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Research Article

Diagnosis and Follow Up of Non Hodgkin Lymphoma in Dakar, Senegal

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Abstract

Introduction: The management of Non-Hodgkin Lymphoma (NHL) in Senegal is challenging due to the lack of exploration tools and the inaccessibility of anticancer drugs. This study aimed to identify the prognostic factors at diagnosis and to assess their outcome under treatment.

Methodology: We conducted a descriptive and analytical prospective study range from 1st January 2018 to 3rd July 2020 covering NHL cases. Initial prognostic factors were assessed according to the International Prognostic Index for diffuse large cell B lymphoma and T-cell lymphoma, the Mantle Cell Lymphoma International Prognostic Index and the Follicular Lymphoma International Index for mantle cell lymphoma and small cell lymphoma respectively. B-cell lymphomas were treated with polychemotherapy with or without rituximab, T-cell lymphomas were treated with polychemotherapy alone. Progression was assessed on the basis of response to treatment, toxicity and survival.

Results: We included 40 patients, 30 males and 10 females with a sex ratio of 3. The mean age was 43.38 years +15.87. The mean time from symptom onset to diagnostic confirmation was 7.4 months. The total follow-up time of the cohort was 30.5 patient-years. B-cell lymphomas accounted for 57.5% of cases, T-cell lymphomas for 27.5% of cases. Twenty-five patients (67.6% of cases) were at an advanced stage at diagnosis. The initial prognosis was unfavourable in 29.7% of cases, all histological types combined. The overall survival at 30 months was 70%.

Conclusion: Our patients were diagnosed with advanced disease stage. The overall survival at 30 months was short. Early diagnosis and better access to immunochemotherapy could improve these results.

Keywords: Non-Hodgkin lymphoma; Diagnosis; Prognosis; Treatment; Africa

Introduction

Non-Hodgkin lymphoma (NHL) is the most common type of haematological malignancy worldwide. In Senegal, a remarkable increase in incidence has been observed. Their prevalence among haematological malignancies rose from 25.6% to 45.4% between 1998 and 2009 [1]. Their management is costly and usually not within the reach of patients. Their prognosis is severe, marked by high mortality and morbidity. This high mortality could be influenced by several factors:

- Diagnostic delay induced by difficulties in access to care.
- Difficulties in confirming the histological type of lymphoma due to the lack of exploration tools such as immunohistochemistry, which is essential for accurate diagnosis and prognosis.
- The inaccessibility of treatments either because of their high cost or the unavailability of certain drugs in our health facilities. In Senegal, the factors that influence the prognosis of lymphoma patients are rarely considered in prospective studies. They are mostly deduced from Western studies despite the difference between epidemiological parameters, diagnostic and therapeutic means and living conditions.

It's against this backdrop that we carried out this work to search for initial prognostic factors related to our context in addition to those already validated in Western studies and to evaluate the results of the treatment of our patients with non-Hodgkin lymphoma.

Methodology

We conducted a descriptive and analytical prospective study from January 1, 2018 to July 3, 2020 (30 months). All patients whose diagnosis of NHL was confirmed by a pathological approach associated or not with an immunohistochemical examination of a tumour sample were included.

Each patient underwent a complete clinical examination, a full blood count, a non-specific inflammatory markers research, a serum creatinine and transaminase level measurement, a haemostasis assessment, a tumour lysis markers assessment and a pathological examination perform on a tumour biopsy specimen, coupled or not with immunohistochemical examination. The tumor extension assessment included either a thoracic-abdominal-pelvic CT scan or a chest X-ray with abdominal ultrasound. The Ann Arbor classification revised by Costwold was used to set extensive assessment. Prognostic

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Table 1: Distribution by histological type.

Histological Type	Frequency	Percentage (%)
Aggressive lymphoma (75%)		
LBDGC	15	37.5
Angioimmunoblastic lymphoma	3	7.5
Lymphoblastic lymphoma	2	5
Anaplastic lymphoma	1	2.5
Plasmablastic lymphoma	1	2.5
Burkiit lymphoma	1	2.5
Mantle Lymphoma	2	5
Peripheral T lymphoma	5	12.5
Indolent lymphoma (12.5%)		
Marginal zone lymphoma	1	2.5
MALT lymphoma	2	5
Small cell B lymphoma	2	5
Not specified (12.5%)	**5**	**12.5**
Total	**40**	**100**

factors were assessed before starting the treatment. We used the International Prognostic Index (IPI) for DLCBL and T-cell lymphomas, the Mantle Cell Lymphoma International Prognostic Index (MIPI) and the Follicular Lymphoma International Index (FLIPI) for mantle cell lymphoma and small cell lymphomas respectively. We then looked for other independent prognostic factors that have yet to be validated. Diffuse large cell, mantle and small cell B-cell lymphomas were treated with cyclophosphamide, doxorubicin, oncovin and prednisone (CHOP) with or without rituximab, T-cell lymphomas with CHOP. Progression was assessed on response to treatment and survival.

Data were collected on a pre-set form. They were entered using the Sphinx software version 5.1.0.2. Data were processed by using the SPSS (Statistical Package for Social Sciences) version 18 software. The descriptive study was carried out with the calculation of frequencies and proportions for the qualitative variables and the calculation of means and standard deviations for the quantitative variables. The Kaplan Meier survival graph was used to assess the probability of survival of patients. The comparison of survival probabilities between the different groups was done using the log rank test with a significance level of $p < 0.05$.

Results

Over a period of 30 months, 40 patients were included, of whom 30 were men and 10 women, corresponding to a sex ratio of 3. The average age was 43.38 years (+15.87 years). The most common age group was between 40 and 49 years, representing 27.5% of cases. The informal sector represented 65.8% of occupational activity. The average time to first consultation was 5.85 months (standard

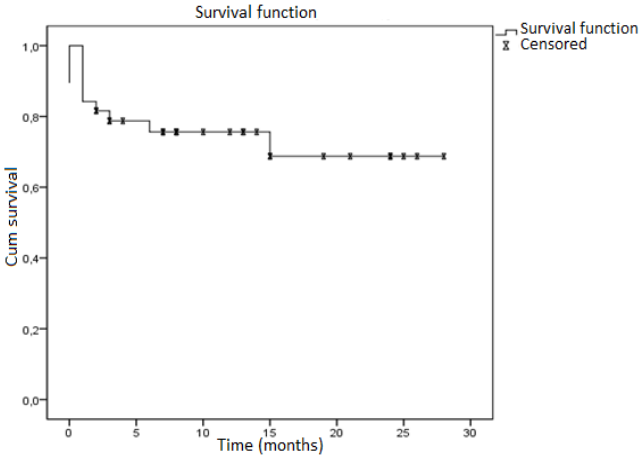

Figure 1: Overall survival.

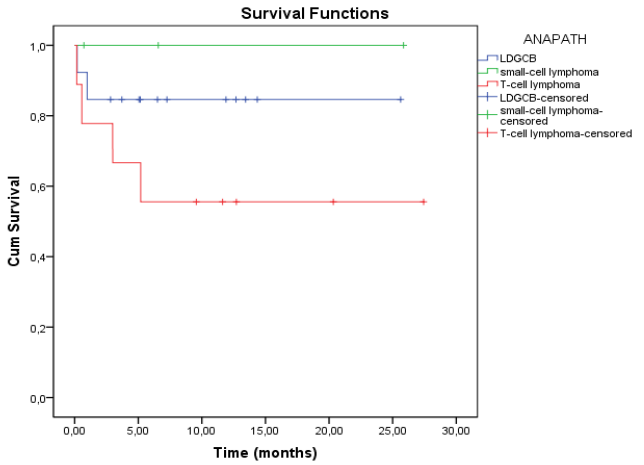

Figure 2: Survival of LDBGC, T-cell Lymphoma and Small Cell Lymphoma.

deviation = 10.6 months), and the time from first consultation to histological diagnosis confirmation was 1.6 months. The total follow-up time of the cohort was 30.5 patient-years. The main clinical signs were polyadenopathy (72.5%), splenomegaly (17.5%) and hepatomegaly (3%). Poor general condition (PS≥2) was found in 50% of cases, clinical and biological signs of evolutivity were respectively found in 60% and 62.5% of cases. LDH was elevated in 66.7% of cases. Spontaneous tumour lysis syndrome (STLS) was observed in 7.5% of cases, renal failure occurred in 5% of cases. B-cell lymphomas accounted for 57.5% of the cases, T-cell lymphomas for 27.5% of the cases, the immunophenotypic form was not determined in 15% of the cases. The aggressive form represented 75% of cases. Diffuse large cell B lymphomas (DLBCL) accounted for 37.5% of all histological forms. The different histological types found are listed in Table 1.

Twenty-five patients (67.6% of cases) were at an advanced stage

Table 2: Outcome modalities according to the type of lymphoma.

Histological type	Frequency (N=40)	Complete remission	Partial remission	Number of deaths	Patients on treatment	Lost follow up
B lymphoma	24	10	1	6	7	0
T lymphoma	13	5	1	4	2	1
Not specified	3	1	0	1	1	0

(Ann Arbor stage III or IV) at diagnosis. The initial prognosis was unfavourable in 29.7% of cases, regardless of histological type. This rate was 26.7% in LBDGC, 50% of small cell B-cell lymphomas, 100% of mantle cell lymphomas and 10% of T-cell lymphomas.

Total remission was noted in 40% of cases, partial remission in 5% of cases. At the end of the study, 25% were undergoing treatment, 2.5% were lost to follow-up. Mortality was estimated at 27.5%. No cases of progression were observed. There were disparities in the evolutionary profile depending on the type of lymphoma (Table 2).

The overall survival at 30 months was 70% (Figure 1), that of small cell lymphoma was 100%, for DLBCL and T-cell lymphoma it was respectively 85% and 55% (Figure 2). There were no difference in survival according to gender, locality, occupation, delay before consultation or diagnosis (p greater than 0.5).

Discussion

Malignant non-Hodgkin lymphomas are rarely considered in African prospective studies. Their diagnosis challenges numerous issues related to the lack of investigation means. Their treatment is hampered by the inaccessibility of anticancer drugs. The recommendations for their management are deduced from those of the West despite the difference between socio-demographic parameters, diagnostic and therapeutic means. Apart from the validated prognostic factors, other parameters could impact the prognosis of our patients. It's against this backdrop that this study was carried out to try to take stock of these different aspects in our context of a developing country. Diagnosis slag of lymphoma remains a reality in our clinical practice with an average delay of 5.85 months. This delay is frequently found in studies conducted in Africa [2]. The revealing symptoms were dominated by polyadenopathy (72.5% of cases), with 60% of patients showing signs of clinical progression.

This very significant clinical course was reported by Ndiaye et al. [1] who described 75% of patients with polyadenopathy. This could be related to the delay in diagnosis experienced by our patients. The STLS observed in our series at a rate of 7.5% of cases deserves special attention because it is favoured by the large tumour mass. Thus it has become rare in the West where the diagnosis is early set on patients. Its seriousness lies in the visceral damage, in particular renal damage. In our study, STLS was complicated by AKI in two patients. Nevertheless, headways has been made in the quality of the diagnosis with immunohistochemistry performed in 82.5% of cases, which is much higher than the rate observed in the study by Diop et al. in 2004 [3] where it was performed in only 3.7% of patients. Advanced stage at diagnosis is found in several studies in Africa; Oyekunle et al. in Nigeria [4] found that 93% of patients were at an advanced stage in Ann Arbor. These data differ from those found in Western countries. Stages I and II were the most common in the Evans study [5] in the UK. This corroborates with the results of Miller [6] in the United States, which revealed that 67% of patients were at stage II. This delay in diagnosis noted in our countries could be attributable to the remoteness and scarcity of specialized haematology unit in health structures and to an insufficiency of diagnostic means.

Despite this advanced Ann arbor stage, 73.3% of LBDGC had a low to intermediate IPI. This distribution in favour of the favourable stage is similar to the data in the literature. In France, Coiffer [7] found 60% of cases with a low-risk LBDGC. However, this prognosis remains unfavourable in most low-grade lymphomas. The FLIPI was unfavourable in 50% of patients with follicular NHL and 100% of cases of Malt lymphoma; the MIPI was unfavourable in all patients (100%) with mantle cell lymphoma. This poor prognosis at diagnosis in low-grade lymphoma is often described in the literature. In Casulo's [8] study of follicular lymphoma, 50% of cases had a poor prognosis. Total remission was achieved in 40% of patients. This rate is higher than that found by Thiam et al. in 1996 [9] who reported a total remission rate of 13.9%. This better result seems to us to be related, on the one hand, to a better precision of the diagnosis by immunohistochemistry and, on the other hand, to the use of immunochemotherapy by rituximab in B lymphoma. The overall patient outcome showed a death rate of 27.5%. These results are similar to African data. In Côte d'Ivoire, Tolo [10] found a mortality rate of 36.16% and Sawadogo [11] reported a death rate of 44%. Ndiaye [1] in Senegal found a mortality rate of 27.4% in his study. This relatively high mortality rate could be related to an advanced prognosis at the time of diagnosis.

The overall 30-month survival of 70% reflects a remarkable advance in the management of malignant non-Hodgkin lymphoma in Senegal compared to previous years. Indeed, the study carried out by Diop et al. in 2004 [3] in Dakar on a population of 107 cases of NHL showed an average survival of 11 months. This result is higher than those usually found in sub-Saharan Africa. In Malawi, Gopal et al. in 2016 [12] found a 2-year survival of 45% in a population of 59 patients. However, this survival is significantly lower than those obtained in developed countries. In the United States of America, Casulo et al. [8] found in 2015, in a prospective multicentre study on a population of 2652 patients, a 30-month survival of 98%. The search for local prognostic factors did not reveal any impact of socio-economic level or time to diagnosis on survival in our cohort (p greater than 0.05).

However, low socio-economic level appeared to be an unfavourable prognostic factor in the study by Sawodogo in Côte d'Ivoire [11] (p=0.004) as well as in the study by Keegan et al. [13] in California. In our study, the poor prognostic value of low socio-economic status would have been erased by the free chemotherapy for all patients and the free immunotherapy for those followed up for LBDGC.

Conclusion

The diagnosis of non-Hodgkin lymphoma is lately made in our centre. Patients often present with advanced disease stage and a poor prognosis. However, compared to previous years, we note a better accuracy of diagnosis with the use of immunohistochemistry. Treatment has significantly improved with the availability of free multidrug therapy and rituximab. These two headways have probably increased overall survival. Improved availability of diagnostics and anti-cancer drugs should further increase survival.

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