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Research Article

Distribution of Lymphoma Cases and Significance of Diagnostic Immunohistochemistry in a Sample of Iraqi Patients: A Cross-Sectional Study in a Tertiary Center in Baghdad

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Abstract

Background: The epidemiological patterns of lymphomas vary regionally, but studies in Baghdad, Iraq's largest population center, remain limited. ***Objective***: To evaluate the prevalence, subtype, and demographics of lymphomas in one of the major centers in Baghdad. ***Methods***: This cross-sectional study evaluated lymphoma prevalence, subtypes, and demographics at the National Center of Teaching Laboratories, Baghdad (June 2022–January 2024) using archival histopathology data confirmed by immunohistochemistry (IHC). ***Results***: 50 cases with complete data were included (41.84±20.4 years). Hodgkin's lymphoma constituted 20 (40%) of all cases, while 30 (60%) were non-Hodgkin's lymphoma. Non-Hodgkin's lymphoma patients were significantly older than those with Hodgkin's lymphoma (31±15.75 *vs*. 48.8±20.4 years). Male predominance was seen in both types of lymphoma, with male-to-female ratios of 1.3:1 in non-Hodgkin's lymphoma and 1.2:1 in Hodgkin's lymphoma. Classical Hodgkin's lymphoma comprised 95% of the cases, with nodular sclerosis being the predominant subtype (65%), followed by mixed cellularity (25%). Reed-Sternberg cell markers CD15 and CD30 were positive in 94.7% and 100% of classical Hodgkin's lymphoma cases. B-cell lymphomas represented 83.3% of non-Hodgkin's lymphoma cases, with diffuse large B-cell lymphoma being the most common subtype (40%), followed by small lymphocytic lymphoma (28%). ***Conclusions***: In Baghdad, there is a higher prevalence of HL than the global average and regional variation in subtype distribution. Small lymphocytic lymphoma rates are relatively high; however, diffuse large B cell lymphoma is the most common non-Hodgkin's lymphoma subtype. These findings emphasize the need for region-specific epidemiological research to improve diagnosis, treatment, and patient outcomes.

Keyword: Baghdad, Hodgkin's lymphoma, non-Hodgkin's lymphoma, Subtypes.

توزيع حالات سرطان الغدد الليمفاوية وأهمية الكيمياء المناعية التشخيصية في عينة من المرضى العراقيين: دراسة مقطعية في مركز من الدرجة الثالثة في بغداد

الخلاصة

الخلفية: تختلف الأنماط الوبائية للأورام اللمفاوية على مستوى المنطقة، لكن الدراسات في بغداد، أكبر مركز سكاني في العراق، لا تزال محدودة. **الهدف**: تقييم انتشار الأورام اللمفاوية والنوع الفرعي والتركيبة السكانية لها في أحد المراكز الرئيسية في بغداد.**الطرائق**: قيمت هذه الدراسة المقطعية انتشار سرطان الغدد الليمفاوية وأنواعها الفرعية والتركيبة السكانية في المركز الوطني للمختبرات التعليمية، بغداد (يونيو 2022 - يناير 2024) باستخدام بيانات الأنسجة المرضية الأرشيفية التي أكدتها الكيمياء المناعية (IHC). **النتائج**: تم تضمين 50 حالة ببيانات كاملة (41.84 سنة). شكلت لمفومة هودجكين 20 (40٪) من جميع الحالات ، بينما كانت 30 (60٪) من سرطان الغدد الليمفاوية اللاهودجكينية. كان مرضى سرطان الغدد الليمفاوية اللاهودجكين أكبر سنا بكثير من المصابين بسرطان الغدد الليمفاوية هودجكين (31 مقابل 48.8 سنة). لوحظ هيمنة الذكور في كلا النوعين من سرطان الغدد الليمفاوية ، مع نسب من الذكور إلى الإناث تبلغ 1.3: 1 في سرطان الغدد الليمفاوية اللاهودجكين و 1.2: 1 في سرطان الغدد الليمفاوية هودجكين. شكلت لمفومة هودجكين الكلاسيكية 95٪ من الحالات ، مع كون التصلب العقدي هو النوع الفرعي السائد (65٪) ، يليه الخلوية المختلطة (25٪). كانت علامات خلايا ريد ستيرنبرغ CD15 و CD30 إيجابية في 94.7٪ و 100٪ من حالات سرطان الغدد الليمفاوية هودجكين الكلاسيكي. مثلت الأورام اللمفاوية للخلايا البائية 83.3٪ من حالات سرطان الغدد الليمفاوية اللاهودجكينية ، مع كون سرطان الغدد الليمفاوية للخلايا البائية الكبيرة المنتشرة هو النوع الفرعي الأكثر شيوعا (40٪) ، يليه سرطان الغدد الليمفاوية الصغير (28٪). **الاستنتاجات**: في بغداد، هناك انتشار HL أعلى من المتوسط العالمي والتباين الإقليمي في توزيع الأنواع الفرعية. معدلات سرطان الغدد الليمفاوية الصغيرة مرتفعة نسبيا. ومع ذلك، فإن سرطان الغدد الليمفاوية للخلايا البائية الكبيرة المنتشرة هو النوع الفرعي الأكثر شيوعا من سرطان الغدد الليمفاوية اللاهودجكيني. تؤكد هذه النتائج على الحاجة إلى البحوث الوبائية الخاصة بالمنطقة لتحسين التشخيص والعلاج ونتائج المرضى.

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INTRODUCTION

Lymphoma is a general term that refers to malignancy that originates from clonal proliferation of lymphoid cells and their precursors [1]. Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL) are the two major forms in addition to plasma cell neoplasms and lymphoid leukemias [2]. Lymphoid neoplasms

accounted for 3.2% of the total new cancer cases globally in 2022 [3]. In Iraq, non-Hodgkin lymphoma was among the top ten malignancies in 2022, with an incidence of 3.2 per 100,000 population [4]. The World Health Organization (WHO) classification of lymphoid neoplasms described over 80 mature and immature lymphoma entities based on morphological, immunophenotypic, and genetic features [5]. Classical HL subtypes include nodular sclerosis (60–65%), mixed cellularity (15–30%), lymphocyte-rich (5%), and lymphocyte-depleted (1%). NHL is predominantly B-cell derived (85–90%), with DLBCL comprising approximately 30% of cases. T-cell and NK-cell lymphomas account for the remaining 10–15% [6]. Geographical variation in the incidence of malignant lymphoma is well established [2,7,8], with a higher incidence in North America, Australia/New Zealand, and Europe, and lower in Asia and Africa, with the exception of regions where Burkitt lymphoma (BL) is endemic [2]. Other known risk factors include age, gender, and ethnicity in addition to radiation, HIV infection, tattoos, and family history of the disease [9,10]. While several local studies from northern [11], middle [12], and southern Iraq [13] have described the lymphoma prevalence, studies from the capital, which has the highest population, are lacking. This study addresses this gap by analyzing the frequency, subtypes, and demographic distribution of lymphoma cases in Baghdad, using the current WHO classification.

METHODS

Study design and setting

This is a cross-sectional study conducted in the National Center of Teaching Laboratories, Baghdad, between June 2022 and January 2024. The study was approved by the Scientific and Ethics Committee of Medical City, Baghdad, Iraq.

Sample collection

The archival material of Histopathology Department was reviewed for malignant lymphoma cases with IHC confirmation of the subtype. Inclusion criteria were nodal or extranodal excisional biopsy with IHC-confirmed HL or NHL with no age or sex restriction. Cases with core biopsy, FNA, inconclusive diagnosis, or incomplete clinical information were excluded from the study. Hematoxylin and eosin (H&E) slides and all available IHC slide of eligible cases were retrieved and reviewed by a Board qualified pathologist to confirm the diagnosis in accordance with the 2016 revision of the World Health Organization's classification of lymphoid neoplasms. Cases with inconsistent diagnoses were reviewed by a consultant pathologist, and the agreed consensus diagnosis was reported. Patients' demographics and clinical information were collected from patients notes.

Immunohistochemistry

The IHC panel employed for lymphoma included CD30, CD23, CD20, CD15, CD79, CD38, CD10, CD8, CD5, CD4, CD3, BCL6, BCL2, Fascine, PAX5, TdT, and Cyclin D1 in addition to Ki67. Markers were stained according to the standard method provided by the manufacturer. Briefly, 4-5 µm slides were deparaffinized and rehydrated with graded alcohol. Heating was employed to acquire epitopes. The primary antibody was applied in accordance with the standard dilution for each marker and incubated at either room temperature for 1 hour or at 4°C overnight. Horseradish peroxidase (HRP) was used to block endogenous peroxidase. 3-3" diaminobenzidine (DAB)-based detection kits were employed to conduct the visualization. A buffer wash was employed after each step. The slides were counterstained with hematoxylin, dehydrated in steadily increasing alcohol concentrations, and cleansed with xylol. Each experiment contained both positive and negative controls.

Statistical analysis

The Statistical Package for Social Sciences software for Windows version 25 (IBM Corp., Armonk, N.Y., USA) was used for all statistical analyses. Observational data was presented in the form of frequencies and percentages. Continuous variables were expressed as mean, standard deviation, or range and were compared using Mann-Whitney and Kruskal-Wallis tests. Statistical comparisons were performed using the Chi-square test or Fisher's exact tests, as appropriate. Statistical significance was defined as a p-value less than 0.05.

RESULTS

A total of 50 patients were included with a mean age of 41.84 ± 20.4 years, ranging between 7 and 79 years. The age group (>40 years) constituted 27 (54%) of all cases, while pediatrics accounted for 9 (18%). Patients' characteristics are summarized in Table 1. Of the 50 cases, 20 (40%) were classified as HL and 30 (60%) as NHL. The subtypes of each group are illustrated in Figure 1. Patients with HL were significantly younger than those with NHL, with a mean age of 31±15.75 *vs*. 48.8±20.4 (Mann-Whitney test: p= 0.002). Half of the patients with HL were young adults (20-40 years). By contrast, 22 (73.3%) of NHL patients were older than 40 years. The cervical lymph nodes were the most frequently affected in both categories. Male predominance was seen in both types of lymphoma, with male-to-female ratios of 1.3:1 in NHL and 1.2:1 in HL. Extranodal involvement was observed in two (10%) of the HL cases that affected the skin and bowel.

Table 1: Patients demographics and clinical features of Hodgkin's Lymphomas (HL) and Non-Hodgkin's Lymphomas (NHL)

Characteristic			Total	HL (n=20)	NHL (n=30)	*p*-value*
Age (year)		<20	9(18)	5(25)	4(13.3)	
		20-40	14(28)	10(50)	4(13.3)	0.002
		>40	27(54)	5(25)	22(73.3)	
Gender		Female	22(44)	9(45)	13(43.3)	0.907
		Male	28(56)	11(55)	17(56.7)	
Distribution		Nodal	42(84)	18(90)	24(80)	0.45
		Extra-nodal	8(16)	2(10)	6(20)	
Number of sites		Single	20(40)	8(40)	12(40)	1.000
		Multiple	30(60)	12(60)	18(60)	
Site of lymph nodes	Nodal	Cervical	27(60)	13(72)	14(51.9)	0.653
		Axillary	6(13.3)	2(11.1)	4(14.8)	
		Abdominal	8(17.8)	2(11.1)	6(22.2)	
		Inguinal	4(8.9)	1(5.6)	3(11.1)	
		Chest wall	1(12.5)	0(0.0)	1(16.7)	
	Extra-nodal sites	Renal	1(12.5)	0(0.0)	1(16.7)	1.000
		Cutaneous	2(25)	1(50)	1(16.7)	
		Bowel	4(50)	1(50)	3(50)	

Values were expressed as frequency and percentage. *Chi Square or Fissure exact tests as appropriate.

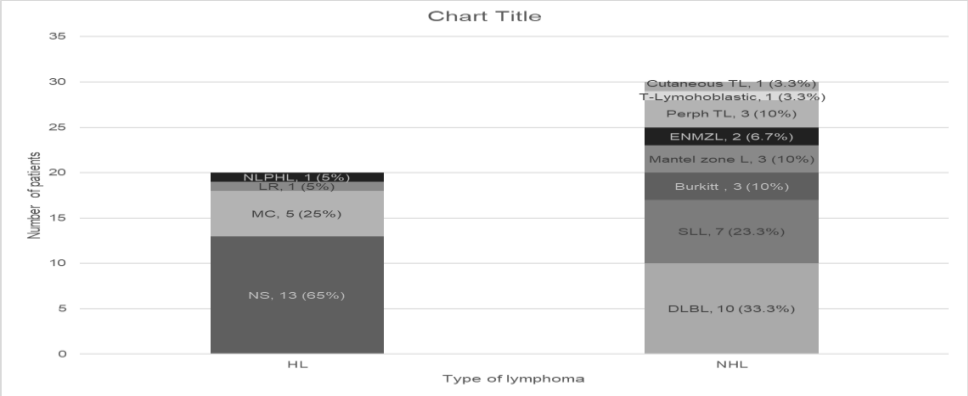

Figure 1: Subtypes of Hodgkin's (HL) and non-Hodgkin's lymphoma (NHL). Abbreviation: nodular sclerosis (NS), mixed cellularity (MC), lymphocyte rich (LR) and nodule lymphocyte predominant HL (NLPHL), diffuse large cell lymphoma (DLBL), small lymphocytic (SLL), Burkitt lymphoma (BL), extra nodal marginal zone lymphoma (ENMZL), peripheral T cell lymphoma (periph TL), cutaneous T cell Lymphoma (TL).

None of the Other clinical characteristics showed a statistical significant difference (Table 1). The morphological and IHC phenotype of lymphomas are demonstrated in Table 2.

Table 2: Immunohistochemistry markers expression in Hodgkins and non-Hodgkin's lymphoma

Marker		Hodgkins's lymphoma	Non-Hodgkin's lymphoma
CD30	+ve	19(95)	0(0.0)
	-Ve	1(5)	9(100)
CD15	+ve	18(90)	0(0.0)
	-Ve	2(10)	6(100)
PAX5	+ve	5(100	2(66.7)
	-Ve	0(0.0)	1(33.3)
Fascin	+ve	2(100)	1(50)
	-Ve	0(0.0)	1(50)
CD20	+ve	1(6.3)	21(77.8)
	-Ve	15(93.8)	6(22.2)
CD3	+ve	0(0.0)	4(19)
	-Ve	16(100)	17(81)
CD5	+ve	0(0.0)	10(45.5)
	-Ve	2(100)	12(54.5)
CD23	+ve	0(0.0)	6(40)
	-Ve	1(100)	9(60)
BCL2	+ve	0(0.0)	17(89.5)
	-Ve	2(100)	2(10.5)
BCL6	+ve	0(0.0)	5(29.4)
	-Ve	2(100)	12(70.6)
CyclinD	+ve	0(0.0)	6(31.6)
	-Ve	1(100)	13(68.4)
CD10	+ve	0(0.0)	1(25)
	-Ve	2(100)	3(75)

Values were expressed as frequency and percentage.

Moreover, the subtypes are shown in Figures 2-4 and Table 3. The classical HL represented 19 (95%), all mixed cellularity (MC) and lymphocyte-rich (LR), and 12 (92.3%) of nodular sclerosis (NS) variants expressed Reed-Sternberg cell (RS) markers (CD15 and CD30) (Figure 2), while one classical RS cell (5.3%) was negative for CD15 but was immunoreactive to PAX5. The lymphocyte-predominant (LP) cell in the only nodular lymphocyte-predominant Hodgkin's lymphoma (NLPHL) case was reactive to CD20, PAX5, and BCL6 cells and negative for CD30 and CD15. The immunophenotypes of NHL (Table 2) and its subtypes are illustrated in Table 4. The most common HL subtype was NS, accounting for 13 (65%) of all HL, with a mean age of 34.2±14.7, ranging between 15 and 59 years, which is relatively older than those with MC, who had a mean age of 20.4±17.9 years, ranging between 8 and 50 years. However, age did not exhibit any discernible variations among various subtypes of HL (Kruskal-Wallis test: p= 0.227) (Figure 5A). Of the 30 NHL cases, B-cell NHL was the more prevalent, accounting for 25 (83.3%). DLBCL was the most frequently encountered subtype of B cell lymphoma, accounting for 10/25 (40%), followed by SLL with 7 (28%). T cell lymphomas represented 5 (16.6%) of all NHL; four were peripheral T cells, one was cutaneous, and the other was T cell

lymphoblastic. As Figure 5B shows, the mean age of different NHL ranged between 45 and 73 years, except for the Burkitt subtype, which was associated with the pediatric age group with a mean age of 9.67 years, ranging between 7 and 11 years (Kruskal-Wallis test: p= 0.012).

DISCUSSION

The epidemiological landscape of lymphomas exhibits significant regional variability [14]. This study evaluated the distribution, immunophenotypic profiles, and clinicodemographic characteristics of Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL) diagnosed at the National Center of Teaching Laboratories in Baghdad over an 18-month period.

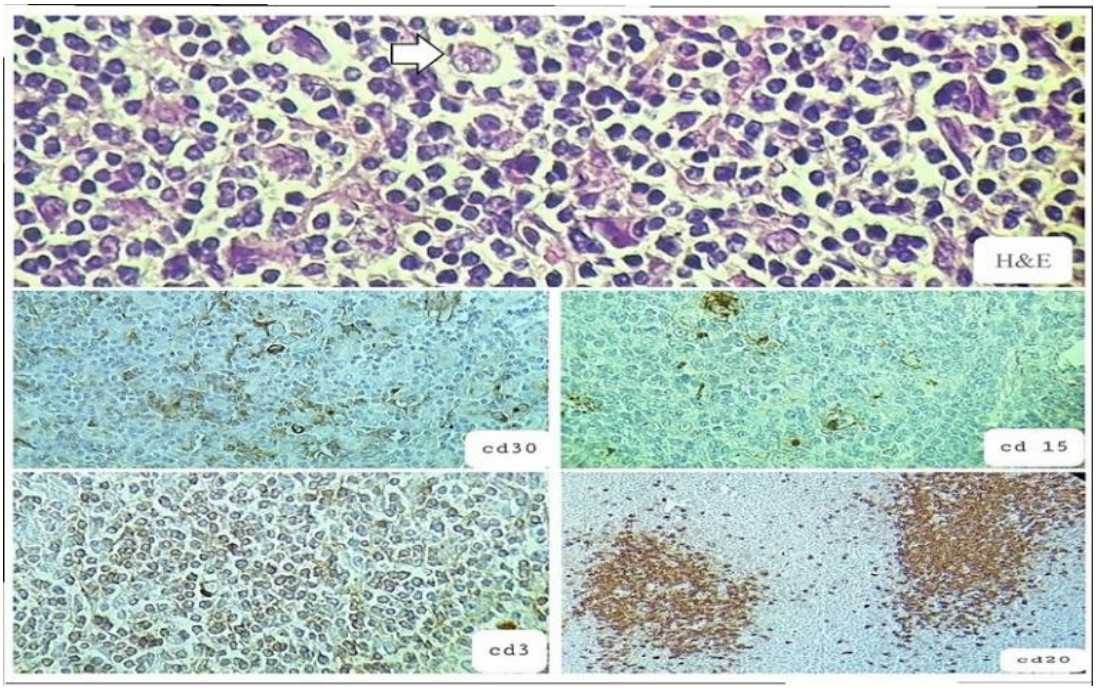

Figure 2: Morphology and immunophenotype of a classical mixed cellularity Hodgkin's lymphoma. Hematoxylin and eosin (H&E) microphotograph of a cervical lymph node illustrating the giant Reed-Sternberg (RS) cells, arrow, which were immunoreactive to CD30 and CD 15 heterogeneous cell population of lymphocytes, eosinophils, neutrophils, plasma cells, histiocytes, and fibroblasts Background was reactive to CD 3 and CD20. X200.

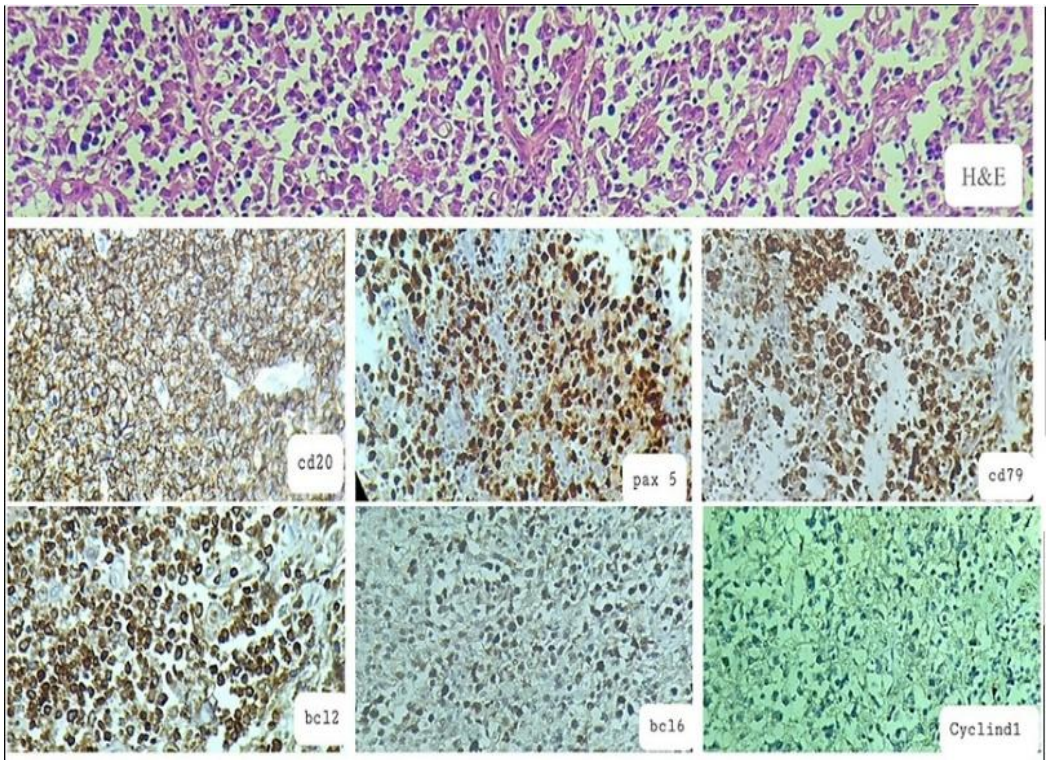

Figure 3: Morphology and immunophenotype of a diffuse large B cell lymphoma (DLBCL). Hematoxylin and eosin (H&E) and immunoreactivity to CD20, CD23, BCL2, BCL6 and Cyclin D. X200.

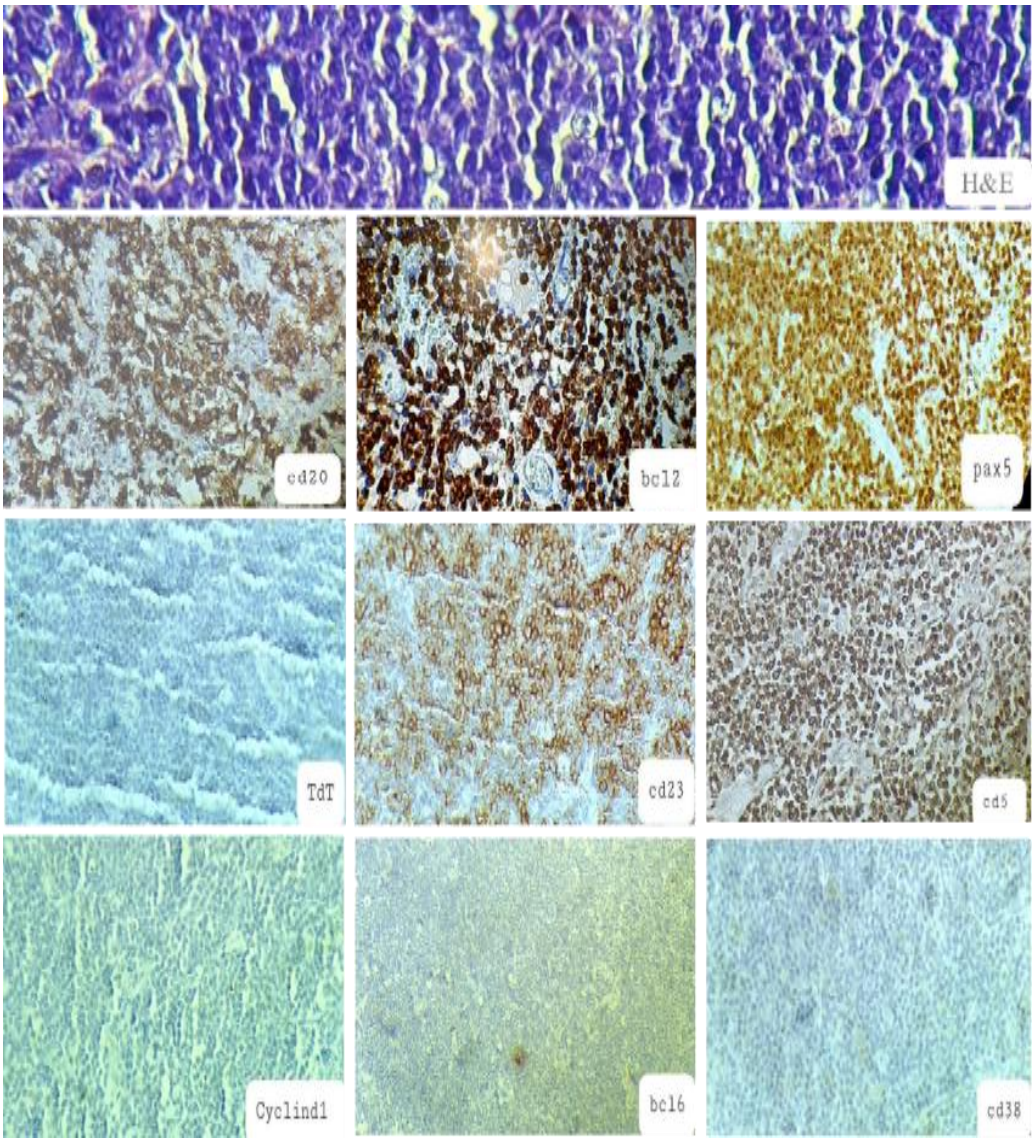

Figure 4: Morphology and immunophenotype of small lymphocytic lymphoma (SLL). Hematoxylene and Eosin (H&E) with immunoreactivity to CD20, CD5, BCL2, PAX5 and CD23 while negative for BCL6, CyclinD, TdT and CD38.

Table 3: Immunoprofile of Hodgkin's lymphoma subtypes

Hodgkin's lymphoma		n(%)	CD15		CD30		PAX5		Fascine		CD20		CD3		BCL6	
			+	-	+	-	+	-	+	-	+	-	+	-	+	-
Classical type	Nodular sclerosis	13(65)	12 (92.3)	0	13 (100)	0	3 (23.1)	0	0	0	0	13 (100)				
	Mixed cellularity	5(25)	5 (100)	0	5 (100)	0	2 (40)	0	2 (40)	0	0	5 (100)				
	Lymphocyte rich	1(5)	1 (100)	0	1 (100)	0	0	0	0	0	0	1 (100)				
Nodular lymphocyte-predominant HL		1(5)	0	0	0	0	1 (100)	0	0	0	1 (100)	0	0	1 (100)	1 (100)	0
	Total	20(100)														

Table 4: Immunoprofile of non- Hodgkin's lymphoma subtypes

Non- Hodgkin's lymphoma	CD15		CD30		PAX5		Fascine		CD20		CD3		CD5		CD23		BCL2		BCL6		Cyclin D		CD10	
	+	-	+	-	+	-	+	-	+	-	+	-	+	-	+	-	+	-	+	-	+	-	+	-
DLBL 10(33.3)		3 (30)	0	3 (30)	1 (10)	2 (20)	1 (10)	2 (20)	8 (80)	2 (20)	1 (10)	9 (90)	0	10 (100)	7 (70)	3 (30)	6 (60)	4 (40)	6 (60)	4 (40)	6 (60)	4 (40)	1 (10)	2 (20)
SLL 7(23.3)	0	7 (100)	0	7 (100)					6 (85.7)	1 (14.3)	1 (14.3)	6 (85.7)	6 (85.7)	1 (14.3)	0	0	5 (71.4)	1 (14.3)	1 (14.3)	5 (71.4)	2 (28.6)	5 (71.4)		
Burkitt 3(10)	0	3 (100)	0	3 (100)	1 (33.3)	2 (66.7)			3 (100)	0	1 (33.3)	2 (66.7)	0	3 (100)	1 (33.3)	2 (66.7)	2 (66.7)	1 (33.3)	1 (33.3)	2 (66.7)	0	3 (100)	3 (42.9)	4 (57.1)
Mantel zone 3(10)	0	3 (100)	0	3 (100)			0		3 (100)		0	3 (100)	2 (66.7)	1 (33.3)	1 (33.3)	2 (66.7)	3 (100)	0	0	3 (100)	3 (100)	0		
ENMZL 2(6.7)	0	2 (100)	0	2 (100)			0	2 (100)	2 (100)		2 (100)	0	1 (50)	1 (50)	0	2 (100)	1 (33.3)	2 (66.7)	1 (33.3)	2 (66.7)	1 (33.3)	2 (66.7)		
Peripheral T cell 3(10)		1 (33.3)	1 (33.3)		1 (33.3)				3 (100)	0	3 (100)	0	2 (66.7)	1 (33.3)	1 (33.3)	2 (66.7)	2 (66.7)	1 (33.3)	1 (33.3)	2 (66.7)	1 (33.3)	2 (66.7)		
T cell Lymphoblastic 1(3.3)									0	0	1 (100)	0	1 (100)	0	0	1 (100)	0	3 (100)			0	3 (100)		
Cutaneous T cell 1(3.3)								0	1 (100)	0	1 (100)	0			0	1 (100)	0	3 (100)			0	3 (100)		

Abbreviations: DLBCL, diffuse large B cell lymphoma; ENMZL, extra nodal marginal zone lymphoma.

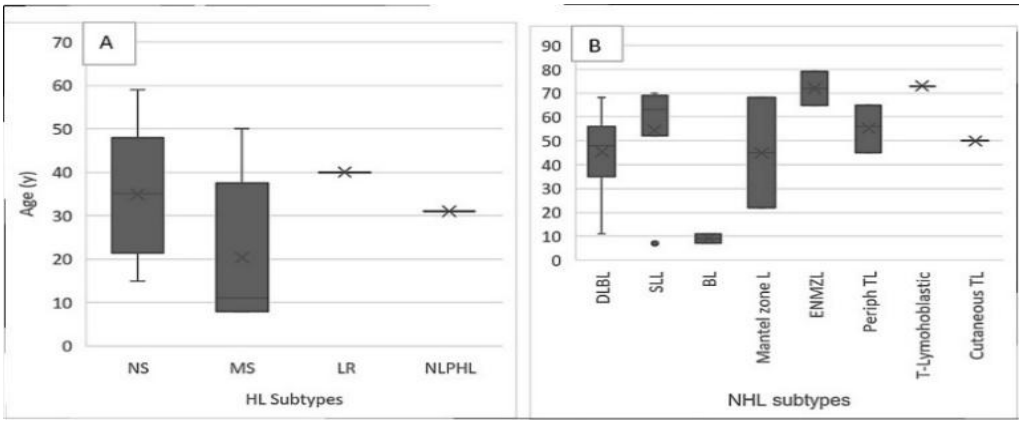

Figure 5: Age distribution of malignant lymphoma subtypes. A) Hodgkin's lymphoma (HL), nodular sclerosis (NS), mixed cellularity (MC), lymphocyte rich (LR) and nodule lymphocyte predominant HL. B) Non- Hodgkin's lymphoma (NHL) subtypes, diffuse large cell lymphoma (DLBL), small lymphocytic (SLL), Burkitt lymphoma (BL), extra nodal marginal zone lymphoma (ENMZL), peripheral T cell lymphoma (periph TL), cutaneous T cell Lymphoma (TL).

In our cohort, NHL accounted for 60% of cases, while HL represented 40%. This contrasts with global data, where NHL constitutes approximately 90% of malignant lymphomas and HL only 10% [15,16]. However, our findings align with regional trends in Iraq and neighboring countries, where HL prevalence is notably higher. For instance, studies from southern Iraq [17] and northern Iraq [11] reported HL rates of 25% and 24%, respectively. Similarly, a large-scale study in Jordan identified HL in 39% of malignant lymphoma cases [18]. The higher HL prevalence in one of the main centers in Baghdad (40%) compared to other Iraqi regions may reflect demographic or diagnostic variations, though our smaller sample size warrants cautious interpretation. Classical HL comprised 95% of HL cases in our study, with NS being the predominant subtype (65%), followed by MC (25%). This mirrors regional reports, such as NS rates of 67% in Jordan [17] and 48.8% in Bahrain [19], though a southern Iraqi study found MC more frequent (57.1%) [17]. Reed-Sternberg cell markers CD15 and CD30 were positive in 94.7% and 100% of classical HL cases, respectively, consistent with the documented CD15 expression range of 75–85% [20]. Discrepancies in CD15 reactivity may arise from technical factors, underscoring the utility of supplementary markers like PAX5 and fascin for diagnostic confirmation. B-cell lymphomas represented 83.3% of NHL cases, with DLBCL being the most common subtype (40%), followed by small lymphocytic lymphoma (SLL) (28%). Globally, DLBCL prevalence ranges widely (20–63.9%), influenced by geographic, socioeconomic, and healthcare access factors [21-23]. Our results are comparable to regional studies: DLBCL accounted for 52.2% of NHL in northern Iraq [11] and 54.02% in Kerbala [13], with similar rates reported in Lebanon (44%), Turkey (53.6%), and Saudi Arabia (59%) [24-26]. In contrast, the proportion of SLL in our study (28%) exceeded rates in northern Iraq (15%) and central Iraq (5%) [11,13]. This variability extends to neighboring countries, where SLL prevalence ranges from 6.7% in Turkey [25] to 17.3% in Hatay [27]. Such disparities may reflect differences in sample size, diagnostic criteria, genetic predisposition, or environmental exposures. Age was a significant differentiating factor: NHL patients were older (mean age: 48.8 ± 20.4 years) than HL patients (mean age: 31.3 ± 15.75 years; p= 0.002), with 73.3% of NHL cases occurring in individuals > 40 years. This aligns with global data linking NHL to advanced age [28]. Conversely, Burkitt lymphoma—an aggressive NHL subtype—affected younger patients (mean age: 9.67 years; p=0.012), consistent with its known predilection for pediatric and adolescent populations [29-31].

Study limitations

This study has several limitations. Its single-center design and small sample size may restrict the generalizability of the findings. Additionally, low numbers in certain categories—such as only one NLPHL case and five T-cell NHL cases—limit statistical power and subgroup analyses. The absence of clinical staging and outcome data further reduces the broader applicability of the results. Future multi-center studies with larger cohorts, detailed molecular profiling, and long-term follow-up would help validate and expand upon these findings.

Conclusions

This study enforces the importance of IHC staining in the diagnosis and subgrouping of lymphoma and highlights the distinct lymphoma epidemiology in one of the main centers in Baghdad, characterized by a higher HL prevalence than global averages and regional variability in subtype distribution. DLBCL remains the predominant NHL subtype, while SLL rates exhibit notable geographic heterogeneity. Age-related patterns underscore the divergent clinical trajectories of HL and NHL. These insights reinforce the importance of region-specific epidemiological research to optimize diagnostic accuracy, therapeutic strategies, and patient outcomes.

Conflict of interests

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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