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Research on blood donation and supply of red blood cell products to medical institutions under the spread of COVID-19 disease in Japan

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ABSTRACT

Due to the spread of SARS-CoV-2 virus infectious disease (COVID-19), blood donation events had to be cancelled, and there were concerns about a decrease in the number of blood donors from late February 2020 in Japan. The purpose of this study is to investigate the numbers of whole blood donation, manufacture and inventory adjustment of red blood cell (RBC) products at the Japanese Red Cross Society (JRCS), and to evaluate the effects of COVID-19 on the donation of blood and the supply of RBC products to medical institutions for transfusion medicine in Japan. We focused on RBC products, which are the most frequently used blood products and are easily reflected under the spread of COVID-19. The status of whole blood donation, manufacture and inventory adjustment of RBC products, and supply to medical institutions. Although there were some fluctuations since January 2020, the amount of estimated donated whole blood, manufactured RBC products, inventory, and supply to medical institutions remained almost stable. The reasons are thought to be the contribution of registered repeaters cooperating in blood donation, the accurate prediction of supply and demand by the JRCS, the call for blood donations in accordance with the prediction, and the timely exchange of products between block centers, and the utilization of a safe supply system established previously by the JRCS. As a result, it can be concluded that the stable provision of medical care was possible without depleting the inventory of RBC products even under the spread of COVID-19.

1. Introduction

In Japan, the JRCS is the only organization that accepts blood donation from volunteers, and all the blood products for transfusion are manufactured from donated blood. Red blood cell (RBC) products are the most widely used blood products for transfusion and are used to provide adequate oxygen to the peripheral tissues in patients. When considering the manufacture, inventory adjustment, and supply of blood products to medical institutions in the event of a spread of COVID-19, we decided to focus on the RBC products because the RBC products with a shelf life of 21 days after blood donation are easier to assess the influence of the COVID-19.

Fig. 1 shows the flow of the supply of RBC products in Japan. Whole blood donation, manufacture of RBC products and supply to medical institutions are all controlled by the JRCS. Whole blood donated at blood donation rooms or sessions across the country (①) are accumulated at blood centers (②) and delivered to a block center located in every region and converted to RBC or whole blood products (④). Because whole blood products are produced in very small quantities, it can be approximated that all whole blood donations are used to produce RBC products. The RBC products are delivered back to blood centers a few times per day, stored there

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and supplied to medical institutions as necessary (⑤). If the amount of RBC products at regional blood centers is sufficient, it is possible that they can be stored at the block centers.

Storage and inventory of blood products are conducted at each block center. Blocks are regional units established in April 2012 to centralize testing and manufacturing operations. As shown in Fig. 2 (a), Japan is divided into seven blocks, and each block region has one block center that controls each block. The population of each block and the gross regional product of each block are shown in Fig. 2 (b) and (c), respectively [1,2]. The characteristics of the blocks are that the Kanto-Koshinetsu block accounts for more than 1/3 of the national population and total block manufacture. Therefore, it is estimated that the Kanto-Koshinetsu block plays an important role in the amount of whole blood donated and the amount of RBC products supply to medical institutions. If there is a possibility that blood products may be out of stock at one block center, a system is activated to supplement this by transferring with other block centers (③).

In COVID-19, the first patient was confirmed in Japan on January 15, 2020, and the infection spread rapidly [3]. Due to the spread of COVID -19 infection, the blood donation event had to be discontinued, and there was a concern about a decrease in the number of blood donors from late February 2020 [4]. On April 1, 2020, the number of patients newly positive for COVID -19 reached 257 per day in Japan, and the number of infected patients is rapidly increasing. Based on the "Act for Partial Revision of the Act on Special Measures Against Pandemic Influenza, etc." passed by the Diet on February 3, 2020, a state of emergency was declared on April 7, 2020 [5,6]. This declaration of a state of emergency is a request from the government to the public and is not legally binding like the lockdown of other countries. Initially, due to the expansion of the number of COVID-19 patients, 7 prefectures across Japan, including Saitama, Chiba, Tokyo, Kanagawa, Osaka, Hyogo, and Fukuoka, were planned to be subject to emergency measures until May 6, 2020; however, due to the spreading of infection, it was decided that the remaining 40 prefectures would be added to the 47 target regions and the emergency measures would be implemented nationwide on April 16, 2020. The implementation period of the emergency measures was also extended to May 31, 2020 on May 4, 2020 [7]. According to the emergency measures, the Japanese government requested prefectural governments for residents to refrain from going out, to restrict the use of their facilities, to provide other necessary cooperation to prevent infections (basic infection control such as wearing a mask, cough etiquette, hand washing, gargling, etc.), and to establish temporary medical facilities. The declaration of a state of emergency was issued 4 times as of October 17, 2021 (1st report: April 7, 2020–May 25, 2nd report: January 8, 2021–March 21, 3rd report: April 25, 2021–June 20, 4th report: July 12, 2021-September 30). Although the first emergency measure was reported to have reduced the person-to-person contact rate to approximately 86 % [8], there is still no clear report on the degree to which the second and subsequent emergency declaration were effective in controlling the flow of people.

In JRCS, the Web membership service of blood donation "Love Blood" provides online reservation and distribution of blood donation requests at blood donation room or session, blood donation in permanent blood donation rooms, and group blood donation by dispatching blood donation buses to schools or companies. However, due to the spread of COVID-19, blood donation events using blood donation bus and open donation in February 2020 had to be canceled compared to those in February 2019 (Fig. S1), and the number of blood donors drastically decreased in February 2020 (Fig. 3). On April 17, 2020, the Japan Society of Blood Transfusion and Cell Therapy called for proper blood transfusion based on medical grounds in accordance with the guidelines for the use of each blood product, because there was a risk of insufficient supply of blood products, as the areas subject to the declaration of a state of emergency spread nationwide [4]. However, there is no report on the actual situation of blood services at that time.

Data on whole blood donation, manufacture and inventory control of RBC products, and supply of the products to medical institutions are annually posted on the website of the JRCS. It can be seen that the number of whole blood donors, the amount of whole blood donated, and the number of RBC products supplied to medical institutions throughout Japan have not changed significantly from 2016 to 2020 [9]. However, some detailed data, such as monthly fluctuations, have not been released, and no study has reported in detail the impact of the spread of COVID-19 as the declaration of a state of emergency. Investigation of the influence of the spread of COVID-19 (1st wave to 5th wave) and the declaration of a state of emergency on whole blood donation, manufacture and inventory

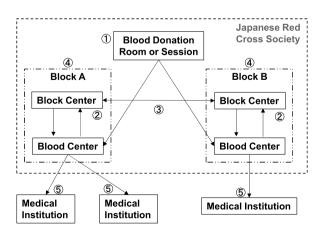


Fig. 1. Flow of RBC products supply in Japan The numbers and corresponding parameters are as follows: ① Estimated amount of whole blood donation, ② amount of manufacture of RBC products, ③ transfer of RBC products between blocks, ④ Inventory of RBC products in blocks at the beginning of month, ⑤ Supply of RBC products to medical institutions.

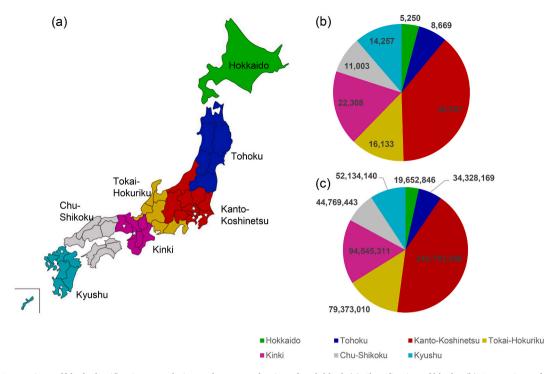


Fig. 2. Comparison of block classification, population and gross production of each block (a) Classification of blocks, (b) Comparison of population of each block (1000 people), (c) Comparison of gross product within each block (1 million yen).

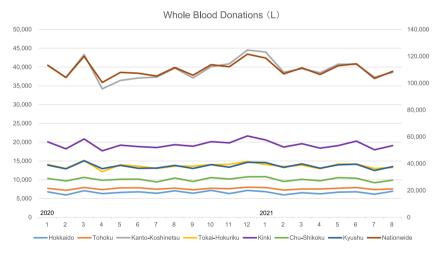


Fig. 3. Amount of whole blood donations (right axis only for nationwide).

control of RBC products, and supply to medical institutions would lead to the securing of medical resources including healthy volunteers who donate blood, and to the evaluation of a system for adjusting inventory for stable supply of blood products to transfusion medicine in the midst of concerns of medical breakdown. This study is believed to be significant in the construction of a future crisis management system.

The objective of this study is to assess the impact of COVID-19 infection on the provision of RBC products to medical institutions by examining JRCS statistical data obtained through data disclosure requests by the authors regarding whole blood donation, manufacture of RBC products and inventory adjustment, and provision to medical institutions at COVID-19 during the spread of infection (January 2020–August 2021).

2. Methods

Based on data provided by the JRCS from January 2020 to August 2021 concerning the whole blood donation, manufacture,

inventory adjustment, and supply of RBC products to medical institutions, the status of whole blood donation and transfusion of RBC products under the spread of COVID-19 infection was investigated. A part of the data is also available on the website of the JRCS [10]. Based on the flow of RBC product supply in Japan shown in Fig. 1, the following data were tabulated and analyzed for each number in the Results. The graphs were divided into national and block sections (see Fig. 2).

- ① Whole Blood Donation
- ② Manufacture of RBC products
- ③ Transfer of RBC products between blocks
- ④ Inventory of RBC products at the beginning of month
- ⑤ Supply of RBC products to medical institutions

All the data provided by the JRCS were cleaned without any missing values by the JRCS staff, and analyzed by the authors in Microsoft Excel 2019.

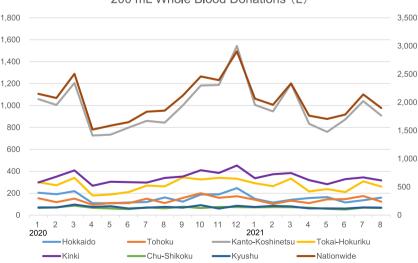
3. Results

As described above, the manufacture and inventory control of RBC products in Japan and their supply to medical institutions are controlled by blood centers and block centers in seven blocks. In the following, the results of each parameter are shown for each block center and the sum of the blocks (expressed as a nationwide).

① Changes in the amount of whole blood donation are shown in Fig. 3. In 2019, the amount of donated whole blood nationwide was about 1,332,000 L [11], and about 111,000 L per month. Table S1 shows changes in the amount of donated whole blood nationwide in 2019. Regarding 2020 (Table S2), January–August, including the period of the first declaration of a state of emergency, the amount of donated whole blood nationwide decreased by 8.0 % in February, increased by 5.9 % in March, decreased by 11.3 %, 4.7 %, 5.3 %, and 7.1 % in April–July 2020, and recovered to the same level as in January 2020 (1.4 % decrease) in August 2020. Compared with Table S1, it can be said that the amount of whole blood donation nationwide varied greatly in the period of February–July 2020 to July compared to February–July 2019.

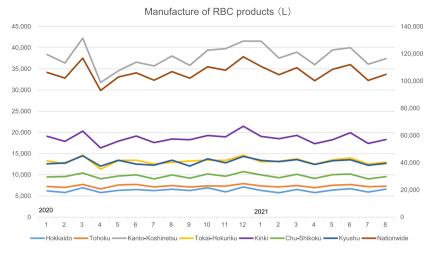
The amount of 200 mL whole blood donation (Fig. 4) showed a tendency different from the amount of donated whole blood (the sum of 200 mL and 400 mL of donated blood), with a peak in March 2020 in nationwide and all blocks, a remarkable decrease from April to June, and an increasing trend after July 2020, while the amount of 400 mL whole blood donation showed almost the same tendency of the amount of donated whole blood since the amount of 200 mL whole blood donation is by far smaller than that of 400 mL. In nationwide and all blocks except for Tokai-Hokuriku, Tohoku, and Hokkaido, it peaked in December 2020 and then declined toward August 2021, although it fluctuated monthly.

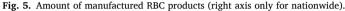
② The manufacture volume of RBC products is shown in Fig. 5, which shows the similar monthly variation to the volume of whole blood donation as shown in Fig. 3. That is, the manufacture volume of RBC products nationwide decreased by 3.9 % in February from January, increased by 9.9 % in March, and decreased by 12.5 % in April. From May 2020 to August 2021, the peak was

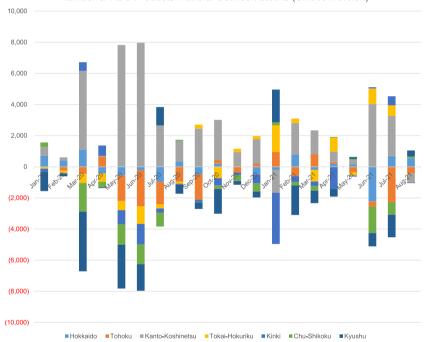


200 mL Whole Blood Donations (L)

Fig. 4. Amount of 200 mL whole blood donations (right axis only for nationwide).







Number of RBC Products Transfer Between Blocks (Unit conversion)

Fig. 6. Amount of RBC products transferred between blocks (unit conversion).

observed in December 2020. Though there were some minor fluctuations, there were no large fluctuations shown in the short period as in March and April 2020. These tendencies were almost common even in each block.

③ The number of RBC products transfer between blocks is shown in Fig. 6. The number of RBC products delivered between the blocks was calculated by subtracting the number of RBC products delivered in each block from the number of RBC products received in each block. Therefore, positive numbers on the vertical axis indicate excess receipt and negative numbers indicate excess sending.

In the Kanto-Koshinetsu block, it is noted that there was an excess of receipt in March 2020, a balance between receipt and sending in April, and a large excess of receipt again in May and June. Except for January and August 2021, the receipts were in excess after June 2020. The Kyushu, Tohoku, and Chu-Shikoku blocks had been rolled to support the receipt excess of the Kanto-Koshinetsu block. Fig 5 and 6 The Kinki, Hokkaido, and Tokai-Hokuriku blocks behaved differently, but the balance between receipt and sending almost equally. In general, other blocks seemed to support the receipt excess of the Kanto-Koshinetsu block. In January 2021, the Kyushu, the Tokai-Hokuriku, and the Tohoku blocks had a large excess of receipt, and the Kanto-Koshinetsu and Kinki blocks sent RBC products to

them. This may have been caused by a series of cancellations of blood donation events due to the effects of the severe cold snap at January 7–10, 2021 in Kyushu [12], the severe cold snap at Tokai-Hokuriku and heavy snow at January 8–15 2021 [13,14], and the heavy snow in Tohoku [15].

- ④ The inventories of RBC products at the beginning of month are shown in Fig. 7. In nationwide the numbers increased from April to July 2020 compared to January 2020 (24.1 %, 10.7 %, 29.2 %, and 18.6 %, respectively), reached transiently the similar levels to January in August, and then maintained approximate 25,000 L in nationwide without significant changes until December. In 2021, the inventories of RBC products nationwide increased significantly from January to March, reaching a peak of 37,403 litters (increased by 45.2 % compared to January 2020), and decreased to approximate 25,000 L until May, and increased again till August. In the Kanto-Koshinetsu block, the trend was similar to that of the nationwide but the increase rate was higher in March 2021 than the nationwide (81.4 % increase compared to January 2020). The Kinki and Tokai-Hokuriku blocks showed the similar variations to that of the nationwide and the Kanto-Koshinetsu block. The other blocks showed their own changes. All of them peaked in March 2021.
- (5) Fig. 8 shows the amount of RBC products supplied to medical institutions. Compared with January 2020, the supply of the products in the nationwide decreased by 7.9 % in February 2020, recovered to the similar level to January in March (2.9 % decrease), decreased from April to May (8.1 % and 9.5 %, respectively), and recovered to the similar level again in June (2.5 % decrease). The amount of RBC products supplied to medical institutions in 2019 is shown in Table S2. By comparison, the decline in supply in April and May 2020 was remarkable. Supply peaked in October and December 2020, dropped significantly in February 2021, and peaked in March 21. This tendency was similar in all blocks. However, it can also be confirmed that they dropped in February and peaked in October and December in 2019 in Table S2. Thus this drop in February and peak in October and December might be a tendency in a year in general.

4. Discussion

In around the declaration of a state of emergency (February–June 2020), the nationwide decrease in blood donations in February 2020 was due to a decrease in the number of blood donors. The reason for this is thought to be that the number of people who refrained from going out increased due to the spread of COVID-19, an unknown infectious disease, and the number of blood donation volunteers drastically decreased at blood donation room or session, and that all blood donation events by blood donation buses at schools and workplaces were cancelled [6]. Fig. S1 shows the number of blood donors at various donation facilities nationwide for January–June 2020. February 2020 showed a decrease in the number of bus and open blood donors compared to February 2019.

The massive increase in blood donations across the country in March (approximately 7.5 % increase from March 2019 and 7.7 % increase from March 2021) was attributed largely to the media coverage of leukemia swimmer Ms. Rikako Ikee on Twitter [16]. Actually, this can be seen from the increase in the amount of 200 mL donated blood (Fig. 4). As a result, it led to an increase in the manufacture volume of RBC products nationwide in March and an increase in the inventory nationwide in April (Fig. 5). According to Fig. S2, though the volume of whole blood donation has been decreasing since 2015 until 2021, the volume of whole blood donations in March 2020 increased significantly compared to that in February 2020 (15.2 % increase, while the volume of whole blood donations in March increased compared to February is much less; 3.4 % (2015), 4.6 % (2016), 5.2 % (2017), 5.0 % (2018), 1.1 % (2019), 4.2 %

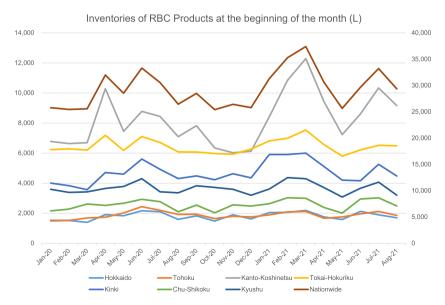


Fig. 7. Inventory amount of RBC products at the beginning of month (right axis only for nationwide).

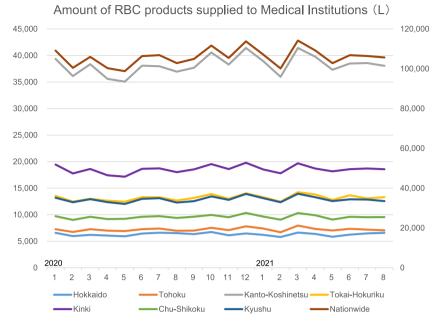


Fig. 8. Amount of RBC products supplied to medical institutions (right axis only for nationwide).

(2021)). From Fig. S1, it can also be seen that the numbers of blood donors in blood donation rooms, buses and blood centers increased significantly in March 2020 in comparison with those in March 2019.

The increase in the manufactured volume of RBC products in March caused the receipt excess of the products at the Kanto-Koshinetsu block in the same month, and the supply of RBC products to medical institutions increased nationwide (Fig. 8), probably because the demand for RBC products increased due to last-minute surgery before the declaration of a state of emergency was announced in April. However, thanks to the increase in manufacture volume in March, the inventory in the Kanto-Koshinetsu block increased in April (Fig. 7).

In April 2020, the supply of RBC products to medical institutions nationwide decreased due to the postponement of surgery using RBC products due to the declaration of a state of emergency [17] (Fig. 8). In addition, due to the suspension of blood donation events in line with the declaration of a state of emergency [6] and the amount of whole blood donation in the same month decreased significantly nationwide (Fig. 3). In fact, compared to March 2020, in April it can be seen a decline in blood donation rooms, buses, blood centers, and open blood donation (Fig. S1). However, the RBC products were sufficiently stocked in the Kanto-Koshinetsu block, which had the largest stock of all blocks, and were used nationwide (Fig. 7). The fact that the numbers of 200 mL blood donations were suppressed during months indicates that the stock was adjusted because 200 mL donation tends to be withheld when there is a large stock of RBC products (Fig. 4). As a result, the receipt and sending (transfer) of RBC products at the Kanto-Koshinetsu block were balanced, so there was no excess of receipt. For the same reason as in April, in May the supply of RBC products to medical institutions was still small (Fig. 8), but the inventory of RBC products at the beginning of May decreased in nationwide and the Kanto-Koshinetsu and Tokai-Hokuriku blocks (Fig. 7). However, the donation of whole blood was on a recovery trend (Fig. 3). Furthermore, the manufacture amounts of RBC products were small but on a recovery trend in all blocks (Fig. 5). So RBC products were over received in the Kanto-Koshinetsu block and nationwide at the beginning of June and July (Figs. 6 and 7).

The first declaration of a state of emergency was reported to have been most effective in curbing human flow but has not been presented with clear data. Fig. S3 shows the daily number of infected people in COVID-19 between January 1, 2020 and October 31, 2021, including the first state of emergency [3]. The first state of emergency was declared on April 7, 2020, and the initial target areas were Saitama, Chiba, Tokyo, Kanagawa, Osaka, Hyogo and Fukuoka Prefectures (See \pm in Figs. 2 (a) and S4 (1)). However, as the number of people infected with COVID-19 continued to increase, on April 16, 2020, all areas of Japan were declared under a state of emergency (Fig. S4 (2)). On the other hand, since the increase in the number of people infected with COVID-19 has been restrained, for May 14, the areas subject to the state of emergency became the following prefectures: Hokkaido, Saitama, Chiba, Tokyo, Kanagawa, Kyoto, Osaka, and Hyogo (Fig. S4 (3)); for May 21, Hokkaido, Saitama, Chiba, Tokyo, and Kanagawa (Fig. S4 (4)); and for May 25, the state of emergency was lifted (Fig. S4 (5)). Thus, the declaration of a state of emergency from April 7 to May 25, 2020, had a major impact on people's lives. On the website of the Cabinet Secretariat [18] on measures against COVID-19, we can refer the frequency and changes of commuting frequency per week for 1 urban commuter, the proportion of trips completed within the municipality where the person lives (weekly average) and the changes thereof, and the changes in the average travel distance per day for 1 urban commuter by the representative means of transportation (railway). When the state of emergency was declared, the commuting frequency of Ibaraki, Saitama, Chiba, Tokyo, and Kanagawa (the Tokyo metropolitan area) decreased, and the areas where people travel on a daily basis

became limited within the municipalities where they live, showing that telework was progressing. In addition, even after the declaration of a state of emergency was lifted, the frequency of commuting had been on a decreasing trend compared to January to March 2020, and commuters living in the city center have tended not to go far. In other words, urban commuters refrain from traveling by rail even after the declaration of a state of emergency was lifted. From the above, we can find in the Tokyo metropolitan area during the declaration of a state of emergency, an increase in telework, an increase in travel within the municipalities where they live, and a decrease in travel distance by rail. As a result of the transformation of people's lifestyles, the modified lifestyles tend to maintain even after the declaration of a state of emergency was lifted. This would have led to a slowdown in the number of whole blood donors since June 2020, and the JRCS will take every possible measure to maintain or to increase the number of whole blood donors in future.

In June, the supply of RBC products to medical institutions increased due to the resumption of surgical operations at medical institutions following the lifting of the state of emergency (Fig. 8). However, due to the spread of telework and distance learning, the amounts of blood donation and manufactured RBC products did not increase nationwide (Figs. 3 and 5). As a result, the inventories of RBC products in all the blocks at the beginning of July decreased significantly from June (Fig. 7).

In July–October 2020, the amount of RBC products supplied to medical institutions increased, which in turn increased the amount of donated whole blood and the amount of manufactured RBC products (Figs. 3, 5 and 8). At the same time, the inventory at the beginning of month decreased from July to August, and it remains low until December (Fig. 7). From January 2021 to March 2021, due to the effect of the 3rd wave (Fig. S3) of December 2020 to February 2021, the inventory of RBC products was significantly increased for all the blocks (Fig. 7), due to the decrease in the supply of the products to medical institutions, and the increase of whole blood donation, and manufacture (Figs. 3, 5 and 8). This reflects on the efforts of JRCS to keep the inventory of RBC products for the spread of COVID-19 were successful. In the fourth wave of April–June 2021 (Fig. S3), the amounts of RBC products supplied to medical institutions decreased from March to May but keeping higher levels by comparing with those in previous year (Fig. 8). The amounts of whole blood donation and manufactured RBC products showed a bottom at April during March to May (Figs. 3 and 5), leading to a bottom at May in the inventories of the RBC products. At that time, adjustment among blocks was little. Therefore, in June the transportation to the Kanto-Koshinetsu block was done as well as the increase of manufacturing, leading to recovery of inventories in June and July. As data up to August 2021 are analyzed, it is not possible to accurately measure the effects of the 5th wave (Fig. S3). However, the situation that RBC products cannot be provided to medical institutions could be avoided at least at the stage of August 2021 because the inventories were kept in high levels.

In January 2021, the large excess of receipt of RBC products in the Kyushu, the Tokai-Hokuriku, and the Tohoku blocks was achieved strategically due to the series of cancellations of blood donation events by the effects of the severe cold snap at January 7–10, 2021 in Kyushu [12], the severe cold snap at Tokai-Hokuriku and heavy snow at January 8–15 2021 [13,14], and the heavy snow in Tohoku [15]. It can be also confirmed that the amount of RBC products supplied to medical institutions in January 2021 was not unstable in the Kyushu, the Tokai-Hokuriku, and the Tohoku blocks compared with those in other blocks.

In general, the amounts of whole blood donation and manufacture of RBC products were kept in normal levels even under declaration of a state of emergency by the spread of COVID-19, and the supply of the products to medical institutions had not been influenced because no shortage of RBC products occurred. The quality of the RBC products was controlled with safety measures taken for the donated blood [19] even under the COVID-19 pandemic and the percentages of donated blood packs which failed the safety test did not change significantly (1.8 % (2019), 1.9 %(2020), 1.8 %(2021)) [10]. It is also revealed that the blood donation volunteers were motivated by the call to action by a famous person (i.e., Ms. Rikako Ikee), while they were demotivated by high risk of COVID-19 infection with a state of emergency and by a bad weather. Several papers reported the blood supplies under the COVID-19 pandemic and it was remarked that there were several operational challenges including loss of staff, blood shortage, and disruption in delivery all over the world [20,21,22,23,24,25,26].

The reasons why the supply of RBC products was not affected significantly by the COVID-19 pandemic in Japan are speculated as follows.

- Volunteers could go out for blood donation without any legal restriction in Japan because declaration of a state of emergency for COVID-19 in Japan did not have a power to bind people legally like lockdowns in other countries. It is important that the volunteers thought that going out for blood donation was required considering the possibility of RBC products shortage.
- No shortage or supply delay of reagents during manufacturing of RBC products were noted in Japan.
- Academia (The Japan Society of Transfusion Medicine and Cell Therapy) issued Urgent Recommendations for Shortage of Blood Product Supply Due to the Spread of Novel Coronavirus on April 17, 2020 [4], resulting in refraining from using too many RBCs for blood transfusion.
- JRCS managed blood donation, manufacturing and delivery of RBC products to medical institutions as a conductor as below during the COVID-19 pandemic while no governance organization of RBC products exists in other developing countries [27,28].
 - 1. JRCS reported the status of the supply and demand of RBC products in Japan to Ministry of Health, Labour and Welfare (MHLW) frequently to get MHLW to understand the current situation.
 - 2. JRCS contacted the main medical institutions frequently where most of the RBC products will be consumed due to the high number of surgeries conducted to confirm future demands of RBC products.
 - 3. JRCS increased the frequency of internal meetings to expect the future demand of RBC products to prevent medical institutions from being in shortage of RBC products.
 - 4. JRCS managed the amount of RBC products at the block level and governed to exchange RBC products among block centers based on future demand (Fig. 6).
 - 5. JRCS encouraged blood donation to public through media continuously.

6. JRCS implemented online service called "Love Blood" in 2018, which led to the close connection between volunteers and blood donation, and decreasing a duration of stay at blood donation places to reduce the risk of COVID-19 infection.

Compared to the current situation of other countries regarding blood donation and supply ecosystem except for Japan [27,28], these points below should be considered to establish a sustainable blood supply even if a disaster like pandemic which could impact on the blood supply happens.

- Depending on the situation of pandemic, it should be considered if movement restrictions like lockdown are required. In case it is determined that the movement restrictions are needed, it should be considered if the movement restrictions could impact on essential social activities like blood donation. Sometimes it is beneficial to discuss which level of movement restrictions will have a significant impact on the essential social activities like blood donation.
- It is important to implement online services of blood donation (e.g., online reservation, online explanation of blood donation), which will reduce the duration of stay at blood donation room or session leading to the risk reduction of pandemic infection, so as not to fail the sustainable blood supply in the countries.
- It is strongly recommended to establish an organization which will manage the entire ecosystem of blood donation and blood supply with multiple stakeholders including health authority, RBC products manufacturing site, transfer vendor of RBC products, and medical institutions. This organization will be a last line of defense dedicated to unwavering blood supply against severe disasters or pandemic.

5. Strengths and limitations

The strength of this research is to analyze the precise fluctuations of parameters regarding blood donation and blood supply per month at each block in Japan based on the accurate monthly data provided by JRCS, which enabled the comparison of the parameters during COVID-19 pandemic period (in 2020) with those during non-COVID-19 period (in 2019) and the description of the situations from January 2020 to August 2021 including the first wave, second wave, third wave, fourth wave, and partial fifth wave (Fig. S3). On the other hand, this research is limited to just analyze the actual data provided by JRCS and it cannot be touched the details of how to control and determine things in JRCS.

Japanese Society of Blood Transfusion and Cell Therapy performed a yearly survey in a large scale to investigate blood transfusion services and annual usage of blood products in Japan [29]. We could not find any notable change of the consumed amount of RBC products at each medical department or at each place of usage from 2019 to 2021. It is suggested that this type of yearly survey cannot reveal significant changes in a short period like under the declaration of a state of emergency. Therefore, it is difficult to identify the fluctuations of true medical needs of RBC products at medical institute under the COVID-19 pandemic.

In this research, blood donation and supply of RBC products after August 2021 was not investigated even though COVID-19 pandemic in Japan was not completely disappeared.

6. Conclusions

Under the spread of COVID-19, the whole blood donations were significantly influenced. However, the amount of RBC products supplied to medical institutions has been conducted with keeping sufficient inventories of the products at each block of the JRCS due to the appropriate transfer of the products between blocks. Such a supplementary system between regional blocks in Japan for blood donation and transfusion has been established through many natural disasters such as earthquakes and typhoons and should be referred to construct smart social security systems not only for infectious diseases such as COVID-19 but also nationwide catastrophes.

CRediT authorship contribution statement

Tomohide Mishiba: Writing – original draft, Visualization, Investigation, Conceptualization. **Shinji Takeoka:** Writing – review & editing, Supervision, Resources, Project administration, Conceptualization.

Ethics statement

Review and/or approval by an ethics committee was not needed for this study because the data used for this research are published on the web site of Japan Red Cross (https://www.jrc.or.jp/donation/blood/data/) and do not include any personal information (only include the amount of blood volume).

Author's information

TM also belongs to Development, Novartis Pharma K. K.

Data availability

No. Data will be made available on request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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