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FREQUENCY DISTRIBUTION OF NON-HODGKIN LYMPHOMA AT THE ANATOMICAL PATHOLOGY LABORATORY. RSUP DR. M. DJAMIL. PADANG. 2020–2023

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ABSTRACT

Background: Malignant lymphoma is a hematological malignancy that affects the body's diffuse lymphatic system. This will occur when white blood cells do not grow normally. Lymphoma can affect areas of the lymphatic system as well as other organs throughout the body. clinically manifesting as nodal or extranodal involvement characterized by enlargement or lumps. Malignant lymphoma is divided into Hodgkin's lymphoma and non-Hodgkin's lymphoma. The frequency of non-Hodgkin's lymphoma is more common than Hodgkin's lymphoma. This study aims to determine the frequency distribution of non-Hodgkin's malignant lymphoma in the Anatomical Pathology Laboratory of RSUP. Dr. M. Djamil Padang in 2020-2023.

Methods: This descriptive observational study employed a total sampling technique from medical records to examine all non-Hodgkin lymphoma patients from 2020 to 2023 who met the inclusion criteria. totaling 211 samples.

Results and discussion: The results indicate a male predominance (66.8%). with the most common age group being > 60 years (33.6%). and a majority located in nodal areas (52.6%). The primary clinical manifestation reported by most patients was enlargement (72.5%). and the most prevalent histopathological type was big cell (35.1%).

Conclusion : In conclusion of this study is that cases of non-Hodgkin's malignant lymphoma at the Anatomical Pathology Laboratory of RSUP. Dr. M. Djamil Padang in 2020-2023 found that the peak occurred at the age of >60 years. more male than female. the most nodal location. the most clinical manifestations of lumps and large cell histopathology type. Therefore. education and early detection of malignant lymphoma cases are needed.

Keywords: non-Hodgkin's lymphoma. Characteristics. Histopathology features

INTRODUCTION

Malignant lymphoma is a hematological malignancy that affects the lymphatic system. The lymphatic system serves as a part of the body's immune system that fights foreign pathogens.[1] It comprises a complex system of vessels. lymph nodes. and various organs. Lymphoma can affect these areas as well as other organs throughout the body. clinically characterized by lymphadenopathy (enlargement of the lymph nodes).[2] When white blood cells—specifically lymphocytes—develop abnormally. they proliferate faster than normal cells or live longer than their physiological lifespan. leading to the development of lymphoma. These abnormal lymphocytes can disseminate to various parts of the body. eventually forming masses known as tumors. Malignant lymphoma is classified into Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). Hodgkin lymphoma arises predominantly from B-lymphocytes and. in a few cases. from T-lymphocytes. whereas NHL originates from B-lymphocytes. T-lymphocytes. or Natural Killer (NK) cells. A very distinctive difference between the two types of

lymphoma is the presence of Reed-Sternberg cells in HL. which are absent in NHL.[2.3]

According to the 2020 Global Burden of Cancer (GLOBOCAN) epidemiological data. NHL ranks 13th in cancer incidence worldwide. Approximately 544.352 (2.8%) new cases and 259.793 (2.6%) deaths were attributed to NHL globally. In Indonesia. NHL holds the 7th position among the top 10 most prevalent cancers. with 16.125 new cases and a total of 9.024 mortalities.[4] Furthermore. the Data and Information Center of the Ministry of Health of the Republic of Indonesia recorded 14.905 cases of malignant lymphoma in Indonesia in 2013.

Age and gender represent significant risk factors for the development of NHL. The risk of NHL increases progressively with age. particularly among the elderly. Data from the Ministry of Health's Data and Information Center indicates that NHL occurs most frequently in individuals over 60 years of age.[3] Regarding gender distribution. males exhibit a higher prevalence of NHL compared to females.

Immunocompromised individuals are more likely to develop NHL. This includes patients infected with infectious agents such as Epstein-Barr Virus. Human T-Cell Leukemia Virus Type 1 (HTLV-1). and Human Immunodeficiency Virus (HIV). Patients who have undergone organ transplantation are also at increased risk for NHL.[5] In addition to the factors mentioned above. environmental exposures such as chemicals and diet are also modifiable risk factors for NHL.[2]

The primary clinical manifestation observed in malignant lymphoma patients is lymphadenopathy. Based on its anatomical distribution. malignant lymphoma can manifest in nodal or extranodal sites. The most frequently affected nodal sites are the cervical and inguinal lymph nodes. Conversely. the most common extranodal sites of involvements are the tonsils. gastrointestinal tract. and bone marrow.[6]

Various factors influence the therapeutic selection and prognosis of NHL. including growth characteristics (indolent/low-grade versus aggressive/high-grade). histological type. clinical stage. patient age. and the patient's general condition.[7] The classification of NHL follows the 2022 World Health Organization (WHO) guidelines. which categorize NHL into two major types: B-cell lymphoproliferative disorders (LPD) and lymphoma. and T-cell/NK-cell LPD and lymphoma. These two types are further subdivided into several subtypes.[8] Notably. Diffuse Large B-Cell Lymphoma (DLBCL) has been identified as the most frequently encountered subtype.[1]

This study aims to determine the frequency distribution of non-Hodgkin lymphoma cases based on patient characteristics and histopathological types. Based on the the above description. the researchers are interested in further presenting the frequency distribution of non-Hodgkin's malignant lymphoma at the Department of Anatomical Pathology. RSUP Dr. M. Djamil Padang. from 2020 to 2023.

MATERIALS AND METHODS

This study is a descriptive study with a retrospective approach. aimed at determining the frequency distribution of non-Hodgkin lymphoma. This study utilized secondary data in the form of anatomical pathology reports archived at the Department of Anatomical Pathology. RSUP Dr. M. Djamil Padang. The study population consisted of all patients with non-Hodgkin lymphoma registered at the laboratory between 2020 and 2023.

The sample in this study includes all members of the population who met the predefined inclusion criteria. These inclusion criteria encompassed all patients histopathologically diagnosed with NHL at the Department of Anatomical Pathology. RSUP Dr. M. Djamil Padang. from 2020 to 2023. whose records contained complete data for the variables under investigation. Conversely. the exclusion criteria consisted of records where NHL was not the primary diagnosis and cases with incomplete clinical information.

Sampling was conducted using total sampling. whereby every individual in the population meeting the inclusion criteria was selected as a research subject. Inclusion was restricted to patients with a confirmed histopathological diagnosis of NHL at the Department of Anatomical Pathology. RSUP Dr. M. Djamil Padang. within the 2020–2023 period. who possessed comprehensive medical records regarding to the studied variables. Exclusion criteria specifically addressed medical records that did not list NHL as the primary diagnosis or those with insufficient clinical data. In this study. a total of 211 samples fulfilled the inclusion criteria and were included as the primary data source.

The data collection procedure began with obtaining ethical and administrative clearances. followed by a review of anatomical pathology examination archives. The variables collected included age. gender. specimen location (categorized into nodal and extranodal). clinical manifestations. and histopathological types. The acquired data underwent systematic processing. including editing. coding. data entry. and cleaning using specialized software applications. Data analysis was conducted univariately to generate frequency distributions and percentages. which are presented in tabular format. This study was granted ethical approval by the Ethics Committee of RSUP Dr. M. Djamil Padang under reference number DP.04.03/D.XVI.XI/594/2023.

RESULTS

Based on the collected data. a total of 211 patients diagnosed with non-Hodgkin lymphoma (NHL) were recorded in the laboratory archives of the Department of Anatomical Pathology. RSUP Dr. M. Djamil Padang. between 2020 and 2023. fulfilling both the inclusion and exclusion criteria.

Table 1. Characteristics of Non-Hodgkin Lymphoma Patients

Patient Characteristics	Frequency (f)	Percentage (%)
Age		
≤ 20 years	11	5.2
21-30 years	12	5.7
31-40 years	20	9.5
41-50 years	30	14.2
51-60 years	67	31.8
> 60 years	71	33.6
Gender		
Male	141	66.8
Female	70	33.2
Location		
Nodal	125	59.2
Colli	36	
Tonsils	20	
Axilla	5	
Abdomen	32	
Inguinal	12	
Spleen	4	
Multiple Nodes (>1)	11	
Extranodal	86	40.8
Brain	1	
Eyes	21	
Oral Cavity	6	
Nasal Cavity	10	
Nasopharynx	5	
Oropharynx	2	
Thyroid	1	
Pleura	1	
Gastrointestinal Tract	23	
Testis	4	
Mandible	1	
Maxilla	4	
Vertebrae	1	
Submandibular	1	
Hepar	1	
Parotid	1	
Ischium	1	
Ileocecal	1	
Sacrum	1	
Clinical Manifestations		
Mass/Lump	153	72.5
Multiple Symptoms (>1)	58	27.5
Mass with fever and weight loss	9	
Mass with odynophagia (painful swallowing)	17	
Mass with nasal congestion	6	
Mass with hearing impairment	1	
Headache and memory impairment	1	
Abdominal pain and constipation	19	
Cough and dyspnea	4	
Bilateral lower limb weakness/ paralysis	1	

According to Table 1. it can be concluded that the most prevalent age group diagnosed with non-Hodgkin lymphoma at the Department of Anatomical Pathology. RSUP Dr. M. Djamil Padang. during the 2020–2023 period was the >60 years age group (33.6%). In terms of gender distribution. NHL was more frequently observed in males (66.8%). The majority of NHL cases were localized in nodal sites (59.2%). Furthermore. the most common clinical manifestation identified among NHL patients was the presence of a mass or lump (72.5%).

Table 2. Frequency Distribution of Histopathological Types in Non-Hodgkin Lymphoma

Histopathological Characteristics	Frequency (f) (n=211)	Percentage (%)
Histopathological Type		
Small-cell type	22	10.4
Intermediate-cell type	49	23.2
Large-cell type	74	35.1
Mixed-cell type	66	31.3

Based on Table 2. it can be inferred that the predominant histopathological characteristic of non-Hodgkin lymphoma at the Department of Anatomical Pathology. RSUP Dr. M. Djamil Padang. from 2020 to 2023. was the large-cell type. accounting for 74 samples (35.1%).

DISCUSSION

Based on the age characteristics. the study found that the age group >60 years represented the largest sample size. accounting for 71 patients (33.6%). This finding aligns with existing literature. which states that the highest incidence of non-Hodgkin lymphoma (NHL) typically occurs within the 45–64 year age range.[9] Furthermore. a study conducted at RSUP Sanglah Bali for the 2016–2018 period reported that the majority of NHL patients were <65 years old.[10] These results also correspond with 2015 data from the Indonesian Ministry of Health. stating that NHL is most frequently identified in individuals older than 60 years.[3]

Generally. NHL can manifest at any age; however. the incidence increases progressively with advancing age. The risk significantly escalates starting from age 50 and above. In the elderly. NHL is closely associated with decline of immune system function. While the human immune system is distributed throughout the body. aging leads to a reduction in immune cell quantity and a loss of functional capacity in neutralizing pathogens or identifying aberrant cells.[11]

Regarding gender distribution. males were more frequently diagnosed with NHL. with a frequency of 141 patients (66.8%) compared to 70 female patients (33.2%). This result is consistent with a study at RSUP Sanglah Bali (2016–2018). where males accounted for 58.2% of the cases (78 patients).[10] Similarly. research at RSUP Dr. Sardjito Yogyakarta from 2012 to 2018 also observed a male predominance. reaching 93.5% (359 patients).[12]

Previous studies suggest that 17β-estradiol in females can spontaneously reduce the production of Interleukin-6 (IL-6). leading to lower IL-6 levels. Conversely. the absence of 17β-estradiol (estrogen) in males leads to elevated IL-6 levels. Increased IL-6 can impair the immune response and function as a growth factor for lymphoma. Thus. estrogen appears to have a protective effect by modulating IL-6 levels. Another mechanism indicates that estrogen affects all lymphocyte types. exhibiting anti-proliferative effects on lymphoid cells through β-estrogen receptor signaling.[13]

In terms of anatomical distribution. NHL occurred most frequently at nodal sites. with 125 samples (59.2%). while extranodal involvement accounted for 86 samples (40.8%). These results correlate with other studies stating that 53.6% of cases are nodal. specifically involving the cervical region (24.6%).[10] Research by Nungki et al. (2021) also found a higher prevalence of nodal (474 samples) compared to extranodal (357 samples) involvement.[12]

However. these findings differ from research by Wibawa (2018). which reported a higher frequency of extranodal sites (73.2%). and Dayang (2020). who found extranodal involvement in 56% of cases compared to 44% in nodal sites.[14]

Theoretically. malignant lymphoma can arise in both nodal and extranodal locations. The site of NHL development depends on the specific subtype; for instance. in Diffuse Large B-Cell Lymphoma (DLBCL). approximately 60% of patients present with lymphadenopathy (nodal). while 40% involve extranodal sites such as the gastrointestinal tract. bone. and spleen. Some extranodal cases are triggered by chronic inflammation or irritation. such as post-mastectomy lymphedema and bone infections.[15.16]

The most common clinical manifestation in this study was the presence of a mass or lump. identified in 144 out of 211 patients (72.5%). Other clinical manifestations observed included a constellation of multiple symptoms (> 1 symptom) in 58 samples (27.5%). which varied as detailed in the results section. In line with clinical theory. lymphadenopathy (nodal enlargement) is the primary complaint in 56.1% of malignant lymphoma cases.[6] A study

at RSUP Sanglah Denpasar in 2014 found that 100% of NHL patients (25 patients) presented with a lump as their primary symptom.[17]

Clinical manifestations in NHL vary based on the affected site. yet a palpable mass remains the most frequent chief complaint. Lymphoma is a solid malignancy originating from lymphoid tissue that can disseminate systemically. In lymphoma patients. lymphocytes that undergo abnormal and uncontrolled proliferation can migrate to various organs and form masses.[18.19] These masses may originate within the lymph nodes (nodal) or outside of them (extranodal). This abnormal proliferation can cause organ damage due to compression or obstruction. and when it involves the lymph nodes. lymphadenopathy occurs. While lymphadenopathy is typically painless. enlargement in the tonsils can cause dysphagia (swallowing difficulties). and masses in the thoracic or abdominal cavities can compress vital organs. leading to respiratory distress. constipation. and abdominal pain.[6]

In this study. the large-cell type was the most common histopathological subtype. accounting for 74 samples (35.1%). No previous studies have categorized NHL using this classification system; however. according to the book titled "A Practical Approach to the Pathological Diagnosis of Lymphoma." lymphomas are categorized based on cell size into small-cell. medium-cell. large-cell. and mixed-cell types. Each of these cell types is further categorized; for instance. the large-cell type includes DLBCL.[8] This study's finding of large-cell predominance aligns with research at RSUP Sanglah Bali (2016–2018). which identified DLBCL as the most common subtype (64.2%).[10] According to other theories. it is also supported that DLBCL is the most commonly found type of NHL. accounting for approximately 50%.[20] Thus. the results of this study are consistent with other studies.

The histopathological subtype in NHL is often influenced by age and location. Theoretically. DLBCL patients have an average age of 60 years.[21] with a median of 64 years.[22] Medium-cell NHL. such as Burkitt Lymphoma (BL). is found 80% more frequently in children. with a peak age of 7 years.[15.22] Meanwhile. small-cell NHL. such as Mantle Cell Lymphoma (MCL). is more prevalent in patients aged 68 to 71 years.[23]

CONCLUSION AND RECOMMENDATIONS

Based on the study conducted at the Department of Anatomical Pathology. RSUP Dr. M. Djamil. from 2020 to 2023. it is concluded that the majority of non-Hodgkin lymphoma (NHL) patients were in the >60 years age group. The demographic profile showed a male predominance. with the majority of cases localized in nodal sites. The most frequent clinical manifestation identified was the presence of a mass. and the large-cell type emerged as the most dominant histopathological subtype.

This study requires further research to investigate the correlation between age and specific histopathological types. Furthermore. it is highly recommended that the diagnosis of malignant lymphoma should include additional immunohistochemical testing to precisely identify the histological subtype.

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