International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

Original Research Article

Immunohistochemical Profiling of Lymphomas in Jos University Teaching Hospital, Jos

Ajetunmobi OI[1], Mandong BM[2], Adelusola KA[3], Silas OA[2]

[1]Department of Histopathology, Federal Medical Centre, Makurdi, Benue State, Nigeria.
[2]Department of Histopathology, Jos University Teaching Hospital, Plateau State.
[3]Department of Morbid Anatomy and Forensic Medicine, Obafemi Awolowo University, Ile-Ife Osun State.

Corresponding Author: Ajetunmobi OI

ABSTRACT

Background: Lymphomas are a significant cause of disease burden globally. In Nigeria, lymphomas are the commonest malignancies in children, and the third commonest in adults. Effectual treatment is dependent on identification of definite lymphoma subtypes.
Objective: This study was undertaken to document the histologic and immunophenotypic subtypes of lymphomas in Jos.
Methods: All lymphomas cases, diagnosed over a period of 5 years, at the Jos University Teaching Hospital, were reviewed and classified according to their morphologic characteristics. Immunostaining with a panel of four monoclonal antibodies, was employed for classification according to cell lineage.
Results: A total of one hundred and eleven (111) histologically diagnosed lymphomas were seen during the 5 year period (2008-2012). Lymphomas were commoner in females with a male to female ratio of 0.8:1. Approximately 48.7% of cases occurred within the 36-65 years age bracket while children accounted for 17.9% of cases. Non-Hodgkin lymphomas were predominant, accounting for 89.7% of cases, while Hodgkin lymphoma made up 10.3%. Diffuse large cell and Burkitt lymphomas were the commonest histologic subtypes of non-Hodgkin lymphoma. The nodular sclerosing subtype was the commonest variant of Hodgkin lymphoma. Immunophenotypically, B cell lymphomas accounted for 77.1% of all non-Hodgkin lymphomas, T cell lymphomas were seen in 5.7% of cases, while phenotyping was inconclusive in 17.1% of cases of non Hodgkin lymphoma.
Conclusion: Immunohistochemistry is invaluable in delineating lymphoid lesions in accordance with their cell of origin, as well as determining the course of therapy.

Keywords: Lymphoma, Hodgkins, Immunohistochemistry, Phenotyping.

INTRODUCTION

Lymphomas are tumours arising from malignant proliferation of lymphoid cells. Globally, lymphomas rank twelfth (12^{th}) highest among all cancers, are the eight (8^{th}) most common cause of cancer deaths in males and the seventh (7^{th}) commonest in females. [1,2] In Nigeria, lymphomas rank third (3^{rd}) amongst the commonest types of cancers. [3] However in children they are reported to be the commonest cause of malignant disease, particularly Burkitt lymphoma which accounts for close to 50% of cases. [4]

Previous studies of malignant diseases in Jos University Teaching Hospital (JUTH) between 1985 and 1994, showed lymphomas as the second (2^{nd}) commonest malignancy. They were the commonest malignancies in males and the second (2^{nd}) commonest in females. [3] A follow up study between 1995 and 2002

showed lymphomas to be the fourth (4^{th}) commonest malignancy in adults, being the second (2^{nd}) commonest in males and the third (3^{rd}) commonest in females. [3] Furthermore a study in JUTH by Okpe et al, carried out between 2006 and 2010 identified Burkitt lymphoma as the commonest tumour in children, accounting for 48.9%, other non Hodgkin lymphomas ranked third (3^{rd}) highest (12.8%). [4]

Appropriate diagnosis and classification of lymphomas enable effective therapeutic management. This constitutes a daunting challenge in the light of the morphological variations in this group of neoplasms. Notwithstanding, ancillary molecular techniques, can identify lymphoid tissue, delineate their nature into reactive or neoplastic, characterize cell lineage (B cell, T cell and NK cell) and grade neoplasms. [5]

Immunohistochemistry has emerged as the most valuable adjunct to routine Hematoxylin and Eosin (H&E) staining in pathology. [6] It possesses remarkable sensitivity and specificity, applicability to paraffin wax-embedded materials and compatibility with most common fixatives. Notably, unlike other human cancers, the success of the treatment for the different types of lymphoma depends on the accurate identification of the disease, rather than its early detection. [7]

This study described the histopathological pattern of lymphomas seen in Jos University Teaching Hospital (JUTH) during the period from 2008 to 2012 and evaluated their immunohistochemical characteristics which served as a basis for their appropriate classification according to cell lineage. It also evaluated the demographic characteristics of patients with lymphomas and determined the relative proportions of Hodgkin and non Hodgkin lymphomas, as well as the various types of non Hodgkin lymphomas.

MATERIALS AND METHODS

This was an hospital based retrospective study, which involved the retrieval of archival records, paraffin wax blocks and Haematoxylin and Eosin (H&E) slides of histologically diagnosed lymphomas at the Jos University Teaching Hospital between 1^{st} January 2008 and 31^{st} December 2012. These were classified according to cell lineage using Immunohistochemistry.

Immunohistochemistry procedure:

Sections of 3-4 microns thickness were cut from FFPEs. Antigen retrieval was performed using citric acid at pH 6.0 in a microwave at power 100 and 121 degrees Celsius for 15 minutes. Endogenous peroxidases were blocked using 3% Hydrogen peroxide for 15 minutes while protein block was performed with Novocastra Protein Block for 15 minutes. Immunostaining was performed using the following monoclonal antibodies, (sourced from Novocastra, Illinois, United States): Leucocyte Common Antigen (LCA), CD20, CD3, and CD30. The procedures for immunohistochemical staining were performed at the Histopathology Laboratory of The National Hospital, Abuja. The polymer technique of the indirect immunoperoxidase method was employed. Tissue from the tonsils and appendix were used as positive control. Ethical clearance was obtained in written form from the Jos University Teaching Hospital Institutional Health Research Committee/Board [IRB]. The IRB approval was granted alongside waiver on patients consent.

RESULTS

A total of one hundred and eleven (111) cases were histologically diagnosed as lymphoma within the study period. These accounted for 0.8% of all surgical pathology biopsies received at the Histopathology department of the Jos University teaching Hospital during the study period. Of these, 78 (71%) met the inclusion criteria.

Of the 78 cases analyzed, 70(89.7%) were diagnosed as non Hodgkin lymphoma, while 8(10.3%) were Hodgkin lymphoma (Table 1). The peak incidence occurred between ages 36 and 45 years, accounting

for 26.9% of all cases. (Table 2) The ages of patients ranged from 2 years to 84 years, the mean age at diagnosis was 35.6 years while the median age was 37.5 years. Middle aged persons, which for the sake of this study were classified to be between 36 and 65years, accounted for 38 (48.7%) of all lymphoma cases, with a male to female ratio of 1:2. Children accounted for 14(17.9%) of all cases (Table 2). Overall, a female predominance was observed in this study, accounting for 43(55.1%) cases, while males account for 35 (44.9%) cases, giving a M:F ratio of 0.8:1 (Table 1).

Out of the 70 cases of non Hodgkin lymphoma, Diffuse large B cell lymphoma (DLBCL) and Burkitt lymphoma were the commonest histologic subtypes, accounting for 27(38.6%) and 15(21.4%) respectively. Other histologic types included small cell lymphoma 10(14.3%), follicular lymphoma 5(7.1%), Lymphoplasmacytic lymphoma 4(5.7%), and a solitary case of lymphoblastic lymphoma (Table 1). There were 30(43%) and 40(57%) cases of non Hodgkin lymphoma in males and females respectively, giving a male to female ratio of 3:4 (Table 1). The mean and median ages of all non Hodgkin lymphomas were 36.3±19.3 and 38years respectively. The peak incidence age was 36-45years and the age range was 2-84 years. Of the 4(4%) cases seen above the age of 65years, 3 were male while only a single case was seen in a female, giving a male to female ratio of 3:1. (Table 2)

The median ages for specific histologic subtypes of non Hodgkin lymphoma were 42 years for Diffuse large B cell, 22years for Burkitt, and 50 years for small cell lymphoma. For follicular lymphoma, and lymphoplasmacytic lymphoma, median ages were 24 years and 52 years respectively. Non Hodgkin lymphomas accounted for 85.7% of cases seen in children, of these, Burkitt (35.7%) and Diffuse large B cell lymphoma (28.6%) were the commonest histologic types.

Hodgkin lymphomas accounted for 8(10.3%) of all lymphomas seen in this study. (Table 1) Nodular sclerosis was the commonest histologic subtype accounting for 6(75%) cases, while 2(25%) cases were of mixed cellularity histology. There were no cases of lymphocyte rich, lymphocyte depleted and nodular lymphocyte predominant variants of Hodgkin lymphoma. (Table 1) Hodgkin lymphoma accounted for only 2(14.3%) cases seen in the pediatric age group, while no case was seen above the age of 50 years. The age range of incidence was 10-50 years. The median age for all cases of Hodgkin lymphoma was 29.5 years. The median age for nodular sclerosis was 29.5 years while that for mixed cellularity was 25.5 years. Overall, the male to female ratio for Hodgkin lymphoma was 1.7:1. The male to female ratio for nodular sclerosis was 1:1 whereas both cases of mixed cellularity occurred in males, giving a male to female ratio of 2:0. (Table 1) All cases of Hodgkin lymphoma were nodal in location with cervical lymph node accounting for 4(50%) cases, axillary lymph node in 2(25%) cases while the nodal site was unknown in 2(25%) cases.

Lymph nodes were the commonest site, accounting for 49 (62.8%) of all cases. Cervical lymph nodes were the most prevalent nodal site, involved in 27(55%) of nodal lymphomas, followed by axillary lymph nodes with 13(27%) and mesenteric lymph nodes 4(8%) (Figure 1). Other lymph node groups involved included, inguinal, epitrochlear and supraclavicular lymph nodes all with 1 case (2%) each. (Figure 1) Two of the lymph nodal sites were unspecified (Figure 1). Lymphomas with primary involvement of cervical lymph nodes had a male to female ratio of 0.8:1, while those arising from axillary lymph nodes had a male to female ratio of 5.5:1. All lymphoma cases arising from mesenteric, inguinal and supraclavicular lymph nodes were seen exclusively in females. The age range for nodal lymphomas was 2-84 years, with a peak at 16-25 years and median of 38 years. Primary extranodal lymphoma occurred in

29(37.2%) cases. The highest number of extranodal lymphomas was seen in the gastrointestinal tract accounting for 8(27.6%). (Figure 2) Other common extranodal sites included ovary 5(17.2%), testis/paratestis 4(13.8%) and the abdominopelvic region 3(10.3%). (Figure 2) The age range of incidence for extranodal lymphomas was between 6 and 80 years. The median age of incidence was 38 years, same as that for nodal lymphomas. Children accounted for 7(24.1%) of extranodal lymphomas. All extranodal lymphomas were of non Hodgkin type. Diffuse large B cell and Burkitt lymphomas both accounted for 10(34.5%) each of all extranodal lymphomas, whereas follicular lymphoma and lymphoplasmacytic lymphoma accounted for 1(3.4%) each. Small lymphocytic lymphoma made up 2(6.9%) of all extranodal lymphomas.

Seventy-seven (77) of all the 78 lymphomas were confirmed as hematolymphoid proliferations, displaying positive immunoreactivity for Leucocyte Common Antigen (LCA). Among the 70 non-Hodgkin lymphomas, a B cell immunophenotype (LCA+, CD20+, CD3-) was predominant, present in 54 (77.1%) cases. The median age for B cell lymphomas was 37.5 years, while the mean was 36.9±18.9 years. The peak age of incidence was between 36 and 45 years while 10(18.5%) cases were seen amidst children.

Amidst B cell lymphomas, the male to female ratio was 0.7:1. Extranodal involvement was seen in 24(44.4%) cases, while 30(55.6%) cases were found in lymph nodes.

A T cell immunophenotype (LCA+, CD20-, CD3+) was observed in 4(5.7%) cases analyzed. T cell lymphomas had a median age of 44 years, and a mean age of 41.0±18.3 years. No case occurred in children, and the elderly. A male to female ratio of 1:3 was seen. T cell lymphomas occurred in lymph nodes in 3(75%) cases, while a solitary case (25%) was seen in an extranodal site.

Phenotyping was inconclusive in 12 of all Non Hodgkin lymphoma cases, 7 of which showed a co expression of both B and T cell antigens, while 5 were non reactive for both monoclonal antibodies indicative of either B cell (CD20) or T cell (CD3) origin. Of the 12 inconclusive cases, only one was negative for LCA. This case was negative for both B cell and T cell antigens.

Table 1: Histologic patterns of lymphomas in JUTH, Jos with their sex distribution

Histologic pattern	Male	Female	Frequency	Percentage
Non Hodgkin Lymphoma				
DLBCL*	12	15	27	38.6
Burkitt	5	10	15	21.4
Small cell lymphoma	3	7	10	14.3
Follicular lymphoma	3	2	5	7.1
LPL**	2	2	4	5.7
Lymphoblastic	1	0	1	1.4
Lymphoma NOS	4	4	8	11.4
Sub-Total	**30**	**40**	**70**	**100**
Hodgkin lymphoma				
Nodular sclerosis	3	3	6	75
Mixed cellularity	2	0	2	25
Lymphocyte Rich	0	0	0	0.0
Lymphocyte depleted	0	0	0	0.0
NLPHL****	0	0	0	0.0
Sub-Total	**5**	**3**	**8**	**100**
Total	**35**	**43**	**78**	

*Diffuse large B cell lymphoma ** Lymphoplasmacytic lymphoma *** Lymphoma None Otherwise Specified. ****Nodular Lymphocyte Predominant Hodgkin Lymphoma

Expression of the B cell antigen CD20 was seen in 96.3% of all cases of Diffuse large B cell lymphoma, but was 100% in cases of small cell lymphoma and lymphoplasmacytic lymphoma. CD20 expression rates were 73.3%, 80% and

87.5% for cases of Burkitt, Follicular lymphoma and Lymphoma NOS (Non Otherwise Specified) respectively. CD3 expression was highest amongst small cell lymphomas (30%), but absent in the case of lymphoblastic lymphoma. CD3 expression was observed in 18.5% of Diffuse large B cell lymphoma, and 25% of both lymphoplasmacytic lymphoma and lymphoma NOS.

Amidst Hodgkin lymphomas, all cases, displayed expression of Leucocyte Common Antigen (LCA) by background reactive lymphoid cells exempting the Reed Sternberg Cells. In 6 of the 8 Hodgkin Lymphomas, Reed Sternberg cells were demonstrated by positive membranous and paranuclear/golgi pattern staining for CD30. (Figure 3) No case of nodular lymphocyte predominance Hodgkin lymphoma was seen.

Table 2: Age and sex distribution of all lymphomas in JUTH, Jos.

Age(years)	Male	Female	Frequency	Percentage
≤ 15	6	8	14	17.9
16-25	9	4	13	16.7
26-35	5	4	9	11.5
36-45	8	13	21	26.9
46-55	2	8	10	12.8
56-65	2	5	7	9.0
66-75	1	1	2	2
>75	2	0	2	2
Total	35	43	78	100

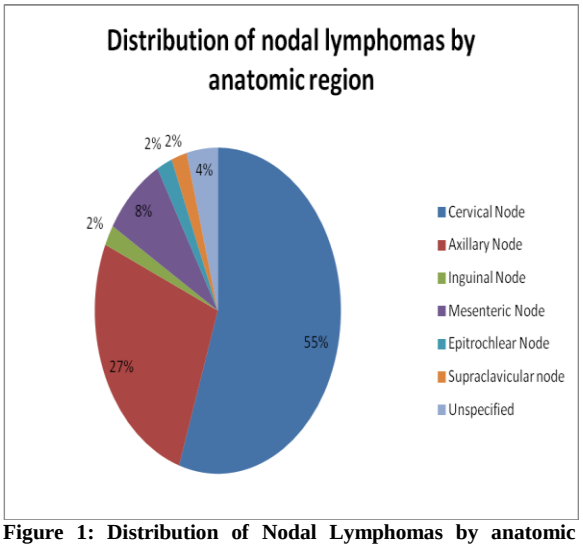

Figure 1: Distribution of Nodal Lymphomas by anatomic region

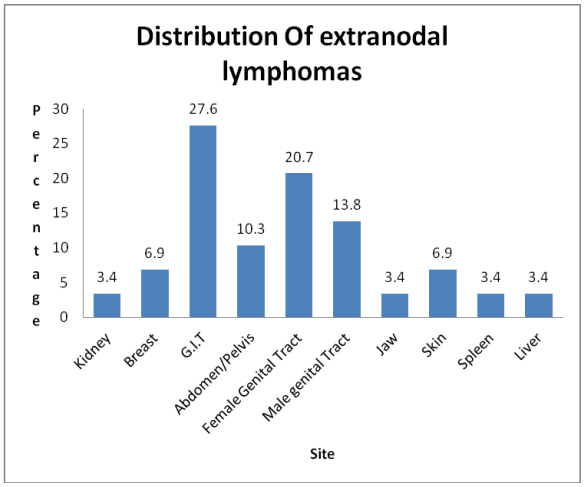

Figure 2: Anatomical sites of extranodal lymphomas

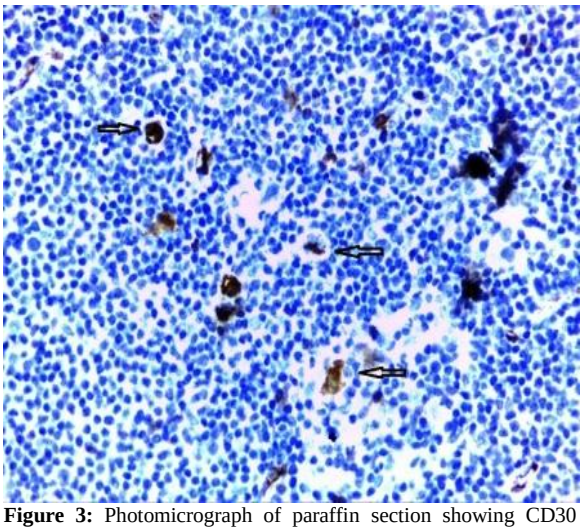

Figure 3: Photomicrograph of paraffin section showing CD30 staining in Hodgkin lymphoma with positive membranous and Golgi pattern staining of Reed Sternberg cells {white arrows}.Indirect immunoperoxidase X100

DISCUSSION

The female predominance in this study differs from the majority of studies carried out in other parts of the country. The previous study carried out in Jos by Obafunwa et al showed a male to female ratio of 3:1 while studies in Lagos and Ibadan showed a male predominance, having ratios 1.8:1 and 1.5:1 respectively. [8-10] However a review in Benin showed a female predominance with a male to female ratio of 1:1.9, an observation similar to findings in this study. [11] Behavioural and social factors could probably account for the variation observed in this study, as females have better health seeking behaviours than males and as such would present at health care facilities more often. However no

definite sex linked factors have been identified in lymphoma aetiology. [12]

A bimodal peak age incidence was observed at ages less than or equal to fifteen (15) years and between thirty six and forty five (36-45) years (Table1). Similarly, a bimodal peak was observed in Gabon at ages less than or equal to fourteen (14) years and between fifty-five and sixty four (55-64) years. [13] In contrast, a single peak in incidence age was observed between forty six and fifty five (46-55) years and between forty seven and sixty seven (47-67) years in studies in Lagos and Sudan respectively. [10,14] The median age observed in this study was 37 years. This is at variance with the median age of incidence of 64 years in the United States and 50 years in China but is similar to a median age of 38 years obtained in Bahrain. [15-17] The median ages of 43 years and 47 years obtained in Ethiopia and Sudan respectively, are higher than that obtained in this study. [14,18] However the mean age in this study is higher than 29.6 years observed in Ibadan. [8]

Lymphoma tends to occur at an earlier age in sub Saharan Africa as compared to Europe and North America. This reflects the greater contribution of childhood cases to the Lymphoma burden in Africa, particularly by Burkitt lymphoma. [19]

Childhood lymphoma formed 17.9% of all the cases seen in this study. This is higher than 12.1% obtained in Malaysia and 14.2% in Ethiopia. [20,18] In this study, non Hodgkin lymphoma accounted for 85.7% of all childhood cases, and this is higher than 74.6% observed in Iraq. [21] Burkitt lymphoma and diffuse large B cell lymphoma jointly accounted for 64.3% of all childhood cases seen in this series. This is similar to observations in a study by Bilic, who stated that Burkitt and diffuse large B cell lymphomas jointly accounted for 60% of childhood lymphomas, but contrasts findings in China where Hodgkin lymphoma was the commonest histologic subtype of childhood lymphoma. [17,22] Burkitt lymphoma alone accounted for 35.7% of all childhood lymphomas seen in this study. This contrasts findings in Uganda, where Burkitt lymphoma accounted for 90% of childhood lymphomas, as well as in Kano and Ife, where it accounted for 48% and 73.2% of childhood lymphomas respectively. [23,24]

The predominance of nodal lymphomas in this study (62.8%), approximates observations in other studies in Denmark (63%), Bahrain (58.3%) and Ethiopia(75.4%), but sharply contrasts with the previous study in Jos by Obafunwa where 90% of cases had a primary extranodal presentation. Of the nodal sites involved in this study, the cervical lymph node was predominant, accounting for more than half of nodal lymphomas, while the inguinal, supraclavicular and epitrochlear lymph nodes all accounted for less than 5% each (Figure1). Cervical lymph nodes were equally the most common site of nodal lymphomas in previous studies in Kano (62%), India (44%) and Sudan (36%). [25,14,26] The predominance of cervical lymph nodes in all the aforementioned studies might reflect the fact that this group of lymph nodes provides ease of access as compared to axillary, mesenteric, epitrochlear and supraclavicular lymph nodes. [27] Axillary lymph nodes were the second commonest site of nodal lymphomas in this study accounting for 27% of cases. This is higher than observations in Kano (21.4%) and Sudan (16%). [25,14] Axillary lymph nodes were also the second most frequent site of nodal lymphomas in Kano, but the 3rd most frequent lymph node site in Sudan. [14,25] Inguinal nodes were the second commonest site of nodal lymphomas in India, whereas they were the fifth (5th) commonest in this study. [26]

Extranodal lymphomas are a less common topographic subtype of lymphomas. They accounted for 37.2% of all cases and 41.4% of all non Hodgkin lymphomas seen in this study. This is similar to findings in Turkey where 46% of all non Hodgkin lymphomas occurred outside lymph nodes, but varies from

observations in Ethiopia where 24.6% of non Hodgkin lymphomas were extranodal. [20,28]

No extra nodal case of Hodgkin lymphoma was identified in this study. This corroborates the finding that 98.7% of the extra nodal lymphomas in Ibadan were non Hodgkin. Similarly a study in Ile-Ife documented that all extranodal lymphomas were non Hodgkin. [29,30]

The commonest sites of extranodal lymphomas were the gastrointestinal tract (27.6%). This varies significantly from findings in Ibadan by Oluwasola with the G.I.T accounting for only 4.9%, while the jaw was the commonest site with 23.5%. [8] The findings in this study however are in consonance with studies in Ife and China which both observed that extranodal lymphomas occurred most frequently in the gastrointestinal tract. [29,17] The high frequency of lymphomas in the gastrointestinal tract is attributable to the abundance of Mucosa Associated Lymphoid Tissue, and the unrelenting antigenic stimuli from microbes.

Hodgkin lymphoma accounted for 8(10.3%) of all lymphomas in this study. This is similar to observations in Zaria and Malaysia where Hodgkin lymphoma made up 12% and 10.3% of all lymphoma cases respectively, but lesser than Omoti's observation in Benin of 17% as well as 22.16% obtained in Tanzania. [2,20,31,32] A male: female ratio of 1:0.6 was derived, contrasting findings in Benin, and the United States with male to female ratios of 3.3:1 and 1.27:1 respectively. [31,33] A mean age of 29.6±14.9 years was observed, which was greater than the mean age of 25.6±2 years obtained in Benin, and 26.42 years reported in Tanzania. [31,32] Nodular sclerosing was the most dominant histologic subtype in this study, accounting for 75% of cases, in correlation with findings in Germany and Malaysia. [20,34] Mixed cellularity made up 25% of Hodgkin lymphoma seen in this study, contrasting findings by Ochicha in Kano, and Adelusola in Ife, where mixed cellularity was predominant in both instances. [29,26] There were no cases of lymphocyte rich Hodgkin lymphoma in this study, similar to observations in South Africa. [35] No case of lymphocyte depleted and nodular lymphocyte predominant subtypes of Hodgkin lymphoma were seen in this study.

All cases of Hodgkin lymphoma in this study occurred in lymph nodes, with cervical lymph nodes accounting for 50% of all Hodgkin lymphomas in this series. The paucity of extranodal Hodgkin lymphomas is corroborated by observations in Ibadan that only 11.3% of cases seen over a fifteen year period occurred in extra nodal sites, whereas a study by Patkar in India observed that only 3 extranodal Hodgkin lymphoma cases were identified in a series of 397 cases. [8,36,37]

The Reed Sternberg cells were identified by positive staining by CD30 in 75% of Hodgkin lymphoma cases. This contrast findings in India and Germany, where CD30 immunoreactivity was 99.74% and 98.4% respectively, but approaches findings by Adelusola in which 62.5% of cases diagnosed were CD30 positive. [37-39] This disparity observed between the local and international studies could be due to much larger sample sizes in the studies in India and Germany.

Non Hodgkin lymphoma constituted 89.7% of cases seen in this study. This is much higher than 57.1% obtained in Kano, but lesser than 93% observed in a study in Gabon. [13,26] A predominance of non Hodgkin lymphomas was equally observed in Tanzania (77.84%), and Ethiopia (73.5%). [32,18]

Diffuse large B cell lymphoma was the commonest non Hodgkin lymphoma seen in this study, accounting for 38.6% of cases seen. This is lesser than the 41% observed in Turkey, but greater than Germany (30%) and Canada (28%). [28,40] For diffuse large B cell lymphomas, a male to female ratio of 0.8:1 was observed in this study which contrasts with what has been observed in Cote d'Ivoire and China with male to female ratios of 2:1 and 1.7:1

respectively. [41,42]

CD20 was expressed in 96% of cases of DLBCL, being absent in a single case. A similar picture was obtained in a study in Texas, United States, with 97% positivity for CD20. [43] In general, the small minority of DLBCLs that fail to express CD20 are reported to be plasmablastic, anaplastic lymphoma kinase positive and HIV associated variants, and have been reported to have worse outcomes. [43] CD 3 was expressed in 18.5% of the cases of DLBCL in this study, in contrast to observations by Nakamura in Japan in which none of the cases of DLBCL was positive for CD3. [44]

Technical factors arising from tissues handling as well as focal involvement by the neoplastic process could account for this "aberrant" expression of T cell antigens in B cell lymphomas. In addition, expression of T cell antigens in diffuse large B cell lymphomas could result from a Richter transformation of low/intermediate grade lymphomas. Although little is known about the significance of CD3 expression in large B cell lymphoma, it indicates that in addition to CD20 and CD3, lineage specific markers such as CD79a, PAX5, CD138, or molecular analysis may be necessary in detecting post therapy minimal residual disease. [45]

Burkitt lymphoma represented 21.4% of all non Hodgkin lymphomas in this study. This is lower than observations in Zaria and Ibadan, with Burkitt accounting for 51% and 29.9% respectively, but is higher than 14.6% obtained in Iraq. [8,11,22] Fifty percent (50%) of the cases occurred in children, similar to findings in Malaysia, with 53.8% of Burkitt occurring children. [20] Overall, abdominopelvic organs were involved in 63.6% of Burkitt, and this mirrors the observation in the previous study in Jos by Obafunwa that an abdominopelvic mass was the major form of presentation in 67.8% of Burkitt Lymphoma cases. [9] In this study, the ovary was the commonest organ affected in the abdomen accounting for 20% of all cases of Burkitt, similar to findings in Uganda with the ovary accounting for 21% of cases. [46] In contrast, the ovary was the third commonest site for Burkitt in Ibadan, accounting for only 7.9% of all cases. [8] In this study, only a solitary case of Burkitt was seen in the jaw, which also contrasts findings in Ibadan, in which the jaw was the commonest site for Burkitt, accounting for 37.1% of cases. [8] The relative lower frequency of Burkitt in this study as well as of endemic Burkitt could be due to the frequent practice of fine needle aspiration cytology (FNAC) in diagnosing head and neck masses in children. The use of FNAC for such lesions precludes the need for surgical biopsies for histology. Equally, a significant number of Burkitt lymphomas are diagnosed by haematologists using bone marrow aspirates. This apparent predominance of sporadic over endemic Burkitt in these studies was also seen in Ghana, where Burkitt lymphoma displayed a pattern of presentation as an abdominal rather than a jaw tumour. [47]

A positive expression of CD20 was seen in 73.3% of all the cases of Burkitt, lower than 99.2% and 97.6% seen in studies performed in Uganda and Italy respectively. [46,48] Expression of T cell antigens was seen in a solitary case, a picture similar to that obtained in Japan in which none of the cases of Burkitt expressed CD3. [44]

***Follicular lymphoma** (FL) made up only 7.1% of all non Hodgkin lymphomas in this study. It varies markedly from the National estimate of 13.3% for Nigeria, and 16% obtained in a study in Zaria, but approaches that of 6.2% in Korea. [11,49] CD20 expression was observed in 80% of cases in this study, less than a 100% expression rate observed in the United States. [50]

A **B cell immunophenotype** was predominant in this study, accounting for 54(77.1%) of all non Hodgkin lymphomas. This is slightly higher than observations made from studies carried out in Ibadan (75%) and India (72%) but is lesser than findings in Greece (88%). [51-53] Interestingly, in Argentina, a 10 year

retrospective study of lymphomas observed that all were of a B cell phenotype. [54] A male to female ratio of 0.7:1, amidst B cell lymphomas, was obtained in this study. This is at variance with a ratio of 1.57:1 obtained in Sudan. [14] The mean age for B cell lymphomas in this study was 36.9±18.9 years, which is lower than 54.4years observed in China. [17] The peak age for B cell lymphomas in this study was between 36 and 45 years, much earlier than the peak age of 47-67 years obtained in Sudan. [14]

T cell lymphomas accounted for 5.7% of all non Hodgkin lymphomas seen in this study. This is lower than 12% and 17.2% reported in Ibadan and Korea respectively, but higher than proportions of 3% and 5.2% obtained in Canada and France respectively. [41,49,55] A female predominance was observed amidst T cell lymphomas in this study, with a male to female ratio of 1:3. This contrasts with a male predominance observed in China, with a male to female ratio of 2.2:1. [17] The mean age for T cell lymphomas in this study was 41.0±18.3 years.

Five (5) of non Hodgkin lymphomas in this study were non reactive for both B and T cell lineage markers. This is similar to findings by Thomas JO, in which 13 of 100 cases were non reactive, and by Kaylan in India, in which 3 of 53 cases were non reactive for lineage specific markers. [51,52] Archival formalin fixed paraffin embedded blocks could be problematic during immunostaining. Notwithstanding, studies carried out by Thomas, Iliyasu and Adelusola have all demonstrated that routinely processed blocks from third world countries were suitable for immunostaining. [11,51,39] Attempts at phenotyping carried out in this region of the world utilized a limited number of lineage specific monoclonal antibodies. This is due to resource limitation. In Sudan, Hamid employed a panel consisting CD45, CD20, CD3, CD15 and CD30 to phenotype lymphomas, whereas Thomas concluded that a panel of three antibodies is adequate for routine immunocharacterisation of lymphomas in this environment. [51,14] However, the limited panel could account for the considerable number of uncharacterized lesions.

In conclusion, this analysis of 78 histologically diagnosed lymphomas has demonstrated the predominance of non Hodgkin lymphomas and of diffuse large B cell and Burkitt lymphomas amidst non Hodgkin lymphomas. Archival paraffin embedded blocks was shown to be suitable for immunostaining, with a vast majority of the lymphomas of B cell lineage.

In this era of personalized medicine, characterizing lymphomas, and malignancies in general should become routine, as techniques such as immunohistochemistry have witnessed proliferation of antigens, improved specificity, and automation.

REFERENCES

1. Sathiya M, Muthuchelian K. Significance of immunological markers in the diagnosis of lymphomas. Acad J Cancer Res 2009;2(1): 40-50
2. Omoti CE, Halim NKD. Adult Malignant Lymphomas in University of Benin Teaching Hospital, Benin City, Nigeria, Incidence and Survival. Nig J Clin Pract 2007;10(1):10-14
3. Mandong BM, Madaki AKJ, Mannaseh AN. Malignant Diseases in Jos: A follow up. Ann Afr Med. 2003; 2(2):49-53
4. Okpe ES, Abok II, Ocheke IE, Okolo SN. Pattern of Childhood Malignancies in Jos, North Central Nigeria. J Med Trop. 2011; 13:2: 109-114
5. Higgins RA, Blankenship JE, Kinney MC. Application of Immunohistochemistry in Diagnosis of Non-Hodgkin and Hodgkin Lymphoma. Arch Pathology Lab Med 2008; 132:441-461
6. Zubair A, Nagamul SA, Yasmen B, Rashida A, Naila K, Shahid P et al. Significance of Immunohistochemistry in accurate characterization of malignant tumours. J Ayub Med Coll Abbottabad 2006;18(2):38-43
7. Sempertegui C. Fluorescent in situ hybridization and its role in lymphoma

diagnosis. Available from; www.ohio.edu. Accessed May 5 2013.
8. Oluwasola AO, Olaniyi JA, Otegbayo JA, Ogun GO, Akingbola TS, Ukah CO et al. A Fifteen year review of lymphomas in a Nigerian Tertiary Healthcare Centre. J Health Popul Nutr 2011; (4): 310-316.
9. Obafunwa JO, Akinsete I. Malignant Lymphomas in Jos, Nigeria. Centr Afr J Med. 1992;38 (1):17-25
10. Anunobi CC, Banjo AA, Abdulkareem FB, Daramola AO, Akinde RO, Abudu EK. Adult Lymphomas in Nigeria; A fourteen year study. Nig Q J Hosp Med 2007; 17(2):63-6
11. Iliyasu Y, Zhao W, Ayesi LW. Malignant Lymphoma Subgroups from Zaria. Infect Agent Cancer. 2010; 5 (1); A54. doi:10.1186/1750-9378-5-S1-A54
12. Horesh N, Horowitz NA. Does Gender Matter in Non-Hodgkin Lymphoma? Differences in Epidemiology, Clinical Behaviour, and Therapy. Rambam Maimonides Med J 2014.5(4):2-6
13. Walter PR, Klotz F, Alfy Gattas T, Minko Mi Etoua D, Nguembi Mbina C. Malignant lymphomas in Gabon Equatorial Africa, a morphologic study of 72 cases. Human Pathology. 1991: 22(10): 1040-1043
14. Hamid KH, Mohamed BMY, Salih MMAF, Elduma AH. Immunophenotyping of Non-Hodgkin lymphomas in Sudan. Pan Afr Med J 2014;18:82. doi:10.11604/pamj.2014.18.82.3732
15. Shome DK, George MS, Al-Hilli F, Satir AA. Spectrum of malignant lymphomas in Bahrain. Saudi Med J. 2004; 25(2):164-167
16. National Cancer Institute. SEER Stat Fact Sheets: Lymphoma; available from; www.cancer.gov. Accessed October 17 2013.
17. Sun J, Yang Q, Lu Z, He M, Gao L, Zhu M et al. Distribution of Lymphoid Neoplasms in China: Analysis of 4,638 Cases According to the World Health Organization Classification. Am J of Clin Path 2012; 138:429-434
18. Bekele A, Ergete W. The Histologic Pattern of Non Hodgkin Lymphoma in Ethiopians. Ethiop. J Health Dev 2000; 14(3):345-351.
19. Orem J, Mbide EK, Lambert B, Silvia DS, Weiderpass E. Burkitt Lymphoma in Africa; a review of the epidemiology and aetiology; Afr Health Sci 2007; 7(3):166-175
20. Chai SP, Peh SC, Kim LH, Lim MY, Gudum HR. The Pattern of lymphomas in East Malaysian patients as experienced in the University Hospital, Kuala Lumpur. Malaysian J Pathol 1999;21(1):45-50
21. AlAllawi NA, Hughson MD, Sulayvani FK, Yaqo RT. Malignant lymphoma in northern Iraq: A retrospective analysis of 270 cases according to the World Health Organization classification Indian J Cancer 2011; 48(4): 446-451
22. Bilic E, Femeni R, Konja J, Simat M, Dubravcic K, Batinic D et al. CD20+ Childhood B-NHL: Morphology, Immunophenotype, and Treatment. Coll Antropol 2010 (34)1:171–175
23. Maxwell PD, Hélène GG, Martine R, Antoine M, Edward KM, Henry W et al. Non-Hodgkin lymphoma in Uganda: a case–control study. AIDS 2000;14(18):2929-2936.
24. Shehu UA, Adegoke SA, Abdulsalam U, Ibrahim M, Oyelami OA, Adeodu OO. Pattern of childhood malignant tumours in two tertiary teaching hospitals in Nigeria: comparative study. Niger J Paed 2013; 40 (2): 175 – 178.
25. Ochicha O, Edino ST, Mohammed AZ, Umar AB, Atanda AT. Pathology of peripheral Lymph node biopsies in Kano, Northern Nigeria. Ann Afr Med 2007;6 (3):104-108
26. Mumtaz T, Roohi N, Akhtar MW. Incidence and Clinical Manifestation of Lymphoma in Central Punjab. Pakistan J Zool 2012; Vol. 44(5): 1367-1372.
27. Olu-eddo AN, Omoti CE. Diagnostic evaluation of primary cervical adenopathies in a developing country. Pan Afr Med J. 2011; 10:52
28. Isikogodan A, Ayyildiz O, Buyukcelik A, Arslan A, Tiftick N, Buyukbayram H, et al. Non-Hodgkin lymphoma in southeast Turkey . Annals of Hematology. 2004; 83(5):265-269.
29. Adelusola KA, Adeniji KA, Somotun GO; Lymphoma in Adult Nigerians; West Afr J Med 2011; 20(2):123-6

30. Thomas JO, Ogunsanwo BO, Ogunbiyi AO. Highlights of extranodal Lymphomas in Ibadan; Centr Afr J Med 1999;45(7):173-176
31. Olu-Eddo AN, Omoti CE. Clinico-pathologic features of Hodgkin lymphoma in Benin City, Nigeria and update on its biology and classification. Nig J Clin Pract 2011; 14 (4): 440-444
32. Mani H, Jaffe ES. Hodgkin Lymphoma: An Update On Its Biology With Newer Insights Into Classification. Clin Lymphoma Myeloma 2009; 9(3):206-216
33. Pareen S, Alison M, Neha M, Flowers CR. Incidence Patterns and Outcomes For Hodgkin Lymphoma Patients in The United States. Advances in Hematology; 2011, Article ID 725219. doi: http://dx.doi.org/10.1371%2Fjournal.pone.0021152
34. Vornhage AS, Haverkamp H, Enget A, BalleisenL, Majunke P, Heil G et al. Lymphocyte Rich Classical Hodgkin lymphoma: Clinical Presentation and Treatment Outcome in 100 patients Treated within German Hodgkin study group trials. J Clin Oncol. 2005; 23(24):5739-5745
35. Engel M, Essop MF, Close P, Hartley P, Pallesen G, Sinclair-Smith C. Improved prognosis of Epstein-Barr virus associated childhood Hodgkin lymphoma: study of 47 South African cases. J Clin Pathol 2000;53:182–186
36. Okpala IE, Akang EE, Okpala UJ. Lymphomas in University College hospital, Ibadan, Nigeria; Cancer 1991; 68:1356-62
37. Patkar N, Mehta J, Kulkarni B, Pande R, Advani S, Borges A. Immunoprofile of Hodgkin Lymphoma In India. Indian J Cancer 2008; 45(2):59-63
38. Von Wasielewski R, Mengel M, Fischer R. Classical Hodgkin disease: clinical impact of the immunophenotype. Am J Pathol. 1997;151(4):1123-1130.
39. Adelusola KA, Titiloye NA, Rotimi O, Durosinmi M. Epstein Barr Virus latent membrane Protein1 in Hodgkin Lymphoma in Nigerians. Afr J Health Sci 2009; 9(3):174-178
40. Flowers CR, Pareen JS, Borate U, Bumpers K, Douglas-Holland T, King N et al. Examining Racial Differences in Diffuse Large B-Cell Lymphoma Presentation and Survival. Leuk Lymphoma. 2013; 54(2): 268–276.
41. Aïssata TD, Boidy K, N'dhatz E, Clotaire DN, N'Dogomo M, Ayémou R et al. Characteristics and Results of the Management of Diffuse Large B-Cell Lymphomas: The Experience of Côte d'Ivoire. Advances in Haematology 2012; Article ID 945138. http://dx.doi.org/10.1155/2012/945138
42. Chen Y, Han T,Iqbal J, Irons R, Wing CC, Zhu X. Diffuse Large B Cell Lymphoma in Chinese patients; Am J Clinical Pathol 2010; 133: 305-313
43. Gaur S, Padilla O, Nahleh Z. Clinical Features and Prognosis of CD20 Negative Aggressive B-Cell Non-Hodgkin Lymphoma. Lymphoma Volume 2013, Article ID 290585, 1-5; http://dx.doi.org/10.1155/2013/290585
44. Nakamura N, Nakamine H, Tamaru J, Nakamura S, Yoshino T, Ohshima K et al. The Distinction between Burkitt lymphoma and Diffuse large B cell lymphoma with c-myc rearrangement. Mod Pathol 2002;15(7):771-776
45. Wang J, Chen C, Lau S, Raghavan RI, Rowsell EH, Said J et al.CD3-positive Large B-cell Lymphoma. Am J Surg Pathol 2009;33:505–512
46. Lukande R, Wabinga HR, Tumwine LK. Burkitt lymphoma in Uganda: the role of immunohistochemistry in diagnosis. East Afr Med J 2008; 85(5): 207-212
47. Biggar RJ, Gardiner C, Lennette ET, Collins WE, Nkrumah FK, Henle W. Malaria, sex, and place of residence as factors in antibody response to Epstein-Barr virus in Ghana, West Africa. Lancet. 1981; 2:115–118.
48. Carbone A, Gloghini A, Gaidano G, Cilia AM, Bassi B, Pollito P et al. AIDS related Burkitt lymphoma. Amer J Clin Pathol 1995;103(5):561-567.
49. Anderson JR, Armitage JO, Weisenburger DD. Epidemiology of the non-Hodgkin lymphomas: Distributions of the major subtypes differ by geographic locations. Ann Oncol 1998.9: 717-720.
50. Contos MJ, Kornstein MJ, Innes DJ, Ben-Ezra J. The utility of CD20 and

CD43 in sub classification of low grade B cell lymphoma on paraffin sections. Mod Pathol 1992;5 (6):6313.

51. Thomas JO, Rafindadi A, Heyyet A, Jones M, Gatter KC, Manson DY. Immunophenotyping of Nigerian cases of non-Hodgkin lymphomas on paraffin sections; Histopathology 1991; 18(6) :505-10.
52. Kaylan K, Basu D, Soundaraghavan J. Immunohistochemical typing of NHL comparing working formulation and WHO classification. Indian J Pathol and Microbiol.2006; 49(2):2003-7.
53. Economopoulos T, Papageorgiou S. Non-Hodgkin's Lymphoma in Greece according to the WHO classification of lymphoid neoplasm. Acta Hematology 2005; 113(2):97-103.
54. Keszler A, Piloni MJ, Paparella ML, Soler Mde D, Ron PC, Narbaitz M. Extranodal oral non-Hodgkin lymphomas: A retrospective study of 40 cases in Argentina. Acta Odentol Latinoam. 2008; 21(1):43-8.
55. Liang R. State of Art on T-cell Lymphomas: The Epidemiology. Hematologic Reports 2006; 2(13):1-3

How to cite this article: Ajetunmobi OI, Mandong BM, Adelusola KA et al. Immunohistochemical profiling of lymphomas in Jos university teaching hospital, Jos. Int J Health Sci Res. 2018; 8(2):7-18.

****