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Original Research

Clinical Characteristics, Treatment Outcomes, and Prognostic Factors in Hodgkin Lymphoma: A Retrospective Cohort Study at King Khalid Hospital, Najran

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Introduction: Hodgkin lymphoma (HL) is characterized by heterogeneous clinical outcomes influenced by a complex interplay of biological and clinical factors. This study aims to delineate presentation patterns, treatment responses, and prognostic indicators within a Saudi Arabian cohort, with consideration of regional epidemiological variations.

Materials and Methods: A retrospective cohort study was conducted involving 23 patients diagnosed with HL at King Khalid Hospital, Najran, between 2014 and 2021. Diagnoses were established according to the World Health Organization (WHO) 2017 classification. Treatment responses were assessed after every two chemotherapy cycles using RECIST version 1.1, due to limited availability of PET imaging modalities. Progression-free survival (PFS) predictors were analyzed using univariate Cox proportional hazards regression, with explicit acknowledgment of the limited statistical precision stemming from the small sample size.

Results: The mean age was 36.3 ± 16.3 years, with males constituting 60.9% of the cohort. Nodular sclerosis was the most common histological subtype (65.2%), and stage III was the most frequent at diagnosis (43.5%). The ABVD chemotherapy regimen yielded an objective response rate of 78.3%, with a complete response observed in 43.5% of patients. At a median follow-up of 33 months, univariate analysis identified significant associations between reduced PFS and advanced disease stage (III/IV vs. I/II; hazard ratio [HR] 3.26, 95% confidence interval [CI] 0.34–31.35; p=0.001), high International Prognostic Score (IPS ≥3 vs.

0–2; HR 17.93, 95% CI 1.85–173.94; p=0.013), and increasing age (per year; HR 1.21, 95% CI 1.10–1.34; p<0.001).

Conclusions: In this cohort, advanced disease stage, elevated IPS, and increasing age were associated with inferior PFS, consistent with established prognostic models despite regional epidemiological differences. These findings underscore the necessity for larger, prospective studies to validate risk stratification tools and optimize management strategies in similar healthcare settings.

Introduction

Hodgkin lymphoma (HL) is a hematologic malignancy exhibiting marked clinical and biological heterogeneity, reflected in variable incidence patterns, prognostic factors, and therapeutic outcomes across global populations [1, 2]. Therapeutic advances have improved 5-year survival rates to over 80% in high-income countries; however, significant geographical disparities persist, underscoring the need for region-specific data to optimize management strategies [3-5].

In Saudi Arabia, HL displays distinct epidemiological characteristics. The age-standardized incidence rate exceeds that of neighboring Gulf countries, with HL accounting for approximately 3.6% of all malignancies nationally [6, 7]. National cancer registry data from 1975 to 2015 indicate HL's rise from the eighth to the sixth most common cancer, signalling a growing disease burden [6, 8]. Saudi patients are diagnosed at a younger median age (30–40 years) compared to Western populations (55–65 years) and exhibit a higher prevalence of Epstein-Barr virus (EBV) association [7-12]. These patterns are consistent with other Middle Eastern populations but contrast with Europe and North America, suggesting underlying biological and environmental determinants that impact disease behavior and prognosis [5, 13, 14].

At the molecular level, classical HL frequently involves dysregulated B-cell signaling pathways, often related to EBV infection, particularly in immunocompromised populations [15]. Prognostic models such as the International Prognostic Score (IPS) show variable predictive performance globally; Middle Eastern cohorts report lower 5-year survival rates (70–75%) compared to Western cohorts (85–90%) and differ in the prevalence of high-risk clinical features [5, 16]. Survival outcomes and prognostic factor distributions in Middle Eastern patients generally reflect an intermediate pattern superior to that reported in low-resource settings yet below the benchmarks established in Western high-income countries. These variations arise from differences in healthcare infrastructure, accessibility to advanced diagnostics and treatments such as PET imaging and bone marrow transplantation, and the burden of adverse prognostic factors [17, 18].

Given the unique clinical and epidemiological features of HL in Saudi Arabia, there is a need for detailed local data on patient characteristics, treatment outcomes, and prognostic factors. This retrospective cohort study conducted at King Khalid Hospital, Najran, aims to fill this gap by investigating these aspects in HL patients. The findings are intended to improve understanding and guide regionally appropriate management strategies.

Materials and Methods

Study Design and Patient Selection

This retrospective cohort study was conducted at the Oncology Centre of King Khalid Hospital in Najran, Saudi Arabia, adhering to STROBE guidelines for observational research. We included all

consecutive adult patients (aged ≥18 years) with histologically confirmed Hodgkin lymphoma diagnosed between January 2014 and December 2021. Patients were excluded if they had a prior malignancy, incomplete staging workup, or were lost to follow-up prior to treatment response assessment. Of 42 initially screened individuals, 19 were excluded due to incomplete clinical data (n=8), concomitant malignancies (n=7), or loss to follow-up (n=4), resulting in a final analytical cohort of 23 treatment-naïve patients (Figure 1A).

Figure 1. Patient Flow and Treatment Response. (A) Flow chart depicting patient inclusion and exclusion criteria, leading to the final cohort of 23 Hodgkin lymphoma patients analyzed in the study. (B) Bar graph illustrating treatment response after first-line therapy according to RECIST 1.1 criteria. The overall objective response rate (ORR) was 78.3%, comprising complete response (CR; 43.5%), partial response (PR; 34.8%), stable disease (SD; 4.3%), and progressive disease (PD; 17.4%).

The study protocol was approved by the Institutional Review Board (KKH/IRB/2021-17), with a waiver of informed consent granted given the retrospective design.

Histopathological Classification

Diagnostic specimens were evaluated according to the 2017 World Health Organization classification of hematopoietic and lymphoid tumors [19, 20]. Two independent hematopathologists reviewed all cases utilizing standardized immunohistochemical panels including CD30, CD15, PAX5, and CD20. Any discordant interpretations were resolved by consensus review. The Revised European-American Lymphoma (REAL) classification system was employed to differentiate classical Hodgkin lymphoma (CHL) from nodular lymphocyte-predominant HL (NLPHL) [21].

Treatment Protocols

First-line chemotherapy predominantly consisted of the ABVD regimen (doxorubicin 25 mg/m^2, bleomycin 10 U/m^2, vinblastine 6 mg/m^2, and dacarbazine 375 mg/m^2) administered biweekly [22]. Treatment duration, ranging from four to eight cycles, was tailored based on disease stage and interim response assessments. Patients presenting with bulky disease defined as mediastinal mass exceeding one-third of thoracic diameter or nodal mass≥10 cm or residual masses after chemotherapy completion, received consolidative involved-field radiotherapy (20–36 Gy). Salvage chemotherapy regimens, such as ICE (ifosfamide, carboplatin, etoposide) or DHAP (dexamethasone, cytarabine, cisplatin), were employed for patients with refractory or relapsed disease, following review by a multidisciplinary tumor board [22].

Response Assessment Criteria

Treatment response was evaluated after every two chemotherapy cycles using the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. This computed tomography (CT)-based approach was selected due to limited access to positron emission tomography (PET) imaging during the study period, consistent with lymphoma response assessment standards in resource-constrained settings [23, 24]. Objective response categories included complete response (CR), defined as disappearance of all target lesions; partial response (PR), indicating a ≥30% reduction in the sum of target lesions; stable disease (SD), where neither PR nor progressive disease (PD) criteria were met; and PD, characterized by ≥20% increase in existing lesions or emergence of new lesions. The objective response rate (ORR) combined CR and PR rates [25].

Prognostic Assessment

The International Prognostic Score (IPS) was calculated for each patient based on seven adverse clinical and laboratory factors: male sex, age ≥45 years, Ann Arbor stage IV, hemoglobin <10.5 g/dL, white blood cell count ≥15×10^9/L, lymphocyte count <0.6×10^9/L or <8%, and albumin <40 g/L [26]. Patients were stratified into low-risk (IPS 0–2) and high-risk (IPS ≥3) groups. Definitions of disease status included refractory disease as<50% reduction in lesion size after 90 days of treatment, progressive disease as new lesions or ≥50% increase in existing lesions, and relapse defined by new lesions following confirmed CR [27].

Study outcomes

The primary outcomes of interest were treatment response rates, including complete response, partial response, and overall objective response rate, as well as disease progression events. Secondary outcomes included identifying clinicopathological factors associated with decreased progression-free survival (PFS).

Data Collection and Statistical Analysis

Demographic, clinical, and laboratory data were retrospectively extracted from electronic health records. Progression-free survival (PFS) was calculated from diagnosis until disease progression, relapse, or death from any cause. Due to the modest cohort size (N=23), univariate Cox proportional hazards regression analyses were conducted to identify predictors of PFS, with acknowledgment of limited power to perform multivariate modeling. Continuous variables were reported as means ± standard deviations or medians with interquartile ranges depending on data distribution; categorical variables were presented as frequencies and percentages. Kaplan–Meier survival analyses with log-rank tests compared survival curves. All statistical analyses were performed using IBM SPSS Statistics version 22, considering p-values <0.05 (two-sided) as statistically significant. Hazard ratios (HRs) and 95% confidence intervals (CIs) are presented, with explicit note of reduced estimate precision related to sample size constraints.

Ethical Considerations

Patient confidentiality was ensured by data anonymization and secure storage on password-protected institutional servers, in compliance with the Declaration of Helsinki. The Institutional Review Board approved the study protocol and waived the requirement for individual informed consent due to its retrospective nature.

Results

Patient Characteristics

The final analytical cohort comprising 23 patients diagnosed with Hodgkin lymphoma, as shown in the patient flow diagram (Figure 1A). The mean age at diagnosis was 36.3 ± 16.3 years (median 33 years; range 19–90 years). For reporting clarity, age groups were categorized as <30 years (39.1%, 9/23), 30–49 years (43.5%, 10/23), and ≥50 years (17.4%, 4/23). The cohort exhibited a male predominance (60.9%, 14/23), resulting in a male-to-female ratio of approximately 1.5:1. Comorbidities included HIV coinfection in 13.0% (3/23) and hepatitis B or C coinfection in 8.7% (2/23). Diabetes mellitus and hypertension were each present in 8.7% (2/23) of patients.

Clinically, lymphadenopathy was the most common presenting symptom (73.9%, 17/23), with lymph nodes serving as the primary disease site in 78.3% (18/23). Histopathological analysis identified classical Hodgkin lymphoma (CHL) as the predominant subtype, accounting for 87.0% (20/23) of cases, with nodular sclerosis representing the most frequent histologic variant (65.2%, 15/23). Advanced-stage disease (Ann Arbor stage III/IV) was observed in 43.5% (10/23) at diagnosis. Detailed demographic and clinicopathological characteristics are summarized in Table 1.

Characteristic	Value
Age at diagnosis (years)	Mean ± SD: 36.3 ± 16.3
	Median (range): 33 (19–90)
Age distribution, n (%)	
<30 years	9 (39.1)
30–49 years	10 (43.5)
≥50 years	4 (17.4)
Sex, n (%)	Female: 9 (39.1)
	Male: 14 (60.9)
Comorbidities, n (%)	
HIV co-infection†	3 (13.0)
Hepatitis B/C co-infection	2 (8.7)
Diabetes mellitus	2 (8.7)
Hypertension	2 (8.7)
Other‡	3 (13.0)
Presenting symptoms, n (%)	
Lymphadenopathy	17 (73.9)
Neck swelling	10 (43.5)
Weight loss	9 (39.1)
Fever	8 (34.8)
Night sweats	5 (21.7)
Abdominal distension	2 (8.7)
Histologic classification, n (%)	
Classical HL	20 (87.0)
	3 (13.0)
Histologic subtype, n (%)	
Nodular sclerosis	15 (65.2)
Mixed cellularity	8 (34.8)
Primary disease site, n (%)	
Lymph node	18 (78.3)
Nasopharynx	2 (8.7)
Liver	2 (8.7)
Spine	1 (4.3)
Ann Arbor stage, n (%)	
I	8 (34.8)
II	4 (17.4)
III	10 (43.5)
IV	1 (4.3)

Table 1. Demographic and Clinicopathological Characteristics of Hodgkin Lymphoma Patients (N=23).

Abbreviations: HL, Hodgkin lymphoma; HIV, human immunodeficiency virus; SD, standard deviation. Notes: Age categories consolidated for clarity per reviewer suggestion. Continuous

variables presented as mean ± SD or median (range); categorical variables as n (%). †HIV co-infection includes patients co-infected with hepatitis B (n=3) or hepatitis C (n=2). ‡Other comorbidities include autoimmune disorders (n=1), asthma (n=1), and chronic kidney disease (n=1).

Baseline Laboratory Parameters

Baseline hematologic parameters were generally within normal reference ranges for the majority of patients. Normal hemoglobin levels were present in 65.2% (15/23), while normal counts for white blood cells (WBC) and platelets were observed in 91.3% (21/23) of patients. Nevertheless, anemia was detected in 34.8% (8/23). Moreover, more than half of the cohort (52.2%, 12/23) exhibited elevated erythrocyte sedimentation rate (ESR > 50 mm/hour), indicative of systemic inflammation. The complete baseline laboratory profile is detailed in Table 2.

Parameter	Category	n (%)
Hemoglobin (g/dL)	Normal (F: ≥12; M: ≥13)	15 (65.2)
	Mild anemia (>10–<12)	2 (8.7)
	Moderate anemia (8–10)	4 (17.4)
	Severe anemia (6.5–8)	1 (4.3)
	Life-threatening anemia (<6.5)	1 (4.3)
White blood cells ($\times 10^9$/L)	Leukopenia (<4.0)	7 (30.4)
	Normal (4.0–11.0)	14 (60.9)
	Leukocytosis (>11.0)	2 (8.7)
Platelets ($\times 10^3$/μL)	Thrombocytopenia (<150)	1 (4.3)
	Normal (150–450)	21 (91.3)
	Thrombocytosis (>450)	1 (4.3)
Lymphocyte count (/μL)	Lymphopenia (<600)	3 (13.0)
	Normal (≥600)	20 (87.0)
ESR (mm/hour)	Normal (<30)	11 (47.8)
	Elevated (>50)	12 (52.2)
LDH (U/L)	Normal (≤280)	21 (91.3)
	Elevated (>280)	2 (8.7)

Table 2. Baseline Laboratory Parameters of Hodgkin Lymphoma Patients (N=23).

Abbreviations: ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase; F, female; M, male. Notes: Reference ranges: Hemoglobin ≥13 g/dL (male), ≥12 g/dL (female). Data presented as n (%).

Treatment Patterns and Initial Response

First-line chemotherapy was administered to 73.9% (17/23) of patients, with 15 receiving the ABVD regimen (doxorubicin, bleomycin, vinblastine, dacarbazine), completing an average of 5.1 ± 1.4 cycles (range 1–6). Salvage second-line chemotherapy was required in 26.1% (6/23). Combined modality therapy, incorporating chemotherapy followed by radiotherapy, was utilized in 30.4% (7/23) of cases.

Treatment response was assessed after every two chemotherapy cycles using RECIST version 1.1 criteria. The overall objective response rate (ORR), defined as complete response (CR) plus partial response (PR), was 78.3% (18/23), comprising 43.5% (10/23) CR and 34.8% (8/23) PR. Stable disease (SD) was documented in 4.3% (1/23) and progressive disease (PD) in 17.4% (4/23).

Treatment outcomes are summarized in Table 3 and illustrated in Figure 1B.

Variable	n (%) or value
Treatment modality	
First-line chemotherapy	17 (73.9)
Second-line chemotherapy	6 (26.1)
Radiotherapy	7 (30.4)
ABVD chemotherapy	
Patients receiving ABVD	17 (73.9)
Cycles completed, mean ± SD	5.1 ± 1.4
Range	1–6
Best treatment response†	
Complete response (CR)	10 (43.5)
Partial response (PR)	8 (34.8)
Stable disease (SD)	1 (4.3)
Progressive disease (PD)	4 (17.4)

Table 3. Treatment Patterns and Therapeutic Responses (N=23).

Abbreviations: ABVD, doxorubicin-bleomycin-vinblastine- dacarbazine; SD, standard deviation.
Notes: †Response assessed after every two chemotherapy cycles using RECIST v1.1 criteria. Data presented as n (%) or mean ± SD.

Disease Course and Survival Outcomes

The median follow-up duration was 33 months (IQR: 31–38), with a mean of 33.5 ± 7.8 months. Disease progression or recurrence occurred in 17.4% (4/23) of patients, with all events occurring within three years post- diagnosis (Figure 2A).

Figure 2. Progression-Free Survival (PFS) and Prognostic Factors. (A) Kaplan-Meier curve showing progression-free survival over a median follow-up period of 33 months (interquartile range 31–38 months). Cumulative incidence of disease progression or relapse events (17.4%) is indicated. (B) Forest plot summarizing univariate Cox proportional hazards regression analysis for predictors of PFS. Hazard ratios (HR) with 95% confidence intervals (CI) are displayed for variables including age, Ann Arbor stage, bulky disease, International Prognostic Score (IPS), sex, histologic subtype, and presence of B symptoms. Significant associations with poorer PFS were observed for increasing age, advanced stage, bulky disease, and high-risk IPS (≥3).

One patient (4.3%) received bone marrow transplantation upon relapse, while others were managed with salvage chemotherapy and/or radiotherapy. Kaplan-Meier analysis estimated median progression- free survival (PFS) at 33 months (IQR: 31–38) (Figure 2A). Univariate Cox proportional hazards regression identified several factors significantly associated with shorter PFS (Table 4, Figure 2B).

Variable	Subgroup	n (%)	HR (95% CI)	p-value
Sex	Female	9 (39.1)	Reference	0.561
	Male	14 (60.9)	1.96 (0.20–18.82)*	
Bulky disease	Absent	17 (73.9)	Reference	0.030*
	Present	6 (26.1)	2.65 (0.37–18.92)	
Histologic subtype	Mixed cellularity	8 (34.8)	Reference	0.384
	Nodular sclerosis	15 (65.2)	0.42 (0.06–2.98)	
Ann Arbor stage	I/II	11 (47.8)	Reference	0.001*
	III/IV	12 (52.2)	3.26 (0.34–31.35)	

IPS category	Low risk (0–2)	19 (82.6)	Reference	0.013*
	High risk (≥3)	4 (17.4)	17.93 (1.85–173.94)	
B symptoms	Absent	16 (69.6)	Reference	0.561
	Present	7 (30.4)	1.96 (0.20–18.82)*	
Age	Per year increase	-	1.21 (1.10–1.34)	<0.001

Table 4. Univariate Analysis of Progression-Free Survival Predictors.

Abbreviations: HR, hazard ratio; CI, confidence interval; IPS, International Prognostic Score. Notes: Statistically significant values ($p < 0.05$) shown in bold and marked with an asterisk ().* Caution: Significant p-values for bulky disease and stage are accompanied by wide confidence intervals crossing 1, indicating limited precision due to small sample size (N=23).

Each additional year of age increased the hazard of progression or death by 21% (hazard ratio [HR] 1.21; 95% confidence interval [CI]: 1.10–1.34; $p < 0.001$). Patients presenting with advanced Ann Arbor stage (III/IV) had a 3.26-fold higher risk of progression compared to those with earlier stages (HR 3.26; 95% CI: 0.34–31.35; $p = 0.001$), although the wide confidence interval crossing 1 indicates limited precision. The presence of bulky disease was associated with a 2.65-fold increased hazard (HR 2.65; 95% CI: 0.37–18.92; $p = 0.03$). A high-risk International Prognostic Score (IPS ≥ 3) was strongly predictive of reduced PFS, with nearly an 18-fold increased risk (HR 17.93; 95% CI: 1.85–173.94; $p = 0.013$). Sex, histologic subtype, and B symptoms were not significant predictors in this cohort. The broad confidence intervals for several hazard ratios underscore the limited statistical power inherent to the small sample size, warranting cautious interpretation of these findings.

Discussion

Hodgkin lymphoma (HL) is a lymphoproliferative malignancy defined by the presence of Reed-Sternberg cells, with clinical presentations and outcomes influenced by patient demographics, comorbidities, and disease characteristics. This study provides a focused analysis of clinical features, treatment patterns, and progression-free survival (PFS) in a cohort of 23 HL patients from Saudi Arabia a region where comprehensive HL data are limited but epidemiology is rapidly evolving [1].

Our analysis found that advanced Ann Arbor stage, bulky disease, elevated International Prognostic Score (IPS), and increasing age at diagnosis were associated with poorer PFS, aligning with established prognostic indicators in major multicenter datasets and recent risk models including EORTC, GHSG, and newer dynamic tools [28-31]. It is essential to interpret these findings as associations rather than causality, given the retrospective design and modest cohort size, which constrain statistical power and precision, as reflected in wide confidence intervals.

Patient demographics in our study showed a mean age at diagnosis of 36.3 years, with over 80% of patients younger than 50 years, confirming the typical young adult peak and bimodal age incidence described in global studies [2, 12, 32]. This age is notably younger than the median age range of 55 to 65 years reported in Western populations [9, 10]. Such a younger age distribution aligns with findings from Middle Eastern and South Asian cohorts and likely reflects underlying demographic, genetic, and environmental differences in these regions [7, 8, 11, 12]. Additionally, the higher prevalence of Epstein-Barr virus (EBV)-associated HL in developing countries, which disproportionately affects younger individuals, may contribute to this epidemiological pattern [5, 13, 14]. The male-to-female ratio of 1.5:1 is slightly higher than the global average (~1.2:1) but parallels patterns seen in large Asian cohorts and population-based reports [5, 33]. Lymphadenopathy as the primary presenting symptom and site was consistent with classical HL [5,

10]. Histologically, the cohort was dominated by classical HL (87%) and nodular sclerosis variant (65.2%), similar to proportions reported in higher-SDI countries [34].

Strikingly, 43.5% of patients presented with Ann Arbor stage III/IV disease, a rate somewhat exceeding the 30–40% typically observed in EORTC and GHSG studies [4, 35]. This finding highlights ongoing challenges around delayed diagnosis, indicating an urgent need for awareness initiatives and improved early detection in Saudi Arabia [6].

Comorbidities, including hepatitis B/C (13%) and HIV (8.7%), were more prevalent than in Western cohorts, where HIV coinfection is commonly <5% [4]. These rates reflect regional infection patterns and carry clinical relevance: increasing therapy-related toxicity, immunosuppression risk, and potential drug interactions, and warrant integrated care approaches for HL patients [2, 12, 32]. Although our analysis did not adjust for these clinical variables due to limited sample size and data availability, their presence represents a potential source of heterogeneity that could have influenced the observed outcomes. Consequently, these factors should be carefully considered when interpreting our findings. Future studies with larger cohorts are warranted to systematically account for such comorbidities, enabling a more precise evaluation of the independent prognostic significance of HL-specific clinical and biological markers.

The ABVD regimen was the principal first-line treatment, administered to 73.9% with an objective response rate (ORR) of 78.3% (CR 43.5%), which is lower than those reported by pivotal multicenter studies but comparable to real-world experience in advanced- stage and comorbid cohorts [3, 35]. In major multicenter trials (e.g., GHSG HD10/HD11), ORR often exceeds 90% and CR approaches 80%, but these studies typically enroll fewer advanced-stage or heavily comorbid patients [3, 4]. The lower response rate in our cohort is likely due to greater disease burden, comorbidity prevalence, and real-world practice variations in adherence and dosing.

Salvage chemotherapy was required in 26.1% of patients and combined modality therapy in 30.4%, mirroring practices and outcomes reported in multicenter and registry studies [36]. The median follow-up of 33 months allowed meaningful outcome assessment, with disease progression or recurrence in 17.4% within three years.

Univariate Cox regression confirmed established adverse prognostic factors advanced age, bulky disease, higher stage, and high-risk IPS consistent with the literature and validation studies [28-31, 36]. Biologically, bulky disease and advanced stage are related to tumor burden and the microenvironment, where immunosuppressive cytokines and immune escape mechanisms diminish conventional and emerging therapy effectiveness [5, 13, 14]. Future inclusion of EBV status and microenvironment profiling could further enhance risk models and personalization.

Response assessment relied on RECIST v1.1 instead of Lugano criteria, reflecting PET resource constraints. This may limit sensitivity and complicate direct international comparisons, highlighting the need for increased PET availability regionally [37]. Recent advances such as brentuximab vedotin and checkpoint inhibitors are reshaping HL therapy in high-resource settings, though cost and access limit their integration in many regions [18]. Their future adoption may necessitate updates in prognostic frameworks and treatment algorithms. The limited use of bone marrow transplantation (BMT) in our cohort only one patient received BMT reflects systemic barriers common in low- and middle-income countries. Restricted access to salvage transplantation adversely affects outcomes for relapsed HL. Furthermore, emerging therapies such as PD-1/PD-L1 inhibitors and histone deacetylase inhibitors, which have demonstrated efficacy in refractory cases, remain largely inaccessible regionally [18]. Adoption of molecular monitoring techniques, including circulating tumor DNA assays, could facilitate earlier detection of minimal residual disease and guide timely interventions once infrastructure improves.

Regional Implications

Our findings emphasize the need for HL management tailored to regional realities in Saudi Arabia and the Asia-Pacific. Risk stratification with clinical parameters (stage, bulk, IPS) remains paramount under resource constraints. Developing pragmatic, validated algorithms for risk, treatment, and surveillance aligned with regional practice will help optimize HL outcomes.

Study Limitations

The main limitations of our study include its retrospective nature, small cohort size, and single-center design, which restrict generalizability and preclude multivariate adjustment for confounders such as comorbidities including HIV coinfection. The use of RECIST version 1.1 for response evaluation instead of the lymphoma-specific Lugano criteria due to limited PET availability may limit comparability with other studies yet reflects clinically pragmatic assessment in our context. Additionally, we did not assess tumor EBV status or the tumor microenvironment, which may influence prognosis. Future prospective, multicenter studies incorporating molecular and sociodemographic profiling are essential to refine prognostic models and optimize individualized treatment strategies.

In conclusion, in this retrospective cohort of Saudi Hodgkin lymphoma patients, advanced Ann Arbor stage, elevated International Prognostic Score, and increasing age at diagnosis were significantly associated with poorer progression-free survival. These findings corroborate established prognostic indicators and emphasize the importance of thorough risk stratification at diagnosis. Despite resource limitations underscoring differences in treatment access and outcomes, our results provide valuable regional insight that can guide tailored management strategies. Future prospective studies involving larger cohorts are warranted to validate these associations and to facilitate the integration of novel diagnostics and therapies aimed at improving long-term outcomes.

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Disclosure of Conflicts of Interest

The authors declare that there are no conflicts of interest related to this work.

Author Contributions

All authors contributed substantially to the conception, design, data acquisition, analysis, and interpretation. All authors contributed to drafting and critical revision and approved the final manuscript.

Human Ethics

The Ethics Research Committees of King Khalid Hospital provided their approval for the study (ID: 2022- 44 E, on September 4, 2022), which adhered to the ethical principles outlined in the

Declaration of Helsinki. Consent was obtained or waived by all participants in this study. The samples represent full coverage.

Data Availability

All data relevant to this study are included within the article.

Use of Artificial Intelligence Tools

The manuscript's English editing was assisted by Perplexity AI. The authors retain full responsibility for the content.

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