ORIGINAL ARTICLE

POST HEMATOPOIETIC STEM CELL TRANSPLANTATION: COST ANALYSIS OF INFECTIONS IN THE FIRST YEAR POST-TRANSPLANT

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Highlights: 1. Infections occurred in 51% of patients in the first year post-transplant. 2. Infections were more frequent in the first 100 days post-transplant. 3. Infections increased both hospitalization time and costs.

PRE-PROOF

(as accepted)

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ABSTRACT

Objective: This study aims to analyze the costs associated with infections within the first year after hematopoietic stem cell transplantation. **Methods:** An analytical, cross-sectional study was conducted using data from patients diagnosed with hematologic cancer who underwent hematopoietic stem cell transplantation in 2018 and were aged 18 years or older at the time of transplantation. Descriptive analyses and correlations between variables were performed. **Results:** Of 71 patients, 36 experienced infections. The highest mean number of infections was

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observed in the haploidentical transplant group (44% vs 9%, p<0.001). Regarding the underlying diseases, the group with infections showed a higher frequency of leukemias (42% vs. 14%, p=0.012). Parameters associated with poor prognosis such as three or more hospitalizations (22% vs 3%, p=0.04), prolonged hospital stay (22.5 [IQR=21-55] vs 19 [IQR=16-23] days, p<0.001), and increased mortality (42% vs 14%, p=0.01) were associated with the presence of infection. The infection group had a significantly higher median cost than the infection-free group (5 5519.8 [25 618.8 - 73 806.6] versus 23 872.5 [23 657.7 - 24 927.6] Brazilian reais, p<0.001). **Conclusions:** Infections pose a significant barrier to transplant success, contributing to increased mortality and complications, thereby escalating the costs associated with hospitalization and procedures.

Keywords: Hematopoietic Stem Cell Transplantation. Infections. Costs and Cost Analysis.

INTRODUCTION

Hematologic neoplasms (HN) are cancers that arise from hematopoietic cells [1]. Therefore, NH can be clinically classified into leukemias, lymphomas, multiple myelomas, plasma cell neoplasms, and myelodysplastic syndromes (MDS) [2].

According to the Brazilian National Cancer Institute (INCA), cancer is a major public health problem in the country, with estimates for Brazil, in the period 2020 to 2022, that for each year of occurrence, there are about 625 thousand new cases. In Brazil, non-Hodgkin's lymphoma is among the 10 most common cancers in men and women, while leukemia ranks 10th in men and 11th in women [3].

However, there are several therapeutic options for the treatment of NH, which consist of the administration of one or more chemotherapeutic drugs or immunotherapies, radiotherapy and hematopoietic stem cell transplantation (HSCT) to replace deficient cells with healthy cells, from the patient's own body or from a donor, depending on the underlying disease [4].

Transplantation can be autologous (when the bone marrow or bone marrow progenitor cells come from the individual being transplanted or the recipient) or allogeneic (when the cells come from another donor). Transplantation can also be performed using bone marrow progenitor cells from a donor's circulating blood, umbilical cord blood, or from the bone marrow itself obtained by aspiration [5].

HSCT is performed worldwide, primarily in wealthier, developed and developing countries. A 2006 retrospective study of patients undergoing autologous and allogeneic HSCT

collected data from 1,327 centers in 71 countries participating in the Worldwide Network for Blood and Marrow Transplantation. The study identified 50,417 initial HSCT cases, including 21,516 allogeneic (43%) and 28,901 autologous (57%) procedures. Average HSCT rates varied by region and country: 48.5 (range, 2.5-505.4) in the Americas, 184 (range, 0.6-488.5) in Asia, 268.9 (range, 5.7-792.1) in Europe, and 47.7 (range, 2.8-95.3) in the Eastern Mediterranean and Africa. Notably, no HSCT procedures were performed in countries with a population of less than 300,000, a land area of less than 960 km^2, or a gross national income per capita of less than $680.00 [6].

In Brazil, 1,695 HSCT cases were recorded in 2010, increasing to 3,490 in 2019. The Northern Region accounted for 2 (2.1%) and the Central-Western Region for 936 (5.3%) of the transplants performed, while the Southeastern Region contributed the majority with 13,317 (50.1%) procedures, followed by the Southern Region with 5,005 (26.3%) and the Northeastern Region with 3,580 (16.2%), for a total of 22,840 procedures in recent years [7]. Specifically, in Ceará, stem cell transplants have been performed for 13 years, reaching 610 HSCTs by September 2021 [8].

However, patients may experience early complications after transplantation, including engraftment failure, rejection, and graft-versus-host disease (GVHD). Graft failure and rejection occur in less than 5% of patients and typically present as persistent pancytopenia or an irreversible decrease in red blood cell count. Treatment typically includes corticosteroids administered over several weeks [9]. In addition, bone marrow recipients may experience early (< 100 days post-transplant) or late complications that contribute to increased healthcare costs [10].

Along these lines, Schelfhout *et al.* (2020) examined the impact of CMV (cytomegalovirus) infection on hospital service utilization and costs during the first 100 days after allogeneic hematopoietic stem cell transplantation. They found that the average total cost of healthcare services (hospitalizations and outpatient visits) during the follow-up period was significantly higher for patients who experienced CMV-related readmissions ($111,729 for one CMV-related readmission; $184,021 for two or more CMV-related readmissions) compared with those without CMV-related readmissions ($46,064) [11].

Using a similar study framework, but extending the observation period to 180 days, Ueno *et al.* (2019) found that the average total medical costs over 180 days following allogeneic transplantation were $122,328 in the CMV-positive group, while the average total medical costs

were $75,344 in the CMV-negative group [12].

HSCT is a complex procedure that can impose significant costs on healthcare institutions in a time of scarce resources. In addition, the incidence of post-transplant infections in patients can add to these hospital costs, a concern for managers within the Brazilian Unified Health System (SUS) [13].

This research is justified in its aim to contribute to the healthcare organization by developing cost management strategies for the procedure. It aims to assist in the formulation of care protocols and provide insights for resource allocation. This endeavor can provide economic data for managers to improve processes and assist in the implementation of a cost center within the institution. In addition, it can provide parameters regarding the incidence of post-transplant infections, as the treatment of infections is associated with an increased risk of readmission and prolonged hospitalization.

Therefore, the guiding question was: "What are the costs of infections in post-hematopoietic stem cell transplant patients to the Unified Health Care System?" In this context, the study aims to analyze the costs of infections in patients who have undergone hematopoietic stem cell transplantation within the first year after transplantation.

METHOD

An analytical, cross-sectional study was conducted using the medical records of patients seen at the hematology outpatient clinic in a specialized HSCT unit in the North-Northeast regions. The study period spanned from 2018 to 2019 and included the one-year post-HSCT follow-up period for patients.

The study was conducted at the Hematology Outpatient Clinic of Walter Cantídio University Hospital (HUWC) and the Hematology and Hemotherapy Center of Ceará (HEMOCE), both recognized as HSCT centers in the North-Northeast regions. HUWC is part of the hospital complex managed by the Brazilian Society of Hospital Services (EBSERH). This facility provides highly complex care and serves as a referral center for kidney, liver and bone marrow transplants, the latter having reached a milestone of 610 HSCTs in Ceará 7.

All 71 medical records of patients who underwent the procedure in 2018 were analyzed, 43 autologous, 20 related allogeneic, 04 unrelated allogeneic (NAP), and 04 haploidentical, aged 18 years or older. Medical records of individuals aged between 18 and 66 years were included, as this is the age range in which HSCT is performed at this institution

during the study period, with the types of HSCT being: autologous, related and unrelated allogeneic, and haploidentical 14 Medical records with incomplete information or data inconsistencies were excluded. Data collection was performed by the principal investigator of the study.

The following patient information was used to extract costs: Individual Hospitalization Authorization Number, National Registry of Health Establishments, patient name, date of birth, year of eligibility, municipality, state, address, procedures performed, primary diagnosis, hospital admission and discharge dates. Direct costs included in the AIH included various aspects such as type of transplant, physiotherapy sessions, pre-transfusion tests, infusion of blood components, biochemical and hematological tests, hemostasis tests, imaging tests, blood cultures, biopsies, endoscopies, electrocardiograms, bronchoscopies, inhalation/nebulization, cyclosporine dosage, daily attendant fees for elderly patients, post-transplant medications, anatomopathological examinations, among others.

All procedural costs were aggregated with transplant costs, covering the period from admission to hospital discharge. The methodology used to assess the cost of infections in patients undergoing HSCT included hospital admissions, infection diagnoses, and outpatient treatment after hospital discharge.

First, patients who underwent transplantation during the study period were identified from a list provided by the HSCT unit. From this list, patient identification, age, sex, medical record numbers, transplant dates, and transplant types were obtained.

Individual patient records were then accessed using their identification numbers. Requests were then made to the Assistance Information Processing Unit for all approved AIHs during the immediate one-year post-transplant period, with reference to HSCT competence. Using spreadsheets provided by the UPIA, the costs of all AIHs were summed for each patient, considering the number of hospitalizations during the first year post-transplant.

Medical records were the primary data source for identifying the infection variable. Information was collected from discharge summaries provided by the treating physician in the HSCT service and from post-transplant outpatient consultations. In cases where the type of infection was not specified in the discharge summary, a search was conducted through daily nursing and medical progress notes. If it was not possible to determine whether a patient had experienced an infection, culture results from laboratory tests available in the hospital's integrated health management system (MASTER) were reviewed.

Infections were categorized into five groups (bacterial, fungal, viral, viral and bacterial, viral, bacterial, and fungal). Infection identification included any period within the one-year horizon, whether during hospitalization or post-discharge outpatient follow-up.

The following control variables were selected Gender (male, female), age, marital status (married, single, divorced, in a stable union, widowed), education (literate, illiterate, high school graduate, high school graduate, college graduate, college graduate), race/ethnicity (mixed race, white), religion (Catholic Protestant), smoking, alcohol use, underlying medical conditions, number of hospitalizations, length of stay, type of transplant (autologous, allogeneic, haploidentical, haploidentical), number of days hospitalized (sum of all AIHs in the first year after transplant), and mortality (yes, no).

For statistical analysis, qualitative variables were expressed as absolute numbers and percentages. All quantitative variables were tested for normal distribution using the Kolmogorov-Smirnov test. Normally distributed data were presented as mean ± standard deviation, while non-normally distributed data were presented as median and interquartile range. Comparisons between qualitative data were made using the chi-squared test and Fisher's exact test, as appropriate. Comparisons of quantitative data between groups were made using Student's t-test or Mann-Whitney test based on normal or non-normal distribution, respectively.

In addition, simple and multiple linear regression analyses were performed with financial costs as the dependent variable. Univariate analysis was first performed to examine the isolated association of each variable with costs. Subsequently, multivariate analysis was performed by sequentially adding variables according to theoretical criteria to evaluate the independent relationship of selected parameters (sex, age, type of transplant, underlying diseases, and type of viral infection) with costs, highlighting variables with $p<0.10$ in the final model. Diagnoses of collinearity between independent variables were checked using tolerance and variance inflation factors (VIF) before inclusion in the multivariate models. Data were analyzed using the Statistical Package for the Social Sciences (SPSS), version 23.

Ethical principles were followed in all phases of the study in accordance with Resolution 466/2012, approved by the Research Ethics Committee under protocol number: 43965121.3.0000.5045.

RESULTS

To investigate factors related to infections in patients who received HSCT, we sought to identify the relationship between sociodemographic and clinical characteristics and costs with the presence of post-transplant infection. The 71 patients were divided into two groups, one with and one without infections, of which 36 had infections. The relationship of other parameters such as the presence of infections, type of transplant, underlying disease, type of infection, number of hospitalizations, length of stay, death, and financial costs was observed (Table 1).

Parameters associated with poor prognosis, such as a higher number of hospitalizations, longer hospital stays, and a higher incidence of death, were associated with the presence of infection. In the group of patients with infections, there was a prevalence of three or more hospitalizations (22% vs 3%, p=0.04). There was a longer median length of stay in the group with infections (22.5 [AIQ=21-55] versus 19 [AIQ=16-23] days, p<0.001). Finally, there was a higher prevalence of death in the infection group (42% vs. 14%, p=0.01) (Table 1).

Regarding financial costs, the group with infections had a significantly higher median than the group without infections (55,519.8 (25,618.8 - 73,806.6) versus 2,3892.5 (23,657.7 - 24,993.4) Brazilian reais, p<0.001) (Table 1).

An increased frequency of allogeneic transplants (44% vs 9%, p<0.001) and a decreased frequency of autologous transplants (33% vs 88%, p<0.001) were observed in patients with infections. Regarding the underlying disease, the group with infections had a higher frequency of leukemias (42% vs. 14%, p=0.012) and patients with multiple myeloma had a lower frequency of infections (19% vs. 54%, p=0.012).

Table 1. Clinical characteristics, type of transplant and costs according to the evolution of infections in patients undergoing HSCT in 2018 and 2019, in a reference hospital. Fortaleza, Ceará, Brazil, 2022.

Infections	**No (n=35)**	**Yes (n=36)**	**p**
Sex			.285
Male	15 (42.9)	20 (55.6)	
Female	20 (57.1)	16 (44.4)	
Age (years)	46 ± 14	43 ± 16	.491
Transplant type			0.001
Autologous	30 (88.2)	12 (33.3)	
Allogeneic	3 (8.8)	16 (44.4)	
Haploidentical	1 (2.9)	4 (11.1)	
Nonmyeloablative	0 (0)	4 (11.1)	
Underlying condition			.012
Leukemia	5 (14.3)	15 (41.7)	
Lymphoma	7 (20)	8 (22.2)	
Multiple myeloma	19 (54.3)	7 (19.4)	
Other	4 (11.4)	6 (16.7)	
Number of hospitalizations			.04
1	28 (80)	22 (61.1)	
2	5 (14.3)	6 (16.7)	
3	1 (2.9)	4 (11.1)	
4	1 (2.9)	3 (8.3)	
5	0 (0)	1 (2.8)	
Length of stay (days)	19 (16 - 23)	28.5 (21.5 - 55.5)	0.001
Death			.01
No	30 (85.7)	21 (58.3)	
Yes	5 (14.3)	15 (41.7)	
Cost (R$)	23 892.5 (23 657.7 – 24 933.4)	5 5519.8 (25 618.8 – 73 806.6)	0.001

Qualitative data expressed as absolute count in percentages in parentheses. Quantitative data expressed as mean ± standard deviation for normal data or as median and interquartile range in parentheses for non-normal data. *Chi-

square test and Fisher's exact test were used to compare qualitative data and the Student's t-test or Mann-Whitney test were used to compare quantitative data, as appropriate.

Regarding the factors associated with higher economic costs for patients who received HSCT, Table 2 shows all categorical parameters with their respective sample sizes and the financial costs of each category to evaluate the association of these factors with higher costs. No association was found between gender and financial costs.

Table 2. Factors associated with higher economic costs in patients who received HSCT in 2018 and 2019, in a reference hospital. Fortaleza, Ceará, Brazil, 2022.

Variables		**Cost (R$)**			
	n	**Median**	**25th percentile**	**75th percentile**	**P***
Sex					0.565
Male	35	24933.4	23 828.7	55 448.9	
Female	36	25209.8	23 810.7	57 158.2	
Infection					<0.001
No	35	23892.5	23 657.7	24 933.4	
Yes	36	55519.8	25 618.8	73 806.6	
Type of infection					
Viral infection	12	76303.1	57 931.7	79 942.6	0.004
Bacterial infection	22	44390.8	24 179.9	72 313.9	0.147
Fungal infection	9	59929.3	56 221.1	79 080.6	0.113
Underlying condition					<0.001
Leukemia	2	58377.8	55 178.5	79 942.6	

	0			
Lymphoma	1	24103.2	23 892.5	33 332.7
	5			
Multiple myeloma	2	23869.9	23 657.7	24 927.6
	6			
Other	1	55618.7	24 355.9	66 141.7
	0			

*The Mann-Whitney test was used for comparisons between two groups, and the Kruskal-Wallis for comparison of the "base disease". # A significant difference was observed between "leukemias" vs "lymphomas" and "multiple myeloma", and between "others" vs "lymphomas" and "multiple myeloma".

Table 3. Classification regarding the type of transplantation in relation to a higher economic cost in patients who received HSCT in 2018 and 2019, in a reference hospital. Fortaleza, Ceará, Brazil, 2022.

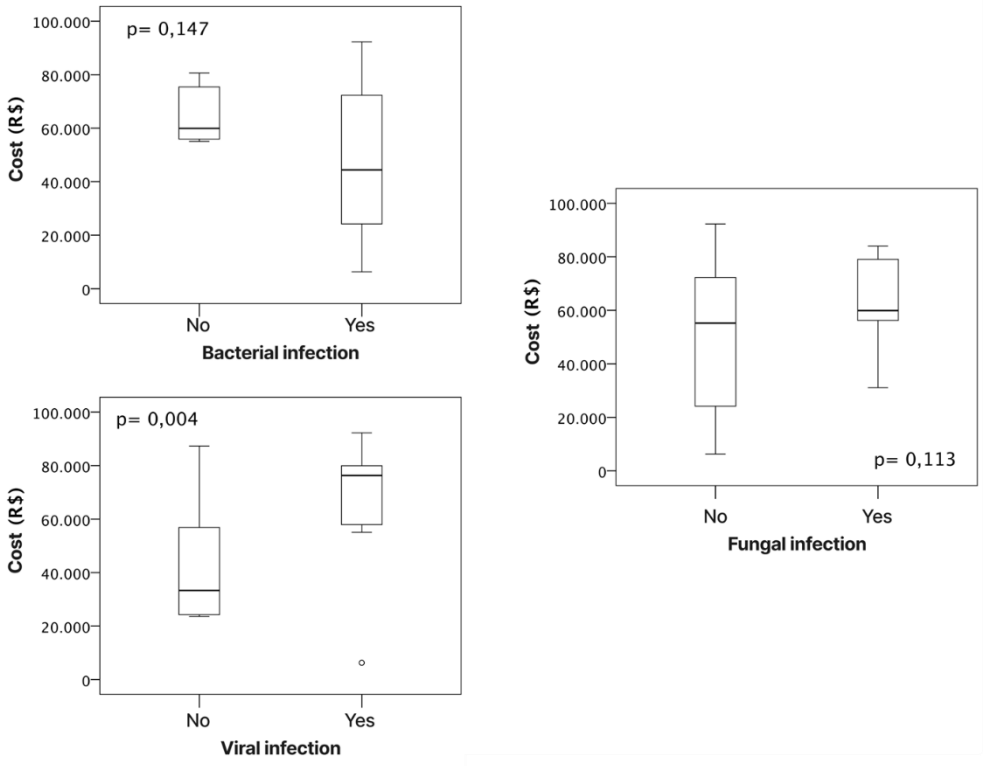
Variables		**Cost (R$)**			
		Median	**25th percentile**	**75th percentile**	**p***
Type of transplant					
Autologous					<0.001
No	2	58377.8	55 519.8	76 303.1	
	8				
Yes	4	24000.7	23 710.3	24 702.6	
	2				
Allogeneic					<0.001
No	51	24 061.9	23 713.8		31 109.5
Yes	19	56 758.4	55 448.9		65 610.3
Haploidentical					0.155
No	65	24 927.6	23 867.4		56 221.1
Yes	5	79 080.6	55 076.8		79 290.9
Nonmyeloablative					0.001
No	66	24 815.1	23 828.7		55 934.1

Yes	4	78 004.4	73 864.1	86 440.1

*The Mann-Whitney test was used for comparisons between two groups, and the Kruskal-Wallis test was used to compare the "underlying disease". # A significant difference was observed between "leukemias" vs "lymphomas" and "multiple myeloma", and between "others" vs "lymphomas" and "multiple myeloma".

Regarding the type of infection, it was observed that viral infection was associated with higher financial costs (p=0.004), but when examining groups with or without bacterial or fungal infection, no statistical association was observed between the groups for financial costs (p=0.113 and 0.147, respectively). (Figure 1).

Figure 1. Costs according to the evolution of viral, bacterial, and fungal infection types in patients who received HSCT in 2018 and 2019, in a reference hospital. Fortaleza, Ceará, Brazil, 2022.



The Mann-Whitney test was used for comparisons.

Regarding the underlying disease, an association with greater financial burden was

observed. The group of patients with leukemia had higher financial expenses compared to the groups with lymphoma and multiple myeloma ($p<0.001$). In addition, patients with other underlying diseases also had higher costs compared to the lymphoma and multiple myeloma groups ($p<0.001$). Therefore, the underlying diseases lymphoma and multiple myeloma had lower financial costs (Table 2).

Regarding the type of transplantation, only autologous transplantation was associated with lower financial costs ($p<0.001$). Allogeneic and nap type transplants had higher financial costs ($p<0.05$) (Table 3). In the simple and multivariate linear regression analysis, considering the financial cost as the dependent variable, it was observed that in the univariate analysis, younger age, type of allogeneic transplant and Nap, leukemia-based diseases and viral infections were associated with higher financial costs.

Type of autologous transplant and underlying multiple myeloma were associated with lower financial costs. However, in the multivariate analysis, an independent association was observed only for the type of allogeneic transplant, the type of NAP transplant, and a statistical trend for the presence of viral and bacterial infections, with all these parameters contributing to increasing financial costs in the multivariate model (Table 4).

Table 4. Multivariate linear regression evaluating factors independently associated with the cost of care of patients who underwent HSCT in 2018 and 2019, in a reference hospital. Fortaleza, Ceará, Brazil, 2022.

	Univariate analysis			**Multivariate analysis**		
	Beta (non-standardized)	**Standard error**	**p**	**Beta (non-standardized)**	**Standard error**	**p**
Sex (female)	3 156	5 409	0.561			
Age (years)	- 648	163	0.000			
Type of transplant						
Autologous (yes)	- 36 788	3 296	0.000			
Allogeneic (yes)	26 662	5 185	0.00	44 745	16 334	0.013

			0			
Haploidentic (yes)	20 502	10 254	0.05			
			0			
Nonmyeloablative (yes)	40 775	10 611	0.00	58 335	18 061	0.004
			0			
Underlying condition						
Leukemia (yes)	30 273	4 799	0.00			
			0			
Lymphoma (yes)	- 10 267	6 525	0.12			
			0			
Multiple myeloma (yes)	- 24 157	4 817	0.00			
			0			
Other (yes)	9 852	7 702	0.20			
			5			
Infection						
Viral (yes)	24 574	7 794	0.00	25 835	13 623	0.073
			4			
Bacterial (yes)	- 17 545	9 128	0.06	24 966	12497	0.060
			4			
Fungal (yes)	15 274	9 268	0.11			
			0			

Unstandardized beta: represents changes in the cost in reais (dependent variable) for each unit of the independent variable.

DISCUSSION

Opportunistic infections may occur between 1 and 6 months after transplantation, with patients commonly affected by bacterial (listeriosis and nocardiosis), viral (BK virus, cytomegalovirus, Epstein-Barr virus, varicella-zoster virus, or hepatitis B or C virus), fungal (aspergillosis, and *Pneumocystis jirovecii* infection), varicella-zoster virus, or hepatitis B or C viruses), fungal (aspergillosis, cryptococcosis, and *Pneumocystis jirovecii* infection), or

parasitic (strongyloidiasis, toxoplasmosis, trypanosomiasis, and leishmaniasis) infections [15].

Regarding the causative agents of infection, other studies also highlight bacteria as the primary culprits, particularly *Klebsiella pneumoniae* and *Klebsiella species* [10,15,16,17]. The development of post-HSCT infections is associated with increased morbidity and mortality, as well as increased financial costs associated with their treatment [13].

A high number of patient deaths have been observed, which may be explained by the fact that HSCT is a complex and aggressive treatment with numerous variables that need to be controlled to protect the lives of patients. Factors such as GVHD, post-transplant relapse, and infection are cited as major causes of failure and mortality [18]. Despite the significant mortality rate, a significant proportion of patients survive HSCT and require support and care throughout the various stages of treatment.

The mortality risk associated with HSCT has improved significantly over the past decade, with a reduction of more than 50% in non-relapse mortality (NRM) and improved long-term survival after HSCT. This improvement is largely due to the introduction of reduced-intensity conditioning regimens, which involve the administration of potent chemotherapeutic agents to destroy neoplastic cells while preventing the recipient's immune system from attacking the donated cells [19].

Studies indicate that the first one hundred days are a critical period of recovery because the patient is more susceptible to infections and other acute complications, requiring careful attention to avoid the occurrence of conditions that predispose to the risk of death. This increased vulnerability results from progressive leukopenia, making the patient susceptible to bacterial, fungal, viral, or other parasitic infections [20].

The treatment of patients with hematopoietic cancers imposes high costs on the public health system, as seen in the reference hospital of the State of Ceará. It is important to understand that the process of developing cancer is a public health issue. In this context, the option of tertiary care, with a focus on highly complex and costly health procedures and treatments, to the detriment of prevention and health promotion, as guaranteed by the 1988 Constitution, favors and naturalizes the marketing logic of health care [21].

In addition, the treatment is complex because it requires the use of immunosuppressive drugs, which very significantly reduce the immunity of the users subjected to it [22-23]. In other words, the individual is exposed to poor health, which requires a lot of care and special conditions for life after the procedure [21]. According to the Brazilian Ministry of Health, Brazil

is a world reference in the field of transplantation and has the largest public transplantation system in the world. Currently, about 96% of the procedures in the country are financed by the SUS. In the case of transplants performed in the SUS, patients receive comprehensive support from the public health network, including preparatory examinations, surgery, follow-up care and post-transplant medication [24].

The financial cost of treating patients who have undergone HSCT is used to purchase medicines, supplies, equipment, to maintain their hospitalization, especially the most complex, so that this material can be used more quickly. This phenomenon occurs in the patients evaluated, without considering the usefulness, the cost-benefit, in relation to the epidemiological profile of the population served, since what is known is the amount spent on the procedure, but the need or not for it to be carried out. is not clearly argued.

Regarding the cost of autologous transplantation being less expensive than allogeneic transplantation in this research, one study showed that hospitalization costs represent a greater component of the total cost, even compared to studies in other countries. Also, according to this study, it was possible to verify that there are higher costs for allogeneic HSCT compared to autologous HSCT [25].

In this sense, in the evaluation of 690 patients (310 allogeneic and 380 autologous), it was observed [26] that cytomegalovirus infection was associated with an increase in total costs (coefficient = 0.21, daily incremental cost estimated at US$ 500), thus being higher in allogeneic HSCT recipients (coefficient = 0.13, US$ 699 vs. US$ 613, or US$ 24,892 per transplant episode) [25]. As a result, some authors analyzed only autologous HSCT 27 and found in bivariate analyses and multivariate studies that the occurrence of >1 episode of cytomegalovirus increased the cost of allogeneic HSCT by 25-30%.

Still in the follow-up of CMV infections, a multicenter retrospective cohort study was conducted and found that all-cause mortality within one year was significantly increased in patients with treated CMV infections (risk ratio, 1.86; 95% CI, 1.16-3.00). Average medical costs during the first year were higher in patients with CMV infection (€46,853 vs. €31,318). These authors suggest that the burden of CMV disease in allogeneic transplant patients may be reduced in the future by appropriate prophylactic strategies [28].

Although there have been major advances in post-transplant supportive care over the past four decades, better strategies to prevent and manage these complications are still needed to reduce the cost of allogeneic transplantation [29].

A retrospective cohort of 102,549 patients, including 37,542 allogeneic and 65,007 autologous, transplanted in 404 centers in 25 European countries between 1996 and 2006, showed that country- and center-specific economic factors are associated with distinct, significant, systematic, and clinical effects relevant to survival after HSCT. They influence the center's experience in treating long-term conditions and complications [30].

This study was able to analyze the costs of infections in patients after hematopoietic stem cell transplantation. The results show an increase in hospital costs due to the occurrence of infections, which can directly affect the success of the proposed treatment.

As limitations of the study, the impossibility of generalizing the results is highlighted, since it covers different realities in a center in Brazil, delimited between 2018 and 2019. The design did not allow to establish the interrelationships between the factors determining the success of the HSCT process. These include health services, food, housing, leisure, employment, transportation, environmental quality, basic sanitation, among others that affect the life and survival of patients. The lack of an electronic medical record for monitoring post-HSCT in case of complications in other health institutions is also highlighted, in addition to the lack of a cost center in the hospital where the research was carried out.

Infection has been shown to be one of the major barriers to transplant success, with a high number of patients dying and developing complications. However, after bone marrow transplantation, patients are expected to have complex defects in their immune system, making them susceptible to a range of infections.

The research generated new knowledge that can innovate, guide, and direct the care of healthcare professionals with patients, families and support services for hematopoietic stem cell transplant recipients. It is therefore suggested that health care teams should be better monitored for the possible occurrence of infections. In addition, sensitive and specific techniques are needed to rapidly diagnose the onset of these infections, allowing early initiation of effective treatments, as well as to assess the immunologic status of the recipient and donor to define the risk of reactivation of these infections after transplantation.

It is also important to monitor the occurrence of diseases detected before transplantation, which could contribute to post-transplant surveillance or secondary prophylaxis. Finally, prevention and control measures for these infections are mainly related to environmental control, prophylaxis and the use of empirical or specific therapies. It is also important to emphasize the importance of continuing education of the multidisciplinary team

in the management of these patients.

In this way, the subsidies generated can serve to qualify teaching, the production of care, to modernize and update new practices, to support the reorientation of public policies aimed at the complexity of demands and innovative technologies in HSCT.

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