

CORRESPONDENCE



Impact of COVID-19 pandemic on global unrelated stem cell donations in 2020—Report from World Marrow Donor Association

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TO THE EDITOR:

The ongoing COVID-19 pandemic has an unprecedented impact on national health care systems including hematopoietic stem cell transplantation (HSCT). Early in the pandemic this prompted the Worldwide Network for Blood and Marrow Transplantation [1] and The European Society for Blood and Marrow Transplantation [2] to publish guidelines regarding the care of patients in need of an HSCT. As World Marrow Donor Association (WMDA) promotes global collaboration for the benefit of stem cell donors and transplant patients, we were interested in examining the impact of the COVID-19 pandemic on unrelated hematopoietic stem cell (HSC) donation numbers. WMDA activities include yearly recording the number and details of unrelated HSC donations performed globally and compiling into a Global Trends Report (GTR). We used the 2020 WMDA GTR to examine trends in unrelated HSC donations during the COVID-19 pandemic globally, per continent and per country/region by comparing it with the 2019 WMDA GTR [3].

Number and details of HSC donations are collected through an online questionnaire and database developed for WMDA, which organisations can access through a secure website using their own account. Quality control measures include validity cross checks within the online questionnaire system and cross checks between years manually by WMDA staff. One-hundred-three (103) donor registries (DRs) and cord blood banks (CBBs) from 61 countries participated in the 2020 GTR, compared to 106 DRs and CBBs from 59 countries in the 2019 GTR. In 2019, 5 organisations reported having no activity and 3 did not respond. In 2020, 8 organisations reported having no activity (2 new organisations) and 8 did not respond. In addition in 2020, 2 organisation merged into 1 and 1 split into 2 reporting organisation. For 104 collections (0.5%) in 2020 and 86 (0.4%) in 2019, no patient country/region was reported. These collections are included in the overall numbers, but not in continent or country/region-specific analyses.

The 10 patient countries/regions with largest absolute increase and the 10 countries/regions with largest absolute decrease in HSC donations (bone marrow (BM) and peripheral blood stem cell (PBSC)) compared to 2019 (i.e. pre-pandemic data) were specifically addressed in the analyses. Country/region-specific cumulative COVID-19 data on cases and deaths on December 31st 2020 were obtained from the data repository operated by Johns Hopkins University Center for Systems Science and Engineering [4]; and population data were retrieved from the Worldometer website [5].

HSC donations from unrelated donors (PBSC and BM) decreased by 3.5% ($n = -707$) from 20,330 in 2019 to 19,623 in 2020, compared to an average annual growth rate of +3.9% from 2015 to 2019. The slowest development in that period was in 2015 with a growth rate of +0.5%. A negative development has not been observed before. The 3.5% decrease is composed of a 29.0% ($n = -1139$) decrease for BM and a 2.6% ($n = +428$) increase for PBSC, resulting in a drop in the BM share of unrelated HSC donations from 19.3% in 2019 to 14.2% in 2020. The percentage of national use of HSC products (PBSC and BM) (i.e. products which did not cross a national border) increased from 51.2 to 53.5%. The share of HSC donations requiring intercontinental transport decreased from 24.6% in 2019 to 21.9% in 2020. The number of cord blood unit (CBU) shipments globally decreased by 3.5% ($n = -101$) from 2851 to 2750.

When considering the continent on which the patient was transplanted (Table 1), the change rate of use of donated HSC products (BM and PBSC) ranged from -28.0% ($n = -155$) in South America to +18.2% ($n = +6$) in Africa in 2020 vs. 2019. In absolute numbers, the largest decrease of HSC donations (BM and PBSC) occurred for patients in Asia ($n = -478$; -9.1%) followed by Europe ($n = -205$; -2.4%), and the largest increase occurred in North America ($n = +88$; +1.7%) followed by Oceania ($n = +19$; +4.8%).

Regarding country/region of transplant (Table 1), in absolute numbers, the largest decrease in HSC donations (BM and PBSC) occurred in Turkey with $n = -147$ (-14.5%), and Japan following with $n = -128$ (-10.5%) (although Japan saw an increase of CBU use of $n = +106$ (+7.5%)). In absolute figures, the greatest increase occurred in Italy ($n = +67$; +8.1%) and the Netherlands ($n = +66$; +17.2%). The two countries for which most HSC products were collected showed no major changes: USA: +0.6% ($n = +30$) (although a decrease for CBU of 21.0% ($n = -149$) was observed) and Germany: -2.4% ($n = -61$).

We did not find any significant correlation between number of COVID-19 cases or COVID-19-related deaths per 1 million inhabitants with HSC donation numbers in 2020 (Spearman's $\rho = 0.098$ ($p = 0.446$) for cases and $\rho = 0.130$ ($p = 0.311$) for deaths).

The decline in number of unrelated HSC donations in 2020 suggests an impact of the COVID-19 pandemic. Reasons could include disrupted courier utilisation due to travel restrictions, lower donor availability, slight changes in donor selection (related and haplo-identical donors vs. unrelated donors) and prioritisation of patients with acute diseases. The noticeable decrease in BM collections and intercontinental/cross-border shipments can be explained by logistically complex processes, and increased risk to the donor of being exposed to COVID-19 during an operative procedure. These observations are in line with published data in the early stages of the pandemic [6, 7]. Use of CBUs as a stem cell source was expected to increase given that the

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Table 1. HSC donations per patient continent and country/region.

Patient continent, country/region	2019 BM/PBSC ^a	2020 BM/PBSC ^a	Δn (%) BM/PBSC ^a	2019 CBU ^b	2020 CBU ^b	Δn (%) CBU ^b	2019 CBU ^b /1 M inhab	2020 CBU ^b /1 M inhab	Δn (%) CBU ^b /1 M inhab
Africa	33	39	+6 (+18.2%)	0	0	0	0	0	0
Asia	5256	4778	-478 (-9.1%)	1637	1662	+25 (+1.5%)	1662	1662	+25 (+1.5%)
Europe	8718	8513	-205 (-2.4%)	332	374	+42 (+12.7%)	374	374	+42 (+12.7%)
North America	5288	5376	+88 (+1.7%)	765	627	-138 (-18.0%)	627	627	-138 (-18.0%)
Oceania	395	414	+19 (+4.8%)	39	27	-12 (-30.8%)	39	27	-12 (-30.8%)
South America	554	399	-155 (-28.0%)	78	60	-18 (-23.1%)	78	60	-18 (-23.1%)
Total ^c	20,330	19,623	-707 (-3.5%)	2851	2750	-101 (-3.5%)	2851	2750	-101 (-3.5%)
Top 10 increased	2019 BM/PBSC^a	2020 BM/PBSC^a	Δn (%) BM/PBSC^a	2019 CBU^b	2020 CBU^b	Δn (%) CBU^b	COVID-19 cases/1 M inhab	COVID-19 cases/1 M inhab	COVID-19 rel deaths/1 M inhab
Italy	827	894	+67 (+8.1%)	24	20	-4 (-16.7%)	34,851	34,851	1227
Netherlands	383	449	+66 (+17.2%)	72	69	-3 (-4.2%)	47,178	47,178	673
Canada	509	557	+48 (+9.4%)	45	57	+12 (+26.7%)	15,564	15,564	418
Iran	136	175	+39 (+28.7%)	20	0	-20 (-100%)	14,586	14,586	657
USA	4773	4,803	+30 (+0.6%)	710	561	-149 (-21.0%)	60,943	60,943	1063
Australia	339	365	+26 (+7.7%)	37	24	-13 (-35.1%)	1115	1115	36
Taiwan	210	235	+25 (+11.9%)	19	11	-8 (-42.1%)	34	34	0
Spain	446	459	+13 (+2.9%)	17	22	+5 (+29.4%)	41,242	41,242	1087
Finland	89	100	+11 (+12.4%)	1	0	-1 (-100%)	6517	6517	101
Portugal	62	72	+10 (+16.1%)	1	0	-1 (-100%)	40,570	40,570	677
Top 10 decreased	2019 BM/PBSC^a	2020 BM/PBSC^a	Δn (%) BM/PBSC^a	2019 CBU^b	2020 CBU^b	Δn (%) CBU^b	COVID-19 cases/1 M inhab	COVID-19 cases/1 M inhab	COVID-19 rel deaths/1 M inhab
Turkey	1013	866	-147 (-14.5%)	4	0	-4 (-100%)	26,188	26,188	248
Japan	1222	1094	-128 (-10.5%)	1416	1522	+106 (+7.5%)	1864	1864	28
China	1571	1469	-102 (-6.5%)	UNK	UNK	NA ^d	66	66	3
Brazil	366	265	-101 (-27.6%)	16	8	-8 (-50%)	36,112	36,112	917
Russia	165	73	-92 (-55.8%)	0	0	0	21,430	21,430	386
UK	1078	989	-89 (-8.3%)	101	140	+39 (+38.6%)	36,771	36,771	1084
India	197	111	-86 (-43.7%)	0	0	0	7454	7454	108
Germany	2540	2479	-61 (-2.4%)	6	2	-4 (-66.7%)	20,850	20,850	403
Argentina	129	96	-33 (-25.6%)	1	1	0	35,966	35,966	957
South Korea	569	539	-30 (-5.3%)	UNK	UNK	NA ^d	1205	1205	18

HSC donations shipped within and to that continent/country/region; *The 2020 numbers for CBU in China were incomplete; ~The 2019 numbers for CBU in South Korea were incomplete.

NA Not available, UNK unknown.

^aBM/PBSC bone marrow/peripheral blood stem cell.

^bCBUs cord blood units.

^cIn 2019 86 BM/PBSC and in 2020 104 BM/PBSC were shipped to unknown continent/country/region and therefore are only included in the total number

product is already available for shipping. However, on a global scale our data does not show increased use of CBU suggesting that clinical decision making about using CBU as a stem cell source did not change during the pandemic.

The success of handling this COVID-19 pandemic as a DR or CBB depended on many factors including: quality and size of the pre-pandemic unrelated donor repository/CBU inventory; having a solid network of collection and transplant centers in place with the ability to move patients and donors to hospitals in less affected regions; shifting towards donations from national donors; fast and adequate response to international transport challenges; cooperation with national/international authorities and collaboration with international colleagues.

Self-reporting is a clear limitation of this data, however the difference in total number of HSC donations reported due to slight differences in participation between the GTR data of 2019 and 2020 was relatively small (BM = 4, PBSC = 8, CBU = 32), and therefore we do not believe explains the trends we observe in HSC donations during the first year of the pandemic.

We were unable to demonstrate a correlation between country/region-specific severity of the pandemic and HSC donation numbers. We suspect this is due to data quality and variability of reported number of COVID-19 cases and COVID-19-related deaths. Furthermore, the amplitude and nature of each wave had a different impact in different countries depending on regional factors, population size, type of travel restrictions and, later in the pandemic, vaccination rates. COVID-19 related changes in HSC donations are dynamic with stronger effects in the beginning of the pandemic and gradual adaptation later on. Unfortunately, we do not gather monthly data in the WMDA GTR and therefore could not specify pandemic waves.

The decrease in unrelated HSCT actually performed could be larger than our figures on HSC donations suggest, because at times during the pandemic a clear majority of all products were cryopreserved. This practice was relatively rare before the pandemic and it is reported by some DRs that a certain amount of these cryopreserved products are not transfused [6, 8, 9].

The emergence of new COVID-19 variants causing potential new waves and the drop in donor recruitment and CBU banking during 2020 (data not shown) could affect the donation rate in the coming years. However, from anecdotal reports by several DRs and CBBs we learned that levels of HSC donation returned to normal or increased in 2021. Therefore, the outlook for HSC donation and transplantation is positive, especially since organisations are now better equipped to deal with any COVID-19 related disturbance to their operations.

In conclusion, despite logistic and other challenges posed by the pandemic, global exchanges of HSC products continued and only decreased slightly. This is an extraordinary achievement by DRs, CBBs, collection/transplant centers, couriers and all willing unrelated donors, and is a testament to the importance of international collaborations facilitated through WMDA.

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DATA AVAILABILITY

The data that support the findings of this study are not openly available. The data was shared with WMDA by donor registries and cord blood banks under a Data Use Agreement (DUA). However, the data are available from the authors (MMJ and LF) upon reasonable request and with permission of donor registries and cord blood banks.

A summary of the data can be found on the WMDA website: <https://wmda.info/wp-content/uploads/2021/05/GTR-2020-Summary-slides.pdf>

REFERENCES

- Algwaiz G, Aljurf M, Koh M, Horowitz MM, Ljungman P, Weisdorf D, et al. Real-World Issues and Potential Solutions in Hematopoietic Cell Transplantation during the COVID-19 Pandemic: Perspectives from the Worldwide Network for Blood and Marrow Transplantation and Center for International Blood and Marrow Transplant Research. *Biol Blood Marrow Transpl*. 2020;26:2181–9.
- Ljungman P, Mikulska M, de la Camara R, Basak GW, Chabannon C, Corbacioglu S, et al. The challenge of COVID-19 and hematopoietic cell transplantation; EBMT recommendations for management of hematopoietic cell transplant recipients, their donors, and patients undergoing CAR T-cell therapy. *Bone Marrow Transpl* [Internet]. 2020;55:2071–6. <https://doi.org/10.1038/s41409-020-0919-0>.
- WMDAWMDA Global Trends Report, copies can be requested via mail@wmda.info [Internet]. <https://data.wmda.info>.
- Data repository operated by the Johns Hopkins University Center for Systems Science and Engineering [Internet]. [cited 2020 Jul 12]. <https://github.com/CSSEGISandData/COVID-19>
- Worldometers.info. Worldometers.info [Internet]. 30 November, 2021. Dover, Delaware, U.S.A. [cited 2020 Jul 12]. <https://www.worldometers.info/>
- Auletta JJ, Novakovich JL, Stritesky GL, Newman J, Fridy-Chesser ST, Hailperin K, et al. Meeting the Demand for Unrelated Donors in the Midst of the COVID-19 Pandemic: Rapid Adaptations by the National Marrow Donor Program and Its Network Partners Ensured a Safe Supply of Donor Products. *Transplant Cell Ther*. 2021; 27:133–41.
- Russo D, Polverelli N, Malagola M, Farina M, Leoni A, Bernardi S, et al. Changes in Stem Cell Transplant activity and procedures during SARS-CoV2 pandemic in Italy: an Italian Bone Marrow Transplant Group (GITMO) nationwide analysis (TransCOVID-19 Survey). *Bone Marrow Transpl*. 2021;56:2272–5.
- Mengling T, Rall G, Bernas SN, Astreou N, Bochart S, Boelk T, et al. Stem cell donor registry activities during the COVID-19 pandemic: a field report by DKMS. *Bone Marrow Transpl* [Internet]. 2021;56:798–806. <https://doi.org/10.1038/s41409-020-01138-0>.
- Fernandez-Sojo J, Azqueta C, Valdivia E, Martorell L, Medina-Boronat L, Martínez-Llonch N, et al. Cryopreservation of unrelated donor hematopoietic stem cells: the right answer for transplantations during the COVID-19 pandemic? *Bone Marrow Transpl* [Internet]. 2021;56:2489–96. <https://doi.org/10.1038/s41409-021-01367-x>.

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AUTHOR CONTRIBUTIONS

MMJ was responsible for collecting data and writing the WMDA GTR 2020 report; extracting, analysing and interpreting the data; writing the paper; creating reference

list; creating table. AHS, SNB and SJF were responsible for the idea for this paper; contributed to interpretation and analyses of the data, writing the paper and provided feedback. JF, NS, HE, DF, FO, DO, KLY, SAM, SM, MA, JV, MMF, GSC, TJ, SMD, PG, RM and CH were responsible for submitting their data for the WMDA GTR 2020 and 2019 and provided feedback. BES, SJF and LF provided feedback. All authors participated in review and approval of the final version of the paper.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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