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Research Article

Correlation of Proliferative Marker in B & T Non-Hodgkin's Lymphoma (NHL) by Immunohistochemical Expression with Ki-67, CD20, and CD3 Tumor Markers: Clinicopathological Study

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Abstract

Background: Tumor proliferation is a fundamental process in cancer progression. Ki-67, a nuclear antigen, is widely recognized as a reliable marker for evaluating cell proliferation through immunohistochemical analysis. Its expression is restricted to the active phases of the cell cycle (G1, S, G2, and M), making it a valuable tool in assessing tumor proliferative activity. In the context of non-Hodgkin lymphomas (NHL), Ki-67 serves as a potential indicator for tumor aggressiveness and clinical behavior. This study aims to evaluate the association between Ki-67, CD20, and CD3 expressions and the clinicopathological features of NHL, including its role in disease progression, response to treatment, and its correlation with variables such as age, gender, type, and tumor location, in order to enhance diagnostic and prognostic accuracy.

Methods: A retrospective analysis was conducted on forty formalin-fixed paraffin-embedded excisional biopsies of NHL cases collected between June 2021 and February 2022 from a specialized surgical center in Baghdad Medical City. All samples were re-evaluated histologically and stained immunohistochemically for Ki-67, CD20, and CD3 markers. Statistical analysis was performed, with significance set at $P<0.05$.

Results: A statistically significant association was found between the Ki-67 labeling index and both lymphoma grade and immunophenotypic type. Based on CD3 and CD20, 30 (75%) had B-cell NHL and 10 (25%) had T-cell NHL.

Conclusions: The study highlights the strong correlation between Ki-67 expression and lymphoma grade. Notably, high-grade lymphomas, especially those with extranodal spread, were predominantly seen in pediatric patients.

Keywords: Non-Hodgkin's lymphoma, Ki-67, CD3, CD20, Proliferative index, Lymphoma grade

Introduction

Non-Hodgkin's lymphoma (NHL) represents a heterogeneous group of lymphoid malignancies that arise from B cells, T cells, or natural killer (NK) cells at various stages of differentiation. It encompasses all lymphoproliferative disorders, excluding Hodgkin lymphoma, and accounts for the majority of malignant lymphomas [1]. NHL may present in nodal or extranodal sites and displays marked variation in clinical behavior, morphology, immunophenotype, and genetic features [2]. B-cell lymphomas constitute approximately 85% of NHL cases, while T-cell lymphomas comprise the remaining 15% [3]. Pretreatment clinical variables such as patient age, sex, Ann Arbor stage of cancer, the presence of B-cell lymphomas symptoms (fever, night sweats, unexplained weight loss), tumor bulk, serum lactate dehydrogenase (LDH) levels, and proliferative indices significantly influence prognosis and therapeutic strategy [4]. The World

Health Organization (WHO) classification of lymphoid neoplasms emphasizes the need for a multiparametric approach, combining morphology, immunophenotyping, cytogenetics, molecular biology, and clinical data to identify distinct clinicopathologic entities with meaningful therapeutic implications [5-6].

Beyond lineage-specific markers, the proliferative activity of lymphoid malignancies provides some key prognostic insights. Ki-67, a nuclear and nucleolar protein, is expressed during the active phases of the cell cycle (G1, S, G2, and M) and absent in resting cells (G0), making it a reliable marker for cellular proliferation [7]. The Ki-67 labeling index (LI), assessed using the MIB-1 monoclonal antibody, and quantifies the fraction of proliferating tumor cells. Studies have shown that a high Ki-67 index correlates with aggressive clinical behavior, poor response to treatment, and decreased overall survival in various NHL subtypes, particularly in diffuse large B-cell lymphoma (DLBCL) and Burkitt lymphoma [8-9]. The prognostic relevance of Ki-67 is further amplified when interpreted alongside other pretreatment variables such as lactate dehydrogenase (LDH) levels, International Prognostic Index (IPI) scores, tumor bulk, and extranodal involvement [4]. Together, these parameters support risk stratification and help guide personalized therapeutic approaches, including intensified chemotherapy regimens or targeted biological therapies. Furthermore, modern advances in immunohistochemistry and flow cytometry have enabled the detection of aberrant expression patterns in leukemic and lymphomatous cells, such as co-expression or loss of lineage-specific antigens [10-11]. These patterns not only refine diagnostic accuracy but also offer insights into clonal evolution, treatment resistance, and potential therapeutic vulnerabilities.

CD3 and CD20 are among the most widely utilized immunohistochemical markers in diagnosing lymphoid neoplasms. CD3 is a T-cell-specific marker that forms part of the T-cell receptor (TCR) complex and is expressed on the surface of nearly all mature T lymphocytes. Its consistent expression in normal and malignant T cells makes it a critical tool for identifying T-cell lineage in suspected cases of T-cell NHL. However, aberrant loss of CD3 expression has been documented in high-grade peripheral T-cell lymphomas and anaplastic large cell lymphoma, necessitating a broader panel of T-cell markers for accurate classification [10-11]. In contrast, CD20 is a membrane-embedded protein expressed on B cells from the pre-B stage until shortly before their terminal differentiation into plasma cells. It is virtually specific for B-cell lineage and is strongly expressed in most B-cell lymphomas, particularly diffuse large B-cell lymphoma and follicular lymphoma. The diagnostic utility of CD20 is complemented by its therapeutic relevance, as it serves as the target for monoclonal antibodies such as rituximab, which have significantly improved outcomes in B-cell lymphoma patients [12-13]. Nonetheless, CD20 expression can be diminished or lost in certain scenarios, including relapsed disease and after exposure to anti-CD20 therapy, complicating subsequent diagnostic and treatment strategies. The combined assessment of CD3 and CD20 expression enables the accurate immunophenotypic distinction between B-cell and T-cell lymphomas and is foundational in current WHO classifications of lymphoid neoplasms [5-2].

Materials and Methods

Study Design and Sample Selection

This retrospective cross-sectional study included 40 formalin-fixed, paraffin-embedded (FFPE) tissue samples from patients diagnosed with non-Hodgkin lymphoma (NHL). The specimens were collected from a specialized surgical center in Baghdad Medical City between June 2021 and February 2022. Cases included both nodal and extranodal lymphoid tumors. Clinical and pathological data, including patient age, sex, tumor location, histological subtype, and tumor grade, were retrieved from histopathology reports.

Histological and Immunohistochemical Evaluation

Three tissue sections, each 4 μm thick, were prepared from each FFPE block and mounted on positively charged slides. One section was stained with hematoxylin and eosin (H&E) for histopathological review. The remaining sections underwent immunohistochemical staining for Ki-67 (MIB-1 clone), CD20 (L26 clone), and CD3, using monoclonal mouse anti-human antibodies (Dako).

Immunostaining was performed according to standard protocols. Antigen retrieval was conducted in a hot water bath at 95°C for 55 minutes. Endogenous peroxidase activity was blocked, followed by incubation with primary antibodies overnight at room temperature. Biotinylated secondary antibodies and streptavidin-HRP-HRP-HRP–HRP complexes were applied, followed by a chromogen solution and hematoxylin counterstaining. Positive controls consisted of reactive lymph node tissues known to

express CD20, CD3, and Ki-67. Negative controls were prepared by omitting the primary antibody while keeping all other conditions identical.

Ki-67 positivity was defined by brown nuclear staining. A minimum of 1,000 tumor cells were counted in 10 high-power fields to determine the labeling index (LI). The proliferative index was categorized as high (>50% positive nuclei), moderate (20–50%), and low (<20%).

CD20 and CD3 expressions were evaluated semi-quantitatively. CD20 positivity was defined as brown staining along the cytoplasmic membrane of B lymphocytes. CD3 positivity was determined by cytoplasmic and/or membranous staining in T lymphocytes.

Ethical approval

The study was conducted using archived, anonymized tissue samples with no patient interaction. Ethical approval was obtained from the institutional review board (Approval No. 04 in 2021). All data were handled in compliance with confidentiality and ethical research standards.

Statistical Analysis

Data were analyzed using SPSS version 28.0 and Real Statistics Pack for Excel 2016. Continuous variables were summarized as mean ± standard deviation or median with interquartile range, depending on distribution. Normality was tested using the Shapiro-Wilk test. The Kruskal-Wallis test was used for comparisons between groups. Correlation between variables was assessed using Spearman's rank correlation. A p-value <0.05 was considered statistically significant. Receiver operating characteristic (ROC) analysis was employed to determine optimal thresholds for diagnostic performance.

Results

The morphology of H&E-stained slides and the immunophenotyping as B or T-NHL by immunostaining with CD20 and CD3, respectively, were used to make the diagnosis and subtyping of NHL. A total of 30 B-cell NHL cases were identified in this study, accounting for 75% of all NHL cases. Diffuse large B-cell lymphoma (DLBCL) was the most prevalent subtype, comprising 14 cases (46.6% of B-NHL and 35% of all NHL). Follicular lymphoma (15%), small lymphocytic lymphoma (12.5%), Burkitt's lymphoma (7.5%), and marginal zone lymphoma (5%) were the other B-cell NHL subtypes observed, as shown in Figure 1. A total of 10 T-cell NHL cases were identified in this study, comprising 25% of all NHL cases. Mycosis fungoides (MF) was the most prevalent subtype, accounting for 6 cases (15% of all NHL). Other T-cell NHL subtypes included lymphoblastic T-cell lymphoma (2 cases, 5% of all NHL), peripheral T-cell lymphoma (1 case, 2.5% of all NHL), and anaplastic large cell lymphoma (1 case, 2.5% of all NHL) (Figure 2).

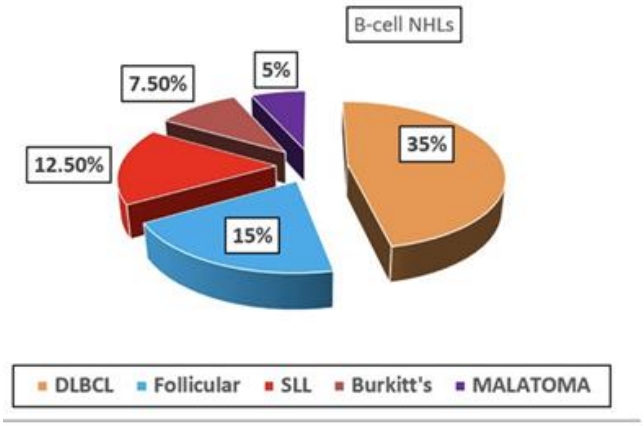

Figure 1: Major types of B-cell NHL

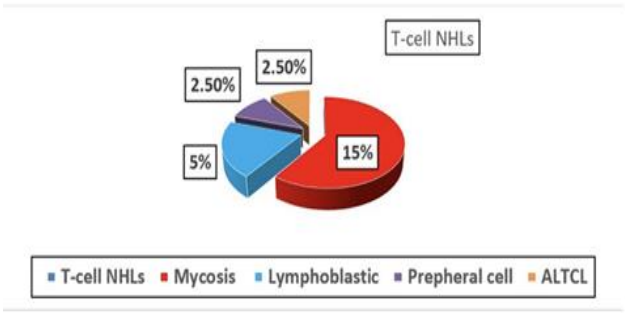

Figure 2: Major types of T-cell NHL

Table 1 revealed a slight male predominance in NHL cases, with 23 male patients and 17 female patients. Both males and females were equally affected by B-cell NHLs, with similar distributions across the different subtypes. A higher proportion of male patients were diagnosed with T-cell NHLs, particularly mycosis fungoides. Table 2 shows that 7 cases (17.5%) were diagnosed in patients aged 0-18 years. About 21 cases (52.5%) were diagnosed in patients aged 50-59 years, while 12 cases (30%) were diagnosed in patients aged 60 years or older. The mean age of all patients was 49.7 ± 2.87 years, with a median age of 55 years. The age range of the patients was 3-81 years. The 24(60%) NHL cases were shown extra- nodal and 16(40%) cases were nodal. The most frequent extra nodal sites were skin, mainly in mycoses fungoides, followed by the GIT, nasopharyngeal, and others. Childhood lymphoma showed extra nodal distribution, among nodal locations, cervical lymph node involvement was seen in 10 cases, axillary lymph nodes in 2 cases, and supraclavicular lymph nodes in one

case, with only 3 patients presenting with deep-seated nodal primary NHL (Figure 3).

Table 1: Distribution of the cases according to the gender

NHL Diagnoses	Male	Female	Total No.
B-cell NHLs			
DLBCL	7	7	14
Follicular	3	3	6
SLL	3	2	5
Burkitt's	2	1	3
MALAT	1	1	2
T-cell NHLs			
Mycosis	5	1	6
Lymphoblastic	0	2	2
Prepheral cell	1	0	1
ALTCL	1	0	1
Totally (B-cell NHLs , T-cell NHLs)	**23**	**17**	**40**

Table 2: Distribution of the cases according to the Age groups

Groups	Age		
	B-cell NHLs	**T-cell NHLs**	**Total No.**
Childhood	4	3	7
50-59 Years	17	4	21
Equal or more than 60 Years	9	3	12
Total No.	**30**	**10**	**40**
Mean age	49.7±2.87		
Median	55		
Rage	3-81		

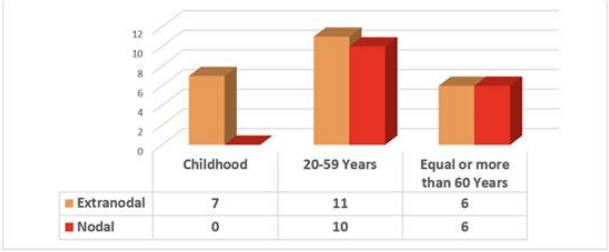

Figure 3: Distribution of the tumor site according to the age groups

The Ki-67 labeling index was assessed in 40 NHL cases to evaluate the proliferative activity of tumor cells. The distribution of cases based on various clinical and pathological parameters can be seen in Table 3. Figure 4 shows strong Ki-67 immunohistochemical expression in an intestinal Burkitt lymphoma, which is more prevalent in the pediatric group. The Key Findings demonstrated that a higher proportion of cases (>50%) with a Ki-67 labeling index were observed in the younger age groups, particularly childhood and the 50-59 years age group. In terms of Immunophenotype, a higher proportion of B-cell NHLs exhibited a Ki-67 labeling index >50% compared to T-cell NHLs. For grade, all cases with a high-grade tumor showed a Ki-67 labeling index >50%. Low-grade tumors exclusively had a Ki-67 labeling index <50%. Intermediate-grade tumors were more frequently associated with a Ki-67 labeling index >50%.

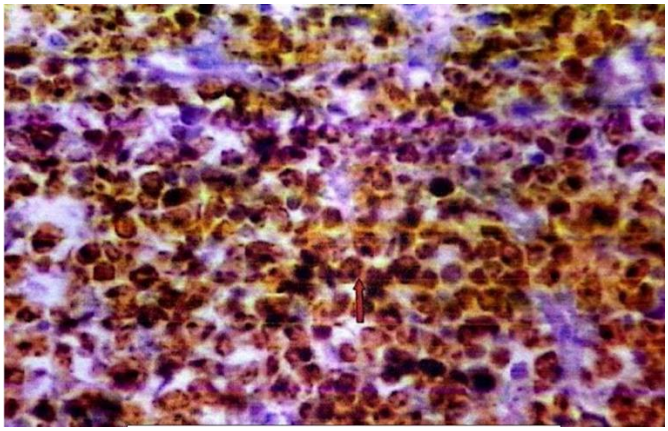

Figure 4: Intestinal Burkett lymphoma showing strong nuclear KI67

Table 3: Distribution the Age groups, gender, immunophenotype and grade according to the Ki67 labeling index

Variable	Ki67>50	Ki67<50	Total No.
Age			
Childhood	7	0	7
50-59 Years	8	13	21
Equal or more than 60 Years	3	9	12
Total No.	18	22	40
Sex			
Male	9	14	23
Female	9	8	17
Total No.	18	22	40
Immunophenotype			
B-cell NHLs	15	15	30
T-cell NHLs	**3**	**7**	**10**
Total No.	**18**	**22**	**40**
	Grade		
Low	**15**	**0**	**15**
Intermediate	**7**	**0**	**7**
High	**0**	**18**	**18**
Total No.	**22**	**18**	**40**

These findings suggest that a higher Ki-67 labeling index is associated with younger age, B-cell phenotype, and higher-grade tumors (Figures 5 and 6). Mycosis Fungoides, a rare variant of T-cell lymphoma, can be differentiated using CD3 immunostain (Figure 7). The same condition clarifies the low proliferative activity of Ki-67(<20%) in this type of lymphoma (Figure 8). Most of the small lymphocytic lymphoma cases enrolled in this study showed Ki-67 less than 25% activity (Figure 9), while the aggressive lymphoblastic lymphoma showed high Ki-67 proliferation rank up to 90% (Figure 10).

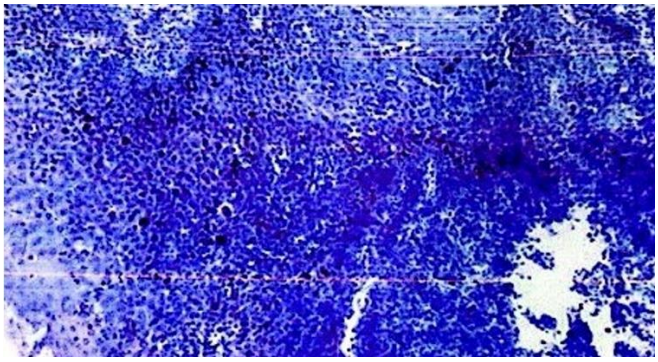

Figure 5: Follicular lymphoma diffuses mixed cell type showing moderate intensity (25%)

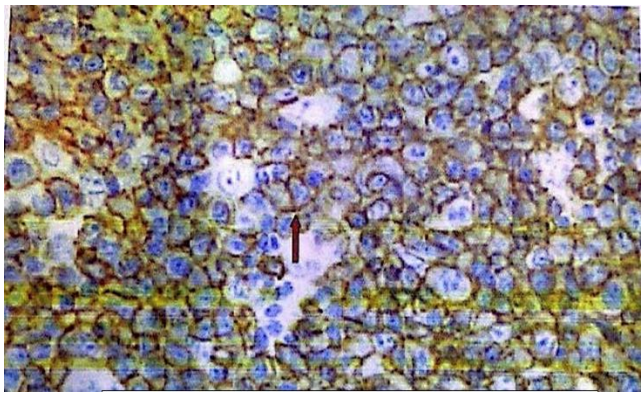

Figure 6: Follicular lymphoma with positive membranous CD20 immunostaining (red arrow)

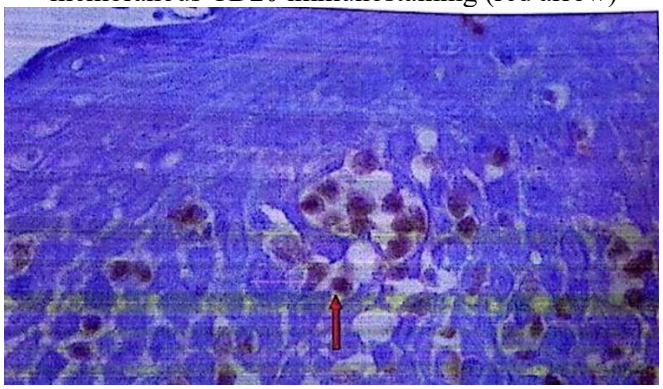

Figure 7: Mycosis fungoides with positive reaction for CD3 epidemiologic cells showing cytoplasmic localization (arrow) (40X)

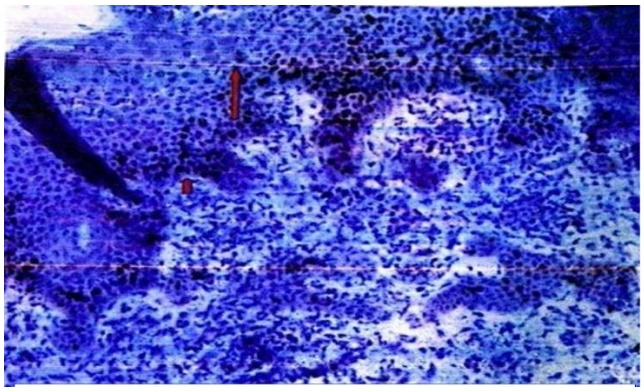

Figure 8: Mycosis fungoides showing Ki67 stains proliferating epidermal basal cell (short arrow) and some neoplastic T-lymphocyte (long arrow) (25%)

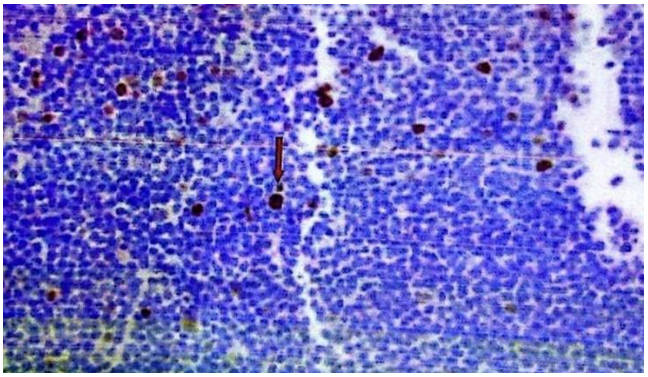

Figure 9: Small lymphocytic lymphoma showing weak Ki67 staining (15%)

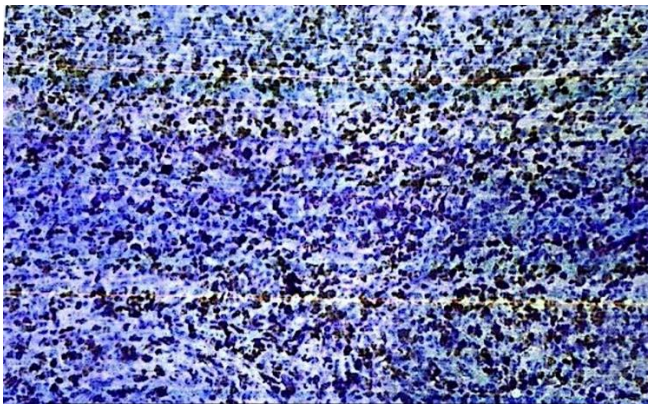

Figure 10: Lymphoblastic lymphoma showing strong Ki67 staining (90%) nuclear localization (X40)

The single case of the anaplastic large cell lymphoma (ALTCL) included in this study showed large-sized sized with eosinophilic cytoplasm and bizzare nuclei (Figure 11) with high Ki-67 activity reaching up to 90% (Figure 12), indicating the aggressive behavior of this T-cell lymphoma.

Discussion

The NHL cases in this study were diagnosed and subclassified based on the morphological assessment of H&E-stained sections, along with immunophenotyping using CD20 and CD3 markers to distinguish B-cell and T-cell lineages, respectively, following the proposed nested classification system.

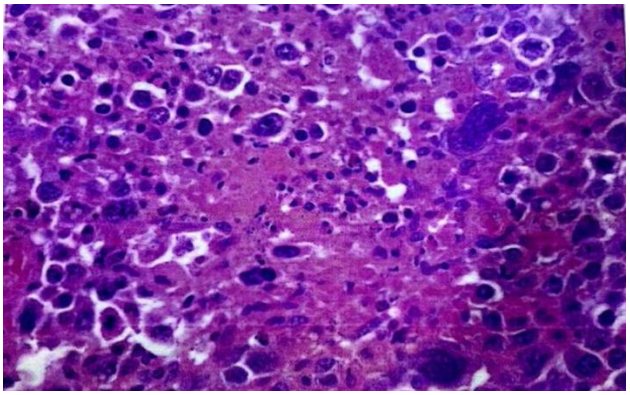

Figure 11: Hematoxylin-Esoin Morphology of ALTCL with bizarre nuclei (X40)

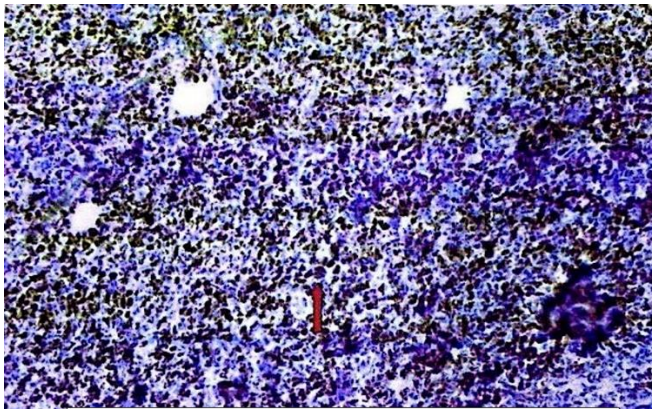

Figure 12: Morphology of ALTCL with bizarre nuclei and strong Ki-67 staining (90%) in ALCL (arrow) (x40)

The CD20-positive to indicate B-cell NHL (B-NHL) was high compared to the CD3-positive to indicate T-cell NHL (T-NHL). This distribution contrasts with findings from a study in Kurdistan, where B-NHL constituted 91% of cases and T-NHL only 9% [14]. Similar proportions were reported in an Iranian study, which showed 89.5% B-NHL and 10.5% T-NHL [15]. These discrepancies may be attributed not only to differences in retrospective versus prospective methodologies but also to sample size limitations and population-specific ethnic or environmental variables [16]. Globally, the distribution of NHL subtypes exhibits significant geographic variation. While B-cell lymphomas predominate in North America and Europe, T-cell lymphomas represent a larger fraction of NHLs in several East and Southeast Asian countries [17]. In the United States, T-cell lymphomas account for approximately 15% of NHLs, but this proportion is notably higher in countries such as Taiwan and Japan. In HTLV-1 endemic regions, the high incidence of adult T-cell leukemia/lymphoma further elevates the T-cell lymphoma frequency, while a lower occurrence of B-cell neoplasms also contributes to this regional disparity [18-19]. These patterns reflect broader differences in environmental exposure, including infections and toxins, as well as a wide range of genetic susceptibilities and lifestyle-related factors that influence host response, particularly across different global populations [19].

Clinicopathological parameters of NHL

This study revealed that the incidence of NHL peaked during the fifth decade of life. The adult age group accounted for the majority of cases, with 21 instances reported in this category. This age distribution applied to both B-cell and T-cell NHL, and these findings were consistent with data from other local and regional studies. For instance, a study conducted in Baghdad reported a mean age of 52 ± 5.3 years at diagnosis [20], while a major study from Kurdistan indicated a median age of 45 years [14-21]. Another study from Baghdad showed a mean age of 51.47 years [22]. Notably, one Iraqi study reported a younger mean age of 32.7 years, whereas another recorded a mean age of 46.2 years [23]. Similarly, research from Iran also identified the fifth decade as the peak age of NHL incidence [24]. In contrast, studies from Western countries have found that NHL primarily affects older adults, with the highest incidence occurring in the seventh decade of life [25]. These differences may be attributed to factors such as genetic polymorphisms, racial variation, environmental exposures, and geographic influences that can alter the biological behavior of the disease in different populations. Additionally, this study observed that aggressive extranodal lymphomas, most notably Burkitt and lymphoblastic subtypes, were more common among pediatric patients. This age-specific distribution supports earlier findings regarding the behavior of these NHL subtypes [26-27].

The current study revealed a slight male predominance in NHL, with a male-to-female (M/F) ratio of 1.35:1, which aligns with findings from several previous studies. In her study on malignant lymphoma reported an M/F ratio of 1.09 [28]. Similarly, another study on B-cell neoplasms observed an M/F ratio of 1.3, while Kareem's study [29] demonstrated a more pronounced male predominance, reporting a ratio of 2:1. A consistent male dominance has also been observed in Western populations, with the ratio exceeding 2:1 for both B-cell and T-cell NHL [30-31]. The present results showed that there was no statistically significant association between gender and either immunophenotypic expression or NHL subtype classification. These findings are in agreement with other studies [32-33]. However, some minor discrepancies in the literature may exist, potentially due to differences in sample size, geographic location, and environmental influences.

The present study showed a high rate of extranodal NHL. This distribution likely reflects the biological behavior and subtype specificity of the disease, as certain NHL subtypes tend to manifest extrabodily. These findings are comparable to previous reports from Kuwait (54%) and Iraq (58%) [34], but contrast with studies conducted in Jordan (40.8%) [35], as well as a significantly lower rate of 26% reported in North America [36]. The observed discrepancies may stem from variations in sample size, diagnostic criteria, or population characteristics. In the current study, the

most common extranodal sites were the tonsils, skin, and gastrointestinal tract locations frequently reported in global literature on extranodal NHL [37].

Diffuse large B-cell lymphoma (DLBCL) was the most prevalent subtype in this study. This finding is consistent with previous reports by Rafil (2016) and comparable to data from Western populations [38]. A high proliferative index was evident, with 12 out of 14 DLBCL cases (85%) showing Ki-67 positivity above 50%, while the remaining two cases exhibited moderate Ki-67 expression between 25% and 50%.

Three cases of Burkitt lymphoma (BL), comprising 7.5% of total NHL cases of the present study, were identified among pediatric patients aged 3 to 9 years, with a median age of 7. According to the WHO classification, BL is divided into three clinical variants: endemic, sporadic (the most frequent in non-malarial regions), and immunodeficiency-associated [20]. Although sporadic BL represents only 1–3% of NHL in Western countries, it accounted for 7.5% of NHL in this study, lower than the 20.5% reported in Dohuk and more recent findings from Jordan [26]. Contrary to the Western trend, this study observed a gender distribution of two males and one female, whereas BL generally showed a male predominance of 3–5:1. All BL cases showed B-cell lineage (CD20+), extranodal involvement (primarily intestinal within the GIT), and a high Ki-67 proliferation index exceeding 80%, supporting the tumor's aggressive nature. These observations are in agreement with findings by Naz et al. (2011) [38] and align with the Working Formulation, which classifies BL as a high-grade lymphoma. In contrast to Western countries, where follicular lymphoma (FL) constitutes up to 40% of all NHL cases [39], only six cases (15%) of FL were identified in this study. This lower prevalence aligns with previous findings from Dohuk [27] and is similarly reflected across other developing and Asian countries, where FL is generally less common. These disparities are likely attributable to genetic and environmental factors that influence lymphomagenesis. The current data suggest that FL in this population exhibits a balanced sex distribution, primarily affects older adults, and typically presents with nodal involvement. All six FL cases showed B-cell lineage and a moderate Ki-67 labeling index, indicating an intermediate level of proliferative activity.

The correlation between the number of Ki–67–positive cells and the histologic grade confirms the role of Ki-67 as a marker of proliferative activity in FL. This is supported by findings that were further explained in the context of the International Working Formulation (IWF) [34], which underscores the prognostic value of proliferation indices in lymphoma classification. Although Mycosis Fungoides is considered a rare cutaneous T-cell lymphoma globally [39], its incidence in the current study was relatively high, accounting for 15% of NHL cases. Six cases were identified, five males and one female, primarily affecting individuals around the age of 55, with the skin as the principal site of involvement.

All cases were confirmed to be of T-cell lineage and exhibited low proliferative activity, with Ki-67 labeling index values consistently below 20%. This low proliferation is characteristic of MF's indolent nature and is consistent with previous findings by Gerdes *et al*. (1987) [40], who described the tumor's slow progression and typically low mitotic activity. The low Ki-67 scores in our series may also reflect the early-stage presentation of T-NHL in these patients.

This study identified five cases of small lymphocytic lymphoma (SLL), which is higher than the global incidence. Similar to findings in other studies [41-42], three cases (60%) showed nodal involvement mainly in the cervical lymph nodes, while two were extranodal, involving the spleen and bone marrow. Approximately one-third of SLL cases are known to demonstrate extranodal extension, as noted by Swerdlow (1999) [43]. These findings are in line with previous studies by Medeiros [44], which describe the characteristically low proliferative activity of SLL. The variability in Ki-67-positive cell counts may reflect the presence of proliferation centers, areas composed of larger, more mitotically active cells such as prolymphocytes and paraimmunoblasts, known to show higher Ki-67 expression [45-46].

Two cases of MALT lymphoma were identified in this study. Both cases demonstrated extranodal involvement and originated from the B-cell lineage. MALT lymphomas are typically indolent and more frequently observed in older adults. In accordance with the International Working Formulation (IWF), MALT lymphoma is classified as a low- to intermediate-grade lymphoma. In both cases, Ki-67 labeling index revealed mild to moderate proliferative activity, which aligns with the histopathological nature of this subtype.

Two cases of lymphoblastic lymphoma of T-cell origin were identified in this study. Both presented in extranodal locations and occurred in pediatric and adolescent age groups, findings that are consistent with previous literature describing this

subtype's predilection for younger populations [47-49]. According to Naz et al. (2011), lymphoblastic lymphoma typically shows a variable gender distribution, elevated mitotic activity, and high Ki-67 labeling index, characteristics that categorize it as a high-grade lymphoma [38]. These features were confirmed in our cases, where a strong Ki-67 expression was observed, supporting the diagnosis of aggressive lymphoid malignancy.

A single case of anaplastic large cell lymphoma (ALCL), constituting 2% of total NHL cases in this study, was observed in a male pediatric patient. The lymphoma displayed T-cell lineage, evidenced by CD3 positivity, and was extranodal in presentation. This case demonstrated highly aggressive features, with a strong Ki-67 labeling index reaching approximately 80%, indicative of intense proliferative activity. These findings are in agreement with earlier reports, which highlighted ALCL's rapid clinical progression, high mitotic index, and frequent extranodal manifestations, particularly in pediatric populations [50-51].

Correlation of Ki-67 Labeling Index (LI) with all parameters

The data of this study revealed a statistically significant increase in Ki-67 index with advancing lymphoma grade, confirming a strong correlation between proliferative activity and tumor grade. These findings align with those reported by other studies [52-53]. Also, the results of this study found a significant association between patient age and Ki-67 LI. These results are consistent with findings from Jordan by Al-Attar et al. (2008) [26]. The lower proliferation indices in adults and older patients may be attributed to the higher prevalence of low-grade lymphomas such as follicular lymphoma, small lymphocytic lymphoma (SLL), and Mycosis fungoides in these age groups. Although Olga (1990) reported T-cell NHL as a high-grade lymphoma, our study did not find a statistically significant correlation between Ki-67 PI and the immunophenotype (T-cell versus B-cell). This discrepancy may be attributed to the relatively high percentage (15%) of mycosis fungoides cases in our cohort, which are typically indolent in nature and exhibit a lower proliferative index [53].

Conclusions

This study highlights the significant correlation between Ki-67 expression and histological grade in NHL, reinforcing its role as a valuable proliferative marker in assessing tumor aggressiveness. High Ki-67 labeling index was predominantly associated with high-grade lymphomas, particularly DLBCL, Burkitt, and lymphoblastic subtypes, while low-grade lymphomas such as SLL and mycosis fungoides exhibited lower expression. Although no statistically significant association was found between Ki-67 and immunophenotype, the marker remains clinically relevant in stratifying risk and guiding treatment intensity. Incorporating Ki-67 evaluation into routine diagnostic practice may improve prognostication and inform therapeutic decisions in NHL patients.

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