DOI:10.31557/APJCC.2026.11.5.707

RESEARCH ARTICLE

Clinicopathological Profile, Treatment Response, and Survival Outcomes of Non-Hodgkin Lymphoma Patients in Southern Iraq: A Retrospective Cross-Sectional Study

Aamer Shareef Mohamed Alhachami*

Department of Internal Medicine, College of Medicine, University of Thi Qar, Nasiriyah, Dhi Qar, Iraq.

Abstract

Introduction: Non-Hodgkin Lymphoma poses a significant health burden, yet detailed epidemiological and clinical data from Southern Iraq are lacking. Understanding local disease patterns is essential for developing effective, region-specific cancer control programs. This study aimed to describe the demographic and clinicopathological characteristics of NHL patients in Nasiriya, Iraq, and to evaluate their treatment response and survival outcomes across different subtypes and disease stages. **Materials and Methods:** A retrospective cross-sectional study was conducted at Al Nasiriya Teaching Hospital from 2017 to 2022. Data from 213 adult patients with histologically confirmed NHL who received at least three cycles of first-line chemotherapy were abstracted. Variables included demographics, disease characteristics, laboratory parameters, treatment response (interim and end-of-therapy), overall survival (OS), and progression-free survival (PFS). **Results:** The cohort's median age was 53 years with a male predominance (54.9%). Diffuse Large B-cell Lymphoma (DLBCL) was the most common subtype (69.5%). Nearly half (46.9%) presented with advanced-stage (III/IV) disease. The interim complete response rate was 70%, declining slightly to 66.2% at end-of-therapy. Response varied significantly by subtype; PTCL NOS had the lowest interim CR rate (35.3%), while MZL and SMZL had the highest (92.9-100%). OS differed significantly by subtype ($p=0.043$) and was most powerfully predicted by disease stage ($p<0.001$), with Stage III/IV conferring a threefold higher mortality risk (HR ~2.8-3.1) compared to Stage I. PFS showed a similar strong association with advanced stage ($p<0.001$). **Conclusion:** This study reveals a high burden of aggressive, late-stage NHL in Southern Iraq, dominated by DLBCL. While first-line therapy is generally effective, PTCL NOS is a high-risk subtype with poor outcomes. Advanced disease stage is the paramount prognostic factor, highlighting an urgent need for public health strategies to enable earlier diagnosis and subtype-specific treatment optimization to improve survival.

Keywords: Non-Hodgkin Lymphoma- Iraq- Epidemiology- Survival Analysis- Treatment Response- Disease Stage

Asian Pac J Cancer Care, **11 (5)**, 707-717

Submission Date: 05/23/2026 Acceptance Date: 07/27/2026

Introduction

Non-Hodgkin Lymphoma (NHL) represents a heterogeneous group of malignancies originating from the lymphatic system, characterized by a wide spectrum of clinical behaviors, histopathological subtypes, and prognostic outcomes. Its global burden is significant, posing a considerable challenge to healthcare systems worldwide. Based on the GLOBOCAN data from the International Agency for Research on Cancer, there were an estimated 553,389 new cases of NHL worldwide in 2022, giving this cancer a rank of 10th among all cancers, with an age-standardized incidence rate (ASR) of 5.6 per 100,000. Mortality from NHL was also substantial, with approximately 250,679 deaths, ranking it 11th, and an ASR of 2.4 per 100,000 [1].

The disease is complex, as highlighted by the diversity of its subtypes, which include entities such as Diffuse Large B-cell Lymphoma (DLBCL) and various T-cell lymphomas, each with distinct biological drivers and clinical courses. This heterogeneity necessitates a precise understanding of its presentation and management, as treatment strategies and survival prospects can vary dramatically [2, 3]. Epidemiological

Corresponding Author:
Dr. Amer Shareef Mohamed
Department of Internal Medicine, College of Medicine, University of Thi Qar, Nasiriyah, Dhi Qar, Iraq.
Emails: amer@utq.edu.iq, aamer.shreef.78@gmail.com

research on NHL plays a crucial role in understanding this complexity. Population-based studies that map the distribution of subtypes, identify risk factors, and track survival trends are fundamental to public health. They inform the development of screening guidelines, guide the allocation of specialized diagnostic and therapeutic resources, and help in assessing the effectiveness of cancer control programs over time [4, 5]. Furthermore, regional epidemiological data can reveal unique patterns linked to genetic predispositions, environmental exposures, or sociodemographic factors, contributing to a more complete global understanding of the disease's etiology. For clinicians, such data provides essential context for diagnosis, prognosis, and treatment planning, enabling care that is tailored to the specific patterns observed within their patient population [6].

Despite the acknowledged importance of such regional data, a significant knowledge gap persists concerning the epidemiological and clinical profile of NHL in Southern Iraq. There is a notable absence of comprehensive, contemporary studies from this area detailing the local burden of NHL, its histological spectrum, the stage at which patients typically present, and their outcomes following standard treatment. This lack of localized evidence limits the ability to evaluate healthcare needs accurately, to identify potential gaps in the diagnostic pathway, and to benchmark local care standards. Without this foundational understanding, efforts to improve early detection, optimize therapeutic protocols, and ultimately enhance survival outcomes for NHL patients in this region are not empirically grounded [7].

To address this gap, this study aims to describe the demographic and clinicopathological characteristics of NHL patients in Nasiriya, Iraq, and evaluate their treatment response and survival outcomes across different subtypes and disease stages. By establishing this crucial baseline profile, the findings are intended to inform local clinical practice and health policy, providing the evidence needed to guide future strategies for improving NHL management and patient prognosis in the region.

Materials and Methods

Study design and Setting

This was a retrospective, cross-sectional study conducted at the outpatient hematology clinic of Al Nasiriya Teaching Hospital located in Nasiriya, Dhi Qar Governorate, Iraq. The center is a major tertiary care facility in the Thi-Qar Governorate, serving a large population in Southern Iraq and managing a high annual load of hematological and oncological malignancies. All NHL cases diagnosed and managed from 2017 through 2022 were identified and reviewed.

Participants / Inclusion and Exclusion Criteria

The study included a total of 213 patients with a confirmed diagnosis of NHL. The inclusion criteria were: adult patients (aged 18 years and above) with a histopathologically confirmed NHL of any subtype, who received at least three cycles of first-line chemotherapy at the study center and for whom complete medical records were available. Patients were excluded if they had a concurrent diagnosis of Hodgkin lymphoma or another malignancy, had incomplete medical records, or were lost to follow-up before the first response assessment.

Sample Size Calculation

Due to the retrospective and comprehensive nature of this study, which aimed to capture all eligible cases over a defined period, a formal sample size calculation was not performed prior to data collection. The final sample size of 213 represents the total population of patients who met the inclusion criteria during the entire study period.

Treatment Regimens

First-line chemotherapy was administered according to histopathological subtype following the National Comprehensive Cancer Network (NCCN) guidelines. Rituximab was available and administered to all patients with CD20-positive B-cell lymphomas, including Diffuse Large B-cell Lymphoma (DLBCL), Marginal Zone Lymphoma (MZL), Splenic Marginal Zone Lymphoma (SMZL), and Mantle Cell Lymphoma (MCL). No patient with a CD20-positive subtype was denied rituximab due to availability or cost constraints during the study period. Patients with Diffuse Large B-cell Lymphoma (DLBCL) received R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone). Patients with Peripheral T-cell lymphoma, not otherwise specified (PTCL NOS) and Angioimmunoblastic T-cell Lymphoma (AITCL) received CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone). Patients with Marginal Zone Lymphoma (MZL) and Splenic Marginal Zone Lymphoma (SMZL) received rituximab monotherapy. Patients with Mantle Cell Lymphoma (MCL) received either R-CHOP or R-DHAP (rituximab, dexamethasone, cytarabine, cisplatin). All patients received at least three cycles of their respective first-line regimen, with response assessed after 3 cycles (interim) and after completion of 6 cycles (end-of-therapy). Patients who did not achieve complete response to first-line therapy (non-responders) were managed according to their performance status and clinical eligibility. All fit patients were offered second-line chemotherapy using the ICE protocol (ifosfamide, carboplatin, etoposide). Frail patients or those with poor performance status were offered best supportive care and palliative measures.

Response Assessment

Treatment response was evaluated according to the Lugano 2014 classification criteria. Interim complete response (CR) was assessed after 3 cycles of chemotherapy, and end-of-therapy response was assessed after completion of 6 cycles. Response assessment was performed using contrast-enhanced computed tomography (CT) scans.

Procedure and Data Collection

Data were extracted from patients' physical and electronic medical records using a standardized data collection form. This form was initially designed as

a structured paper sheet to systematically capture all variables. Subsequently, the data from these paper forms were entered into a Microsoft Excel spreadsheet (Microsoft Office 365) to create a digital database for analysis. The form was designed to capture the following variables:

• Demographic and Baseline Clinical Characteristics: Age at diagnosis, sex.

• Laboratory Parameters at Diagnosis: Hemoglobin (Hb), White Blood Cell count (WBCs), Absolute Monocyte Count (AMC).

• Disease Characteristics: Primary disease site (cervical, mediastinal, abdominal, inguinal), presence of organomegaly, extranodal involvement, and histopathological subtype (AITCL: Angioimmunoblastic T-cell Lymphoma, DLBCL: Diffuse Large B-cell Lymphoma, MCL: Mantle Cell Lymphoma, MZL: Marginal Zone Lymphoma, PTCL NOS: Peripheral T-cell lymphoma, not otherwise specified, SMZL: Splenic Marginal Zone Lymphoma).

• Staging: Ann Arbor stage (I-IV) at diagnosis.

• Treatment and Response: Interim complete response (CR) after 3 cycles, and end-of-therapy response after 6 cycles.

• Outcome and Survival Analysis Variables: Number of patients who died (survival events), Number of patients who were alive at the end of follow-up.

OS was defined as the time from diagnosis to death from any cause. PFS was defined as the time from diagnosis to the first documented disease progression or death from any cause.

Ethical considerations

The study was conducted in accordance with the ethical standards of the Declaration of Helsinki. It received approval from the Institutional Review Board of Thi Qar Medical College prior to the initiation of data collection (IRB Log No: ----------). Given the retrospective nature of the study, the requirement for informed consent was waived by the approving ethics committee. All patient data were anonymized and de-identified prior to analysis to ensure confidentiality and privacy.

Statistical analysis

Statistical analysis was done by SPSS version 28 (IBM Co., Armonk, NY, USA). Numerical data were presented as the median and interquartile range (Q1, Q3) due to the non-normality of the distribution and analyzed using Kruskal-Wallis test. Categorical data were presented as the frequency and percentage and analyzed using the Chi-square test or exact test, as appropriate. OS and PFS were analyzed using Kaplan-Meier curve with Log-rank test. Multivariable Cox proportional hazards regression model was fitted to identify independent predictors of OS and PFS, incorporating: disease stage (I, II, III, IV), histological subtype (grouped as DLBCL, PTCL NOS group [AITCL + PTCL NOS], Indolent B-cell [MZL + SMZL], and Other [MCL + Other]), age at diagnosis, and sex. A two tailed P-value < 0.05 was considered statistically significant.

Results

The demographic and clinicopathological characteristics of the studied patients are presented in Table 1 and Figure 1. The study included 213 patients with a median age at diagnosis of 53 years (Q1-Q3: 39-64) and a slight male predominance of 54.9% (n=117). The most common involved sites were the abdomen in 109 patients (51.2%), the cervical region in 104 (48.8%), and the mediastinum in 75 (35.2%), with organomegaly present in 110 patients (51.6%). DLBCL was the most frequent

Table 1. Demographic and Clinicopathological Characteristics of the Study Patients (N=213)

Item	Total patients (n=213) (%)
Sex	
Male	117 (54.9)
Female	96 (45.1)
Age at diagnosis (years)	53 (39, 64), mean±SD (51.47±18.37)
Hb (g/dL)	11.3 (10, 13) mean±SD (11.27±2.06)
WBCs (x10^3/µl)	7 (5.28, 10) mean±SD (9.01±9.3)
Site	
Cervical	104 (48.8)
Mediastinum	75 (35.2)
Abdomen	109 (51.2)
Inguinal	49 (23)
Extra nodal	78 (36.6)
Organomegaly	110 (51.6)
Histopathological subtype	
AITCL	5 (2.3)
DLBCL	148 (69.5)
MCL	10 (4.7)
MZL	14 (6.6)
PTCL NOS	17 (8)
SMZL	5 (2.3)
Other	14 (6.6)
Stage	
I	66 (31)
II	47 (22.1)
III	28 (13.1)
IV	72 (33.8)
Interim CR (after 3 cycles)	
No	64 (30)
Yes	149 (70)
End of therapy response (after 6 cycles)	
No	72 (33.8)
Yes	141 (66.2)
AMC (x10^9/L)	0.4 (0.3, 0.73) mean±SD (0.6±0.54)

Numerical data are presented as median (Q1, Q3), mean±SD and categorical data are presented as frequency (%), Hb: Hemoglobin, WBCs: White Blood Cells, AITCL: Angioimmunoblastic T-cell Lymphoma, DLBCL: Diffuse Large B-cell Lymphoma, MCL: Mantle Cell Lymphoma, MZL: Marginal Zone Lymphoma, PTCL NOS: Peripheral T-cell lymphoma, not otherwise specified, SMZL: Splenic Marginal Zone Lymphoma, CR: Complete Response, AMC: Absolute Monocyte Count

Table 2. Demographic and Clinicopathological Characteristics of Patients According to NHL Subtypes

Item	Histopathological subtype							P-value
	AITCL (n=5)	DLBCL (n=148)	MCL (n=10)	MZL (n=14)	PTCL NOS (n=17)	SMZL (n=5)	Other (n=14)	
Sex								
Male	4 (80)	76 (51.4)	7 (70)	8 (57.1)	9 (52.9)	3 (60)	10 (71.4)	0.613
Female	1 (20)	72 (48.6)	3 (30)	6 (42.9)	8 (47.1)	2 (40)	4 (28.6)	
Age at diagnosis (years)	55 (26.5, 57.5)	52 (38, 62)	56 (47.5, 81.5)	60.5 (49.75, 74.5)	59 (36, 69)	60 (51, 65.5)	40 (22, 64.5)	0.171
Hb (g/dL)	10 (9, 11.5)	11 (10, 12.95)	11.5 (10.45, 12.55)	12 (10.6, 13)	11 (8, 13.25)	12 (9.3, 13.5)	12 (10.88, 13.78)	0.522
WBCs (x10^3/µl)	6 (4.8, 15.44)	7 (5.16, 10)	8 (6.75, 9.68)	6.15 (4.42, 10.25)	7 (6, 11.28)	8.4 (7.33, 19)	8.25 (5.75, 11.85)	0.628
Stage								
I	2 (40)	44 (29.7)	4 (40)	5 (35.7)	4 (23.5)	3 (60)	4 (28.6)	0.467
II	0 (0)	34 (23)	1 (10)	5 (35.7)	3 (17.6)	0 (0)	4 (28.6)	
III	0 (0)	19 (12.8)	0 (0)	1 (7.1)	4 (23.5)	0 (0)	4 (28.6)	
IV	3 (60)	51 (34.5)	5 (50)	3 (21.4)	6 (35.3)	2 (40)	2 (14.3)	
Interim CR (after 3 cycles)								
No	2 (40)	46 (31.1)	2 (20)	1 (7.1)	11 (64.7)	0 (0)	2 (14.3)	0.006
Yes	3 (60)	102 (68.9)	8 (80)	13 (92.9)	6 (35.3)	5 (100)	12 (85.7)	
End of therapy response (after 6 cycles)								
No	2 (40)	51 (34.5)	3 (30)	1 (7.1)	12 (70.6)	0 (0)	3 (21.4)	0.004
Yes	3 (60)	97 (65.5)	7 (70)	13 (92.9)	5 (29.4)	5 (100)	11 (78.6)	

Numerical data are presented as median (Q1, Q3) and categorical data are presented as frequency (%), Statistical significance at P-value<0.05

histopathological subtype at 69.5% (n=148), while others included PTCL NOS (8%, n=17), MZL (6.6%, n=14), MCL (4.7%, n=10), and AITCL and SMZL (each 2.3%, n=5). The disease stage was distributed as Stage I in 66 patients (31%), Stage II in 47 (22.1%), Stage III in 28 (13.1%), and Stage IV in 72 (33.8%). The interim complete response after 3 cycles was 70% (n=149), and the end-of-therapy response after 6 cycles was 66.2% (n=141). The median laboratory values were 11.3 g/dL (Q1-Q3: 10, 13) for Hb, 7 x10^3/µl (Q1-Q3: 5.28, 10) for WBCs, and 0.4 x10^9/L (Q1-Q3: 0.3, 0.73) for AMC.

The demographic and clinicopathological characteristics of patients according to NHL subtypes are presented in Table 2. No statistically significant differences were observed among the subtypes in terms of sex (p=0.613), age at diagnosis (p=0.171), Hb level (p=0.522), WBC count (p=0.628), and the distribution across Ann Arbor stages I-IV (p=0.467). However, a significant difference was found in the interim complete response after 3 cycles (p=0.006), with rates ranging from 35.3% in PTCL NOS to 100% in SMZL. This significant difference was also present for the end-of-therapy response after 6 cycles (p=0.004), where PTCL NOS again had the lowest rate at 29.4%, while SMZL and MZL maintained the highest rates at 100% and 92.9%, respectively.

The OS analysis of patients according to NHL histopathological subtype and stage is presented in Table 3, Figure 2, and Figure 3. A significant difference was observed across the different histopathological subtypes

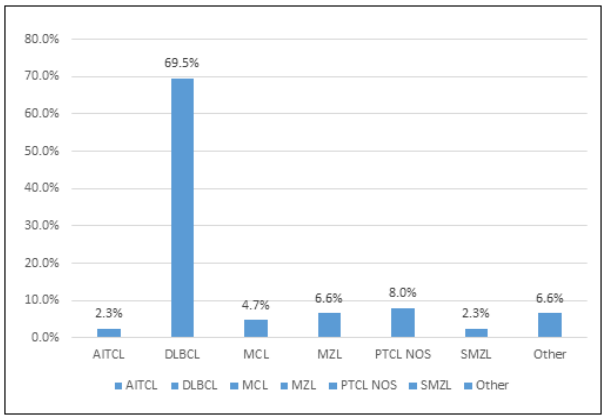

Figure 1. Distribution of NHL Cases According to Histopathological Subtype

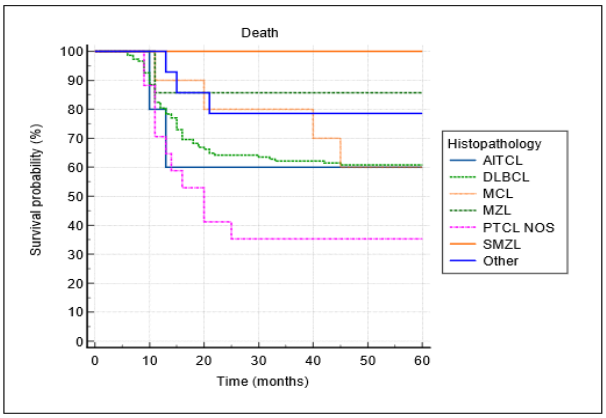

Figure 2. Kaplan-Meier Curve for Overall Survival Analysis of NHL Patients According to Histopathological Subtype

(p=0.043). The number of events varied considerably, from 0% in SMZL with a mean survival of 60 months, to 64.7% in PTCL NOS with a mean survival of 30.53 months. The corresponding hazard ratios, using AITCL as reference, were 0.91 (95% CI: 0.20-4.17) for DLBCL, 0.81 (95% CI: 0.14-4.78) for MCL, 0.29 (95% CI: 0.05-1.59) for MZL, and 1.75 (95% CI: 0.31-9.76) for PTCL NOS. Furthermore, disease stage at diagnosis was a significant predictor of OS (p<0.001), with patients in advanced stages (III and IV) showing significantly higher hazard ratios compared to Stage I. In Figure 3 (OS by stage), the Kaplan-Meier curves for survival by stage show that the curves for Stages III and IV separate markedly downward from those of Stages I and II, with this divergence widening over time. The risk of death increased with stage, from HR=1.18 (95% CI: 0.66-2.12) for Stage II, to HR=2.78 (95% CI: 1.33-5.83) for Stage III, and HR=3.05 (95% CI: 1.76-5.26) for Stage IV.

The PFS analysis of patients according to NHL histopathological subtype and stage is presented in Table 4, Figure 4, and Figure 5. The difference across histopathological subtypes did not reach statistical significance (p=0.076). Disease stage was a highly significant factor for PFS (p<0.001). For Figure 5 (PFS by stage), the PFS curves for Stages III and IV diverge visibly and substantially from those of early-stage disease (I and II), with this separation apparent from the initial months of follow-up and persisting throughout. The Hazard Ratios for progression or death showed a clear gradient, from HR 1.13 (95% CI: 0.64-2.02) for Stage II, to HR 2.85 (95% CI: 1.37-5.92) for Stage III, and HR 2.93 (95% CI: 1.71-5.02) for Stage IV, confirming that advanced stage at diagnosis was strongly associated with worse progression-free survival.

Cox proportional hazards models were developed for OS and PFS after merging some histopathological types (Table 5). The key findings of the multivariable analysis are as follows: Disease stage was confirmed as a highly significant independent predictor of both OS and PFS. Compared to Stage I, Stages III and IV carried significantly higher mortality and progression risk after adjustment for subtype, age, and sex (Stage III: OS aHR=2.68 [95% CI: 1.28–5.58], p=0.009; PFS aHR=2.74 [95% CI: 1.34–5.57], p=0.006; Stage IV: OS aHR=2.73 [95% CI: 1.50–5.00], p=0.001; PFS aHR=2.65 [95% CI: 1.47–4.78], p=0.001). Stage II did not differ significantly from Stage I in either model. Histological subtype also emerged as an independent prognostic factor. The Indolent B-cell subtype (MZL + SMZL) had significantly better survival than DLBCL in both OS (aHR=0.22 [95% CI: 0.05–0.89], p=0.034) and PFS (aHR=0.21 [95% CI: 0.05–0.88], p=0.033) models. The PTCL NOS group did not reach independent significance. Age at diagnosis was a statistically significant independent predictor in both models (OS aHR=1.01 per year [95% CI: 1.00–1.03], p=0.034; PFS aHR=1.01 [95% CI: 1.00–1.03], p=0.043). Sex was not an independent predictor of OS (aHR=0.89, p=0.603) or PFS (aHR=0.96, p=0.843) after adjustment.

Discussion

This study provides a detailed analysis of NHL in Nasiriya, Southern Iraq, characterizing the demographic profile, histopathological distribution, treatment response, and survival outcomes of 213 patients. The findings offer critical insights into the local epidemiological and clinical patterns of NHL.

The demographic and clinicopathological results reveal distinctive epidemiological and clinical patterns. The observed slight male predominance (54.9%) and a median age at diagnosis in the sixth decade of life (53 years) characterize the demographic context of the disease in this population, closely mirroring regional patterns observed in Lebanon (mean age 53.5 years, 54.4% male) by Touma et al., 2021 [8] and Saudi Arabia (male:female ratio 1.27:1) by Alyahya et al., 2019 [9]. A central finding is the overwhelming predominance of Diffuse Large B-cell Lymphoma (DLBCL), which constituted the vast majority of cases (69.5%). This suggests the clinical burden of NHL in this region is primarily driven by this aggressive subtype. While DLBCL is consistently the most common subtype globally, its proportion in our cohort exceeds the 54% reported in Lebanon [8] and the 59-71% in Saudi Arabian studies [9, 10], suggesting a potentially unique epidemiological profile in Southern Iraq with a higher relative burden of aggressive disease, possibly influenced by local environmental or genetic

Table 3. Overall Survival Analysis of Patients According to NHL Histopathological Subtype and Stage

Item	N of events (%)	N. Censored (%)	Mean (months)	HR (95%CI)	Log-rank P-value
Histopathological subtype					
AITCL	2 (40)	3 (60)	40.6	Ref	0.043
DLBCL	58 (39.19)	90 (60.81)	42.3	0.91 (0.2 to 4.17)	
MCL	4 (40%)	6 (60)	47.6	0.81 (0.14 to 4.78)	
MZL	2 (14.29)	12 (85.71)	53	0.29 (0.05 to 1.59)	
PTCL NOS	11 (64.71)	6 (35.29)	30.53	1.75 (0.31 to 9.76)	
SMZL	0 (0)	5 (100)	60	---	
Other	3 (21.43)	11 (78.57)	50.64	0.43 (0.08 to 2.34)	
Stage					
I	15 (22.73)	51 (77.27)	50.58	Ref	<0.001
II	12 (25.53)	35 (74.47)	48.55	1.18 (0.66 to 2.12)	
III	14 (50%)	14 (50)	36.79	2.78 (1.33 to 5.83)	
IV	39 (54.17)	33 (45.83)	35.54	3.05 (1.76 to 5.26)	

Table 4. Progression-free Survival Analysis of Patients According to NHL Histopathological Subtype and Stage

Item	N of events (%)	N. Censored (%)	Mean (months)	HR (95%CI)	Log-rank P-value
Histopathological subtype					
AITCL	2 (40)	3 (60)	38.4	Ref	0.076
DLBCL	59 (39.86)	89 (60.14)	39.7	0.933 (0.20 to 4.18)	
MCL	4 (40)	6 (60)	43.9	0.83 (0.14 to 4.78)	
MZL	2 (14.29)	12 (85.71)	52.21	0.29 (0.05 to 1.57)	
PTCL NOS	11 (64.71)	6 (35.29)	26.94	1.71 (0.31 to 9.26)	
SMZL	0 (0)	5 (100)	60	---	
Other	4 (28.57)	10 (71.43)	46.21	0.57 (0.11 to 3.05)	
Stage					
I	16 (24.24)	50 (75.76)	48.47	Ref	<0.001
II	12 (25.53)	35 (74.47)	47	1.13 (0.64 to 2.02)	
III	15 (53.57)	13 (46.43)	33.46	2.85 (1.37 to 5.92)	
IV	39 (54.17)	33 (45.83)	31.92	2.93 (1.71 to 5.02)	

HR: Hazard ratio, CI: Confidence interval, Statistical significance at P-value<0.05; HR could not be calculated due to the absence of events (0%) in the SMZL group

factors not yet characterized. The clinical presentation of patients in this cohort was marked by features suggestive of a high disease burden. The high frequency of abdominal involvement (51.2%) and organomegaly (51.6%) points towards significant visceral disease, aligning with regional data where extranodal presentations are common [9]. A critical finding is that nearly half of the patients (46.9%) presented with advanced-stage (III or IV) disease at diagnosis, with Stage IV alone accounting for 33.8%. This stage distribution, which is more severe than the 25% Stage IV reported in the Aseer region of Saudi Arabia [9] but similar to the 48.8% Stage IV in Riyadh [10], suggests that diagnosis often occurs at a late point in the disease course, which has direct implications for prognosis and treatment strategy and underscores a critical healthcare challenge shared across the region. Despite this advanced presentation, the initial treatment response to first-line chemotherapy was notably high, with 70% achieving an interim complete response after 3 cycles. This indicates that these regimens can be effective even in patients with advanced disease within this setting, a finding that reinforces the importance of treatment access and completion, as highlighted in an Indian study where completed chemotherapy was a key factor for longer mean survival [11]. The slight decrease in response rate by the end of therapy to 66.2% is a common clinical observation, reflecting that a subset of patients who respond initially may not sustain that response, a trend often linked to the biological aggressiveness of the predominant DLBCL subtype and advanced stage at presentation.

The analysis across different NHL subtypes revealed a fundamental contrast between baseline presentation and therapeutic outcome. The subgroups were well-balanced in terms of demographics, basic laboratory parameters, and crucially, the stage at diagnosis, with no statistically significant differences (all p-values >0.05). This similarity

at presentation allows for a more focused interpretation of subsequent differences in outcome, a methodological strength not always highlighted in regional studies where stage distribution can vary widely by subtype, as seen in an Indian cohort where DLBCL cases were predominantly Stage 1A [11]. The most critical finding from this analysis is the profound and statistically significant disparity in treatment response. PTCL NOS emerged as a distinct high-risk entity, demonstrating markedly poor chemo-sensitivity. With only 35.3% of patients achieving an interim complete response and 29.4% achieving an end-of-therapy response, this subtype presents a major therapeutic challenge within our cohort. This poor response is a primary factor that would logically contribute to unfavorable survival outcomes and underscores a subtype-specific vulnerability that may be amplified in our setting, in contrast to studies where response disparities were less pronounced among subtypes [12]. This finding aligns with current international treatment guidelines, which recognize PTCL NOS as a particularly challenging subtype with poor outcomes to conventional chemotherapy. Both the National Comprehensive Cancer Network (NCCN) [13] and European Society for Medical Oncology (ESMO) guidelines [14] emphasize that for PTCL NOS, enrollment in clinical trials should be prioritized whenever possible, and for eligible patients, consolidation with autologous stem cell transplantation in first remission is recommended . In contrast, the indolent B-cell lymphomas, specifically MZL and SMZL, exhibited exceptional sensitivity to first-line chemotherapy, with response rates of 92.9% and 100%, respectively. It is important to note that all patients with MZL and SMZL in this cohort were symptomatic at presentation, meeting criteria for treatment initiation according to standard guidelines. For SMZL specifically, indications for treatment included symptomatic splenomegaly, cytopenias, or systemic symptoms. No patient underwent splenectomy as a primary treatment modality; all received immunochemotherapy with rituximab monotherapy as outlined in the Methods section. This excellent response profile aligns with the expected behavior of these subtypes and establishes a benchmark for treatment success in our setting, and it notably exceeds the overall first-line complete remission rate of 77.5% reported in a Turkish series, highlighting the efficacy achievable for specific indolent lymphomas even within broader regional treatment frameworks [12]. The consistency of this pattern from the interim assessment to the end of therapy reinforces the robustness of these observations. Furthermore, a higher proportion of PTCL NOS patients presented with Stage III disease (23.5%) compared to other subtypes, a trend that, while not statistically significant in our cohort, aligns with its known aggressive nature. This pattern, observed alongside its poor treatment response, indicates that PTCL NOS in our population presents a dual clinical challenge: a tendency for more advanced disease at diagnosis coupled with intrinsic resistance to standard chemotherapy. This observation reinforces the high-risk profile of this subtype and underscores the need for heightened clinical vigilance and alternative treatment strategies from the point of diagnosis [15].

The OS analysis reveals the real-world impact of the patterns observed in disease presentation and treatment response. Patients with different NHL subtypes had significantly different OS (p=0.043), a direct result of how well each subtype responded to treatment. The poor chemo-sensitivity of PTCL NOS translated into the most severe survival outcomes, with 64.71% of patients dying from the disease and a mean survival of just 30.53 months. This solidifies its identification as the highest-risk subtype within this population, a finding that aligns with and intensifies global observations where PTCL-NOS consistently portends a poor prognosis, with studies noting its negative impact on survival even after initial treatment and very poor outcomes upon relapse [16, 17]. Conversely, the excellent treatment response in SMZL correlated with flawless survival in our cohort, with no deaths (0%) and a mean survival of 60 months. This outcome surpasses the high 5-year relative survival rates reported in Western registries and highlights the curative potential of frontline therapy for this indolent subtype in our setting [18, 19]. It should be noted, however, that the long-term risk of histologic transformation, a risk that is particularly high in SMZL, may influence survival outcomes beyond the follow-up duration of this study. The survival of DLBCL patients, representing the majority, occupied an intermediate position, with an event rate of

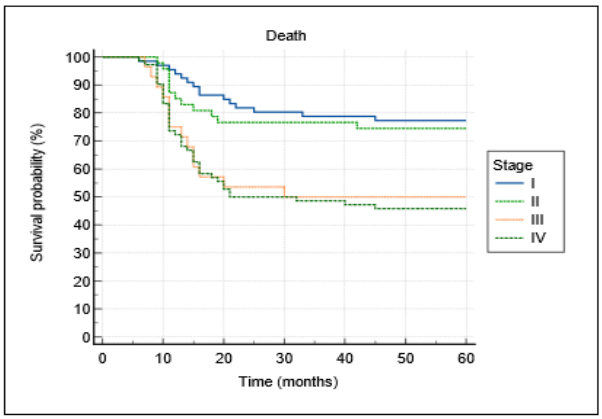

Figure 3. Kaplan-Meier Curve for Overall Survival Analysis of NHL Patients According to Stage

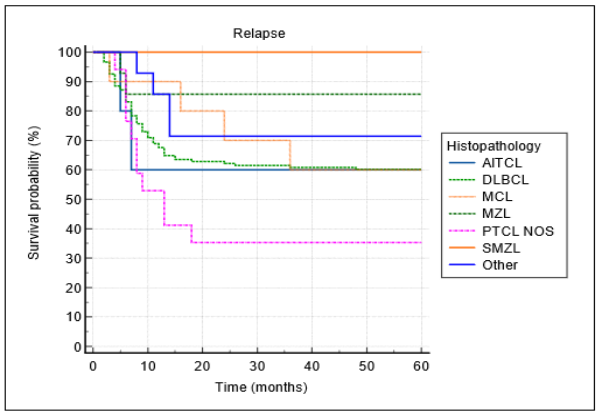

Figure 4. Kaplan-Meier Curve for Progression-free Survival Analysis of NHL Patients According to Histopathological Subtype

Table 5. Multivariable Cox Proportional Hazards Regression Analysis for Overall Survival (OS) and Progression-Free Survival (PFS)

Variable	N (%)	Univariable HR — OS (95% CI, p-value)	Multivariable HR — OS (95% CI, p-value)	Univariable HR — PFS (95% CI, p-value)	Multivariable HR — PFS (95% CI, p-value)
Stage					
I (ref)	66 (31.0)	—	—	—	—
II	47 (22.1)	1.19 (0.56–2.55)	1.21 (0.57–2.60)	1.14 (0.54-2.40) p=0.736	1.16 (0.55–2.46)
		p=0.651	p=0.618		p=0.698
III	28 (13.1)	2.85 (1.37–5.91)	2.68 (1.28–5.58)	2.91 (1.44-5.89) p=0.003	2.74 (1.34–5.57)
		p=0.005	p=0.009		p=0.006
IV	72 (33.8)	3.13 (1.72–5.68)	2.73 (1.50–5.00)	3.00 (1.67-5.37 p<0.001)	2.65 (1.47–4.78)
		p<0.001	p=0.001		p=0.001
Histological subtype					
DLBCL (ref)	148 (69.5)	—	—		—
PTCL NOS group	22 (10.3)	1.75 (0.96–3.20)	1.34 (0.72–2.48)	1.68 (0.92-3.07)	1.28 (0.69–2.37)
(AITCL + PTCL NOS)		p=0.067	p=0.356	p=0.090	p=0.432
Indolent B-cell	19 (8.9)	0.23 (0.06–0.93)	0.22 (0.05–0.89)	0.22 (0.05-0.91)	0.21 (0.05–0.88)
(MZL + SMZL)		p=0.039	p=0.034	p=0.036	p=0.033
Other (MCL + Other)	24 (11.3)	0.64 (0.29–1.40)	0.56 (0.25–1.24)	0.72 (0.34-1.50)	0.64 (0.30–1.36)
		p=0.261	p=0.153	p=0.377	p=0.249
Sex					
Male (ref)	117 (54.9)	—	—		—
Female	96 (45.1)	0.97 (0.63–1.51)	0.89 (0.57–1.39)	1.02 (0.66-1.58)	0.96 (0.61–1.49)
		p=0.903	p=0.603	p=0.915	p=0.843
Age at diagnosis	Mean 51.5 (SD 18.4)	1.01 (1.00–1.03)	1.01 (1.00–1.03)	1.01 (1.00-1.03)	1.01 (1.00–1.03)
(per year, continuous)		p=0.019	p=0.034	p=0.026	p=0.043

HR: Hazard Ratio; CI: Confidence Interval; OS: Overall Survival; PFS: Progression-Free Survival; DLBCL: Diffuse Large B-cell Lymphoma; PTCL NOS: Peripheral T-cell Lymphoma, Not Otherwise Specified; AITCL: Angioimmunoblastic T-cell Lymphoma; MZL: Marginal Zone Lymphoma; SMZL: Splenic Marginal Zone Lymphoma; MCL: Mantle Cell Lymphoma. Bold cells indicate statistically significant results (p<0.05).

39.19% and a mean survival of 42.3 months, a result that contextualizes the OS burden within a cohort dominated by this aggressive but treatable subtype. Beyond subtype, the analysis clearly identifies the Ann Arbor stage at diagnosis as the most powerful prognostic determinant in this cohort (p <0.001). The hazard for death increased dramatically, approximately threefold, for patients presenting with Stage III (HR=2.78 (95% CI: 1.33-5.83)) or IV (HR=3.05 (95% CI: 1.76-5.26)) disease compared to those with Stage I. This creates a clear clinical threshold; while survival outcomes between early stages (I and II) were comparable, advancement to Stage III marked a pivotal point associated with a steep decline in survival probability, as seen in the drop in mean survival from 50.58 months in Stage I to 35.54 months in Stage IV. This finding forcefully highlights that efforts to improve survival outcomes must address the systemic challenge of late diagnosis, a universal theme echoed in studies from Brunei Darussalam [20] and Saudi Arabia [10] where advanced stage was similarly linked to significantly increased mortality risk and poorer survival . The clear prognosis for advanced-stage disease in our cohort underscores an urgent need for public health strategies aimed at earlier detection, as this modifiable factor appears to exert a stronger influence on survival than even the inherent biology of the most common subtype, DLBCL.

The analysis of PFS reinforces and refines the findings established by the OS data. The trend observed across subtypes, though not meeting the threshold for statistical significance (p=0.076), consistently mirrors the OS pattern. PTCL NOS exhibited the most rapid disease progression or relapse, with 64.71% experiencing an event and the shortest mean time to progression of 26.94 months. This pattern of early treatment failure in aggressive T-cell lymphomas is supported by regional studies, such as one from Iran which also identified the T-cell subtype and advanced stage as key determinants of shorter survival [21]. The sustained excellent outcome for SMZL, with no progression events (0%) recorded

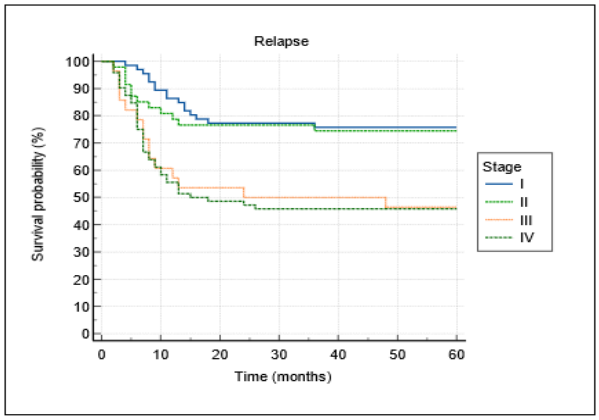

Figure 5. Kaplan-Meier Curve for Progression-free Survival Analysis of NHL Patients According to NHL Stage

and a mean PFS of 60 months, confirms the durable effectiveness of therapy for this indolent subtype in our setting, contrasting with the more variable PFS rates (e.g., 69.7% at 2-years) reported for other indolent lymphomas like follicular lymphoma in different populations [22]. The PFS analysis most powerfully confirms the main prognostic role of disease stage ($p < 0.001$). The impact of advanced stage at diagnosis was nearly identical in magnitude for both progression-free and overall survival, with hazards increasing approximately threefold for Stage III HR 2.85 (95% CI: 1.37-5.92) and IV HR 2.93 (95% CI: 1.71-5.02) disease. This indicates that the poor prognosis associated with late-stage presentation is mechanistically rooted in an early failure of first-line therapy. This finding is strongly consistent with the Indian study where 77.4% of relapses occurred in patients diagnosed at Stage III or higher, directly linking advanced stage to treatment failure [11]. The sharp decline in mean PFS from 48.47 months in Stage I to approximately 33-32 months in Stages III and IV quantifies this accelerated treatment failure. The consistent finding that Stage II (HR 1.13 (95% CI: 0.64-2.02)) disease did not confer a significantly worse prognosis than Stage I, for both PFS and OS, suggests that the major negative shift in disease behavior occurs at the transition to Stage III. This threshold effect aligns with other studies where Stage III/IV, but not necessarily Stage II, was an independent risk factor for worse survival in extranodal lymphomas [23]. Therefore, our findings support a risk-adapted approach to treatment. Based on our data, the similar outcomes for Stage I and II disease suggest that Stage II NHL may be managed effectively with standard early-stage protocols. Conversely, the pronounced survival detriment observed at Stage III in our cohort underscores the need for more intensive therapeutic strategies. This could involve considering intensified regimens, such as those incorporating etoposide or consolidative stem cell transplantation as suggested by a study in PTCL [24], which may be relevant for high-risk, advanced-stage B-cell lymphomas in our context.

Multivariable analysis confirmed that advanced stage (III/IV) was the dominant independent predictor of both inferior OS and PFS, with adjusted hazard ratios of approximately 2.7 (Stage III: aHR= 2.68, 95% CI: 1.28-5.58; Stage IV: aHR =2.73, 95% CI: 1.50-5.00 for OS). Indolent B-cell lymphomas (MZL/SMZL) retained their favorable prognosis even after adjustment (aHR= 0.22, 95% CI: 0.05-0.89 for OS; aHR= 0.21, 95% CI :0.05-0.88 for PFS). These findings underscore that the survival disadvantage of late-stage disease is not explained by confounding factors, reinforcing the critical need for earlier diagnosis.

Strengths and Limitations

This study possesses notable strengths that enhance the validity of its findings. The research provides a comprehensive, real-world assessment of NHL in a previously understudied region, capturing the full spectrum of patients managed at a major tertiary referral center over a multi-year period. The application of strict, predefined inclusion criteria ensured a homogeneous cohort of patients who received definitive first-line therapy at the study site, which improves the internal consistency of the treatment response and survival analyses. Moreover, the use of a standardized data collection form and the systematic capture of a wide range of clinicopathological and outcome variables allowed for a robust, multi-faceted analysis. Certain limitations inherent to the retrospective, single-center design must be acknowledged. The findings are influenced by the specific referral patterns and diagnostic capabilities of the center, which may not be fully representative of the broader community, potentially limiting generalizability to primary care settings or other regions. The reliance on archived medical records introduces the possibility of incomplete data or variability in documentation practices over time, particularly for details not routinely captured in standard clinic notes. The absence of a formal, pre-study sample size calculation means the study was powered by the available cohort rather than a specific effect size, which may affect the statistical power to detect delicate differences, particularly among the rarer lymphoma subtypes. Additionally, while survival data were collected, the analysis did not account for all potential confounding prognostic factors beyond stage and subtype, such as specific chemotherapy regimens, dose intensities, or the molecular profile of tumors, which could provide a more nuanced understanding of the outcomes observed. Related to this, we were unable to calculate established prognostic indices like the International Prognostic Index (IPI) for DLBCL patients, as key components (performance status and LDH levels) were not consistently available in the retrospective records. This limits direct comparison with studies reporting IPI-stratified outcomes and represents an important area for prospective data collection in future research.

In conclusion, this study establishes the clinicopathological profile of NHL in Southern Iraq, revealing a high burden of aggressive disease characterized by a DLBCL predominance and frequent late-stage presentation. While treatment is effective overall, outcomes are sharply stratified by histology and, most critically, by disease stage. PTCL NOS is identified as a high-risk subtype with poor chemo-sensitivity, whereas indolent B-cell lymphomas have excellent outcomes. The pronounced survival declines at Stage III underscores late diagnosis as the paramount challenge. These findings necessitate a dual-focused strategy: public health measures for earlier detection and the development of optimized, subtype-specific treatment protocols to improve survival.

Clinical Implications

The findings from this cohort translate into actionable insights for patient management. The alarming rate of advanced-stage diagnosis underscores a critical need to overhaul the diagnostic journey, prioritizing faster access to imaging and biopsy to shift the stage distribution toward earlier, more curable disease. Clinically, the stark disparity in outcomes demands a subtype-aware approach at diagnosis. The poor chemo-sensitivity of

PTCL NOS should prompt clinicians to consider this subtype a therapeutic emergency, warranting early discussion of protocol-based treatment intensification, including consideration of consolidation with autologous stem cell transplantation (ASCT) in first remission for eligible patients, as well as clinical trial enrollment. Conversely, the documented excellence of standard therapy for marginal zone lymphomas supports their management with conventional immunochemotherapy, avoiding overtreatment. The powerful, stage-dependent gradient in survival provides a clear and immediate tool for prognostication and resource allocation, identifying patients with Stage III/IV disease as a high-priority group requiring more vigilant monitoring and comprehensive support.

Future Research Directions

This study outlines several key priorities for subsequent investigation. Establishing a prospective, population-based national lymphoma registry is fundamental to confirm the epidemiological patterns observed here and to explore underlying etiological factors. Translational research focusing on the molecular characterization of prevalent subtypes, particularly the high-risk PTCL NOS and the dominant DLBCL cases, is needed to uncover biomarkers for risk stratification and novel therapeutic targets. Operational research should evaluate the implementation and impact of interventions designed to reduce diagnostic delays, such as public symptom awareness campaigns and optimized referral pathways. Furthermore, the clinical challenge posed by PTCL NOS specifically calls for the design and conduction of tailored clinical trials within the region to test modified frontline regimens, with particular emphasis on incorporating novel agents that have shown promise in this subtype, such as histone deacetylase inhibitors (e.g., romidepsin, belinostat), antifolates (pralatrexate), or antibody-drug conjugates (brentuximab vedotin for CD30-positive cases). For the predominant DLBCL population, future studies should explore the feasibility and efficacy of incorporating targeted therapies that may be cost-effective and feasible in resource-limited settings, including polatuzumab vedotin-based regimens or lenalidomide for non-germinal center B-cell (non-GCB) subtypes, as well as exploring biosimilar rituximab to maintain cost-effectiveness. Finally, extending follow-up to capture long-term outcomes, including the risk of late transformation in indolent lymphomas and the durability of response in aggressive subtypes, will be essential for refining lifelong care strategies.

Acknowledgments

Statement of Transparency and Principles

• The authors declare no conflict of interest.

• The study was approved by the Research Ethics Committee of the authors' affiliated institution.

• The study data are available upon reasonable request.

• All authors contributed to the implementation of this research.

References

1. Non-Hodgkin Lymphoma, International Agency for Research on Cancer, GLOBOCAN. World Health Organization. 2022. Available from: https://gco.iarc.fr/today/en/fact-sheets-cancers...
2. Xu J, Shi Y, Cui M. Development and validation of a hierarchical approach for lymphoma classification using immunohistochemical markers. Cancer Med. 2024;13(20). https://doi.org/10.1002/cam4.70120
3. Lisson C, Götz M, Wolf D. Non-Hodgkin's lymphoma classification using 3D radiomics machine learning models for precision imaging in oncology. BMC Med Imaging. 2025;25(1):435 10 1186 12880–025–02006–3.
4. Thandra K, Barsouk A, Saginala K. Epidemiology of Non-Hodgkin's Lymphoma. Med Sci (Basel. 2021;9(1).
5. Bamodu OA, Chung C. Cancer Care Disparities: Overcoming Barriers to Cancer Control in Low- and Middle-Income Countries. JCO Global Oncology.2024(10). https://doi.org/10.1200/go.23.00439
6. Luo J, Craver A, Bahl K. Etiology of non-Hodgkin lymphoma: A review from epidemiologic studies. J Natl Cancer Cent. 2022;2(4):226–234 10 1016 2022 08 003.
7. Zisis K, Pavi E, Geitona M. Real-world data: a comprehensive literature review on the barriers, challenges, and opportunities associated with their inclusion in the health technology assessment process. Journal of Pharmacy & Pharmaceutical Sciences. 2024;27:– 2024 10 3389 2024 12302.
8. Touma E, Antoun L, Hallit S. Non Hodgkin lymphoma in Lebanon: a retrospective epidemiological study between 1984 and 2019. 2021;21.
9. Alyahya N, Adiga B, Alwadei A. The clinico-pathological profile of non-Hodgkin's lymphoma in Aseer region of Saudi Arabia. BMC Research Notes. 2019;12(1):418. https://doi.org/10.1186/s13104-019-4447-1
10. Mahmood N, Aamir S, Alseraye A. A Retrospective Analysis of the Clinicopathological Spectrum and Survival Outcome of Non-Hodgkin Lymphoma From a Tertiary Care Hospital in Saudi Arabia. Cureus. 2025;17(11):97251 10 7759 97251.
11. Wani U, Jeelani U, Aziz S. Evaluation of NHL subtypes, staging, and prognostic factors: A single-centric retrospective cohort study. J Cancer Res Ther. 2025;21(1):34–39 10 4103 25 24.
12. Yildirim R, Sincan G. The clinicopathologic features and response to treatment of patients with Nonhodgkin Lymphoma: A single-center experiment in Turkey. Pak J Med Sci. 2019;35(1):82–85 10 12669 35 1 415.
13. NCCN Guidelines: Treatment by Cancer Type, (NCCN), National Comprehensive Cancer Network. 2026. Available from: https://www.nccn.org/guidelines/category_1..
14. ESMO Clinical Practice Guideline: Lymphomas, European Society for Medical Oncology (ESMO). 2026. Available from: https://www.esmo.org/content/search?searchText=PTCL...
15. Iqbal, Zafar, Batoul Mustafa Almusawi, Fatimah Fouad Alhashim, et al., Demographic and Clinical Characteristics of Lymphoma Patients from Al-Ahsa, Saudi Arabia. Journal of Applied Hematology, 2020. 11(3)https://journals.lww.com/jaht/fulltext/2020/11030/demographic_and_clinical_characteristics_of.6.aspx.
16. Chihara D, Fanale M, Miranda R. The survival outcome of patients with relapsed/refractory peripheral T-cell lymphoma-not otherwise specified and angioimmunoblastic T-cell lymphoma. Br J Haematol. 2017;176(5):750–758 10 1111 14477.
17. Gao H, Ji X, Liu X, Mi L, Liu W, Wang X, Zhu J, Song Y.

Conditional survival and hazards of death for peripheral T-cell lymphomas. Aging. 2021;13:10225–10239.
18. Vaughn J, Pinheiro L, Olszewski A. Survival of patients with marginal zone lymphoma in the United States: A population-based cohort study (2000 to 2017. Am J Hematol. 2021;96(4):123– 126 10 1002 26103.
19. Xie S, Yu Z, Feng A. Analysis and prediction of relative survival trends in patients with non-Hodgkin lymphoma in the United States using a model-based period analysis method. Front Oncol. 2022;12:942122 10 3389 2022 942122.
20. Mwalim M, Leong E, Ong S. Non-Hodgkin lymphoma incidence, mortality, and survival trends in Brunei Darussalam from 2011 to 2020. BMC Cancer. 2024;24(1):994 10 1186 12885–024–12725–5.
21. Fallahzadeh H, Mortazavizadeh SMR, Momayyezi M. Bayesian Parametric Survival Analysis of Patients With Non-Hodgkin's Lymphoma in Yazd, Iran, During 2009-2019. Epidemiol Health System J. 2024;11(2):88–93 10 34172 26111.
22. Su Y, Hu Q, Zhao W. Clinical features and prognosis analysis of patients with follicular lymphoma: a real-world study in China. Ann Hematol. 2025;104(10):5257–5271 10 1007 00277–025–06617–2.
23. Lv J, Jiang Y, Yu T. Clinical characteristics and prognostic analysis of primary extranodal non-Hodgkin lymphoma of the head and neck. Aging (Albany NY. 2024;.
24. Baek D, Lee J, Jang Y. Real-world data on long-term outcomes in patients with T-cell lymphomas: a nationwide study of Korea. Blood Res. 2025;60(1):47 10 1007 44313–