

Survival and Epidemiologic Trends of Lymphomas in Saudi Arabia: A 10-Year Report from a Tertiary Care Hospital

Masha'el Yahya Altowairqi, Mohammed Yousef Alyousef, Mohammed Khaled Ghandour, Abdulrahman Abdulmohsen Alrashed, Yousef Jebrin Aljebrin, Ghadah Abdulkarim Alotheem, Aamer Aleem, Farjah Algahtani, Musa F. Alzahrani

Department of Medicine, King Saud University, Riyadh, Saudi Arabia

Abstract

Background: The current trends in lymphoma cases from Saudi Arabia and their long-term survival are unknown. This study was conducted to evaluate the trends of lymphoma diagnoses and survival from a major tertiary care hospital in Saudi Arabia.

Methods: This retrospective study included all new cases of lymphoma diagnosed in adults (age ≥ 18 years) at King Saud University Medical City, Riyadh, Saudi Arabia, from 2008 to 2018, as identified from the Saudi Cancer Registry. Data on the demographics and clinical characteristics were collected, the survival outcomes were estimated, and multivariate analysis of the overall survival was calculated.

Results: A total of 422 patients were included (median age: 46 years). The number new cases of lymphoma diagnosed variably increased over the study period: From 28 (7%) cases in 2009 to 48 (11%) in 2018. The most common lymphoma was diffuse large B-cell lymphoma (175; 41%); and extranodal site was GI involvement (33.5%). In terms of survival, 79% were alive at the last follow-up. On multivariable analysis, the hazard ratio (HR) for patients aged ≥ 60 years was 3.44 (95% CI: 2–5.9; $P = 0.0000069$), adjusted for lactate dehydrogenase level (LDH) and disease stage. For advanced-stage disease and high LDH, the HR was 4.2 (95% CI: 1.5–11.8, $P = 0.00637$) and 0.5 (95% CI: 0.28–0.97; $P = 0.04106$), respectively.

Conclusions: The lymphoma trend in the Saudi Arabian population showed variable increase in cases over the study period, with most patients presenting with advanced-stage disease and at a younger age. The overall survival was comparable with studies from Western countries.

Keywords: Epidemiology, Hodgkin, lymphoma, non-Hodgkin, Saudi Arabia, survival analysis

Address for correspondence: Dr. Musa F. Alzahrani, Department of Medicine, King Saud University, Saudi Arabia, P O Box: 55068 (37), Riyadh 12372, Saudi Arabia.

E-mail: malzahrani@ksu.edu.sa

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INTRODUCTION

The incidence of cancer continues to rise worldwide, in high-income and especially in low/middle-income countries.^[1] Lymphomas, which are malignancies that

arise from the lymphoid tissues,^[2,3] account for about 5% of all types of cancer in countries such as the United States.^[4] In fact, according to the WHO's Globocan 2020

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report, non-Hodgkin's lymphoma (NHL) and Hodgkin's lymphoma (HL) account for 2.8% and 0.43% of all new cases of cancer worldwide, respectively.^[5]

The distribution of lymphoma subtype and survival rates vary, but NHL and HL generally account for the vast majority of the cases. For example, in the United Kingdom, the most common subtype between 2004 and 2014 were NHL (85.5%) and HL (14.4%). The estimated 5-year overall survival with NHL was 53.7% and with HL it was 78.9%.^[6] Similarly, in Spain, between 2014 and 2018, NHL of B-cell origin and HL represented 80% and 12.4% of all lymphomas, respectively; the overall 2-year survival rate after diagnosis was 92% in HL.^[7] In Canada, a study found that NHL and HL accounted for 90% and 6% of all lymphomas, respectively,^[8] while in the United States, these two subtypes accounted for 90% and 10% of the lymphomas, respectively.^[4]

In Saudi Arabia, between 1975 and 2012, NHL and HL comprised 7.5% and 4% of all cancers, making it the third and eight most common type of cancer, respectively.^[9] More recently, NHL and HL represented 6.9% and 3.6% of all new cases of cancer in 2015, ranking it as the fourth and sixth most common cancer types among Saudis, respectively.^[10] However, there is limited data focusing on the general trend of lymphoma diagnoses and the long-term survival data from Saudi Arabia. Accordingly, this study was conducted with the objective of presenting a 10-year data from a major tertiary care academic center with relevant demographic and clinical data, trends of different lymphoma pathologies, and mature follow-up survival data.

METHODS

This retrospective study included all new cases of lymphoma diagnosed in adults (aged ≥ 18 years) at King Saud University Medical City (KSUMC), Riyadh, Saudi Arabia, from 2008 to 2018, as identified from the Saudi Cancer Registry. KSUMC is one of the largest governmental tertiary care hospitals in Saudi Arabia. Oncology cases at KSUMC comprises those diagnosed within the hospital or referred from other hospitals.

The study was conducted after the protocol was approved by the Institutional Review Board (IRB) of King Saud University. Patient data confidentiality was ensured during the study and access to, collection, and analysis of the data were only by the investigators. Missing data were handled through calculating the ratio from the number of evaluable patients. The manuscript was prepared following the STROBE reporting guidelines.

Data collection

The primary assessed variables pertained to demographic, clinical characteristics, and long-term survival data. Accordingly, the following data were collected: Age, gender, nationality, date of diagnosis, disease stage, presence of B symptoms, lactate dehydrogenase (LDH) level, biopsy site, histology, bone marrow (BM) involvement, gastrointestinal (GI) tract involvement, central nervous system (CNS) involvement, date of last follow up, and survival status (alive or dead). The first six authors completed the data extraction, which was then verified by the last author.

Lymphoma subtypes under histology were classified according to the WHO classification of lymphoid neoplasms.^[3] The lymphoma staging was done following the modified Ann–Arbor staging classification.^[11]

Statistical analysis

The survival outcomes for the univariate analysis were estimated using the Kaplan–Meier method, and *P* values were determined using the log-rank test. Multivariate analysis of overall survival (OS) was conducted including the following variables: Age, stage, and LDH level. OS was defined as the time from diagnoses until death from any cause. Multivariable Cox proportional hazard regression models was used to assess the effects of the prognostic variables on OS, hazard ratio (HR), and Wald 95% confidence intervals (CIs). All analyses were performed using two-tailed tests, with the type 1 error rate fixed at 0.05. Simple frequency statistics were used to summarize the remaining variables. Data were analyzed using R Studio version 1.3.1056^[12] and R for Statistical Computing version 4.0.2.^[13]

RESULTS

Epidemiological data

A total of 422 new lymphoma cases were diagnosed during the study period. The number of cases/year ranged from 28 (7%) in 2009 to 48 (11%) in 2018 [Figure 1]. The majority of the patients were aged < 60 years (76%) (median age: 46 years; range: 18–87 years). In addition, males accounted for 59% of the cases, and most were of Saudi nationality (85%). Patients with advanced-stage disease accounted for about three-quarters (72%) of the evaluable cases [Table 1].

Lymphoma stages and subtypes

In terms of staging, 45 (11%), 67 (16%), 70 (17%), and 226 (55%) cases were of Stages I, II, III, and IV, respectively. In addition, B symptoms were present in 227 of 373 evaluable cases (61%). LDL was elevated in 185 of 322 evaluable cases (57%). Regarding extra-nodal disease, GI

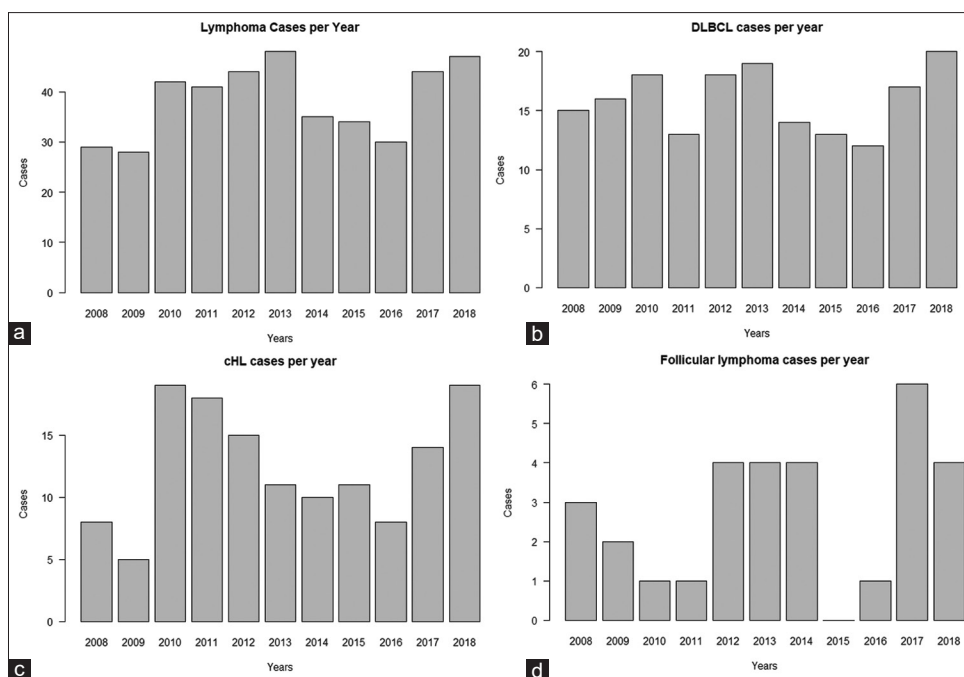


Figure 1: Newly diagnosed cases per year for (a) whole group, (b) DLBCL, (c) cHL and (d) follicular lymphoma

Table 1: Baseline characteristics of the patients (n=422, unless stated otherwise)

Variable	n (%)
Age (years)	
<60	319 (76)
≥60	103 (24)
Median (range)	46 (18-87)
Gender	
Male	247 (59)
Female	175 (41)
Nationality	
Saudi	358 (85)
Non-Saudi	64 (15)
Stage (n=408)	
Advanced	295 (72)
Limited	113 (28)
B symptoms (n=373)	
Present	227 (61)
Absent	146 (39)
Pathologic subtype	
DLBCL	175 (41)
CHL	138 (33)
FL	30 (7)
NHL, unclassifiable	22 (5)
Others	57 (14)
Status on last follow up	
Alive	333 (79)
Dead	89 (21)

DLBCL – Diffuse large B-cell lymphoma; CHL – Classical Hodgkin's lymphoma; FL – Follicular lymphoma; NHL – Non-Hodgkin's lymphoma

involvement was the most common (136 of 405 evaluable patients; 33.5%), followed by BM (82 of 347; 24%), and central nervous system (19 of 405; 0.05%) involvement.

Nineteen subtypes of lymphoma were identified, and are listed as follows in descending order: diffuse

large B-cell lymphoma (DLBCL), 175 (41%); classical Hodgkin's lymphoma (cHL), 138 (33%); FL, 30 (7%) cases; non-Hodgkin's lymphoma, unclassifiable, 22 (5%); T-cell lymphoma, 11 (3%); Burkitt lymphoma, 7 (2%); marginal zone lymphoma (MZL), 7 (2%); mantle cell lymphoma (MCL), 6 (1%); cutaneous T-cell lymphoma, 5 (1%); lymphoplasmacytic lymphoma (LPL), 4 (1%); mucosa-associated lymphoid tissue (MALT) lymphoma, 4 (1%); non-Hodgkin's lymphoma, 3 (0.7%), gray zone lymphoma, 2 (0.5%); plasmablastic lymphoma, 2 (0.5%), T-cell lymphoblastic lymphoma, 2 (0.5%); nodular lymphocyte predominant Hodgkin's lymphoma (NLPHL), 1 (0.2%), peripheral T-cell lymphoma, 1 (0.2%); and case and small lymphocytic lymphoma, 1 (0.2%) [Table 1].

Survival data

On the last follow up, 333 (79%) patients were alive and 89 (21%) had died. Univariate survival analysis was done using log-rank test and KM curves for the whole group, LDH level, age, DLBCL, and cHL groups were created [Figures 2 and 3]. The median follow-up period was 18 months (range: 0–139 months). The multivariable Cox proportional hazard regression model for age, LDH, and disease stage showed that HR for patients aged ≥60 years is 3.44 (95% CI 2–5.9) adjusted for LDH level and disease stage ($P = 0.0000069$). In advanced-stage disease, the HR is 4.2 (95% CI 1.5–11.8), adjusted for age and LDH level ($P = 0.00637$). For the elevated LDH level, the HR is 0.5 (95% CI 0.28-0.97), adjusted for age and disease stage ($P = 0.04106$).

DISCUSSION

Our study is one of the largest single institution data regarding survival and epidemiological trends of lymphomas from Saudi Arabia. It was found that the number of cases each year increased slightly and variably during the study period. Most of them were males of a younger age with advanced-stage disease at presentation. The GI system was found to be the most common site of extranodal involvement in our patient population, which is similar to that reported in the international literature.^[14-17] The younger age at diagnosis may be because of the high proportion of young population in Saudi Arabia or a unique biologic difference, which may warrant further studies. Advanced-stage disease on diagnosis could be because of

multiple reasons such as delays in patient seeking medical attention due to lack of knowledge or underestimation of the symptoms, visiting multiple institutions before reaching an accurate diagnosis, and/or the aggressiveness of the biologic lymphoma subtype.

The most common lymphoma subtypes reported were DLBCL, cHL, and FL. Compared with previous studies from Saudi Arabia,^[9,10] our findings showed similar pattern of male predominance, median age, and advanced-disease stage at presentation. Moreover, the current and previously available data showed that the most common subtype was DLBCL. Slight male predominance and NHL being the most common type of lymphoma have been reported in studies from different countries.^[4-8]

In our univariate survival analysis, being aged ≥ 60 years, having high LDH, and an advanced-stage disease were found to be associated with lower survival. In the multivariate Cox proportional hazard regression models including age, LDH level and stage, patients of aged ≥ 60 years were more likely to die as compared to younger patients, adjusting for disease stage and LDH level. This is an expected finding and goes well with what is reported in many prognostic scores in lymphoma.^[18-22]

Our study has several limitations, including the weakness inherent in retrospective studies. Relapsed data and treatment received were also not collected, as this was beyond the scope of the study. We also recognize that

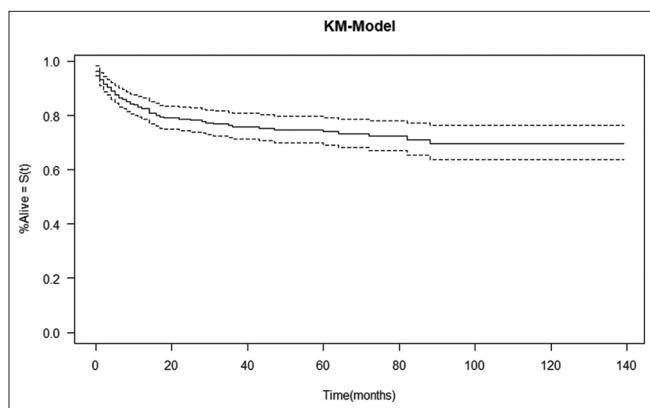


Figure 2: KM curve for OS for whole group. The dotted lines represent 95% CI

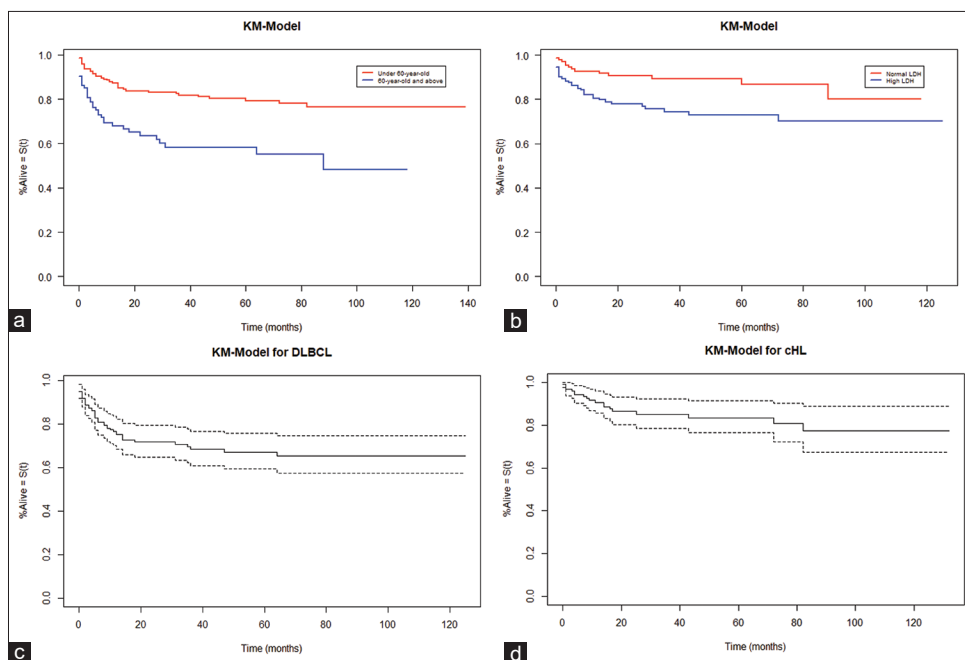


Figure 3: KM survival curves for (a) Age for whole group, (b) LDH level for whole group, (c) DLBCL and (d) cHL. The dotted lines represent 95% CI

survival analyses in some subgroups could be underpowered because of the small number of patients. Despite these limitations, the study has several strengths such as mature survival data being reported with a long-term follow-up. Furthermore, the study had a large population, as the single institution is a major tertiary care hospital.

CONCLUSIONS

This study provides a current benchmark of lymphoma cases in Saudi Arabia. A variable increase in the number of cases was observed during the study period. The study found that the survival trends are comparable with those from Western countries; however, some clinical features and patterns differed such as a higher proportion of cHL cases, more cases presenting with advanced stage and at a younger age. Future studies should focus on defining the etiology of these unique differences.

Ethical considerations

The study was approved by the IRB at the College of Medicine, King Saud University, Riyadh, Saudi Arabia, with approval no.: E-19-4176 on August 28, 2019, and renewed on October 20, 2020, for additional contributors. The requirement of patient consent was waived by the IRB based on the study design. The patient's data confidentiality was ensured as access to data for collection and analysis was limited to the investigators, who adhered to the principles of the Declaration of Helsinki 2013.

Data availability statement

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

Peer review

This article was peer-reviewed by two independent and anonymous reviewers.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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