Ugwu *et. al.,* Babcock Univ. Med. J.2026 9(1):135-143
https://doi.org/10.38029/babcockuniv.med.j..v9i1.933
eISSN: 2756-4657

RESEARCH ARTICLE OPEN ACCESS

Pattern of distribution of Hodgkin lymphoma and non-Hodgkin lymphoma subtypes among adults: An experience of a Nigerian tertiary health facility

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Submitted: 18th May 2025
Accepted: 4th October 2025
Published: 31st March 2026
ID: Orcid ID

Abstract
Objective: Lymphomas are a heterogeneous group of malignancies with varying geographic and demographic distributions. This study aimed to describe the pattern of distribution of Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL) subtypes among adults.
Methods: This was a retrospective study of patients diagnosed with lymphoma at our institution between January 2019 and December 2023. Data were extracted from the record of the histopathology department of the institution. Lymphoma subtypes were classified according to the World Health Organisation (WHO) classification.
Results: There were 59 cases of lymphoma during the study period, made up of 30 (50.8%) males and 29 (49.2%) females. The overall mean age at diagnosis was 45±18 years. HL accounted for 35.6% (21/59) of the cases, while NHL accounted for 64.4% (38/59) of the cases. Among the HL, classical HL contributed 85.7% while Nodular lymphocyte-predominant HL contributed 14.3%. The distribution of the different histologic subtypes of HL showed mixed cellularity 10 (47.6%) as the commonest subtype, followed by nodular sclerosis 5 (23.8%) subtype. Among the NHL, B-cell lymphoma accounted for 76.3% while T-cell lymphoma accounted for 23.7%. Overall, Small Lymphocytic Lymphoma (SLL)/ Chronic Lymphocytic Leukaemia (CLL) was the commonest subtype and accounted for 42,1% (16/38), followed by diffuse large B-cell lymphoma (DLBCL) 18.5% (7/38), and follicular lymphoma (FL) 7.9% (4/38).
Conclusion: This study provides insight into the distribution pattern of lymphoma subtypes among adults in our environment, with mixed cellularity as the most common HL histologic subtype and SLL/CLL as the predominant NHL subtype.

Keywords: Adult, Histological subtypes, Hodgkin lymphoma

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Plain English Summary
Lymphoma is a type of cancer that affects the blood cells called lymphocytes, and the abnormal cells can settle in any part of the body and continue to divide and multiply to form a mass. There are different types, some common in certain geographical locations and others rare in others. Research done in other places in Nigeria and outside Nigeria has shown different patterns of distribution of these cancers at different geographical locations, but none has been done in our locality. This study looked at the pattern of distribution of lymphomas among adults in our locality. The result showed that non-Hodgkin lymphoma is common than Hodgkin lymphoma. Overall, SLL/CLL was the most common, followed by DLBCL and FL. B-cell lymphomas were more common than T-cell lymphomas. Among the B-cell lymphomas, SLL/CLL was the most common, followed by the DLBCL and FL, while T-lymphoblastic and anaplastic large-cell lymphoma were the most common. Among the HL, mixed cellularity was the most common, followed by the nodular sclerosis subtype. Males were slightly more affected than females by lymphoma. Young adults were affected more by HL than middle-aged adults, while NHL affects all age groups.
The distribution pattern of lymphoma in a particular location will help to look for possible causes so that preventive measures can be applied.

Introduction
Lymphomas are a group of blood malignancies that develop from lymphocytes because of neoplastic transformation of the normal lymphoid cells that reside predominantly in lymphoid tissues (1). Lymphomas are the most common haematological malignancy (2). They are broadly classified into two main categories: Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL) based on the presence or absence of the Reed-Sternberg (RS) cell on histology (2). HL and NHL are further subtyped into individual entities displaying distinct behavioural, prognostic and epidemiological characteristics, with varying responses to treatment (3).
NHL subtypes include diffuse large B cell lymphoma (DLBCL), Follicular lymphoma (FL), small lymphocytic lymphoma (SLL), Burkitt's lymphoma (BL), and marginal zone B cell lymphoma, among others.
Hodgkin Lymphoma is subtyped into classical Hodgkin lymphoma (cHL) and nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL). Classical Hodgkin Lymphoma is further subdivided into four subtypes, which include nodular sclerosis, mixed cellularity, lymphocyte-rich and lymphocyte-depleted subtypes (3).
Lymphomas show a broad spectrum of clinical and pathological presentations, and continue to be one of the primary causes of morbidity and mortality (4). NHL is reported as the 10th most common cancer by GLOBOCAN estimates, and its definition and characteristics are ever-increasing and more complex since molecular and genetic features are constantly being identified to allow a more accurate diagnosis and prognosis (5).
The World Health Organisation (WHO) classification of lymphoma is still evolving, and it comprises different subtypes of Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL), which are fairly heterogeneous concerning their morphological, molecular, and clinical course (3). About 90–95% of lymphomas arise from neoplastic transformation of B-cells, whereas the rest originate from either T or NK-cells (6).
Studies have shown that the subtype distribution of malignant lymphomas varies among countries and also across the geographic regions within the countries, the reason for which remains largely unknown (7, 8). However, genetic and ethnic differences, as well as environmental factors such as socioeconomic issues, have been proposed to explain these geographical differences in the distribution of lymphoma subtypes.
Lymphomas have been recognised as a major public health problem globally due to the associated increase in morbidity and mortality. Non-Hodgkin Lymphoma accounts for 2.8% of all cancers globally and contributes to 2.6% of cancer deaths, while HL accounts for 0.4% of all cancers and contributes to 0.2% of cancer deaths (3). However, the incidence and mortality patterns vary considerably across different geographical regions (7).
Previous studies have reported the distribution pattern of lymphoma subtypes in different geographical regions. A study done in France reported DLBCL as the commonest subtype of NHL, followed by FL, while nodular sclerosis is the commonest subtype of HL, followed by the nodular lymphocyte predominant subtype (9). In a study conducted in Zambia, Burkitt lymphoma and DLBCL were the most common subtypes of NHL, while mixed cellularity and lymphocyte-rich were the most common subtypes of HL, both occurring in equal proportion (10). In Nigeria, a study done in Ile-Ife reported DLBCL as the commonest NHL subtype, while mixed cellularity was reported as the commonest HL subtype (11). Another study done in Uyo reported SLL/CLL as the most common NHL subtype, while the nodular lymphocyte-

predominant subtype is the most common HL subtype (12).
Although several reports exist regarding the distribution of subtypes of malignant lymphomas in different parts of the world, including Nigeria, no study has previously reported on the pattern of distribution of malignant lymphoma in our locality. This study aimed to describe the pattern of distribution of HL and NHL subtypes among adults in Abakaliki, Nigeria.

Materials and Methods

A retrospective study was conducted at the Alex Ekwueme Federal University Teaching Hospital, Abakaliki, Nigeria. A record of histology reports of all lymph node biopsies taken from adults diagnosed with lymphoma within 5 years (January 2019 to December 2023) was retrieved from the register of the histopathology department of the hospital.
Adult was defined as aged 18 years and above. Included in the study were records of confirmed diagnoses made by a consultant histopathologist through histology with or without immunophenotyping, and the patients were at least 18 years old at the time of diagnosis. Records without a definitive diagnosis or with incomplete data were excluded. Information collected from the departmental register included age, sex and diagnosis.
The data generated were analysed using IBM Statistical Package for Social Sciences (SPSS) software, version 26 (IBM, Armonk, NY, USA). Descriptive statistics were used to compute proportions and percentages, mean and standard deviation, and the results were presented in tables and charts.

Results

There were 59 cases of lymphoma during the study period, made up of 30 (50.8%) males and 29 (49.2%) females, with a male-to-female ratio of 1.1:1. The overall mean age at diagnosis was 44±18 years.
Hodgkin Lymphoma accounted for 21(35.6%) of the cases, while NHL accounted for 38 (64.4%) of the cases (Figure 1).

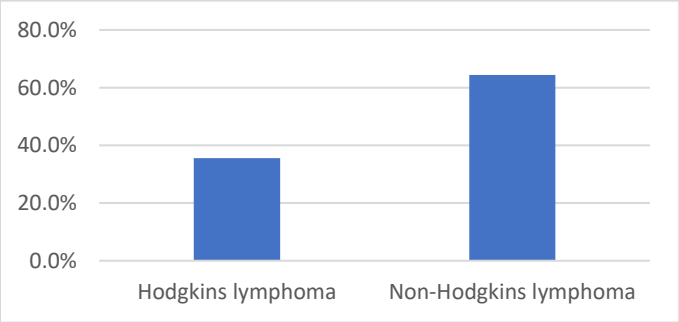

Figure 1: Distribution of lymphomas into Hodgkin and Non-Hodgkin Lymphoma

Among the HL cases, classic HL accounted for 85.7%, and NLPHL accounted for 14.3% (Figure 2).

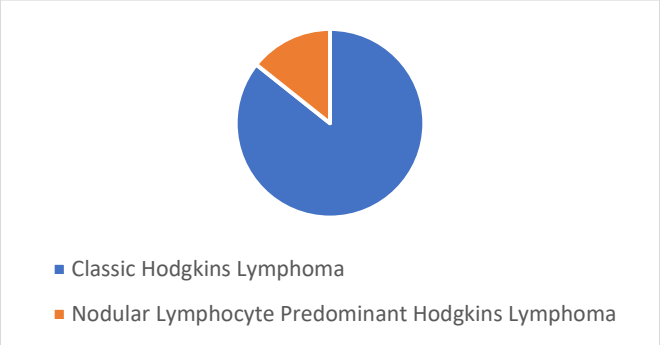

Figure 2: Distribution of Hodgkin lymphomas into Classical Hodgkin Lymphoma and Nodular Lymphocyte-Predominant Hodgkin Lymphoma

The distribution of the different histologic subtypes of HL showed that mixed cellularity (47.6%) was the most common subtype, followed by nodular sclerosis 5 (23.8%) subtype (Figure 3).

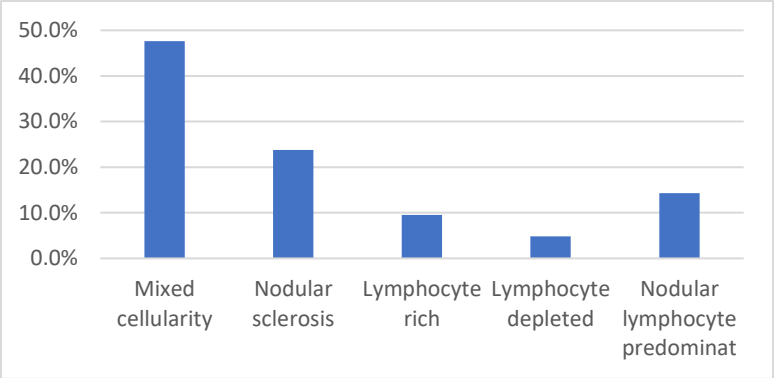

Figure 3: Distribution of Hodgkin lymphoma subtypes

Among the NHL, B-cell lymphoma accounted for most of the cases (76.3%; 29/38) while T-cell lymphoma contributed 23.7% (9/38) (Figure 4).

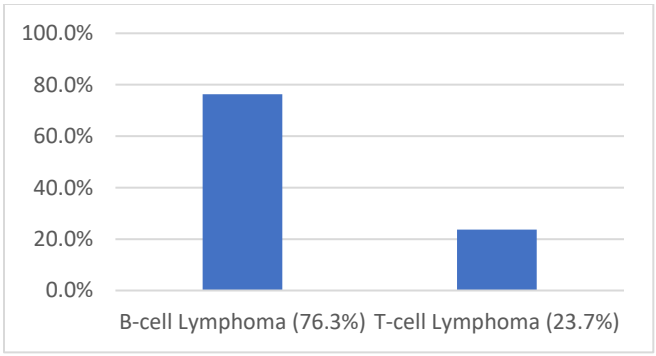

Figure 4: Distribution of non-Hodgkin lymphomas into B-cell and T-cell Lymphoma

Overall, Small Lymphocytic Lymphoma/ Chronic Lymphocytic Leukaemia (SLL/ CLL), which accounted for 42.1% (16), was the most common subtype, followed by diffuse large B-cell lymphoma (DLBCL) 18.5% (7), and follicular lymphoma (FL) 7.9% (4) subtype (Table 1).

Table 1: Distribution of non-Hodgkin lymphoma subtypes

Non-Hodgkin Lymphoma subtype	Frequency	Percentage
Small lymphocytic lymphoma/Chronic Lymphocytic Leukaemia	16	42.1
Diffuse large B-cell lymphoma	7	18.5
Follicular lymphoma	4	10.5
T-cell Lymphoblastic lymphoma	3	7.9
Mycosis Fungoides	1	2.6
Anaplastic Large Cell Lymphoma	3	7.9
Splenic lymphoma with villus lymphocyte	1	2.6
Angioimmunoblastic T-cell lymphoma	2	5.3
Lymphoplasmacytic lymphoma	1	2.6
Total	38	100

Among the B-cell lymphomas, the majority of the cases were SLL/CLL (55.2%; 16/29), followed by DLBCL (24.1%; 7/29), and FL (14.0%; 4/29) (Table 2). Among the T-cell lymphomas, lymphoblastic lymphoma and anaplastic large cell lymphoma were the most common, each contributing 33.3%, followed by Angioimmunoblastic T-cell lymphoma (22.3%) (Table 2).

Table 2: Distribution of Non-Hodgkin Lymphoma according to B-cell and T-cell type.

Non-Hodgkin Lymphoma (NHL) subtype	Frequency	Percentage
B-cell NHL		
Small Lymphocytic Lymphoma/ Chronic Lymphocytic Leukaemia	16	55.2
Diffuse large B-cell Lymphoma	7	24.0
Follicular Lymphoma	4	14.0
Splenic Lymphoma with Villous Lymphocytes	1	3.4
Lymphoplasmacytic Lymphoma	1	3.4
Total	29	100
T-cell NHL		
T-cell Lymphoblastic Lymphoma	3	33.3
Anaplastic Large Cell Lymphoma	3	33.3
Angioimmunoblastic T-cell Lymphoma	2	22.3
Mycosis Fungoides	1	11.1
Total	9	100

The distribution of HL and NHL, according to sex, was not statistically significant (P = 0.789).
The mean age of the HL patients was 31 ±13 years, while the mean age of patients diagnosed with NHL was 51± 17 years. Subjects with NHL were significantly older than those with HL (P = 0.003). Hodgkin Lymphoma was observed to be more common in young adults of 20-39 years, and no case of HL was recorded in those older than 60years. However, NHL was seen in all age groups (Table 3).

Table 3: Distribution of Lymphoma in relation to age group

Age group	Hodgkins Lymphoma	Non-Hodgkin Lymphoma	Total
Young adults (<40 years)	16	13	29
Middle age (40 – 60 years)	5	12	17
Elderly (>60 years)	0	13	13
Total	21	38	59

Discussion

This study provides insight into the pattern of distribution of HL and NHL subtypes among adults in Abakaliki, Nigeria. The findings showed that NHL is more common than HL. This is consistent with reports from previous studies, which also showed that the majority of malignant lymphoma cases are NHL subtype (11, 12). Among the NHL, B-cell lymphoma was found to account for most of the cases. This is in keeping with the report of previous studies (11, 12, 13, 14). Immune system abnormality is a known risk factor for B-cell lymphoma, and immunodeficient individuals have an increased risk of B-cell lymphoma. Some autoimmune diseases, such as rheumatoid arthritis and Hashimoto thyroiditis, have been associated with increased risk of developing B-cell lymphomas (15), and these may have contributed to the higher prevalence of B-cell lymphomas compared to those of T-cell lymphomas.
Overall, the most common NHL subtype in this study was SLL/CLL, followed by DLBCL and FL. This is consistent with the report in Uyo by Akpan *et al* (12), who also found SLL/CLL and DLBC as the first and second most common subtypes of NHL. Similarly, a study conducted in India by Shanmugasundaram et al (13) found that SLL/CLL was the most common subtype of NHL, followed by the DLBCL subtype. On the contrary, a study conducted in Zambia by Polepole et al (10) reported Burkitt lymphoma and DLBCL as the top two NHL subtypes. Yakubu *et al* (16). In another study done in Maiduguri, Northern Nigeria, Burkitt Lymphoma was the commonest subtype of NHL. The differences in findings could partly be since their study population were children, and Burkitt lymphoma has been reported to be more common in children (17), while the study population in this study were adults. A previous study done in our centre to determine the pattern of childhood malignancies reported lymphoma as the commonest childhood malignancy, and Burkitt lymphoma was the most common (18).
Among the B-cell lymphoma, this study found that SLL/CLL was the most common, followed by DLBCL and follicular lymphoma. This corroborates the findings of previous studies, which also reported SLL/CLL as the most common B-cell lymphoma (12, 13). However, Dei-Adomakoh *et al* (19), in Ghana reported DLBCL as the most

common B-cell lymphoma. These different findings may be due to different etiologic, host risk factors and environmental factors (7).

Among the T-cell lymphoma, this study found T-cell Lymphoblastic Lymphoma and Anaplastic Large Cell Lymphoma to top the list in equal proportion. However, the study by Mahanta *et al* (20) in Eastern India reported peripheral T-cell lymphoma was reported to be the most common, followed by anaplastic large cell lymphoma and T-lymphoblastic lymphoma. Another study by Yoon *et al* (21) in some Asian countries reported extranodal NK/T-cell lymphoma was reported as the most common subtype, followed by angioimmunoblastic T-cell lymphoma. Variation in the distribution of subtypes may be due to genetic, environmental and socioeconomic factors.

Among the HL, classical HL contributed more cases compared to the nodular lymphocyte-predominant subtype. Previous studies have also reported that nodular lymphocyte-predominant HL contributed a minority of all cases of HL (11, 12). The most common classical HL subtype in this study was mixed cellularity, followed by nodular sclerosis. This corroborates the findings of previous studies, especially those from Africa and Asia, while Europe and America have been reported to have more of the nodular sclerosis subtype (13, 22). Factors such as early Epstein-Barr virus infection and HIV infection, as well as host-related factors such as nutritional status, among other factors, could explain these differences.

A slight male predominance over females was observed in this study. Previous studies have also shown a male preponderance more than females (20, 23). The reason for male preponderance is not clear. However, the possible explanation might be the fact that males are comparatively more exposed to environmental and occupational carcinogenic agents, such as industrial chemicals and herbicides and are therefore at higher risk of developing lymphoma (24).

In this study, HL showed a gradual decline in the number of cases with advancing age. Most of our patients were young adults, and there was no case seen in those above the age of 60 years. This is consistent with studies done in other parts of Nigeria and Africa (11, 12, 25). In Western countries, HL shows a bimodal age distribution with a peak incidence in the third and sixth decades of life (26).

This may be due to variation in environmental, genetic and socioeconomic factors.

NHL was observed to vary across different age groups. This is similar to reports from studies in other parts of Nigeria and Africa (12, 24, 27) where NHL has been reported to vary across age groups, with certain subtypes showing a higher prevalence in specific age groups. Similar findings have also been reported in advanced countries (25).

Study Limitations

Diagnosis of lymphoma was based only on morphology with haematoxylin and eosin, and this may have contributed to some degree of misdiagnosis. Immunohistochemistry, cytogenetics, and molecular diagnostic techniques were not employed to better characterise lymphomas, as these are not available in our laboratory at the time of the study.

Another limitation is the retrospective nature and possible information bias, as data were extracted from records, and some of the information may be missing.

Conclusion

This study provides an overview of the distribution of NHL subtypes among adult patients in our locality. In this study, lymphomas are predominantly NHL, mostly of B-cell lineage, affecting slightly more males than females. The most common NHL subtype is SLL/CLL, followed by DLBCL, while mixed cellularity, followed by nodular sclerosis, were the most common subtypes of HL. The highest number of HL patients were seen in young adults (less than 40 years), but absent in the elderly (>60 years), while NHL was seen in all age groups.

Further studies, including larger samples with an improved method of diagnosis, are essential to understand the difference in subtype distribution in our population.

List of Abbreviations

DLBCL: Diffused Large B-cell Lymphoma
FL: Follicular Lymphoma
HIV: Human Immunodeficiency Virus
NK/T-cell: Natural Killer/ T-cell
HL: Hodgkin Lymphoma
NHL: Non-Hodgkin Lymphoma
NLPHL: Nodular Lymphocyte-Predominant Hodgkin Lymphoma
SLL/CLL: Small Lymphocytic Lymphoma/ Chronic Lymphocytic Leukaemia

Declaration

Ethics Approval and Consent to Participate

Ethical approval for the study was obtained from the Research and Ethics Committee of Alex Ekwueme Federal University Teaching Hospital,

Abakaliki, with protocol number AEFETHA/REC/VOL 3/2022/041

Consent for publication
All the authors gave consent for the publication of the work under the Creative Commons Attribution-Non-Commercial 4.0 license.

Availability of data and materials
The datasets used and/or analysed in this study are available from the corresponding author upon reasonable request.

Competing interests
The authors have no conflicts of interest to declare

Funding
Financial support was borne by the author. There was no external funding.

Authors' contributions
UNI conceived the research idea. UCN, OS, EU, IU, UJC, and UCL were involved in designing the study. OS, UJC, EU and EEO participated in data collection and writing up the manuscript. UNI analysed the data, and with UCN, UCL, and IU, participated in the interpretation and drafting of the manuscript. All authors reviewed and approved the final manuscript.

Acknowledgments
The staff of the Morbid Anatomy department of the hospital are appreciated for their assistance in data collection.

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