Malignant lymphoma in Hadhramout Sector, Yemen: a retrospective study of 170 cases classified according to the WHO classification

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Introduction
Malignant lymphoma is a primary neoplasm of lymphoid tissue. It is the third most common cancer in children worldwide. There are two broad categories of malignant lymphomas: non-Hodgkin's lymphoma (NHL) and Hodgkin's lymphoma (HL). Both have different microscopic features, follow different treatment modalities, and have different prognoses.

Aim of the work
The aim of the study was to determine the different types of lymphoma in all age groups, and find its relation to sex and site of lymph node involvement in Hadhramout Governorate.

Materials and methods
This is a retrospective descriptive study of 170 cases of lymphomas retrieved from the archives of the National Oncology Center, Hadhramout, during the period between 2008 and 2013. The diagnosis was assessed with immunohistochemical results and categorized according to the WHO classification of lymphoid neoplasms.

Results
Out of 170 patients, 116 (68.2%) had NHL and 54 (31.8%) had HL. A male predominance was observed (103/170, 60.6%). B-cell lymphomas were the most frequent type of NHL (95/116, 81.9%) and diffuse large B-cell lymphoma was the most common pattern of NHL (58/95, 61.1%), followed by Burkitt's lymphoma (20/95, 21.1%). The distribution of HL showed predominance of nodular sclerosis classical HL (38/54, 70.4%). The proportion of lymph node involvement of lymphomas was higher than extranodal involvement, being seen in 91/116 cases (78.5%) of all NHLs and 49/54 cases (90.8%) of all HLs.

Conclusion
NHL is the most common type of malignant lymphoma, and diffuse large B-cell lymphoma is the most common pattern among all NHL types, whereas nodular sclerosis classical HL is the most common type of HL. The nodal involvement of malignant lymphoma is higher than extranodal involvement.

Keywords:
Hodgkin's disease, lymphoma, nodal and extranodal, non-Hodgkin's lymphoma, WHO classification

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Introduction

Lymphoma is the primary neoplasm of the lymphoid tissue. It is considered the third most common type of cancer in children worldwide. There are two broad categories of lymphomas – non-Hodgkin's lymphoma (NHL) and Hodgkin's disease (HL) – diagnosed through histopathological biopsy. They have different clinical manifestations, microscopic morphology, treatment modalities, and prognoses [1]. The WHO classification of lymphoma has gained popularity and has been applied in various populations around the world [2].

The incidence of lymphomas has been increasing worldwide the past several decades [3]. In 2006 in the USA, the American Cancer Society estimated 66 670 new cases of lymphoma, resulting in 20 330 deaths, which included 7800 HLs and 58 870 NHLs, 34 870 in men and 31 800 in women, making lymphoma the fourth most common malignant neoplasm in both sexes in the USA [4]. In 2007, the projections in the USA were 8190 cases of HL and 63 190 cases of NHL [5].

NHL was considered the third most common type of cancer after breast cancer and leukemia. HL was the fourth most common type of cancer. This is considerably higher than their proportion in developed

countries such as the UK, where NHL is the sixth most common cancer (2011), accounting for 4% of all new cases, whereas HL is around 1% [6].

There are marked geographic variations in HL incidence [3]. A higher incidence occurs in western countries and in westernized populations including in those who immigrate from low incidence sites to the USA [7].

Lymphoid malignancies are generally more common in men than in women. For both NHL and HL, the age-standardized rates and numbers are consistently higher for men than for women, the differences tending to be slightly more pronounced in less developed regions of the world [8].

In Yemen, there are few published studies, but some studies revealed that the most common cancer was that of the gastrointestinal tract, followed by lymphomas and then head and neck cancers [9]. As per the Aden Cancer Registry hematopoietic cancers were the most common [10].

Badheeb and Baamer [11] reported that lymphoma represents 12.5% of all cancers in the Hadhramout Sector (Hadhramout, Shabwah, and Al Mahrah) in the east of Yemen, as per the Hadhramout Cancer Registry of Hadhramout Cancer Foundation.

No studies have been previously reported on the pattern of lymphoma in Hadhramout, Yemen. Because the clinical management of lymphomas depends on correct diagnosis and classification, the aim of this study was to determine the types of lymphoma in all ages, and in relation to sex and site in Hadhramout Governorate.

Materials and methods

This is a retrospective descriptive study of all lymphomas retrieved from the archives of National Oncology Center, Hadhramout. The related data were abstracted from patient medical records based on clinical, histological, and immunohistochemical staining results using a special form designed for this purpose. The data included residence, sex, and age of the patients, site of lymphoma, histological type, and immunohistochemical staining results during the period from January 2008 to December 2013. The study was approved by the ethical committee based on the best practice of ethics in medicine and in concordance with the principals of Helsinki declaration. The data were checked for completeness, coded, then entered into the computer using the statistical package for social sciences, version 20 (SPSS Inc., Chicago, Illinois, USA). The obtained data were analyzed using descriptive statistical tables (frequencies, percentages, χ^2-test, and *P* value).

Results

Age

There were 170 lymphoma patients included in this study; 116/170 (68.2%) had NHL and 54/170 (31.8%) had HL. We observed a wide age range from 5 to 90 years (mean age 41.2 years). The frequency of lymphomas in all ages was not statistically significant (P = 0.11). In children, 31/51 (60.8%) had NHL and 20/51 (39.2%) had HL (Table 1).

Sex

The present study showed male predominance: 103/170 (60.6%) patients were male and 67/170 (39.4%) were female (Table 2 and Fig. 1).

Histopathological types of non-Hodgkin's lymphomas

Among the 116 cases of NHL, 75 (64.7%) were male and 41 (35.3%) were female. The age of the patients ranged from 5 to 90 years (median age is 45). Out of 116 cases of NHL 95 (81.9%) lymphomas were immunophenotyped as B-cell lymphomas, and the remaining 21 (18.1%) expressed the T-cell immunophenotype. Among B-cell lymphomas, diffuse large B-cell lymphoma (DLBCL) was the

Table 1 The frequency of lymphomas in adults and children

Lymphoma	Children (up to 15 years) (*n* (%))	Adults (from 15 years) (*n* (%))	Total (*n* (%))
NHL	31 (60.8)	85 (71.4)	116 (68.2)
HL	20 (39.2)	34 (28.6)	54 (31.8)
Total	51 (100.0)	119 (100.0)	170 (100.0)

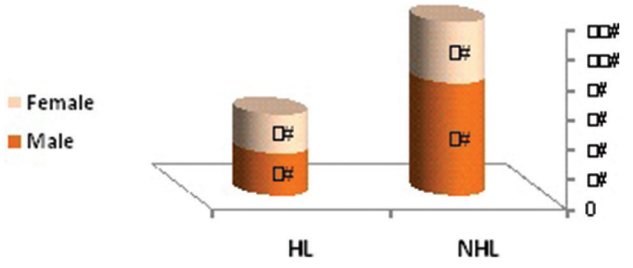
χ^2=1.866[a]. HL, Hodgkin's lymphoma; NHL, non-Hodgkin's lymphoma. *P*=0.11.

Table 2 The frequency of lymphomas according to sex

Sex	NHL (*n* (%))	HL (*n* (%))	Total (*n* (%))
Male	75 (72.8)	28 (27.2)	103 (100.0)
Female	41 (61.2)	26 (38.8)	67 (100.0)
Total	116 (68.2)	54 (31.8)	170 (100.0)

Pearson χ^2=2.529[a]. HL, hodgkin's lymphoma; NHL, non-Hodgkin's lymphoma. *P*=0.112.

Figure 1



The sex of malignant lymphomas. HL, Hodgkin's lymphoma; NHL, non-Hodgkin's lymphoma.

most common subtype (58/95, 61.1%) with a median patient age of 42 years at diagnosis, and it was common in men. This was followed by Burkitt's lymphoma (BL) with 20/95 cases (21.1%). All 20 cases of BL were seen in children with a median age of 10.5 years. Of 21 cases of T-cell lymphoma, lymphoblastic T-cell lymphoma was the predominant type, accounting for 11/21 cases (52.4%), followed by anaplastic large-cell lymphoma in 7/21 cases (33.3%) and mycosis fungoides in 3/21 cases (14.3%) (Table 3).

Histopathological types of Hodgkin's lymphomas

Among the 54 patients diagnosed with HL, 28 (51.9%) were male and 26 (48.1%) were female, with ages ranging from 8 to 69 years (median age 20 years) (Fig. 1).

Of the 54 cases of HL, nodular sclerosis classical HL was the most common variant of HL (38/54, 70.4%). Mixed cellularity HL was the second most frequent (8/54, 14.8%), followed by nodular lymphocytic predominant HL (4/54, 7.4%) and lymphocytic-rich classic HL (4/54, 7.4%) (Table 4).

Site distribution of lymphomas (nodal and extranodal)

There was significant statistical relation between the lymphoma and site of involvement. A total of 91/116 lymphomas (78.5%) showed lymph node involvement and 25/116 (21.5%) were extranodal sites. The most frequent nodal location was in the neck and cervical lymph nodes (39/116, 33.6%), followed by the abdominal and pelvic (30/116, 25.9%), the axillary (11/116, 9.5%), and the meditational lymph nodes (11/116, 9.5%). The most frequent extranodal location was the limbs (14/116, 12%) (Table 4).

There was significant statistical relation between lymphoma type and site of involvement in HL; lymph node involvement was seen in 49/54 cases (90.8%) and extranodal in 5/54 cases (9.2%; four in the limbs and one in the jaw). The most frequent nodal location was in the cervical lymph nodes (29/54, 53.7%), followed by the meditational nodes (9/54, 16.7%) and the abdominal and pelvic nodes (7/54, 13%) (Table 5).

Discussion

The classification of lymphomas has changed over the years, and nowadays most centers are adopting the WHO classification (2008). The latter represents a worldwide consensual set of criteria for the diagnosis of these tumors and is adopted by pathologists and clinicians. The objective of the present study is to determine the common types of malignant lymphoma

Table 3 The histopathological types of non-Hodgkin's lymphomas according to age and sex

Types of NHL	Age group (*n* (%))					Total (*n* (%))	Age (median)	Male (*n* (%))	Female (*n* (%))
	≤15	16-30	31-45	46-60	>60				
B-cell NHL 95 (81.9)									
DLBCL	7 (25.9)	25 (75.8)	9 (60.0)	17 (85.0)	0	58 (61.1)	42	35 (60)	23 (40)
BL	20 (74.1)	0 (0.0)	0 (0.0)	0 (0.0)	0	20 (21.1)	10.5	17 (85)	3 (15)
FL	0 (0.0)	3 (9.1)	4 (26.7)	2 (10.0)	0	9 (9.5)	54	4 (45)	5 (55)
SLL	0 (0.0)	5 (15.2)	1 (6.7)	0 (0.0)	0	6 (6.3)	42	4 (67)	2 (33)
MCL	0 (0.0)	0 (0.0)	1 (6.7)	1 (5.0)	0	2 (2.1)	61.5	1 (50)	1 (50)
Total	27 (100.0)	33 (100.0)	15 (100.0)	20 (100.0)	0	95 (100.0)		61 (64)	34 (36)
T-cell NHL 21 (18.1)									
LL	4 (100.0)	2 (66.7)	2 (100.0)	1 (25.0)	2 (25.0)	11 (52.4)	30	10 (90)	1 (10)
Anapla	0 (0.0)	1 (33.3)	0 (0.0)	3 (75.0)	3 (37.5)	7 (33.3)	60	4 (57)	3 (43)
MF	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (37.5)	3 (14.3)	65	0 (0)	3 (100)
Total	4 (100.0)	3 (100.0)	2 (100.0)	4 (100.0)	8 (100.0)	21 (100.0)			

χ^2=76.719[a]. Anapla, anaplastic lymphoma; BL, burkitt's lymphoma; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; LL, lymphoblastic lymphoma; MCL, mantle cell lymphoma; MF, mycosis fungoides; NHL, non-Hodgkin's lymphoma; SLL, small lymphocytic lymphoma. *P*=0.00% within age group.

Table 4 The histopathological types of Hodgkin's lymphomas according to age and sex

HL subtype	Age group (*n* (%))					Total (*n* (%))	Age (median)	Male (*n* (%))	Female (*n* (%))
	≤15	16-30	31-45	46-60	>60				
NSCHL	16 (80.0)	12 (66.7)	5 (50.0)	2 (66.7)	3 (100.0)	38 (70.4)	24.5	16 (42)	22 (48)
MC	2 (10.0)	5 (27.8)	1 (10.0)	0 (0.0)	0 (0.0)	8 (14.8)	18	7 (87.5)	1 (12.55)
NLPHL	2 (10.0)	1 (5.6)	1 (10.0)	0 (0.0)	0 (0.0)	4 (7.4)	17.5	3 (75)	1 (25)
LRCHL	0 (0.0)	0 (0.0)	3 (30.0)	1 (33.3)	0 (0.0)	4 (7.4)	34	2 (50)	2 (50)
Total	20 (100.0)	18 (100.0)	10 (100.0)	3 (100.0)	3 (100.0)	54 (100.0)			

Pearson χ=18.118[a]. HL, hodgkin's lymphoma; LRCHL, lymphocytic-rich classical Hodgkin's lymphoma; MC, mixed cellularity; NLPHL, nodular lymphocytic predominant Hodgkin's lymphoma; NSCHL, nodular sclerosis classical Hodgkin's lymphoma. *P*=0.112% within age group.

Table 5 Site distribution of lymphomas (nodal and extranodal sites)

Site	NHL (*n* (%))	HL (*n* (%))	Total (*n* (%))	
Nodal lymphomas				
Cervical (neck)	39 (33.6)	29 (53.7)	68 (40.0)	140 (82.4)
Abdomen and pelvis	30 (25.9)	7 (13.0)	37 (21.8)	
Meditational	11 (9.5)	9 (16.7)	20 (11.8)	
Axilla	11 (9.5)	4 (7.4)	15 (8.8)	
Extranodal lymphomas				
Limbs	14 (12)	4 (7.4)	18 (10.6)	30 (17.6)
Jaw	3 (2.6)	1 (1.8)	4 (2.4)	
Tonsils	8 (6.9)	0 (0.0)	8 (4.7)	
Total	116 (100.0)	54 (100.0)	170 (100.0)	

Pearson χ^2=12.893[a]. HL, hodgkin's lymphoma; NHL, non-Hodgkin's lymphoma. *P*=0.045% within the diagnosis of lymphoma HL or NHL

in children and adults in Hadhramout, Yemen, classified according to the recently published WHO system (2008) [2].

Our study showed a predominance of NHL, with the majority seen in the male population. These data are in agreement with those reported by Akhtar *et al.* [12] in Saudi Arabia, who reported that NHL (65.2%) was more common than HL (30.4%). Aminian *et al.* [13] in Iran also made similar observations. Previous studies have shown that the occurrence of HL is less frequent compared with NHL in Saudi Arabia [14], Bahrain [15], United Arab Emirates [16], and Nigeria [17]. The relative frequency of HL is the least in the Far East, Japan (5%), Thailand (7.9%), and Malaysia (13.3%) [18–20]. These differences might be explained by geographical variations in the distribution of the different types of malignant lymphoma.

NHL tended to be more common in men (median age 45 years at the time of diagnosis). Al-Samawi *et al.* [21] in Sana'a (Yemen) and Almasri *et al.* [22] in Jordon made a similar observation (median age 44 years). This might be explained by the greater exposure of men to different carcinogens like air and water pollution, which is common in Hadhramout.

In the current study, B-cell NHL lymphomas were more frequent than T-cell lymphomas, and DLBCLs represented the most common B-cell lymphoma, followed by BL. DLBCL has been reported to be the most common NHL in most studies worldwide, but it varies considerably from region to region – for example, United Arab Emirates 59% [16], Egypt 49% [27], Kuwait 47.6% [24], Jordan 43.8–53% [22,25], and Turkey 41% [26]. The relative proportion of DLBCL in this study is much higher than that reported in India [27].

In the current study, the second most common NHL, and the most common NHL in children, was BL. Such a predominance of BL is similar to that found in recent studies from Jordan, Saudi Arabia, and the United Arab Emirates [16,23,25], but is different from Indian reports, where BL ranks only third in frequency among children, following precursor T-lymphoblastic lymphoma and DLBCL [28]. The frequencies of BL do not exceed 5% of NHL, and in most countries are in the range of 1 – 3% [2,27,29]). Such high frequency of BL in the populations of the eastern Mediterranean region requires further scrutiny.

In the present study, DLBCL was common in younger adults and all cases of BL occurred in male children. This is a pattern that has been reported in many studies [12,21].

In this study, T-cell lymphomas were uncommon. The proportion seen is similar to that in studies conducted in some neighboring countries [12,16,25], but Far Eastern countries like Japan, Thailand, and China show high frequency of T-cell lymphomas, where it constitutes 27–30.5% of NHL [30,31], and to a lesser extent the 15–18% reported from India [20,27,32]. Such significant variation in the geographical distribution of T-cell lymphomas has long been recognized and has been attributed to racial predisposition, human T-cell lymphotropic virus-I infection, and lower relative incidence of B-cell NHL in the Far East [33].

In the current study, the majority of NHL cases presented with nodal involvement, the cervical lymph nodes being the most commonly affected site. Similar figures have been observed in other studies in the region, such as the United Arab Emirates. Castella *et al.* [16] noticed that 87 (71%) cases of NHL were nodal and the most frequent nodal locations at the time of presentation were the cervical lymph nodes (30 cases, 24%). But in Bahrain, Shome *et al.* [15] found a slightly higher proportion of extranodal involvement (41%). This variation could be due to differences in the number of cases, geographical distribution, and the differences in environmental factors in various communities.

The current study shows a low rate of HL and a somewhat higher prevalence in men. These findings are similar to those observed by Castella *et al.* [16] and Haddadin [25].

The nodular sclerosis classical HL was found to be the most common variant of HL in this study and the most common childhood HL variant, followed by mixed cellularity type. These results are in agreement with the percentage of HL types in other studies conducted in some Gulf countries and Northen Iraq [12,14,16,34]. This high frequency of nodular sclerosis has been attributed to reduced risk for early childhood exposure

to Epstein Barr virus, which is more likely to be associated with mixed cellularity rather than nodular sclerosis. Our result differs from those of other studies in Bahrain [19] and Jordan [35] in which mixed cellularity HL was more frequent than the nodular sclerosis variant. This discrepancy, however, might be explained by sample size, geographical, or molecular pathway differences.

The majority of HL cases presented with nodal involvement. The most frequent nodal location was in the cervical nodes, followed by meditational nodes. Castella *et al*. [16] in the United Arab Emirates noticed that the most common location of HL at the time of diagnosis was in the cervical lymph nodes (45 cases, 53%), followed by the axillary lymph nodes (13 cases, 15%) and meditational lymph nodes (12 cases, 14%). Only two cases of HL were extranodal and involved the parotid gland and the pleura, respectively.

Conclusion

Our study was the first conducted in Hadhramout on the pattern of malignant lymphomas using immunohistochemical staining and based on the current WHO classification of lymphoid neoplasm. NHL is more common than HL, with male predominance in both types. B-cell lymphomas were the most frequent NHL compared with T-cell lymphomas, and DLBCL was the most common pattern of NHL in all ages, followed by Burkitt's type, which is most common in the pediatric group. The distribution of HL showed a predominance of nodular sclerosis HL predominantly in the pediatric group. The proportion of nodal involvement of malignant lymphomas is higher than extranodal involvement. Further studies are recommended to elucidate the relation between higher prevalence of lymphoma in men and exposure to various environmental factors.

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Conflicts of interest

There are no conflicts of interest.

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