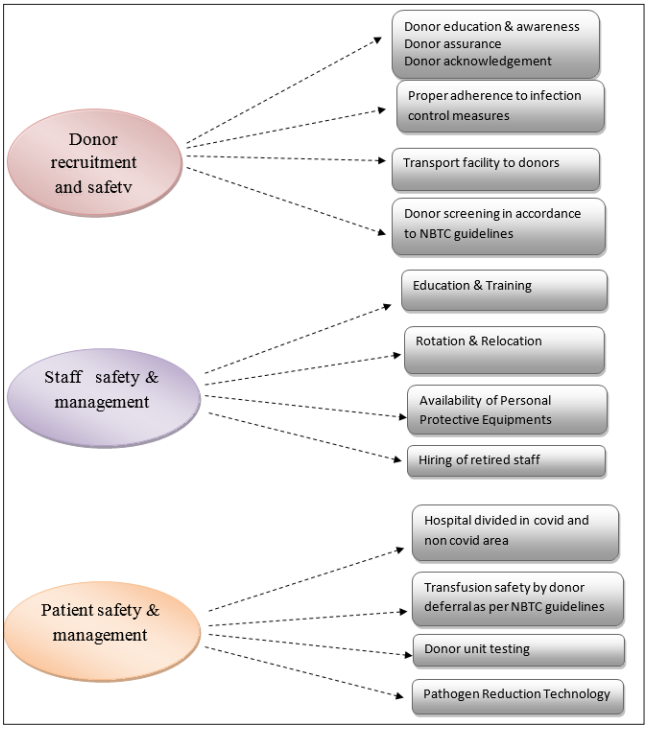

Figure 1: Challenges and their management in Blood Transfusion Services

Staff Safety and Its Management

Safety of staff is equally important as the safety of donors. Adequate education and training on infection prevention and control measures is provided and updated periodically. Concerns about contracting the disease or worrying about family exposure is also to be addressed. Only 50% of staff is put on duty on rotation basis thus reducing exposure risk. Rotation may also call for relocation of the staff in different laboratory areas highlighting the importance of training in all sections of laboratory. The available staff is protected from exposure risk by providing adequate number of masks, gloves, hand sanitizers and other personal protective equipment (PPE) based on level of exposure. In addition to blood donors, the body temperature of staff members is to be checked at the entrance of blood bank. Staff members are advised not to come for work if they feel any symptom of COVID-19 or have come in contact with confirmed case. The staff is not to be penalized for absence due to illness. Measures should be in place to maintain the uninterrupted emergency and routine services in case of shortage of staff. One such measure could be hiring the retired staff. Centers for Disease Control and Prevention advocates following measures to be followed by laboratory staff while handling the sample of suspected or confirmed case of COVID-19 in laboratory for pre transfusion testing i)Proper information and timely communication between clinical and laboratory workers ii) proper Labeling of sample iii) use of proper personal protective equipment as per standard laboratory practices if procedure is likely to generate droplets or aerosols iv) the sample be discarded as all other biohazardous wastes [24].

Patients Safety and Its Management

Our center is a tertiary care referral center with a mandate for research, patient care and receives referred patients from different part of the country. So, our hospital divided in two areas: one exclusive for COVID and suspected COVID patients and other one is for non COVID patients. However non COVID patients getting treatment in our hospital can contract corona infection from two sides. One is the risk of exposure due to contact with other patients and second is the risk of transfusion transmission of COVID-19 if evidence suggests so. To mitigate the risk of contracting infection from other patients, emergency plan is activated and hospital has shut all the routine OPDs and surgeries to decrease the patient rush attending hospital and only emergency services are being carried out. This has also helped to decrease the blood demand and better management of blood inventory. In addition to adequate supply, safe supply of blood is also very important. For COVID-19 to be a transfusion transmissible infection, it should fulfill following criteria: i) the infectious agent must be present in the blood ii) the donor must be free of signs and symptoms of the disease iii) Infectious agent must gain entry into host intravenously iv) Infectious agent must remain in blood, either free in plasma or within cellular component of blood [25].

Till now SARS CoV-2 has not been reported to be transfusion transmissible neither the previous pandemic causing infectious agents SARS-CoV and MERS were reported. Also, respiratory viruses in general are not transmitted by transfusion. However, SARS CoV-2 has got the properties that suggest its transmission via blood and thus there is a theoretical risk of transmission as Viral RNA has been reported in plasma/serum of the patients. Also, there is as incubation period of 14 days during which the patient remains asymptomatic but infectious and some patients remains asymptomatic even during the course of disease increasing probability of carrier donating blood [8]. American association of blood bank (AABB) advocates there is no action is required on blood collection and testing facility because there are no data suggesting a risk of transfusion transmission of SARS-CoV-2 [26]. To mitigate this risk, precautionary donor deferral policy is implemented however this should be applied in accordance with the level of community transmission and not in an imprudent manner as it can lead to loss of potential donor pool which will have a negative impact on the blood supply. The other measure to mitigate this risk is testing the donor units which will help to maintain both safety and sufficiency. However, there is no recommended licensed molecular or serological test for screening of blood or plasma for COVID-19, in view of no

reported case of transfusion transmission. Also, no SARS-CoV-2 genome has been detected in asymptomatic donors and only very low level of virus genome in symptomatic patients [27].

Third measure to reduce the threat and enhance blood safety is the Pathogen Reduction technology (PRT). A PRT should either remove/inactivate the pathogen or reduce the level of pathogen to such an extent that it ceases to cause infection in the recipient. Past studies demonstrate PRTs to be effective on SARS-CoV and MERS to varying degrees and same is being applied to SARS CoV-2 due to its similar nature. Heat and Solvent/Detergent treatment has been found effective to reduce SARS-CoV from plasma. For cellular products illumination with UV-A, UV-B at different wave lengths in presence of amotasalen or riboflavin could inactivate the nucleic acid. However, given the lack of evidence of transmission by blood transfusion and the cost of various PRTs, the decision of using such methods on regular basis has not been taken in our setting so far [28-34].

WHO votes on notifying the clinician if the donor tests positive for COVID-19 post donation and NBTC guidelines advocate recalling and discarding of blood products collected from such donor and reporting the same to HvPI. If such a unit is transfused, we must identify and properly investigate the risk of transmission by transfusion [22]. The patient safety is also maintained by preventing unnecessary transfusions and thus decreased chances of exposure. For this careful planning and management of blood inventory should be at the upper shelf. To secure the patient safety, a clear communication with clinicians regarding strict adherence to transfusion guidelines and emphasis on use of alternatives to blood transfusion should be made.

Our Experience

Management of Adequate and Sustained Supply of Blood

Due to complete lock-down blood donors were unable to reach the blood collection center. Although demand of blood was less because of postponement of elective surgery but collection of blood was drastically reduced and we faced acute shortage of blood for time being. To overcome this problem, we started to motivate resident doctors and hospital staff through WhatsApp group and personal calling (mobile) for voluntary blood donation. BTS started issuing curfew passes to allow blood donors for blood donation. As soon as NBTC granted permission to conduct blood donation camp BTS worked closely with voluntary blood donor organization (VBDO) and started blood donation camp in green zone with appropriate precautionary measure.

Prevention of Spread of COVID-19 among Blood Donors and Staff

Our preventive measures mainly focus on to prevent infection between one blood donor to another and between blood donor to staff. So, blood donors and staff were thoroughly thermal screened and given triple layer masks before entering the blood bank. We maintained strict social distancing among donors and staff. Our screening doctors and phlebotomist were provided proper PPE based on the hospital guidelines and level of exposure. Blood donation couch was sterilized after completion of each blood donation.

Contribution of Our Blood Bank in Treatment of COVID-19 Patients

In some patients severe COVID-19 present with coagulation abnormalities that indicate systemic coagulopathies which may be associated with severe infections, may cause disseminated intravascular coagulation (DIC) or thrombotic microangiopathy [35]. Coagulopathy is associated with an increased risk of death in patients with COVID-19 [36]. The presence of cold agglutinins in COVID 19 patients have also been reported in many studies [37]. To deal with COVID 19 associated coagulopathy, we assured to make available sufficient quantity of fresh frozen plasma (FFP), cryoprecipitate, platelet concentrate (PC) and single donor apheresis platelet (SDAP) for COVID-19 patients in our blood bank.

Due to non-availability of specific anti-viral treatment for COVID-19, an empirical treatment with convalescent plasma collected from cured COVID-19 patients has been seen beneficial as it has been used to treat various other viral infections in the past. It is based on the concept of neutralization of virus by antibodies generated during recovery phase or mediation of effective immune response. Previously convalescent plasma therapy was used for the treatment of SARS-CoV-1 epidemic, H1N1 influenza virus pandemic, MERS-CoV epidemic and Ebola epidemic [38]. In India Indian council of medical research (ICMR) developed a protocol for convalescent plasma therapy in moderately ill COVID-19 patients by starting a multi-center, two-arm, prospective, Phase II, open label, randomized controlled trial [39]. Results of the trial was not very encouraging for using convalescent plasma therapy.

Conclusion and Limitation of Study

The COVID-19 pandemic is spreading across the globe at an alarming rate. In India COVID 19 cases were increased due to second wave of pandemic. As cases have been decreased again lockdown has been relaxed and economic activity has been started. Government of India has realized that we have to learn to live with COVID-19. As a citizen we must follow COVID appropriate behavior. In our hospital administration outpatient department (OPD) has been started and routine services starting in phased manner. So, requirement of blood and blood components will be increasing in upcoming days. Our efforts must focus on donor recruitment, to conduct regular blood donation camp with maintaining safety of blood donors as well as our staff. Patient safety is a key challenge and blood donors must be selected with strict criteria according with national guidelines. India and other parts of world can get advantage from our experience in the management of blood bank services. Our review is limited by the fact that we focused only on blood bank services and convalescent plasma therapy in the treatment of COVID 19. In future more research and trials are required on convalescent plasma therapy with other treatment modality in COVID 19 patients.

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