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Impact of the COVID-19 outbreak on the field of hematopoietic cell transplantation in the Asia-Pacific region: APBMT Activity Survey 2020/2021

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Abstract

COVID-19 became a global pandemic in 2020 and significantly affected the activity of hematopoietic cell transplants (HCT) worldwide. Despite these challenges, a total of 28,793 transplants, including 18,518 allogeneic and 10,275 autologous transplants, were performed in 719 facilities in 2020 in the Asia-Pacific (AP) region. This represented a 5.1% increase in allogeneic transplants and a 3.1% increase in autologous transplants, an overall increase of 4.4% compared to the numbers in 2019. With respect to the donor source, haploidentical transplants increased significantly by 18.6%, related transplants by 8.8%, and cord blood transplants (CBT) by 9.2%. However, the number of unrelated transplants, excluding CBT, decreased for the first time by 8.2%. As a result, COVID-19 facilitated the growth of haploidentical transplants due to cross-border restrictions. Regarding the changes in the total number of transplants by country/region in 2020, it increased by 2,048 transplants in China, followed by Japan (210 transplants) and Korea (230 transplants); however, 14 of the 22 countries and regions decreased their number of transplants in 2020 compared to the previous year. There was no correlation between the increase or decrease in the number of transplants in 2020 and the Gross National Income (GNI) per capita of each country/region in 2020, as well as Domestic General Government Health Expenditure as a percentage of General Government Expenditure (GGHE-D/GGE). In 2021, the total number of transplants in this region was 34,754. With the exception of a few countries/regions that decreased the number of transplants in 2020, most countries/regions have started to see a recovery in 2021. The COVID-19 pandemic significantly affected the supply chain and logistics involved in HCT rather than its numbers; however, we have found ways to overcome logistical challenges to carry out transplant medicine without delay, even under these circumstances.

Key words COVID-19, Asia-Pacific region, hematopoietic cell transplantation, number of transplants

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Introduction

The COVID-19 pandemic caused by SARS-CoV-2 has significantly affected the activity of hematopoietic cell transplantation (HCT) in both developed and emerging countries/regions worldwide. Since the first documented case of COVID-19 was reported in December 2019, the infection spread globally with a high mortality rate from 2020 and 2021[1]. As COVID-19 spread worldwide, the global medical community had to prioritize its treatments, so routine medical care could no longer be maintained. In particular, as COVID-19 infection is likely to become severe in immunocompromised hosts, HCT recipients needed to take strict precautions against infection for an extended period before, during, and after treatment. On the other hand, allogeneic HCT requires unique preparations before the treatment, such as securing donors and stem cell collection and transportation, and this process requires in-person work by many stakeholders. However, social restrictions for infection control significantly interfered with this series of tasks. Under these severe circumstances, organizations involved in HCT have made efforts to maintain transplant medicine as usual, coping with the pandemic, by reframing the entire medical system, adjusting HCT programs, and formulating HCT guidelines under COVID-19, both in international societies[2] and in individual countries/regions[3]. Here, we report the changes in the number of transplants in the Asia-Pacific (AP) region during the two years from 2020 to 2021, at the beginning of the epidemic, compared with the previous period.

Materials and Methods

Data collection

In 2023, 23 countries and regions are participating in the Asia-Pacific Blood and Marrow Transplantation Group (APBMT). Those include Australia, Bangladesh, Cambodia, China, Hong Kong, India, Indonesia, Iran, Japan, Korea (the Republic of Korea will be referred to as Korea in this paper), Malaysia, Mongolia, Myanmar, Nepal, New Zealand, Pakistan, Philippines, Singapore, Sri Lanka, Taiwan, Thailand, Uzbekistan, and Vietnam. As shown in **Figure 1**, excluding Cambodia where HCT has not yet started, 22 out of 23 countries/regions submitted the activity survey reports and reporting facility lists to the APBMT Data Center by email through

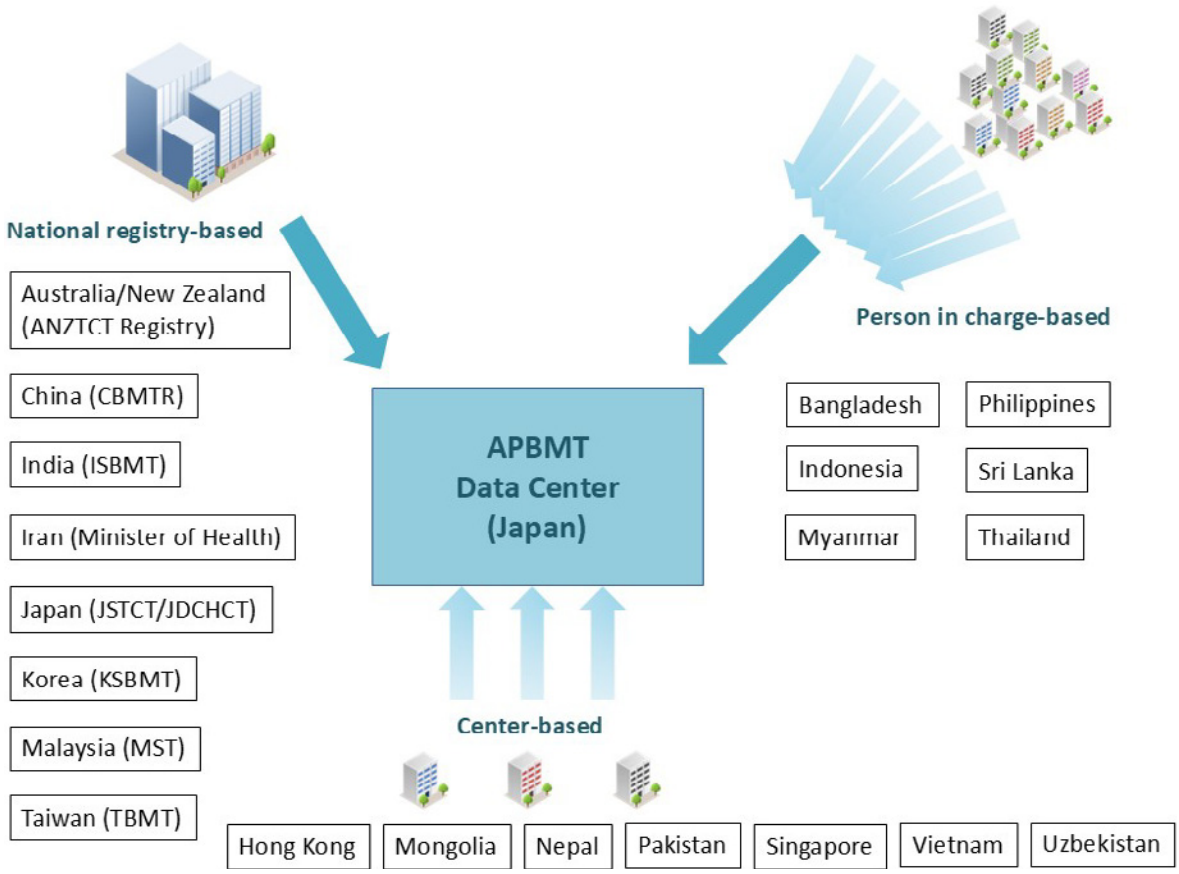

Figure 1. Routes of data submission
Activity Survey data from China, India, Japan, Korea, Malaysia, and Taiwan were submitted through their national registry: Chinese Blood and Marrow Transplantation Registry (CBMTR), Indian Society for Blood and Marrow Transplantation Registry (ISBMT), Japan Society for Transplantation and Cellular Therapy (JSTCT)/Japanese Data Center for Hematopoietic Cell Transplantation (JDCHCT), Korean Society of Blood and Marrow Transplantation (KSBMT), Malaysian Society of Transplantation (MST), and Taiwan Society of Blood and Marrow Transplantation (TBMT). The Australasian Bone Marrow Transplant Recipient Registry (ABMTRR) submitted the national data for Australia and New Zealand. Iran submitted the national data from the Minister of Health and Medical Education of the Islamic Republic of Iran. Data were collected by a particular contact person and submitted to the Data Center from Bangladesh, Indonesia, Myanmar, the Philippines, Sri Lanka, and Thailand. The Data Center directly contacts major transplantation centers and receives data from Hong Kong, Mongolia, Nepal, Pakistan, Singapore, Vietnam, and Uzbekistan.

different routes owing to the differences in the data collection systems in each country/region.

Statistical analyses and ethical approval

The APBMT Data Center performed all necessary analyses for this survey using Excel functions. To clarify the change of stem cell source selection in this period, unrelated transplants excluded cord blood transplants (CBT). As a result, unrelated transplants included only bone marrow (BM) and peripheral blood stem cells (PBSC) transplants. To avoid overestimating the increasing rate of the HCT activity in 2021, the increasing/decreasing rates of the year 2021 were calculated with the number of 2019 as the reference. We evaluated the increase or decrease in the number of transplants in each country/region in 2019 and 2020, the delta value was calculated using the following formula:

$$\frac{\text{HCT number in 2020 - HCT number in 2019}}{\text{HCT number in 2019}} \times 100\ (\%)$$

The total population of each country/region was extracted from World Bank[4]. The Gross National Income (GNI) indicates the total income calculated by adding the gross domestic product (GDP), which represents the total amount of value generated in the country, to income from abroad, and was extracted from World Bank Group[5]. GNI per capita in each country/region was calculated and expressed in US dollars for 2020. Domestic General Government Health Expenditure as a percentage of General Government Expenditure (GGHE-D/GGE) is defined as the ratio of general government health expenditure to general government expenditure in each country/region and was extracted from the World Health Organization[6]. The correlation between GNI/capita or GGHE-D/GGE and the delta value was evaluated by a coefficient of determination (R^2) using Excel func-

Table 1. The number of total transplants and facilities in 2020 and 2021 and the differences between the previous year

	The number of total transplants and facilities				The differences between previous year			
	2020		2021		2020-2019		2021-2020	
	Facilities	Transplants	Facilities	Transplants	Facilities	Transplants	Facilities	Transplants
Australia	37	1,792	37	1,854	**-5**	**-80**	0	62
Bangladesh	4	23	4	41	2	3	0	18
China	166	13,415	174	18,110	17	2,048	8	4,695
Hong Kong	4	199	3	195	2	47	**-1**	**-4**
India	84	1,675	84	2,497	3	**-757**	0	822
Indonesia	3	3	1	4	0	**-2**	**-2**	1
Iran	10	758	9	851	0	**-322**	**-1**	93
Japan	317	6,070	312	5,852	4	210	**-5**	**-218**
Korea	44	2,937	44	3,158	0	230	0	221
Malaysia	9	386	14	391	**-6**	9	5	5
Mongolia	1	4	1	7	0	**-2**	0	3
Myanmar	2	4	0	0	0	**-2**	**-2**	**-4**
Nepal	1	17	1	26	0	**-8**	0	9
New Zealand	6	335	6	344	0	34	0	9
Pakistan	3	143	3	204	0	**-34**	0	61
Philippines	6	30	1	45	0	**-14**	**-5**	15
Singapore	3	228	3	210	0	**-16**	0	**-18**
Sri Lanka	4	33	3	72	0	**-40**	**-1**	39
Taiwan	5	332	7	422	0	**-58**	2	90
Thailand	7	301	6	345	**-2**	**-41**	**-1**	44
Uzbekistan	1	0	1	9	0	**-6**	0	9
Vietnam	2	108	3	117	0	5	1	9
Total	719	28,793	717	34,754	15	1,204	-2	5,961

Numbers that decreased from the previous year are highlighted in bold.

tions.

As we collected only the annual number of all types of HCTs, the Data Center and registries/facilities did not obtain informed consent from each patient. The APBMT Activity Survey was approved by the Institutional Review Board of the Aichi Medical University School of Medicine (2016-M029) and the APBMT Registry Committee.

Results

Number of reported facilities and all transplants

The number of facilities reporting data was 719 and 722 in 2020 and 2021, respectively (**Table 1**). Despite the COVID-19 pandemic, the number of transplant facilities in this region has increased continuously since 2016 (**Figure 2A**). As shown in **Figure 2B**, the total number of annual transplants did not decrease in 2020 and increased steeply in 2021. The total number of transplants in 2020 was 28,793, an increase of 1,204 compared to 2019, and that in 2021 was 34,754, an increase of 5,961 compared to 2020 (**Figure 2B**).

Trends of HCT by stem cell sources

The number of allogeneic and autologous transplants has continuously increased in 2020 and 2021. Although the increase rate of allogeneic and autologous transplants was lower in 2020 than in the previous three years, it increased steeply in 2021; it was 19.7% and 24.9% for allogeneic and autologous transplants, respectively (**Figure 3A**). The change in unrelated transplants in 2020 was -8.2%; however, it recovered steeply in 2021, and the rate raised to 17.2%. Compared with unrelated transplants, the number of related transplants increased in 2020 and 2021, and the number of related transplants exceeded 15,000 for the first time in 2021 (**Figure 3B**). The number of haploidentical transplants has also steadily increased in 2020 and 2021. The growth rate of CBT was 9.2% in 2020; however, it decreased by 5.6% in 2021 (**Figure 3C**).

Trends of all transplants in each country/region

Figure 4 shows the trends in the number of all transplants by country and region since 2017. Excluding Indonesia, Mongolia, Myanmar, and Uzbekistan, which had ten or fewer transplants per year in 2020, the number of all transplants per year in 2020 did not decrease in Bangladesh, China, Hong Kong, Japan, Korea, Malaysia, New Zealand, and Vietnam. As opposed to this, the number of transplants temporally decreased in Aus-

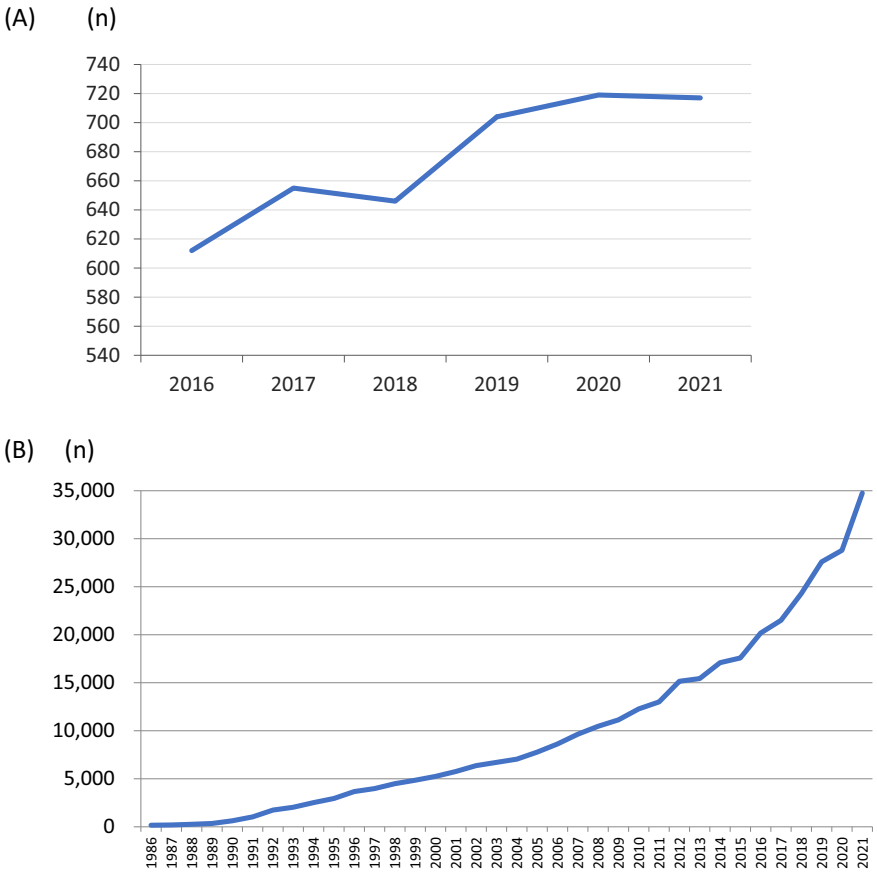

Figure 2. Trends in the number of facilities and all transplants
(A) The number of facilities that reported Activity Survey data did not decrease in 2020 and 2021. (B) The number of transplants in this region has increased continuously, even in 2020 and 2021.

tralia, India, Iran, Nepal, Pakistan, the Philippines, Singapore, Sri Lanka, Taiwan, and Thailand in 2020 compared to the previous year, and then recovered in 2021, except for Singapore. Notable changes were found in India and China. India saw a decrease of 757 transplant cases in 2020 compared to the previous year, followed by an increase of 822 cases in 2021. In China, which increased by 2,048 cases in 2020 compared to 2019 and saw a greater increase of 4,695 cases in 2021. The detailed number of facilities and transplants in 2020 and 2021 and the differences between the previous year in each country and region are shown in **Table 1**.

Relationship between economic indicators of figures or index and the increase/decrease of the transplants number in each country/region

No correlation was found between the GNI per capita of each country/region in 2020 or the GGHE-D/GGE and the delta value of the number of transplants in 2020 compared to 2019 (**Figure 5A** and **B**). **Supplementary 1** provides the number of transplants by disease category and stem cell source in 2021.

Discussion

The APBMT Data Center commenced the HCT Activity Survey in 2007 and the initial report was published in 2010[7]. Since then, we conducted the survey every year and reported on trends in HCT in the AP region[8-11]. During this period, the total annual number of all kind of HCTs exceeded 10,000 in 2008[7] and 20,000 in 2016[9], indicating that it took eight years for the number of transplants to increase from 10,000 to 20,000. In this report, the total number of transplants in 2021 exceeded 30,000 for the first time; however, it took only five years to increase the number from 20,000 to 30,000. This finding indicates that HCT has recently become increasingly active in the AP region.

The COVID-19 pandemic caused by SARS-CoV-2 has spread throughout the world since 2020, both in developed and emerging countries/regions, and has had a significant impact on the activity of HCT. EBMT Activity Survey reported a 6.5% decrease in total transplants, 5.1% in allogeneic transplants, and 7.5% in autologous transplants in 2020[12]. In the United States, the number of allogeneic and autologous transplants has also de-

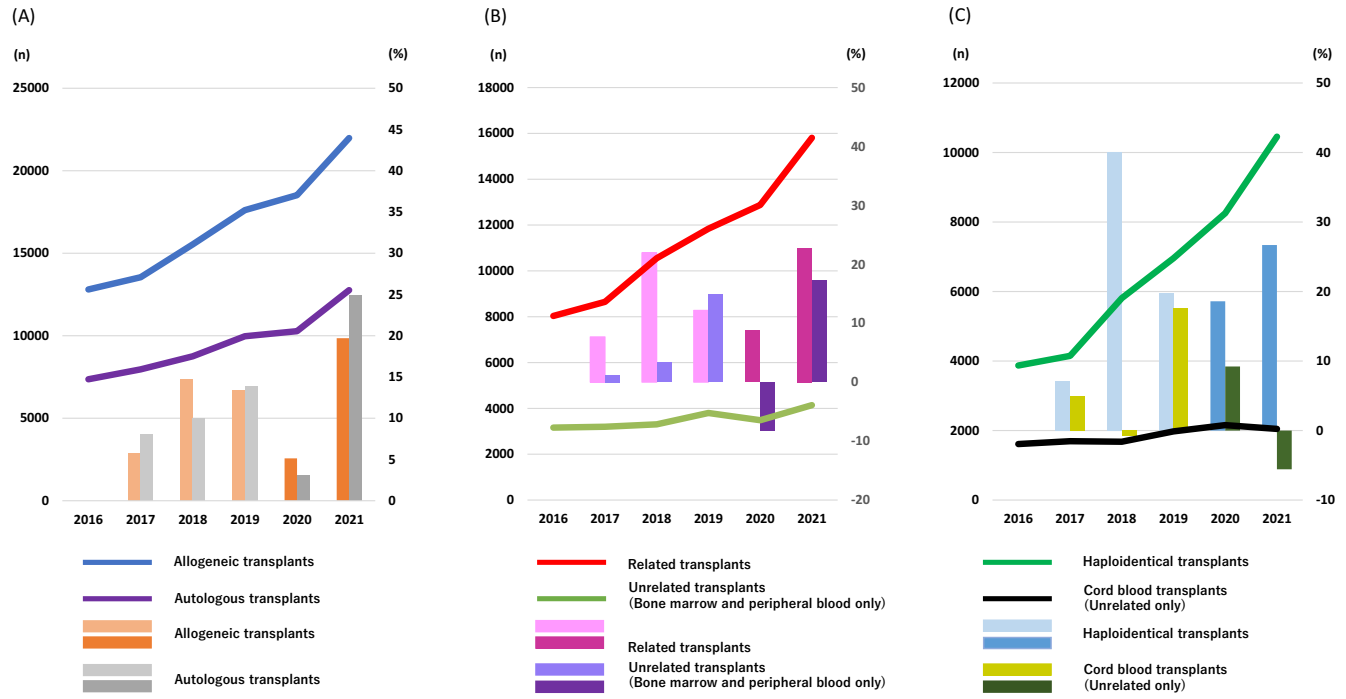

Figure 3. Trends in absolute numbers of hematopoietic cell transplantations from 2016 to 2021 (left axis; line chart) and their increasing/decreasing rates compared to the previous year (right axis; column chart)
The increasing/decreasing rates until 2019 were compared to the previous year (faint color), and those in 2020 and 2021 were compared to 2019 (dark color).
(A) The number of allogeneic and autologous transplants has continuously increased since 2016, and their increasing ratios exceeded more than 15% in 2021. (B) The number of related transplants has rapidly increased since 2016. The number of unrelated transplants has steadily increased; however, the ratio became negative for the first time in 2020. (C) Compared to the rapid growth of haplo-transplants since 2017, the number of cord blood transplants has remained at around 2,000 for the past five years; however, its increasing ratio was -5.1% in 2021.

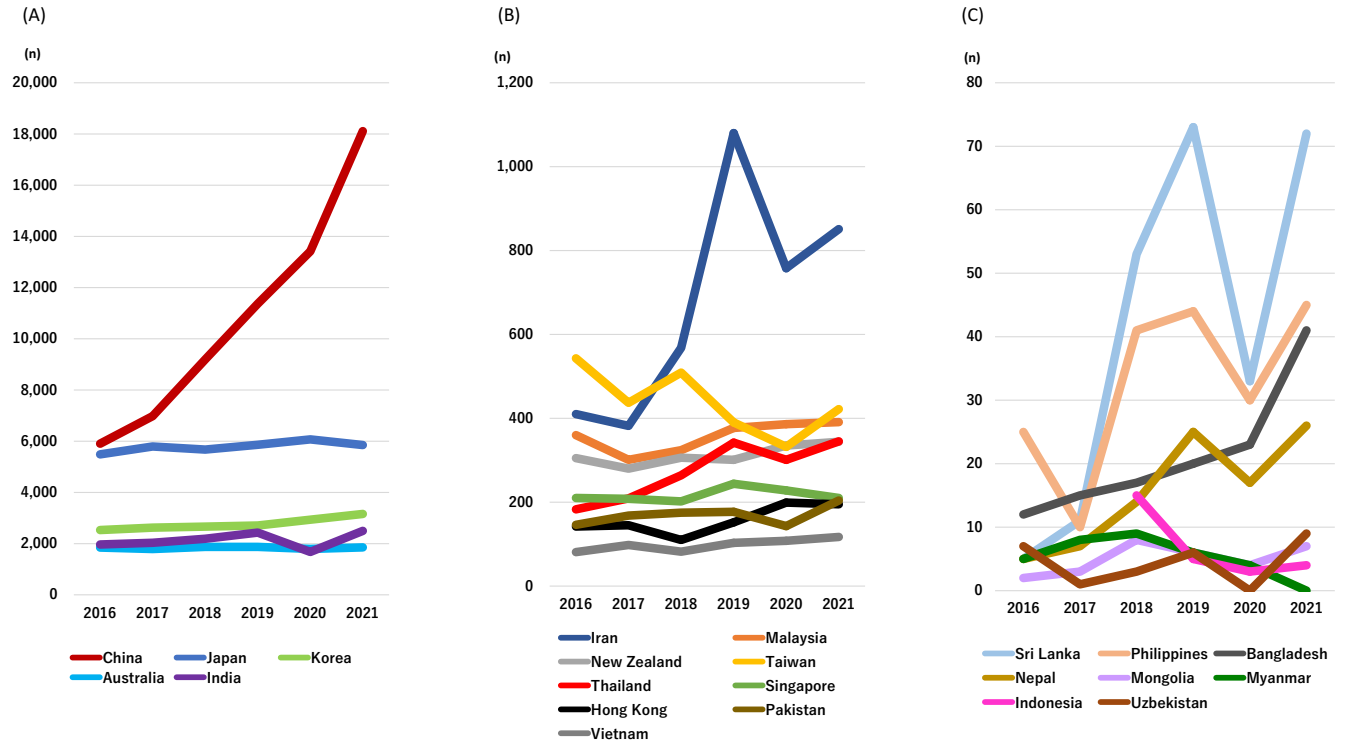

Figure 4. Trends in absolute numbers of transplantations from 2016 to 2021 by country/region
(A) n>1,500, (B) 1,500>n>100, (C) 100>n

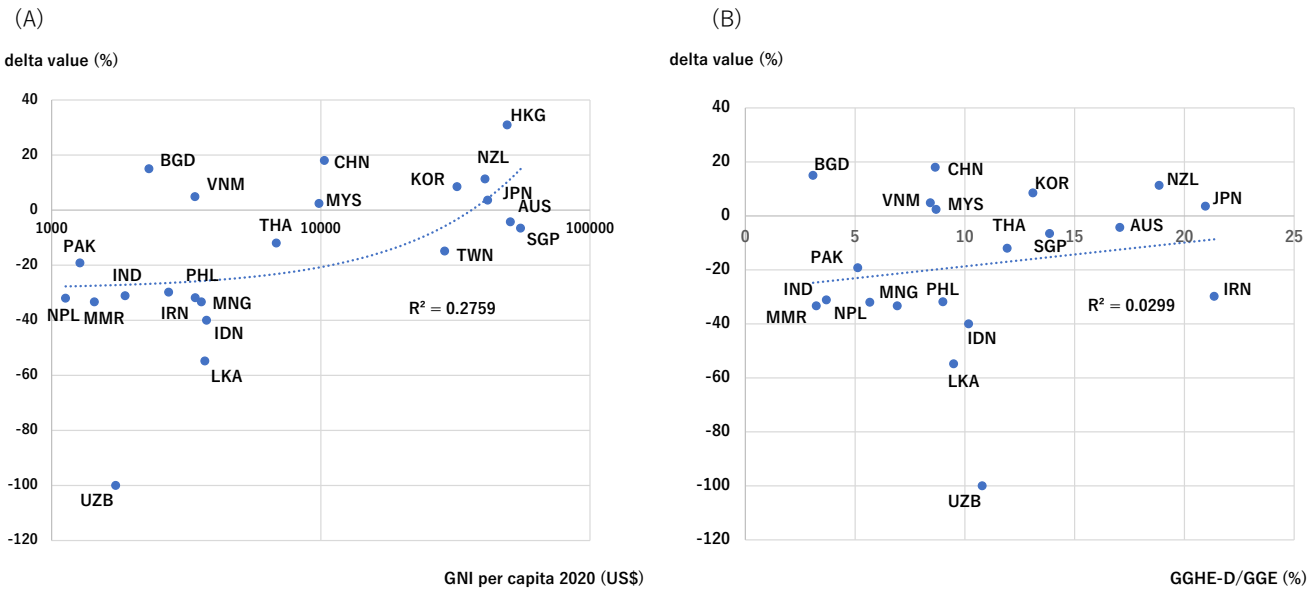

Figure 5. Correlation between the delta value of the number of transplants in 2019 and 2020 and (A) the gross national income (GNI) per capita 2020 and (B) Domestic General Government Health Expenditure as a percentage of General Government Expenditure (GGHE-D/GGE)
The coefficient of determination (R^2) were 0.2759 and 0.0299 for the GNI per capita and GGHE-D/GGE, respectively. There are no GGHE-D/GGE data for Hong Kong or Taiwan.

creased in 2020 compared to 2019[13]. As opposed to those reports, we found that the number of HCTs in the AP region did not decrease in the number of autologous and allogeneic transplants, and both of which recorded the highest activity ever in 2020 and 2021. Despite the COVID-19 epidemic, the number of autologous and allogeneic transplants in this region did not decrease because the number of both transplants in China showed a significant increase, covering a decrease in the number of transplants in other countries/regions. Xu et al. explained the reason for their uptrend that the number of medium and large HCT groups increased, and transplant care was carried out smoothly as usual because of the basic principles of infection prevention, namely social distancing, masking, and thorough education of patients and donors[14]. As we previously reported[9], the number of haploidentical transplants, which had been on the rise before 2020, has continued to increase in 2020 and 2021. One possible reason is that donors for haploidentical transplants are relatively easier to select than unrelated donors, even under social restrictions. On the other hand, the growth rate of unrelated transplants in 2020 was negative compared to the previous year for the first time. It is because of delays in transplant coordination to prevent infection and cancellations and postponements of transplants due to donor infection. Like haploidentical transplants, since CB was easy to use as a transplant source even in social restrictions and complemented other donor sources, the number of CBTs in 2020 increased from the previous year. However, it decreased in 2021, which may reflect a decrease in CBT due to the increase in haploidentical transplants in Japan[15]. In other words, as we reported in our most recent publication[11], the choice of stem cell sources in this region varies significantly across countries and regions, and these differences may have influenced the increase or decrease in HCT numbers during the COVID-19 pandemic in each country and region.

Atsuta et al. have shown the correlation between economic growth indicators and the number of transplants by transplant type in each region of Europe, America, Asia-Pacific, the Middle East, and Africa and they have reported that the number of autologous transplants tends to be more strongly correlated with GNI per capita in the region compared to allogeneic transplants[16]; however, there was no direct implication between the increase and decrease in the number of transplants and the economic situation of the country and region in this analyses. The economic situation obviously impacts transplant medicine, but the Asia-Pacific region is vast and has a wide variety of populations, age structures, politics, and financial systems, the increase or decrease in the number of transplants in each country and region is thought to be the result of not only the economic situation but also a complex interaction of multiple factors, such as when the government started substantial restrictions on going out, how strictly they were implemented, thorough implementation of basic infection prevention measures, and the availability of human and material medical resources.

The guidelines have played a major role in continu-

ing transplant medicine during the COVID-19 pandemic. In India, the Indian Society for Blood and Marrow Transplantation (ISBMT) took the lead in publishing guidelines for COVID-19[17], and as a result, the number of transplants recovered to pre-COVID-19 levels in 2021. By December 2020, guidelines were issued by EBMT[18], WMDA[19], ASTCT[20], and other organizations in the field of HCT. Because transplantation, especially allogeneic transplantation, requires the involvement of various allied health professionals and donors, these guidelines helped create a system in which patients with blood diseases could receive transplantation. It is thought that each country and region used them as a reference to modify their own transplantation care.

There are some limitations to our report. Our survey covered data from the first two years of the COVID-19 pandemic, so long-term data collection and analysis will be necessary to see how the COVID-19 pandemic has affected transplant care in this region. Secondly, the AP region is vast, and it is likely that there were significant differences in the approach to transplant care in each country/region during the pandemic, so this report cannot be used to discuss its success or failure. Thirdly, the Activity Survey only collects data on the number of transplants, so the results cannot reflect the disease background of individual patients.

The COVID-19 pandemic showed us how we should control the supply chain and logistics involved in transplantation under unexpected circumstances and overcome some challenges so that patients can receive the transplant care they need. Taking the above limitations into consideration, APBMT will continue analyzing the Activity Survey and start patient-specific data analyses in the future.

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Author Contributions

MI and YA designed the study, and MI wrote the manuscript. LW, AD, MA, ML, JS, VL, KML, DA, AAH, YA, JHM, YSC, KWH, KB, AAG, BSP, TF, MRB, UB, SH, MD, and PCD submitted the data. MI and APBMT Data Center analyzed the data. All coauthors reviewed the manuscript, and YA, AH, AD, DS, YSC, CCL, UA, MD, PCD, and SO revised it.

Conflicts of Interest

The authors declare no conflict of interest. Disclosure forms provided by the authors are available on the website.

MI, AS, AAH, NK, MB, and SO are editors of *Blood Cell Therapy*. They were not involved in the editorial evaluation and the decision to accept this article for publication.

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