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Review article

Impact of the COVID-19 Pandemic on Blood Transfusion Systems: International Review and the Moroccan Blood Transfusion System Experience

Sabah Meham[1,2*], Khilan Lahjouji[1], Mohammed Benab[1], Azlarab Mascar[2,3]

[1]National Centre for Blood Transfusion and Hematology, Rabat, Morocco; [2]Hematology Research Team, Hematology Laboratory, Faculty of Medicine and Pharmacy, Mohammed V University, Rabat, Morocco; [3]Central Hematology Laboratory, Ibn Sina University Hospital Centre, Rabat, Morocco

ABSTRACT

Introduction: The COVID-19 pandemic is considered by several Scientifics and transfusion experts 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 term search strategy to identify necessary information about the impact of some previous health crisis on the availability and the safety of blood products and the impact of the COVID-19 pandemic on the availability and the safety of blood products in some blood establishments around the world. 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 a good management of this health crisis on the availability and the safety blood products in Morocco.

Results: Virus like Severe Acute Respiratory Syndrome, Influenza A (H1N1) virus, Chikungunya virus and Zika virus 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 impacted blood collections and caused an important decrease in the number of blood donors nationally. The pandemic impacted other activities of the blood transfusion system in Morocco like as continuing education program, 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.

Keywords: Impact; COVID-19 pandemic; Transfusion; Blood donation; Blood supply; Safety; Availability; Moroccan transfusion system

INTRODUCTION

Since the international health crisis relating to the Spanish flu in 1918, transfusion systems around the world have had to face many challenges against the emergence or the re-emergence of numerous infectious diseases. Some of that virus has posed major public health problems. All of this has led the health authorities to draw up response plans and to imagine new organizations of health care systems to propose appropriate control measures and to ensure good management of these diseases [1]. On the side of blood establishments, considerable efforts have been made to catalogue these responsible viruses,

Correspondence to: Sabah Meham, National Centre for Blood Transfusion and Hematology, Rabat, Morocco, Tel/Fax:+ 212 658936955; E-mail: sabahbouhou@hotmail.com

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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 since its beginning 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 a risk analysis in order to propose appropriate response measures [2-5]. Several blood establishments around the world had reported a great impact of the COVID-19 pandemic on the availability of blood products because of various factors such as: restrictive measures established by local authorities to control 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 Haematology 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.

LITERATURE REVIEW

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. Some previous virus like Severe Acute Respiratory Syndrome, Influenza A (H1N1) virus, Chikungunya virus and Zika virus were of great concern because of the virulence, mortality, mode of transmission and especially the impact on maternal-foetal 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. 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 a large proportion of people infected with the virus remain asymptomatic and the duration of viremia and viral shedding is uncertain. 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. In Brazil, several cases of possible viral transmission by blood transfusion were studied in early 2016. The WHO and the Food and Drug Administration FDA have recommended delaying or stopping blood donations from people in or returning from areas of active Zika virus transmission. 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 Zika virus. As part of securing blood donation from this virus, many countries and organizations have recommended delaying blood donation 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. In a meta-analysis study published by Liu 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% [8]. The prevalence varied considerably by geographic region. Donated blood was more than twice as likely to be infected with Zika Virus during a Zika epidemic than during a non-epidemic. 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. According to the authors, the results suggest that nucleic acid testing (NAT) for blood screening and pathogen reduction/inactivation (PRT) technology should be implemented in Zika endemic areas and appropriate strategies should be designed according to different conditions.

B) Influenza A (H1N1) virus: A new influenza A (H1N1) virus of swine origin appeared among residents of Mexico in the spring of 2009 and spread among travellers around the world, resulting in the first influenza pandemic since 1968 [9]. In view of the scale of the epidemic, 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. In December 2009, the Superior Health Council of Belgium, as part of 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, reported that European Commission Directive of November 3, 2009 authorized temporary exemptions from certain 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 [10]. These temporary exemptions relate, on the one hand, to a reduction of the haemoglobin threshold from 125 grams to 120 grams per litre of blood for women and from 135 grams to 130 grams per litre of blood for men. 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.

On August 2010, Tsubokura et al. published an assessment of the number of blood donors presenting for blood donation at fixed or mobile collection sites using a Red Cross Hyogo Prefectural Blood Centre blood donation database between 4 weeks before and after May 16, 2009, respectively, when the first case of H1N1 flu was confirmed in Kobe (Japan) [11]. The number of blood donors fell by 21% and whole blood donations fell by 1,329 units in the week following the first case. This rapid decrease in blood donation has had a great impact on clinical practice. The number of blood donors in mobile clinics has decreased by 39%. The Department of Health, Labour 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 centres in other prefectures.

C) Chikungunya virus: Since March 2005, the Chikungunya virus has been responsible for an epidemic in the Comoros, in the south-western area of the Indian Ocean, with the 1st case in Reunion in April 2005, the peak of the epidemic having been reached during the 5th week of 2006 with more than 45,000 weekly cases, and reached 35% of the population or 244,000 people, in April 2006 [1]. A pressing situation was experienced during the Chikungunya epidemic which broke out in 2005-2006 on Reunion Island. On January 20, 2006, faced with the scale of the epidemic (with 10,000 to 40,000 new cases per week), the French Blood Establishment suspended whole blood collection on the Island and set up two measures that had never been tested on a large scale for platelet donations : unit qualification by quantitative RT-PCR and systematic inactivation of platelet concentrates by the Intercept® system capable of reducing the viral load of a product by more than 5 log10 blood [12,13]. According to a model from the National Institute for Public Health Surveillance, considering 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), the number of positive donations avoided was 29 at the peak of the epidemic and 40 for the whole of it [13,14]. Ultimately, no case of transfusion contamination has been observed either in Reunion or elsewhere in the world. 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.

D) SARS-CoV virus: The year 2003 was marked by the emergence of severe acute respiratory syndrome (SARS), a disease linked to the SARS-CoV virus of the Coronavirus family, which is characterized by mainly respiratory symptoms. The epidemic quickly took on an international dimension, leaving more than 8,000 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]. Regarding the impact of the SARS epidemic on blood donation, previous studies have shown that during the SARS epidemic, daily blood donation collections in Beijing declined due to the unavailability of blood donors, the avoidance of public places and the closure of workplaces and universities which are places of blood collection in normal times [11]. During the peak of the SARS epidemic in Singapore, a 60% decrease was observed in donors presenting to donate blood. 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. An additional 4% of potential donors were postponed during the SARS outbreak due to risk reduction measures [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. The much more pronounced effect was the significant decrease in the volume of blood drawn. As of mid-April 2003, daily collections in Beijing have dropped at times to a tenth or less of a usual daily collection. This decrease was mainly caused by the unavailability of blood donors due to the avoidance of public places and the closure of workplaces and universities. In Beijing during the SARS epidemic, to ensure the availability of blood, 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 other parts of China to ensure the availability of blood for clinical use.

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 on November 16, 2019, in Hubei province before spreading around the world. 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 spreads 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 found to be a new type of beta-CoV with over 99.98% genetic identity among 10 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 [15].

WHO declares 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 made on October 2020, Dragoslav Domanovic from the European Centre for Disease Control ECDC reported that comparing March and April 2020 to March and April 2019, many countries in Europe had expressed decrease in blood collections and distribution with 9% as a median decrease in collections (ranging from 1% to 27%) and 12% as a median decrease in distribution (ranging from 1% to 18%) [16]. Thus, Croatia had expressed-27% as a difference on blood collections

and-17% as a difference on blood and blood components distribution. Slovenia expressed-23% in blood collections and-12% in blood and blood components distribution. In the same context, Italy expressed-8% in blood collections and-15% in blood and blood components distribution in comparison with March and April 2019. For Portugal, a decrease of 14% was observed on blood collections between 2019 and 2020 and a decrease of 5% on blood distribution between 2019 and 2020.

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 9 factories and plasma fractionators with 100% response. 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 in place to avoid any disruption to the European PDP market.

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 cancelled since February 5, 2020 due to the suspension from school, the switch to work from home and the advised suspension from public activities [17]. As of Week 5 2020, 2362 blood collections were expressed in comparison with 4074 in the same week on 2019. An emergency appeal for blood donations was made on February 11, 2020 through social networks and media. This made it possible to increase the number of blood collections to 6401 in week 7 2020 in comparison with 4890 blood collections on the same period on 2019.

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. Only 58% of the available meeting slots were secured. To face this situation, direct phone calls were made to donors and public service announcements were made by Prime Minister [18]. 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. Some donor selection criteria were altered to help mitigate blood supply shortages. The haemoglobin 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 1,000 women to be able to donate per month. In October 2020, the haemoglobin criteria reverted to pre-pandemic criteria as no shortage in LBP were observed.

D) Impact of the COVID-19 pandemic on the availability of blood products in WHO African Region: A rapid investigation into the impact of COVID-19 on the blood supply and demand in the WHO African Region was done and 47 countries in the Region were invited to complete a structured questionnaire and send their response from May 21 to June 14, 2020. For comparison purposes, countries were requested to provide data for the period running from January 1 to May 31, 2019 and from January 1 to May 31, 2020. A second round of investigations was carried out during the first two weeks of September 2020 with a particular focus on the COVID-19 convalescent plasma. Thirty-seven countries provided responses from 47. 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 of the countries [19]. 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. 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 eleven (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.

E1) 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 in 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 [20-24].

The analysis of this data makes it possible to report these 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.

-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 [25-27].

-Cases of product transfusion from COVID-19 positive donors after donation have provided no evidence of transmission of the virus to recipients [28-34].

-As a precautionary measure, blood centres should take the necessary measures to reduce the risk of transmission of SARS-CoV-2 through blood products and to ensure the safety of donors and recipients [3-5].

-Strengthening the haemovigilance system and post-donation information is a very important link for blood safety during the COVID-19 pandemic.

-SARS-CoV-2 is not a direct threat to blood safety, but raises problems with the blood supply.

-The measures put in place by blood centres to minimize the risk of transfusion transmission must take into account the need to ensure the availability of blood products.

E2) 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 in place several measures to face on the theoretical risk of transmission of SARS-CoV-2 through blood and blood

products. One of the important aspect of these measures consisted on the strengthening and updating the medical selection of donors against SARS-CoV-2 infection. Thus, the criteria of blood donor eligibility were updated according to the international and local epidemic evolution of each country 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 travellers returning from China, 21 days for travellers from countries at risk other than China and 21 days for contact cases. In the same context, Australia, Canada and Japan postponed blood donors for a period of 4 months after their return 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. In March 09, 2021, the High Council of Public Health published a report with new SARS-CoV-2 blood donor eligibility criteria [35]. 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 [35].

With the introduction of COVID-19 vaccination campaigns, several blood centres updated recommendations concerning the eligibility criteria for blood donation after receiving COVID-19 vaccine in according to the types of COVID-19 vaccines adopted in their countries. As an example, the Scottish National Blood Transfusion Service on December 21, 2020, stipulated that blood donor how had the vaccine as part of the UK vaccination programme, can give blood 7 days after the jab. The blood donor also has to be recovered from any reaction to the vaccine [36]. On December 16, 2020 the Canadian Blood Services in its COVID-19 update stipulated that for COVID-19 vaccine, there is no deferral period post-vaccination with Moderna vaccine [37]. For the American Red Cross, there is no deferral time for eligible blood donors who are vaccinated with an inactivated or RNA based COVID-19 vaccine manufactured by Moderna or Pfizer [38].

The others 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 centre 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 haemovigilance 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 products that did not benefit of pathogen inactivation awaiting post donation feedback. Blood centres that already have the inactivation technique had a reduction in this theoretical risk.

E3) 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 centres 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 [39-40].

In a multicenter study in Hubei, all donated blood from the week of 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 [40,25]. All donations were negative for SARS-CoV-2 RNA in the past 12 weeks and 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.

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 a variety of clinical manifestations with tree clinical forms: light, moderate to severe disease. The mortality rate is high in patients admitted to the Intensive Care Unit ICU [41,42]. In according to several publications, blood transfusion has been used in COVID-19 patients for different reasons such as:

-Spontaneous haemorrhage or during a procedure (tracheostomy, central venous route, break in a cannula).

-COVID-19 patients with chronic and non-tolerated anaemia.

-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, Grandone et al. published results of a study about mortality and transfusion requirements in COVID-19 hospitalized Italian Patients according to severity of the disease [41]. They retrospectively explored 422 patients with 179 admitted to the ICU at 04 Italian academic hospitals from 3 March to 30 August 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. In patients admitted to the ICU, the

number of Red Blood Cells (RBC) units strongly predicts the overall mortality, which increases by 37% per unit of transfused RBC unit. By April 2020, FAN 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. From 572 patients with COVID-19 infection, they present clinical profiles of the 9 patients who required transfusion: 2 from 553 non ICU COVID-19 patients and 7 out 19 ICU COVID-19 patients. They found that 0.36% (two out of 553) of non-ICU COVID-19 patient's required RBC transfusion [42]. However, 36.8% (seven out of 19) of ICU patients required RBC transfusion, with lesser requirements for FFP and platelet transfusion. 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. The non-ICU patients who require transfusions were pre-menopausal females who had 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 infections, 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 VIIa [42]. The authors concluded that most patients with mild COVID-19 infection do not require blood transfusions and that a subset of critically ill patients with severe COVID-19 infection in the ICU, especially those with overt gastrointestinal bleeding, requires mostly RBC transfusion, with lesser requirements for FFP and platelet products.

On September 2020, a nationwide study in South Korea focused on transfusion demand in 7512 COVID-19 patients from the Korean population [43]. They found that 1.2% of all patients (n=93) required blood transfusion during COVID-19 treatment periods. 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. In the same context, Sanz et al. published on November 2020, the results of a cross-sectional study, where they reviewed 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 a period of 60 days, from mid-March to mid-May 2020 [44]. Bleeding was the indication for transfusion in 55 patients, and included either large haematomas in 22 and external haemorrhage in 31. Anaemia of critical illness 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. Tracheostomy with endotracheal intubation, surgical interventions, and cannulation of femoral vessels were the main procedures behind non-spontaneous bleeding. Seventeen patients died during the period of study, but none of the deaths was ascribed to haemorrhage or the blood transfusion.

G) Information's on the link between SARS-CoV-2 infection and blood group type: From the start of the COVID-19 pandemic, scientists were interested in the link between the blood group of individuals and the risk of developing the COVID-19 disease. In one year, some 40 studies have been published on the subject, using various methods and focusing on various populations in several countries [45]. Several methods have been employed by different research groups and most assume that the blood group has an impact on 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 infection and in uninfected people. 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. Also, a genome-wide association study (GWAS) found that blood group O carriers have IL-6 levels higher compared to individuals with other blood groups, suggesting the benefits of blood group O over other types in maintaining the dominant role of ACE2 and therefore a reduced risk of developing hypertension and therefore fewer cardiovascular complications [46,47].

A second group of studies has looked more specifically at the impact of the blood group on the severity of the disease. A Canadian study conducted a multicentre retrospective analysis and nested prospective observational sub study of critically ill patients with COVID-19 and aimed to determine whether ABO blood groups are associated with different severities of COVID-19 [48]. Data were collected from consecutively admitted ICU patients in 6 metropolitan Vancouver hospitals between 21 February 2020 and 28 April 2020. A total of 125 critically ill COVID-19 patients were admitted to the ICU from 1 March 2020 to 28 April 2020. Of these 125 patients, 95 had ABO blood group data available 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.

In France, a study made and published on 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 [49]. The study sample consisted of 702 patients. They found that patients with COVID-19 more frequently had the A blood group than those without (81.8% vs. 41.3%, respectively). Conversely, the O (18.2% vs. 46.5%, respectively), B (0% vs. 9.3%, respectively), and AB (0% vs. 2.9%, respectively) groups were underrepresented in patients with COVID-19. 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.

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 [50]. 464 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. They found a low prevalence with 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. In conclusion, the authors reported that blood group O persons are less at risk of being infected and that an increased risk of infections associated with blood group A is likely but remains to be formally established in non-hospitalized persons.

H) Impact of the COVID-19 pandemic on the continuity of transfusion care in patients with chronical diseases such as haemoglobinopathies: The COVID-19 pandemic could have a major impact on the capacity of health systems to continue the delivery of essential health services [51]. While health systems around the world are being challenged by increasing demand for care of COVID-19 patients, it is critical to maintain preventive and curative services, especially for the most vulnerable populations such people living with chronic conditions [51,52]. 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 [51-53]. In the same context, Intezar et al. stipulated that COVID-19 pandemic has posed significant challenges for children with cancers and blood disorders such haemoglobinopathies [54]. They report that interruption or postponement of treatment would be an additional challenge, either due to COVID-19 infection or inability to reach the centres for treatment due to lockdowns. Farmakis et al. reported that the COVID-19 pandemic represents a significant challenge for haemoglobinopathies patients, their families and their attending physicians [55]. They present a statement who summarizes the key challenges concerning the management of haemoglobinopathies, with particular focus on patients with either transfusion-dependent or non-transfusion-dependent thalassaemia. They illustrate that adaptation of thalassaemia care during the present and potential future similar pandemics requires on 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.

Fattizo et al. reported the strategies of progressive systematic reorganization of haematologic care in a large public university hospital in Milan (Lombardy) during the first 6 weeks of the COVID-19 pandemic [56]. They observed that urgent transfusions were guaranteed, and transfusion-dependent patients adapted their schedules to fit with donor availability (1 unit per week instead of 2 units per 14 days), because the transfusion centre experienced a marked reduction in donors. With regard to hospitalization, admissions to the haematology and transplant wards showed a decrease at week 1. In the same way, a multi-centre 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 haemoglobin disorders and compares the pre-COVID-19 prevailing environment with regard to haemoglobin disorders across with the post COVID-19 period [57,58]. This study was based on:

-A survey that was conducted prior to COVID-19 pandemic between January-December 2018 with the contribution of 62 National Thalassaemia Associations, in 48 countries representing 3,500 patients globally and on.

-A second survey that was conducted during the COVID-19 pandemic between March 15th to May 15th 2020 with the contribution of 48 National Thalassaemia Associations in 42 countries representing 3,200 patients globally.

The results showed that the moderate to severe blood shortage during the COVID-19 pandemic has resulted in moderate to severe drop in haemoglobin (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) [57]. Half of the respondents reported severe interruption with the frequency and/or the quantity of blood provided; all these respondents were from developing countries. This has resulted in the provision of unmatched or non-leukoreduced units, and even the reliance on whole blood for transfusion. Interruption and/or shortages in chelation therapy have also been reported. As expected, the impact on patients from western countries was mild to nil despite initial blood shortages [57,58].

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 Haematology, 18 Regional Blood Transfusion Centres, 14 Blood Banks and 24 Blood Transfusion Units (Antenna). The Moroccan National Centre for Blood Transfusion and Haematology is a scientific reference on a national scale. He is responsible for implementing the policy of the Moroccan Ministry of Health in the field of blood transfusion. His main 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 Centres (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 centres of Morocco, cell therapy, genetic and cellular engineering, molecular biology activities.

During the COVID-19 pandemic, several activities of the MNBTCH 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 on technical missions: Before the pandemic, the MNBTCH used to hold several meetings, divided into:

-Daily emergency meeting for the management of blood products availability problems at the level of the 18 MRBTC, reagent supply problems and critical equipment failures.

-One weekly meeting for the discussion of priority actions launched by the centre on technical plan, financial plan, computerization of the activities of the regional blood centres, promotion of blood donation.

-One weekly meeting for monitoring state of progress of technical project.

-One weekly quality meeting for the evaluation and the validation of quality procedures.

Since the declaration of the first case of COVID-19 in Morocco on 02 March, 2020 and because of the restrictive measures introduced by the competent Moroccan authorities, all meetings at the MNCBTH have been suspended. Some meetings were held by videoconference. Other meetings were authorized in a case of emergency need with respect to the measures recommended by the Moroccan authorities: distancing, mask wearing.

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

B) Impact on the continuing education program for staff: Each year, in its annual action plan, the MNBTCH establishes a continuing training program for the staff of blood transfusion in Morocco. This program includes the participation of the staff of the MNBTCH, those of Regional Blood Transfusion Centres 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 in Morocco and the meeting for the presentation and the discussion of scientific articles in the field of blood transfusion and haematology.

In 2020, the COVID-19 pandemic had impacted the achievement of actions planned by the MNCBTH in its continuing education program. Two meeting of bibliographical research sessions held before the declaration of the first case of COVID-19 in Morocco on March 2, 2020. Also, the 2020 annual meeting of responsible for blood transfusion system in Morocco was assured in February 2020 because it was programmed before the declaration of the first case of COVID-19 in Morocco and before the implementation of restrictive measures by Moroccan authorities. Information's about the achievement of continuing education program of MNCBTH in 2020 compared with 2019 were presented in Table 1.

	Bibliographic researches sessions meeting	Scientific seminars	National congress	International congress	workshops	Scientific days	Quality training	Computer training
2019	34	1	2	2	2	5	2	4
2020	2	0	0	0	0	0	0	0

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

C) Impact on blood donation: The MNBTCH has made considerable efforts in recent years in order 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 Centres and Blood Banks have been requested to strengthen the processes of promotion and sensitisation to blood donation and also to strengthen the collection activities by using all the necessary logistics for this purpose. In 2018, the number of donations made by all MRBTC and all blood banks was 321,336 donations in Morocco compared to 318,164 made in 2017 with an increase of 3172 donations. In 2019, more efforts have been done by all MRBTC and blood banks under the technical guidance of the MNBTCH and the total number of blood donations made in Morocco was 334,510 donations with an increase of 13,174 donations.

Unfortunately, in 2020, and like other blood transfusion establishments worldwide, blood donation activities have been impacted in Morocco and epically after the declaration of the first case of COVID-19 on 02 March 2020. The number of donors has started to decrease, and this situation has worsened from 21 March 2020 due to the installation by Moroccan authorities of restrictive measures regarding prohibition of displacement within and between cities. These measures including, also, the prohibition of gatherings, caused limiting blood donor's displacement to fixed sites of blood transfusion centres and the suspension of mobile blood collections in mobiles sites. As a consequent, in March, the number of donations made nationally was 27,812 donations, in April it was 22,415 donations and on May 17,147 donations. As an example, in the Regional Blood Transfusion Centre of the city of Oujda which is located in the eastern region of Morocco, only 7 blood collections were carried out in mobile sites until May 2020 in comparison with 30 done in 2019 [59]. From January to May, this centre had collected a total of 8445 donations (fixed site and mobile site) on 2019 compared with 7510 donations (fixed site and mobile site) made in 2020 with a decrease of 11%.

Another aspect of blood donation that has been affected by the COVID-19 pandemic is blood collections during the month of 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 to this, the fixed

sites are also open after the break of the fast for blood collection according to a well-established programme by the MRBTC and blood banks. In 2019, the number of blood donations made in Morocco during the month of Ramadan (from 07 May to 04 June 2019) was 29,240 donations. In 2020, as part of the Moroccan surveillance and response plan against COVID-19 and from the beginning of the month of Ramadan (which lasted from 24 April to 23 May 2020), the Moroccan authorities have introduced a national nightly curfew from 7pm to 5am. Travelling on foot or by any other means of transport was prohibited, except for those working in essential and vital sectors. Donors were unable to travel to the collection sites and the number of donations has fallen sharply in the first two weeks of this month registering 0 donations in some transfusion centres. As a result, the number of blood donations made in this month was 11,658 donations nationally with a decrease of 17,582 donations in comparison with 29,240 donations made in 2019.

Data provided from all regional blood transfusion centres and all blood banks in Morocco show that the total number of blood donation made in 2020 was 297, 841 blood donations nationally in comparison with 334,510 blood donations made in 2019 with a decrease of 36 669 blood donations. Information's about number of blood donations and Labile Blood Products production made in Morocco on 2019 and on 2020 are represented in Table 2.

	Number of blood donation	Number of labile blood products produced			Total production
		RBC (Red Blood Cell's)	FFP(Fresh Frozen Plasma	PC(Platelet Concentrate)	All type of LBP included
2019	334 510	304 089	207 130	184 755	695 974
2020	297 841	275 522	188 170	174 628	638 320
Difference	**-36 669**	**-28 567**	**-18 960**	**-10 127**	**-57 654**

Table 2: Information's about the number of blood donation and LBP production made in Morocco on 2019 and on 2020.

D) Impact on other activities: In 1999, in order 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 FFBL to fractionate Moroccan plasma. Since this date some Moroccan regional blood transfusion centers have been approved for the preparation of plasma for fractionation and each year the FFBL collects this plasma. Follow-up audits are programmed by FFBL 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 MNBTCH. The plasma removal already planned for 2020 has been postponed due to disruptions to air and sea transport, and this removal was not assured until April 2021.In the same way, the audit programmed by FFBL in March 2020 for Regional blood transfusion center of Rabat was postponed to December 2021.

The MNBTCH 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 on December 31, 2019 in China, the MNBTCH followed up closely all information's and scientific data published about this new coronavirus specially to know in one hand the real risk of this virus in blood donors and in transfused patients and in the other hand the impact of the epidemic on the continuity of the various activities at the level of 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 in relation to this health crisis.

A) Scientific and epidemiological watch: In this context and since the start of the SARS-CoV-2 health crisis, the MNBTCH has strengthened its scientific and epidemiological monitoring system to ensure several activities.

A1) Participation in the meetings of the Ministry of Health COVID-19 monitoring committee: Since 30 January 2020, the MNBTCH has appointed a representative to take part daily in the meetings of the monitoring and response committee against the novel coronavirus epidemic at the direction of epidemiology and disease control of 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 national level, the discussion of data on the evolution of the daily 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.

A2) Health monitoring and bibliographic research: Since 27 January 2020, a MNBTCH 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).

The data provided by these reports was transmitted by e-mail to the directorate of the MNBTCH and was used for the continuous update of the measures taken by the MRBTC with regard to this new coronavirus as and when they become available. This team was also responsible for ensuring a monitoring of all the documentation and all the circulars issued by the Moroccan Ministry of Health as part of the monitoring and response plan against COVID-19.

A3) Updating of the eligibility criteria for donating blood: Information notes with recommendations concerning actualization of blood donation eligibility criteria intended for blood transfusion centres 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 MNBTCH published on January 28, 2020 the first information note on the first criteria for the medical selection of blood donors as a measure 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, diarrhoea or vomiting.

-The temperature measurement at any suspicion of fever in a blood donor.

-Temporary eviction for a period of 28 days for any person having stayed in a country considered at risk of SARS-CoV-2 or having been in contact with a 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 07 October 2020, the MNBTCH established a novel information note about actualization of the criteria of medical selection 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 aetiology, accompanied by myalgia or headache or

-If there has been contact with a person likely or confirmed to have COVID-19.

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

On 06 January 2021, The MNBTCH established novel masseurs about the blood donation eligibility after COVID-19 vaccination. Taking into account the multitude of vaccine candidates that are being launched internationally and which are 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 two vaccines: an inactivated vaccine from Sinopharm (Wuhan) and a non-replicating viral vector vaccine (chimpanzee adenovirus) from AstraZeneca. But, there are other types of COVID-19 vaccine that are in use by other countries. So, on 06 January 2021, the MNBTCH recommended that as part of the donation pre-selection, blood donors are required to provide all the necessary information about their vaccination: the date of vaccination, the type of vaccine received as well as any side effects developed after the COVID-19 vaccination. So, the MNBTCH established that for donors who receive inactivated vaccine, mRNA-based vaccine, vaccine with protein sub-particles and non-replicative viral vaccine and don't develop any side effects after vaccination, they can donate blood 07 days after COVID-19 vaccination. If the donor develops side effects, he should wait 07 days after the complete resolution of symptoms. If the donor receives live attenuated vaccine or replicative viral vaccine, a deferral of 04 weeks should be applied. With these MNBTCH 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.

A4) Scientific research on the place of SARS-CoV-2 screening in blood donors: The MNBTCH scientific team carried out close and daily research on the recommendations of international scientific bodies in the context of the interest of the introduction of molecular and serological techniques for screening for SARS-CoV-2 in blood donation. Taking into consideration all the scientific data currently available on SARS-CoV-2, no international body recommends screening for SARS-CoV-2 in blood donors, either by molecular test or by serological test. So, the MNBTCH has not introduced any screening for SARS-CoV-2 for blood donation.

A5) The Moroccan COVID-19 convalescence plasma project: Like other countries in the world, the MNBTCH has prepared and submitted to Ministry of Health a clinical trial project based on the use of 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 [60-63]. This efficiency concerned:

-An improvement of clinical and radiological signs.

-A Decreased viral load.

-The stopping the use of invasive and non-invasive mechanical supports after administration.

-An earlier discharge rate from 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 [64]. The Ministry of Health response was made later based on Moroccan law and considered this project to be a biomedical interventional research that must be conducted by an industrial pharmaceutical company that has been authorized in accordance with the provisions of Moroccan Law 17-04 on the Medicines and Pharmaceuticals Code. As the MNBTCH does not have the status of an industrial establishment, he has decided to stop all actions related to pursue this project.

A6) Sharing the experience of the MNBTCH: Since the start of the COVID-19 pandemic, experts and scientists from blood

transfusion establishments around the world have continued to share their experiences in the context of managing the impact of the COVID-19 pandemic on availability and safety of blood products. Sharing experience helps to learn from each experience and improve planning and response plans for this pandemic and for the next health crisis.

The MNCBTH experience of 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 [65].

-The impact of the COVID-19 pandemic on the continuity of transfusion care for thalassemia patients: a case report [52].

-The impact of COVID-19 pandemic on blood supplies and transfusion services in Eastern Mediterranean Region [66].

-Proactive strategies during a COVID-19 pandemic on regional centre for blood transfusion in Oujda city and its impact on blood supply management [59].

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 MNBTCH established:

-The possibility for donors to make previously an appointment with the Blood Transfusion Centre to minimize the risk of gathering.

-A COVID-19 self-exclusion document with man information's about the criteria for excluding the donor from donating before the process of medical selection and with the possibility to have feedback after the donation through Blood Transfusion Centre phone numbers and 'email address.

-Measurement of the donor's temperature before accessing blood transfusion centres.

-The exclusion of at-risk donors by strengthening and updating the criteria for the medical selection of donors, based on the updating of 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 centres laboratories and the establishment of 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 re-organization 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 where the donor is required to inform the transfusion centre of any suggestive sign that may suspect a SARS-CoV-2 infection.

-The strengthening of the haemovigilance system and collaboration with healthcare services.

-The quarantine of the plasma produced by the MRBTC for a period of 28 days to obtain information on the clinical status of donors after the blood donation.

-The implementation of protective measures at the level of blood transfusion centres 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. But, 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 MNBTCH 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 centre.

-Inter-regional regulation when a Moroccan regional blood transfusion centre expressed a particular need for LBP, this deficit centres was supplied from other blood transfusion centres and the necessary logistics are provided by the MNBTCH.

In the same context, to compensate for the drop in the number of blood donors observed nationally especially after the introduction of restrictive travel measures by the Moroccan Authorities on 21 March 2020, the MNBTCH has established measures to maintain transfusion activities in all Moroccan blood transfusion structures. The MNBTCH 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 MNBTCH such as:

-Encouraging the competent authorities to issue special authorizations for blood donors to move to blood centres.

-The establishment of a blood donation permanence at all blood transfusion centres from 9 a.m. to 7 p.m. to recruit as many donors as possible at fixed sites.

-Encouraging associations working in the field of blood donation to provide assistance to blood transfusion centres, in particular raising awareness and transporting donors from their homes to transfusion centres and vice versa.

-The coordination and organization of several blood donation campaigns in partnership with several institutions.

-A call for blood donations was made by the Director of the MNBTCH on April 30, 2020.

-A call for blood donations was made by the president of the national council of the order of doctors on 04 May 2020 to doctors at national level to donate their blood. Also, the national council invited all Moroccan regional councils of the order of doctors to contact responsible of blood transfusion centres in order 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 in comparison with 17,147 donations made in May 2020. This has had a positive impact on the national stock in LBP and has made it possible to satisfied the demands for blood, in particular 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 haemoglobin, 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 this date, the MNBTCH has ranked among its priorities ensuring the availability and proximity of quality blood products to these patients and continued provided adequate management of patients with thalassemia. In 2020, despite the decrease in the number of blood donors after the declaration of the first case of COVID-19 in Morocco on March 2, 2020, the MNBTCH and all Moroccan Regional Blood Transfusion Centres have continued to ensure as much as possible the availability of blood products for thalassemia patients. Moreover, The MNCBTH intervened to support the case of 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.

It is a 15-year-old patient with β-thalassemia living in Al hoceima city and followed since the discovery of her disease at the haemato-oncology department of the university hospital of Rabat. She receives transfusion care according a well identified protocol established by her attending physician, and she is already immunologically known to have two antibodies: anti-Jka and anti-S. Her last transfusion goes back to March 03, 2020, and she had an appointment of hospitalization for blood transfusion on March 23, 2020. Note that the Al Hoceima city is at 457 kilometres away from Rabat city and at 260 kilometres away from Oujda city.

Following the lockdown established by Moroccan authorities on March 21, 2020, this patient had a problem of moving from Al Hoceima city to Rabat city. The MNBTCH was informed of the difficulty encountered by this patient and coordinated her transfusion management in her city of residence with the intervention of several actors. The first MNBTCH intervention was on 21 March 2020 when her biological assessment reported a haemoglobin level at 5, 8 g/dl and for which she was transfused in Mohammed V hospital of Al Hoceima city with two red blood cells products, compatible with its current immunological status, prepared by the Regional blood centre of Oujda who is qualified for the preparation of qualified blood products for thalassemia patients in the region. The red blood cells products were transported to Al Hoceima city with the assistance of the local health authorities and delivered by the Regional Blood Transfusion Centre of Al Hoceima after having ensured leucocyte free products. The second intervention of MNBTCH was on April 06, when the patient has done a biological assessment with a haemoglobin level at: 6.2 g/dl. The National Blood Centre has started the procedure of regulation and coordination between the Regional Centre of Oujda, the Regional Blood Centre of Al Hoceima and the health authorities of the region and the patient was hospitalized and transfused on April 10 with 03 red blood cell pellets, compatible with its current immunological status, prepared by Regional Blood Centre of Oujda and delivered by the Regional Blood centre of Al Hoceima. The third intervention of the MNBTC was on April 28 regarding the patient's clinical and biological status with tiredness and a haemoglobin level at: 5.9 g/dl. Faced with the suspicion of transfusion inefficiency, the National Blood Centre contacted the responsible for the paediatric department of the Oujda University Hospital Centre in order to hospitalize the patient for a complete biological and immunohematological assessment. On May 01, the patient was hospitalized and put on corticosteroid treatment. The erythrocyte genotyping carried out at the Regional Blood Centre of Rabat had found the patient to be Fya-. This new information could explain her transfusion inefficiency. This information was helpful for the Blood Centre of Oujda to prepare appropriate blood units for this patient. So, after clinical improvement and stabilization, the patient was transfused with 4 red blood cell pellets Jka-, S-and Fya-compatible with her new immunohematological status. These blood products were prepared and delivered by the Oujda Regional Blood Transfusion Centre. The patient left the hospital after 15 days of hospitalization and presented a good clinical and biological evolution with a haemoglobin level at 11 g/dl. On June 03, the MNBTCH was informed that the patient had a follow-up appointment at the Paediatric department of the University Hospital of Oujda. A biological assessment shows a haemoglobin level at 9.5 g/dl. She has been transfused with three red blood cells products with good biological recovery. From July 01, the patient's medical file was transferred from the Rabat University Hospital to the Oujda University Hospital, where she is regularly monitored and taken care of according to a transfusion protocol well established by her new attending physician.

This effective and efficient intervention and coordination that the MNBTCH ensured between the three regional blood transfusion centres involved in this case (Oujda, Al Hoceima and Rabat), the regional and local health authorities and the thalassemia association allowed the patient to continue to receive her therapeutic transfusion protocol in the best conditions and with the appropriate blood products compatibles with her new immune hematological status.

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

the declaration of the first case of COVID-19 in Morocco on March 02, 2020, the staff of the transfusion centres have been made aware of protective measures against COVID-19 infection and of measures to be taken in the event of a suspected COVID-19 case or in case of contact with a suspected or confirmed COVID-19 person. In the same context, since the beginning of November 2020, COVID-19 screening campaigns were carried out for the benefit of the staff of the RBTC of Rabat and the staff of MNBTCH. 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 this transfusion staff was taken care in according to the therapeutic protocol recommended in 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 IV. Initially, this campaign prioritized some populations like health care's workers over 40, authorities, teachers over 45 age-old and people over 75 age-old. Then it was gradually extended to other age groups and other populations [67,68]. Staff of blood transfusion centres was among the staff targeted by this campaign and with 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's workers 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's 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 Ig G serological analysis and focused on plasma samples from blood donors of 18 Regional Blood Transfusion Centres of Morocco over a period from February 14 to August 08, 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 results of this study 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 [69].

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 represents 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 10 populations, including the population of blood donors and staff of blood transfusion in 18 regional blood transfusion centres. For blood donors, automated SARS-CoV-2 IgG serological analyses have been made with a rhythmicity of 03 months and 01 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 the automated SARS-CoV-2 IgG serological analyses of this strategy and the official results are being validated by the technical committee responsible for the activities of this strategy.

To note that the activities of this COVID-19 serosurveillance strategy were the subject of a protocol that was also validated by the ethics committee of Faculty of Medicine and Pharmacy of Casablanca.

Conclusion

Transfusion systems around the world have been confronted with several health crises relating to numerous emerging or re-emerging infectious diseases. Some have posed major public health problems, but also 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 around the world had activated their emergency plans to deal with the impact of this health crisis. Although SARS-CoV-2 has had a direct impact on the availability of blood products, no direct impact on the safety of these products was reported. But, Haemovigilance and post-donation information still an essential link in reducing the theoretical risk of transmission of SARS-CoV-2 through blood products.

By strengthening its scientific and epidemiological monitoring system, the MNBTCH has expressed great 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 to learn from each experience to improve our pandemic or epidemic response plans for a good management of the next health crisis.

Competing Interests

The authors declare no competing interest.

Authors' Contributions

The first author did the bibliographic research necessary for the preparation of the review, compiled all available information on the subject of this paper, and wrote the draft of the article. Then, all the authors had revised and approved the final contents of this paper.

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ORCID ID

ORCID ID: https://orcid.org/0000-0003-4432-1431

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