



Research Article

**Non-Hodgkin Lymphoma: A Retrospective Descriptive Analysis
of 82 cases.**

Dr. Rania Chtir, Professor Hicham Eddou, Dr. Chaymae Chbihi, Dr. Lamyae Elansari*

***Correspondence to:** Dr. Rania Chtir, Morocco.

Copyright.

© 2024 **Dr. Rania Chtir**. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Received: 13 September 2024

Published: 01 October 2024

Abstract

Background: NHLs consist of a diverse group of hematologic malignancies deriving from mature or immature lymphocytes (B, T or NK) which can infiltrate both lymphoid and hematopoietic tissues but can also extend to other organs.

These lymphomas are characterised by significant clinical, anatomopathological, and biological diversity, which reflects the complexity of the different classification systems. Moreover, several factors can be involved in the evolution of malignant lymphomas which can be genetic, infectious, toxic or even environmental.

The objective of this study was to evaluate the epidemiological profile, clinicopathological characteristics and survival rates of NHL patients treated at Moulay Ismail Military Hospital in Meknes, Morocco.

Methods: This is a retrospective study carried out within the Clinical Haematology department of the Moulay Ismail Military Hospital in Meknes covering a series of 82 cases of non-Hodgkin lymphoma over a period of 8 years (between January 2014 and December 2021).

We analysed the clinical, biological and anatomopathological profiles, along with survival rates. Standardised data collection sheets have been used to collect information.

Results: The median age was 54 years (between 16 and 85 years) and the male/female ratio was 2.57.

The average time between the initial symptoms and the first medical consultation was 5 months (1 to 24 months) and the main presenting complaint was lymph node swelling (39%). It was seen that 28 of the patients (35 %) had extra nodal involvement, CNS involvement was only in 2 patient (2.4 %). Diffuse large B-cell lymphoma was the most common morphologic type (48%), and 57.3 % of the patients were in the advanced stage (stages III-IV). The highest survival rates were seen in B cell lymphomas (67%), while the lowest rate was observed in T cell lymphoma (15%).

Conclusion: The research highlights the diverse nature of NHL cases, with a significant proportion being diagnosed at an advanced stage and in the middle age. It suggests that survival rates are poor amongst patients with T cell Lymphomas.

Material and Methods

Study design:

We performed a descriptive retrospective analysis within the Clinical Haematology department of Moulay Ismail Military Hospital, Meknes. Patients aged above 16 diagnosed with NHL between 2014 and 2022 were included in this study.

The aim of our study is to analyse the epidemiological, clinicopathological, therapeutic, and prognostic profiles of non-Hodgkin lymphomas based on 82 diagnosed cases and contemporary literature.

Data collection and analysis:

Data were collected from medical records using a standardised clinical data sheet for each patient, which included the following variables: Patient's name, age, sex, the time between the initial symptoms and the first medical consultation, personal and family history, presenting complaint, clinical examination findings, histologic type, stage, chest x-ray, scans, bone marrow, management approach and survival rates.

The collected data was then entered in Excel spreadsheets to determine the variables and assess the baseline characteristics associated with each NHL case.

Mean and standard deviation was used to report quantitative data, while frequencies and percentages were used for qualitative variables.

Results

In present study, the median age of patients is 54 years (range 16-85) with 43% of them aged more than 60 years. We also observe a significant rise in frequency within the 60-69 age group (Figure 1).

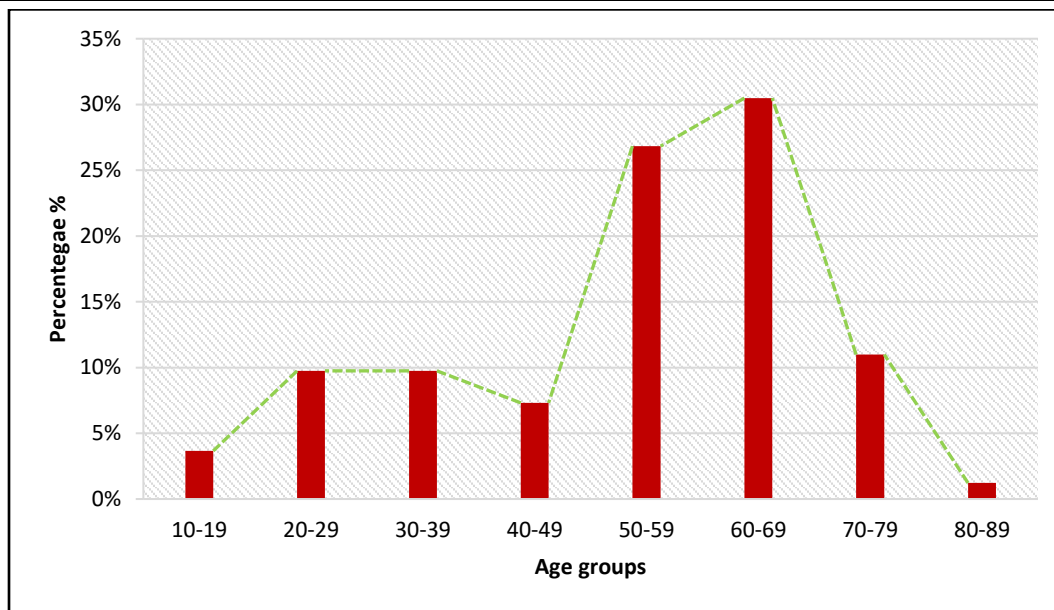


Figure 1: Age Group Distribution

The sex distribution of patients revealed a higher prevalence of males, with 59 men (72%) and 23 women (28%), resulting in a male-to-female ratio of 2.57.

After analysing the past medical history of our patients, 48 of patients (58.5%) had no significant medical history, however: 16 cases were chronic smokers, 2 cases had chronic alcoholism, 9 cases had high blood pressure, 1 case had tuberculosis, 9 cases were diabetic under treatment, and 1 case had treated and cured hepatitis C.

The time gap between symptom onset and specialist consultation and diagnosis varied widely in our study, spanning from 1 month to 2 years. About 67% of patients sought specialist advice between 2 to 6 months after their symptoms initially appeared.

Peripheral lymphadenopathies were the primary reason for consultations. They were found in 32 patients, accounting for 39% of cases.

Non-Hodgkin lymphomas (NHL) were also discovered due to extra-nodal symptoms, particularly digestive symptoms, in 27 patients in our series (32.9%). These symptoms included epigastric pain, diffuse abdominal pain, jaundice, and anorectal disorders.

Seven patients presented with signs of ENT involvement, such as odynophagia, swallowing disorders, or foul-smelling nasal discharge (8.5%).

Neurological signs were observed in 2 cases (2.4%), including hemiplegia and intracranial hypertension syndrome.

Six patients in our series consulted for respiratory symptoms and 2 cases for isolated asthenia.

Additionally, the following were noted: skin problems in 2 patients in our series, exophthalmos in 1 patient, gynaecological signs reported by 2 female patients, consisting of pelvic pain and a breast mass, 1 case presented with a swollen and painful leg.

The diagnosis of NHL was established through histological examination of lymph node or tissue biopsy, complemented by immunohistochemical staining according to the World Health Organization (WHO) classification criteria [1].

Type B NHL was the most frequent, affecting 69 patients and accounting for 84% of the cases. Among these, diffuse large B-cell lymphoma (DLBCL) was the predominant histological type, identified in 39 patients.

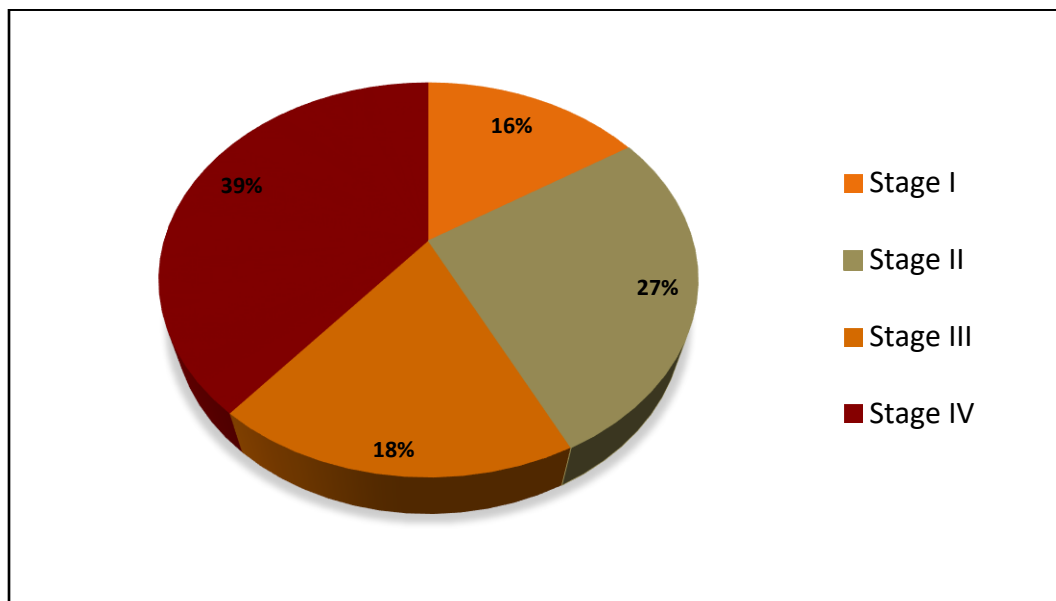
Among the cases diagnosed, various other B-cell lymphomas were observed: Burkitt's Lymphoma in 9 patients (11%), Mantle cell lymphoma in 8 cases (10%), Marginal zone lymphomas in 7 cases (9%), Primary mediastinal large B-cell lymphoma (PMBCL) in 5 patients (6%), and Follicular Lymphoma in 1 patient (1%).

In our series, T-cell lymphoma was found in 12 patients, comprising 16% of the cases. The specific histological types observed were: 1 case of T-cell lymphoma Gamma Delta, 5 cases of peripheral T-cell lymphoma Not Otherwise Specified (PTCL-NOS), 3 cases of T/NK Nasal lymphoma, 3 patients with Anaplastic T-cell lymphoma, and 1 case of Mycosis Fungoides (Table1).

	Histological Type	Cases	Percentage
Lymphomes B	DLBCL	39	48%
	Burkitt Lymphoma	9	11%
	Marginal zone lymphoma	7	9%
	Mantle cell lymphoma	8	10%
	Mediastinal lymphoma	5	6%
	Follicular lymphoma	1	1%
Lymphomes T	T Gamma Delta lymphoma	1	1%
	T lymphoma NOS	5	6%
	T/NK nasal lymphoma	3	4%
	Anaplastic large cell lymphoma	3	4%
	Mycosis Fungoïde	1	1%

Table 1: *Distribution of NHLs according to histological type.*

After completing the extensive diagnostic workup, which included thorough clinical examination, chest x-ray, body CT scan, PET scan and bone marrow biopsy, patients were staged according to the ANN ARBOR classification. This resulted in 43% of patients classified as having localised stages (I, II) and 57% as having advanced stage disease (II-IV).

**Figure 2:** *Distribution of NHLs according to the ANN ARBOR classification.*

The patients in our series were treated with protocols specifically designed according to their histological type, existing comorbidities, and the stage of disease progression. This personalised strategy ensured that each patient received the most suitable and effective treatment.

The majority of patients with DLBCL were treated with the R-CHOP protocol (37 patients), while one patient with primary cerebral lymphoma received the RMPV protocol, and another patient was treated with the COP regimen.

In cases with mantle cell lymphoma, 4 cases received RCHOP protocol which was complemented by RDHAP protocol in one patient. Moreover, 3 patients were treated by RDHAOX protocol and 4 patients had BEAM high dose chemotherapy with autologous stem cell transplantation.

Patients with mediastinal lymphoma underwent R-DAEPOCH chemotherapy, while patients with follicular lymphoma and marginal zone lymphoma received R-CHOP regimen.

7 patients with Burkitt lymphoma were treated by LMBA02 protocol, whereas 2 patients had R-DAEPOCH

protocol.

On the other hand, patients with T lymphoma NOS received CHOEP protocol and 1 patient was treated by Cop protocol. All patients with T/ NK nasal lymphoma were treated by SMILE regimen.

The progression-free survival rates at 50 months are estimated to be 59% for diffuse large B-cell lymphomas (DLBCL), 77% for Burkitt lymphomas, 80% for mediastinal large B-cell lymphomas, 62% for mantle cell lymphomas, 71% for marginal zone lymphomas, and 23% for T-cell lymphomas.

Discussion

In our study, the mean age of NHL patients was 54 years. This finding is slightly higher compared to several studies from Arab countries. For instance, in Egypt, the mean age from 1995 to 2004 was 51.6 years [2], while in Lebanon, the mean age from 1984 to 2009 was 53.52 [3].

In the United States, the mean age of NHL patients between 2012 and 2016 was significantly higher at 67 years [4]. This substantial difference may reflect variations in healthcare access, lifestyle factors, and population demographics across regions.

The predominance of males in our cohort (72%) also reflects broader epidemiological trends, as many studies report a higher incidence amongst males [5] [3] [6] [7].

Non-Hodgkin lymphomas comprise a wide variety of lymphoproliferative malignancies, each with unique pathogenetic mechanisms. These mechanisms often include immunosuppression, especially in relation to T-cell activity, Epstein-Barr virus (EBV) infections, and chronic antigen stimulation [8]. In our study, some patients were exposed to these risk factors, while others were not.

The delay in seeking care, ranging from 1 month to 2 years, underlines the challenges in early diagnosis. In our study, the mean time between symptom onset and specialist consultation was 5 months, with 67% of patients consulting a specialist within 2 to 6 months. This finding is slightly longer than another study, which reports a mean delay of 3.4 months [9].

Peripheral lymphadenopathy was the primary reason for consultation in 39% of our patients, a finding consistent with the literature where lymphadenopathy is a common presenting symptom [8]. The observation that 32.9% of NHL cases were discovered due to extra-nodal symptoms, such as digestive issues, aligns with reports indicating that NHL can present with a range of extra-nodal manifestations [10].

Type B NHL was the most frequent in our study, representing 84% of cases, with diffuse large B-cell lymphoma (DLBCL) being the predominant subtype (56%). This distribution is similar findings from other

studies, which also identified DLBCL as the most common subtype in B-cell NHL [11] [12], [13] T cell lymphoma represented 16% of all the cases, which is similar to other studies where TCL represented similar proportions [14], however this percentage is relatively low compared to other studies in China [15] (30% of all NHL) and Japan [16] (27%).

Amongst T cell lymphomas, Peripheral T cell lymphoma not otherwise specified (PTCL-NOS) was the most common histological subtype, which is a similar finding in a study conducted in Spain [17] However, a study in Mexico reported higher frequency of T/NK subtype [11].

Our study found 43% of patients in localised stages and 57% in advanced stages, which is comparable to findings in the literature where a significant proportion of NHL patients present at advanced stages [3], [9] [18]

The use of R-CHOP for DLBCL and the varied regimens for other subtypes are in line with standard practices, though specific regimen choices and their outcomes can vary based on local practices and patient characteristics.

Our reported progression-free survival (PFS) rates at 50 months vary by subtype, with DLBCL at 59%, Burkitt lymphoma at 77%, and T-cell lymphomas at 23%. These rates are consistent with the literature, where DLBCL and Burkitt lymphoma typically have higher survival rates compared to T-cell lymphoma [11] [17]. The lower survival rate for T-cell lymphomas reflects the generally poorer prognosis associated with these types, as noted in various studies [19] [20].

Conclusion

The research underscores the heterogeneous nature of Non-Hodgkin Lymphoma (NHL) cases, revealing that a considerable number of patients are diagnosed at an advanced stage of the disease, often during middle age. This late-stage diagnosis significantly impacts treatment outcomes and prognosis. Furthermore, the study draws attention to the particularly poor survival rates observed in patients with T-cell lymphomas, a more aggressive subtype of NHL. These findings suggest a pressing need for earlier detection strategies, improved therapeutic options, and tailored treatment approaches to address the distinct challenges posed by T-cell lymphomas.

References

1. Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R, Advani R, Ghielmini M, Salles GA, Zelenetz AD, Jaffe ES., "The 2016 revision of the World Health Organization classification of lymphoid neoplasms.," *Blood*, no. 9;127(20):2375-90, 2016.
2. Abdel-Fattah MM, Yassine OG, "Non-Hodgkin's lymphomas in Alexandria,Egypt; incidence rates and trend study (1995–2004).," *Eur J Cancer Prev.*, p. 16(5):479–85., 2007.
3. Touma E, Antoun L, Hallit S, Nasr F, Massoud M, El Othman R, Chahine G., "Non Hodgkin lymphoma in Lebanon: a retrospective epidemiological study between 1984 and 2019.," *BMC Public Health.*, no. 9;21(1):1820., 2021 Oct.
4. Müller AMS, Ihorst G, Mertelsmann R, Engelhardt M., "Epidemiology of non- Hodgkin's lymphoma (NHL): trends, geographic distribution, and etiology.," *Ann Hematol*, vol. 84(1):1–12., 2005.
5. "Office for National Statistics. Index of cancer survival for Clinical Commissioning Groups in England: adults diagnosed 2001 to 2016 and followed up to 2017.".
6. Lal A, Bhurgri Y, Vaziri I, Rizvi NB, Sadaf A, Sartajuddin S, Islam M, Kumar P, Adil S, Kakepoto GN, Masood N, Khurshed M, Alidina A., "Extranodal non-Hodgkin's lymphomas--a retrospective review of clinico-pathologic features and outcomes in comparison with nodal non-Hodgkin's lymphomas.," *Asian Pac J Cancer Prev*, pp. 9(3):453-8, 2008.
7. Grulich, A. E., & Vajdic, C. M., "Grulich AE, Vajdic CM. The epidemiology of non-Hodgkin lymphoma," *Pathology*, pp. 37(6):409-19, 2005 Dec.
8. Singh, Rohit & Shaik, Shabana & Negi, Bhupender & Rajguru, JagadishPrasad & Patil, PankajBajirao & Parihar, AnujSingh & Sharma, Uma, "Non-Hodgkin's lymphoma: A review.," *Journal of Family Medicine and Primary Care.*, p. 9. 1834. 10.4103, 2020.
9. Allgar VL, Neal RD, "Delays in the diagnosis of six cancers: analysis of data from the National Survey of NHS Patients: Cancer," *Br J Cancer*, pp. 6;92(11):1959-70, 2005 Jun.
10. R. Otter, W.B.J. Gerrits, M.M.V.D. Sandt, J. Hermans, R. Willemze, "Primary extranodal and nodal non-Hodgkin's lymphoma: A survey of a population-based registry," *European Journal of Cancer and Clinical Oncology*, vol. 25, no. 8, pp. 1203-12010, 1989.
11. Hernandez-Ruiz E, Alvarado-Ibarra M, Juan Lien-Chang LE, Banda-Garcia L, Aquino-Salgado JL, Barragan-Ibanez G, Ramirez-Romero EF, Nolasco-Cancino C, Herrera-Olivares W, Morales-Adrian JJ, Paredes-Lozano EP, Espitia-Rios ME, Gonzalez Lopez-Elizalde MM, Lop, "Epidemiology and Clinical Characteristics of Non-Hodgkin Lymphoma in Mexico.," *World J Oncol.*, no. World J Oncol., 2021.

12. Badheeb, Ahmed Mohamed & Ahmed, Faisal & Alyami, Nasher & Badheeb, Mohamed & Elhadi, Musadag., "Clinical and Therapeutic Profile of Non-Hodgkin's Lymphoma: A Retrospective Study From a Najran Oncology Center.," *Cureus*, no. 8;15(6):e40125, 2023.
13. Akhter, A and Rahman, MR and Majid, N and Shermin, S and Saleheen, MS and Rajib, RC and Ullah, SMA and Haque, N and Akond, AK, "Histological subtypes of Non-Hodgkin's Lymphoma in different age and sex groups," *Bangladesh Medical Journal*, vol. 41, pp. 32-36, 2012.
14. Naz E, Mirza T, Aziz S, Danish F, Siddiqui ST, Ali A., "Frequency and clinicopathologic correlation of different types of non Hodgkin's lymphoma according to WHO classification," *J Pak Med Assoc.*, pp. 61(3):260-3., 2011.
15. Yang, QP., Zhang, WY., Yu, JB. et al., "Subtype distribution of lymphomas in Southwest China: Analysis of 6,382 cases using WHO classification in a single institution.," *Diagn Pathol* 6, 77, 2011.
16. Ryosuke Aoki, Kennosuke Karube, Yasuo Sugita, Yuko Nomura, Kay Shimizu, Yoshizo Kimura, Keiko Hashikawa, Nobuko Suefuji, Masahiro Kikuchi and Koichi Ohshima, "Distribution of malignant lymphoma in Japan: Analysis of 2260 cases, 2001–2006," *Pathology International*, 2008.
17. Bastos-Oreiro M, Muntañola A, Panizo C, Gonzalez-Barca E, de Villambrosia SG, Córdoba R, López JLB, González-Sierra P, Terol MJ, Gutierrez A, Grande C, Ramirez MJ, Iserte L, Perez E, Navarro B, Gomez P, Salar A, Luzardo H, López A, Del Campo R, García-Bel, "RELINF: prospective epidemiological registry of lymphoid neoplasms," *Ann Hematol*, 2020.
18. Zeynep Deniz Tutun, Ganiye Begül Küpeli, Buğra Tutun., "NON-HODGKIN'S LYMPHOMA: A RETROSPECTIVE ASSESSMENT OF CLINICAL FEATURES AND TREATMENT OUTCOMES," *Hematology, Transfusion and Cell Therapy*, vol. 44, no. 1, p. 42, 2022.
19. Escalón, M.P., Liu, N.S., Yang, Y., Hess, M., Walker, P.L., Smith, T.L. and Dang, N.H., "Prognostic factors and treatment of patients with T-cell non-Hodgkin lymphoma. *Cancer*, 103: 2091-2098. <https://doi.org/10.1002/cncr.20999>".



Medtronic