

Hodgkin's lymphoma in North Jordan

Does it have a different pattern?

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ABSTRACT

Objective: To study the pattern of Hodgkin's lymphoma (HL) in North Jordan, identify the epidemiological features of this disease, and to see if these patterns are unique or follow the patterns seen in developed or developing countries.

Methods: All of the cases of HL diagnosed at the Department of Pathology, Jordan University of Science and Technology, Irbid, Jordan between January 1996 and September 2002 were retrieved and reviewed histologically. Seventy-five confirmed HL cases were classified according to the WHO classification of hematological malignancies. Data on the age and gender of the patients were correlated with those of the histopathologic types of the disease.

Results: Patients range in age from 3-72 years with a median of 20 years. The young adult population (15-34 years) was the largest group in this study accounting for 45.9% of all cases followed by the childhood group (0-14 years), which accounted for 25.6% of the cases. The age

distribution displayed only one peak between 11 and 20 years. Classic HL accounted for 91% of the cases, half of these cases belong to the mixed cellularity (MC) type and 46% belong to the nodular sclerosis (NS) type. The overall male to female ratio was 1.7:1; but the ratio was the highest (3.75:1) among children, and reversed among patients with NS type in the young adult group (0.78:1).

Conclusion: The MC and NS types of HL accounted for the vast majority of HL in North Jordan. Similar to other developing countries the MC type of HL was the most common type followed by the NS type. The age distribution displayed a unimodal pattern with a peak between 11 and 20 years of age, which is a decade earlier than the first peak seen in the West. This pattern is also different from developing countries, where HL peaks in children less than 10 years of age. Hodgkin's lymphoma in Jordan appears to have an intermediate pattern between developing countries and the West.

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Hodgkin's lymphoma (HL) is a peculiar neoplasm with unique epidemiological features. Early studies have found that HL is associated with the socio-economic level of the patients, and factors such as early birth order, small family size and high maternal education are all associated with increased risk of developing HL especially among young adults.¹⁻³ These associations have led to the suggestion that HL may be related to an infectious agent. This probably is not a surprising assumption,

after all HL was believed to represent an infectious disease by Thomas Hodgkin himself and even by Dr. Reed and Dr. Sternberg who eloquently described the morphology of the neoplastic cells in this disease.⁴ From an epidemiological point of view, HL is composed of 3 distinct diseases: a childhood form (0-14 years), a young adult form (15-34 years), and an older adult form (≥ 55 years).^{5,6} The young adult form is more common in the West and is responsible for the bimodal age distribution

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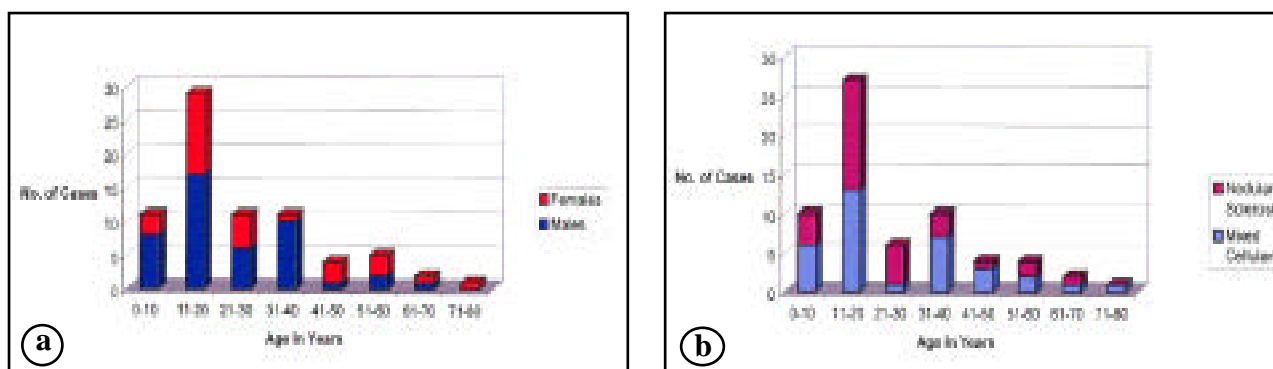


Figure 1 - Age distribution of Hodgkin's lymphoma in North Jordan. a) Distribution according to gender. b) Distribution of the 2 most common histopathologic types: mixed cellularity and nodular sclerosis types.

with a first peak seen between 20 and 35 years of age and a second peak, affecting patients beyond the age of 55 years. In developing countries, the young adult peak is not seen, and instead a higher incidence of HL is seen among children <15 years of age.^{7,8} Another major difference between developed and developing countries is the distribution of the histological subtypes of HL. In the West, the nodular sclerosis subtype of HL predominates, whereas in developing countries there is predominance of the mixed cellularity (MC) subtype.⁷ In this study, we will try to examine the pathological features of HL in Jordan, and see if the patterns of this disease and its subtypes follow those of the West or those of developing countries.

Methods. All cases of Hodgkin lymphoma diagnosed between January 1996 and September 2002, at the Department of Pathology at the Jordan University of Science and Technology (JUST), were retrieved. The Department of Pathology at JUST is located in Irbid and is the provider of surgical pathology services to all Ministry of Health hospitals as well as private hospitals in the entire North of Jordan.

Paraffin blocks were retrieved, and 4-micron thick paraffin sections were stained with Hematoxylin and Eosin. All the slides were re-examined by the author at the Department of Pathology in the year 2002. The diagnoses were confirmed or re-classified using morphologic and immunophenotypic findings, according to the World Health Organization (WHO) classification.⁹ The total number of HL cases included in this study was 75 cases.

Immunostains were performed on the cases to confirm the diagnosis. Leukocyte markers used included antibodies against the leukocyte common antigen (CD45), the T-cell antigens CD3, CD43 and CD45RO (UCHL1), the B-cell antigen CD20 (L26),

in addition to the Hodgkin's markers CD15 (Leu-M1) and CD30 (BerH2). Autoclaving was used for antigen recovery. All antibodies were obtained from DAKO (Glostrup, Denmark).

Results. The total number of patients included in this study was 75. The mean age of all the patients was 25.3 (SD 17.2); the median age was 20 years with a wide age distribution ranging from 3-72 years. There was a male predominance with a male to female ratio of 1.68. The median age of presentation for males and females was similar. The mean age for female patients was higher than that of males; however this difference was not statistically significant ($p=0.28$). **Figure 1a and 1b** illustrates the age distribution of all patients; the age group 11-20 years dominated all other groups.

The young adult population (15-34 years) was the largest group in this study accounting for 45.9% of all cases followed by the childhood group (0-14 years), which accounted for 25.6% of the cases (**Table 1**). The adult group (35-54 years) and the elderly group (≥ 55 years) accounted for 17.6% and 10.8% of all cases.

Table 2 shows a summary of the histopathological features of all cases in this study. Classic HL was the predominant form seen in this series comprising 91% of all cases. Nodular lymphocyte predominant type accounted for 9% of the cases. Among classic HL cases, the MC type was the most common type accounting for 50% of all the classic HL cases. Nodular sclerosis type was the second most common form accounting for 46% of cases. Lymphocyte depleted type and unclassified cases accounted for 2.9% and 1.5% of classic HL cases respectively. The mean age for patients with MC type was 27.1 years, which is slightly higher than the 23.4 years mean age for the nodular sclerosis type; this difference was not statistically significant ($p=0.7$). The male to female ratio among the MC

Table 1 - Major age groups distribution of 75 cases of Hodgkin's lymphoma from North Jordan.

Age groups (years)	Patients n (%)	Male to female ratio	Mixed cellularity	Nodular sclerosis	Lymphocyte depleted	Unclassified	Nodular lymphocyte predominant
0-14	19 (25.6)	15 : 4	10	7	0	1	1
15-34	34 (45.9)	18 : 16	12	16	2	0	4
35-54	13 (17.6)	10 : 3	8	4	0	0	1
≥55	8 (10.8)	3 : 5	4	3	0	0	1
Unknown	1 (1.3)	1 : 0	0	1	0	0	0
Total	75 (100)	47 : 28	34	31	2	1	7

Table 2 - Distribution of the histologic types of 75 Hodgkin's lymphoma cases from North Jordan.

Histologic type	Cases	Mean age (years)	Median age (years)	Range (years)	Male to female ratio
Mixed cellularity	34	27.09	19.5	3-72	23 : 11
Nodular sclerosis	31	23.43	18.5	4-62	18 : 13
Lymphocyte depleted	2				2 : 0
Unclassified	1				0 : 1
Nodular lymphocyte predominant	7	28.14	22	12-58	4 : 3
Total	75	25.28	20	3-72	47 : 28

type was 2:1. Males also predominated by females in the other subtypes of HL, but the ratios were much lower, 1.38 in the nodular sclerosis type and 1.33 among the nodular lymphocyte predominant type. Among children <15 years of age, there was a striking male predominance with a male to female ratio of 3.75. On the other hand, the male to female ratio dropped significantly among the young adult group to reach 1.13. The young adult group has peculiar features in that the nodular sclerosis type was the most common form of HL seen in this group. Sixteen nodular sclerosis cases were seen, and only 12 MC cases were seen in this group. When limiting the analysis to the nodular sclerosis type in the young adult group, we found that females became more common than males. The male to female ratio in this subset is 0.78:1. On the other hand, the male to female ratio in the remaining histologic types in the young adult group was 3:1.

Discussion. Malignant lymphomas (ML) are among the most common tumors affecting Jordanians; they rank as the third most common malignancy among males and the second most common malignancy among females.¹⁰ According to the 1997 report by the Jordan Cancer Registry, ML represents 10.2% of all cancers in Jordan,¹⁰ this is considerably higher than their proportion in the United States of America (USA), which is approximately 4%.¹¹

The annual incidence rate for ML as reported by the Jordan Cancer Registry in 1997 was 13.0/100000, with a rate of 4.4/100000 for HL and 8.6/100000 for non-Hodgkin's lymphoma.¹⁰ We believe that these rates may be slightly underestimated due to non- and misdiagnosis, and under-reporting of ML cases. The incidence of ML in Jordan seems to be lower than that of the USA, which is 19.3/100000 for NHL and 2.8/100000 for HL.¹²

Hodgkin's lymphoma (HL) comprises a substantial fraction of lymphomas accounting for 34-44% of all ML in Jordan.^{10,13} This figure appears to be in line with those reports from the Middle East. Hodgkin's lymphoma accounts for 35% of all ML in Oman,¹⁴ 32% in Kuwait,¹⁵ 33% in Bahrain,¹⁶ 41% in United Arab Emirates (UAE),¹⁷ 31% in Sudan,¹⁸ and Kingdom of Saudi Arabia (KSA).¹⁹ Such figures are higher than the 12% fraction seen in the USA.¹² It is also higher than the rates seen in East Asia where it is known that the incidence of HL is very low.^{20,21} Therefore, it would be reasonable to conclude that the Middle East represents one of the geographic areas with high incidence of HL. Classical HL subtypes comprised the vast majority of HL cases in this study. The MC type is the most common histologic type of HL in this group of Jordanian patients, followed by the nodular sclerosis (NS) type, which is similar to findings from other developing countries,²²⁻²⁵ and to countries in our region, including Oman,¹⁴ KSA,²⁶ Kuwait,²⁷ Bahrain,¹⁶ Iraq,²⁸ Egypt,²⁹ Greece,³⁰ Turkey,³¹ and Iran.³² This pattern is opposite to what is seen in Western countries, where the NS type of HL is the most common type, followed by MC.^{7,33} The lymphocyte depleted (LD) type of classical HL comprised 3% of HL cases, which is consistent with the rates reported in the developing countries,³³ and it is comparable to neighboring countries. Nodular lymphocyte predominant HL, which is now considered as a distinct entity of HL according to the recent classification systems of lymphoma,^{9,34} accounted for 9% of all HL cases. This figure is slightly higher than the 2-5% figures reported in the West,³³ and falls in the upper range of figures from neighboring countries, which range from 4-8.3%.^{16,19,27,32} No cases of lymphocyte-rich classic HL were diagnosed in this series. This entity is currently separated from the nodular lymphocyte predominant HL for clinical purposes and separated from the other types of classic HL for research purposes.³⁴

On epidemiological grounds, Correa and O'Connor⁷ described 4 patterns of HL: 1) developing countries pattern characterized by high incidence in male children and a low incidence in the third decade; 2) developed countries pattern characterized by predominance of NS, and high incidence in young adults and low incidence in children; 3) intermediate pattern seen in rural areas of developed countries with features intermediate between patterns 1 and 2; and 4) oriental pattern with low incidence in all age groups.^{7,33} Age distribution of HL in Jordan showed that the young age group (15-34 years) was the largest group affected, accounting for almost 46% of HL cases. This age group is the one responsible for the first peak of the bimodal distribution of HL seen in the West. However, unlike Western HL, we were unable to

show a bimodal age distribution in this study. Furthermore, a closer look at the age distribution of our patients has shown that the peak in our patients was seen in the age group 11-20 years (**Figure 1**), which is a decade earlier than the first peak seen in the West.¹² This unimodal age distribution of HL in Jordan with a peak occurring between 11 and 20 years of age is also different from the pattern associated with developing countries with its peak occurring primarily in children <10 years of age.^{7,8,22} The findings from this study would indicate that HL in Jordan has features intermediate between those of developed countries and those of developing countries, and probably best corresponds to the third pattern described by Correa et al.⁷ The lack of developed countries' bimodal age distribution in conjunction with absent childhood peak highly characteristic of developing countries HL, has been recently documented in a series from Kuwait and in the data from the Saudi Cancer Registry.^{19,27} Al-Diab et al³⁵ have shown that HL patterns in KSA have shifted in recent years with increasing frequency among young adults, and predominance of the NS type which became the most frequent type. Similarly Macfarlane et al⁵ have shown that incidence data of HL in Latin America are shifting towards patterns of developed countries. It seems that the patterns of HL are changing not only in developing countries, but also in developed countries, Hjalgrim et al³⁶ have shown that the first peak of HL in Nordic countries has shifted towards younger ages with a 9.9% annual increase among Finish women between 10-19 years of age. Because there are no previous reports on HL from Jordan, we were unable to confirm or exclude the possibility of a shift in the pattern of this malignancy. The only study on HL in Jordan addressed the childhood form of this disease.³⁷ When limiting the analysis to patients <15 years of age, we noted that the age distribution, and predominance of the MC type have not changed. However, the number of NS type cases has increased from 15% in that study to 37% in the current study. This finding may indicate that a shift in the histopathology of Jordanian HL towards the NS type has taken place recently. There was a male predominance in all of the histological subtypes of HL, a pattern similar to other developing and developed countries.⁷ The male predominance was most striking in the childhood group where it reaches 3.75:1. The only exception to the male predominance was seen in the NS subtype involving young adults between 15 and 34 years of age. In this group, the male to female ratio was 0.8:1. This finding is compatible with earlier reports on the epidemiology of HL, where male predominance was documented in all types of HL except the NS type.⁵

In summary, the results from this study indicate that HL in Jordan affects primarily patients between 11 and 20 years of age. Hodgkin's lymphoma in Jordan lacks both the bimodal age distribution

characteristic of Western HL, and the childhood peak characteristic of developing countries. The MC histology is the most common type followed closely by the NS type. On epidemiological grounds, HL in Jordan appears to have an intermediate pattern between developing countries and developed countries.

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