IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 21, Issue 12 Ser.5 (December. 2022), PP 22-26
www.iosrjournals.org

Cost burden of diffuse large B-cell lymphoma in the internal medicine and ONCO-hematology department of the University Hospital of Fez

N. ALAMI DRIDEB, B. KACHOUR, H. MASROUR, M. BOUZAYD, S. BOUCHNAFATI, N. OUBELKACEM, M. OUAZZANI, Z. KHAMMAR, R. BERRADY

Internal medicine and onco-hematology department, HASSAN II university hospital, Sidi Mohammed Ben Abdellah university, Fez, Morocco

Abstract:
Introduction: *Diffuse large B-cell lymphoma (DLBCL) represents 30 to 40% of all non-Hodgkin's lymphomas. About 60% of patients are recovred with standard treatment. Targeted therapies, that may improve disease outcomes, are currently investigated; however, their effect on anticancer drug budgets seems to be huge. In our study, we analyzed the direct medical cost of DLBCL in our unit, to assess its impact and lead care management strategies and health plans.*
Methods: *this is a retrospective study of patients diagnosed with DLBCL at the department of internal medicine and Onco-Hematology at Hassan II University Hospital in Fez in 2019. We evaluated the direct medical costs of managing newly diagnosed DLBCL during the first year of follow-up.*
Results: *30 patients were included in this study. The main direct medical cost of each patient's management during the first year after diagnosis is about 168124 MAD. This cost is considered high and challenging for our health system. We spread the costs into several components designed as acts to determine which act has the greatest impact on the direct medical cost of managing DLBCL (histology, radiology, biology, chemotherapy, medical consultations, and hospitalizations, as well as the various medical and paramedical acts). Chemotherapy was the largest cost factor in the first year after diagnosis, responsible for 75.7% of the total cost. Furthermore, most patients (80%) were in remission at the end of the follow-up period.*
Conclusion: *The economic burden of DLBCL is significant, especially in the first year of diagnosis, which is the period when the majority of patients receive treatments. The study of direct non-medical costs and indirect costs should also be considered for a more precise and accurate results.*
Keywords: *diffuse large B-cell lymphoma, direct medical cost, chemotherapy.*

Date of Submission: 04-12-2022 Date of Acceptance: 16-12-2022

I. INTRODUCTION:

For many years, the Moroccan health system was face up to difficulties in financing health spending [1]. Onco-hematology, which is a national issue, is precisely part of this problem.

The preventive, diagnosis, therapeutic, and, more generally, societal management of patients with hematological malignancies is consuming more and more resources. Their management is becoming more effective but also more expensive, and explaining the therapeutic choices is essential.

In Morocco, cancer is recognized as a long-term illness and is therefore fully covered. The Moroccan social protection system covers both public and private sector employees. The compulsory health insurance system, was instituted in 2002 by law 65.00 on the code of compulsory basic medical coverage, and guarantees universal access to health care. It is managed by two organisms (CNOPS and CNSS). A second system, the medical assistance scheme (RAMED), covers the most dis-advantaged. About two-thirds of the population is covered.

Our attention has been drawn to Diffuse Large B-Cell Lymphoma (DLBCL), a lymphoid malignancy characterized by the proliferation of mature B-cells of larger-than-normal size [2]. DLBCL is the most common form of non-Hodgkin's lymphoma (NHL), accounting for 25% to 40% of all NHL cases [3]. The standard first line of treatment consists of a combination of chemotherapy, it includes the drugs cyclophosphamide, doxorubicin, vincristine sulfate, and prednisone (CHOP) plus Rituximab, an anti-CD20 monoclonal antibody, and is referred to as the R-CHOP protocol [4]. Although associated with a significant survival benefit, the use of RCHOP has put upward pressure on anti-cancer drug budgets.

The objective of our study is to estimate the direct medical cost of DLBCL management during the first year after diagnosis and to identify the most important expenditure items.

II. METHODS :

This is a retrospective, descriptive and analytical study, spread over 1 year from 01 January 2019 to 01 January 2020, including 30 patients. This study is an evaluation of the direct medical costs of patients followed for diffuse large B-cell lymphoma during the first year after the initial diagnosis, carried out at the internal medicine and onco-hematology department at the Hassan II University Hospital of Fez.

In this work, we are limited to the direct medical costs of DLBCL, which represent the value of all resources consumed directly to make the diagnosis and treat the disease.

The statistical analysis was done in collaboration with the laboratory of epidemiology, clinical research, and community health of the Faculty of Medicine and Pharmacy of Fez.

III. RESULTS :

1. Epidemiological data :

Thirty patients were included in our study. The mean age of our patients was 56.7 years +/- 14.6 years with extremes between 22 and 77 years. The male sex was dominant with a sex ratio of 1.3. The geographical distribution of the patients according to their place of residence noted the existence of a maximum of patients residing in the region of Fez-Meknes (60%), and the redistributed between the various regions of the East and North-East of Morocco. 53.4% of our patients were jobless.

Only 9 patients in our series were covered by health insurance (CNSS, CNOPS, and FAR), 30%, while 70% of the patients were covered by RAMED (Table I).

Table I: Socio-demographic characteristics of the study population

Features	n	%
Age		
<50 ans	10	33,4
≥ 50 ans	20	66,6
Gender		
Men	17	56,7
Women	13	43,3
Origin		
Fez	18	60
East	8	26,6
North East	4	13,4
Profession		
Yes	14	46,6
No	16	53,4
Sanitary coverage		
Health insurance	9	30
RAMED	21	70

2. Direct medical cost study:

We split the costs into several components called acts, in order to determine which act has the greatest impact on the direct medical cost of managing DLBCL:

-The histological act, which includes biopsies and pathology studies that led to a positive diagnosis of DLBCL.

-The radiological procedure includes the radiological assessment of extension, re-evaluation, and pre-therapeutic trans-cardiac echography (TTE).

-Biological procedures include all biological examinations carried out in the context of hematological malignancy, whether the initial biology, the pre-therapeutic work-up, or the biological work-up carried out during the follow-up.

-Endoscopy, performed as part of the extension workup.

-Chemotherapy, which includes all the anti-cancers molecules used to treat DLBCL.

-Consulting, which include onco-hematology (OH) consulting at the diagnostic center and day hospital (DH)consultations.

-Hospitalizations.

-Blood product transfusions.

-Costs of management of complications related to the disease and adverse effects of the various treatments.

The diagnosis of lymphoma is based on the histological analysis of a lymph node biopsy, a biopsy of an extra-ganglionic mass, or a bone marrow biopsy. In our study, all our patients had at least one biopsy with a pathology study confirming the diagnosis of DLBCL. The average fee of histology was 649.67 MAD with a standard deviation of 546.4 MAD.

We calculated all radiological examinations, including standard radiographs, ultrasound (cervical, abdominal, soft tissue, and cardiac), full body scans as part of the extension and re-evaluation workup, MRI, and PET scans. The mean cost of radiological examinations was 19634.27 MAD.

Concerning endoscopic examinations performed either for the initial diagnosis or as part of the extension work-up, the average supply was 553MAD.

The average cost for biological exams was 8846.4 MAD. This cost includes all the biological tests performed during the study period, including the initial standard workup and viral serology, as well as all the biological statements performed before and during the chemotherapy treatment.

We calculated separately the costs of medical consults in OH at the diagnostic center and medical consultations in DH. The DH had the highest cost with an average of 3850 MAD compared to the average cost of OH consultations of 281 MAD.

The mean total cost of hospitalizations was 1571.67 MAD. It only concerns the cost of hospitalization days at the University Hospital and does not include the cost of medical and non-medical procedures performed.

Once the diagnosis of DLBCL is confirmed, the management is defined in the framework of a Multidisciplinary Consultation Meeting (MCM). All decisions are then communicated and discussed with the patient. The patient is thus informed of all the therapeutic options available in his or her situation, the expected benefits, risks and potential adverse effects. The reference protocol for immune-chemotherapy generally combines 6 to 8 cycles of the R-CHOP protocol.

All our patients received R-CHOP as first-line therapy. Ten patients received a debulking chemotherapy COP regimen (cyclophosphamide, vincristine sulfate, and prednisone), 14 days before the first RCHOP cycle. Fourteen patients (46.6%) received intrathecal chemotherapy. However, only 2 DLBCL patients received second-line RDHAOX therapy.

The costs of the RCHOP, RDHAOX, and intrathecal chemotherapy with methotrexate, cytarabine, and hydrocortisone protocol drugs were calculated for each patient based on 2013 drug prices [5]. For each patient, the doses of the drugs were adjusted to the body's surface area. As a result, the drug costs will show some variations.

The average cost of chemotherapy was 127472.73 MAD with a standard deviation of 26801.866 MAD.

The median fee of granulocyte growth factors used routinely or during post-chemotherapy neutropenia was 3010.50 MAD for an average of 4.5 days.

Many of our patients required blood product transfusions. The average cost of transfusions was 629 MAD for an average of 1.2 transfusions per unit (Packed red blood cells and/or platelet).

The average cost of medical treatments other than chemotherapy was 2011.77 MAD per person during our study period. This fee includes all drugs consumed by the patient outside chemotherapy, whether preventive treatments (Valaciclovir, Sulfamethoxazole/Trimethoprim, Lamivudine), preventive or curative anticoagulant therapy , oral or IV antibiotics, and any other drugs used to manage complications of DLBCL and side effects of chemotherapy (zoledronic acid, rasburicase ...).

We conclude that the overall average cost of managing DLBCL, involving direct medical costs, during the first year after diagnosis is 168124 MAD per patient (Table II).

Table II : Average direct cost of DLBCL management by expenditure item (act)

Type of act	**Averagecost (MAD)**
Histology	649,67
Radiology	19634,27
Endoscopy	553
Biology	8846,4
Chemotherapy	127472,73
Oncohematology consultations	281
Day Hospital consultations	3850
Hospitalizations	1571,67
GCSF	3010,50
Transfusion	629
Other treatments	2011,77
AVERAGE OVERALL COST	**168124**

We split the different costs of the various procedures; chemotherapy was the procedure that weighed most heavily on the management of DLBCL, occupying 75.5% of the average overall cost (Figure).

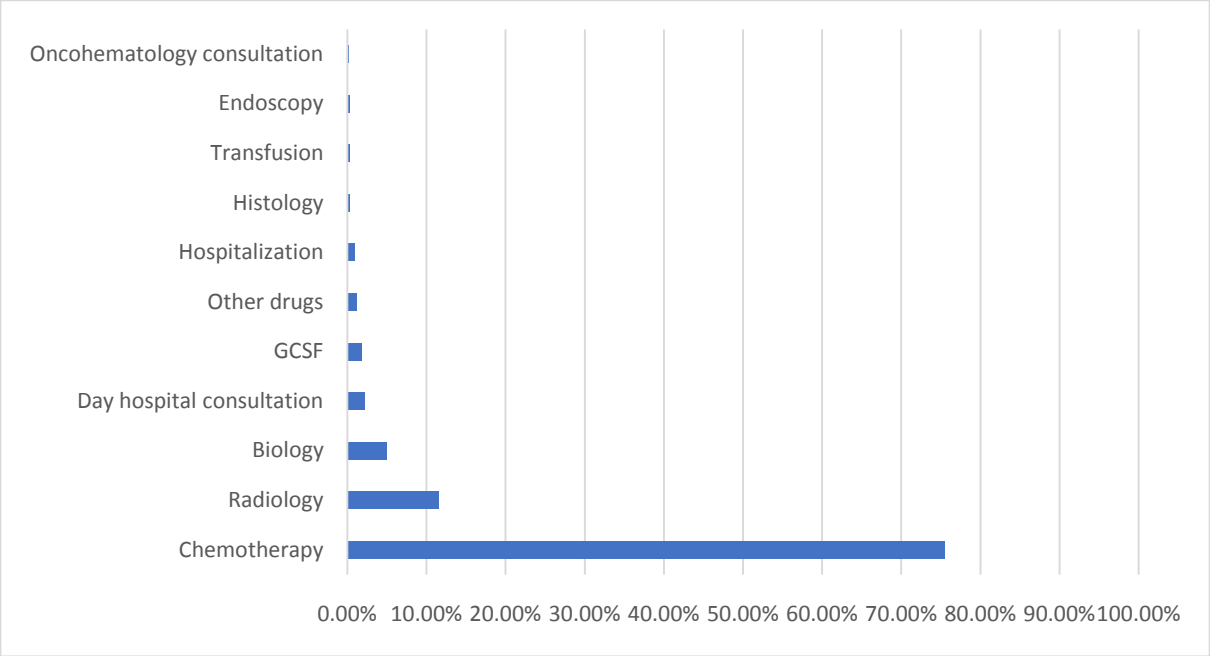

Figure: illustrates the important cost impact of chemotherapy in the management of DLBCL.

The evolution of DLBCL at the end of the follow-up year was marked by a complete remission rate of 80%. Lymphoma progression was noted in 3 patients (10%) and refractory disease in 10% of cases.

IV. DISCUSSION:

The evaluation of the costs of management and care for a complex disease such as diffuse large B-cell lymphoma reveals major challenges in the collection of economic and health organization, both nationally and internationally. It is very difficult to collect this data referring to the disease nature, given the diversity of data sources of the various stakeholders in the health care system, and the non-integration of these data in large data bases across centers and countries. The real cost is yet harder, since it also includes some expenses provided by patients or their relative. The disease has another important impact, which is the loss of labor supply during the disease period.

No study in Morocco has so far evaluated the cost of lymphoma in the general population. Our study is the first to estimate the direct medical cost of diffuse large B-cell lymphoma.

On average, the estimated direct medical cost of DLBCL management was about 168124 MAD per patient with a minimum of 75772 MAD and a maximum of 248660 MAD, for a follow-up of one year after the discovery of the disease. This constitutes a considerable burden for our health system and represents a huge challenge to confront in the context of important socioeconomic, demographic, and epidemiological transitions.

The variability of the methods used by the various international studies conducted on this subject, the diversity of the economic evaluation methods according to the countries, and the difference in prices make it difficult to compare the costs of managing this disease. In France, a few studies have evaluated the cost of lymphoma. These studies have focused on non-Hodgkin lymphoma (NHL). The first study by Best et *al* evaluated the cost of managing patients with DLBCL over a 15-year time horizon, depending on whether they were treated with CHOP or R-CHOP [6]. The costs considered were direct medical costs limited to the costs of hospital days related to treatment administration, treatment costs, and management of associated adverse events, monitoring, recurrence, transplantation, and palliative care. The average cost associated with the management of a DLBCL patient treated with R-CHOP was estimated at €41,952 (445153.15 MAD) over 15 years. The second study by Decconick et *al*, evaluated the cost of managing Follicular Lymphoma in complete or partial remission following induction therapy, depending on whether they received rituximab maintenance therapy or not [7]. The costs considered were limited to direct medical costs. The cost of managing follicular lymphoma from rituximab maintenance therapy over the lifetime horizon was estimated to be €71,314 (756713.67 MAD). Costs associated with induction therapy were not considered, nor were direct non-medical costs and indirect costs. These studies are efficiency studies in which the cost was evaluated to associate it with an effectiveness criterion. They do not evaluate the real cost of the disease.

In the United Kingdom, the average cost per patient treated for DLBCL was approximately $18,000 (167085.00 MAD). This cost was consistent regardless of the time horizon chosen ($18,096, $18,396, $18,396 for 5 years, 15 years, and lifetime, respectively), this reflects that for most DLBCL patients, treatment is

completed within 5 years [8].The microcosting study conducted in Canada estimated an average cost of $40,191 (294223.99 MAD) for first-line treatment of DLBCL, $5,294 (38755.49 MAD) for disease assessment, and $3,905 (28587.11 MAD) for follow-up costs over an average of 450 days (all costs in Canadian dollars) [9].
Our observation reflects that Chemotherapy represented the largest cost driver in the first year after diagnosis with a frequency of 75.5%. The corresponding expenses are mainly related to Rituximab, which is similar to several studies [6-8]. This cost can be largely reduced in the future by the availability of biosimilars.

Chemotherapy is toxic and resulting complications are common during a chemotherapy cycle. Nevertheless, they are managed during the next admission for chemotherapy, which explains our results and justify the low cost related to complications alone. This shows the importance of preventions.

The second cost factor of DLBCL was radiology, corresponded to 11.6% of the overall cost, mainly involving full body scans and PET scans, which is explained by the important role of medical imaging in the extension, re-evaluation, and follow-up.

As for efficacy, most of our patients (80%) were in remission at the end of the follow-up period, results comparable to other studies [6, 8].

Our results may be under estimated. The study protocol allowed us to evaluate only the cost of care procedures mentioned in the medical records. It is also possible that some procedures were performed without being recorded in the file. The estimated cost of care at the national levels only an approximation of the cost of care for DLBCL in Morocco. Indeed, the rates used in the public sector are much lower than those used in the liberal practice sector. This sector is currently undergoing significant development.

Our study did not evaluate the costs separately for patients who progressed versus those who did not; these costs were taken into account in the overall cost of lymphoma. Other studies have shown that patients with indolent NHL who progressed incurred more costs than those who did not progress [10].

V. CONCLUSION

This study led to providing the mean costs over time for DLBCL, this information is useful for resource allocation planning and operational decisions. These approaches may be beneficial for future research involving cost modeling both technically (radiological and biological) and therapeutically (the potential effects that targeted therapies may have on the management of DLBCL).

Prospects: A larger, multi-center study would be beneficial to confirm or refute some of the non-statistically significant trends in total hospital costs, and it is recommended that organizations involved in cancer care coordinate data collection and integrate data bases to allow more accurate and precise cost burden studies.

REFERENCES

[1]. STRATÉGIE NATIONALE DE FINANCEMENT DE LA SANTÉ. rapport_SNFS VD avril 2021.pdf (sante.gov.ma).
[2]. Rodriguez-Abreu D, Bordoni A, Zucca E. Épidémiologie des hémopathies malignes. Ann Oncol. 2007;18(Suppl 1):i3–i8.
[3]. Morton LM, Wang SS, Devesa SS, Hartge P, Weisenburger DD, Linet MS. Profils d'incidence des lymphomes selon le sous-type de l'OMS aux États-Unis, 1992-2001. Blood 107(1), 265-276 (2006).
[4]. Wästerlid T, Harrysson S, Andersson TM, et al. Outcome and determinants of failure to completeprimary R-CHOP treatment for reasonsotherthannon-responseamong patients with diffuse large B-celllymphoma. Am J Hematol 2020; 95 : 740–8.
[5]. Décret n° 2-13-852.https://www.sante.gov.ma/Reglementation/TARIFICATION/2-13-852.pdf.
[6]. Best JH, Hornberger J, Proctor SJ, Omnes LF, Jost F. Cost-effectivenessanalysis of rituximab combinedwith chop for treatment of diffuse large B-celllymphoma. Value Health. 2005 Jul-Aug;8(4):462-70.
[7]. Deconinck E, Miadi-Fargier H, Pen CL, Brice P. Costeffectiveness of rituximab maintenance therapy in follicularlymphoma: long-termeconomicevaluation. Pharmacoeconomics. 2010;28(1):35-46.
[8]. Treatmentcost and life expectancy of diffuse large B-celllymphoma (DLBCL): adiscreteevent simulation model on a UK population-basedobservationalcohort. DOI 10.1007/s10198-016-0775-4.
[9]. Lee RC, Zou D, Demetrick DJ, Difrancesco LM, Fassbender K, Stewart D. Costsassociatedwith diffuse large B-celllymphoma patient treatment in a Canadian integrated cancer care center. Value Health 2008;11:221–30.
[10]. Beveridge R, Satram-Hoang S, Sail K et al. Impact économique de la progression de la maladie dans le lymphome folliculaire non hodgkinien. Leuk. Lymphome 52(11), 2117-2123 (2011).

N. ALAMI DRIDEB, et. al. " Cost burden of diffuse large B-cell lymphoma in the internal medicine and ONCO-hematology department of the University Hospital of Fez." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 21(12), 2022, pp. 22-26.