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DOI:

10.4103/joah.joah\_30\_20

# Demographic and Clinical Characteristics of Lymphoma Patients from Al-Ahsa, Saudi Arabia

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Submitted: 26-Mar-2020

Revised: 13-Apr-2020

Accepted: 21-Apr-2020

Published: 16-Sep-2020

## Abstract:

**BACKGROUND:** Lymphoma is a malignancy of the lymphatic system. As no studies have previously been conducted about lymphoma in Al-Ahsa, Saudi Arabia, we hereby present first report on demographic and clinical characteristics of lymphoma patients from Al Ahsa, Saudi Arabia from 2009 to 2018.

**PATIENTS AND METHODS:** All histologically confirmed lymphoma patients from 2009-2018 attending KAH were included in the study. BCL2, BCL6 and C-MYC rearrangements were detected by fluorescence in situ hybridization. Data was analyzed using SPSS.

**RESULTS:** Male to female ratio was 1:1.52 with 23 (39.7%) male and 35 (60.3%) female patients. Mean age was 35.9 years in Hodgkin lymphoma (HL) and 54.4 years in non-Hodgkin lymphoma (NHL). HL was found to be more common in the young age group (0-18 years, 85.7%), which is a new finding. NHL was more common in age group (41-60 years) (80%,  $P=0.002$ ). Overall, HL was more common than NHL (60.3% vs 39.7%). The most common subtype of HL was nodular Sclerosis type (52.2%), while diffuse large B cell lymphoma (DLBCL) was the most common subtype (74.3%) of NHL. The most common sites of involvement (other than lymph nodes) in HL were liver and mediastinum (19% and 18% respectively). However, the most common sites of involvement in the NHL were liver and bone marrow (12.90%), followed by the spleen and stomach (9.67%). BCL-2 and BCL-6 were the most frequently positive markers in NHL, especially in DLBCL. Moreover, it was found that DLBCL had a more aggressive course and associated with more deaths (5/26; 19.2%,  $P=0.047$ ). Triple hit lymphoma was only found in follicular lymphoma patients with overall frequency of 1.7%.

**CONCLUSIONS:** Our study shows that in Al-Ahsa area, HL is more prevalent in pediatric patients. Moreover, there is high frequency of DLBCL among NHL subtypes as compared to the western world.

## Keywords:

Al-Ahsa, cancer, Eastern province, lymphoma, Saudi Arabia

## Introduction

Lymphoma is a type of cancer that arises from lymphoid tissue.<sup>[1]</sup> There are two main types of lymphoma, Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL).<sup>[2]</sup> Under a microscope, HL is classified by the presence of an abnormal cell called Reed-Sternberg cell (RSC). However, if the RSCs are not present, the lymphoma is classified as NHL.

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NHL may arise from B- or T-lymphocytes, although majority of NHL cases are of B-cell in origin.<sup>[3]</sup> Approximately 85%–90% of patients diagnosed with lymphoma have NHL in Western populations.<sup>[3]</sup> Systemic symptoms such as night sweats, weight loss, and fever are commonly found in both types of lymphomas.<sup>[4]</sup>

The primary cause of lymphoma is unknown. Many factors that can increase

**How to cite this article:** Iqbal Z, Almusawi BM, Alhashim FF, Aleassa WA, Albueisa ZY, Malik A, *et al.* Demographic and clinical characteristics of lymphoma patients from Al-Ahsa, Saudi Arabia. *J Appl Hematol* 2020;11:122-5.

its risk include age, sex, autoimmune diseases, and a diet rich in meat.<sup>[5]</sup> However, contribution of different risk factors to lymphoma development may vary in different regions. Lymphoma is diagnosed by analysis of lymph node biopsy by immunophenotyping, karyotyping, etc. and by imaging techniques such as chest X-ray, magnetic response imaging, etc.<sup>[6,7]</sup>

The frequency of lymphoma and its clinical characteristics may vary in different regions. Only few studies have been carried on lymphoma in Saudi Arabia. One such study determined the frequency of different types of lymphoma in Al-Qassim region from 1988 to 2007, according to the World Health Organization classification.<sup>[8]</sup> The results of this study showed that NHL was the most common type found in that region. In 2008, NHL was one of the most common type of cancer in Saudi Arabia and ranked second in cancer incidence among the male population, with a male-to-female ratio of 1.22:1.<sup>[9]</sup> King Faisal Specialist Hospital and Research Center registry reported 5493 (7.6%) cases of NHL from 1975 to 2011.<sup>[10]</sup> Another study was carried out in Abha to analyze the pattern of NHL at Asir Central Hospital, from October 1987 to May 1994.<sup>[11]</sup> The result of this study showed that NHL third most common cancer in Abha. In Egypt, NHL was the 5<sup>th</sup> most common cancer in both males and females.<sup>[12]</sup> In Yogyakarta, a city on the Indonesian island, there was a noticeable increase in the incidence of Lymphoma from 2010 to 2014, and it was more common in 45–64-year age group with a male predominance.<sup>[13]</sup> NHL was the most common cancer in the USA during 2018.<sup>[14]</sup> In Jordan, B-cell lymphoma was found to be more common in adults, whereas T-cell lymphoma was more common in children.<sup>[15]</sup> It shows that frequencies of lymphoma and its different subtypes may vary in different regions.

No studies about lymphoma patients have been conducted in Al-Ahsa. Hence, the goal of our study was to find out demographic and clinical characteristics of lymphoma patients at King Abdulaziz Hospital (KAH) in Al-Ahsa.

## Materials and Methods

All histologically confirmed lymphoma patients from 2009 to 2018 attending KAH were included in the study. BCL2, BCL6, and C-MYC rearrangements were detected by fluorescence *in situ* hybridization analyses using Vysis probes per manufacturer's instructions (Abbott Molecular, Des Plaines, IL, USA).

Data obtained from the files/records of the patient were collected from patient data collection form and stored in the Microsoft Excel. Statistical analysis conducted in a form of descriptive and inferential statistics, categorical variables like gender were analyzed and reported as proportions and

continuous variables, and age was analyzed and reported as mean  $\pm$  standard deviation. Chi-square test was used for categorical variables.  $P \leq 0.05$  was considered statistically significant for all the statistical tests.

## Results

A total of 58 patients of lymphoma at King Abdul-Aziz Hospital-Al Ahsa from 2009 to 2018 were included in the study. There were 23 (39.7%) males and 35 (60.3%) females, with male-to-female ratio of 1:1.52. Patients were divided into HL (23, 39.7%) and NHL (35, 60.3%). Twelve (52.2%) HL patients had nodular sclerosis histology, 8 (34.8%) had mixed cellularity type, and 2 (8.7%) had classical HL. In the NHL category, 26 (74.3%) patients had diffuse large B-cell lymphoma (DLBCL), 2 (5.7%) had follicular lymphoma, 2 (5.7%) marginal zone lymphoma, 3 (8.6%) had T-cell lymphoblastic lymphoma, 1 (2.9%) a Burkitt's lymphoma, and 1 (2.9%) had mucosa-associated lymphoid tissue lymphoma.

We found that the HL had the highest association with the age group of 0–18 years (85.7%). NHL had the highest association with the age group of 41–60 years (80%) ( $P = 0.002$ ) [Figure 1].

In our study, we found that the most common sites of involvement (metastasis) in HL were live and mediastinum (19% and 18%, respectively). However, the most common sites of involvement in the NHL were liver and bone marrow (12.90%), followed by the spleen and stomach (9.67%) [Figures 2 and 3].

In NHL subtypes, it was found that the DLBCL has significant association with BCL2 and BCL6 (77.8%) as compared to follicular lymphoma, marginal zone lymphoma, T-cell lymphoblastic lymphoma, and Burkitt's lymphoma subtypes. It is important to mention that triple-hit (BCL2, BCL6, and c-MYC positive) lymphoma was found only in follicular lymphoma patients, with overall frequency of 1.7% and 50% of FL cases.

Moreover, it was found that DLBCL is the subtype of NHL with high levels of ALT and AST (80% and 85.7%, respectively) followed by T-cell lymphoblastic lymphoma ( $P = 0.047$ ). However, there is no statistical

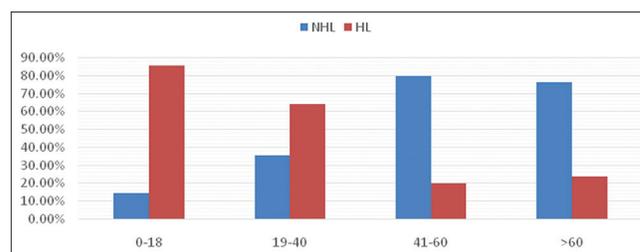


Figure 1: Association of age groups with lymphoma

significance was found between different subtypes of HL and liver enzymes. Elevated liver enzyme levels may be clinically relevant, as these are associated with the most aggressive and common type of NHL (DLBCL) in our study.

The trend in the disease pattern observed over a period of 2009–2018. The data records in 2013 and 2016 showed the highest number of cases in patients diagnosed with lymphoma as compared to the lowest number of patients in 2009 [Figure 4].

Overall, our results indicate higher frequency of DLBCL among NHL subtypes and HL more prevalent in the pediatric group as compared to Western populations.

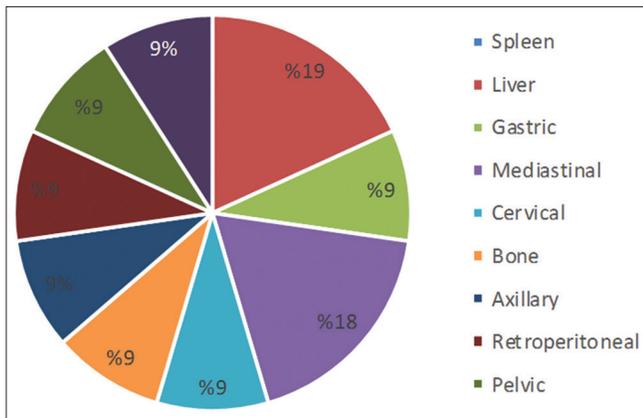


Figure 2: Different sites of involvement in Hodgkin lymphoma patients

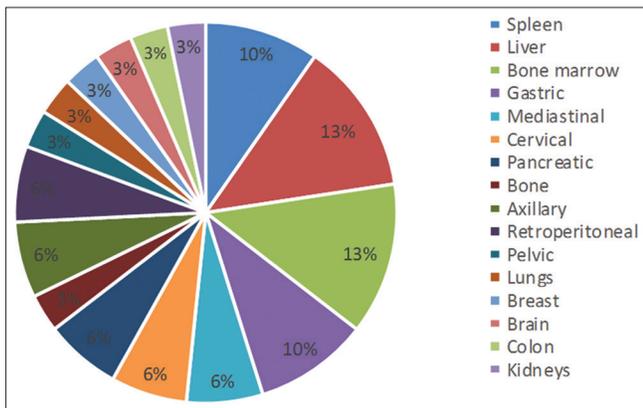


Figure 3: Different sites of involvement in non-Hodgkin lymphoma patients

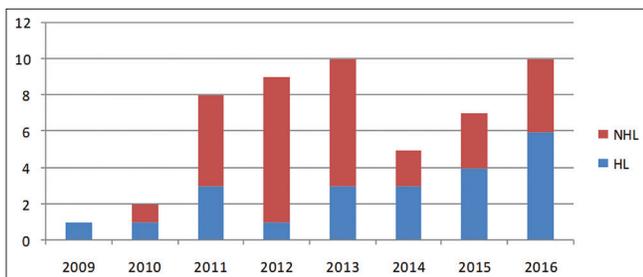


Figure 4: Year-wise frequency of lymphoma in Al-Ahsa region

## Discussion

The aim of our study was to find out the association of different parameters with lymphoma patients at King Abdul-Aziz Hospital Al-Ahsa. The study included 58 patients of HL and NHL with male-to-female ratio of 1:1.52. The mean age in HL was 35.9± (0–18 years) and 54.4± (41–60) years for NHL. A study conducted in America in 2019 showed that the mean age associated with HL is 39 years<sup>[16]</sup> which supports our findings.

HL was more common in the age group of 0–18 years, which is unique to Al-Ahsa area, as HL is rarely detected in children in developing countries.<sup>[17,18]</sup> NHL was more common in the age group of 45–60 years. A study conducted in Northern Saudi Arabia from 2009 to 2016 reported the association of NHL patients with age ≥ 60 years.<sup>[19]</sup> In 2013, another study including 567 patients found the increased frequency of young adults with HL.<sup>[20]</sup>

In HL, the most common subtype was nodular sclerosis (52.2%), which is in accordance with other studies.<sup>[21]</sup> In the case of NHL, DLBCL was the most common subtype 74.3%. Khelfa *et al.* reported the frequency of 25% DLBCL among NHL worldwide.<sup>[22]</sup> Furthermore, there was a study performed in Europe that showed DLBCL constitutes 30%–58% of NHL subtypes.<sup>[23]</sup> Our study shows that Al-Ahsa has a very high frequency of DLBCL among NHL subtypes as compared to Western populations.

In our study, we found that the most common sites of involvement in HL were liver and mediastinum (19% and 18%, respectively). A study conducted in the USA included 190 cases of patients with Hodgkin’s disease showed that spleen, liver, and lung organs are the most frequent sites of involvement in lymphoma.<sup>[24]</sup> However, the most common sites of involvement in NHL were liver and bone marrow (12.90%), followed by the spleen and stomach (9.67%). Another study reported that the most frequently involved sites in patients with NHL are liver, stomach, lung, and spleen.<sup>[25]</sup>

Liver function profile can be a helpful test to rule out the liver abnormalities resulting from lymphoma. We found that DLBCL is the only subtype of NHL that is related to an increased level of aspartate transaminase and alanine aminotransferase (80%). Our results are supported by another study that carried out in France during 2017 included 363 patients with DLBCL that showed that most of the patients had elevated liver function enzyme levels.<sup>[26]</sup> This is especially important as 19% of HL and 12.9% of NHL patients in our study population had liver infiltration.

Our results showed that most of DLBCL patients were positive for both BCL-2 and BCL-6 (77.8% each). These molecular biomarkers are reliable prognostic markers. It has been reported that BCL2 and BCL-6 are the most frequently found markers in DLBCL (23.07%),<sup>[27]</sup> which is in accordance with our findings.

Despite some interesting results, our study has certain limitations. We have small number of patients as Al-Ahsa is a smaller city as compared to Dammam and Riyadh. Moreover, most of the patients after initial diagnosis are referred to other oncology centers with better facilities. We aim to continue our studies to recruit more patients and to improve patient care services at our hospital.

### Conclusions

Our study shows that the HL is more common in the pediatric age group. Among the lymphoma patients, DLBCL is the most common subtype of NHL, whereas nodular sclerosis is more frequent subtype in HL. The liver and spleen showed the highest percentage of involvement with HL, whereas NHL involved bone marrow and liver frequently. DLBCL was commonly associated with BCL2/BCL6 and elevated liver enzymes. Overall, our study shows that Al-Ahsa region has a high frequency of DLBCL among NHL subtypes as compared to the Western world.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

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