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HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) FOR ALL SESSION SBTMO 2023 ACCESS TO HEMATOPOIETIC STEM CELL TRANSPLANTATION: FACING OUR CHALLENGES

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There are major challenges for HSCT in Brazil. The access to the transplant due to an insufficient number of active beds for adults and even less for pediatric patients and lack of access to some critical medications such as antiviral drugs and GVHD therapies were discussed with SBTMO associates and the coordinator of the Government National Transplant System (SNT), in order to improve this scenario.

HSCT IN BRAZIL: WHERE ARE WE?

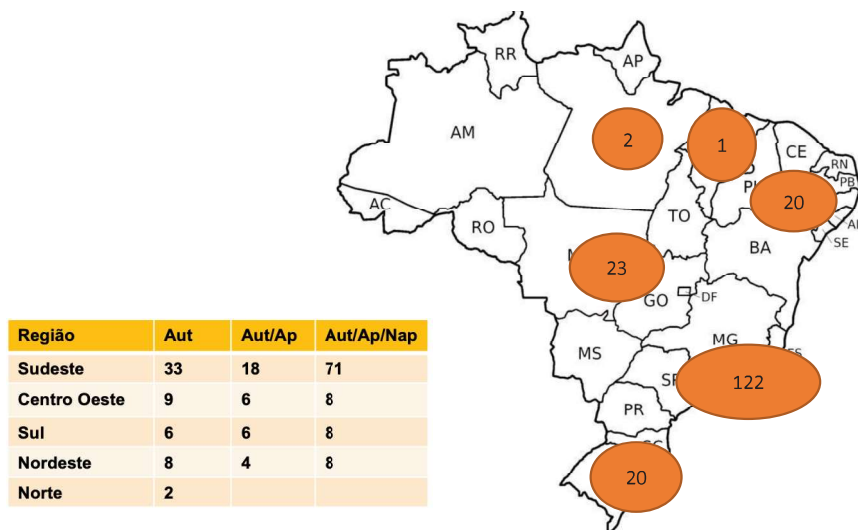
Brazil has one of the biggest transplant programs in the world. In the HSCT scenario, 70% of the HSCT is

performed by our Public Health System (SUS) and about 30% is performed at private Hospitals.

Currently, Brazil has 261 transplant centers in 124 establishments, being 247 public: 124 for autologous only, 80 for auto and allogeneic related, and 57 for autologous, allogeneic related and unrelated HSCT. Most centers are concentrated in Southeast and South Brazil (figure 1).¹

Furthermore, Brazil has the third donor registry in the world: REDOME has more than five million donors registered.²

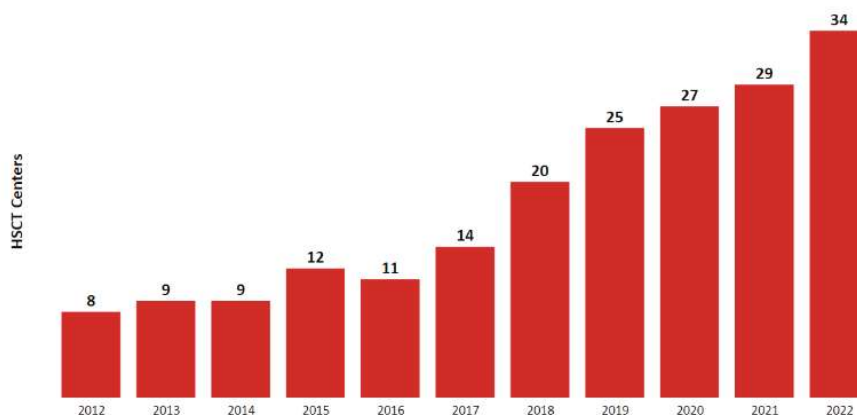
FIGURE 1. Transplant Centers in Brazil



We have very few centers in the north, northeast and central regions of Brazil. This concentration generates a higher cost to the public system to take the patients to centers far away from their cities of origin. Family support, essential to these patient's quality of life, is also often limited when they are far from their cities.¹

Nevertheless, thirteen new centers were authorized in 2023 and we can see that the number of active centers has been increasing through the last few years, as well as the proportion of allogeneic transplants (Figure 2)¹

FIGURE 2. Brazilian Active Centers in the CIBMTR by year¹



However, with a population of 200 millions of inhabitants, in 2022, Brazil performed only 2840 transplants by SUS, being 1745 autologous, 866 related and 229 unrelated transplants. We estimate only 160 beds for HSCT in SUS. Therefore, we can see long lines of unattended patients either waiting for autologous (myeloma, lymphomas, and germ cell tumors) or allogeneic HSCT (especially acute leukemia, bone marrow failure, myelodysplastic syndrome, myeloproliferative disorders and falciform anemia).

Even with a limited number of unrelated HSCT performed, there is great difficulty in finding centers for marrow harvest or peripheral blood collection. For autologous transplants, strategies for simplifying the requirements can be discussed (perform autologous transplants in hematology units, for example). Despite many achievements in recent years, Brazilian centers still have problems to registering these transplants. When collected and sent to regional state transplant coordination, these data seem not to reach SNT, which claims to have insufficient information about HSCT around the country. There is also no monitoring, to make sure the data is collected, by the government. Besides, the lack of data manager staff at the centers limits their ability to register their results.

Another important difficulty in HSCT in Brazil is the lack of access to important tests and medications. With the increment of unrelated and particularly haploidentical transplants in Brazil, we had an increment of infection, which is the leading cause of

death for our patients.¹ Viral infections are frequent in this scenario. However, there is no reimbursement for viral identification by PCR, which is the recommended method for monitorization. Diagnosis by PCR for CMV, EBV, adenovirus and respiratory virus are crucial to HSCT. Besides, specific evaluations of engraftment by chimerism (STR analysis) are not reimbursed. This is very important to guide immunosuppressive drugs management and the requirement of strategies, like donor lymphocyte infusions, which is not reimbursed either. The absence of viral monitorization and therapy is a matter of great concern given Brazil's remarkable increment of haploidentical transplants.

Regarding the drugs important to HSCT we have diverse difficulties. Some of them are no longer produced by pharmaceutical companies without any advice or time to be substituted. It was the case for melphalan and busulfan, which are essential to the conditioning phase of HSCT. Other medications are not reimbursed by the public health system. It is the case of some immunosuppressive agents which are available for other types of transplants (solid organs) but not for HSCT, such as tacrolimus, mycophenolate mofetil and sirolimus. It is also the case of important antiviral drugs like cidofovir and foscarnet, which are not available in our country. Some other new drugs or new developments which would be very important for conditioning (treosulfan, thiotepa), GVHD therapy (ruxolitinib, ibrutinib or extracorporeal photopheresis) or for CMV prophylaxis (letermovir) and

therapy (maribavir) are not available.^{3,4} It usually takes too long for new medications or procedures to be incorporated into our regulatory system, which can certainly impact the results. There are many established indications for HSCT that are not included in the regulation either for public or private scenarios, and this is an urgent matter. There is also no financial support from the government for clinical research protocols in this field.⁵

Total body irradiation is not available in many centers, which can compromise the results of the HSCT for Acute Lymphoblastic Leukemia (ALL).

PEDIATRIC HSCT IN BRAZIL

One important unattended need is the pediatric transplant. SBTMO Pediatric Group estimates that around 400 kids would need transplants for a year only because of leukemia. Besides acute leukemia, taking into consideration many other diagnoses (SCID, falciform anemia, inherited disorders), there is a clear need for an increment in pediatric transplants in the country. Amplifying screening measures for inherited disorders will tend to worsen this situation. 400 hundred pediatric transplants were performed in 2022 in Brazil. Transplants have also been centralized in a few centers in the southeast and south of the country. Infection is the main cause of death, suggesting that these children have been referred late to the transplant centers. Acute Lymphoblastic leukemia is the main diagnosis among pediatric transplants performed in our country.¹

MAIN ACHIEVEMENTS

Since its foundation on April 15th, 1996, the Brazilian Society of Transplant and Cellular Therapy (SBTMO) has had great development. With 1171 associates, SBTMO has an important online journal (the first transplant journal in Latin America), and has established partnerships with other societies in the field (EBMT, ASBMT, LABMT, WBMT). SBTMO Consensus guidelines have been important to guide current practices in the country and in the Latin American Continent. With the partnership with CIBMTR, there are an increasing number of centers which report their data to this platform, currently more than 86 centers, with the important coordination of SBTMO data managers group. Reporting centers are certified by SNT. Through the data back to center tool, these data could come back to SBTMO and establish the Brazilian HSCT Registry (RBTMO), which captures data from both HSCT and Car-T cell infusions.²

Summary slides with general results of HSCT in Brazil are then published at JBMTCT annually.¹ Aside from the information, many educational initiatives have been taken as regional and national meetings, meetings with FACT and “Young Transplanter Program”, which has been an important source of education for our residents and young staff. GEDECO, the scientific working group of SBTMO, has published in the last years many collaborative trials in important peer review journals.²

As a result of this robust society and a government disposition to discuss and solve current problems we also have some regulatory achievements at the public health system such as the increment of age of transplant and a recent improvement in the reimbursement according to the qualification of the center.

PROPOSALS AND PERSPECTIVES

During the discussion, many proposals were discussed and can therefore be summarized to guide future efforts of improvement of HSCT in Brazil:

- Increment of active beds for both adult and pediatric HSCT;
- Expansion of centers in North, Northeast and Central Region of Brazil, with the proposal of Tutorials and continuous educational programs;
- Improvement and expansion of RBTMO through mandatory hiring of data managers and mandatory registry of data;
- Reporting data to SNT for adequate diagnosis and working in collaboration with the government to solve the problems identified;
- Discuss strategies of implementation of cellular therapy programs;
- Establish a special group for discussing the autologous transplant regulation in Brazil
- Partnership with Anvisa to discuss notification of industries which do not respect the required time to discontinuation of products;
- Partnership with Anvisa and MS to stimulate other industries for production of critical drugs;
- Revision of transplant indications and continuous actualization;
- Discussion about incorporation of drugs and procedures.
- Establishment/ funding for clinical research national protocols.

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