ISSN : 2350-0743

International Journal of Recent Advances in Multidisciplinary Research

Vol. 12, Issue 07, pp.11411-11417, July, 2025

RESEARCH ARTICLE

THERAPEUTIC POTENTIAL AND LIMITATIONS OF USING HEMATOPOIETIC STEM CELLS AS A TREATMENT FOR PATIENTS WITH SICKLE CELL ANEMIA

Yasmim Vitoria Santos Sampaio[1], Alexia Costa Santos de Santana[2], Ana Carolina Santana de Oliveira[3] and João Ronaldo Tavares de Vasconcellos Neto[4]

[1]Biomedicine student- Higher Education Unit of Feira de Santana- UNEF; [2]Biomedicine student- Higher Education Unit of Feira de Santana- UNEF; [3]Professor of Biomedicine- Higher Education Unit of Feira de Santana- UNEF; [4] Professor of Biomedicine- Higher Education Unit of Feira de Santana- UNEF

ARTICLE INFO

Article History

Received 24th April, 2025
Received in revised form
27th May, 2025
Accepted 20th June, 2025
Published online 30th July, 2025

Keywords:

Sickle Cell Anemia, Hematopoietic Stem Cell Transplantation and Cell and Tissue Transplant-Based Therapy.

****Corresponding author:***
Dr. Amadou Abdourazac

ABSTRACT

Introduction: Hematopoietic stem cell transplantation (HSCT) is a promising therapy for sickle cell anemia, offering a potential cure. However, its access is limited by economic obstacles, such as high costs, shortage of compatible donors, and specialized infrastructure. The lack of financial resources in developing countries and the scarcity of public policies aggravate the situation. **Objective:** To investigate the therapeutic potential of stem cells in the treatment of patients with sickle cell anemia, evaluating their efficacy, safety, and impact on patients' quality of life. **Methodology:** an integrative review of articles published between 2013 and 2024 in the PubMed/MEDLINE and BVS databases was carried out, focusing on clinical outcomes and impact on quality of life. The analysis was divided into three axes: benefits, risks and limitations, and economic and social obstacles. **Results and Discussion:** HSCT has been an effective option for sickle cell anemia since the 1990s, with success rates of up to 95%. It offers cure in up to 90% of cases, but presents risks such as graft-versus-host disease and long-term complications. Alternatives, such as umbilical cord blood stem cell transplantation and gene therapies, are being explored, but with lower success rates and safety and cost challenges. **Conclusion:** Although effective, HSCT faces economic, clinical and social barriers to its large-scale implementation. Reducing clinical risks and overcoming economic barriers, in addition to public policies to finance treatment and improve health infrastructure, are essential to make HSCT accessible, especially in low-income countries.

Citation: Yasmim Vitoria Santos Sampaio, Alexia Costa Santos de Santana, Ana Carolina Santana de Oliveira and João Ronaldo Tavares de Vasconcellos Neto. 2025. "Therapeutic potential and limitations of using hematopoietic stem cells as a treatment for patients with sickle cell anemia.". *International Journal of Recent Advances in Multidisciplinary Research,* 12, (04), xxxx-xxxx.

INTRODUCTION

Sickle cell anemia (SCA) is one of the most prevalent hereditary hemoglobinopathies in the world, especially in Afro-descendant populations, with a major impact on quality of life, increased morbidity in childhood and risk of early mortality (Khemani *et al*., 2018). It is characterized by a mutation in the HBB gene, which alters a single amino acid in the beta globin chain. This alteration results in abnormal hemoglobin that, when it loses oxygen, polymerizes. Due to this, red blood cells become rigid and sickle-shaped, which impairs oxygen transport and causes problems in blood flow (Arnold *et al*., 2016). The deformation of red blood cells causes vaso-occlusive crises, chronic kidney disease, ulcers, osteomyelitis, bacterial infections, especially by Streptococcus pneumoniae, and progressive involvement of specific organs, such as the brain (in cases of stroke), liver, spleen, lungs, eyes, among others. This genetic disease affects millions of people globally, with high infant mortality in low-income countries and a significant reduction in quality of life in adults due to the serious complications of the disease (Hosoya *et al*, 2018). Palliative treatments, such as hydroxyurea and blood transfusions, control the symptoms but do not act on the underlying cause of the disease (Abraham *et al*., 2016). Epidemiologically, sickle cell anemia affects approximately 300,000 children born annually worldwide, being more prevalent in regions with a high frequency of consanguineous marriages. In the United States, approximately 1 in 600 African Americans is reported to have the disease. In Brazil, it is estimated that one child is born with the disease for every thousand live births, with the incidence ranging from 1:650 in Bahia to 1:13,000 in Rio Grande do Sul. The prevalence of sickle cell trait (HbAS) in the country is heterogeneous, being higher in the North and Northeast regions (6% to 10%) and lower in the South and Southeast regions (2% to 3%) (Silva *et*

al., 2016). In 2022, it was estimated that approximately 9 million Brazilians had sickle cell trait, while between 60,000 and 100,000 had the disease (Silva-Pinto *et al*., 2022). In high-income countries, advances in clinical management have significantly reduced pediatric mortality; However, the survival rate in adults is still challenging due to complications accumulated over time (Dalle *et al*., 2014). In low-income countries, where health infrastructure is limited, infant mortality rates remain alarming, highlighting the need for affordable and effective therapeutic alternatives (Meier *et al*, 2018). In the context of therapeutic options, hematopoietic stem cell transplantation (HSCT) emerges as the only curative approach for sickle cell anemia. This treatment replaces defective hematopoietic cells with healthy cells from a donor, promoting the normalization of hematological parameters and stopping disease progression. However, the procedure presents considerable challenges, including the risk of serious complications, such as graft-versus-host disease, infertility, and graft exclusion. Furthermore, access to HSCT is limited by the availability of compatible donors, making it difficult to universalize this curative intervention (Gluckman *et al*., 2017; Azevedo *et al*., 2021). Stem cell transplantation offers a unique opportunity to treat the cause of sickle cell anemia, with disease-free survival rates in successful cases of around 90% and overall survival of 95% in pediatric patients with compatible donors. Despite these promising figures, high costs and structural and social limitations make access to HSCT challenging, especially in developing countries. The central problem is the lack of compatible donors and the high risk of complications, especially in adults, who have a longer exposure time to harmful agents and a greater burden of organ damage (Dalle, 2014; Rotin *et al*, 2022).

In view of this scenario, this study aimed to investigate the therapeutic potential of stem cells in the treatment of patients with sickle cell anemia, evaluating their efficacy, safety, and financial and social impact on the quality of life of patients. The justification for this investigation lies in the need for curative solutions for the disease, with emphasis on HSCT as an alternative capable of transforming the clinical and social reality of affected patients. This study sought to contribute with robust scientific evidence that can support more inclusive and accessible health policies.

METHODOLOGY

This study used an integrative review methodology with a qualitative approach, based on the selection and analysis of scientific texts on the topic. Data collection was carried out through a bibliographic survey in indexed databases, covering the period from 2013 to 2024. The sources consulted included the States National Library of Medicine (PubMed/MEDLINE) and the Virtual Health Library (VHL). To ensure the relevance of the research, we used descriptors in Health Sciences (DeCS), such as “Sickle Cell Anemia”, “Hematopoietic Stem Cell Transplantation”, and “Cell and Tissue Transplant Based Therapy”. In English, the corresponding descriptors were: “Sickle Cell Anemia”, “Hematopoietic Stem Cell Transplantation”, “Cell-and Tissue-Based Therapy”, with the help of the Boolean operator “AND”. Alternative terms relevant to the topic were also considered. The inclusion criteria were scientific articles published in full in the databases between 2013 and 2024, in Portuguese, English or Spanish, which addressed clinical results, biological mechanisms and impact on the quality of life of patients treated with hematopoietic stem cells. The exclusion criteria included articles with no direct relation to the topic, duplicates, incomplete, reviews, debates, abstracts or unavailable in full. The selected material was organized in tables, categorizing the relevant articles found in each database. After eliminating duplicates, an initial screening was performed based on the titles. The abstracts of the selected articles were evaluated, and those that met the inclusion criteria were subjected to full reading. For data analysis, the results were grouped into three thematic axes defined based on the specific objectives of the study: main benefits of stem cell transplantation compared with conventional therapies available; risks and limitations associated with hematopoietic stem cell transplantation in patients with sickle cell anemia; and the main economic and social obstacles that hinder access to stem cell transplantation for patients with sickle cell anemia. The guided questions that were developed based on these axes guided the critical interpretation of the specific literature, allowing a systematic and robust analysis. The analyzed data were used to compose the specifications of results and discussion, aligning them with the established theoretical framework. This structured methodology ensured the validity and reliability of the data presented, contributing to an in-depth investigation into the efficacy and challenges of stem cell therapy in patients with sickle cell anemia.

RESULTS AND DISCUSSION

The use of hematopoietic stem cells as a therapeutic option began in the late 19th century. In 1902, hematopoietic progenitor cells, responsible for the production of mature blood cells, were discovered, and the concept of stem cells was solidified. The term "stem cells" was introduced by Ernst Haeckel in 1888, but it was not until 1939 that the first bone marrow transplant was successfully performed to treat aplastic anemia. In the 1950s, French oncologist George Mathe performed the first hematopoietic stem cell transplant to treat people exposed to radioactive substances. In 1957, Dr. E. Donnall Thomas initiated the first allogeneic hematopoietic stem cell transplant, but early results were challenging due to high failure rates. The revolution in stem cell transplantation occurred in 1972, with the discovery of cyclosporine, an immunosuppressant that improved outcomes, making treatments successful for leukemia and aplastic anemia (Hoang *et al*., 2022). The use of stem cells in the treatment of sickle cell anemia began to be explored in the 1990s, after the molecular basis of the disease was identified in 1949 by Linus Pauling, who discovered that SCA is caused by hemoglobin S, an abnormal form of hemoglobin resulting from a mutation in the beta-globin gene (Eaton, 2022). Research on the disease advanced throughout the 20th century, but until the 1970s, the focus was limited, in part due to lack of funding and the fact that the disease primarily affects people of African descent. In 1972, the creation of the Sickle Cell Anemia Act and the founding of the Sickle Cell Disease Association of America increased awareness and investment in the fight against the disease. The first hematopoietic stem cell transplant for patients with sickle cell anemia was performed in 1993. The therapy involved transplanting hematopoietic stem cells from matched donors to replace defective blood cells with normal donor cells. Although a major advance, early transplants were associated with high risks, such as graft rejection and graft-versus-host disease (GVHD). Over time, protocols were

refined, including newborn screening, the use of hydroxyurea to increase fetal hemoglobin levels, and blood transfusions. In 2018, the National Heart, Lung, and Blood Institute (NHLBI) launched the Cure Sickle Cell Initiative, driving research into gene therapies to cure SCA. Although advances in gene therapies have shown promising results in clinical trials, the big leap forward came in 2019, when the FDA approved the LentiGlobin™ gene therapy, an alternative that is less dependent on matched donors and has shown promising results, marking a new chapter in the cure of the disease. However, HSCT still remains a more accessible and viable cure option for SCA patients (Hoang *et al*., 2022).

Benefits of stem cell transplantation compared to conventional therapies available: Conventional palliative therapies for sickle cell anemia, such as hydroxyurea and blood transfusions, are reasonably effective in managing symptoms, such as chronic anemia, vaso-occlusive crises, jaundice, and complications, such as acute chest syndrome, leg ulcers, stroke, bone complications, priapism, acute chest syndrome, renal impairment, among others, when trying to raise Hb levels in anemic patients (Demirci *et al*., 2023). The use of hydroxyurea reduces the frequency of these painful crises and complications, and is especially recommended for adults with recurrent episodes of acute chest syndrome. Frequent transfusions help prevent serious complications by keeping hemoglobin levels within a safe range, reducing the risk of vaso-occlusive crises and organ damage. However, conventional treatments do not offer a definitive solution (Ozdogu *et al*., 2015). The use of hydroxyurea has disadvantages such as dizziness, seizures, infertility and an increased risk of infections (Shet *et al*., 2017). On the other hand, constant transfusions of packed red blood cells help prevent serious complications, but carry risks such as iron overload, alloimmunization and possible changes in blood viscosity due to the rapid increase in hemoglobin levels. This increase, if not properly monitored, can affect blood flow and contribute to complications such as strokes and severe headaches. However, treatments such as hydroxycarbamide have shown efficacy in raising hemoglobin in a controlled manner, reducing associated risks (Ballas *et al*., 2021). Although essential, these approaches are insufficient to alter the course of the disease, regarding the cure, highlighting the relevance of HSCT.

By exchanging hematopoietic stem cells for others free of FA, changing the abnormal hematopoiesis for those carried out by healthy cells, the patient can achieve a cure (Brandow *et al*., 2022). According to the Haute Autorité de Santé (HAS), this is the only curative therapy, especially indicated for young people with HLA-compatible sibling donors. Studies show that survival after transplantation exceeds 95% and the cure rate is 90%, especially when performed at preschool age, before the onset of chronic complications (Dalle, 2014; Cairo *et al*., 2021). Furthermore, HSCT can also reduce the need for ongoing treatments such as hydroxyurea and transfusions, reducing dependence on frequent interventions and significantly improving quality of life by allowing greater freedom and fewer limitations in patients' daily lives (Gallo, 2019; Patel *et al*, 2022). HSCT remains the gold standard for the treatment of sickle cell anemia, especially for patients with severe complications, with a success rate of over 90% (Ware *et al*., 2024). For the transplant to be successful, it is necessary to prepare the patient with conditioning regimens, which are protocols that help destroy diseased cells and create space for new stem cells (Rostami *et al*, 2024). These regimens vary in intensity according to the patient's clinical conditions. Myeloablative regimens, which are more intense, are used to treat patients with severe complications, destroying the bone marrow to ensure that the transplant is successful. On the other hand, milder conditioning regimens, such as non-myeloablative ones, have allowed younger patients or those with milder symptoms to benefit from transplantation. These milder regimens offer a good chance of success, while reducing the risk of complications. In addition, they expand eligibility for the procedure, making it possible to treat patients with pre-existing organ dysfunctions, achieving positive results and improved quality of life (Guilcher *et al*., 2018). The impact of HSCT goes beyond physical symptoms and also involves improvements in the emotional and psychosocial aspects of patients. Studies indicate that transplantation reduces hospitalizations and the need for opioids, improving the quality of life of both patients and their caregivers (Bhatia *et al*., 2015; Hulbert *et al*.; 2022). Despite the risks, such as infertility and neurological complications, many patients report that the procedure has transformed their lives, allowing greater freedom and a fuller life (Scott, 2014; Cappelli *et al*, 2019). Thus, HSCT represents not only a solution for physical healing, but also a profound change in the quality of life of patients with sickle cell anemia.

The use of haploidentical transplants and umbilical cord blood transplants emerge as promising alternatives for patients with sickle cell anemia, especially given the shortage of fully compatible donors. Umbilical cord blood transplantation, although more common in young patients, has a lower success rate compared to transplants with compatible donors. Haploidentical transplants, which involve partial compatibility between donor and recipient, offer a viable solution for patients whose siblings are HLA-incompatible or have sickle cell disease, representing an important alternative given the low probability of finding a fully compatible donor (25%) (Fitzhugh, *et al*.; 2014). Recent advances have also expanded the treatment possibilities for sickle cell anemia. Gene therapy, for example, offers an innovative approach to correcting the genetic mutation that causes the disease. Lentiviral vectors are used to introduce therapeutic genes into the patient's stem cells, eliminating the need for donors and the risks of exclusion (Shet *et al*., 2017). Although this technique has shown promising results, it still faces challenges, such as high costs and the need for further studies to ensure its safety and efficacy, especially in relation to the effects of myelobalancing (Ferraresi *et al*., 2023). Another approach, autologous transplantation with genetic modification, also reduces the risks of GVHD, but is in the experimental stage (Germino-Watnick *et al*., 2022; Fitzhugh, 2022). CRISPR-Cas9 therapy, a recent therapeutic possibility, uses genetic editing of the patient's blood stem cells to increase the production of fetal hemoglobin (HbF), which can replace defective sickle cell hemoglobin (HbS), improving blood flow and reducing vaso-occlusive crises, bone crises, abdominal crises, and pulmonary crises. Gene editing with CRISPR/Cas9 has been a promising approach to curing sickle cell disease (SCD) by correcting the mutation in the HBB gene that causes the hemoglobin abnormality. Studies have shown that it is possible to modify up to 80% of allelopathies at this locus, with few unwanted changes elsewhere in the DNA. Before receiving the therapy, patients must undergo preparatory treatment with high-dose chemotherapy, which helps create space in the bone marrow for the modified stem cells (Adashi *et al*., 2024). These

innovations offer significant hope for patients, although there are still hurdles to overcome before they become affordable and widely effective treatments, as many of these treatments are still in the clinical trials phase.

Risks associated with hematopoietic stem cell transplantation in patients with sickle cell anemia: Despite its numerous advantages, HSCT has limitations that prevent the full use of this technology by patients in need. Chronic graft-versus-host disease (GVHD) is one of the most serious complications, occurring in patients undergoing myeloablative conditioning regimens. This condition, in which the donor's immune cells attack the recipient's tissues, can cause damage to organs such as the skin, liver, and intestines, as well as late complications such as infertility, hypothyroidism, and diabetes mellitus. On the other hand, non-myeloablative regimens reduce toxicity but increase the risks of graft rejection and disease recurrence, compromising the success of the transplant (Ozdogu *et al*., 2015). Risks associated with transplantation include early and late mortality, as well as long-term complications. In a study of 1,000 patients transplanted between 1986 and 2013 at 106 centers in 23 countries, reported to the European Society for Blood and Marrow Transplantation, the five-year survival rate was 95% in children, but complications such as infection, organ toxicity, and GVHD were observed. Late mortality, associated with organ involvement, highlighted the need for prolonged follow-up. Furthermore, the choice of graft type significantly influences outcomes, with better success rates associated with the use of bone marrow compared with peripheral or cord blood (Gluckman *et al*., 2017).

Chemotherapy used pre-transplant also carries risks, including organ toxicity and infertility (Meacham *et al*, 2023). Studies show that patients undergoing myeloablative regimens have a higher chance of reproductive complications, such as ovarian failure and sperm dysfunction (Whitley, 2014). In addition, transplantation in patients with preexisting organ damage can precipitate organ failure, worsening the clinical picture (Leonard *et al*., 2020; Lawal *et al*, 2022). Fertility preservation should be discussed before transplantation, especially in women, who may opt for cryopreservation of oocytes or ovarian tissue (George *et al*, 2022). Despite advances, HSCT still presents risks associated with the development of hematologic malignancies and solid tumors. Studies show an incidence of neoplasms of 2.4% in 10 years, with a higher frequency of acute myeloid leukemia, myelodysplastic syndrome (MDS), and chronic myeloid leukemia. In addition, cases of acute T-lymphoblastic leukemia, large T-cell granulocytic leukemia, and solid tumors such as medulloblastoma, grade 2 ependymoma, embryonal rhabdomyosarcoma, Kaposi sarcoma, myxofibrosarcoma, unspecified sarcoma, and myofibroblastic tumor of the liver have been reported. These risks are exacerbated by the use of low-dose radiation regimens, which, although effective and less toxic, are intended to destroy the patient's bone marrow prior to transplantation, creating space for healthy donor stem cells. However, this approach may affect the surviving host cells, increasing the risk of mutations and malignant transformations. Graft failure, where the donor cells do not establish themselves properly, is another serious complication that can compromise the efficacy of the transplant (Eapen *et al*., 2023; Gorur *et al*, 2024). The patient's age and donor compatibility play key roles in the success of the transplant. Younger patients, particularly children, have a higher survival rate and face fewer complications, as they have a more resilient immune system and a faster recovery. On the other hand, adults have a higher risk of complications, such as Graft-versus-Host Disease and organ damage, due to a more intense immune response and the aging of the immune system, which makes recovery and control of adverse effects difficult (Shenoy *et al*., 2018). Despite being a curative method, HSCT presents challenges, such as the identification of compatible donors, which is hampered by the underrepresentation of HLA haplotypes in donor banks, which limits access to treatment for many patients (Kassim *et al*., 2017). Only 14% of patients with sickle cell anemia find an HLA-identical donor, due to the complexity of matching HLA antigens, which are necessary for a successful transplant. The chance of two siblings being HLA-identical is only 25%, and the limited genetic diversity in some populations also makes the search difficult. This requires alternative strategies, such as the use of umbilical cord blood and haploidentical transplants, to expand treatment possibilities. Studies show that starting the search for donors before 43 months of age significantly improves the chances of finding a suitable match, increasing transplant success rates (Justus *et al*., 2015).

In this scenario, the use of stem cell transplant-based therapies must follow strict protocols that ensure the safety of the procedure, with guidelines that individually evaluate factors such as the type of transplant, the donor profile, and the patient's age (Kanter *et al*., 2021). Detailed clinical evaluation and pre-transplant management are especially critical for patients with damage to vital organs, reducing risks such as graft rejection and infections (Kogel *et al*., 2020). These factors become essential for a careful evaluation, determining the best therapeutic approach for each patient. Despite the risks, the procedure is particularly effective when performed in the early stages of the disease, before irreversible damage develops (Jang *et al*., 2021). Advances in less toxic conditioning regimens and gene therapies promise to make the treatment safer and more accessible, but the decision to opt for transplantation should always consider the benefits and risks involved (Stenger *et al*., 2019).

The main economic obstacles that hinder access to stem cell transplantation for patients with sickle cell anemia: Despite its indescribable advantages, HSCT faces significant barriers related to economic and social accessibility. Limitations related to the availability of donors and the costs of the procedure, ethical and legal issues also present considerable challenges, especially in situations involving children and adolescents. The decision on the use of stem cells by individuals under 18 years of age is exclusively made by their legal guardians, which can impact the initiation or delay of treatment, regardless of the recipient's wishes (Níckel *et al*., 2018). HSCT faces significant economic and social challenges. A study conducted in Florida using data from the Medicaid program showed that the average health care cost per patient is $1,389 per month (approximately R$7,547.69, based on the conversion of $1 = R$5.43). These values increase with age, ranging from $892 (R$4,847.04) for children aged 0 to 9 years to $2,562 (R$13,921.65) for patients aged 50 to 64 years. In addition, the annual cost of chronic transfusions and chelation therapy in the United States is estimated at $40,000 per patient (R$217,356.00) (Ozdogu *et al*., 2015). Even though these costs refer to traditional treatment, such as transfusions, they directly affect access to other more complex options, such as HSCT. Conventional

treatment is already very expensive, placing a huge financial burden on patients and their families. When one considers transplantation, which involves additional costs for patient preparation, the procedure, and post-transplant follow-up, access becomes even more restricted, especially for families with lower incomes. Medicaid, a health care program of the United States government, provides health coverage for low-income individuals and families, helping to cover the costs of essential medical treatments, including high-cost therapies such as HSCT. This facilitates access and ongoing care for patients with sickle cell anemia. However, the complexity of treatment and high costs still limit access, even with the help of Medicaid. However, in high-income countries, the majority reach adulthood due to access to advanced medical programs, while in low-income regions such as Africa, the survival rate is dramatically lower, with only 20% of children reaching adulthood. This scenario reflects economic barriers and inequalities in access to adequate health care (Montalembert *et al*, 2017).

The economic context of low-income countries exacerbates inequality in access to HSCT. The lack of adequate hospital infrastructure, shortage of blood products, and absence of post-transplant support prevent low-income patients from being treated locally, forcing the wealthier to seek care abroad, at high costs and beyond the reach of the majority (Kassim *et al*., 2017). Furthermore, inequalities in the health system are reflected in infant mortality rates in regions such as Africa, where more than 50% of children with SCA die before the age of five due to the lack of adequate treatment and the high prevalence of serious complications (Crossley *et al*., 2022).
In the United States, the Affordable Care Act (ACA), enacted in 2010, brought groundbreaking advances, such as expanding access to health insurance and prohibiting denial of coverage for pre-existing conditions. Patients with SCA benefit from these changes, with greater access to specialized medical services and preventive therapies. However, even with these improvements, financial and social barriers persist, especially for racial minorities and low-income populations (Leonard *et al*., 2018).

Patients with sickle cell disease benefit from continuous follow-up in specialized centers, where a multidisciplinary team can monitor the evolution of symptoms and manage associated complications. However, the availability of such centers is still limited, even in countries with well-structured health systems, which makes access to treatment a challenge for many patients (Azar *et al*., 2017). In Bahia, there are support centers for people with sickle cell anemia, such as the Bahian Association of People with Sickle Cell Disease (ABADFAL), located in Salvador/BA, and the State Reference Center for People with Sickle Cell Anemia, located in Salvador/BA, managed by the Hemoba Foundation, which is also responsible for the State Blood Bank, which is a reference in the care of patients with sickle cell anemia in Bahia, offering transfunctional and pharmaceutical assistance. The high incidence of complications of sickle cell anemia and the lack of basic resources in low-income countries aggravate the situation, resulting in alarmingly high infant mortality associated with the disease. This scenario reinforces the urgent need to promote equitable access to advanced treatments, such as hematopoietic stem cell transplantation (John *et al*., 2022). In addition, clear and accessible communication strategies are essential to increase adherence and promote the best clinical advances in the treatment of SCA, especially for patients who depend on assistance programs to cover long-term expenses (Kumar *et al*., 2018; Sharma *et al*., 2024).

CONCLUSION

Overcoming the economic challenges associated with HSCT requires a multidimensional approach. This includes public policies to finance advanced treatments, health education programs to increase patient adherence, improvements in low-income countries, and innovative strategies to expand donor availability. With these combined efforts, it will be possible to make HSCT accessible to a greater number of patients with SCA, offering them an opportunity for effective and affordable treatment. Although hematopoietic stem cell transplantation represents a significant advance in the treatment of hematologic diseases such as sickle cell anemia, its widespread adoption requires a coordinated effort to overcome the clinical, economic, and social challenges associated with this procedure. Reducing clinical risks, reducing economic barriers, and promoting equity in access to treatment are essential to ensuring that the benefits of HSCT are widely disseminated. Only through an integrated approach, involving improvements in health infrastructure, public financing policies, and ongoing education of health professionals, will it be possible to maximize the positive impact of this innovative therapy, making it a viable and accessible option for all patients who need it.

REFERÊNCIAS

Abraham, A., Jacobsohn, D. A., & Bollard, C. M.Catherine M. Cellular therapy for sickle cell disease. Cytotherapy, v. 18, n. 11, p. 1360-1369, 2016.

ADASHI, Eli Y.; GRUPPUSO, Philip A.; COHEN, I. Glenn. CRISPR therapy of sickle cell disease: the dawning of the gene editing era. The American journal of medicine, p. S0002-9343 (23) 00798-2, 2024.

Arnold, S. D., Bhatia, M., Horan, J., & Krishnamurti, L.Haematopoietic stem cell transplantation for sickle cell disease–current practice and new approaches. British journal of haematology, v. 174, n. 4, p. 515-525, 2016.

Azar, S., & Wong, T. E. Sickle cell disease: a brief update. Medical Clinics, v. 101, n. 2, p. 375-393, 2017.

Azevedo, J. T. C., Costa, T. C. D. M., Lima, K. C., Maciel, T. T., Palma, P. V. B., Darrigo-Júnior, L. G., ... & Malmegrim, K. C. R. Long-term effects of allogeneic hematopoietic stem cell transplantation on systemic inflammation in sickle cell disease patients. Frontiers in Immunology, v. 12, 2021.

Ballas, S. K., Kuypers, F. A., Gordeuk, V. R., Hankins, J. S., Thompson, A. A., & Vichinsky, E. Time to rethink haemoglobin threshold guidelines in sickle cell disease. British Journal of Haematology, v. 195, n. 4, p. 518-522, 2021.

Bhatia, M., Kolva, E., Cimini, L., Jin, Z., Satwani, P., Savone, M., ... & Sands, S. Health-related quality of life after allogeneic hematopoietic stem cell transplantation for sickle cell disease. Biology of Blood and Marrow Transplantation, v. 21, n. 4, p. 666-672, 2015.

Brandow, A. M., & Liem, R. I.Advances in the diagnosis and treatment of sickle cell disease. Journal of Hematology & Oncology, v. 15, n. 1, p. 20, 2022.

Cairo, MS, & Savani, BN. Transplante de células progenitoras hematopoiéticas em adultos com anemia falciforme

sintomática: chegou a hora. British Journal of Hematology , v. 192, n. 4, 2021.

Cappelli, B., Volt, F., Tozatto-Maio, K., Scigliuolo, G. M., Ferster, A., Dupont, S., ... & Gluckman, E. Risk factors and outcomes according to age at transplantation with an HLA-identical sibling for sickle cell disease. Haematologica, v. 104, n. 12, p. e543, 2019.

Crossley, M., Christakopoulos, G. E., & Weiss, M. J.Effective therapies for sickle cell disease: are we there yet?. Trends in Genetics, v. 38, n. 12, p. 1284-1298, 2022.

DALLE, Jean-Hugues. Hematopoietic stem cell transplantation in SCD. Comptes Rendus. Biologies, v. 336, n. 3, p. 148-151, 2013.

Demirci, S., Uchida, N., & Tisdale, J. F. Gene therapy for sickle cell disease: An update. Cytotherapy, v. 20, n. 7, p. 899-910, 2018.

Eapen, M., Brazauskas, R., Williams, D. A., Walters, M. C., St Martin, A., Jacobs, B. L., ... & Horowitz, M. M. Secondary neoplasms after hematopoietic cell transplant for sickle cell disease. Journal of Clinical Oncology, v. 41, n. 12, p. 2227-2237, 2023.

EATON, William A. Impact of hemoglobin biophysical studies on molecular pathogenesis and drug therapy for sickle cell disease. Molecular aspects of medicine, v. 84, p. 100971, 2022.

Ferraresi, M., Panzieri, D. L., Leoni, S., Cappellini, M. D., Kattamis, A., & Motta, I. Therapeutic perspective for children and young adults living with thalassemia and sickle cell disease. European Journal of Pediatrics, v. 182, n. 6, p. 2509-2519, 2023.

Fitzhugh, C. D. Knowledge to date on secondary malignancy following hematopoietic cell transplantation for sickle cell disease. Hematology, v. 2022, n. 1, p. 266-271, 2022.

Fitzhugh, C. D., Abraham, A. A., Tisdale, J. F., & Hsieh, M. M.Hematopoietic stem cell transplantation for patients with sickle cell disease: progress and future directions. Hematology/Oncology Clinics, v. 28, n. 6, p. 1171-1185, 2014.

Gallo, A. M., Patil, C., Adeniyi, T., Hsu, L. L., Rondelli, D., & Saraf, S.Health-related quality of life and personal life goals of adults with sickle cell disease after hematopoietic stem cell transplantation. Western journal of nursing research, v. 41, n. 4, p. 555-575, 2019.

George, S. A., Lai, K. W., Lewis, R. W., Bryson, E. W., Haight, A. E., & Meacham, L. R. Comparison of anti-Mullerian hormone levels pre-and post-hematopoietic cell transplantation in pediatric and adolescent females with sickle cell disease. Transplantation and Cellular Therapy, v. 28, n. 11, p. 770. e1-770. e6, 2022.

Germino-Watnick, P., Hinds, M., Le, A., Chu, R., Liu, X., & Uchida, N.Hematopoietic stem cell gene-addition/editing therapy in sickle cell disease. Cells, v. 11, n. 11, p. 1843, 2022.

Gluckman, E., Cappelli, B., Bernaudin, F., Labopin, M., Volt, F., Carreras, J., ... & Eapen, M.Sickle cell disease: an international survey of results of HLA-identical sibling hematopoietic stem cell transplantation. Blood, The Journal of the American Society of Hematology, v. 129, n. 11, p. 1548-1556, 2017.

Gorur, V., Kranc, K. R., Ganuza, M., & Telfer, P. Haematopoietic stem cell health in sickle cell disease and its implications for stem cell therapies and secondary haematological disorders. Blood Reviews, v. 63, p. 101137, 2024.

Guilcher, G. M., Truong, T. H., Saraf, S. L., Joseph, J. J., Rondelli, D., & Hsieh, M. M. Curative therapies: Allogeneic hematopoietic cell transplantation from matched related donors using myeloablative, reduced intensity, and nonmyeloablative conditioning in sickle cell disease. In: Seminars in hematology. WB Saunders, 2018. p. 87-93.

Hoang, D. M., Pham, P. T., Bach, T. Q., Ngo, A. T., Nguyen, Q. T., Phan, T. T., ... & Nguyen, L. T.Stem cell-based therapy for human diseases. Signal transduction and targeted therapy, v. 7, n. 1, p. 1-41, 2022.

Hosoya, H., Levine, J., Abt, P., Henry, D., Porter, DL, & Gill, S. Toward dual hematopoietic stem-cell transplantation and solid-organ transplantation for sickle-cell disease. Blood Advances, v. 2, n. 5, p. 575-585, 2018.

Hulbert, M. L., King, A. A., & Shenoy, S. Organ function indications and potential improvements following curative therapy for sickle cell disease. Hematology, v. 2022, n. 1, p. 277-282, 2022.

Jang, T., Mo, G., Stewart, C., Khoury, L., Ferguson, N., Egini, O., ... & Lim, S. H. Hematopoietic stem cell transplant for sickle cell disease: patient selection and timing based on sickle cell-related multiple chronic conditions. Cell Transplantation, v. 30, 2021.

John, T. D., Namazzi, R., Chirande, L., & Tubman, V. N. Global perspectives on cellular therapy for children with sickle cell disease. Current opinion in hematology, v. 29, n. 6, p. 275-280, 2022.

Justus, D., Perez-Albuerne, E., Dioguardi, J., Jacobsohn, D., & Abraham, A. Allogeneic donor availability for hematopoietic stem cell transplantation in children with sickle cell disease. Pediatric blood & cancer, v. 62, n. 7, p. 1285-1287, 2015.

Kanter, J., Liem, RI, Bernaudin, F., Bolaños-Meade, J., Fitzhugh, CD, Hankins, JS, ... & Tisdale, J. American Society of Hematology 2021 guidelines for sickle cell disease: stem cell transplantation. Blood advances, v. 5, n. 18, p. 3668-3689, 2021.

Kassim, A. A., & Sharma, D. Hematopoietic stem cell transplantation for sickle cell disease: The changing landscape. Hematology/oncology and stem cell therapy, v. 10, n. 4, p. 259-266, 2017.

Khemani, K., Ross, D., Sinha, C., Haight, A., Bakshi, N., & Krishnamurti, L. Experiences and decision making in hematopoietic stem cell transplant in sickle cell disease: patients' and caregivers' perspectives. Biology of Blood and Marrow Transplantation, v. 24, n. 5, p. 1041-1048, 2018.

Kogel, F., Hakimeh, D., Sodani, P., Lang, P., Kühl, J. S., Hundsdoerfer, P., ... & Schulte, J. H.Allogeneic hematopoietic stem cell transplantation from sibling and unrelated donors in pediatric patients with sickle cell disease—a single center experience. Pediatric Transplantation, v. 25, n. 2, 2021.

Kumar, A., Ahmed, J., Anwar, A., Fanucchi, M., & Lim, S. H. Applicability of and potential barriers preventing allogeneic stem cell transplant in sickle cell patients treated outside a sickle cell program. American Journal of Hematology, v. 93, n. 6, p. E150-E152, 2018.

Lawal, R. A., Walters, M. C., & Fitzhugh, C. D.Allogeneic transplant and gene therapy: evolving toward a cure. Hematology/oncology clinics of North America, v. 36, n. 6, p. 1313-1335, 2022.

Leonard, A., & Tisdale, J. F. Stem cell transplantation in sickle cell disease: therapeutic potential and challenges faced. Expert review of hematology, v. 11, n. 7, p. 547-565, 2018.

Leonard, A., Tisdale, J., & Abraham, A.Curative options for sickle cell disease: haploidentical stem cell transplantation or gene therapy?. British journal of haematology, v. 189, n. 3, p. 408-423, 2020.

Meacham, L. R., George, S., Veludhandi, A., Pruett, M. C., Haight, A. E., Arnold, S. D., ... & Krishnamurti, L. Female Reproductive Health Outcomes after Hematopoietic Cell Transplantation for Sickle Cell Disease: Is Reduced Intensity Better Than Myeloablative Conditioning?. Transplantation and Cellular Therapy, v. 29, n. 8, p. 531. e1-531. e4, 2023.

Meier, ER, Johnson, T., Pinkney, K., Velez, MC, Kamani, N., & Odame, I. Acesso ao transplante de células-tronco hematopoiéticas para pacientes com anemia falciforme. Pediatric Blood & Cancer , v. 65, n. 9, p. 27105, 2018.

Montalembert, M., Brousse, V., Chakravorty, S., Pagliuca, A., Porter, J., Telfer, P., ... & Rees, D. C. Are the risks of treatment to cure a child with severe sickle cell disease too high?. Bmj, v. 359, 2017.

Nickel, R. S., & Kamani, N. R. Ethical challenges in hematopoietic cell transplantation for sickle cell disease. Biology of Blood and Marrow Transplantation, v. 24, n. 2, p. 219-227, 2018.

ÖZDOĞU, Hakan; BOĞA, Can. Hematopoietic stem cell transplantation in adult sickle cell disease: problems and solutions. Turkish Journal of Hematology, v. 32, n. 3, p. 195, 2015.

Patel, A., Wilkerson, K., Chen, H., Sharma, D., Byrne, M., Green, J., ... & Kassim, A. Reduction in the prevalence of thrombotic events in sickle cell disease after allogeneic hematopoietic transplantation. Transplantation and Cellular Therapy, v. 28, n. 5, p. 277. e1-277. e6, 2022.

Rostami, T., Rad, S., Rostami, M. R., Mirhosseini, S. A., Alemi, H., Khavandgar, N., ... & Mousavi, S. A. Hematopoietic stem cell transplantation in sickle cell disease: A multidimentional review. Cell Transplantation, v. 33, 2024.

Rotin, LE, Viswabandya, A., Kumar, R., Patriquin, CJ, & Kuo, KH.A systematic review comparing allogeneic hematopoietic stem cell transplant to gene therapy in sickle cell disease. Hematology, v. 28, n. 1, 2023.

Scott, AR. Stem cells: Creating a cure-all. Nature, v. 515, n. 7526, p. S14-S15, 2014.

Sharma, A., Young, A., Carroll, Y., Darji, H., Li, Y., Mandrell, B. N., ... & Johnson, L. M. Gene therapy in sickle cell disease: Attitudes and informational needs of patients and caregivers. Pediatric blood & cancer, v. 70, n. 6, p. e30319, 2023.

Shenoy, S., Gaziev, J., Angelucci, E., King, A., Bhatia, M., Smith, A., & Walters, M. C. Late effects screening guidelines after hematopoietic cell transplantation (HCT) for hemoglobinopathy: consensus statement from the second pediatric blood and marrow transplant consortium international conference on late effects after pediatric HCT. Biology of Blood and Marrow Transplantation, v. 24, n. 7, p. 1313-1321, 2018.

Shet, A. S., & Thein, S. L. Therapeutic advances in sickle cell disease in the last decade. Indian Journal of Medical Research, v. 145, n. 6, p. 708-712, 2017.

Silva-Pinto, A. C., Costa, F. F., Gualandro, S. F. M., Fonseca, P. B. B., Grindler, C. M., Souza Filho, H. C., ... & Cançado, R. D. Economic burden of sickle cell disease in Brazil. PLoS One, v. 17, n. 6, 2022.

Silva, W. S., De Oliveira, R. F., Ribeiro, S. B., Da Silva, I. B., De Araújo, E. M., & Baptista, A. F. Screening for structural hemoglobin variants in Bahia, Brazil. International journal of environmental research and public health, v. 13, n. 2, p. 225, 2016.

Smith-Whitley, K. Reproductive issues in sickle cell disease. Hematology 2014, the American Society of Hematology Education Program Book, v. 2014, n. 1, p. 418-424, 2014.

Stenger, EO, Shenoy, S., & Krishnamurti, L. How I treat sickle cell disease with hematopoietic cell transplantation. Blood, The Journal of the American Society of Hematology, v. 134, n. 25, p. 2249-2260, 2019.

Ware, R. E., & Quinn, C. T. The bold promise of gene therapy for sickle cell disease. British Journal of Haematology, v. 204, n. 2, p. 381-382, 2024.

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