

## CLINICAL-EPIDEMIOLOGICAL EVALUATION OF HODGKIN AND NON-HODGKIN LYMPHOMAS AT LONDRINA CANCER HOSPITAL IN THE YEAR OF 2018

### AVALIAÇÃO CLÍNICO-EPIDEMIOLÓGICA DOS LINFOMAS DE HODGKIN E NÃO HODGKIN NO HOSPITAL DO CÂNCER DE LONDRINA NO ANO DE 2018

Luana Ferreira **Ferri\*** , Eduardo Ramiro **Pasiani** , Jeissi Camila **Furlan** , Carlos Eduardo Coral de **Oliveira** , Laura Cinquino **Franco** , Adriano Morita Fernandes da **Silva** 

Pontifical Catholic University of Parana, Londrina, PR, Brazil.

\*luanafferri@hotmail.com

#### ABSTRACT

Lymphomas are a heterogeneous group of hematological neoplasms that can occur in individuals of both sexes and of all ages. They are subdivided into Hodgkin's and non-Hodgkin's lymphoma, and originate from lymphocytes at different stages of development and can affect any organ. Its diagnosis is not always easy since it presents with varied symptoms, and for this reason, it is often diagnosed at an advanced stage. National data on the epidemiology of lymphomas are limited. The objective of this study is to analyze clinical and epidemiological data of individuals with lymphoma in a cancer treatment reference center in Paraná. Observational, retrospective study of analysis of medical records of patients over 18 years of age, of both genders, diagnosed with Hodgkin's and non-Hodgkin's lymphoma followed by the Londrina Cancer Hospital in the year of 2018. The data collected were number of cases, age, sex, municipality of origin and Ann Arbor clinical staging. Our study found a low incidence of non-Hodgkin's lymphoma and a high frequency of advanced disease compared to other centers. Patients with advanced disease came from cities with a lower median Human Development Index (HDI) compared to those with early disease. The analysis of patients with Hodgkin's lymphoma found data similar to that of other centers. The low incidence of non-Hodgkin's lymphoma and the high number of cases with advanced disease allows the development of strategies for recognizing the disease and improve assistance to the population in Londrina region.

**Keywords:** Epidemiology. Hodgkin's Lymphoma. Non-Hodgkin's Lymphoma.

#### RESUMO

Os linfomas são um grupo heterogêneo de neoplasias hematológicas que podem ocorrer em indivíduos de ambos os sexos e de todas as idades. São subdivididos em linfoma de Hodgkin e não Hodgkin, e têm origem em linfócitos em diferentes fases de desenvolvimento, podendo afetar qualquer órgão. Seu diagnóstico nem sempre é fácil já que se apresenta com sintomas variados e, por isso, frequentemente é diagnosticado em fase avançada. Dados nacionais sobre a epidemiologia dos linfomas são limitados. Este trabalho tem como objetivo analisar dados clínicos e epidemiológicos de indivíduos com linfoma em um centro de referência de tratamento oncológico no Paraná. Estudo observacional, retrospectivo, de análise de prontuários médicos de pacientes acima de 18 anos, de ambos os sexos, com diagnóstico de linfoma de Hodgkin e não Hodgkin acompanhados pelo Hospital de Câncer de Londrina no ano de 2018. Os dados coletados foram número de casos, idade, sexo, município de procedência estadiamento clínico de Ann Arbor. Nosso estudo observou baixa incidência de linfoma não Hodgkin e frequência elevada de doença avançada em comparação com outros centros. Pacientes com doença avançada eram provenientes de municípios com menor mediana do Índice de Desenvolvimento Humano (IDH) em comparação com aqueles com doença precoce. A análise de pacientes com linfoma de Hodgkin encontrou dados semelhantes ao de outros centros. A baixa incidência de linfoma não Hodgkin e número alto de casos com doença avançada permite a elaboração de estratégias para reconhecer precocemente a doença e melhorar a assistência à população na região de Londrina.

**Palavras-chave:** Epidemiologia. Linfoma de Hodgkin. Linfoma não Hodgkin.

## INTRODUCTION

Cancer is a potentially life-threatening clinical condition that affects individuals of all ages and it is estimated that in 2018 there were approximately 18.1 million new cases of cancer in the world (PAHO, 2018). In Brazil, according to the Brazilian National Cancer Institute (INCA), it is assumed that between 2018 and 2019 there were 600 thousand new cases (INCA, 2018).

The term cancer is used to define a group of more than one hundred diseases that share disorderly cell growth (MINISTÉRIO DA SAÚDE, 2011). In Brazil, it is estimated that hematological neoplasms are responsible for approximately 5% of cases and 7% of all cancer deaths (CORREA, 2019). The most common hematological neoplasm is lymphoma, which is classically subdivided into Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). Lymphomas arise from lymphocytes at different stages of development and are characterized by masses of lymphoid tissue that can affect any organ in the body, and present with very varied clinical manifestations. Therefore, suspected cases of lymphoma can be seen by the general practitioner or by doctors of different specialties who must be attentive to its recognition (SILVA, ARAÚJO, FRIZZO, 2015). Non-Hodgkin lymphoma is responsible for the vast majority of lymphoma cases (85-90% of cases) and approximately 4% of new cancer cases. It is a heterogeneous group of diseases that has its origin mainly in the B cell (85-90%), it is more common in men, in white people and in those over 50 years old (ARAÚJO *et al.*, 2008; GOUVEIA *et al.*, 2011).

Hodgkin lymphoma, on the other hand, affects 10-15% of individuals with lymphoma, and is characterized by being a mature B cell neoplasia affecting from young to elderly individuals (INCA, 2018). North American data show the occurrence of two peaks of incidence, being more common in young adults up to 30 years old and in the elderly (NATIONAL CANCER INSTITUTE, 2020).

National data on the incidence of lymphomas are limited and do not reflect all regions of the country, therefore, this study aims to provide data on the epidemiology of lymphomas in a reference center for cancer treatment in Paraná.

## METHODOLOGY

Retrospective descriptive study, submitted and approved by the Research Ethics Committee (CEP), on November 28, 2018, number 3.043.54, through Plataforma Brasil. It was conducted through the analysis of medical records of patients diagnosed with lymphoma and followed up at the Londrina Cancer Hospital from January 1st to December 31st, 2018. Inclusion criteria: diagnosis of HL or NHL, including all subtypes, as criteria established by the World Health Organization, age greater than or equal to 18 years, both sexes. Exclusion criteria: absence of specific diagnostic criteria for the aforementioned hematological neoplasms, age below 18 years.

The data collected by the medical record analysis include: age, sex, origin, type of lymphoma and Ann Arbor staging, which classifies patients into four clinical stages (CS) ranging from I to IV, according to lymph node involvement and involvement of organs, and subclassified according to the presence or absence of B symptoms (fever, night sweats or loss of more than 10% of body weight in 6 months) (MINISTÉRIO DA SAÚDE, 2020). Patients with CS I and II are considered to have an early disease and CS III or IV as an advanced disease (HALLACK NETO *et al.*, 2006; LOPES *et al.*, 2012). For the analysis of the incidence, the coverage area of the Londrina Cancer Hospital and its population assisted, which consists of approximately 1.5 million inhabitants, were considered. And from the source data, the HDI of each city was identified, based on the database of the Brazilian Institute for Applied Economic Research (PNUD, 2013).

Exploratory analyzes were performed on the data obtained. For continuous variables the data were described as median (interquartile range) and for dichotomous variables as a percentage.

Graphs were created showing the distribution according to the age of involvement and staging of the different diseases. The analysis of the HDI in patients with early and advanced disease was performed using the Mann-Whitney test.

## RESULTS AND DISCUSSION

In 2018, a total of 128 new cases of lymphoma were identified, with 96 cases of NHL and 32 cases of HL.

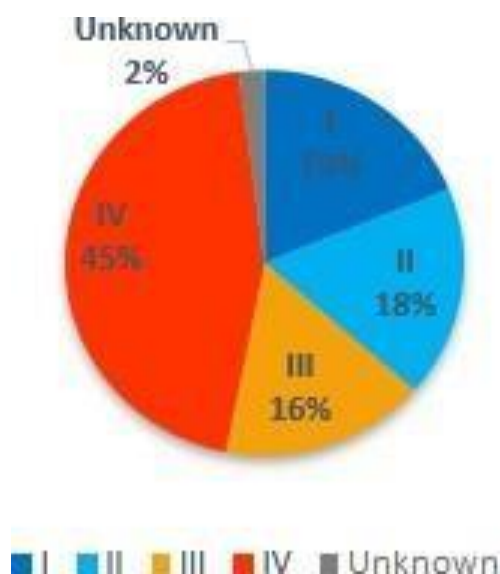
### Non-Hodgkin lymphoma

Ninety-six NHL cases with similar distribution between genders (47 men and 49 women) were evaluated, unlike another study that found a predominance in the male population (1.39: 1). The median age was 63 years (IQR 53-72 years), compatible with data from the literature (NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE, 2016).

The incidence of NHL found in our study was 6.44 cases per 100,000 inhabitants. Data from a study conducted in the United States showed an incidence rate approximately 3 times higher (FISHER, FISHER, 2004). This discrepancy may be related to difficulty in diagnosing the disease since the clinical manifestations are very varied and can be confused with other ones. The low incidence observed highlights the importance of reinforcing the continuing education of doctors to minimize possible failures in the early recognition of NHL.

As for staging, 37% of patients with early disease (19% CS I, 18% CS II), 61% advanced disease (16% CS III, 45% CS IV) were observed and in 2% of cases it was unknown (Figure 1). Our result is different from a study conducted in the United States, with a sample of 13,691 patients, which found a higher incidence of patients at an early stage (58%) (SHENOY *et al.*, 2011). Another data observed in our study was that approximately half of the patients had symptoms B (52%), unlike the literature that verifies the presence of symptoms B in 40% of the cases (ARAÚJO *et al.*, 2008). These discrepancies may be related to socioeconomic or cultural factors that are associated with difficulty in accessing health services as well as failures in the recognition of the disease by doctors in earlier CS.

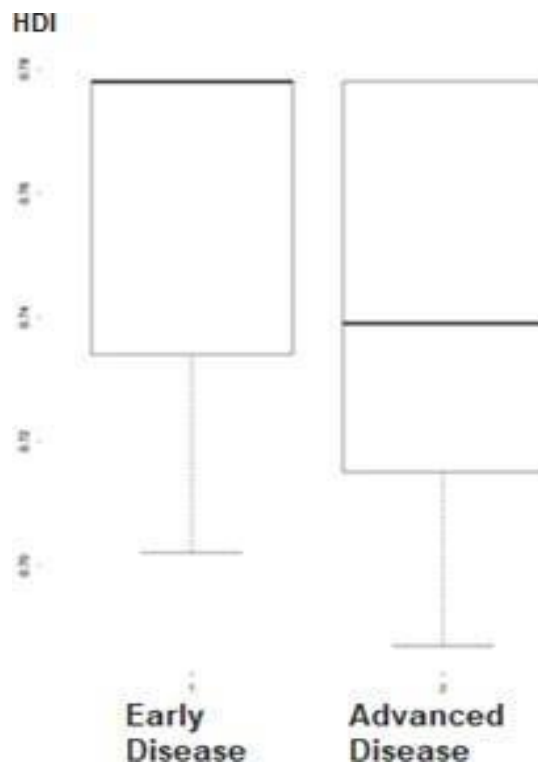
**Figure 1** - Distribution of staging by the Ann Arbor system of non-Hodgkin lymphoma



**Source:** the authors.

Ninety-three patients were evaluated, belonging to 27 cities, of which 44% were from Londrina-PR, then analyzing the HDI of each location. We found that the median HDI was significantly higher in patients with early disease (HDI = 0.778) compared to the advanced disease group (HDI = 0.739) ( $p = 0.02689$ ) (Figure 2). This difference in the HDI can be explained by the greater difficulty in accessing these patients to the specialized health service, leading to a delay in diagnosis.

**Figure 2** - Comparison of median HDI in patients with NHL in early and advanced CS



Source: the authors.

### Hodgkin lymphoma

Of the 32 cases of HL, 16 were men and 16 women, in agreement with data from the literature in which there is no predominance of the disease in any gender.

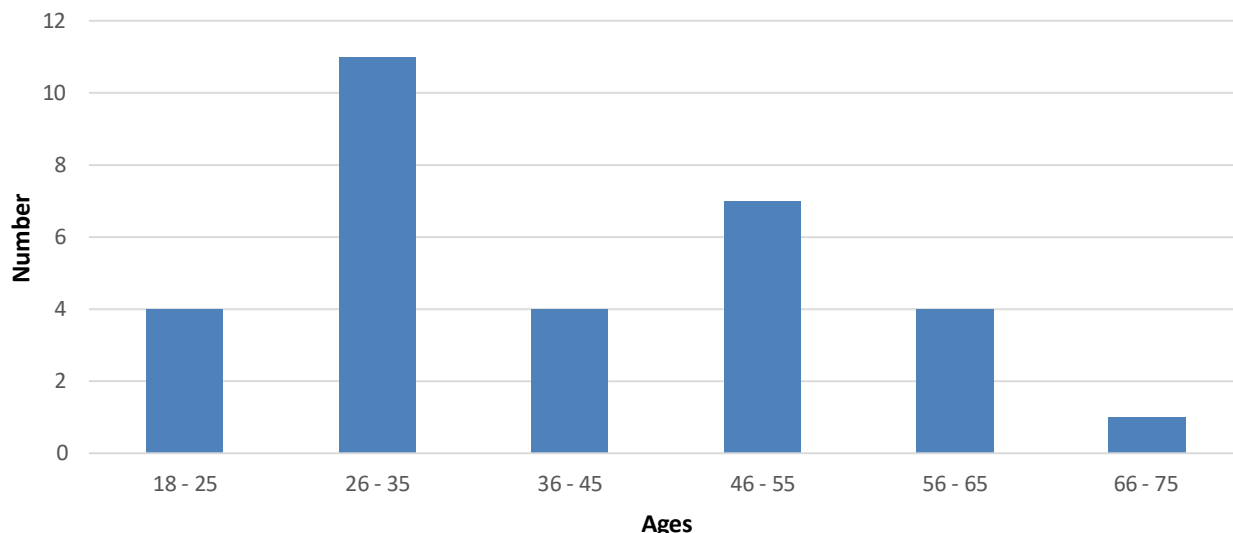
The incidence of cases of HL in 2018 was 2.15 cases per 100,000 inhabitants, similarly to that found in a study conducted in Europe (2.4/100,000 inhabitants) (ASTER; FREEDMAN; ROSMARIN, 2018).

The median age was 36 years with an interquartile range (IQR) of 29.7-50.2 years. The age distribution showed two peaks of incidence - one around 26-35 years and the other around 46-55 years (Figure 3). We observed that the second peak of incidence in our study was at a younger age than that found in other studies, however, the number of patients evaluated was small and we did not analyze the histological subtypes (NATIONAL CANCER INSTITUTE, 2020).

Concerning staging, we observed 35% with early disease (10% CS I, 25% CS II) and 65% with advanced disease (31% CS III and 34% CS IV). The staging distribution observed in our study is similar to that found in other studies in which approximately 70-80% of patients diagnosed with advanced disease are observed (SPECTOR, 2004). We also observed that men had a higher frequency of illness in CS IV (44%) compared to women (25%), which could be explained by the fact that women seek care earlier than men (Figure 4). In addition, we observed a high frequency of B symptoms in the patients analyzed in our study (88%), differently from other studies that found

rates around 25% (MACHADO *et al.*, 2004). This discrepancy in relation to B symptoms may reflect difficulties in recognizing the disease at earlier stages.

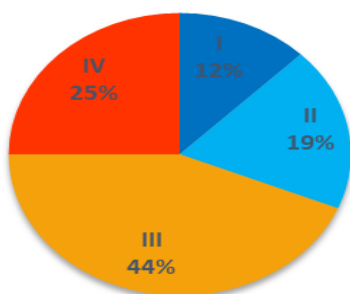
**Figure 3 -** Age distribution at diagnosis of Hodgkin lymphoma



Source: the authors.

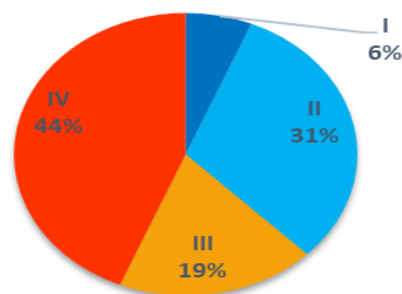
**Figure 4 -** Comparison between staging by the Ann Arbor system in Hodgkin Lymphoma in both genders.

**HL staging Women**



■ I ■ II ■ III ■ IV

**HL staging Men**

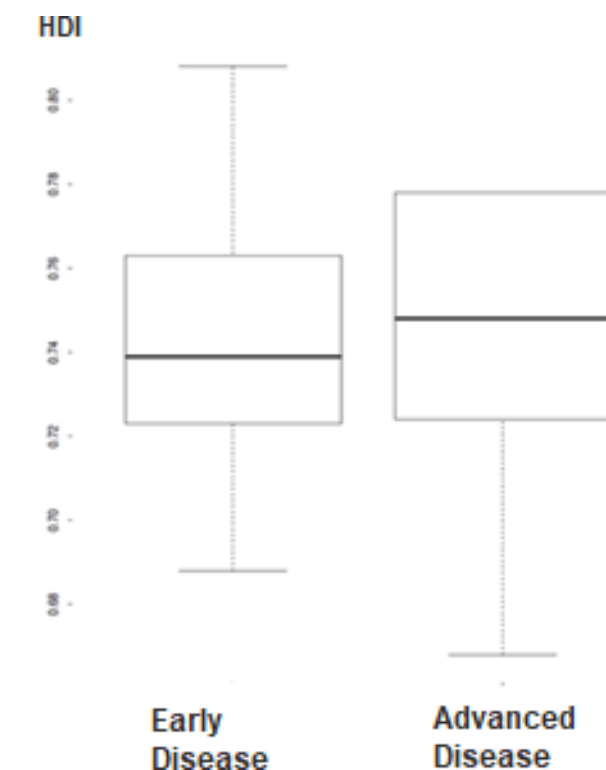


■ I ■ II ■ III ■ IV

Source: the authors.

Thirty-one patients were evaluated regarding the HDI of the municipality of origin, which corresponded to 16 municipalities, with Londrina-PR being responsible for 31% of the cases. We found no difference in the median HDI between the group of patients with early disease (HDI = 0.739) compared to the group of advanced disease (HDI = 0.748) ( $p = 0.7847$ ) (Figure 5).

**Figure 5** - Comparison of median HDI in the municipality of origin of patients with early and advanced Hodgkin lymphoma



Source: the authors.

## CONCLUSION

The incidence of NHL observed in our study was lower than that of other centers and there was a predominance of disease in advanced staging. Patients with advanced NHL came from municipalities with a lower HDI. Regarding HL, we observed that the incidence was similar to data in the literature. Most were diagnosed with advanced disease and there was no relationship with the municipality of origin.

These data help to understand the local reality, contribute to the development of strategies to improve the early diagnosis of lymphomas and serve as a parameter for planning assistance to the population in the city of Londrina and region.

## REFERENCES

ARAÚJO, L. H. L. *et al.* Linfoma não Hodgkin de alto grau – revisão da literatura. **Revista Brasileira de Cancerologia**, v. 54, n. 2, p. 175-183, 2008.

ASTER, J. C.; FREEDMAN, A. S.; ROSMARIN, A. G. Epidemiology, pathologic features, and diagnosis of classic Hodgkin lymphoma. **UpToDate**, junho de 2018. Disponível em: <https://www.uptodate.com/contents/epidemiology-pathologic-features-and-diagnosis-of-classic-hodgkin-lymphoma>. Acesso em 15 de maio de 2019.

CORREA, N. Trajetória da Incidência e Mortalidade das Neoplasias Hematológicas no Brasil. **Observatório de Oncologia**, 2019. Disponível em: <https://observatoriodeoncologia.com.br/trajetoria-da-incidencia-e-mortalidade-das-neoplasias-hematologicas-no-brasil>. Acesso em 12 nov. 2020.

FISHER, S. G.; FISHER, R. I. The epidemiology of non-Hodgkin's lymphoma. **Oncogene**, v. 23, n. 38, p. 6524-6534, 2004.

GOUVEIA, G. *et al.* Prevalence of non-Hodgkin lymphomas in São Paulo, Brazil. **Revista Brasileira de Hematologia e Hemoterapia**, v. 33, n. 4, p. 317, 2011.

HALLACK NETO, A. E. H. *et al.* Estratificação de risco em linfoma difuso de grandes células B. **Revista Brasileira em Hematologia e Hemoterapia**, v. 28, n. 4, p. 296-300, 2006.

HOFFBRAND, A. V.; MOSS, P. A. H. **Fundamentos em hematologia**. 6. ed. Artmed: Porto Alegre, 2013. 464 p.

INSTITUTO NACIONAL DE CÂNCER JOSÉ ALENCAR GOMES DA SILVA. Estimativa 2018: Incidência de Câncer no Brasil. **Revista Brasileira de Cancerologia**, v. 64, n. 1, p. 119-120, 2018.

LOPES, G. C. B.; MOREIRA, W. B.; SOARES, A. N. Avaliação dos resultados do tratamento de pacientes portadores de linfoma de Hodgkin com esquema ABVD em primeira linha. **Revista Brasileira de Oncologia Clínica**, v. 8, n. 29, p. 112-120, 2012.

MACHADO, M. *et al.* Linfoma de Hodgkin – Conceitos atuais. **Medicina Interna** v. 11, n. 4, p. 207-215, 2004.

MINISTÉRIO DA SAÚDE. **ABC do câncer – abordagens básicas para o controle do câncer**, p. 14. Rio de Janeiro: INCA, 2011.

MINISTÉRIO DA SAÚDE. Diretrizes Diagnósticas e Terapêuticas do Linfoma de Hodgkin. **Coordenação de Gestão de Protocolos Clínicos e Diretrizes Terapêuticas**, Brasília, p. 11-12, 2020.

NATIONAL CANCER INSTITUTE. SEER Cancer Statistics Review 1975-2017. Surveillance Epidemiology and End Results. **National Institute of Health**, 2020. Disponível em: [https://seer.cancer.gov/csr/1975\\_2017](https://seer.cancer.gov/csr/1975_2017). Acesso em 03 dez. 2020.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE. Non-Hodgkin's lymphoma: diagnosis and management. **NICE guideline**, p. 1-25, 2016. Disponível em: <https://www.nice.org.uk/guidance/ng52/resources/nonhodgkins-lymphomadiagnosis-and-management-pdf-1837509936325>. Acesso em: 23 maio 2019.

ORGANIZAÇÃO PAN-AMERICANA DA SAÚDE BRASIL. Folha informativa – Câncer. **Agência Internacional de Pesquisa em Câncer (International Agency for Research on Cancer – IARC)**, 2018. Disponível em: [https://www.paho.org/bra/index.php?option=com\\_content&view=article&id=5588:folha-informativa-cancer&Itemid=1094](https://www.paho.org/bra/index.php?option=com_content&view=article&id=5588:folha-informativa-cancer&Itemid=1094). Acesso em: 15 nov. 2020.

PROGRAMA DAS NAÇÕES UNIDAS PARA O DESENVOLVIMENTO. O Índice de Desenvolvimento Humano Municipal Brasileiro. **Série Atlas do Desenvolvimento Humano no Brasil**. Brasília, 2. ed., 2013.

SHENOY, P. *et al.* Incidence Patterns and Outcomes for Hodgkin Lymphoma Patients in the United States. **Advances in Hematology**, v. 2011, p. 1-11, 2011. Disponível em <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3010617/>. Acesso 7 jun. 2019.

SILVA, F. C.; ARAÚJO, L. S.; FRIZZO, M. N. Neoplasias hematológicas no idoso: uma revisão. **Revista Saúde Integrada**, v. 8, n. 15-16, 2015.

SPECTOR, N. Abordagem atual dos pacientes com doença de Hodgkin. **Revista Brasileira de Hematologia e Hemoterapia**, v. 26, n. 1, p. 35-42, 2004. Disponível em: <http://www.scielo.br/pdf/rbhh/v26n1/v26n1a07.pdf>. Acesso em: 14 maio 2019.