

ORIGINAL ARTICLE

The Typical Patterns of Lymphomas in Northwestern Saudi Arabia

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SUMMARY

Background: Lymphoma is one of the leading cancers in Saudi Arabia. Because there is a paucity of data about the prevalence of lymphomas in Saudi Arabia, numerous extensive investigations are still required. Thus, the present study aimed to assess the common patterns of lymphomas in Northwestern Saudi Arabia.

Methods: This is a retrospective study conducted at the Histopathology Departments of King Khalid and King Salman Hospitals in Hail city, Saudi Arabia, between 2008-2020. The present study comprised 134 lymphoma patients, and all data referring to these patients, such as gender, age, lymphoma type, grade, and cancer site, were retrieved.

Results: The most common lymphoma type was NHL, followed by HL, constituting 32.8% and 20%, respectively. There was a clear difference between male and female patients of HL type where the male was higher than the female (24% versus 15.3%). The risk of HL associated with male gender, the relative risk (RR) CI (95% Confidence interval) = 2.0077 (0.9447 - 4.2667), $p = 0.0700$, z statistic = 1.812.

Conclusions: Lymphoma is prevalent in the Hail region with an exceptionally ever-increasing incidence of HL. Wide-ranging lymphoma varieties have been explored in the Hail region, denoting large groups of unattributable etiologic modifiable risk factors.

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KEYWORDS

Lymphoma, Hodgkin lymphoma, non-Hodgkin lymphoma, Hail, Saudi Arabia

LIST OF ABBREVIATIONS

HL - Hodgkin lymphoma
NHL - Non-Hodgkin lymphoma

INTRODUCTION

Lymphoma is a cancer of lymphoid tissue that is classically divided into Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). NHL represents the most common type originating from mature or precursors B cells or T lymphoid cells. The most common NHL types (indolent or aggressive) include follicular lymphoma (FL), Burkitt's lymphoma (BL), diffuse large B cell lymphoma (DLBL), Mantle cell lymphoma (MCL), marginal zone lymphoma, primary central nervous system lymphoma (PCNSL), adult T cell lymphoma, and Mycosis fungoides (MF) [1]. On the other hand, HL mainly originates from B cell lymphoid cancer, and it is characterized by a few cancer cells and many immune cells tumor microenvironment and is rare with high cure rates. HL is classified into nodular sclerosis (dominant subtype), lymphocyte-rich HL, lymphocyte-depleted, and mixed cellularity [2,3].

Lymphomas including (HL and NHL types) represent 9.2% of all cancers in Saudi Arabia with odds ratio (OR) (95% CI) = 3.02 (1.48 - 6.17). The recent shift in the Saudi lifestyle to adopt a western lifestyle after the country's prosperity, has been linked to several diseases, including lymphoma [4]. NHL, with approximately sixty subtypes, has been linked to numerous etiological factors [5], including a family history of leukemia and multiple myeloma, cigarette smoking and alcohol consumption, autoimmune diseases, eczema, blood transfusion, hepatitis C infection [6]. Besides Epstein Barr virus (EBV), HL has been linked to many lifestyles and environmental factors [7,8].

Recognition of the lymphoma risk factors, and the appropriate management option depends chiefly on identifying the typical patterns of lymphoma in a particular geographical region. Accordingly, the present study aimed to report the specific types of lymphomas in northwestern Saudi Arabia.

MATERIALS AND METHODS

Data collection and processing

This study included a retrospective analysis of a series of lymphoma patients diagnosed between 2008 to 2020 at the Histopathology Departments of King Khalid and King Salman Hospitals in northwestern Saudi Arabia. Data relating to 134 lymphoma patients (including total coverage sample) referred to King Salam hospital in 13 years. Besides essential patients' identification data, such as gender, age, etc., information regarding lymphoma type, grade, and cancer site, were also obtained from patients' records. Lymphoma diagnosis was based on histopathology and immunohistochemistry methods, as described elsewhere [9,10].

Statistical analysis

Retrieved data were entered into computer software (SPSS) and analyzed to produce frequencies, percent-

ages, crosstabs, statistically significant values such as p-value, relative risk (RR), and odds ratio (OR), considering 95% confidence intervals. p-value < 0.05 was considered statistically significant.

RESULTS

This study included 134 lymphoma patients aged 4 to 85 with a mean age \pm SD of 45.5 ± 21.4 . Males embodied 75/134 (56%), while 59/134 (44%) were females, providing a male/female ratio of 1.27:1.00. Most patients were aged between 30 - 39 years (25/134; 18.7%), followed by 50 - 59 and ≥ 70 years (each 22/134; 16.4%). However, the age distribution was relatively similar for both males and females (Table 1, Figure 1). Because the data availability between 2008 - 2014 was limited, the samples diagnosed during these years were accounted for together. The available records indicated that most patients attended in the year 2019, followed by 2020, 2015, and 2016, representing 34/134 (25.4%), 14/134 (10.4%), 11/134 (8.2%), and 10/134 (7.5%), respectively (Table 1, Figure 1).

The most common lymphoma type was NHL followed by HL and B cell/NHL, constituting 44/134 (32.8%) [24/75 (32%) males and 20/59 (33.9%) females], 27/134 (20%) [18/75 (24%) males and 9/59 (15.3%) females], and 26/134 (19.4%) [13/75 (17.3%) males and 13/59 (22%) females], respectively (Table 2, Figure 2). In HL, the difference in the percentage between male and female patients was the highest. The risk of HL associated with male gender, the relative risk (RR) and the 95% confidence interval (95% CI); RR (95% CI) = 2.0077 (0.9447 - 4.2667), p = 0.0700, z statistic = 1.812. T cell/NHL and undifferentiated lymphoma (UL), NLP/HL, T cell/NHL, and lymphocytic lymphoma (LL) were identified in 6/134 (4.5%) cases [4/75 (5.3%) males and 2/59 (3.4%) females], 5/134 (3.7%) [3/75 (4%) males and 2/59 (3.4%) females], 5/134 (3.7%) [3/75 (4%) males and 2/59 (3.4%) females], and 4/134 (3%) [2/75 (2.7%) males and 2/59 (3.4%) females], respectively (Table 2, Figure 2).

A cancer site was available for 97 cases. Most patients presented with cervical lymph node (CLN) site, followed by unclassified site of lymph node (LN), and axillary, representing 27/97 (27.8%) [19/54 (35.2%) males and 8/43 (18.6%) females], 22/97 (22.7%) [10/54 (18.5%) males and 12/43 (28%) females], and 7/97 (7.2%) [2/54 (3.7%) males and 5/43 (11.6%) females], respectively (Table 2, Figure 2). The highest percentage based on gender was in CLN of male patients. The risk of CLN site associated with male gender, RR (95% CI) = 2.1192 (1.0047 - 4.4701), p = 0.0486, z statistics = 1.972. Data referred to cancer grade was available for 28 patients, 12/28 (42.9%) with high grade [8/16 (50%) males and 4/12 (33.3%) females], and 16/28 (57%) with low grade [8/16 (50%) males and 8/12 (66.7%) females] (Table 2, Figure 2).

Table 1. Lymphoma patients distributed by age and years of presentation.

Category	Variable	Male	Female	Total
Age group	≤ 18 years	11	6	17
	19 - 29	8	8	16
	30 - 39	15	10	25
	40 - 49	7	6	13
	50 - 59	10	12	22
	60 - 69	12	7	19
	70+	12	10	22
	Total	75	59	134
Year of presentation	Years *	26	19	45
	2015	6	5	11
	2016	8	2	10
	2017	7	2	9
	2018	5	3	8
	2019	15	19	34
	2020	8	9	17
	Total	75	59	134

Years * - 2008 - 2014.

Regardless of the year of record loss, the highest lymphoma prevalence was seen in the year 2019, which shows 34/134 (25.4%) (with predominant B cell/NHL 12/34 (35.3%) and HL 5/34 (14.7%)), followed by 2020 representing 14/134 (10.4%) (with predominant HL 5/14 (35.7%) and NHL 3/14 (21.4%)) (Table 3). In addition, most patients were seen in the age range 30 - 39 years, followed by 50 - 59 and ≥ 70 years, constituting 25/134 (18.7%) and 22/134 (16.4%) for the last two age groups. Although NHL was the highest percentage in most age groups, the age group 30 - 39 years represented HL as the major lymphoma type 9/25 (36%).

DISCUSSION

Contemplating the lack of lymphoma literature from Saudi Arabia and absence from the Hail region, the present study revealed a series of lymphoma cases materialized in Hail Region, Saudi Arabia, for 14 years. The current data showed that the prevalence rate of lymphoma in Hail was 9.6%/year, which is relatively higher than the previously stated report of 9.2% [4]. The prevalent patients in this study were males (56%). Such findings align with the previously reported literature that lymphoma is more frequent among men than women [11,12]. Additionally, the results of this study display a relatively equal age distribution in all age groups. NHL, which represents the commonest lymphoma subtype, can occur at different ages, and portrays

numerous age-related disparities in tumorigenesis and survival. High-grade lymphomas, such as anaplastic large cell lymphoma, diffuse large B-cell lymphoma, lymphoblastic lymphoma, and Burkitt lymphoma, usually occur in children.

In contrast, low-grade lymphomas, such as follicular lymphoma, outgrow with age [13]. However, wide variations in lymphoma biology regarding gender and age are unknown. This changes only sluggishly, even with the latest upsurge in attention about these mechanisms [14]. Therefore, investigations to explore the entire biological variations of lymphomas regarding age and gender are deemed necessary. In addition, identifying possible risk factors and increasing public awareness of early cancer detection could improve patients' survival rates and reduce its impact on human health and economics.

According to histopathology diagnosis, besides classical HL and primary NHL, several lymphoma types have been identified. According to our histopathology diagnosis scale, these lymphoma patterns were investigated at King Khalid and King Salman regional hospitals. The overall prevalence of classical HL (24.6%) among the studied patients is very high in the present study, particularly among men. However, such indicators were reported in Saudi Arabia, and HL represents the third leading cancer among Saudi males [15,16].

On the other hand, primary NHL has been demonstrated in about 56.7% of the patients in the current series. A previous study has shown an incidence rate of 51% for

Table 2. Distribution of lymphoma type, size, and grade by gender.

Category	Variable	Male	Female	Total
Lymphoma type	Hodgkin lymphoma (HL)	18	9	27
	Non-Hodgkin lymphoma (NHL)	24	20	44
	B cell/NHL	13	13	26
	T cell/NHL	4	2	6
	T cell/HL	2	2	4
	Nodular lymphocyte-predominant (NLP)/HL	3	2	5
	B cell/HL	0	1	1
	Nodular sclerosis (NS)/HL	1	1	2
	Mucosa-associated lymphoid tissue (MALT)/NHL	0	2	2
	Anaplastic lymphoma (AL)/NHL	0	2	2
	Lymphocytic lymphoma (LL)/NHL	3	2	5
	Lymphoma/sarcoma (L/S)	2	0	2
	Lymphoid neoplasm (LN)	1	1	2
	Undifferentiated lymphoma (UL)	4	2	6
Total	75	59	134	
Cancer sites	Cervical lymph node (CLN)	19	8	27
	Unclassified site of lymph node (LN)	10	12	22
	Thyroid	3	3	6
	Supraclavicular	1	4	5
	Axillary	2	5	7
	thigh	1	1	2
	Submandibular	3	3	6
	Tonsils	2	1	3
	Pleural effusion	3	0	3
	other	10	6	16
Total	54	43	97	
Cancer grade	High grade	8	4	12
	Low grade	8	8	16
	Total	16	12	28

A previous study has shown an incidence rate of 51% for NHL in Saudi Arabia [17]. Another study from Saudi Arabia demonstrated that NHL was the third most common male cancer with an incidence rate of 8.4% [18]. It was well-documented that hepatitis C virus (HCV) is associated with NHL [19,20]. Seroprevalence of HCV was reported to be 2.2% in Saudi Arabia, which might contribute to the mentioned cases of NHL [21]. Regarding specific lymphoma patterns, NLP/HL was detected in 19.4% of the patients. NLP/HL is a subtype of HL with a preserved B-cell phenotype and T-helper cells resetting around the tumor cells [22]. NLP/HL is an uncommon histological variant for some population patterns [23].

Even though nodular sclerosis (NS) was identified in this study to be among 1.5% of the patients, other

studies in Saudi Arabia (middle and eastern regions) showed NS as the common subtype of Hodgkin lymphoma [24,25]. Thus, NS is not common in northern Saudi Arabia, which might differ due to environmental or lifestyle factors. In India, mixed cellularity is the most common type, which has been reasoned as the infection of Epstein Bar Virus (EBV) and other environmental factors [26]. Although there is a paucity of data regarding EBV from Saudi Arabia, a former study has reported that EBV infection was more commonly seen in mixed cellularity Hodgkin's lymphoma (52.4%) compared to nodular sclerosing Hodgkin lymphoma (26.1%) [27].

Mucosa-associated lymphoid tissue (MALT)/NHL represented 1.5% of this study. MALT/NHL is a rare NHL type representing about 5% of all NHL types. Gastric

Table 3. Distribution of lymphoma types by year of presentation.

Variable	Years *	2015	2016	2017	2018	2019	2020	2021	Total
Lymphoma Type									
HL	7	4	3	2	0	5	5	1	27
NHL	34	2	0	1	1	3	3	0	44
B cell/NHL	2	1	1	2	5	12	1	2	26
T cell/NHL	0	2	1	0	0	1	2	0	6
T cell/HL	0	0	1	0	0	3	0	0	4
NLP/HL	0	0	0	2	0	3	0	0	5
B cell/HL	0	0	0	0	0	1	0	0	1
NS/HL	0	1	0	0	0	1	0	0	2
MALT/NHL	0	1	0	1	0	0	0	0	2
AL/NHL	0	0	0	0	0	1	1	0	2
LL/NHL	1	0	3	0	0	0	1	0	5
L/S	0	0	0	0	2	0	0	0	2
LN	0	0	1	1	0	0	0	0	2
UL	1	0	0	0	0	4	1	0	6
Total	45	11	10	9	8	34	14	3	134

Years * - 2008-2014.

Table 4. Number of patients by lymphoma type and age.

Variable	≤ 18 years	19 - 29	30 - 39	40 - 49	50 - 59	60 - 69	≥ 70	Total
Lymphoma Type								
HL	6	8	9	1	1	0	2	27
NHL	3	4	5	3	8	9	12	44
B cell/NHL	3	1	2	5	10	4	1	26
T cell/NHL	0	1	1	0	1	2	1	6
T cell/HL	0	0	2	1	1	0	0	4
NLP/HL	1	1	3	0	0	0	0	5
B cell/HL	0	0	0	1	0	0	0	1
NS/HL	1	1	0	0	0	0	0	2
MALT/NHL	0	0	0	0	0	1	1	2
AL/NHL	1	0	0	0	1	0	0	2
LL/NHL	1	0	1	1	0	1	1	5
L/S	0	0	2	0	0	0	0	2
AL	0	0	0	0	0	2	0	2
UL	1	0	0	1	0	0	4	6
Total	17	16	25	13	22	19	22	134

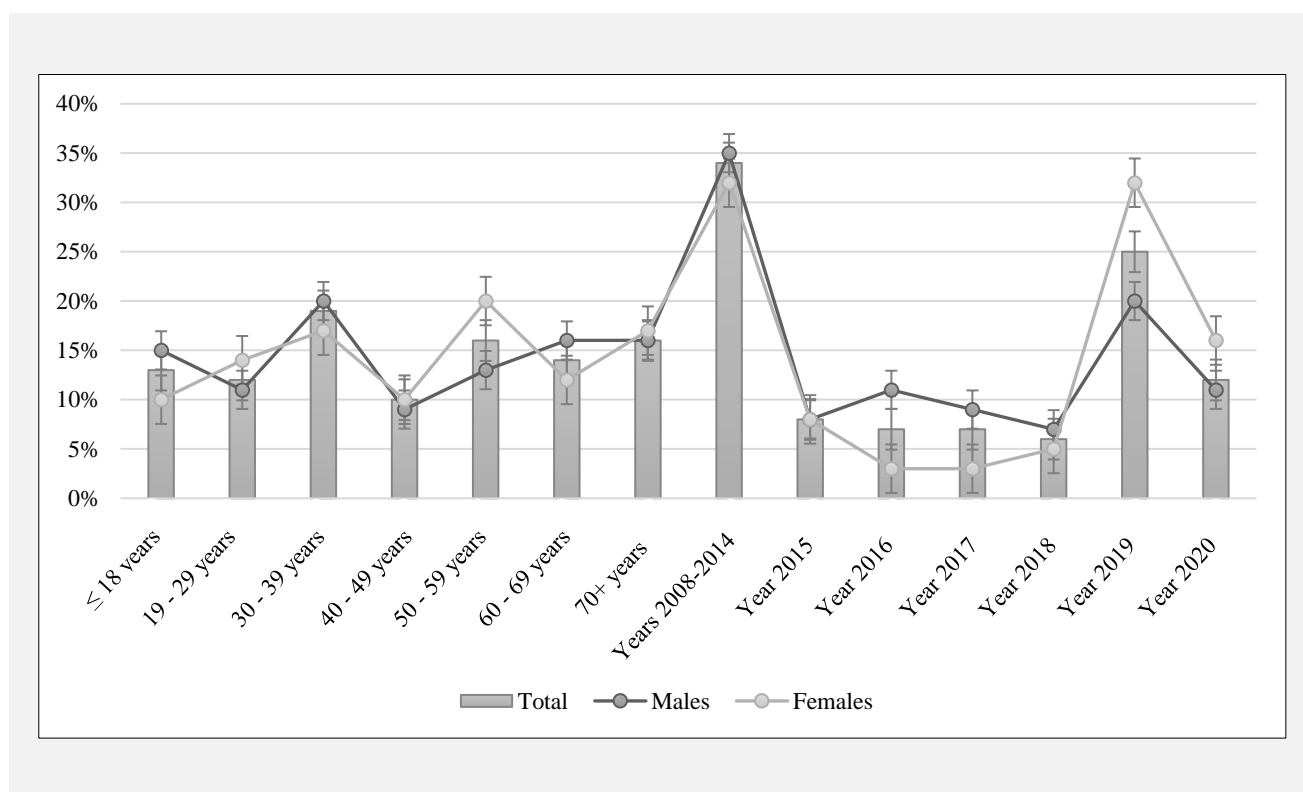


Figure 1. Description of lymphoma patients by age, year of presentation, and gender.

MALT/NHL is associated with *Helicobacter Pylori* [28]. It has been reported that *Helicobacter Pylori* is a major cause of lymphoma in the Middle East region [17].

Anaplastic large cell lymphoma (ALCL) was identified in 1.5% of the patients. ALCL originates from mature post-thymic T-cells and has distinctive lymphoid neoplasm in terms of pathogenesis and aggressive clinical presentation [29]. Lymphocytic lymphoma was found in 3.7% of the patients in the current study. Small lymphocytic lymphoma/chronic lymphocytic leukemia is an uncommon variant representing around 1% of all lymphomas [30]. Undifferentiated lymphoma (UL) represented about 4.5% of the patients, and 66.7% of the cases were males. UL usually consists of undifferentiated lymphoma cells that lack distinct morphologic evidence of maturation, such as those associated with certain Burkitt lymphoma types [31].

In addition, the cervical lymph nodes were found in this study to be the most typical site for lymphoma cancer, confirming the previous findings in the literature [31]. Furthermore, our results showed no significant association between specific lymphoma types and distinct age ranges. This variant, alongside various other variants in lymphoma cancer, is still poorly investigated and requires further studies to understand their associations with lymphoma cancer progression and treatment strategies. This changes only sluggishly, even with the latest

upsurge in attention to these mechanisms. Therefore, investigations to explore the entire biological variations of lymphomas regarding age and gender are deemed necessary.

Though the present study has some limitations, including its retrospective setting, it provides essential data insight into the lack of literature from Saudi Arabia in this context. Moreover, it increases the current knowledge in this field and identifies the common lymphoma subtypes with higher incidence rates. In addition, it clearly states and confirms the previous findings that males are more susceptible to lymphoma, suggesting the need for taking measures to target this group to reduce its occurrence. Such matters could include increasing their awareness about lymphoma cancer, early diagnosis, and avoiding risk factors.

CONCLUSION

Lymphoma is prevalent in the Hail region, Saudi Arabia, with an exceptional, ever-increasing incidence of HL. Wide-ranging lymphoma types have been explored in the Hail region, denoting large groups of unattributable etiologic modifiable risk factors. Therefore, further investigations are essential to explore the possible etiology of lymphoma in the Hail region.

Prevalence of Lymphomas in Saudi Arabia

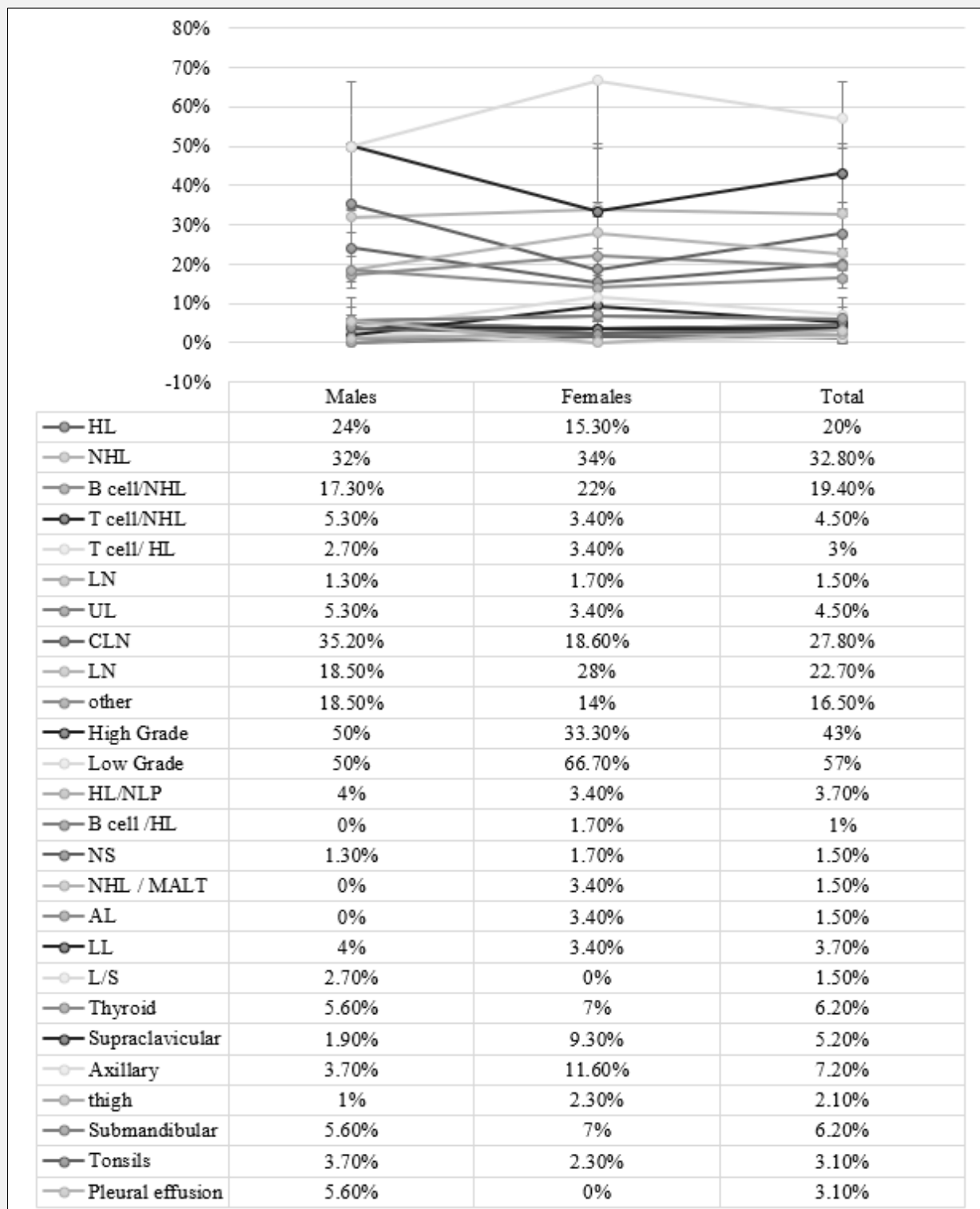


Figure 2. Description of lymphoma types, size, and grade within the gender category.

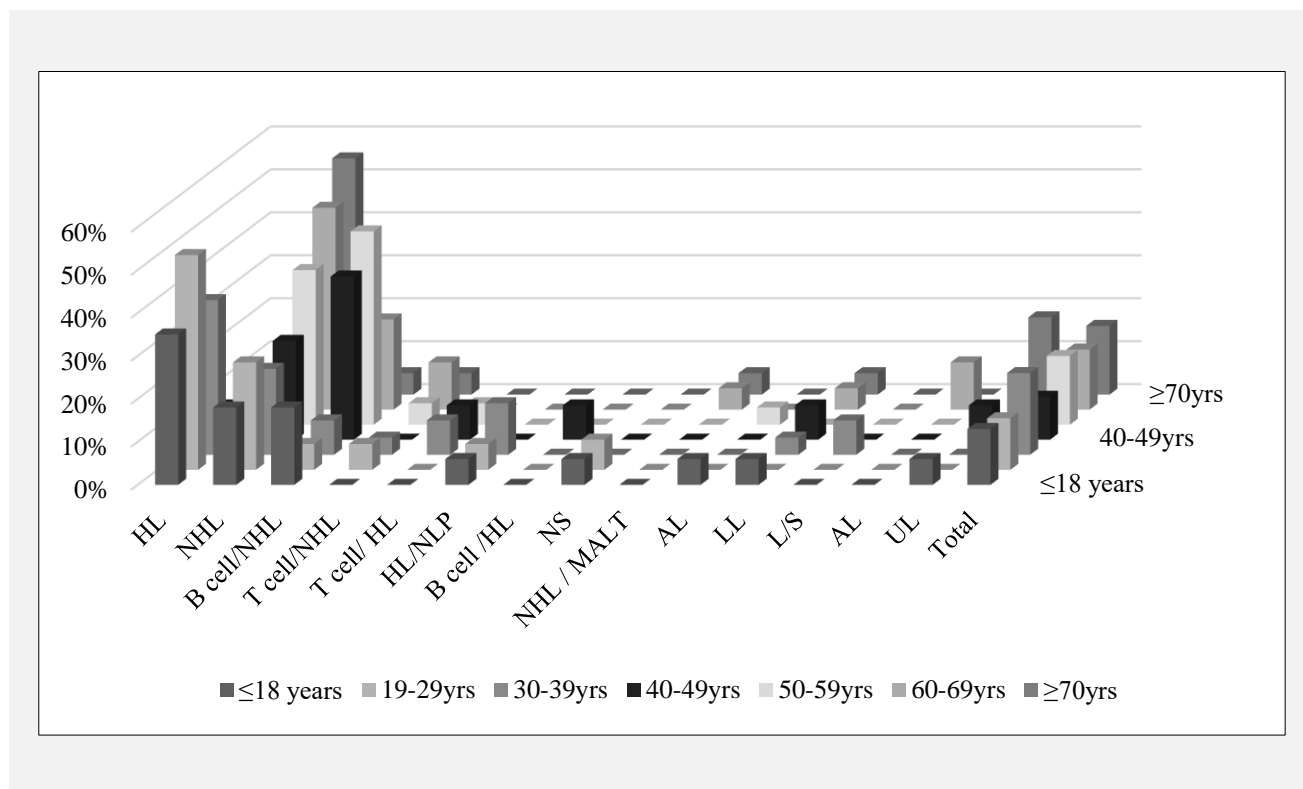


Figure 3. Percentage of patients by lymphoma type and proportions with entire age group.

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Ethics Committee Statement:

The study was conducted according to the guidelines of the Declaration of Helsinki, and the research ethics was approved by the Ethics Committee at the University of Hail (Ref. No. H-2020-173). Patient privacy and confidentiality of data were maintained in accordance with the Declaration of Helsinki.

Data Availability Statement:

Data that support the findings of this study are available within the article, and from the corresponding author upon request.

Declaration of Interest:

All authors declare no competing interests.

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