

## **Adult Lymphomas in a Tertiary Hospital in South – South Nigeria: A Review of Clinicopathologic Features and Treatment Outcome**

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### **Authors' contributions**

*This work was carried out in collaboration between all authors. Author ISA contributed substantially to the conception and design, acquisition of data, analysis and interpretation of data, drafting the article and revising it critically for important intellectual content. Author MOT contributed substantially to study design, acquisition of data, drafting of the article and revising it critically for important intellectual content. Author EIB contributed to analysis and interpretation of data, drafting the article and revising it critically for important intellectual content. Author EEU contributed to analysis and interpretation of data, drafting the article and revising it critically for important intellectual content. Author RIA contributed to analysis and interpretation of data, drafting the article and revising it critically for important intellectual content. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Background:** There has been an increase in the prevalence of Lymphomas in our environment lately. Thorough literature search reveals a limited number of reports on the prevalence of Lymphoma and no information on the clinicopathologic pattern and outcome of treatment of this disease in our centre. Data on the burden of Lymphoma across different regions are important, as

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there may be variation in incidence in different locations even within the same country. This will keep healthcare providers informed about the current trend of Lymphomas in the region and facilitate prompt and appropriate diagnosis and treatment as well as assist Government agencies in better healthcare planning.

**Aim:** To determine the burden, clinicopathologic characteristics and treatment outcome of Lymphoma among a cohort of adult patients accessing care in a Referral Hospital in Southern Nigeria

**Methods:** This was a longitudinal prospective study of all lymphoma cases managed in the Department of Haematology, University of Uyo Teaching Hospital, Uyo, between January 1, 2014 and December 31, 2018

**Results:** There were 59 cases. Forty 40 (67.8%) were males and 19(32.2%) were females giving a male to female ratio of 4.4:1. Hodgkin Lymphoma(HL) accounted for 11(18.6%) of the cases while Non-Hodgkin Lymphoma(NHL) accounted for 48( 81.4%)of the cases , with the mean ages for HL and NHL patients being 32.09 +9.22 years and 40.88 + 12.21 years, respectively. The distribution of the different histologic subtypes of the malignancy were as follows: HL; Nodular Lymphocyte Predominant(7cases;63.6%), Nodular Sclerosis(2 cases;18.2%) and Lymphocyte Depleted(2 cases;18.2%). NHL; Small Lymphocytic Lymphoma(23cases;47.9%),Diffuse Large Cell Lymphoma(15 cases;31.3%),unspecified

(4 cases;8.3%), Follicular Lymphoma(2 cases;4.2%),Lymphoblastic Lymphoma(2 cases;4.2%), Mantle Cell Lymphoma(1 case;2.1%) and Adult T-Cell Lymphoma(1 case;2.1%). Fourteen 14 (29.2%) out of all the NHL patients had immunohistochemistry and only nine 9 of them were CD20 positive. Relapse rate among the cohort was 11.9% (7/59), while 15.3% (9/59) were still in remission. The cure rate was 5.1%, loss to follow up was 22.0% and 37.3% of patients died in the course of therapy either from advanced disease, non -compliance to treatment or late presentation. All the HL patients received ABVD (Adriamycin, Bleomycin, Vinblastine and Dacarbazine) regimen alone. Majority of the NHL patients (91.7%, 44/48) received CHOP (Cyclophosphamide, Doxorubicin, Oncovin and Prednisolone) regimen alone, while 8.3% (4/48) received Rituximab with CHOP (R-CHOP).

**Conclusion:** The clinicopathological profile, age and sex distribution of lymphoma in our study were comparable to those reported by other authors with nodular lymphocyte predominant being the most common HL histologic subtype and small lymphocytic lymphoma the predominant NHL histologic subtype in our environment. The general outcome was very poor with a high default rate and unsettling mortality figures.

**Keywords:** Hodgkin lymphoma; non-hodgkin lymphoma; ABVD, CHOP; rituximab; Nigeria.

## 1. INTRODUCTION

Lymphomas are a heterogeneous group of primary solid clonal malignant disorders of the lymphoid tissues. These malignancies are broadly classified into Hodgkin lymphoma (HL) and Non-Hodgkin (NHL), each characterized by distinct behavioural, prognostic and epidemiological features, with variable responses to treatment [1].

The burden of lymphomas as a major public health problem is increasingly being recognized the world over owing to the associated increase in morbidity and mortality. Globally, lymphomas account for 3-4% of all cancers and are ranked twelfth and eleventh respectively among the commonest types of cancers diagnosed in males and females. HL accounts for 0.5% of all cancers and 0.5% of cancer deaths, while NHL is the tenth most common cancer diagnosis and the

eleventh leading cause of cancer mortality worldwide [2,3,4]. However, the incidence and mortality patterns vary considerably across different geographical regions [2,4].

In the United States, HL represents approximately 10% of cases of newly diagnosed lymphoma, and the remainder are NHL. Of 21,210 estimated deaths annually from lymphoma, about 1070 (5%) are due to HL. It comprises about 0.5% of newly diagnosed cases of cancer and about 0.2% of all cancer deaths [5]. NHL accounts for about 4% of all cancer cases in the United States. It is the seventh leading cause of cancer death and represents 3.3% of all cancer deaths in the country [5,6]. The prevalence and mortality rates are much less in Eastern European and Asian countries [7,8]. World Health Organization (WHO) fact sheet on lymphoma records HL and NHL prevalence in Korea as 0.12% and 2.3% and

mortality rates as 0.08% and 2.4%, respectively [9]. In Africa, a study conducted in Kenya showed a HL prevalence of 2.8% and NHL prevalence of 7.4% whereas the prevalence of 1.2% and 2.4% was observed for HL and NHL in Kano, North-Central region of Nigeria [10,11] when compared to other cancers. These disorders are associated with escalating mortality figures in African cohorts, owing to the endemic menace of ravaging human immunodeficiency virus (HIV) infection as well as ill equipped health systems to deal with the challenge [12].

Tremendous improvement in the diagnosis and treatment of lymphomas has been made over the past couple of decades. However, it is important to note that most of these advances have occurred in high – income countries. Caring for patients with lymphoma poses a substantial challenge to families and healthcare systems, especially in middle-income and low-income countries. This is so, because most patients present when the disease is at such an advanced stage that effective treatment and cure are not possible. This usually portends prolonged hospitalization, varied invasive and non-invasive diagnostic investigations and health care cost incurrence. It is also disquieting that in these countries, including Nigeria, access to healthcare is a huge problem, lymphoma awareness is limited, the general public seems to know little about lymphomas and their public health importance [13,14]. The lack of knowledge and poor health seeking behaviour are possibly due to poverty, illiteracy, pertinacious religious and cultural barriers and the often unspoken belief that cancers are caused by demons and are undeserving of medical attention [15].

Furthermore, unavailability of state – of – the art diagnostic facilities in many centres in resource constrained countries like ours, therapeutic issues like lack of needed chemotherapeutic agents, especially the novel drugs, and where available, are very expensive and unaffordable to the majority of patients. Lack of radiotherapy equipment and healthcare professional skilled in administering radiotherapy, lack of surgeons, inadequate hospitals equipped with operating theatres and patients' inability to access and pay for surgical services pose real problems. Huge advanced, inoperable lymphomatous tumours for which they only tenable option is palliative care are still a common occurrence in these countries [12].

Regrettably, despite the avalanche of statistics on the epidemiology of lymphoma around the

world, information on the prevalence and pattern of this disorder in most African countries, including our country is scarce. This study, the first in our locality, was therefore carried out to document the spectrum of adult lymphoma and describe the clinicopathological profile and outcome of treatment among patients in the South-South region of Nigeria. Data generated from this work will underpin the importance of lymphoma as a disease with a considerable burden on health in African populations, and will draw attention to a disease that needs funding and research to improve treatment strategies.

## **2. MATERIALS AND METHODS**

### **2.1 Study Location**

The study was conducted in the Department of Haematology, University of Uyo Teaching Hospital (UUTH) Uyo, Akwa Ibom State. Uyo is the capital city of Akwa Ibom State, situated in the South-South geo-political zone of Nigeria. University of Uyo Teaching Hospital is the only tertiary healthcare facility in Akwa Ibom State, located on the outskirts of Uyo about six kilometers from the centre of the city. The hospital is a four hundred bed referral health facility that provides specialized healthcare services to residents of Uyo and its environs. It also serves as a referral centre for its neighbouring states that include Cross River, Abia and Rivers. The Department of Haematology attends to Adult patients with various haematological disorders including lymphomas.

### **2.2 Study Population**

This consists of male and female adult patients diagnosed with lymphoma in the last five years from January, 2014 to December, 2018 in Haematology Department. A total of 59 adult patients with lymphoma were reviewed during the study period.

### **2.3 Study Design**

This was a longitudinal prospective study of all lymphoma admissions into the Department of Haematology, UUTH over a five year period (Jan, 2014 – Dec., 2018). A register for documentation of lymphoma cases was opened in the Department. Patients aged 20 years and above presenting with features suggestive of lymphoma, who were admitted for investigations and treatment were registered.

Information including age, sex, duration of illness before presentation, symptoms, clinical findings on examination, laboratory results, diagnosis, treatment were recorded in the register as the patients were admitted and data entered into excel spreadsheet. Routine laboratory tests tailored towards making a diagnosis included a full blood count, bone marrow examinations, lymph node biopsy, histology and immunohistochemistry on tissue specimens. Other ancillary investigations which were carried out to assist in diagnosis and management of the patients included Xrays, ECG, abdominal ultrasound scan, serum urea, electrolytes and creatinine, and uric acid, liver function tests, urinalysis, Hepatitis B surface antigen and Anti-HCV antibody detection, Human Immunodeficiency virus 1 and 2 screening.

## 2.4 Inclusion And Exclusion Criteria

Adult patients aged 20 years and above with confirmed diagnoses of lymphoma were recruited for the study. Patients with presumptive diagnoses of lymphoma were excluded from the study. Also, all paediatric patients were excluded from the study.

## 2.5 Data Analysis

Data obtained were analyzed using STATA software for windows version 10.0. The results were summarized using simple descriptive statistics (frequencies and percentages), and presented in tables and graphical charts.

## 3. RESULTS

A total of fifty-nine (59) cases of lymphoma were recorded in patients aged 20-79 years between January 1, 2014 and December 31, 2018 at the Department of Haematology, University of Uyo Teaching Hospital. The mean age of the HL patients was  $32.09 \pm 9.22$  years with a range of 22-55 years; while the mean age of patients diagnosed with NHL was  $40.88 \pm 12.21$  years with a range of 20 – 79 years. Eleven (18.6%) of the cases were HL, with male to female ratio of 1.8:1; while forty-eight (82.4%) cases were NHL with male to female ratio of 2.2:1. The distribution of HL and NHL, according to sex, was not statistically significant ( $P = 0.73$ ). Subjects with NHL were significantly older than those with HL ( $P = 0.03$ ). The peak age incidence of the disorders was within the fourth to the fifth decades of life. HL was also observed to be common in patients between the age bracket of 20-29 years but no case was recorded in those

older than 55years. NHL was seen in all age groups Table 1.

The distribution of primary sites of lymphoma is presented in Fig. 1. The axilla was the commonest site of lymphoma (49.2%), followed by cervical lymphadenopathy (39.0%). Inguinal lymphadenopathy and intra-abdominal lymph nodes and organs (para-aortic nodes, omentum and peritoneum) accounted for 8.2% and 3.6%, respectively. Table 2 shows the clinical features of lymphoma which demonstrated that most of the patients had fever, weight loss, pallor, and abdominal distension. The features clearly show that majority of the patients had B symptoms. All the patients presented with peripheral lymphadenopathy.

Of the histologic subtypes of HL, nodular lymphocyte predominant constituted 7(63.6%) while the classical variant of HL were made up of two cases each of nodular sclerosis and lymphocyte depleted. Cases of lymphocyte rich and mixed cellularity were not encountered. Small lymphocytic lymphoma was the most common subtype of NHL, accounting for 47.9% of 48 cases, followed by diffuse large cell lymphoma accounting for 31.3%. Four cases (8.3%) of NHL were not specified. Among the remaining cases of NHL, there were two cases each of follicular lymphoma(4.2%) and lymphoblastic lymphoma(4.2%), one case each of mantle cell lymphoma(2.1%) and Adult T-cell lymphoma (2.1%) [Table 3]. HIV, Hepatitis B and C screening tests were negative in all the HL patients whereas HIV test was positive in 6/48 of the NHL patients, and one patient each was found to be sero-positive for Hepatitis B and C. Immunohistochemistry is not routinely done for patients in our centre because of cost and lack of facilities; the test (CD3, CD5, CD 15, CD20, CD23, CD 30, CD40, CD56, Cyclin D1, LCA, Pax5, Tdt, Ki-67, BCL-2 and or MUM1) was however done in another centre for fourteen (29.2%) patients who could afford and CD20 positivity was noted in 9 of them. Fig. 2 shows the Ann Arbor staging distribution of the lymphoma. Five cases (45.59%) of HL presented with stage II disease, while four (36.4%), one (9.1%), and one (9.1%) patients, presented with stage I, III, and IV diseases, respectively. On the other hand, most of the patients with NHL presented with stage III disease fifteen (31.3%), while twelve (25%), eleven (22.9%) and ten (20.8%) patients presented with stages II, IV and I diseases, respectively.

**Table 1. Age and sex distribution of HL and NHL**

| Diagnosis | Age 20 -29 (n((%)) |        | Age 30 -39 (n((%)) |        | Age 40 - 49 (n((%)) |        | Age 50 -59 (n((%)) |        | Age 60 - 69 (n((%)) |        | Age ≥ 70 (n((%)) |        |
|-----------|--------------------|--------|--------------------|--------|---------------------|--------|--------------------|--------|---------------------|--------|------------------|--------|
|           | Male               | Female | Male               | Female | Male                | Female | Male               | Female | Male                | Female | Male             | Female |
| HL        | 3(5)               | 1(2)   | 2(3)               | 2(3)   | 1(2)                | 1(2)   | 1(2)               | 0(0)   | 0(0)                | 0(0)   | 0(0)             | 0(0)   |
| NHL       | 3(5)               | 1(2)   | 8(14)              | 2(3)   | 10(17)              | 5(8)   | 5(8)               | 4(7)   | 4(7)                | 3(5)   | 3(5)             | 0(0)   |
| Total     | 6(10)              | 2(3)   | 10(17)             | 4(7)   | 11(19)              | 6(10)  | 6(10)              | 4(7)   | 4(7)                | 3(5)   | 3(5)             | 0(0)   |

$P^a$  = Pearson's chi-square, \* $P \leq 0.05$  (significant), HL = Hodgkin Lymphoma, NHL – Non-Hodgkin Lymphoma  $P^a$  0.03, 0.73

**Table 2. Clinical manifestations of lymphoma**

| Clinical features symptoms             | HL cases |     | NHL cases |     | Signs                       | HL cases |     | NHL cases |     |
|--|----------|-----|-----------|-----|-----------------------------|----------|-----|-----------|-----|
|  | cases    | %   | cases     | %   |                             | cases    | %   | cases     | %   |
| Fever                                  | 5        | 45  | 18        | 38  | Pallor                      | 6        | 55  | 20        | 42  |
| Weight loss                            | 6        | 55  | 27        | 56  | Jaundice                    | 3        | 27  | 10        | 21  |
| Night sweat                            | 4        | 36  | 8         | 17  | Chest signs                 | 6        | 55  | 15        | 31  |
| Swellings in the neck, axilla or groin | 11       | 100 | 48        | 100 | Hepatomegaly                | 4        | 36  | 24        | 50  |
| Abdominal pain                         | 2        | 18  | 15        | 31  | Splenomegaly                | 2        | 18  | 11        | 23  |
| Abdominal swelling                     | 4        | 36  | 20        | 42  | Generalized lymphadenopathy | 11       | 100 | 48        | 100 |
| Bone pain                              | 3        | 27  | 9         | 19  | Ascites                     | 2        | 18  | 8         | 17  |
| Pruritus                               | 3        | 27  | 0         | 0   | Abdominal tenderness        | 2        | 18  | 18        | 38  |
|  |          |     |           |     | Peripheral edema            | 3        | 27  | 9         | 19  |
|  |          |     |           |     | Erythroderma with Scaling   | 0        | 0   | 2         | 4   |

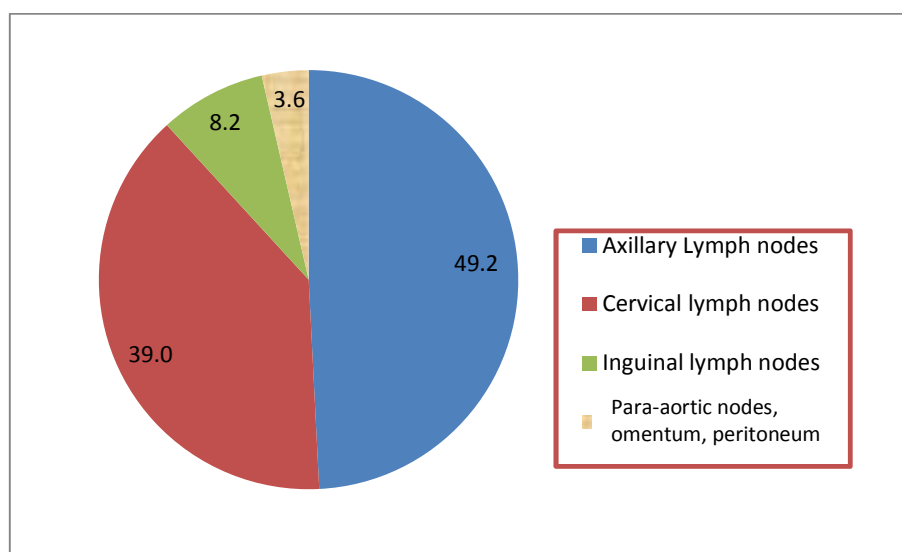


Fig. 1. Pie chart distribution showing primary sites of lymphoma

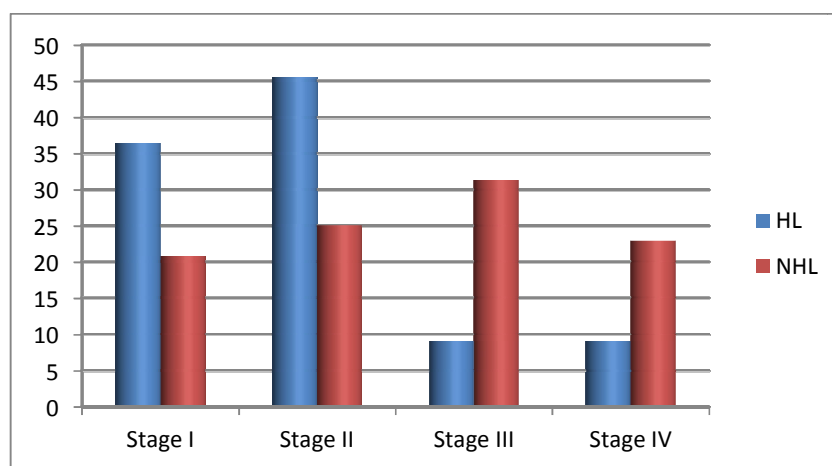
Table 3. Distribution of histologic subtypes of hodgkin lymphoma and non-hodgkin lymphoma

| Types of lymphoma | Histologic subtypes            | Cases | Percentage |
|-------------------|--------------------------------|-------|------------|
| HL                | Nodular Sclerosis              | 2     | 18.2       |
|                   | Mixed Cellularity              | 0     | 0          |
|                   | Lymphocyte Rich                | 0     | 0          |
|                   | Lymphocyte Depleted            | 2     | 18.2       |
|                   | Nodular Lymphocyte Predominant | 7     | 63.6       |
| NHL               | Small Lymphocytic Lymphoma     | 23    | 47.9       |
|                   | Diffuse large cell Lymphoma    | 15    | 31.3       |
|                   | Unspecified                    | 4     | 8.3        |
|                   | Follicular Lymphoma            | 2     | 4.2        |
|                   | Lymphoblastic Lymphoma         | 2     | 4.2        |
|                   | Mantle cell Lymphoma           | 1     | 2.1        |
|                   | Adult T – cell Lymphoma        | 1     | 2.1        |

Table 4. Treatment outcome of patients with lymphoma

| Treatment outcome n (%)                   | n(%)     |           |       | Statistical test |
|---|----------|-----------|-------|------------------|
|   | HL       | NHL       | Total |                  |
| Cure                                      | 2 (18.2) | 1 (2.1)   | 3     | P = 0.15         |
| Remission                                 | 2 (18.2) | 7(14.6)   | 9     |                  |
| Relapse after first year of chemotherapy  | 1 (9.1)  | 2 (4.2)   | 3     |                  |
| Relapse after second year of chemotherapy | 1(9.1)   | 3 (6.3)   | 4     |                  |
| Poor Response                             | 0 (0.0)  | 0(0.0)    | 0     |                  |
| No response                               | 0(0.0)   | 0(0.0)    | 0     |                  |
| Left against Medical Advice               | 1 (9.1)  | 1(2.1)    | 2     |                  |
| Referred                                  | 0(0.0)   | 3(6.3)    | 3     |                  |
| Loss to follow up                         | 1(9.1)   | 12(25.0)  | 13    |                  |
| Death                                     | 3(27.3)  | 19 (39.6) | 22    |                  |

Fishers exact p There is no significant difference in treatment outcome between respondents with HL and NHL [ P = 0.15]



**Fig. 2. Ann arbor staging distribution of HL and NHL**

Table 4 shows the treatment outcome. All the HL patients (100%, 11/11) received ABVD (Adriamycin, Bleomycin, Vinblastine and Dacarbazine) regimen alone. The NPLHL patients in our series could not afford Rituximab and therefore were not placed on R-CHOP. Majority of the NHL patients (91.7%, 44/48) received CHOP (Cyclophosphamide, Doxorubicin, Oncovin and Prednisolone) regimen alone, while 8.3% (4/48) received Rituximab with CHOP (R-CHOP). The SLL patients received CHOP regimen alone, they could not afford Bendamustine, Rituximab and Fludarabine which are essential for their treatment. Sixteen 16(27.1%) patients achieved complete remission. However, three 3(5.1%) patients relapsed after the first year of chemotherapy, four 4(6.8%) patients relapsed after the second year while nine 9(15.3%) patients were still in remission. The HL and NHL patients who relapsed were given the same first line chemotherapeutic regimens, they did not switch to other first line drugs or the second line chemotherapeutic combinations because of the prohibitive cost and inaccessibility of most of the agents. The cure rate was very low 5.1%, losses to follow up accounted for 22.0%, 0.03% of patients left against medical advice and 37.3% of patients died in the course of therapy either from advanced disease or complications of chemotherapy. This study had a follow up period of 5 years and more than one third of the patients had died as at the time of this evaluation.

#### 4. DISCUSSION

Lymphomas are malignancies that have been widely studied across the globe [16]. In the US,

Europe and Asian countries, a lot of literature on the epidemiological profile of these neoplasms has been published [5,8,13,15,17,18]. In spite of the availability of this literature, published studies on lymphomas in Africa, Nigeria in particular are few and far between. In addition, most of the Nigerian studies were not conducted in South – South Nigeria. Therefore, the results may not reflect the actual prevalence and characteristics of lymphoma in the geographical region. The present study sought to determine the prevalence, treatment outcome and clinicopathological features of the subtypes of lymphoma in Uyo, South-South Nigeria with the aim of improving understanding of the demographic profile of the local population affected by the disease and to provide invaluable baseline data with which to compare findings with those of other workers.

These neoplasms have been reported to be the commonest haematological malignancies among adults [3,6,7,10-15]. There is variation in incidence rates with respect to age, sex, race, socioeconomic status and histologic subtypes [3]. The male preponderance in the current study is consistent with findings from other studies including studies from United Kingdom and less developed countries of Central and South America, Africa and Asia [12-14,19-23]. However, higher female to male ratios of 1.6 – 1.8 in Asia and Africa, and 1.1-1.2 in Europe and North America have been reported [24,25]. The gender of an individual confers one of the major risks for contracting lymphomas [26]. In 1998, Hasenclever et al. [27] examined pooled patients' data and the male sex factor was identified as an adverse prognostic index for advanced lymphomas.

An increased occurrence of HL in young adult population has been associated with higher socioeconomic status [28-30] and this lends credence to the bewildering etiologic heterogeneity of this tumour. In keeping with the studies, majority of our patients (73%) were young adults. There was paucity of cases above the age of 55 years, which is in dissonance with the incidence peak of over 60 years seen in advanced economies [31,32]. This may be due to variation in sample size, genetic and racial factors. Nonetheless, a significant higher incidence has been reported among adolescents and young adults in some Western countries, while less developed nations commonly show higher rates in the pediatric age group [33]. The latter finding was not demonstrated in the present study because the study population consists entirely of adults. These observations underscore the need to identify risk factors and define etiological hypotheses for HL in the young. The bimodal incidence peak of 20-29 and 30-39 years age brackets in this study displays a striking variation compared with the classic bimodality of peaks in young adults and the elderly seen in the developed world [28]. The differences observed in the age incidence in our clime and the western world could be attributed largely to our relatively younger population, shorter life expectancy among the populace owing to appalling socioeconomic conditions and environmental factors.

NHL was majorly observed among patients aged 30-49 years, similar to reports from studies conducted in Jos [34] and Lagos [35]. The mean age of diagnosis of NHL in this study was 40.88±12.21 years. This agrees with studies from other centres [35,36], though contrasts with values that were reported by Dei – Adomakoh et.al [37] in Ghana and Shen et.al in China [38]. Also, our finding is inconsistent with studies by Thieblemont et al. [39] and Grossoeuvre et.al [40] who observed that one half of newly diagnosed NHL occurred in patients older than 60 years.

HL accounted for 18.6% of all lymphoma cases in our review. This is comparable with 17% reported by Omoti [3] in Benin, but contrasts findings in Zaria [41], Tanzania [42] and Malaysia [43] where HL constituted 12%, 10.3% and 22.16% of all lymphoma cases respectively. Nodular lymphocyte predominant was the most dominant histologic subtype, accounting for 63.6% of cases, this correlates with findings in Maiduguri, North-East Nigeria, where Nodular

lymphocyte predominant was equally the dominant histological subtype [44]. The finding is however at variance with the general observation in most studies in which nodular sclerosis is catalogued as the most prevalent subtype [25,26,30,33,45,46]. Nodular sclerosis made up 18.2% of HL seen in this study. Lymphocyte depleted also accounted for 18.2% of the cases, this figure closely approximates with 18% [47] and 19.6% [48] reported by Okpala et al and Olu-Eddo et al in Ibadan and Benin respectively, but lower than 24% reported in Iraq [49]. There were no cases of lymphocyte-rich NHL in our series, similar to findings in South Africa [50]. However lymphocyte-rich HL made up 10% of cases seen in Lagos [45]. No cases of mixed cellularity subtype of HL were seen in the present study. In contrast, mixed cellularity HL constituted 64.3% and 14.7% of HL in Benin [48] and Brazil respectively [46].

Non-Hodgkin lymphoma made up 81.4% of cases seen in the current review. This is comparable to 80% observed in Maiduguri [44], though much higher than 57.1% obtained in Kano [51] and lower than 93% reported in a study in Gabon [52]. A predominance of NHL has equally been observed in other studies [42,46]. Small lymphocytic lymphoma formed the vast majority of the NHL cases encountered in our study. It constituted 47.9% of the cases. This is in contrast to studies conducted in Africa [53], South America [48] and Asia [8,54], which showed diffuse large cell lymphoma to be the commonest. Diffuse large cell lymphoma was the second most common subtype in our report, accounting for 31.3% of cases seen. This figure is lower than a proportion of 41% observed in Turkey [55], but greater than figures reported in Enugu (26.3%) [56] and Ibadan (15.5%) [57]. The Other histologic subtypes seen were follicular lymphoma 4.2%, lymphoblastic lymphoma 4.2%, Mantle cell lymphoma 2.1%, Adult T – cell lymphoma 2.1% and 8.3% of the cases had no clarification of type and therefore designated as unspecified. Immunohistochemical examination was not performed on these unspecified cases because the patients could not afford the test. The rarity of follicular lymphoma in the present work reflects a general trend found in NHL series from African countries [53,58] but is inconsistent with observations in studies from the US, Canada and Western Europe, where this variant of lymphoma has increased in frequency in the past few decades [6,26,31]. The reason for the low percentage of follicular lymphoma in African nations remains to be elucidated. The



plausible explanation for the small proportion of cases in our study could be due to the young mean age ( $40.88 \pm 12.21$  years) of the NHL patients. Since follicular lymphoma is seen most frequently in older age groups, the younger age distribution of our patient population could partly account for the percentage of this lymphoma. Similarly, the low percentage of lymphoblastic lymphoma, mantle cell lymphoma and Adult T-Cell lymphoma found in our study corroborates the observations in reports from other African studies [3,21,47,52,53,56,57,58].

The predominant occurrence of lymphomas in lymph nodes in our review (96.4%) is comparable with 88.5% reported by Mozaheb et al (23) in Iran, but sharply contrasts with the previous study of lymphomas in Jos by Obafunwa et al. [59] who found that 90% of cases had a primary extranodal presentation. Of the nodal sites involved in this study, the axillary lymph node was predominant, accounting for 49.2% of nodal lymphomas, while the cervical and inguinal lymph nodes accounted for 39.0% and 8.2% respectively. The para-aortic nodes, omentum and peritoneum were the least common sites of lymphoma in the present study accounting for 3.6% of cases. However, several studies [41-46] have shown cervical lymph nodes to be the commonest nodal site of lymphoma, followed by the axillary nodes and other lymph nodes. The predominance of cervical lymph nodes in the aforementioned studies might be due to the fact that this group of lymph nodes provide ease of access compared to axillary, mesenteric, epitrochlear, supraclavicular and inguinal lymph nodes. Also, the anatomic location of cervical lymph nodes provides a morphologic picture unperturbed by fibrosis following chronic inflammation, in contradistinction to what obtains in the inguinal lymph nodes [48]. The only sites of extranodal lymphoma in the current study were the omentum and peritoneum). This extranodal lymphoma was of the NHL subtype. We did not encounter any extranodal case of HL in our review. This compares favourably with findings in Ibadan and Ile-Ife where extranodal lymphoma of the NHL variant accounted for 98.7% and 100% of the lymphomas, respectively [57,60]. The clinical features of lymphoma, demonstrated in this study showed that all the patients presented with generalized lymphadenopathy. Worthy of note also is that most of the patients presented with B symptoms [Table 2], other presentations were bone pain, pallor, jaundice, hepatomegaly, splenomegaly, ascites and chest signs. These

features were more common in NHL compared to HL. This shows that most of the NHL patients in this review presented late to the hospital. NHL stage III disease dominated in our series, while majority of the HL patients were diagnosed with stage 1 and stage II diseases. This scenario has been reported by other authors [3,44,61]. In our country, just like any other developing nation, the tendency to go for routine medical checkup is inadmissibly low. Self-medication or prior consultation of other Healthcare Providers such as Nurses, Pharmacists, Medical Laboratory Scientists and Patent Medicine Dealers aside from Physicians delays visits to hospitals for proper medical evaluation, hence a lot of patients are diagnosed with advanced disease. Other reasons for late presentation to our referral centre may include inappropriate diagnosis and mismanagement at various primary and secondary health facilities or financial constraints that was observed to plague a vast majority of our patients. Patients presenting with late stage disease have poor prognosis and experience untold psychological and socioeconomic deprivation, occasioned by besetting pecuniary obligations from soaring medical bills.

Combination chemotherapy was the mainstay of treatment in our centre. The role of surgery was primarily for diagnostic purposes and no radiotherapy was used in the management of the patients. All the patients received supportive care during the course of treatment. Major challenges encountered during the management of patients included unavailability of some prescribed cytotoxic agents such as Bleomycin, Vinblastine, Darcabazine and Rituximab, exorbitant cost where available and reluctance on the part of the patients and their caregivers to continue spending endlessly after protracted hospital admission, coupled with no clinical improvement, especially in those who presented with advanced stages of the disease. Similar experience have been reported in other centres in the country [44,62-64].

The mortality figures, default rate and number of patients lost to follow up noted in the study are true reflections of the abysmal outcome of lymphoma management in our environment. In most developing countries, cancer is still being viewed as incurable, and a condition that cannot be treated with orthodox methods. Rather, traditional healers, spiritual or faith healers are highly patronized, especially in this study locality [15,65]. This may possibly have accounted for the number of patients who were lost to follow up

as well as those who left against medical advice. Most of the patients lost to follow up were presumed dead or too demoralized to continue hospital treatment owing to the mounting bills. Majority of the patients had no form of health insurance cover and therefore bore the cost of treatment directly.

With the use of ABVD-type Chemotherapy for HL and R-CHOP for NHL the outcome of these conditions have improved remarkably during the last few decades with 70-80% complete remission [66,67]. Achievement of complete remission with frontline chemotherapeutic drugs is the initial step towards cure of any chemosensitive neoplasm and adequacy of treatment determines this. ABVD was used in 100% of our HL cases. The treatment was sustained and all the patients received six courses. Of the patients who had complete remission at the end of 6 cycles of ABVD, two (18.2%) were cured, one (9.1%) relapsed after the first year of chemotherapy, one (9.1%) relapsed after the second year while two (18.2%) were still in remission. A previous survival study in HL in Lebanon had recorded similar pattern [68].

The combination of Rituximab with CHOP (R-CHOP) is the gold standard in NHL treatment. R-CHOP or CHOP is the most commonly employed treatment for NHL [69]. Similarly in this study treatment was mainly with CHOP, with 91.7% of the patients receiving this chemotherapeutic regimen, while 8.3% received Rituximab with CHOP (R-CHOP). It is known that response rates diminish significantly in the absence of Rituximab [66,70]. Majority of the patients did not have immunohistochemistry done and of those who were CD 20 positive only 4 of them could afford and receive Rituximab. This may have adversely affected the survival and underscores the need for public-spirited individuals and Government to assist in defraying the expenses incurred during treatment with this drug. This is quite imperative as the cost of investigations and procuring the drug is not affordable for the generality of the populace.

## 5. CONCLUSION

The clinicopathological characteristics, age and sex distribution of lymphoma in our study are comparable to those reported in other studies conducted within and outside Nigeria. There is need for establishment of more molecular laboratories throughout the country to cater for

the increasing demand for molecular genetic studies and to ensure that immunohistochemistry, cytogenetics and other molecular-based tests, which are required for the definitive diagnosis of lymphoma and other cancers, are made affordable and accessible. The government should also be sensitized on the need to subsidize cancer treatment or make it free to reduce default and increase survival. Finally, medical personnel should be reawakened to the consciousness that lymphoma is not uncommon in our environment.

## CONSENT

It's not applicable.

## ETHICAL APPROVAL

Ethical approval was obtained from The Institutional Health Research Ethical Committee of the Hospital before the commencement of the study.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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