# Lymphoma at King Hussein Medical Center: A Histopathologic Review

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## ABSTRACT

**Objective:** To determine the spectrum of various types of malignant lymphoma in children and adults at King Hussein Medical Center according to the World Health Organization classification 2001.

**Methods:** A retrospective review of the histopathological subtypes of all primary lymphoma cases was conducted at Princess Iman Research and Laboratory Sciences Center at King Hussein Medical Center during the period between January 2004 and December 2008. A total of 485 patients were studied regarding: age, gender, and Lymphoma type using the World Health Organization classification of lymphoid neoplasms. Descriptive analysis using frequencies was used to describe the study variables.

**Results:** Two hundred seventy-four (56.5%) cases were males and 211 (43.5%) were females. Their ages ranged between two and ninety years. A total of 61 (12.6%) patients were children and 424 (87.4%) patients were > 14 years old. Of 485 patients included in the study, 342 patients (70.5%) had non-Hodgkin's lymphoma and 143(29.5%) had Hodgkin's lymphoma. Two hundred twenty nine (47.2%) of affected patients aged 50 years and above, non-Hodgkin's Lymphoma accounted for 206 patients (90%) of them. Of all pediatric lymphoma cases, Hodgkin's lymphoma accounted for 41 % (25 cases) and Non-Hodgkin's Lymphoma 59% (36 cases). Burkitt's lymphoma was the predominant lymphoma in children. In the adult NHL group, diffuse large B-cell lymphoma was the most common followed by follicular lymphoma .In the HL group, the nodular sclerosis variant was the most frequent (63.6%, 91 patient) followed by the mixed cellularity type (20.3%, 29 patient).

**Conclusion:** Distribution and patterns of lymphoma differs between children and adults. Diffuse large B-cell lymphoma is the most commonly encountered lymphoma in adults. Burkitt's lymphoma and Hodgkin's lymphoma are the predominant childhood lymphomas.

**Key words:** Lymphoma, Hodgkin's, Histopathology.

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## Introduction

Neoplasms originating in lymphoid tissue comprise a diverse yet closely related group of neoplasms, including Non-Hodgkin lymphoma (NHL), Hodgkin's lymphoma, multiple myeloma, and acute and chronic lymphocytic leukemia.[1] In the United States, Lymphoma accounts for 5% of new cancer cases and 3.6% of cancer deaths annually.[2] Jordan Cancer Registry data between January 2004 and December 2008 showed that lymphoma is one of the ten most

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common cancers affecting Jordanian population in both adults and pediatric subgroups. Hodgkin's lymphoma (HL) was first described by Thomas Hodgkin's in 1832. For more than a century, this disease was regarded as a chronic inflammatory disorder, which is reflected by the old term lymphogranulomatosis. However, because aneuploidy and monoclonality were detected in the cells, Hodgkin's disease, or in terms of the World Health Organization (WHO) classification of malignant lymphomas, HL, today is considered a malignant tumor.[3] Hodgkin's lymphoma (HL) is characterized by progressive enlargement of the lymph nodes. It is considered unicentric in origin and has a predictable pattern of spread by extension to contiguous nodes.[4] The new WHO classification distinguishes only two groups-the nodular lymphocyte-predominant HL and the classical HL. The latter is subdivided in four forms (Lymphocyte-rich HL, Nodular-sclerosis HL, Mixed-cellularity HL and Lymphocytic-depletion HL.[3,4,5] In most developed countries, the incidence of Non-Hodgkin's lymphoma (NHL) is increasing steadily at an annual rate of approximately 4%, indicating a doubling of incidence every 20 years.[6,7] The United States has one of the highest rates of NHL incidence in the world. NHL is the second-fastest growing cancer in terms of mortality rates [2] Non-Hodgkin's lymphoma (NHL) is defined as Neoplasia of the lymphoid system and its precursor cells with genetically disturbed regulation of proliferation, differentiation and apoptosis.[8] Childhood NHL represents a heterogeneous group of disorders that are different from adult NHL in that they are commonly disseminated; diffuse not nodular; high grade; of mature and immature T- or B-cell lineage; and have frequent extranodal disease, marrow and central nervous system (CNS) involvement.[9] In 1994, the International Lymphoma Study Group developed the Revised European-American Lymphoma (REAL) classification, which classified lymphomas based on the cell of origin (B, T, or NK) and included morphology, immunophenotype, genetic, and clinical features to define diseases. In 1997, the International Lymphoma Classification Project performed a clinical evaluation of the REAL classification in a cohort of 1403 cases of NHL.

In 2001, the WHO updated the classification of hematopoietic and lymphoid neoplasms to apply the principles of the REAL classification, representing the first international consensus on classification of hematologic malignancies. In 2008, the International T-Cell Lymphoma Project evaluated the WHO classification of T-cell lymphoma.[10] This study was conducted to study and analyze lymphoma cases in children and adults at King Hussein Medical Center over five years.

## Methods

A retrospective review of the histopathological subtypes of all primary lymphoma cases was conducted at Princess Iman Research and Laboratory Sciences Center at King Hussein Medical Center during the period between January 2004 and December 2008. The inclusion criteria was, all newly diagnosed patients of lymphoma with appropriate clinical information regarding age, gender. A total of 485 patients were studied regarding: age, gender, and lymphoma type .The cases were subtyped according to the 2001 WHO classification of lymphoid neoplasms, although a new 2008 WHO classification of lymphomas was introduced and still running on. The histopathologic examination was based on the hematoxylin and eosin staining (H & E) and immunohistochemistry using a panel of antibodies. The age was categorized into two groups (≤14 years as children group and >14 years as adult group). The adult age group was further stratified into two age intervals (15-49 years and >50 years). Descriptive analysis using frequencies was used to describe the study variables.

## Results

Two hundred seventy-four (56.5%) cases were males and 211 (43.5%) were females. Their ages ranged between two and ninety years. A total of 61 (12.6%) patients were children (age ≤ 14 years) and 424 (87.4%) patients were > 14 years old. Table I shows, the age and gender distribution of Hodgkin's and Non-Hodgkin's lymphoma among the study group.

Of the 485 patients with lymphoma, there were 342 cases (70.5%) of non-Hodgkin's Lymphoma

**Table I:** Age and sex distribution of HL and NHL

| Variables | Number of lymphoma cases | Number of HL cases (%) | Number of NHL cases (%) |
|---|---|---|---|
| Age group | | | |
| ≤ 14 years | 61(12.6) | 25 (41) | 36(59) |
| >14 years | 424(87.4) | 118(27.8) | 306(72.2) |
| 15-49years | 195(40.2) | 95(48.7) | 100(51.3) |
| >50 years | 229(47.2) | 23(10) | 206(90) |
| Gender | | | |
| Males | 274 (56.5) | 76(27.7) | 198(72.3) |
| Females | 211(43.5) | 67(31.8) | 144(68.2) |
| Total | 485 | 143(29.5) | 342 (70.5) |

**Table II:** Age distribution of HL according to WHO classification

| Age group | Number of HL cases | nodular lymphocyte predominant n (%) | Lymphocyte-rich n (%) | Nodular-sclerosis n (%) | Mixed-cellularity n (%) | Lymphocytic-depletion n (%) | Non-otherwise specified |
|---|---|---|---|---|---|---|---|
| ≤ 14 years | 25 | 0 | 4(16) | 14(56) | 7(28) | 0 | 0 |
| 15-49years | 95 | 5(5.3) | 5(5.3) | 66(69.5) | 14(14.7) | 2(2.1) | 3(3.2) |
| >50 years | 23 | 2(8.7) | 1(4.3) | 11(47.8) | 8(34.8) | 1(4.3) | 0 |
| Total | 143 | 7(4.9) | 10(7.0) | 91(63.6) | 29(20.3) | 3(2.1) | 3(2.1) |

and 143 cases (29.5%) of Hodgkin's Lymphoma. Two hundred twenty-nine (47.2%) of all lymphoma cases aged 50 years and above. Non-Hodgkin's Lymphoma accounted 206 patients (90%) of them. Table II presents the age distribution of HL according to WHO classification among the study group. In all age groups, the Nodular-sclerosis classical subtype was the most frequent in Hodgkin's lymphoma cases (63.6%), followed by the mixed cellularity classical Hodgkin's Lymphoma type (20.3%). Of the 143 patients with Hodgkin's lymphoma, 95 cases (66.4%) aged 15-49 years. Table III illustrates the age distribution of NHL according to WHO classification among the study group. In pediatric age group Burkitt's lymphoma was the predominant type of NHL constituting 55.6%, followed by diffuse large B-cell lymphoma (22.2%). In the adult NHL group, diffuse large B-cell lymphoma was the most common, comprising 64% and 58.3% in both age groups 15-49 years and >50 years respectively followed by follicular lymphoma.

## Discussion

During the past decade, there have been many advances in our understanding of lymphoma, especially after the WHO updated classification of hematopoietic and lymphoid neoplasma. Our study showed that NHL was predominant in Jordanian lymphoma cases representing 70.5% compared with HL (29.5%). These results are closely comparable to several studies conducted in the Middle East region, where the incidence of HL was 33% in Bahrain, 27% in Saudi Arabia, 35% in Oman, but much lower than United Arab Emirates patients where the incidence of HL was 41%.[11-14] In comparison with other studies from the Far East and Western countries, our study results were intermediate. Notably, the Far East incidence of HL ranges between 5%-10%.[15] A Jordanian study over a 3 year period between January 2001 and December 2003 reported that HL incidence was 21.6%. In our study, the most common type of NHL was diffuse larger B-cell lymphoma (DLBCL) comprising 85.8%, followed by follicular lymphoma (FL) (10.8%), B-small lymphocytic lymphoma (B-SLL) (8.5%) and peripheral T-cell lymphoma (5.2%) as shown in Table III. DLBCL was reported to be the commonest subtype of adult NHL in several studies. Xiao *et al*. reported in 2005 in China that Overall, six subtypes including diffuse larger B-cell lymphoma (DLBCL) follicular lymphoma (FL), unspecified peripheral T-cell lymphoma (PT-un), precursor T-lymphoblastic lymphoma

**Table III:** Age distribution of NHL according to WHO classification

| NHL type | ≤ 14 years n (%) | 15-49 years n (%) | >50 years n (%) |
|---|---|---|---|
| B-cell lymphoma | | | |
| Precursor lymphoblastic | 0 | 1 (1) | 1(0.5) |
| Small lymphocytic | 0 | 2(2) | 24(11.6) |
| Lymphoblasmacytic | 0 | | 2(1) |
| Splenic marginal zone | 0 | 1(1) | 2(1) |
| Extranodal marginal (Malt type) | 0 | 1(1) | 3(1.5) |
| Follicular | 0 | 10(10) | 23(11.2) |
| Mantle cell | 0 | 1(1) | 6(2.9) |
| Diffuse large B-cell | 8(22.2) | 64(64) | 120(58.3) |
| Burkitt's | 20(55.6) | 3(3) | 3(1.5) |
| T- cell lymphoma | | | |
| Precursor lymphoblastic | 6(16.7) | 3(1) | 2(1) |
| Peripheral T-cell | 0 | 10(10) | 6(2.9) |
| Extranodal NK/T-cell, nasal type | 0 | 1(1) | 3(1.5) |
| Angioimmunoblastic | 0 | 1(1) | 1(0.5) |
| Anaplastic large cell | 0 | 2(2) | 6(2.9) |
| Not otherwise specified | 2(5.5) | | 4(1.9) |
| Total | 36 | 100 | 206 |

(T-LBL), extranodal marginal zone B-cell lymphoma of MALT type (MALT) and B-small lymphocytic lymphoma (B-SLL) were among the most common subtypes.[17] Zelenetz *et al.* reported that the International Lymphoma Classification Project performed a clinical evaluation of the REAL classification in a cohort of 1403 cases of NHL confirming the diagnosis of NHL in 1378 (98.2%). This study identified the 13 most common histologic types, constituting approximately 90% of the cases of NHL in the United States. The findings were as follows: DLBCL, 31%; follicular lymphoma (FL), 22%; small lymphocytic lymphoma/chronic lymphocytic leukemia (SLL/CLL), 6%; mantle cell lymphoma (MCL), 6%; peripheral T-cell lymphoma (PTCL), 6%; and mucosa-associated lymphoid tissue (MALT) lymphoma, 5%. The remaining subtypes each occurred in fewer than 2% of cases. Importantly, in the United States more than 50% of lymphoma cases are either DLBCL or FL.[10] These results are comparable to our study regarding the commonest three subtypes. Kuwaiti experience of non-Hodgkin's lymphoma subtypes revealed that the three most common subtypes in Kuwaiti Arabs were diffuse large B-cell lymphoma (46.5%), follicular lymphoma (15.5%), and mycosis fungoides (9.3%). In non-Kuwaiti Arabs, the most common subtypes were diffuse large B-cell lymphoma (48%), B-cell small lymphocytic lymphoma / chronic lymphocytic leukemia (15.8%), and follicular lymphoma (12.7%) (18), these results are also comparable to our results.

Regarding the pediatric age group, our study showed that NHL is more frequent than HL; considering the various subtypes of NHL and their frequencies we conclude that, HL is the most common lymphoma in Jordanian children followed by Burkitt's lymphoma. This result was comparable to the earlier Jordanian study.[16] Our study described the pattern of NHL in pediatric age group. In which, Burkitt's lymphoma was the predominant 20 cases (55.6%), followed by DLBCL 8 cases (22.2%) and Precursor T-lymphoblastic lymphoma 6 cases (16.7%). The Jordanian study done by Haddadin, between Jan 2001 and Dec 2003 identified the three most common types of pediatric lymphoma. The findings were Burkitt's lymphoma and HL followed closely by lymphoblastic lymphoma.[16] Comparing our results with the earlier Jordanian experience, we found that Burkitt's lymphoma is still the most common pediatric NHL, while DLBCL ranked second and lymphoblastic lymphoma became third among all newly diagnosed NHL in children during the study period between Jan 2004 and Dec 2008.

Regarding HL in our study, the Nodular-sclerosis classical subtype was the most frequent; 91 cases (63.6%) followed by the mixed cellularity classical Hodgkin's Lymphoma

subtype 29 cases (20.3%). This was true in the three age groups as seen in Table II. This is similar to several studies done in Middle East region where Nodular-sclerosis type is the commonest.[12,14] On contrary, in Oman, Bamanikar S *et al.* reported that Among the HD, mixed cellularity (MC) appeared in nine cases (56%).[13] A recent study done in Pakistan by Mushtaq *et al*. in 2008 agreed that Mixed cellularity and nodular sclerosis were the main histological variants of Hodgkin's disease.[19] A comparison of histological appearances of Hodgkin's disease in Pakistani and Saudi patients in 2008 showed that Mixed cellularity HD (MCHD) was the commonest subtype among Pakistani patients whereas Nodular Sclerotic HD (NSHD) was more common among Saudis.[20] The earlier Jordanian experience about HL between Jan 2001 and Dec 2003 revealed that also that Nodular-sclerosis type is the commonest.[16] This indicates that the relative incidence of HL subtypes in Jordan is not changing since 2001. Although Hodgkin's lymphoma in North Jordan has a different pattern that half of these cases belong to the mixed cellularity (MC) type and 46% belong to the nodular sclerosis (NS) type.[21] Our study showed that the age distribution of HL peaks in the age group (15-49 years) as shown in Table II. On contrary, Punnett *et al*. reported that HL is rare among children <5 years of age and relatively rare in the adult population, but is the most commonly diagnosed cancer among adolescents aged 15 to 19. In developed countries, there is a bimodal age distribution for HL with a peak in the adolescent/young adult population and again after age >55 years.[22]

## Conclusion

Childhood and adulthood lymphoma differ significantly in distribution. While, diffuse large B-cell lymphoma is the most commonly encountered lymphoma in Jordanian adults, Hodgkin's lymphoma and Burkitt's lymphoma are the predominant childhood lymphomas. The relative incidence of DLBCL is increasing and exceeding T-lymphoblastic lymphoma in Jordanian children.

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