DOI: http://dx.doi.org/10.33846/hn50405 http://heanoti.com/index.php/hn



URL of this article: http://heanoti.com/index.php/hn/article/view/hn50405

# The Relationship Between Clinical Manifestation and Histopatological Result in Non-Hodgkin Lymphoma: RSUD Dr. Soetomo Surabaya

Glazydia Juwita Rachma<sup>1(CA)</sup>, Ugroseno Yudho Bintoro<sup>2</sup>, Mia Ratwita Andarsini<sup>3</sup>, Novira Widajanti<sup>4</sup>
<sup>1(CA)</sup>Faculty of Medicine, Universitas Airlangga, Indonesia; jemyjuju@gmail.com (Corresponding Author)

<sup>2</sup>Department of Haematology, RSUD DR. Soetomo, Surabaya, Indonesia; ugrosenoyb@yahoo.com

<sup>3</sup>Department of Pediatrics, RSUD Dr. Soetomo Surabaya, Indonesia; dr.intanidewi@gmail.com

<sup>4</sup>Department of Geriatrics Interna, RSUD Dr. Soetomo, Surabaya, Indonesia; novirawidajanti@fk.unair.ac.id

#### **ABSTRACT**

Non-Hodgkin's lymphoma is a major public health problem with over 14.1 million people are diagnosed with it (2012). In the same year there were 8.2 million deaths due to cancer. The purpose of this study was to determine the relationship between clinical manifestations and the degree of malignancy based on histopathological features in patients with Non-Hodgkin's Lymphoma. This study used a retrospective analytical method with a cross-sectional approach using the patient's medical record at RSUD Dr. Soetomo, Surabaya who was diagnosed with Non-Hodgkin Lymphoma from 1st January 2015 to 31st December 2017. In this study, there were 139 samples include those criteria, with a greater number of male samples (62.6%) compared to women (37.4%). This study showed that 49.3% of patients with non- Hodgkin's lymphoma in RSUD Dr. Soetomo with clinical manifestations without symptoms actually experience malignancy with a high degree, this showed that clinical manifestations without symptoms are not always associated with a low level of malignancy. Then, based on the Chi Square test results obtained p-value of 0.289 (>0.05), so there was no significant relationship between clinical manifestations and the degree of malignancy.

**Keywords:** lymphoma; manifestation; histopatological

# INTRODUCTION

## **Background**

According to GLOBOCAN (IARC) data for 2012, Non-Hodgkin's Lymphoma ranks eighth out of ten most cancers in the world <sup>(1)</sup>. In the same year a mortality rate of 8.2 million was recorded due to cancer. The symptoms are often non-specific in lymphoma sufferers <sup>(2)</sup>. Symptoms of weight loss, fever and night sweats should be watched because they are associated with poor prognosis. There are complicated and difficult problems regarding the histological classification of LNH, moreover its still very varied treatment can affect various aspects of healing. The Histological classification of IWF has a good predictive value to determine the clinical behavior of this malignancy.

This system is the basis for therapeutic action <sup>(3)</sup> Non-Hodgkin's Lymphoma Classification in Dr. RSUD patients Soetomo allegedly showed linear results with clinical manifestations. For that reason, the researcher wanted to find a link between the clinical manifestation of non-Hodgkin's lymphoma patients in Dr. Soetomo with the IWF classification.

## Purpose

This study aims to determine the relationship between clinical manifestations with the results of histopathological examination of patients with non-Hodgkin's lymphoma in Dr. Soetomo.

## **METHODS**

This study used an analytical retrospective method with a cross-sectional approach of all patient folders and medical records from 1st January 2015 to 31st December 2017, was carried out. Institutional approval was obtained from ethical clearance RSUD Dr. Soetomo. The research was located on the RSUD Dr. Soetomo Surabaya and conducted at the Outpatient Unit POSA (*Poli Onkologi Satu Atap*) RSUD Dr. Soetomo with the time of the study which began on 24th July 2018. The sampling used a total population sampling method within the study period that meets the inclusion criteria; (i) female or male patient, (ii) patients over the age of 18 years. Exclusion criteria: incomplete medical record data. The data collected from the medical records were limited to only information that was necessary to the study. No personal identifiable data was collected. Only the authors had access to the data. In this study using the SPSS 16.0.0 software program for Windows, 2007, SPSS Inc. Chicago, IL, USA and Microsoft Office 2007.

# RESULTS Clinical Manifestations with Degrees of Malignancy Based on Histopathological Features

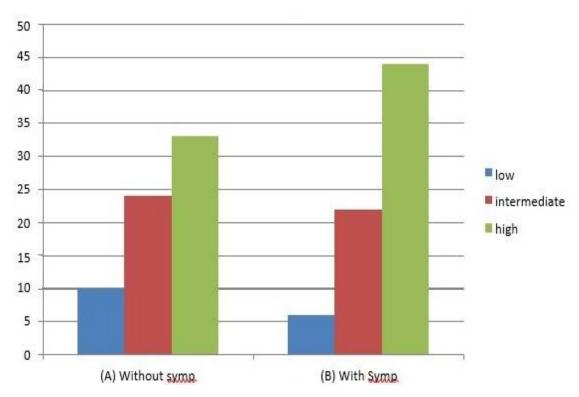


Figure 1. Distribution of Non-Hodgkin's Lymphoma patients based on clinical manifestations with degrees of malignancy

The 44 people (61.1%) patients with systemic symptoms experienced malignancies with a high degree. Then the highest number of patients without systemic symptoms experienced malignancies with a high degree of 33 people (49.3%). In addition, patients with clinical manifestations in the form of systemic symptoms, had a very low prevalence of malignancy with a mild degree, as many as 6 people (8.3%).

# Degree of Malignancies Based on Age

Patients within <60 years old experienced a high degree of malignancy that was 58 people. In the age range >60 years, the lowest number of patients with low malignancy is 2 people.

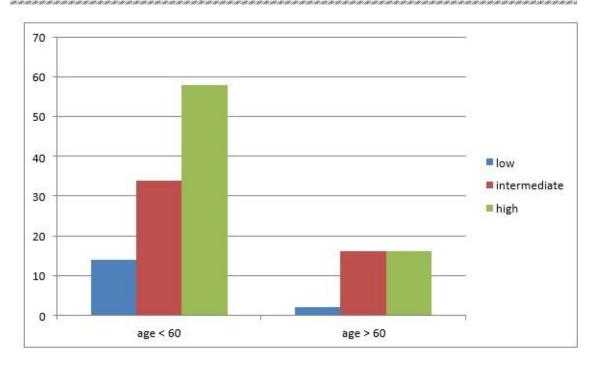


Figure 2. Distribution of Non-Hodgkin's Lymphoma patients by age and degrees of malignancy

Table 1. Distribution of research subjects

# **Description of Variables**

Variables	n = 139	Percentege
Gender		
Male	87	62.6
Female	52	37.4
Age		
18-60	107	76.42
> 60	33	23.58
Clinical manifestation		
Without symptoms (A)	67	48.2
With symptoms (B)	72	51.8
Grade Histo PA		
Low	16	11.5
Intermediate	46	33.1
High	77	55.4

Non-Hodgkin's Lymphoma patients were more common in male (table 1). Above 60 years old, only 33 people were found affected by non-Hodgkin's Lymphoma. There was no significant differences in clinical manifestation. 139 samples of Non- Hodgkin's Lymphoma patients was found that most patients with a high degree of malignancy were 77 people (55.4%).

# The Relationship Between Clinical Manifestation and Histopatological Result in Non-Hodgkin Lymphoma

To determine the relationship between clinical manifestation and histopatological result in non-hodgkin lymphoma, a logistic regression statistical analysis was carried out with the following result (table 2). It can be interpreted (4) that there was no significant relationship between clinical manifestations and degree of malignancy in non-Hodgkin's Lymphoma at RSUD Dr. Soetomo 2015-2017.

Table 2. The results of Chi Square test

	Value	df	p-value
Pearson Chi-square	2,482	2	0,289

#### DISCUSSION

#### **Distribution of Research Subjects**

The sampling was carried out in the medical record section of the One-Stop Poly Oncology (POSA). In this study, the sample of 139 met the inclusion criteria, with a greater number of male samples (62.6%) compared to women (37.4%). This is in line with the concept of the theory which explains that the prevalence of non-Hodgkin's lymphoma is more common in men than in women <sup>(5)</sup>. The same thing can also be explained because of the better resistance of women than men <sup>(6)</sup>. Some previous research states that 17-beta-estradiol which is owned by women, can spontaneously reduce the production of IL6. High levels of IL6 can reduce body immunity and work as a growth factor for lymphoma development. Other mechanisms show that estrogen has an anti- proliferation effect on lymphoid cells through estrogen receptor Beta signaling <sup>(7)</sup>. Men are suspected of having a greater risk for lymphoma due to smoking, occupational factors, and environmental exposure which is more experienced by men <sup>(8), (9)</sup>.

## Age Distribution, Clinical Manifestations and Degrees of Malignancy

According to International Prognostic Index (1990) Non-Hodgkin's lymphoma is a malignancy that has a poor prognosis at the age above 60 years <sup>(10)</sup>. From the data obtained, it is known that 23.58% of patients are in the age range above 60 years. In this study also showed that the highest incidence of the age range <60 years was 76.42%, and there was a decrease in the age range >60 years. This is in line with other studies which explain that the incidence of non-Hodgkin's lymphoma has the highest incidence in the age range 45-64 years <sup>(11)</sup>. This study showed a decrease in incidence in the age range >70 years. There was an increase in life expectancy in 2010-2015 from 69.1 to 70.1 <sup>(12)</sup>. Based on the data Ministry of Health in Indonesia, the elderly population in Indonesia is dominated by women. As explained earlier, women have a stronger resistance to lymphoma compared to men.

#### Distribution of Clinical Manifestations and Degrees of Malignancy

The most common clinical manifestations are "B" symptoms in the form of non-typical symptoms such as fever, night sweats, weight loss (13) as many as 51.8% of patients with non-Hodgkin's lymphoma in RSUD Dr. Soetomo came with clinical manifestations of systemic symptoms. This was also followed by the highest number (55.4%) of Non-Hodgkin's Lymphoma patients who came with the highest degree of malignancy. Different from Dehghani M. et al. (2015) studies which state that intermediate degree are most often found when diagnosis is made. The majority of non-Hodgkin's Lymphoma patients at RSUD Dr. Soetomo without symptoms actually experience malignancy with a high degree (Figure 1). The Chi Square test showed p> 0.05, indicating that there was no significant relationship between clinical manifestations and the degree of malignancy in patients with non-Hodgkin's lymphoma at RSUD Dr. Soetomo for the 2015-2017 period. This contrasts with Dwiyaningsih, et al (2016) studies which state that there is a significant relationship between clinical manifestations and histopathological features of lymphoma (11). High-grade Lymphoma generally present B symptoms (ie fever, night sweats and weight loss), as well as elevated serum LDH and uric acid levels. These systemic symptoms are caused by the body's reaction to inflammation and the chemicals produced by Lymphoma. In this study also supported by other studies which said that systemic symptoms were less common in people with low levels of non-Hodgkin's lymphoma (14).

B symptoms are indicators of the systemic inflammatory response and have been linked to increased plasma CRP concentrations and proinflammatory cytokines. There is increasing evidence that systemic inflammatory responses often occur in patients with malignancy, and generally associated with poorer clinical outcomes <sup>(15)</sup>.

Lymph glands contain immune cells that can help fight infection by attacking and destroying germs (16). This shows that aggressiveness influences lymph function which affects the clinical symptoms of the body's reaction to having a fever due to infection. In addition, the degree of malignancy also affects systemic symptoms such as weight loss. Sometimes, several cancer tends to reduce appetite but also increases basal calorie expenditure by cytokine-mediated mechanisms (17).

In this study, the division of clinical manifestations group was only divided into A (without symptoms) and B (with symptoms). This raises a bias that results in no significant relationship between the two variables. This is also in line with the results of research conducted by Dwiyaningsih E. K. et al in 2016 which states that the weak correlation is caused by many incompatibilities between clinical diagnosis with histopathological

features. This mismatch can be caused by several factors (11).

In this study, there are other factors that affect the level of lymphoma aggressiveness, namely the classification of extranodal involvement as a clinical manifestation that is not included as a variable in this study. As explained in other studies that Non-Hodgkin's Lymphoma with clinical manifestations involving extranodal has increased more rapidly, especially in developing countries with increasing diffuse patterns and becoming more aggressive types (18). With a simple classification carried out in this study, we cannot obtain a specific picture regarding clinical manifestations and factors that can affect the degree of malignancy.

#### CONCLUSION

Non-Hogkin's lymphoma attacks men more often than women. In this study it was also found that the highest incidence was in the age range >60 years old. In addition, more patients with severe clinical manifestations when diagnosed with non-Hodgkin's lymphoma. In this study the highest number of patients with non-Hodgkin's lymphoma in RSUD Dr. Soetomo with clinical manifestations without symptoms actually experience malignancy with a high degree. In this study the results showed that there was no significant correlation between clinical manifestations and the degree of malignancy based on histopathological features.

#### REFERENCES

- 1. Globocan.iarc.fr. Globocan 2012 –Estimated Cancer Incidence, Mortality, Prevalence Worldwide in 2012 [Internet]. 2018 [cited 2020 Aug 2]. Available from: http://globocan.iarc.fr/Default.aspx
- 2. National Institutes of Health (NIH). National Cancer Institute (NCI) [Internet]. 2018 [cited 2018 May 3]. Available from: https://www.nih.gov/about-nih/what-we-do/nih-almanac/national-cancer-institute-nci
- 3. Patel S, Morreale S, Panagopoulou A, Bailey H, Robinson N, Paladino F, Margaritoulis D, Spotila J. Changepoint analysis: a new approach for revealing animal movements and behaviors from satellite telemetry data. Ecosphere. 2015;6(12):291.
- 4. Supranto J. Statistik Teori dan Aplikasi. Jakarta: Erlangga; 2008.
- Ansell S, Lesokhin A, Borrello I, Halwani A, Scott E, Gutierrez M, Schuster S, Millenson M, Cattry D, Freeman G, Rodig S, Chapuy B, Ligon A, Zhu L, Grosso J, Kim S, Timmerman J, Shipp M, Armand P. PD-1 Blockade with Nivolumab in Relapsed or Refractory Hodgkin's Lymphoma. New England Journal of Medicine. 2015;372(4):311-319.
- Hoppe RT, Mauch PT, Armitage JO, et al. Hodgkin Lymphoma. Philadelphia: Lippincott Williams & Wilkins; 2007.
- 7. Horesh N, Horowitz N. Does Gender Matter in Non-Hodgkin Lymphoma? Differences in Epidemiology, Clinical Behavior, and Therapy. Rambam Maimonides Medical Journal. 2014;5(4):e0038.
- 8. Morton LM, Hartge P, Holford TR, et al. Cigarette smoking and risk of non-Jodgkin Lymphoma: a pooled analysis from the International Lymphoma Epidemiology Consortium (interlymph). Cancer Epidemiol Biomarkers Prev. 2015;14:925-33.
- 9. Reksodiputro AH. Multicentre epidemiology and survival study of B cell non Hodgkin lymphoma patients in Indonesia. J Blood Disorder Transfusion. 2015;6:1-5.
- 10. Kemenkes RI. Infodatin. Data dan Kondisi Penyakit di Indonesia. Jakarta: Kemenkes RI; 2018.
- 11. Dwiyaningsih EK, Indrawati, Hardianti MS, Malueka RG, Iswar RR, Sutapa SA, Triningsih FX. Histopathological Features of Lymphoma in Yogyakarta, Indonesia. Asian Pacific Cancer Prev. 2016;17(9):4213-4216.
- 12. BPS. Global Health Data Exchange. Jakarta: BPS; 2015.
- 13. Dehghani M, Haddadi S, Vojdani R. Signs, Symptoms and Complications of Non-Hodgkin's Lymphoma According to Grade and Stage in South Iran. Asian Pacific Journal of Cancer Prevention. 2015;16(8):3551-3557.
- 14. Freedman A. Follicular lymphoma: 2018 update on diagnosis and management. American Journal of Hematology. 2018;93(2):296-305.
- 15. Sharma R, Cunningham D, Smith P, Robertson G, Dent O, Clarke S. Inflammatory (B) symptoms are independent predictors of myelosuppression from chemotherapy in Non-Hodgkin Lymphoma patients analysis of data from a British National Lymphoma Investigation phase III trial comparing CHOP to PMitCEBO. BMC Cancer. 2009;9(1).
- 16. American Cancer Society. Cancer. 1981;48(6):1289-1289.
- 17. Sharp M, Corp D. Amneal Pharmaceuticals LLCUnited States Court of Appeals of the Federal Circuit, 2018881 F.3d 1376. Biotechnology Law Report. 2018;37(2):109-114.
- 18. Chattopadhyay B, Choudhury K, Mitra D, Bhattacharya B. Primary extranodal non-Hodgkin's lymphoma: A retrospective analysis of its clinicopathological features and treatment outcomes in a tertiary cancer center of eastern India. Clinical Cancer Investigation Journal. 2013;2(3):218.