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Impact of the COVID-19 pandemic on blood transfusion systems: International review and the Moroccan blood transfusion system experience

Sabah Bouhou, Khadija Lahjouji, Mohammed Benajiba, Azlarab Masrar

ABSTRACT

Introduction: Transfusion systems worldwide have had to face many challenges against the emergence or the re-emergence of numerous infectious diseases. Some of those viruses have posed significant impacts on blood transfusion activities. Several scientific and transfusion experts consider the current COVID-19 pandemic to present a potential risk of reducing and compromising the supply of blood products. Blood establishments had to activate their emergency plans and to propose appropriate response measures.

Method: It is an international review where we used key terms search strategy to identify necessary information about: (i) the impact of some previous emergent viruses on the availability and the safety of blood products and (ii) the impact of the current COVID-19 pandemic on the blood transfusion activities worldwide. Additionally, we presented the impact of the COVID-19 pandemic on the Moroccan transfusion system activities and the measures established by the Moroccan National Centre of Blood Transfusion and Hematology (MNCBTH) to ensure management of this health crisis on the availability and the safety of blood products in Morocco.

Results: Viruses like Zika, Influenza A (H1N1), Chikungunya, SARS-CoV, MERS-CoV, and Ebola have been of great concern in terms of virulence, modes of transmission, and impact on blood transfusion activities. The COVID-19 pandemic has impacted the availability of blood products in blood establishments worldwide. In Morocco, the COVID-19 pandemic affected blood collections and caused a significant decrease in the number of blood donors nationally. Data provided from all regional blood transfusion centers and blood banks in Morocco show that the total number of blood donations made in 2020 was 297,841 blood donations nationally compared to 334,510 blood donations made in 2019, with a decrease of 36,669 blood donations. The number of labile blood products (LBP) produced in 2020 was 455,805 units compared to 695,974 units produced in 2019, which corresponds to a reduction of 57,654 units. The number of LBP delivered in 2020 is 455,805 units against 451,736 delivered in 2019, with an increase of 4069 units. The pandemic impacted other activities of the blood transfusion system in Morocco like continuing education programs, meeting activities, technical missions, and the Moroccan plasma removal for the fractionation.

Conclusion: The COVID-19 pandemic has had a significant impact on blood transfusion activities worldwide. The MNCBTH has expressed continued adaptability to ensure proper management of the impact of the COVID-19 pandemic on the availability and safety of blood products in Morocco.

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INTRODUCTION

Since the international health crisis relating to the Spanish flu in 1918, transfusion systems worldwide have had to face many challenges against the emergence or the re-emergence of numerous infectious diseases. Some of those viruses have posed significant public health problems [1]. All of this has led the health authorities to draw up response plans and imagine new healthcare systems organizations to propose appropriate control measures and ensure good management of these diseases [1]. On the side of blood establishments, considerable efforts have been made to catalog these responsible viruses, understand their respective specificities, put in place means of securing transfusion, and monitor the possible consequences of each epidemic on the availability and the safety of blood products.

For several international scientific societies and blood transfusion experts, the current COVID-19 pandemic has been considered to present a potential risk of reducing and compromising the supply of blood products [2, 3]. Blood establishments had to activate their emergency plans and risk analysis to propose appropriate response measures [2–5]. Several blood establishments worldwide have reported a significant impact of the COVID-19 pandemic on the availability of blood products because of several factors. They are cited restrictive measures established by local authorities to control the transmission of SARS-CoV-2, difficulty in moving donors to blood collections sites because of lockdown, cancellation of mobile blood donation drives, and the fear expressed by donors regarding the risk of SARS-CoV-2 infection in the event of displacement to transfusion centers.

By strengthening its scientific and epidemiological monitoring system, the National Centre of Blood Transfusion and Hematology of Morocco (MNCBTH) has put in place several measures to ensure good management of the impact of the COVID-19 pandemic on transfusion activities in Morocco. These measures have been updated as the national and international epidemiological situation regarding SARS-CoV-2 evolves.

METHOD

Previous viruses' impact on transfusion activities was identified using keys terms like *Influenza and blood donation, SRAS blood safety, EBOLA and blood donation impact, Blood collection and Chikungunya virus, epidemics and blood collection, Blood safety in epidemics, MERS and blood donation, Zika virus transmission, Zika virus transfusion risk.*

For information on the COVID-19 pandemic effect on the transfusion activities worldwide, we used terms such as *COVID-19 impact on blood collection, COVID-19 and blood safety, SARS-CoV-2 transmission by blood, COVID-19 impact on transfusion cares continuity, COVID-19 infection and blood type, Transfusion in COVID-19 infected patients, Blood products use in COVID-19 disease.*

In the final section, we presented the experience of the Moroccan blood transfusion system about the management of the impact of the COVID-19 pandemic on several blood transfusion activities in Morocco.

RESULTS

Impact of some previous epidemics or pandemics on the availability and safety of blood products

Each epidemic or pandemic outbreak has been unique by its epidemiological characteristics and its consequences [6]. So the response scenario plans had to adapt quickly according to each situation [6]. Viruses like Zika, Influenza A (H1N1), Chikungunya, SARS-CoV, MERS-CoV, and Ebola have been of great concern in terms of virulence, modes of transmission, and especially the impact on maternal-fetal transmission, as is the case with Zika virus [1].

(A) Zika virus

Zika virus was isolated from humans in 1952. The four recent epidemics (Micronesia on the island of Yap in 2007, French Polynesia in October 2013, New Caledonia in January 2014, and Brazil in May 2015) are due to strains of lineage Asia and have occurred in immunologically naive populations [1]. From May 1 to July 28, 2016, in mainland France, 200 imported cases and 2 cases of sexual transmission have been confirmed. There have been no cases of indigenous vector transmission [1].

In early 2016, the World Health Organization (WHO) declared a public health emergency of international concern due to the explosion in the number of people infected with the Zika virus in Central and South America and due to indications that the virus was responsible for an epidemic of microcephaly in Brazil [7]. The potential transmission by blood transfusion is of concern because many people infected with the virus remain asymptomatic, and the duration of viremia and viral shedding is uncertain [7]. During the Zika virus outbreak in French Polynesia in 2013 and 2014, researchers found that 3% of asymptomatic blood donors were infected with the Zika virus [7]. In Brazil, several cases of possible viral transmission by blood transfusion were studied in early 2016. Puerto Rico began importing blood components on March 5, 2016, although local donations resumed on April 2, 2016, after the FDA approved an experimental

nucleic acid test for the Zika virus [7]. Many countries have established blood donation deferral for up to 28 days after symptoms resolve or after a serological test result or virology positive for an asymptomatic individual, as recommended by the WHO. The FDA recommended 28 days, the Brazilian Ministry of Health recommended 30 days, and Canadian Blood Services recommended 21 days [7]. At this time, FDA determined that Zika virus was a "relevant transfusion-transmitted infection" and that testing for Zika virus was necessary to reduce adequately and appropriately the risk of transmission of Zika virus by blood and blood components [8]. FDA issued guidance recommending nationwide and territorial implementation of individual-donor nucleic acid testing on all blood donations, or pathogen reduction [8].

In a meta-analysis study published by Liu Rongfei et al. in 2019, about the information provided by ten literatures (528,947 blood samples), the overall pooled prevalence of Zika virus (RNA and antibody) in donated blood was 1.02% [9]. The prevalence varied considerably by geographic region. Donated blood was more infected (likely double) with Zika virus during a Zika epidemic than during a non-epidemic [9]. In addition, a total of 122 Zika virus-positive blood donors were followed up, of whom 48 (39%) reported symptoms after donation, but none of the 13 recipients followed reported clinical symptoms related to Zika infection after transfusion [9].

In May 12, 2021, the FDA published an information paper for Blood Establishments regarding ZiKa virus and determined that Zika virus is no longer a Relevant Transfusion-Transmitted Infection [8]. The FDA Withdrawal the Guidance titled "Revised Recommendations for Reducing the Risk of Zika Virus Transmission by Blood and Blood Components"; where it says that if change in the epidemiology that leads FDA to conclude that ZiKa virus "may again have sufficient incidence and/or prevalence to affect the potential donor population," the FDA may then re-determine that ZIKV is a transfusion-transmitted infection and issue guidance with recommendations for blood donor screening and testing, if necessary, to ensure donor safety [8].

(B) Influenza A (H1N1) virus

A new influenza A (H1N1) virus of swine-origin appeared among residents of Mexico in the spring of 2009. It spread among travelers worldwide, resulting in the first influenza pandemic since 1968 [10]. Given the epidemic scale, on June 11, 2009, WHO raised the alert level for H1N1 influenza to the highest level, phase 6, and qualifies the situation as a pandemic [10].

In December 2009, the Superior Health Council of Belgium published a paper about the assessment of the risk of a shortage in the supply of blood and blood components that may be caused by an influenza A (H1N1) pandemic [11]. It reported that the European Commission Directive of November 3, 2009, authorized temporary exemptions from specific eligibility criteria for donors of whole blood and blood components in the context of a risk of shortage directly caused by the influenza A (H1N1) pandemic [11]. On the one hand, these temporary exemptions relate to a reduction of the hemoglobin threshold from 125 to 120 grams per liter of blood for women and from 135 to 130 grams per liter of blood for men [11]. On the other hand, the minimum exclusion period of two weeks after the disappearance of symptoms of donors with an influenza-like episode is replaced by a one-week exclusion period. The Superior Health Council of Belgium has also reported that the impact of a pandemic on transfusion needs is difficult to assess and unpredictable [11].

In August 2010, Masaharu Tsubokura et al. published an assessment of the number of blood donors presenting for blood donation at fixed or mobile collection sites [12]. They use a Red Cross Hyogo Prefectural Blood Centre blood donation database between four weeks before and after May 16, 2009, when the first case of H1N1 flu was confirmed in Kobe (Japan) [12]. The number of blood donors fell by 21%, and whole blood donations fell by 1329 units in the week following the first case. This rapid decrease in blood donation has had a significant impact on clinical practice. The number of blood donors in mobile clinics has decreased by 39% [12]. The Department of Health, Labor, and Welfare has repeatedly called on hospitals to restrict blood consumption. The Hyogo Red Cross Prefecture blood establishment has requested blood products from Red Cross blood centers in other prefectures [12].

(C) Chikungunya virus

Since March 2005, the Chikungunya virus has been responsible for an epidemic in Comoros, in the southwestern area of the Indian Ocean [1]. The 1st case was detected in Reunion in April 2005. The epidemic peaked during the 5th week of 2006 with more than 45,000 weekly cases. It got 35% of the population or 244,000 people in April 2006 [1]. Reunion Island experienced a critical situation during the Chikungunya epidemic, which broke out in 2005–2006. On January 20, 2006, given the epidemic scale (with 10,000 to 40,000 new cases per week), the French Blood Establishment suspended whole blood collection on the Island. Also, the French Establishment set up two measures never been tested on a large scale for platelet donations: unit qualification by quantitative reverse transcription-polymerase chain reaction (RT-PCR) and systematic inactivation of platelet concentrates by the Intercept system. This system can reduce the viral load of a product by more than five log10 blood [13, 14]. A model made by the National Institute for Public Health Surveillance considered that the average duration of viremia is 7.5 days and that 38% of the Reunionese population has been exposed to the virus (including about 6% of asymptomatic). Consequently, the number of positive donations avoided was 29 at the peak of the epidemic and 40 for the whole of it [13, 14, 15]. Ultimately, no case of transfusion contamination has been observed either in Reunion or elsewhere in the world [13, 14, 15].

However, the risk of blood transmission is proven by several cases of contamination of laboratory workers and by one case of contamination of a nurse during a blood sample from an infected patient [13, 14, 15].

(D) SARS-CoV virus

The year 2003 was marked by the emergence of a Severe Acute Respiratory Syndrome (SARS), a disease linked to the SARS-CoV virus of the Coronavirus family, which is characterized by mainly respiratory symptoms [1]. The epidemic quickly took on an international dimension, leaving more than 8000 sick and 774 dead in some 30 countries. In February 2003, a Chinese doctor from the province of Guangdong who was staying at the Metropolis Hotel in Hong Kong infected some fifteen guests and visitors to this hotel, who were responsible for the various outbreaks around the world [1].

During the peak of the SARS epidemic in Singapore, a 60% decrease was observed in donors presenting to donate blood [6]. Various planning scenarios estimate that up to 30–40% of the population may be infected during the peak of an influenza pandemic and that a 10–30% loss of donors may occur. Due to risk reduction measures, an additional 4% of potential donors were postponed during the SARS outbreak [6]. During the SARS epidemic in Beijing (April–June 2003), there was an initial decrease in blood requirements, mainly due to the postponement of certain elective surgeries due to the closure of hospitals [6]. The epidemic caused a significant reduction in the volume of blood collected because of the unavailability of blood donors because of the avoidance of public places and the closure of mobile blood collection sites such as workplaces and universities. By mid-April 2003, daily blood collections sometimes dropped to one-tenth or less of the number of daily collections usually made in the pre-epidemic period [6]. To ensure the availability of blood in Beijing, a centrally coordinated program for monitoring and restricting clinical blood use and a contingency plan was initiated to coordinate imports from other regions. Between April and July 2003, Beijing had to import a significant number of blood products from different parts of China to ensure the availability of blood for clinical use [6].

In Hong Kong, the SARS epidemic impacted the blood supply and demand. The demand number reduced by 12.8% due to the change in health care [16]. Also, there has been a reduction of about 16.9% in blood donations due to a decrease in donor's attendance at blood donation centers and mobile clinics and the cancellation of a large number of scheduled mobile clinics. There was a drop in blood collection by 6445 units during the SARS epidemic in 2003 in Hong Kong [16].

(E) MERS-CoV virus

The Middle East Respiratory Syndrome-coronavirus (MERS-CoV) is a zoonotic pathogen that caused an epidemic in Saudi Arabia and other countries of the Arabian Peninsula since 2012 [17]. From 27 countries worldwide, 1905 confirmed infections due to MERS-CoV, including 677 deaths, were reported as of February 24, 2017 [17]. The number of asymptomatic cases was estimated to be much higher than reported cases, which was considered a risk for blood safety [17].

Through our review, no information is available on the impact of MERS-CoV on the availability of blood products but some information on the implications for transfusion safety. Viroj Wiwantikit published a paper in June 2016 and stipulated that MERS-CoV was for significant concern on transfusion medicine [18]. The author reported a study made by a Saudi Arabian team on donated blood samples by immunofluorescence assay with no positive findings. The author confirmed that the method used was not a gold standard and concluded a low chance of transmission by blood donation [18]. To minimize the risk of any possible transfusion-related MERS-CoV transmission. Some studies investigated the efficacy of inactivation of the MERS-CoV in human plasma. Salwa Hindawi et al. reported data showing efficient inactivation of this virus in therapeutic human plasma units of 4.67 logs using amotosalen and ultraviolet A light [17].

(F) Ebola virus

On March 21, 2014, the Republic of Guinea confirmed an Ebola virus outbreak, with WHO subsequently reporting an expansion into Sierra Leone and Liberia primarily, and then into Nigeria [1]. The epidemic was characterized very quickly by high mortality and transmission to health care workers. The outbreak in West Africa has resulted in 28,616 confirmed, probable, and suspected cases in Guinea, Liberia, and Sierra Leone, of which 11,310 have died. In June 2016, WHO declared the end of transmission in Guinea and Liberia [1]. On June 28, 2019, the ECDC reported that the risk of transmission of the Ebola virus through substances of human origin is related to the presence of the Ebola virus in the donor's blood, tissues, and organs [19]. The presence and concentration of virus in organs, tissues, blood, and other body fluids changes during infection [19]. The concentration of the virus peaks when symptoms are most severe. However, viruses can be detected and isolated from breast milk and semen weeks after recovery. Ebola virus has been isolated by cell culture from blood, saliva, urine, aqueous humor, semen, and breast milk of recovering patients' days and months after recovery. The risk of transmission of the Ebola virus through substances from human origin was assessed as high [19].

(G) Convalescent plasma use in the treatment of infections caused by the previous virus

Convalescent plasma taken from individuals who have recovered from a previous viral infection has been used at various times over the last century. Based on the principle of passive antibody transfer, this therapy has proven beneficial against several infections (including

hepatitis B, polio, measles, influenza, Ebola) and, of course, the SARS and MERS epidemics. Results from a small documented series of cases in previous outbreaks have shown faster viral clearance after administration of convalescent plasma, particularly when given early in the disease [20].

A retrospective meta-analysis of eight studies on the use of convalescent sera involving 1703 patients during the 1918 H1N1 pandemic suggested that those who received serum had lower mortality. The effectiveness of convalescent sera varied with the virus and the study. Still, there was a consensus that this intervention was helpful and used in many epidemics [21]. In a 2009 study of 20 H1N1 positive patients who received A H1N1 convalescent plasma, the researchers observed a reduction in viral load in the respiratory tract, cytokine levels, and a decrease in mortality [22]. Cheng et al. in 2005 reported the results of the administration of convalescent plasma in 80 patients with SARS-positive disease. This administration was associated with an increase in the hospital discharge rate on day 22 of symptom onset compared to those who did not receive convalescent plasma [23].

A data from Saudi Arabia explored the feasibility of collecting convalescent plasma for the treatment of MERS-CoV infection. Many persons' samples were screened using ELISA to detect MERS-CoV antibodies [24]. These authors reported that such testing should be mandatory for convalescent plasma donations due to the low prevalence of anti-MERS-CoV antibodies, even in patients with previous laboratory-confirmed MERS-CoV infection. This testing is essential to confirm antibodies to MERS-CoV and the protective effect of the MERS-CoV convalescent plasma [24]. The authors reported that two patients in the 2015 MERS-CoV outbreak in South Korea were reported to have received convalescent plasma collected from recovered patients but without information on the effect of this transfused plasma in recipients [24]. Convalescent sera were also used during the Ebola outbreak in West Africa in 2013. A small non-randomized study in Sierra Leone found significantly longer survival for those treated with whole convalescent blood than those who received standard treatment [25].

Impact of the COVID-19 pandemic on the availability and the safety of blood products

COVID-19 is an emerging infectious disease caused by the SARS-CoV-2 coronavirus, which appeared in Wuhan, Hubei Province on November 16, 2019, before spreading worldwide. The first diagnosed patient was identified on December 1, 2019, in central China's Hubei Province. On December 16, 2019, the first hospitalization due to this infection was noted. The disease spread out of China as early as January, and on February 25, 2020, the number of new cases reported daily outside China is higher than in the country. The first genomic sequence of SARS-CoV-2 was reported on January 10, 2020. SARS-CoV-2 was a new type of beta-CoV with over 99.98% genetic identity among ten sequenced samples taken from the original outbreak site, the seafood market from Huanan to Wuhan. SARS-CoV-2 is genetically more similar to SARS-CoV than to MERS-CoV [26].

WHO declared a state of public health emergency of international concern on January 30, 2020. On March 11, 2020, the COVID-19 epidemic was declared a pandemic by the WHO. As of June 14, 2021, have been notified 176,702,468 cases and 3,813,133 deaths worldwide.

(A) Impact of the COVID-19 pandemic on the availability of blood products in Europe

During the European Directorate for the Quality of Medicines & Health Care (EQDM) webinar in October 2020, data from the European Centre for Disease Control (ECDC) reported the impact of the CIVID-19 pandemic on blood collection and distribution. Comparing March and April 2020 to March and April 2019, many countries in Europe had expressed 9% as a median decrease in blood collections (ranging from 1% to 27%) and 12% as a median decrease in distribution (ranging from 1% to 18%) [27]. Thus, Croatia had expressed –27% as a difference in blood collections and –17% in blood and blood components distribution [27]. Slovenia reported –23% in blood collections and –12% in blood and blood components distribution. In the same context, Italy reported –8% in blood collections and –15% in blood and blood components distribution compared to March and April 2019 [27]. Portugal observed a decrease of 14% in blood collections between 2019 and 2020 and 5% in blood distribution between 2019 and 2020 [27].

For the impact of the COVID-19 pandemic on plasma-derived medicinal products (PDP), as of April 16, 2020, a questionnaire has been sent to nine factories and plasma fractionators with 100% response [27]. The results were that there was no drop in production of PDP in Europe. Some disturbances in the source plasma supply have been reported, but all manufacturers have emergency plans to avoid any disruption to the European PDP market [27].

(B) Impact of the COVID-19 pandemic on the availability of blood products in Hong Kong

In Hong Kong, all mobile blood drives have been canceled since February 5, 2020, due to the suspension from school, the switch to work from home, and the advised break from public activities [28]. As of week 5 2020, 2362 blood collections were reported compared to 4074 in the same week in 2019 [28]. Using social networks and media, they made an emergency appeal for blood donations on February 11, 2020. Consequently, the number of blood collections increased to 6401 in week 7 2020 compared to 4890 in the same period in 2019 [28].

(C) Impact of the COVID-19 pandemic on the availability of blood products in Canada

In Canada, between February and May 2020, there was a drop in the number of donations ranging from 70,000 donors per month in pre-pandemic to 54,738 donors in May 2020 [29]. Only 58% of the available meeting slots were secured. Direct phone calls were made to donors, and public service announcements were made by Prime Minister [29]. Both Canadian Blood Services and Héma-Québec, the organization tasked with collecting blood in Quebec, adapted their donor assessment policies and donor eligibility criteria in response to the pandemic [29]. Some donor selection criteria were altered to help mitigate blood supply shortages. The hemoglobin cut-off threshold for donors was temporarily reduced, meaning more people were eligible to donate at a time when donations were needed. In August 2020, this allowed an additional 1000 women to donate blood per month. In October 2020, the hemoglobin criteria reverted to pre-pandemic standards as no shortage in LBP was observed [29].

(D) Impact of the COVID-19 pandemic on the availability of blood products in WHO African Region

Lou et al. made an investigation on the impact of COVID-19 on blood supply and demand in the WHO African Region. Forty-seven countries were asked to complete a questionnaire and submit their responses from May 21 to June 14, 2020 [30]. Countries were asked to provide data for the period January 1–May 31, 2019 and January1–May 31, 2020 to ensure a comparison of information between those two periods. A second survey focused on COVID-19 convalescent plasma activity was conducted during the first two weeks of September 2020 [30]. Thirty-seven countries responded. The total number of donated blood fell in 32 countries while it rose in five countries. The proportion of blood donations also decreased in 21 countries and increased in nine countries [30].

On 2019, 1,800,236 blood collections were made in those countries but on 2020 1,498,773 blood collections were made with −301,463 as a difference [30]. Blood requested and delivered for transfusion has declined in 30 countries. The risk of out-of-stock reagents and consumables used along the blood transfusion chain, from blood collection to transfusion to patients, increased in 11 (29.7%) countries in 2019 to 22 (59.5%) in 2020. Ten countries reported some convalescent plasma activity. However, very few units of these collected products have been transfused to patients with COVID-19 [30].

(E) Impact of the COVID-19 pandemic on the safety of blood products

(E-1) Is SARS-CoV-2 transfusion-transmitted?

Data available to date on the real risk of transmission of SARS-CoV-2 through blood and blood products such as publications of international scientific societies, studies about the detection of SARS-CoV-2 RNA in the blood of COVID-19 patients and blood donors, and all published cases of the transfusion of blood products from donors confirmed COVID-19 positive after donation and the progress in recipients of these products, speaks about a theoretical risk [31–35].

The analysis of this data makes it possible to report the main following points:

- SARS-CoV-2 is a new infectious agent and not enough information to exclude with certainty the risk of transfusion transmission, which remains a theoretical risk [31–35].
- SARS-CoV-2 RNA has been detected with a very low load, but the infectivity of the virus has not been confirmed in blood donors [36–38].
- Cases of product transfusion from COVID-19 positive donors after the donation have provided no evidence of transmission of the virus to recipients [39–45].
- As a precautionary measure, blood centers should take the necessary measures to reduce the risk of transmission of SARS-CoV-2 through blood products and ensure the safety of donors and recipients [3–5].
- Strengthening the hemovigilance system and post-donation information is an essential link for blood safety during the COVID-19 pandemic [3–5].
- SARS-CoV-2 is not a direct threat to blood safety but raises problems with the blood supply [36].
- The measures put in place by blood centers to minimize the risk of transfusion transmission must consider the need to ensure the availability of blood products [36].

(E-2) Measures to mitigate the risk of transmission of SARS-CoV-2 through blood products

Since the beginning of the COVID-19 pandemic and according to publications from international scientific societies, blood establishments around the world put several measures to face the theoretical risk of transmission of SARS-CoV-2 through blood and blood products. One of the critical aspects of these measures consisted of strengthening and updating the medical selection of donors against SARS-CoV-2 infection. Blood establishment updated blood donor eligibility criteria according to each country's international and local epidemic evolution relating to SARS-CoV-2. In this context, as of January 27, 2020, Germany, Austria, Belgium, Denmark, Finland, Malta, the Netherlands, the United Kingdom, Sweden, Switzerland, Slovenia have introduced 28 days of postponement of blood donation for travelers returning from China, 21 days for travelers from other countries at risk other than China and 21 days for contact cases [2]. In the same context, Australia, Canada, and Japan postponed blood donors four months after returning from China [2]. For the United States, as

of January 31, 2020, in the absence of data suggesting a risk of transmission of SARS-CoV-2 by transfusion, the AABB (American Association of Blood Banks), the FDA (Food and Drug Administration), and the CDC (Centre of Diseases Control) do not recommend any action to be taken by blood establishments [2]. On March 09, 2021, the High Council of Public Health published a new SARS-CoV-2 blood donor eligibility criteria [46]. Considering the latest European and international recommendations, the HCPH recommends reducing from 28 to 14 days' deferral period for donors who have had a confirmed SARS-CoV-2 virus infection after resolution of symptoms or who have been in contact with a subject infected with this agent [46].

With the introduction of COVID-19 vaccination campaigns, several blood centers updated recommendations concerning the eligibility criteria for blood donation after receiving the COVID-19 vaccine according to the types of COVID-19 vaccines adopted in their countries. For example, the Scottish National Blood Transfusion Service on December 21, 2020, stipulated that blood donors how had the vaccine as part of the UK vaccination program can give blood seven days after the jab. The blood donor also has to be recovered from any reaction to the vaccine [47].

On December 16, 2020, in its COVID-19 update, the Canadian Blood Services stipulated that for the COVID-19 vaccine, there is no deferral period post-vaccination with the Moderna vaccine [48]. For the American Red Cross, there is no deferral time for eligible blood donors vaccinated with an inactivated or RNA-based COVID-19 vaccine manufactured by Moderna or Pfizer [49].

The other measures implemented by blood establishments to mitigate the risk of transmission of SARS-CoV-2 through blood products are:

- The implementation of protective measures against SARS-CoV-2 infection for donors and staff.
- The reinforcement of post-donation information.
- The strengthening of dialogue and collaboration between the blood center and the care services to consult on the delivery of blood products based on the concept of Patient Blood Management.
- The monitoring and strengthening of the recipient's hemovigilance to detect and to follow recipients how are received blood products derived from donors confirmed with COVID-19 infection in post-donation.
- The quarantine of blood products like Fresh Frozen Plasma (FFP) products that did not benefit from pathogen inactivation while awaiting post-donation feedback. Blood centers that already have the inactivation technique had a reduction in this theoretical risk.

(E-3) Place of screening for SARS-CoV-2 in blood donors

In the absence of clear evidence on the real risk of transmission of SARS-CoV-2 through blood and blood products, the majority of blood centers around the world have not introduced a screening technique for SARS-CoV-2 for blood donation. But, SARS-CoV-2 nucleic acid detection has been added to the blood screening process since the end of January 2020 in Wuhan and other cities in Hubei province because Wuhan was considered the epicenter of the epidemic at the start of 2020 [50–52].

In a multicenter study in Hubei, all donated blood from February 9 to April 30, 2020, was tested at 12 blood establishments in Hubei province. A total of 98,342 donations, including 87,095 whole blood donations and 11,247 platelet donations, were tested by nucleic acid screening test (NAT): individually for 3831 and in a mini pool for 94,511 donations [51, 52]. All donations were negative for SARS-CoV-2 RNA in the past 12 weeks. For the authors, these results indicate that the novel coronavirus may not pose a direct threat to blood safety but raises serious concerns for the general blood supply [51, 52].

(F) Blood transfusion need in patients with COVID-19 infection

All the data available to date stipulate that SARS-CoV-2 is not a direct threat to blood safety but can compromise and decrease the supply of blood products to meet the need expressed by the care structures for both non-COVID-19 and COVID-19 patients. COVID-19 infection can present various clinical manifestations with three clinical forms: light, moderate, to severe disease. The mortality rate is high in patients admitted to the Intensive Care Unit (ICU) [53, 54]. According to several publications, blood transfusion has been used in COVID-19 patients for different reasons such as:

- Spontaneous hemorrhage or procedure (tracheostomy, central venous route, break in a cannula).
- COVID-19 patients with chronic and non-tolerated anemia.
- Bleeding under anticoagulants.
- Bleeding disorder for intensive care unit COVID-19 patients.
- Disseminated Intravascular Coagulation (DIC) in critically ill COVID-19 patients.

On January 11, 2021, Elvira Grandone et al. published a study about mortality and transfusion requirements in COVID-19 hospitalized Italian patients according to the severity of the disease [53]. They retrospectively explored 422 patients with 179 admitted to the ICU at 4 Italian academic hospitals from March 3 to August 30, 2020. They found that the percentage of transfused patients was significantly higher in those admitted to the ICU (41.9%) than in those admitted to medical wards (10.3%). Patients undergoing non-invasive and invasive ventilation are significantly more transfused than those who do not need ventilation [53]. In patients admitted to the ICU, the number of Red Blood Cells (RBC) units strongly predicts overall mortality, increasing by 37% per transfused RBC unit [53]. By April 2020, Bingwen Eugene et al. evaluated

in a paper the indications and requirements of blood and blood products in patients with COVID-19 infection at the National Centre for Infectious Diseases (NCID) in Singapore [54]. From 572 patients with COVID-19 infection, they present clinical profiles of the nine patients who required transfusion: two from 553 non-ICU COVID-19 patients and seven out 19 ICU COVID-19 patients. They found that 0.36% (two out of 553) of non-ICU COVID-19 patients required RBC transfusion [54]. However, 36.8% (seven out of 19) of ICU patients required RBC transfusion, with lesser FFP and platelet transfusion requirements. Most transfusions consisted of red cell concentrates (total of 48 units of RBC) and occurred mainly in the ICU setting. Three out of seven ICU patients suffered from severe gastrointestinal bleeding, requiring high volumes of RBC transfusion [54]. The non-ICU patients who needed transfusions were pre-menopausal females with iron deficiency anemia, whose symptoms of anemia were exacerbated by concurrent COVID-19 infection. The use of FFP and platelet transfusions was minimal in their patients with COVID-19 diseases, with one patient having major bleeding while being on Extracorporeal Membrane Oxygenation ECMO. Platelet transfusions were used to mitigate peri-procedural risks of bleeding. They did not use specialized blood products in their patients with COVID-19 infection, such as factor VIII concentrates, 4-Factor prothrombin complex concentrates, or recombinant Factor VII a [54]. The authors concluded that most patients with mild COVID-19 infection do not require blood transfusions. A subset of critically ill patients with severe COVID-19 disease in the ICU, especially those with overt gastrointestinal bleeding, requires mostly RBC transfusion, with lesser requirements for FFP and platelet products [54].

In September 2020, a nationwide study in South Korea focused on transfusion demand in 7512 COVID-19 patients from the Korean population [55]. They found that 1·2% of all patients (n = 93) required blood transfusion during COVID-19 treatment periods [55]. The proportion of RBC transfusion was predominant (n = 88), PC and FFP transfusion were also observed (n = 28 and n = 18, respectively) with 30 patients receiving multiple types of transfusion product. The median amounts of RBC, PC, FFP, and cryoprecipitate received in the transfusion group during COVID-19 treatment periods were 3, 11, 4, and 27 units, respectively [55]. In the same context, Cristina Sanz et al. published on November 2020 the results of a cross-sectional study with a review of the blood bank and clinic records of 80 consecutive patients diagnosed with COVID-19, who required red blood cells (RBC) transfusion at the Hospital Clinic of Barcelona over 60 days, from mid-March to mid-May 2020 [56]. Bleeding indicated transfusion in 55 patients and included either large hematomas in 22 or external hemorrhage in 31 [56]. Critical illness anemia was the reason for transfusion in 22 patients. Most patients were on anticoagulants at the time of transfusion or the two days before. In total, 138 of the 261 transfusion episodes, 59% were related to 94 spontaneous or 44 procedure-related bleeding. Spontaneous bleeding was more frequent in the retroperitoneal space and the gastrointestinal apparatus [56]. Tracheostomy with endotracheal intubation, surgical interventions, and femoral vessels cannulation were the main procedures behind non-spontaneous bleeding. Seventeen patients died during the study period, but none of the deaths was ascribed to bleeding or blood transfusion [56].

(G) Information's on the link between SARS-CoV-2 infection and blood group type

Since the beginning of the COVID-19 pandemic, scientists have been interested in studying the link between individuals' blood groups and the risk of developing COVID-19. Some 40 studies have been published on the subject in one year, using various methods and focusing on multiple populations in several countries [57]. Different research groups have employed several ways. Most assume that the blood group impacts the risk of infection and attempt to confirm this by comparing the frequency of each blood group in the ABO system in patients with COVID-19 disease and uninfected people [57]. These studies have reported a reduced risk for people with blood type O, even if this reduction remains relative. These initial data have also already been confirmed by several meta-analyses [57]. A genome-wide association study (GWAS) found that blood group O carriers have IL-6 levels higher compared to individuals with other blood groups. They suggested the benefits of blood group O over different types in maintaining the dominant role of ACE2 and, therefore, reduced risk of developing hypertension and fewer cardiovascular complications [58, 59].

The second group of studies has looked more specifically at the impact of the blood group on the severity of the disease [57]. A Canadian study conducted a multicenter retrospective analysis and nested prospective observational sub-study of critically ill patients with COVID-19. It aimed to determine whether ABO blood groups are associated with different severities of COVID-19 [60]. The study involved six hospitals in the Greater Vancouver area and included patients admitted to intensive care units between February 21, 2020 and April 28, 2020 [60]. One hundred twenty-five critically ill COVID-19 patients were admitted to the ICU from March 1, 2020 to April 28, 2020 [60]. Of these 125 patients, 95 had ABO blood group data from an ICU admission group and screen and were included in the analyses. This data indicates that critically ill COVID-19 patients with blood group A or AB are associated with an increased risk for requiring mechanical ventilation, continuous renal replacement therapy (CRRT), and prolonged ICU length of stay compared with patients with blood groups O or B [60].

In France, a study made and published in November 2020 about hospitalized COVID-19 patients who had previously undergone aortic valve replacement surgery

highlighted that belonging to group A was the most significant predictor of mortality [61]. The study sample consisted of 702 patients. They found that COVID-19 patients were more likely to have blood group A (81.8%) than others (41.3%). Conversely, groups O, B, and AB were under-represented in COVID-19 patients [61]. Additionally, patients with the A blood group more frequently experienced COVID-19-related death as well as the combined endpoint of COVID-19-related death or hospitalization [61].

Pierre Gallian et al. published on July 3, 2020, the results about the investigation of the distribution of antibodies neutralizing SARS-CoV-2 according to age, sex, or blood group in French blood donors [62]. Four hundred sixty-four samples, collected before the emergence of SARS-CoV-2 (2017 and 2018), were used to test the virus neutralization assay specificity. With a 100% specificity, the test was used to test 998 samples collected from blood donors during the last week of March or the first week of April 2020 [62]. They found a low prevalence of 2.7%, but they observed that the proportion of seropositive was significantly lower in group O donors (1.32% vs. 3.86% in other donors, $p = 0.014$). The authors concluded that blood group O persons are less at risk of being infected and not only of suffering from severe clinical presentations, as previously suggested [62]. In conclusion, the authors reported that blood group O persons are less at risk of being infected. An increased risk of infections associated with blood group A is likely but remains formally established in non-hospitalized persons [62].

(H) Impact of the COVID-19 pandemic on the continuity of transfusion care in patients with chronic diseases such as hemoglobinopathies

The COVID-19 pandemic could have a significant impact on the ability of health systems to continue providing essential health services [63]. As health systems worldwide face increasing demand for care for COVID-19 patients, it is crucial to maintain both preventive and curative services, especially for people living with chronic conditions that represent the most vulnerable populations [63, 64]. Analyses from the 2014–2015 Ebola outbreak suggest that the increased number of deaths caused by measles, malaria, HIV/AIDS, and tuberculosis attributable to health system failures exceeded deaths from Ebola [63–65].

In the same context, Intezar Mehdi et al. stipulated that the COVID-19 pandemic has posed significant challenges for children with cancers and blood disorders such as hemoglobinopathies [66]. They report that interruption or postponement of treatment would be an additional challenge, either due to COVID-19 infection or inability to reach the centers for treatment due to lockdowns [66]. For Dimitrios Farmakis et al. the COVID-19 pandemic represents a significant challenge for hemoglobinopathies patients, their families, and their attending physicians [67]. The authors reported management methods of either transfusion-dependent or non-transfusion-dependent thalassemia patients [67]. They illustrate that adaptation of thalassemia care during the present and potential future similar pandemics requires, on the one hand, the strengthening of existing and creation of new communication channels between healthcare professionals and patients and on the other the promotion of a modified patient pathway for access to care including visits to medical facilities [67].

Bruno Fattizo et al. published the results of progressive reorganization strategies of hematological care in a large public university hospital in Milan (Lombardy) during the first six weeks of the COVID-19 pandemic [68]. As the transfusion center observed a reduction in the number of blood donations, patients' dependent on transfusions adapted their schedules according to the availability of donors, and they were transfused with 1 unit a week instead of 2 units in 14 days [68]. A decrease in the admissions to hematology and transplantation departments was observed at week 1 [68]. In the same way, a multi-center survey was run by the Thalassemia International Federation (TIF) and was focused on COVID-19 and its medical, public health, social, and economic impact on hemoglobin disorders and compares the pre-COVID-19 prevailing environment concerning hemoglobin disorders across the post-COVID-19 period [69, 70]. This study was based on:

- a survey conducted before the COVID-19 pandemic between January and December 2018 with the contribution of 62 National Thalassemia Associations, in 48 countries representing 3500 patients globally;
- a second survey was conducted during the COVID-19 pandemic, between March 15 and May 15, 2020, with the contribution of 48 National Thalassemia Associations in 42 countries representing 3200 patients globally.

The results showed that the moderate to severe blood shortage during the COVID-19 pandemic has resulted in a medium to a severe drop in hemoglobin (Hb) in β-Thalassemia Major (BTM) patients, with pre-transfusion Hb levels between 5–7 g/dL, with some reported to be very low (<5 g/dL) [69]. Half of the respondents said a severe interruption in the frequency and/or quantity of blood supplied, all from developing countries. They assured the supply with unpaired or non-leukoreduced units and even transfusion with whole blood units. Concerning chelation therapy, interruptions and/or shortages were reported. There was little to no impact on patients in Western countries despite the blood shortages reported at the beginning of the pandemic [69, 70].

Impact of the COVID-19 pandemic on blood transfusion system activities in Morocco

The Moroccan blood transfusion system includes one National Centre of Blood Transfusion and Hematology, 18 Regional Blood Transfusion Centers, 14 Blood Banks, and 24 Blood Transfusion Units (Antenna). The Moroccan National Centre for Blood Transfusion and Hematology is a scientific reference on a national scale. He is responsible for implementing the Moroccan Ministry of Health policy in the field of blood transfusion. His primary mission is to ensure national self-sufficiency in blood products for the benefit of patients in need. The MNCBTH provides other activities, including scientific and epidemiological monitoring, technical support for 18 Moroccan Regional Blood Transfusion Centers (MRBTC), administrative activities, management activities, basic training, and continuing education for all staff of blood transfusion in Morocco, supply of fungible reagents and consumables for 18 regional blood transfusion centers of Morocco, cell therapy, genetic and cellular engineering, molecular biology activities.

During the COVID-19 pandemic, several activities of the MNCBTH have been impacted, and some activities were reinforced and maintained to allow the MNCBTH to ensure good management of this health crisis.

(A) Impact on meetings activities and technical missions

Before the pandemic, the MNCBTH used to hold several meetings, divided into:

- Daily emergency meeting to manage blood products availability problems at the level of the 18 MRBTC, reagent supply problems, and critical equipment failures.
- One weekly meeting to discuss priority actions launched by the center on the technical plan, financial plan, computerization of the activities of the regional blood centers, promotion of blood donation.
- One weekly meeting for monitoring the state of progress of technical projects.
- One weekly quality meeting for the evaluation and the validation of quality procedures.

After the declaration of the first case of COVID-19 in Morocco on March 2, 2020, competent Moroccan authorities established restrictive measures to control the transmission of the virus. All meetings at the MNCBTH have been suspended. Some sessions were held by videoconference. Other meetings were authorized in case of emergency need with strict compliance with measures recommended by the Moroccan authorities: distancing, mask-wearing.

In the same way, all 2020 programmed displacement technical support missions for MRBTC, blood banks, and transfusion units were postponed.

(B) Impact on the continuing education program for staff

Each year, in its annual action plan, the MNCBTH establishes a continuing training program for blood transfusion staff in Morocco. This program includes the participation of the staff of the MNCBTH, those of Regional Blood Transfusion Centers, and staff of Blood Banks in scientific seminars, national and international scientific congresses, workshops, scientific days, quality training, computer training, training during the installation of medico-technical equipment, the annual meeting of those in charge of blood transfusion system in Morocco and the sessions for the presentation and the discussion of scientific articles in the field of blood transfusion and hematology.

In 2020, the COVID-19 pandemic had impacted the achievement of actions planned by the MNCBTH in its continuing education program. Two bibliographical research sessions were held before the first case of COVID-19 in Morocco on March 2, 2020. Also, the MNCBTH organized and hosted the annual meeting responsible for the blood transfusion system in Morocco in February 2020. This yearly meeting was assured because it was programmed before the implementation of restrictive measures by Moroccan authorities.

As the majority of scientific congresses programmed in 2020 have switched to virtual mode and webinars, some staff of the MNCBTH has been able to attend some webinars. Blood transfusion and SARS-CoV-2 are the main themes of these webinars, especially concerning blood safety in the era of the COVID-19 pandemic and the place of serological and molecular SARS-CoV-2 tests in the qualification of the blood donations process.

Information's about the achievement of continuing education program of MNCBTH in 2020 compared with 2019 is presented in Table 1.

(C) Impact on blood donation

The MNCBTH has made considerable efforts in recent years to reach the minimum rate recommended by the WHO to meet the need for blood products, which is 1%. In this context, aiming for a 4% annual increase in blood donations, all Moroccan Regional Blood Transfusion Centers and Blood Banks have been requested to strengthen the processes of promotion and sensitization to blood donation and strengthen the collection activities by using all the necessary logistics for this purpose. In 2018, the number of blood donations made by all MRBTC and blood banks was 321,336 donations in Morocco compared to 318,164 made in 2017, with an increase of 3172 blood donations. In 2019, more efforts were made by all MRBTC and blood banks under the technical guidance of the MNCBTH, and the total number of blood donations made in Morocco was 334,510 donations with an increase of 13,174 blood donations.

Unfortunately, in 2020, and like other blood transfusion establishments worldwide, blood donation

Table 1: Comparison between the achievement of 2019 and 2020 continuing education program of MNCBTH

	Bibliographic researches sessions meeting	Scientific seminars	National congress	International congress	Workshops	Scientific days	Quality training	Computer training
2019	34 sessions	1 seminar for the benefit of 52 staff members over a period of 2 days	2 national congresses : one for the benefit of 2 staff members and the other for the benefit of 100 staff members	2 international congresses: one for the benefit of 1 staff and the other for the benefit of 3 staff members	2 national workshop for the benefit of one staff each one	6 different sessions with a total of 19 beneficiaries from staff members	1 session for the benefit of 07 staff members over a period of 1 week	4 sessions of different duration and for the benefit of three staff members each
2020	2 sessions	0	0	3 international conferences webinars	0	0	01 session for 1 staff member over a duration of 3 days	0

activities have been impacted in Morocco and epically after the first case of COVID-19 on March 2, 2020. The number of blood donors has started to decrease. This situation has worsened from March 21, 2020, given the prohibition of displacement in and within cities established by Moroccan authorities. These measures, including the ban on gatherings, caused limiting blood donors' displacement to fixed sites of blood transfusion centers and the suspension of mobile blood collections in mobiles sites. Consequently, in March, the number of donations made nationally was 27,812 donations; in April, it was 22,415 donations, and in May 17,147 donations. For example, in the Regional Blood Transfusion Centre of the city of Oujda, which is located in the eastern region of Morocco, only seven blood collections were carried out in mobile sites until May 2020 compared to 30 made in 2019 [71]. From January to May, this center had collected a total of 8445 donations (fixed site and mobile site) in 2019 compared with 7510 donations (fixed site and mobile site) made in 2020 with a decrease of 11% [71]. For the Regional Blood Transfusion Center of Oujda, the number of LBP demand received by this center increased by 23% comparing 2020 to 2019 [71]. The RBTC of Oujda received 3998 demands in 2019 and 4951 demands in 2020 [71]. For the LBP delivered, during the first Five months of 2020, the RBTC of Oujda delivered 13,109 LBP in 2020 compared to 10,078 LBP in the same period of 2019. An increase of 30% was noted [71].

The number of LBP produced by the 18 MRBTC in 2020 was 455,805 units compared to 695,974 units produced in 2019, which corresponds to a reduction of 57,654 units. The number of LBP delivered nationally in 2020 is 455,805 units against 451,736 delivered in 2019, with an increase of 4069 units.

Another aspect of blood donation that has been affected by the COVID-19 pandemic is blood collection during Ramadan in Morocco. Indeed, during this month of fasting, blood collections are usually and essentially done at mosques at night after the break of fasting. In addition, the fixed sites are also open after the suspension of the fast for blood collection, according to a well-established program by the MRBTC and blood banks. In 2019, the number of blood donations made in Morocco during Ramadan (from May 7 to June 4, 2019) was 29,240 donations. In 2020, from the beginning of the month of Ramadan (which lasted from April 24 to May 23, 2020), the Moroccan authorities had introduced a national nightly curfew from 7 pm to 5 am. Traveling on foot or any other means of transport was prohibited, except for those working in vital sectors. Donors were unable to travel to the collection sites. The number of donations has fallen sharply in the first two weeks of this month, registering zero blood donations in some transfusion centers. As a result, the number of blood donations made this month was 11,658 donations nationally, with a decrease of 17,582 blood donations compared to 29,240 donations made in 2019.

Data provided from all regional blood transfusion centers and blood banks in Morocco show that the total number of blood donations made in 2020 was 297,841 blood donations nationally compared to 334,510 blood donations made in 2019 with a decrease of 36,669 blood donations. Information's about the number of blood donations, LBP production, and LBP deliverance made in Morocco in 2019 and 2020 are represented in Table 2.

(D) Impact on other activities

In 1999, to ensure the availability of blood-derived medicines at affordable prices for Moroccan patients, the MNCBTH signed a contract with the French fractionation and biotechnology laboratory LFB to fractionate Moroccan plasma. Since this date, some

Moroccan regional blood transfusion centers have been approved to prepare plasma for fractionation, and each year the LFB collects this plasma. LFB programs follow-up audits for these approved centers according to a well-established plan. In 2020, this activity was impacted by the COVID-19 pandemic. Thus, this French fractionation and biotechnology laboratory used to do two removals per year for Moroccan plasma intended for fractionation and the production of blood-derived products for MNCBTH. The plasma removal planned for 2020 has been postponed due to air and sea transport disruptions. The LFB did not assure plasma removal until April 2021. In the same way, the LFB delayed to December 2021 the audit program in March 2020 for the Regional blood transfusion center of Rabat.

The MNCBTH experience to ensure a good management of the impact of the COVID-19 pandemic on the availability and the safety of blood products in Morocco

Since the outbreak of the new coronavirus SARS-CoV-2, the MNCBTH followed up all information and scientific data published about this virus. The MNCBTH searched to know the real risk of this virus in blood donors and transfused patients. On the other hand, the epidemic's impact on the continuity of the various activities at blood transfusion establishments. Thus, several measures have been issued as the national and international epidemiological situation evolves. These measures have been updated, taking into account updated data from national health authorities and international scientific bodies concerning this health crisis.

(A) Scientific and epidemiological watch

In this context and since the start of the SARS-CoV-2 health crisis, the MNCBTH has strengthened its scientific and epidemiological monitoring system to ensure several activities.

(A.1): Participation in the meetings of the Ministry of Health COVID-19 Monitoring Committee

Since January 30, 2020, the MNCBTH has appointed a representative to take part daily in the monitoring and response committee meetings against the novel coronavirus epidemic at the direction of epidemiology and disease control of the Moroccan Ministry of Health. This committee organizes a meeting every day for the discussion of the daily activities of the COVID-19 Moroccan response plan at the national level, the discussion of data on the evolution of the everyday SARS-CoV-2 epidemiological situation at the national and international level, and the coordination of the logistics necessary to carry out all COVID-19 response plan programmed actions of the day.

(A.2): Health monitoring and bibliographic research

Since January 27, 2020, an MNCBTH team was responsible for carrying out bibliographic research through daily consultation of all scientific publications concerning this new coronavirus and particularly all reports issued by scientific societies working in the field of blood transfusion and blood donation (WHO, HAS, HCSP, ECDC, FDA, AABB, etc.).

Data provided through these reports were transmitted to the directorate of the MNCBTH and used to update MNCBTH measures to face this new coronavirus. This team was also responsible for monitoring all the documentation and circulars issued by the Moroccan Ministry of Health as part of the monitoring and response plan against COVID-19.

(A.3): Updating of the eligibility criteria for donating blood

Information notes with recommendations concerning the actualization of blood donation eligibility criteria intended for blood transfusion centers and blood banks responsible have been issued and updated according to the evolution of the national and international SARS-CoV-2 epidemiological situation. In this context, the MNCBTH published on January 28, 2020, the first information note on the first criteria for the medical selection of blood donors to mitigate the risk of transmission of SARS-CoV-2. The first information note consisted on:

- The need to deepen the blood donor questionnaire by looking for signs such as cough, fever, runny nose, diarrhea, or vomiting.
- The temperature measurement at any suspicion of fever in a blood donor.
- Temporary eviction for 28 days for any person having stayed in a country considered at risk of SARS-CoV-2 or having been in contact with a

Table 2: Information's about the number of blood donations, LBP production, and LBP deliverance made in Morocco in 2019 and 2020

	Number of blood donation	Number of Labile blood products produced			Total production number	Total of Labile blood products delivred
		RBC (red blood cells)	FFP (fresh frozen plasma)	PC (platelet concentrate)	All type of LBP included	
2019	334,510	304,089	207,130	184,755	695,974	451,736
2020	297,841	275,522	188,170	174,628	638,320	455,805
Difference	−36,669	−28,567	−18,960	−10,127	−57,654	+4069

subject returning from a country at risk of SARS-CoV-2 or having presented recent respiratory symptoms of viral appearance.
- Informing blood donors about the need to take all necessary preventive measures against infection with this virus.

On October 7, 2020, the MNCBTH established a novel information note about the actualization of medical selection criteria of blood donors. Thus, any donor who has presented during the last 14 days one of the following conditions must be postponed donating blood for two weeks:

- If there were symptoms such as cough, sore throat, difficulty breathing ... with or without fever or
- If there was a notion of fever ≥ 38 °C not explained by another obvious etiology, accompanied by myalgia or headache or
- If the donor was in contact with a person likely or confirmed to have COVID-19.

On the same note, taking into account the evolution of scientific data and information transmitted by international bodies, the MNCBTH established that a confirmed and recovered COVID-19 person can donate blood 28 days after the official declaration of his recovery.

On January 6, 2021, the MNCBTH established novel measures about the blood donation eligibility after COVID-19 vaccination. Considering the multitude of vaccine candidates that are being launched internationally and produced by different technical platforms, the deferral period for donating blood may vary depending on the type of COVID-19 vaccine received and whether the donor develops symptoms after receiving the vaccine. In Morocco, the authorities have adopted the Sinopharm vaccine (Wuhan) and AstraZeneca vaccine for the vaccination campaign. But, there are other types of COVID-19 vaccines that are in use by other countries. So, on January 6, 2021, the MNCBTH recommended that as part of the donation preselection, blood donors are required to provide all the necessary information about their vaccination: the date of vaccination, the type of vaccine received, and any side effects developed after the COVID-19 vaccination. So, the MNCBTH established that donors who receive inactivated vaccines, mRNA-based vaccine, a vaccine with protein sub-particles, and non-replicative viral vaccine and don't develop any side effects after vaccination could donate blood 7 days after COVID-19 vaccination. If the donor develops side effects, he should wait 7 days after the complete resolution of symptoms. If the donor receives a live attenuated vaccine or replicative viral vaccine, a deferral of 4 weeks should be applied. With this MNCBTH new criteria recommendations, all MRBTC were notified and prepared early before the official launch of the COVID-19 vaccination campaign in Morocco on January 28, 2021.

(A.4): Scientific research on the place of SARS-CoV-2 screening in blood donors

The MNCBTH scientific team carried out close and daily research on the recommendations of international scientific bodies to introduce molecular and serological techniques for screening for SARS-CoV-2 in blood donation. Considering all the scientific data on SARS-CoV-2, no international body recommends screening for SARS-CoV-2 in blood donors, either by a molecular or serological test. So, the MNCBTH has not introduced any screening for SARS-CoV-2 for blood donation.

(A.5): The Moroccan COVID-19 convalescence plasma project

Like other countries globally, the MNCBTH has prepared and submitted to the Ministry of Health a clinical trial project based on using COVID-19 convalescent plasma in patients infected with SARS-CoV-2 in Morocco. Thus, the various clinical trial studies published at the start of the COVID-19 pandemic have proven the effectiveness of the administration of COVID-19 convalescent plasma in patients infected with SARS-CoV-2 [72–74]. This efficiency concerned:

- An improvement of clinical and radiological signs.
- A decreased viral load.
- The stopping of the use of invasive and non-invasive mechanical supports after administration.
- An earlier discharge rate from the hospital compared to those who did not receive convalescent plasma.
- The absence of side effects following the use of convalescent plasma.

The Moroccan project was based on the recommendations of the WHO and the European Commission [75]. The Ministry of Health response was made later based on Moroccan law and considered this project to be biomedical interventional research that must be conducted by an industrial pharmaceutical company authorized under the provisions of Moroccan Law 17-04 on the Medicines and Pharmaceuticals Code. As the MNCBTH does not have the status of an industrial establishment, he has decided to stop all actions related to pursuing this project.

(A.6) Sharing the experience of the MNCBTH

Since the start of the COVID-19 pandemic, experts and scientists from blood transfusion establishments worldwide have continued to share their experiences in the context of managing the impact of the COVID-19 pandemic on the availability and safety of blood products. Sharing experience helps to learn from each experience and improve planning and response plans for this pandemic and the subsequent health crisis.

The MNCBTH experience on the management of the impact of the COVID-19 pandemic has been the subject of some publications titled:

- Ensuring a safe and adequate blood supply during the COVID-19 pandemic: The Moroccan National Blood Centre experience [76].
- The impact of the COVID-19 pandemic on the continuity of transfusion care for thalassemia patients: a case report [64].
- The impact of COVID-19 pandemic on blood supplies and transfusion services in Eastern Mediterranean Region [77].
- Proactive strategies during a COVID-19 pandemic on regional center for blood transfusion in Oujda city and its impact on blood supply management [71].

(B) Implementation of measures to protect donors, staff and recipients from the risk of SARS-CoV-2 infection

According to recommendations of international societies and with the restrictive measures recommended by the Moroccan Health authorities against the COVID-19 pandemic, the MNCBTH established:

- The possibility for donors to make an appointment with the Blood Transfusion Centre to minimize the risk of gathering.
- A COVID-19 self-exclusion document with man information about the criteria for excluding the donor from donating before the medical selection process and with the possibility to have feedback after the donation through using Centre phone numbers and email addresses.
- Measurement of the donor's temperature before accessing blood transfusion centers.
- The exclusion of at-risk donors by strengthening and updating the criteria for the medical selection of donors, based on updating the definition of COVID-19 confirmed cases issued by the Ministry of Health.
- Continuous ventilation of premises and offices.
- The monitoring of standard bio-security practices in blood centers laboratories and establishing a well-identified circuit of samples from suspect or infected COVID-19 patients received by MRBC as part of a request for LBP for blood transfusion.
- The reorganization of the workflow at the donation biological qualification laboratories to ensure continuity of work in this critical process even in the event of contamination of laboratory staff.
- The reinforcement of post-donation information, with particular attention during the 28 days following the donation, requires the donor to inform the transfusion center of any suggestive sign that may suspect a SARS-CoV-2 infection.
- The strengthening of the hemovigilance system and collaboration with healthcare services.
- The quarantine of the plasma produced by the MRBTC for 28 days to obtain information on the clinical status of donors after the blood donation.
- Implementing protective measures at the level of blood transfusion centers through the acquisition and distribution of products and protective devices like single-use over blouse, overshoes, masks, gloves, hydro-alcoholic gel, hydro-alcoholic gel dispensers, frontal thermometers, disposable chair covers.

(C) Maintaining and strengthening transfusion activities and blood donation at the national level

Before the pandemic, the MNCBTH provides weekly monitoring of the state of stock in LBP at the national level. Since the start of the pandemic and particularly from the date of the declaration of the 1st case of COVID-19 in Morocco on March 2, 2020, the MNCBTH has launched an emergency plan and set up a committee in charge of:

- Twice daily monitoring of the national LBP stock and daily collection of the number of blood donations made at each regional blood transfusion center.
- Inter-regional regulation between MRBTC. When a Moroccan regional blood transfusion center expressed a need for LBP, the MNCBTH assured the supply from other blood transfusion centers, and the MNCBTH provided the necessary logistics.

In the same context, to compensate for the drop in the number of blood donors observed nationally, especially after introducing restrictive travel measures by the Moroccan Authorities on March 21, 2020, the MNCBTH has established measures to maintain transfusion activities in all Moroccan blood transfusion structures. The MNCBTH has ensured a continuous supply of equipment, reagents, fungibles necessary for the continuity and smooth running of activities at these structures since the start of the pandemic. Other actions were made by the MNCBTH such as:

- Encouraging the competent authorities to issue special authorizations for blood donors to move to blood centers.
- Establish a blood donation permanence at all blood transfusion centers from 9 am to 7 pm to recruit as many donors as possible at fixed sites.
- Encouraging associations working in blood donation to assist blood transfusion centers, particularly raising awareness and transporting donors from their homes to transfusion centers and vice versa.
- The coordination and organization of several blood donation campaigns in partnership with several institutions.
- The director made a call for blood donations of the MNCBTH on April 30, 2020.
- A call for blood donations was made by the president of the national council of doctors' order on May 4, 2020 to doctors at the national level to donate their blood. Also, the national council invited all Moroccan regional councils of the

order of doctors to contact responsible for blood transfusion centers to organize blood donation campaigns in their regions as soon as possible.

All these actions have led to an increase in the number of donors, with 25,157 blood donations nationally in June 2020 compared to 17,147 donations made in May 2020. This positive impact on the national stock in LBP has made it possible to satisfy the demands for blood, particularly the urgent demands and the demands of chronic multiple transfusion patients.

(D) Ensuring continuity of care for chronic poly transfused patients like thalassemia patients

Since 2011, the Moroccan health ministry launched a program to fight hereditary diseases of hemoglobin, particularly thalassemia. This program aims for: (i) the generalization by 2012 of care to all patients; (ii) the establishment of a budget for the purchase of blood products and all drugs for poor patients; (iii) the creation of medical care structures in different regions of the country to avoid long trips to Rabat. Since then, the MNCBTH has prioritized ensuring the availability and proximity of quality blood products for these patients and providing adequate care for thalassemia patients. In 2020, despite the decrease of blood donations number after the declaration of the first case of COVID-19 in Morocco on March 2, 2020, the MNCBTH and all Moroccan Regional Blood Transfusion Centers have continued to ensure as much as possible the availability of blood products for thalassemia patients. Moreover, the MNCBTH intervened to support a young thalassemia patient who expressed difficulty in continuing to receive her usual transfusion protocol not because of a lack of blood products but because of the restrictive measures introduced by the Moroccan authorities as part of the surveillance and response plan against COVID-19.

The patient is 15 years old, has β-thalassemia, and lives in the city of Al Hoceima. Since discovering her disease in the pediatric hematooncology department of the University Hospital of Rabat, she has followed a transfusion management protocol established by her attending physician. On the immunohematological status, she is already known to have two antibodies: anti-Jka and anti-S. Her last transfusion goes back to March 3, 2020, and she had an appointment of hospitalization for blood transfusion on March 23, 2020. Following the lockdown established by Moroccan authorities on March 21, 2020, this patient had a problem moving from Al Hoceima to Rabat. The MNCBTH was informed and coordinated her transfusion in her city of residence with the intervention of several actors. On March 21, 2020, her biological assessment reported a hemoglobin level at 5.8 g/dl. She was transfused to Mohammed V hospital of Al Hoceima city with two compatibles red blood cells products, prepared by the Regional blood center of Oujda and delivered by the Regional Blood Transfusion Centre of Al Hoceima after having ensured leucocyte free products. On April 6, the patient had done a biological assessment with a hemoglobin level at: 6.2 g/dL. She was hospitalized and transfused on April 10 in Al Hoceima hospital with three compatibles red blood cell (RBC) pellets. On April 28, the patient's clinical and biological status with tiredness and hemoglobin level at: 5.9 g/dL. Faced with the suspicion of transfusion inefficiency, the MNCBTH contacted the responsible pediatric department of the Oujda University Hospital Centre to hospitalize the patient for a complete biological assessment. On May 1, the patient was hospitalized and started a corticosteroid treatment. The erythrocyte genotyping was done at the molecular biology laboratory of the Regional Blood Transfusion Centre of Rabat and had found the patient to be Fya-. The Regional Blood Transfusion Centre of Oujda prepared appropriate blood units for this patient. After clinical improvement under corticosteroid treatment, the patient has transfused with four compatibles red blood cell pellets: Jka-, S- and Fya-. The patient left the hospital 15 days after hospitalization and presented an excellent clinical and biological evolution with an 11 g/dl hemoglobin level. On June 3, the patient had a follow-up appointment at the pediatric department of the University Hospital of Oujda. A biological assessment shows a hemoglobin level at 9.5 g/dL. She has been transfused with three red blood cells products with good biological recovery. From July 1, the patient's medical file was transferred from the Rabat University Hospital to the Oujda University Hospital. She is regularly monitored and taken care of according to a transfusion protocol well established by her new attending physician.

(E) COVID-19 screening activities and follow-up of COVID-19 contact cases among Moroccan blood transfusion staff

Since the first case of COVID-19 was reported in Morocco, blood centers staff have been made aware of the COVID-19 protectives measures and actions to be taken in a suspected case of COVID-19 or contact with a person suspected or confirmed of having COVID-19. In addition, since November 2020, COVID-19 screening campaigns have been carried out to benefit the staff of the RBTC of Rabat and the team of MNCBTH. In collaboration with the health authorities, the management of COVID-19 suspected person or confirmed cases or having been a contact case, followed the recommendations of the Ministry of Health, and the staff taken care of according to the therapeutic protocol recommended Morocco.

(F) Vaccination of blood transfusion staff against COVID-19

The COVID-19 vaccination campaign in Morocco was officially launched on January 28, 2021, by His Majesty King Mohammed VI. Initially, this campaign prioritized some populations like health care workers over 40, authorities, teachers over 45 years old, and people over

75 years old. Then, the vaccination campaign gradually extended to other age groups and other populations [78, 79]. The staff of blood transfusion centers was among the people targeted by this campaign. By the end of March 2021, the majority of the blood transfusion staff were vaccinated with two doses of the AstraZeneca vaccine recommended by the Moroccan authorities for the health care worker's category.

(G) Coordination of the activities of the SARS-CoV-2 seroprevalence study launched by the Ministry of Health in the blood donor population

It is a study launched by the Ministry of Health on June 25, 2020, to monitor the prevalence of COVID-19 infection in the blood donor population. It was based on automated SARS-CoV-2 IgG serological analysis and focused on plasma samples from blood donors of 18 Regional Blood Transfusion Centers of Morocco from February 14 to August 8, 2020. Several Moroccan Ministry of Health institutes, departments, and laboratories were involved in this study, the protocol of which was validated by the ethics committee of the Faculty of Medicine and Pharmacy of Casablanca.

On September 17, 2020, the study results were officially communicated by the Ministry of Health through a press release reporting a SARS-CoV-2 prevalence of 0.7% nationally compared to 85,000 treated samples [80].

(H) Coordination of the activities of the national serosurveillance strategy for COVID-19 launched by the Ministry of Health

This COVID-19 Moroccan National Serosurveillance strategy represented a continuity of the study of SARS-CoV-2 seroprevalence mentioned above and was launched by the Moroccan Ministry of Health at the end of July 2020. This strategy targets ten populations, including blood donors and staff of blood transfusion in 18 regional blood transfusion centers. Laboratories used automated SARS-CoV-2 IgG serological analyses for blood samples. The rhythmicity was 1 per three months for blood donors and 1 per month for blood transfusion staff. Between September 2020 and March 2021, around 84,000 samples were sent and processed by the reference laboratory responsible for carrying out this strategy's automated SARS-CoV-2 IgG serological analyses. The official results are being validated by the technical committee responsible for the activities of this strategy.

The COVID-19 serosurveillance strategy protocol was validated by the ethics committee of the Faculty of Medicine and Pharmacy of Casablanca.

CONCLUSION

Transfusion systems worldwide have been confronted with several health crises relating to numerous emerging or re-emerging infectious diseases. Some have posed major public health problems and significant impacts on the availability and safety of blood products.

The COVID-19 pandemic has had a significant impact on blood transfusion activities internationally. Blood establishments worldwide had activated their emergency plans to deal with the effects of this health crisis. Although SARS-CoV-2 has directly impacted the availability of blood products, no direct impact on the safety of these products was reported. But, hemovigilance and post-donation information are still essential links in reducing the theoretical risk of transmission of SARS-CoV-2 through blood products.

By strengthening its scientific and epidemiological monitoring system, the MNCBTH has expressed excellent responsiveness and adaptability as updated scientific data on SARS-CoV-2 become available. He has assured several actions to ensure good management of the impact of the COVID-19 pandemic on transfusion activities in Morocco. These measures have been updated as the national and international epidemiological situation regarding SARS-CoV-2 evolves.

Finally, we can say that the impact of a newly emerging virus can have multifaceted and unforeseen ramifications on blood products. Therefore, we must continue to share our experiences and learn from each experience to improve our pandemic or epidemic response plans to manage the next health crisis.

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Author Contributions
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Khadija Lahjouji – Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Data Availability
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