ORIGINAL RESEARCH

TRANSFUSION

National level adjustments to the challenges of the SARS-CoV2 pandemic on blood banking operations

Andrea Matusovits¹ | Sándor Nagy¹ | Klára Baróti-Tóth¹ | János Nacsa¹ | Mária Lázár² | Imelda Marton^{3,4} | Hajnalka Andrikovics^{5,6} | Zoltan Vokó⁷ | Attila Tordai⁶

Correspondence

Attila Tordai, Department of Transfusion Medicine, Semmelweis University, Budapest 1089, Hungary. Email: tordai.attila@med.semmelweisuniv.hu

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Abstract

Background: SARS-CoV2 causing coronavirus disease (COVID-19) is responsible for an unprecedented worldwide pandemic severely affecting all activities of societies including blood banking. We aimed to systematically collect key indicators in a nationally centralized blood banking system and to perform comparisons between 2020 and 2019.

Methods: Count data for January–December 2020 and 2019 were extracted from the integrated informatics system of Hungarian National Blood Transfusion Service and analyzed by simple graphics, tabulations, and statistics.

Results: Whole blood donation activity showed a highly significant decline due to a sharp decrease in field donations by an average fall of 24% (range:17%–28%) during March–May 2020 compared to identical period of 2019. A second, more moderate decline accompanied the second wave in late fall. The simultaneous increase in institutional donations did not counterbalance this decline. Donor exclusion rates fell significantly by an average of 1,1% (range:0.9%–1.6%) in the three spring lockdown-affected months. First-time and repeat donors showed decreased turn-out in larger proportions compared to highly repeat donors. Interestingly, among repeat and highly repeat donors, females showed less-pronounced declines compared to males while this was not observed among first-time donors. In June–September, a remarkable swing-back was observed among highly repeat female donors. Product utilization fell most notably for RBC (mean:26.2%) but also for PLT (mean:19.8%) and FFP (mean:24.3%) and showed a full recovery in June–September followed by a second decline.

Conclusion: Trends and reaction patterns of blood banking reported by our study may be useful in future planning and adjustments of blood banking activities.

KEYWORDS

blood banking, blood donors, COVID-19, SARS-CoV2

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¹Hungarian National Blood Transfusion Service, Budapest, Hungary

²Hungarian National Blood Transfusion Service, Szeged, Hungary

 ³Department of Transfusion Medicine, University of Szeged, Szeged, Hungary
 ⁴2nd Department of Internal Medicine, University of Szeged, Szeged, Hungary

⁵Laboratory of Molecular Genetics, Central Hospital of Southern Pest, Budapest, Hungary

⁶Department of Transfusion Medicine, Semmelweis University, Budapest, Hungary

⁷Center for Health Technology Assessment, Semmelweis University, Budapest, Hungary

1 | INTRODUCTION

The novel coronavirus (initially called nCoV later renamed as SARS-CoV2) causing a severe respiratory syndrome, coronavirus disease (COVID-19) is responsible for a worldwide pandemic never seen before. 1,2 The pandemic initiated early January 2020 from Wuhan, China reached the entire world with confirmed cases exceeding 100 million and death toll exceeding 2.1 million at the time of this writing.3 This unprecedented pandemic prompted previously unimaginable restrictions by governments severely affecting societies and economies. Health care systems were among the ones most hardly hit by the handling of the massive inflow of COVID-19 patients with acute respiratory insufficiency with one or more comorbidities, and the unavailability of specific treatment. Excessive exposure of health care workers to SARS-CoV2 and their subsequent fall-out from work also imposed serious problems. The immediate restructuring of the normal health care services included the complete halt of all elective areas of patient care.

Similarly to many countries, the Hungarian government announced a state of health-emergency on March 11, 2020 and introduced severe restrictions including border control, immediate closure of universities, shop, and restaurant opening restrictions and banning indoor events (>100) or outdoor events (>500). In response to the worsening of the pandemic, on March 28, restrictions were strengthened by a stay-at-home order (lockdown) practically shutting the entire country down. However, several exceptions as "well founded reasons" were also defined, and its enforcement was rather permissive. This stay-at-home order lasted for a total of 7 weeks and was lifted on May 18. The state of health emergency was canceled a months later, on June 18, resulting a duration of the milder restrictions of practically 3 months. Society life essentially normalized for the holiday months but, in parallel with school start in September a steady recurrence of the pandemic was observed with rising case numbers and death toll. In response to this that is also known as the second wave of the COVID-19 pandemic, on November 11, 2020, the Hungarian government decided to introduce a second set of restrictions which were less severe (e.g., elementary schools stayed open) compared to the spring lockdown. These milder set of restrictions have still been in effect at the time of this writing.

During the spring lockdown, blood banking services were also profoundly affected by the widespread immediate cancellations of planned blood drive events outside blood banks. In addition, donors themselves may have been deterred of traveling and even entering blood banks due to a fearful collective perception. A parallel major

consequence was the prompt decline of blood product utilization by elective surgery activities. 4,5 The net result of these counterbalancing effects was an unpredictable blood banking operation with lower output numbers and realistic threats of severe blood shortages. Furthermore, blood bank workers required additional protection from potential SARS-CoV2 exposure from donors. In addition, a sharply increasing demand arose for compatible and appropriately processed convalescent plasma product from donors earlier infected with SARS-CoV2. 10,11

The aim of the current study was to systematically collect and analyze key indicators of the national blood banking activities during the first 6 months of 2020. The chosen study time frame was deemed sufficiently broad to cover the 2 months period of national lockdown and the 3 months period of state of health emergency.

2 | METHODS

2.1 Data sources

Systematic data collection was performed from the integrated informatics system (Progesa) of the Hungarian National Blood Transfusion Service (HNBTS) covering two time periods: January 01, 2019 to December 31, 2019 versus January 01, 2020 to December 31, 2020. Since HNBTS provides integrated blood banking services for the entire Hungarian health care system, our data represent such activities on the national level.

2.2 | Definitions

Whole blood donations were categorized as "Institutional" ("Ins") if they took place on any premise of HNIBTS or in a small proportion at a hospital-based blood donation facility. In contrast, all other donation events qualified as "Field". Such events include scheduled visits to larger working establishments, universities, community centers, mass organized events with the help of the Hungarian Red Cross (mobile drives). As an indicator of loyalty, blood donors were categorized in 3 subgroups according to the number of their previous successful whole blood donations regardless of the dates: (i) "first-time" donors with 0 previous donations; (ii) "repeat donors" with 1-9 previous donations; and (iii) "highly repeat donors" with ≥ 10 previous donations. Among blood products from whole blood donations, full units of packed red blood cell (RBC) products were considered without fractionated units. Regarding platelet (PLT) products, pooled and single donor (apheresis) products were collectively considered.

considered significant. SPSS Statistics Software v.22 was used.

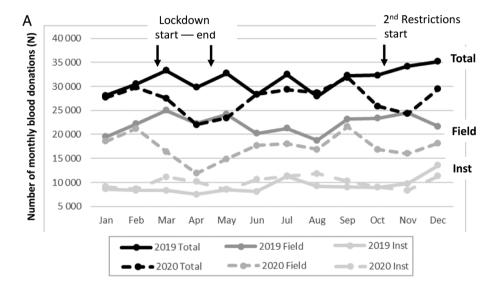
2.3 | Statistics

Count time series and proportion (composition) time series were analyzed either for the entire 12 months period or for the 3 most relevant, spring lockdown-affected months (March, April, May) with Poisson regression and with the chi-square test. 12 p values <.05 were

3 | RESULTS

3.1 | Whole blood donations

Taking advantage of the fully integrated informatics system of HNBTS, we performed systematic comparisons of nationwide key indicators of blood banking activities



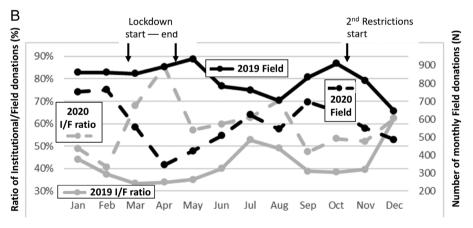


FIGURE 1 Comparisons of selected indicators of monthly whole blood donation activities between 2020 and 2019. (A) Total numbers of completed whole blood donations nationwide by all months of 2019 and 2020 with two pairs of additional curves indicating the numbers of subgroups "institutional" and "field" donations (see methods), see bold signs on the right-hand side. Black lines: Number of total donations; medium gray lines: Number of "field" donations; light gray lines: Number of "institutional" ("Inst") donations. (B) Changes in the relative proportion (%) of "institutional" versus "field" donations (left axis, 2 lower, gray curves, 1 solid +1 dashed line at left) and changes in the numbers of "field" donation (mobile) events that does not reflect actual unit numbers donated (right axis, 2 upper, black curves, 1 dashed +1 solid line at left) by all 12 months of 2019 and 2020. Black lines: Number of field donation events; gray lines: Ratio of institutional versus field donations. On both panels, solid lines represent data for 2019 (comparator) while dashed lines those for 2020. On both panels, months legends indicate cumulative data for the particular month. To translate this to a timescale, the center positions of legend text (months abbreviations) equal to ends of the months. Approximate timepoints of the start (March 28) and end (May 18) of lockdown as well as the start of the second set of restrictions on November 11, 2020 are indicated on top by arrows. Abbreviations: F, field (mobile); I, institutional

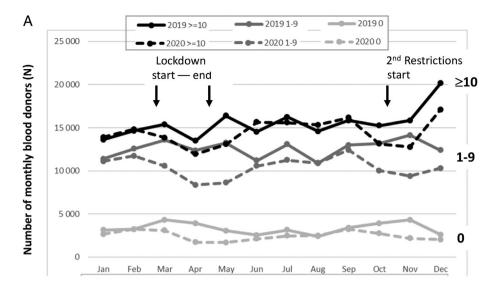
between all 12 months of 2020 versus 2019. We observed the similarities between the 2020 and 2019 values for the first 2 months (January and February) yet unaffected by the COVID-19 pandemic as well as a partial (March), fully developed (April, May), and recovering (June) effects of the pandemic. The two summer months and September show a practical overlap between the 2 years while a marked second drop can be observed during the final 3 months of 2020 mirroring the second wave. As shown in Figure 1(A), it was March when the total number of completed whole blood donations showed a substantial decrease by 5793 donations (17% of the 2019 value of 33,312). Similarly, dramatic, further declines characterized April and May of 2020 with 26% and 28% decreases, respectively, averaging a decline of 24% for these 3 months. In June 2020, a full recovery of donor appearances was observed with an equal total number of above 28,000 compared to 2019. Poisson regression analyses indicated that, the 2020/2019 ratios of total monthly donations were highly significantly altered in the 3 months (March, April, and May) initially affected by the pandemic with 0.83 (95% CI: 0.81-0.84), 0.74 (0.73-0.75) and 0.72 (0.70-0.73), respectively, compared to the three unaffected months with 0.99 (0.97-1.00), 0.98 (0.96-0.99) and 1.00 (0.98-1.02) respectively. Interestingly, the profound setbacks of donation activities exclusively affected the field activities with dramatic decreases by 52%, 87%, and 63% compared to 2019 in March, April, and May of 2020, respectively. Conversely, the numbers of completed institutional whole blood donations showed compensatory increases in March (25%), April (26%), and June (24%). Such an increase was lacking in May (0%) with closely overlapping values of above 8500 donations. The comparisons of the second halves of 2020 versus 2019 indicated similar differences. Numbers of donations were essentially overlapping between July and September 2020 with those of 2019. Reflecting the second wave, they were profoundly decreased in October through December 2020. Similarly to the spring lockdown period, this decline was primarily was due to the fall of the numbers of field donations. Interestingly, institutional donations of 2020 did not exceed those in 2019 during these final 3 months.

Next, we calculated ratios of the numbers of institutional/field donations and compared them between the respective months of the examined and the comparator years. As shown in Figure 1(B) (two lower curves on the left), this ratio showed a steady level between 45% and 33% for 2019 (lowest, solid gray line) while a dramatic increase was observed in 2020 with a maximum of 85% in April (10,143 institutional vs. 11,879 field donations). These numbers during the only full month lockdown translate to a close to 1:1 ratio instead of the usual 1:2

ratio between institutional and field whole blood donations. The ratio stayed elevated (60%) even in June 2020 indicating a potentially more skewed, long-term pandemic effect. A chi-square test comparison of combined institutional/field ratios (37% in 2019 vs. 58% in 2020) indicated a significant (p < .001) difference. The ratio values during the second halves of the years analyzed showed more variability also during the comparator year, 2019. In 2020, this indicator stayed elevated compared to 2019 except for December when in 2019, a parallel decrease of field events and increased institutional donations caused a profound "base-effect". As shown in Figure 2(B), the numbers of field events (2 black curves starting in the top left corner and corresponding to the right "y" ordinate scale) showed substantial variations throughout both years. The 2020 values were markedly decreased with minimum values of n = 346(April) and 486 (December). Average exclusion rates of 11.9% (range: 9.5%-13.0%) for the 12 months of 2020 were significantly (p < .001) lower compared to those of 2019 with 13.2% (range: 10.7%-15.1%). A similar difference was found regarding the 3 pandemic months with the average exclusion rate of 12.0% (range: 11.5%-12.4%) in 2020 versus 13.1% (range: 12.4%-13.5%) in 2019 (p < .001).

3.2 | Analyses of further donor characteristics

Not surprisingly, blood donors did not uniformly react to the COVID-19 pandemic and to the severe restrictions imposed. Data of Figure 2(A) substantiate this in as much as the most committed and active ("highly repeat", with ≥10 donations – solid and dashed black lines on top) donors were able to relatively preserve their donation activities during the critical months of severe restrictions with decreases of 11% and 20% in April and May 2020, respectively (upper, black lines). Moreover, in June 2020, their turn-out even exceeded that recorded in 2019 by about 8%. Those with medium number (1-9) of previous donations ("repeat" donors -- solid and dashed medium gray lines in the middle) showed profoundly larger decreases in numbers with 32% and 34% drops, while first-time donors solid and dashed light gray lines in the bottom) were the most pandemic sensitive with 55% and 44% drops in April and May 2020, respectively, compared to identical time periods in 2019. Second half year data indicated similar trends with marked decreases of donor turn-out in October-December 2020 that most profoundly affected first time donors. Due to special, Christmas-related campaigns, the turn-out of "highly repeat" donors increased temporarily in December of



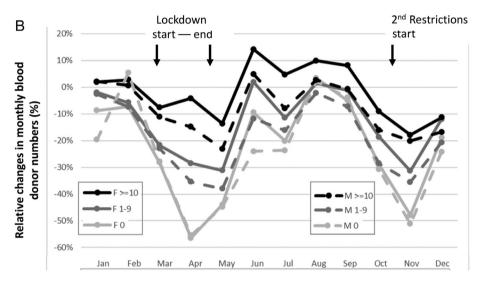


FIGURE 2 Comparisons of selected indicators of blood donors between 2020 and 2019. (A) Total numbers of blood donors nationwide by all months of 2019 (solid lines) and of 2020 (dashed lines) according to the number of their previous donations dividing them into the following 3 categories: (i) "0" no previous donation (first-time donors, light gray lines); (ii) "1–9" previous donations ("repeat" donors, medium gray lines) and "> = 10" 10 or more previous donations ("highly repeat" donors, black lines), also see bold signs on the right-hand side. Solid lines of all colors represent data for 2019 (comparator) while dashed lines those for 2020. (B) Relative changes in blood donor numbers during 2019 and 2020 by sex and the number of previous donations. Ordinate values represent simple ratios in percentage values (2019 = 100%) between 2020 and 2019 for the respective months. Black lines: "Highly repeat" donors; medium gray lines: "Repeat" donors; light gray lines: First-time donors. Solid lines of all colors represent data for females while dashed lines those for males. On both panels, months legends indicate cumulative data for the particular month. To translate this to a timescale, the center positions of legends (months abbreviations) equal to ends of the months. Approximate timepoints of the start (March 28) and end (May 18) of lockdown as well as the start of the second set of restrictions on November 11, 2020 are indicated on top by arrows. Abbreviations: F, female, M, male

both years. Interestingly, as seen on Figure 2(B), female donors showed relatively higher activity during the pandemic compared to men as indicated by the relative (2020 vs. 2019) changes of monthly donor numbers. This difference was only noticeable among repeat and highly repeat donors (black and medium gray lines) while no sex-difference was observed among first-time donors

(light gray lines). In June, a clear rebound was observed that even exceeded the comparator 2019 values among "highly repeat" female (14% increase) and male (5% increase) donors. Turn-out of highly repeat female donors stayed above 2019 values in July through September 2020. Subsequently, corresponding to the second wave, all donor activities reached their minimum in

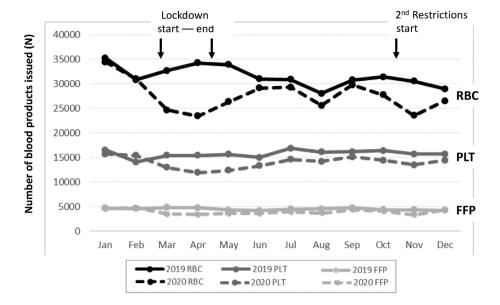


FIGURE 3 Comparisons of monthly blood product utilization between 2020 and 2019. Total numbers of various blood products issued by all months of 2019 (solid lines) and of 2020 (dashed lines). Black lines: RBC; medium gray lines: PLT; light gray lines: FFP; also see bold signs on the right-hand side. Months legends indicate cumulative data for the particular month. To translate this to a timescale, the center positions of legend texts (months abbreviations) equal to ends of the months. Approximate timepoints of the start (March 28) and end (May 18) of lockdown as well as the start of the second set of restrictions on November 11, 2020 are indicated on top by arrows. Abbreviations: FFP, fresh frozen plasma; PLT, platelet; RBC, red blood cells

November 2020 followed by a marked but incomplete rebound in December.

(mean:24.3%) and the data showed a similar picture to those for PLT.

3.3 | Blood product utilization

As expected, changes in the numbers of issued blood products showed a characteristic and COVID-19 pandemic-dependent decline for all three major unstable blood products reflecting a strong decrease in demand. As shown in Figure 3, monthly utilization of packed red blood cells (RBC) decreased profoundly by 24.6%, 31.6%, and 22.3% (mean:26.2%) in March, April, and May, respectively, comparing the two neighboring years. In June 2020, the reduction of this difference to 6% signaled a return of elective activities requiring primarily RBC products. This returned RBC utilization activity was preserved during July through September while a profound decrease by 11.6% was observed in October followed by a drop by 22.9% in November and a marked rebound to an 8.4% drop in December. Quantities of issued platelet (PLT) showed a similar but more moderate decline by 15.8%, 22.6% and 21% (mean:19.8%) in the spring lockdown-effected 3 months. PLT utilization essentially stayed declined during the entire second half of 2020. During the spring lockdown-effected 3 months, the utilization of fresh frozen plasma (FFP) also decreased in a more fluctuating manner by 27.6%, 29.3%, and 15.9%

4 | DISCUSSION

Our approach represents an opportunity to gain unique insights into processes of blood banking initiated by the COVID-19 pandemic. Our systematic dataset of the first half year of 2020 presented here encompass the entire critical SARS-CoV2 pandemic time period in Hungary with 3 months of health emergency state and 2 months of stay-at-home order (lockdown). Such unusual circumstances did not characterize the identical time period in 2019 allowing us to use it as comparator. As expected, we observed a sharp decline in blood donor turn-out translating to strongly decreased numbers of monthly whole blood donations similarly to data from other countries, including China, 5,13 the USA, 14 Italy, 15 India, 17,18 and Iran. 19 The sharp fall in blood donations was exclusively a result of abrupt cancellations of donations outside HNBTS premises classified here as "field" donations. During normal operations, field donations represent approximately two thirds of total. As a result of the spring lockdown lasting for 7 weeks, the output of this mode of donor drives declined by an average of 50% (range: 35%-61%). This reaction was also observed in several other countries. 6,7,18,20 The swing-back of field

donation activity was only partial in terms of number of field events (Figure 1(B) solid lines), however, eventefficiency improved substantially with a total number of field donations close to our comparator value (Figure 1 (A) middle curves). Due to various immediate changes of HNBTS activities including emergency contacting private apheresis centers, community facilities, and an active communication campaign, a marked increase in institutional donations occurred. These approaches are in agreement with recommended strategies to avoid blood shortages.^{7,14} Trends of the second halves of the 2 years examined gave a logical reflection of the introduction of a second, somewhat milder set of society restrictions on November 11, 2020. Starting already prior to this, a decline was observed in our indicators in October followed by minimum values in November not reaching the magnitude associated with the spring lockdown.

Returning blood donors are characterized by substantially higher commitment and motivation²¹ which is also illustrated by our data (Figure 2(A)). In June 2020, an unequivocal rise among "highly repeat" donors offset the minor declines among other donors and translated to a full recovery of donor activity compared to 2019. As shown in Figure 2(B), analyzing sex-related difference in donor attitudes demonstrated a clear advantage of women compared to men in coping with the challenges of the pandemic and in managing to provide help by an increased turn-out in the three critical spring lockdownaffected months of 2020. This difference was not present among first-time donors as curves for female and male first-time donors (light gray solid and dashed lines) are overlapping. An increasing trend for female advantage was observed with larger differences among "highly repeat" donors. In this donor subgroup, among women, the swing back stably stayed above 2019 values in June (14%) through September (8%). The observed sex difference in donor turnout favoring women was repeatedly present during the second wave albeit with a lower intensity. A possible explanation for the above differences may be that women may generally be more prone to altruistic attitudes. These data further emphasize the importance of returning donors and can be taken into consideration if public relations efforts and valuable resources must be allocated toward certain target populations.²¹

The primary major RBC concentrate users, elective surgical interventions were halted between the second half of March and end of May 2020. Our data (Figure 3) reflect these changes with a dramatic decline in RBC utilization (number of issued RBC products) in the three spring lockdown-affected months averaging to more than 25%. A similar, albeit more moderate decline occurred in association with the second set of society restrictions in October through December 2020. Decreases of PLT

products were less pronounced averaging 20% in March through May, possibly indicating that, during the majority of elective surgery interventions PLT transfusions are less prevalent. Similar trends have recently been described by others with reporting weekly hospital blood product utilization between the middle of February through the end of April 2020 in the Seattle area. There, more profound declines in PLT use were found compared to RBC, however, their comparator was less clearly defined.²⁰ In another report, an overall fall of 42% in daily transfusions was documented in the Baltimore area in March and April of 2020 and returning to normal in May but without comparing to similar unaltered time periods.²² In a brief report, Spanish colleagues performed comparisons for March and April 2020 to the same months of 2019 and found a fall of 26% and 40% for RBC and PLT transfusions, respectively.¹⁶

In summary, we performed a series of systematic comparisons of time series of key blood bank activity indicators between half year periods of 2020 and 2019, with the former entirely covering the unprecedented society shock elicited by the SARS-CoV2 pandemic. Our data substantiate expected changes such as a remarkable decrease in blood donor activities. We point out interesting trends for example, the less intense decline of donor activities of returning donors and the more committed loyalty pattern of women compared to man. These trends more moderately repeated themselves in response to the second wave of the COVID-19 pandemic during the late fall period of 2020 providing additional support for the existence of the proposed associations and creating a situation somewhat resembling to that in clinical research with discovery and validation cohorts. These attitude differences may be useful for blood bank management during resource allocation planning. Our approach may serve as an example for future analyses in larger geographical areas or blood bank service communities regarding the influence of this extensive shock on societies. Based on these observations, the increased commitment of resources and widened communication modalities toward reaching repeat donors can be recommended in such unusual situations.

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AUTHORSHIP CONTRIBUTIONS

AM, SN, and AT conceptualized and coordinated the study, SN, KB, ML, IM collected, adjusted, and analyzed

the data from HNIBT centralized informatics system; AH, VZ and AT performed the statistical analysis. All authors participated in the creation of the manuscript and approved the final version of the paper.

CONFLICT OF INTEREST

The authors declare no conflict of interest in relation to the work described.

ORCID

Attila Tordai https://orcid.org/0000-0001-6966-1622

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