JOURNAL OF MARKET ACCESS & HEALTH POLICY
2023, VOL. 11, 2236851
https://doi.org/10.1080/20016689.2023.2236851

Routledge
Taylor & Francis Group

RESEARCH ARTICLE

OPEN ACCESS Check for updates

Economic analysis of allogeneic hematopoietic stem cell transplantation in the Bone Marrow Transplant Center of Tunisia

Leila Achour[a], Chema Drira[a], Mohamed Zied Sboui[a], Ikram Fazaa[a], Mohamed Ali Soussi[a], Senda Hammami[a], Tarek Ben Othman[b] and Myriam Razgallah Khrouf[a]

[a]Pharmacy department, Bone Marrow Transplant Center of Tunisia, Tunis, Tunisia; [b]Hematopoietic Stem Cell Transplantation Unit, Hematology Department, Bone Marrow Transplant Center of Tunisia, Tunis, Tunisia

ABSTRACT

Introduction: New procedures and diagnostic tests in hematopoietic stem cell transplantation (HSCT) are associated with a significant increase in costs. The last cost estimate of allogeneic HSCT done in Tunisia was in 1996 and concerned only direct medical costs. Therefore, an updated cost analysis is needed.

Objective: Analysis of direct costs during the first-year post-allogeneic HSCT in two groups of patients: Bone Marrow Transplant (Allo-BMT) and Peripheral Blood Stem Cell Transplant (Allo-PBSCT) and identification of factors leading to interindividual variations in costs in order to compare these costs with the budget allocated by the payer (CNAM).

Methods: Pharmacoeconomic retrospective study, concerning patients who underwent allogeneic HSCT in 2013. Clinical and unit cost data were obtained from medical and administration records.

Results: This study showed that the average direct cost of allogeneic HSCT in the population during the first year reached 56 638€. The average cost of Allo-BMT was 63 612€, and Allo-PBSCT was 45 966€ ($p > 0.05$). The initial hospitalization counted for 88% of total direct cost with an average cost of 41 441€ in Allo-BMT and 24 672€ in Allo-PBSCT ($p < 0.05$). Direct medical costs represented more than 70% of total direct costs, drugs, and laboratory tests occupied the largest share. Antifungals, antitumors, and antiviral drugs were the most expensive pharmaceutical classes with a mean cost, respectively, of 4 526€; 3 737€ and 3 268€. Some clinical criteria were significantly related to total direct costs like length of aplasia ($p < 0.01$) and GVHD ($p < 0.05$). However, the type of blood disease, its risk, length of mucositis, and the treatment protocol have no effect on the costs for all allogeneic patients.

Conclusion: Our results showed that the costs of Allo HSCT have exceeded by far the budget allocated by the CNAM to the center, since the 90s to this day. That's why the total reimbursement mechanism should be revised.

ARTICLE HISTORY
Received 18 April 2023
Revised 11 July 2023
Accepted 11 July 2023

KEYWORDS
Costs; allogeneic hematopoietic cell transplantation; bone marrow transplantation; peripheral blood stem cell transplantation

Introduction

Hematopoietic Stem Cell Transplantation (HSCT) has become a first-line indication for several malignant and non-malignant hematological diseases.

However, this technique has evolved over the past decade due to technological and scientific advances, which has improved outcomes and increased costs exponentially [1, 2,3].

In fact, the care required by patients with hemopathy and treated with Bone Marrow transplant (BMT) or peripheral stem cells (PSCT) has become increasingly costly, such as the introduction of new, very expensive molecules (Anti-infective, immunosuppressant, etc.) and the use of new tools for the diagnosis and follow-up of post-transplant patients (viral PCR, molecular chimerism, residual disease study, etc.).

Between 2004 and 2007, HCT was one of the 10 procedures with the greatest increase in hospital costs in the United States, from 694 million to 1.3 billion dollars [4].

In Tunisia, the National Bone Marrow Transplant Center (CNGMO) financing mechanism is based on patient classification in DRGs (DiagnosisRelated Groups). Indeed, the CNGMO signed a convention with the National Social Insurance (CNAM) in 1996 which includes 34 821€ per patient limited to the first-year post-transplant.

Furthermore, the last cost estimate of allogeneic HSCT done in Tunisia, was in 1997.

CONTACT Leila Achour leila.achourr@gmail.com Pharmacy department, Bone Marrow Transplant Center of Tunisia, Tunis, Tunisia

Thus, new cost study has become essential to estimate recent costs of HSCT in order to better identify these progresses and to analyze the evolution of these costs over time.

Patients and methods

Patients

This study was focused on all patients allowed for Allo-HSCT [BMT and PBSCT] from 1January 2013 to 31 December 2013 in CNGMO.

Study design

This is a pharmacoeconomic retrospective study, from the perspective of CNGMO, which analyzes medical and non-medical direct costs for 1 year after an allo-HSCT is performed in the hematology department of the CNGMO. The year of support begins on the first day of patient admission and lasts 1 year.

Studied variables

- **Patients' characteristics**: gender, age, allogeneic HSCT source (BMT or PSCT), blood disease (malignant or benign hemopathies), risk of blood disease, ABO compatibility and protocols were collected
- **Clinical outcomes**: Presence of Graft-Versus-Host Disease (GVHD), duration of aplasia and mucositis, number and length of all hospitalizations, and prophylaxis (primary or secondary prophylaxis) were recorded.
- **Direct costs**: Direct costs represent all the expenses directly attributed to the therapeutic management (medical and non-medical direct costs).
- In this study, direct costs included pre-transplant phase, transplantation phase, and outpatient costs during the first year following transplantation.
  - Direct medical costs included drugs, diagnostic and laboratory tests, medical devices, radiological investigations, blood products, parenteral nutrition, hygiene, and anesthesia.
  - Direct non-medical costs included medical and paramedic staff salaries, hospital expenses, and amortization.
- **Data source**: Patients' characteristics, clinical outcomes, and direct medical costs were obtained from medical individual patient records.
  Direct non-medical costs were obtained from the administration. Costs attributed to the medical and paramedical staff were accounted for from the yearly gross salary of staff involved in the treatment adjusted to the number of days spent by each patient in CNGMO. Costs attributed to hospital expenses were calculated in reference to the annual budget of the centre in 2013 granted by the Ministry of Health.
  Drug costs were calculated using purchasing product prices for 2013 according to the hospital list of drugs. The purchase of drugs is counted on the annual budget of the CNGMO pharmacy.
  Costs of biological analyses (virology, bacteriology, hematology, and biochemistry) were defined according to a national hospital codification, where each code is allocated a price.
  Costs of medical devices were those negotiated in 2013 as contracts with firms.
  Costs attributed to the medical and paramedical staff were accounted for from the yearly gross salary of staff involved in the treatment adjusted for the number of days spent by each patient in the CNGMO.
  Costs attributed to hospitalizations were calculated with reference to the annual budget of the center in 2013, granted by the Ministry of Health.
- **Statistical analysis**: To examine the equality of the means of quantitative and qualitative variables, the independent samples t test was applied, with equal variances assumed. In this statistical test, a p value less than 0.05 was considered significant.

Results

Patients' characteristics

A total of 43 patients who underwent Allo-HSCT were included in our cost analysis, they were classified on:

- 26 patients admitted for Allo-BMT.
- 17 patients admitted for Allo-PSCT.

The characteristics of the included patients are shown in Table I.

Clinical outcomes

The average length of the first hospitalization in allograft patients was 45 days ±18 days with a median of 39 days. The extreme durations were 22 days and 112 days.

Our study showed that 42% of patients had more than one hospitalization and one of them had until four hospitalizations (Table II).

Table I. Patients' characteristics.

	Allo-HCT (*n*= 43)	
	BMT (*n*=26)	PBSCT (*n*=17)
Male sex, no. (%)	16 (62%)	11 (65%)
Female sex, no. (%)	10 (38%)	6 (35%)
Age at transplant, median (range)	27 [-]48)	33 [-]50)
Mismatched no.	11	8
ABO compatibility	22	15
Protocols (%)	MyeloA: 43 (100%)	MyeloA: 14 (82%)
	NMA: 0	NMA: 3 (18%)
Blood diseases (n)	Malignant hemopathies:	Malignant hemopathies:
	AML (10)	AML (8)
	ALL (6)	ALL (2)
	CML (1)	CML (0)
	NHL (1)	NHL (5)
	MM (0)	MM (1)
	Benign hemopathy:	Benign hemopathy:
	MA (8)	MA (1)
Risks/stages of blood diseases	Malignant hemopathies:	Malignant hemopathies:
	SR (13)	SR (12)
	HR (5)	HR (4)
	Benign hemopathy:	Benign hemopathy:
	SR (8)	SR (1)

Abbreviations: ALL: Acute Lymphoblastic Leukemia; AML: Acute Myeloid Leukemia; CML: Chronic Myeloid Leukemia; GVHD: Graft-Versus-Host Disease; HR: High Risk; SR: Standard Risk; MA: Medullary Aplasia; MM: Multiple Myeloma; NHL: Non Hodgkin Lymphoma; MyeloA: Myeloablative conditioning protocols; NMA: Non-Myeloablative conditioning protocols.

Table II. Clinical outcomes.

	Allo-HSCT (*n*= 43)	
	BMT (*n*=26)	PBSCT (*n*=17)
Number of hospitalizations (%)	1 hospitalization: 15 (58%)	1 hospitalization: 8 (47%)
	2 hospitalizations: 9 (34%)	2 hospitalizations: 7 (41%)
	3 hospitalizations: 1 (4%)	3 hospitalizations: 2 (12%)
	4 hospitalizations: 1 (4%)	
Reason of hospitalization (%)	Complication: 11 (42%)	Complication: 6 (36%)
	Rejection: 0	Rejection: 0
	Relapse: 0	Relapse: 3 (18%)
Length of stay, median (range) d	65 (30–168)	49 (26–116)
Length of the initial hospitalization, median (range) d	52 (30–112)	34 (22–51)
Prophylaxis (n)	Primary prophylaxis (20)	Pri
	Secondary prophylaxis []	mary prophylaxis []
		Secondary prophylaxis []
Length of aplasia, median (range) d	31 (9–112)	13 (4-30)
Length of mucositis, median (range) d	13 (1-37)	12 (1-25)
GVHD no (%)	No GVHD: 10 (38%)	No GVHD: 6 (35%)
	Acute GVHD: 5 (19%)	Acute GVHD: 2 (11%)
	Chronic GVHD: 5 (19%)	Chronic GVHD: 4 (23%)
	Acute and chronic GVHD: 6 (23%)	Acute and chronic GVHD: 5 (30%)

The difference in the average length of the first hospitalization between Allo-BMT and Allo-PBSCT was statistically significant ($p < 0.001$)

Total direct costs

The average cost of Allo-HSCT in the population during the first-year post-transplant attended 56 638€ with a minimum of 25 051€ and a maximum of 196 824€. The median of total direct cost was 44 495€.

Results showed that Allo-BMT was more expensive than Allo-PBSCT. Indeed, the mean cost in Allo-BMT was 63 612€ (Min: 25 051€; Max: 196 824€; Median: 52 161€) and the mean cost in Allo-PBSCT was 45 966€ (Min: 28 712€; Max: 89 739€; Median: 41 117€), but this difference was not significant between the two groups ($p < 0.05$)

The costs related to hospitalization were the major cost contributors across this study and the relation between the length of stay and total direct costs for all allogeneic patients was significant ($p < 0.01$) with a correlation coefficient of 0.910.

The costs associated with the initial hospitalization were the main driver of total costs in the first 100 days post transplantation and the most expensive costs during the post-transplant year for all patients with an average cost of 34 811€ which represent 88% of total

direct cost. The relationship between costs of the initial hospitalization and total costs during the post-transplant year was statistically significant ($p < 0.01$).

The average cost of the initial hospitalization for Allo-BMT and Allo-PBSCT was, respectively, 41 441€ and 24 672€ and the difference was statistically significant ($p < 0.05$).

Some clinical criteria were significantly related to total direct costs in Allo-HSCT: length of aplasia. In fact, the link between the length of aplasia and total direct costs was positive for allogeneic patients ($p < 0.01$).

Nevertheless, analyses showed that the type of blood disease, its risk, length of mucositis, and the protocol have not any effect on the costs for all allogeneic patients.

Direct medical costs represent 74% of total direct cost (Table III).

Drugs and laboratory tests were the most costly medical items (Table IV).

The relationship between costs of drugs and total medical costs, on the one hand, and costs of laboratory tests and total direct costs, on the other hand, were statistically significant ($p < 0.05$) with correlation factors, respectively, 0.988 and 0.811.

Similar results have been found for Allo-BMT and Allo-PBSCT: direct medical costs were the most costly in direct costs (74.79% and 71.40%). Costs of drugs and laboratory tests were the most expensive of all medical costs (Table V).

Concerning drugs for allogeneic patients, antifungals followed by antitumors and antivirals were the most expensive pharmaceutical classes 4 526€; 3 737€ and 3 268€ with, respectively, 23.22%, 19.18%, and 16.67% of total drug costs.

The link between the costs of these drugs and the costs of total drugs was statistically significant ($p < 0.001$) with correlation factors, respectively, 0.840; 0.518 and 0.784

The same pharmaceutical classes were the most costly in Allo-BMT and Allo-PBSCT (Table VI).

Table III. Medical and non-medical direct cost.

Cost type		Mean cost €
Total Direct cost		56 638
Direct cost	Medical (74%)	41 749
	Non-medical (26%)	14 896

Discussion

There are limited studies on the cost of HSCT. The purpose of this pharmaco-economic study was to analyze direct costs during the first-year post-allogeneic HSCT in two groups of patients admitted for allo-BMT or allo-PBSCT and to identify factors leading to inter-individual variations in costs.

This study showed that the average direct cost of allogeneic HSCT in the population during the first year reached 56 638€. The average cost of allo-BMT was 63 612€ and allo-PBSCT was 45 966€ ($p > 0.05$).

One American study using a large national database showed that within the first 100 days, hospitalization for HSC transplantation was associated with the majority of total costs and the median of total inpatient costs was 88 429$ [5].

The initial hospitalization for all allogeneic patients had the largest temporal and financial share among all the successive hospitalizations. Indeed, costs of the initial hospitalization were the main driver of total costs in the first 100 days post transplantation (which represented alone more than 70% of total direct costs) and the most expensive costs during the post-transplant year with a mean of 34 811€ which represent 88% of total direct cost.

Table IV. Direct medical costs in Allo-HSCT.

Medical parameters	Mean cost of Allo-HSCT (€)	Mean cost of Allo-HSCT (%)
Drugs	23 621	57%
Laboratory tests	16 664	28%
Medical devices	982	2%
Radiological investigations	803	2%
Anatomopathology	33	0.1%
Transfusion	845	4%
Pharmacovigilance	870	2%
Hygiene	158	0.4%
Parenteral nutrition	205	0.5%
Treatment of graft	1 558	4%
Total	**41 741**	**100%**

Table V. Mean costs of drugs and laboratory tests in Allo-BMT and Allo-PBSCT.

Medical parameters	Allo-BMT (€)		Allo-PBSCT (€)	
Drugs (%)	27 695	(58%)	17 392	(53%)
Laboratory tests (%)	12 602	(26%)	10 230	(31%)

Table VI. Mean costs of Antifungals, Antitumors, and Antivirals in Allo-BMT and Allo-PBSCT.

Drugs	Allo-BMT (€)	Allo-PBSCT (€)
Antifungals (%)	5 752 (25.04%)	2 652 (18.51%)
Antitumors (%)	3 946 (17.18%)	3 419 (23.85%)
Antivirals (%)	4 000 (17.41%)	2 100 (14.65%)

The mean cost of the initial hospitalization for Allo-BMT and Allo-PBSCT was, respectively, 41 441€ and 24 672€ and the difference was statistically significant ($p < 0.05$).

This could be explained by the costs associated with the act of graft, the costs of chemotherapy protocols and primarily the complications that took place during the first hospitalization. In fact, some clinical criteria such as the length of aplasia ($p < 0.01$) were significantly related to direct costs.

Our results showed that there is a difference in cost between patients who developed chronic GVHD. The average direct cost was three times higher than for those who did not present this complication ($p = 0.032$). The patients with chronic GVHD were treated with immunosuppressive therapy and were therefore more susceptible to the occurrence of potentially severe and life-threatening opportunistic viral and fungal infections.

A recent study conducted in 2019 has demonstrated that patients who developed a GVHD during hospitalization for allo-HSCT had an inpatient mortality rate approximately three times higher and total costs approximately two times higher than those who did not develop GVHD [6] Additionally, a US report between 2009 and 2013 showed that any diagnosis of a GVHD during the year following allo-HSCT increased hospital stay by 17 days and total health-care costs by 100,000$ compared with patients without a GVHD [7]

Direct medical costs occupied the most costly part of total direct costs (73.70%).

Drug costs represented 56% of direct medical costs in Allo-SCT with a total cost of 23 621€. In Allo-BMT and Allo-PBSCT, these costs were, respectively, 27 695€ (58.21%) and 17 392€ (52.96%).

In most studies, the cost of drugs had an important part in the health-care budget of developed [8] and developing countries [9].

Concerning drugs, antifungals, antitumors, and antivirals were the most expensive pharmaceutical classes in the two groups with, respectively, 23% (4 526€), 19% (3 737€), and 17% (3 269€) of total drug costs.

Indeed, in order to reduce costs, it is important to detect patients with higher risk of transplant-related complications, especially GVH. Besides, new method of financing with the CNAM could be considered.

Through our study, some limitations should be mentioned:

As it was a retrospective one, our study has assessed total direct costs in 2013 but since that time and until today an increase of prices in several medical parameters (principally medicines) has been occurred.

In addition, the indirect and intangible costs of HSCT were not concidered in this study, which would have provided a global vision of total cost.

The follow-up post-transplant was also among the weak points of our study. Indeed, this follow-up has lasted only 1 year and not long term, from where other studies with follow-up arriving at 5 years post-transplant [10,11] or even more should be conducted in order to address cost-utility studies or even comparative effectiveness ones [12,13].

Conclusion

Regarding our study, the average total direct costs in allograft was 56 638€ and some factors were responsible for interindividual differences in costs.

A significant imbalance between hospital spending and reimbursement is to report, from where an urgent reaction from the health authorities is needed.

Disclosure statement

No potential conflict of interest was reported by the author(s).

References

[1] Greenberg D, Earle C, Fang CH, et al. When is cancer care cost-effective? A systematic overview of cost-utility analyses in oncology. J Natl Cancer I. 2010;102(2):82–88. doi: 10.1093/jnci/djp472

[2] Warren JL, Yabroff KR, Meekins A, et al. Evaluation of trends in the cost of initial cancer treatment. J Natl Cancer I. 2008;100(12):888–897. doi: 10.1093/jnci/djn175

[3] Preussler JM, Denzen EM, Majhail NS. Costs and cost-effectiveness of hematopoietic cell transplantation. Biol Blood Marrow Tr. 2012;18(11):1620–1628. doi: 10.1016/j.bbmt.2012.04.001

[4] Clement FM, Harris A, Li JJ, et al. Using effectiveness and cost-effectiveness to make drug coverage decisions: a comparison of Britain, Australia, and Canada. J Amer Med Assoc. 2009;302(13):1437–1443. doi: 10.1001/jama.2009.1409

[5] Wang HI, Aas E, Howell D, et al. Long-term medical costs and life expectancy of acute myeloid leukemia: a probabilistic decision model. Value Health. 2014;17 (2):205–214. doi: 10.1016/j.jval.2013.12.007

[6] Yu J, Parasuraman S, Shah A, et al. Mortality, length of stay and costs associated with acute graft-versus-host disease during hospitalization for allogeneic hematopoietic stem cell transplantation. Curr Med Res Opin. 2019 Jun 3;35(6):983–988. doi: 10.1080/03007995.2018.1551193

[7] Mariotto AB, Yabroff KR, Shao Y, et al. Projections of the cost of cancer care in the United States: 2010-2020. J Natl Cancer I. 2011;103(2):117–128. doi: 10.1093/jnci/djq495

[8] Majhail NS, Mau LW, Denzen EM, Arneson TJ. Costs of autologous and allogeneic hematopoietic cell transplantation in the United States: a study using a large national private claims database. Bone Marrow Transplant. 2013 Feb;48(2):294–300. doi: 10.1038/bmt.2012.133

[9] Subedi P, Perfetto EM, Ali R. Something old, something new, something borrowed…comparative effectiveness research: a policy perspective. J Manage Care Pharm. 2011;17(9 Suppl A):S05–9. doi: 10.18553/jmcp.2011.17.s9-a.S05

[10] Dreyer NA, Tunis SR, Berger M, et al. Why observational studies should be among the tools used in comparative effectiveness research. Health Affair. 2010;29 (10):1818–1825. doi: 10.1377/hlthaff.2010.0666

[11] Cameron A, Ewen M, Ross-Degnan D, et al. Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. Lancet. 2009;373(9659):240–249. doi: 10.1016/S0140-6736(08)61762-6

[12] Grubb WW, Huse S, Alam N, Dychter S, Wingard JR, Majhail NS, et al. Economic Burden of Acute Graft-Versus-Host Disease (GvHD) Following Allogeneic Hematopoietic Cell Transplant (HCT) for Hematologic Malignancies. Blood. 2016 Dec 2;128(22):1187–1187. doi: 10.1182/blood.V128.22.1187.1187

[13] Yu YB, Gau JP, You JY, et al. Cost-effectiveness of postremission intensive therapy in patients with acute leukemia. Ann Oncol. 2007;18(3):529–534. doi: 10.1093/annonc/mdl420