



# Evaluating the Importance of Patient Blood Management During COVID-19 Pandemic

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## Abstract

Due to the COVID-19 pandemic, the demand for blood products may decrease as the health care system shifts toward treating the increased number of patients afflicted with COVID-19 and delaying selective surgeries and emergency procedures. One of the most important problems for blood transfusion services during COVID-19 pandemic is the reduction in the number of donors and a decrease in blood stocks. This happens due to the limitations of attendance of donors in blood centers, lack of awareness, misinformation, fear of being infected while donating blood, and restricting the freedom of blood collection teams to attend public places. Blood transfusion services should be prepared and well-responded in a timely manner. In this regard, appropriate use of blood, diminishing unnecessary transfusions, and implementation of patient blood management (PBM) principles are considered as significant measurements. PBM can help maintain blood supply throughout the crisis and reduce the pressure on blood demand. As a result, blood products can be saved for patients who need it urgently. PBM focuses on the patient, as well as the conditions that make patients transfuse blood, such as blood loss, coagulopathy, platelet dysfunction, and anemia. Thus, the majority of health systems in different countries have made recommendations to the PBM in hospitals.

**Keywords:** Blood Transfusion, COVID-19 Pandemic, Blood Loss Surgical, Anemia

## 1. Introduction

In December 2019, the first cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) were reported (1). Then, the World Health Organization (WHO) declared it as a pandemic disease (2). The emergence of this new virus was a challenge for global health systems, such that 15 - 20% of them had an overwhelming load of patients (3).

Due to the COVID-19 pandemic, the demand for blood products decreased as the health care system shifts toward treating the increased number of patients afflicted with COVID-19 and delayed selective surgeries and emergency procedures. Meanwhile, blood transfusions were increased in emergencies, such as trauma (4), postpartum hemorrhage, severe neonatal anemia, blood dyscrasia, and immediate surgeries. However, blood transfusion can support patients with severe COVID-19 sepsis or mechanical ventilation (5-7). Different countries adopted various strategies to control COVID-19 epidemics, which might hinder donors to attend the blood donation centers. One of the most important problems for blood transfusion services during COVID-19 pandemic is the reduction in the number of donors. For instance, the mean number of

blood donations decreased to a critical level ( $2828.45 \pm 1587$  per day) between 26 February and 6 March 2020 in Iran (8), as well as in 32 countries in the WHO regional office for Africa (9). Moreover, during COVID-19 pandemic, there were severe reductions in the number of voluntary blood donations, blood components, and stock maintenance in India (10). Moreover, blood supply was decreased in the most centers of Eastern Mediterranean region, ranging from 26 - 50% (11).

One of the most important problems for blood transfusion services during COVID-19 pandemic is the reduction in the number of donors and a decrease in blood stocks. This happens due to the limitations of attendance of donors in blood centers, lack of awareness, misinformation, fear of being infected while donating blood, and restricting the freedom of blood collection teams to attend public places. The number of blood donations was closely monitored so that the necessary steps were taken to prevent any reduction. Under such circumstances, blood transfusion services were prepared and well-responded in a timely manner. This was especially vital for short-lived products, such as platelets, particularly for patients who were dependent on platelet transfusion (12).

However, the number of blood requests for emergency cases, including chronic patients such as those with malignancies, blood diseases (eg, sickle cell disease, thalassemia, myelodysplastic syndrome, etc.), chemotherapy, and surgeries increased. In some cases, cancellation of elective surgery in COVID-19 pandemic might lead to disease progression, resulting in more complex and immediate conditions. While the demand for blood donation was evolving, the nature of the COVID-19 pandemic might also change rapidly (13). During crisis and the increase in the number of patients, physicians experienced limitations, and new scientific findings in this regard led to changes in their daily clinical practice (14).

Blood transfusion services should make the necessary predictions and regularly assess the blood stocks. The methods for overcoming this problem might include a quick change for blood collection where possible, transferring the donors to blood centers, and scheduling online appointments for donations or even working hours. Blood collection activities might be more purposeful with the call of repeated healthy donors. Sometimes blood center calls could not increase the number of donors and reduce this problem (12).

To alleviate the anxiety of donors, leading communication strategies and effective awareness campaigns are critically needed. During this period, the routine methods for donor management and testing for infectious diseases did not change. However, in the case of severe blood stock deficiency, a complete reduction in blood donation might consider donors with lower hemoglobin levels able to tolerate repeated donations. In addition, systems had to be established to reintroduce infected donors after complete recovery (28 days after recovery) (12).

Therefore, the pandemic situation puts more pressure on blood transfusion services and hospitals, so that sometimes they are forced to care patients with less staff (13, 15). Blood transfusion services should communicate effectively with health care professionals about blood transfusion activities to ensure that blood products are used in appropriate clinical settings (12). In this regard, patient blood management (PBM) could help maintain blood supply throughout the crisis (12).

## 2. Methods

In this narrative review, databases including Embase, CINAHL, Scopus, Google Scholar, Google, Science Direct, ProQuest, ISI Web of Knowledge, and PubMed were searched to obtain the related literature published in English language. The key words were: PBM, COVID-19 pandemic, transfusion medicine challenges, clinical practice,

supply and use of blood, blood inventory, blood transfusion utilization in COVID-19 pandemic, evidence-based management, blood supply and demand, blood product use, strategies in COVID-19 pandemic, anemia, perioperative bleeding, coronaviruses and blood safety, guideline of PBM, implementation of PBM, pandemic outbreak and outcome. Out of 189 articles retrieved, 55 studies were selected after reading the abstracts. Then, the final choice was based on a careful study of the articles.

### 2.1. Patient Blood Management

PBM is a multifaceted and multidisciplinary approach based on scientific evidence improve the outcome of patients at risk (16). Restrictions and limitations on the crisis have led to decrease in blood donations (13). However, there is still no proven evidence for the transmission of COVID-19 through blood products (13). The majority of health systems in European countries have made recommendations to prevent the transmission of the virus through blood donation, as well as the PBM in hospitals (17).

As mentioned above, in COVID-19 epidemics, there was a significant reduction in blood donors and blood stocks. Sometimes, this problem could not be overcome by calls from blood centers meaning that other solutions were needed. By applying the principles of PBM, the pressure on blood demand would be reduced, and these valuable resources (blood) would be protected for patients who need them urgently. Blood products deficiency during the COVID-19 pandemic led to the cancellation of elective surgery. However, with the rapid and effective implementation of PBM principles, despite limited blood supply, many patients could safely undergo surgery and other interventions.

These are some methods for the implementation of PBM Principles:

(1) A triage system must be established to delay the choice of surgery at any hospital. This rescheduling of surgeries should be done with the aim of preserving the necessary personnel and resources of the health care system, regardless of the need for blood products.

(2) The hematopoiesis status in elective surgery patients should be optimized and then prepared for surgery. Anesthesiologists should work together with other physicians in the hospital to make the necessary and effective efforts in developing PBM.

(3) Identification, diagnosis, and treatment of anemia should be considered throughout surgery and even after it.

(4) Coagulation disease should be identified, monitored, and treated before, during, and after surgeries with emphasis on exact monitoring and proper use of instruments and interventions to support the patient's home-

ostasis (eg, innovative surgical techniques and coagulation factors, such as fibrinogen concentrate) (18, 19).

(5) Comprehensive use of effective methods to maintain patients' own blood, such as precise surgical technique, intra-, and post-operative cell recovery, use of acute normovolemic hemodilution (ANH), proper management and treatment of fluids, and minimization of iatrogenic blood loss.

(6) Continuous evaluation and monitoring of surgery patients to estimate bleeding, blood clotting, and anemia. It should be noted that acute anemia is common after surgery and, in many cases, may be treated with iron replacement with or without concomitant use of bone marrows stimulating drugs and red blood cell. The goal is to maintain patients' own blood and save allogeneic blood.

(7) Training and participation of medical professionals, as well as patients and their families in the PBM is utterly important in crisis of blood deficiency (20).

Hence, the national Blood Organization of Australia conducted a comprehensive systematic review on the PBM's six modules, 52 recommendations, 142 practical points of view, and 56 experts' views (20, 21). Several randomized controlled trials, observational studies, and meta-analysis showed that patients with PBM had significantly improved outcomes and reduced blood utilization (22-28). PBM focuses on the patient, as well as the conditions that make patients transfuse blood, such as blood loss, coagulopathy, platelet dysfunction, and anemia. PBM shifts its attention from blood transfusions and outpatients to self-medication and transfusion of blood-derived products to maintain the patient's own blood and effectively manage the patient's condition (22-28).

Thus, the PBM concept was approved by the WHO in 2010 through WHA63.12. The European Health Care Commission recommended PBM as a standard in 2017. The WHO's action plan for access to safe blood had been changed to qualified and effective blood components. Implementation of PBM was introduced in one of six recommendations (29).

The strong recommendations and available evidence suggested that the PBM model was not only an option but also a necessity. Nevertheless, essential changes in hospitals still lagged far behind scientific evidence. In addition, it was approved that PBM model improved the patient's clinical outcomes, increased patient safety, and reduced costs, but there were few hospitals with an organized PBM program. In the face of the current crisis, the European Center for Disease Control and Prevention (ECDC), in considering its COVID-19 risks on March 12, 2020, specified that the implementation of PBM was highly recommended. In addition, the WHO interim guide on March 20, 2020, on PBM acclaimed that the patient's blood manage-

ment could protect blood stocks (29).

## 2.2. Anemia

Anemia is putting up patients at risk for blood transfusions, and usually, it gets worse after surgery (29, 30). The patients should be screened for anemia before surgery, especially those who are scheduled to undergo major surgery. The WHO describes anemia as hemoglobin level of less than 120 g/L in non-pregnant women over 15 years of age and 130 g/L in men. However, recently it was introduced as hemoglobin levels less than 13 in all patients (31, 32).

In a study conducted in Spain, the overall prevalence of anemia before surgery was 36%. In more than 70% of these anemic patients, complete or functional iron deficiency was reported as a result of limited iron erythropoiesis (33). So, iron deficiency in patients before cardiac surgery has resulted in a 3.5-fold increase in 90-day mortality (34). It was expected that anemia would increase due to changes in diet and lifestyle following the COVID-19 pandemic, including lower incomes and less consumption of fresh foods containing vitamin C and folic acid (fruits and vegetables), vitamin D, fish, and meat (iron, vitamin B6, vitamin B12). On the other hand, staying at home due to social restrictions caused the lack of sunlight which triggered muscle atrophy. As a result of the proliferation of red blood cells, iron homeostasis and hemoglobin synthesis were affected, and the overall mental and physical function were affected (35, 36). Eventually, the public health of communities with the highest elderly people was affected (37).

### 2.2.1. Diagnosis and Treatment of Anemic Patients Awaiting Surgery During COVID-19 Pandemic

During the COVID-19 pandemic, most of elective surgeries were postponed, emergency surgeries were prioritized, and the number of elective surgeries was significantly reduced. Preoperative anemia clinics that were tasked with screening, diagnosing, and treating iron deficiency and other causes of anemia were closed and patient visits were cancelled. However, the possibility of telephone and video counseling for iron deficiency increased. The common symptoms of severe iron deficiency include feeling tiredness, confusion, palpitations, shortness of breath, anxiety, low mood, depression, restless legs, alopecia, brittle and spoon-shaped nails, and tendency to eat dirt or ice. Intravenous iron administration (IV iron) was preferred for rapid results in anemia clinics or through general practitioners. However, access to injectable iron might be possible during COVID-19 pandemic (38).

The new formulation of oral iron increased the absorption and tolerance of iron (such as sucrose iron) in the di-

gestive tract (39), which was also practical for people who could not leave their homes due to quarantine (40).

### 2.2.2. Diagnosis and Treatment of Anemia

In patients admitted for emergency surgery, the diagnostic tests for anemia include hemoglobin, ferritin, CRP, and transferrin saturation in preoperative evaluation. As mentioned above, the prevalence and severity of anemia was likely to increase during the COVID-19 pandemic due to changes in diet and lifestyle. Therefore, we might have more anemic patients in the hospitals. Low ferritin is usually considered a sign of very low iron stores and iron deficiency, but it increases in the acute phase of inflammation, as in viral infections. As a result, the use of ferritin in the diagnosis of anemia in patients with COVID-19 would be problematic, and it is not reliable in acute inflammation phase and viremia. These people would have normal or even high ferritin levels, despite severe iron deficiency (40, 41). An increase (CRP > 4 mg/L) indicates that ferritin level in the acute phase of inflammation or viremia is not trustworthy (41). Consequently, the evaluation of CRP and transferrin saturation < 20% with low ferritin can indicate the severity of iron deficiency (33).

### 2.3. Intra-operative Methods

Further intraoperative approaches to reduce bleeding and prevent unnecessary blood transfusions include maintaining perioperative normothermia, using cell salvage, employment minimally invasive surgical techniques, acute normovolemic hemodilution (ANH), pharmaceutical agents such as tranexamic acid, restrictive transfusion triggers, massive hemorrhage protocols, and guidelines, and point of care coagulation testing (42). Although maintaining normothermia, pH > 7.2, Calcium > 1.1 mmol/L, and other physiological conditions intra-operative is very important in this period (42-44).

One of the easiest methods to establish PBM and make balance between supply and demand of blood in COVID-19 pandemic is to use one RBC unit and assess the patient's condition and then transfuse, which is called a single-unit transfusion plan (45). With the implementation of these methods, some meta-analysis studies showed a decrease in transfusion request by 55% in orthopedic surgery, as well as 50% in heart surgery. Moreover, they reported decrease in thrombotic events, morbidity, and mortality in patients (27, 46).

### 2.4. PBM and COVID-19 Pandemic

The COVID-19 pandemic did not increase blood demand in Zhejiang Province of China, but low donors caused the shortage due to panic of infection (47). Blood

transfusion services had to provide blood products even during the COVID-19 pandemic. Admittedly, the blood supply was incessant. In these circumstances, social media could play an important role in the enrollment of healthy blood donors. On the other hand, there could be a strategic plan for maintaining blood supply, focusing on blood shortage, and decreasing blood wastage (48).

Also, according to the WHO guidelines, a suitable inventory management system should be run to maintain blood stocks. Inventory management included such principles as reduction of blood demand by closure of outpatient departments, postponing elective surgeries, and decreasing the wastage using the FIFO (first in first out) principle (14). Chinese people learned from the experience of COVID-19 pandemic that it is vital to extend donor sources and reduce blood use scientifically. Autologous transfusions could be increased, elective surgery postponed, surgical procedures with less bleeding used, the PBM expanded, and strict blood transfusion strategies employed (49). Appropriate use of blood, diminishing unnecessary transfusions, and implementation of PBM were significant measurements in this regard. There were more than 20 PBM methods for decreasing blood utilization (50). Thus, various specialists, including surgeons, obstetrics, gynecologists, and anesthesiologists, were involved in the PBM (51). During February and March 2020, postponing the elective surgeries and low hospital beds declined the request for blood products. Hospitals should have an emergency strategic PBM plan to prepare blood for patients (52). Accordingly, the medical community needs other solutions to care for patients, and implementation of immediate PBM principles must be mandatory worldwide (53).

## 3. Conclusions

One of the most important problems for blood transfusion services in COVID-19 outbreak is the reduction in the number of donors and blood stocks. Strategies such as PBM can be used to reduce blood demand. These strategies include pillars in pre-, intra-, and post-operative periods. Maintaining the patient's own blood is very important in the strategy. Methods such as treatment of anemia, maintenance of normothermia during surgery, use of cell salvage and minimally invasive surgical techniques, acute normovolemic hemodilution (ANH), and pharmacological agents such as tranexamic acid should be used to maintain the patient's own blood. Adherence to the existing protocols and guidelines and the use of point of care tests are methods that can help reduce the blood demand. Thus, implementation of immediate PBM principles must be mandatory worldwide.



## Footnotes

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