The patterns and clinical manifestations of lymphoma in adults in South Yemen

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Abstract

Lymphoid neoplasms are clonal lymphoproliferations and are heterogeneous in clinical presentation, histopathology, immunophenotype, and prognosis.
The objectives of the study are to determine the main subtypes of lymphoma at the National Oncology Center in Aden and to analyze the clinical parameters including age, gender, anatomic distribution (nodal and extra nodal), signs, symptoms, grading, and to compare our results with other geographic regions.

A total number of 127 cases of lymphoma were collected during two years, the diagnosis was based on histological morphology following the International Working Formulation Classification System. Data were subjected to statistical software; Statistical Package for Social Sciences SPSS version 19. Age, gender, type of lymphoma, anatomic location, signs and symptoms were computed in term of frequency.

This is a retrospective study of 127 cases of lymphoma during the years 2013-2014, the ratio of NHL to HL was 1.59: 1. NHL was 61.4% ,38.6% were males and 22.8% were females, with a male to female ratio of 1.68:1. Hodgkin lymphoma was 38.6%; 22.0% were males and 16.5% were females, with a male to female ratio was 1.3:1.

The most common age groups affected for NHL in both sexes was ≥ 60& 45-59, 22.8%& 15.0%, respectively, together accounting for more than 50% of NHL, while the most common age groups affected for HL was 30-44& 15-29, 14.2% &10.2% respectively, together accounting for more than 50% of HL. According to the grading of NHL, high grade lymphoma was 14.1%, intermediate grade 48.7%, low grade 37.2 %. Regarding the subtypes of HL, the most common subtypes were mixed cellularity and nodular sclerosis 57.1% & 38.8% respectively. NHL with nodal presentation was seen in 39.37% of cases, and extranodal 22.04%, while HL mainly was manifested as nodal in 37.79% and only 0.78% extra nodal. Swelling in neck, axilla, groin was the most common symptom for NHL and HL 48.7%& 67.3% respectively. Anemia was the most common sign for NHL and HL (62.8%&67.3% respectively), followed by hepatomegaly and splenomegaly in HL (38.8% & 51.0% respectively).

Non-Hodgkin lymphoma was twice the Hodgkin lymphoma. NHL was the most common in elder age group, while HL was in younger age group. Histological grade of NHL revealed the highest frequency of intermediate grade. Mixed cellularity was the most common subtype of HL. Nodal presentation predominate than extranodal. Lymphoma presents commonly as lymphadenopathy, fever, wt. loss, hepatomegaly, splenomegaly.

Keywords: Lymphoma, Non-Hodgkin, Hodgkin, grading, clinical manifestations.

Introduction:

Lymphoid neoplasms are clonal lymphoproliferations and are heterogeneous in clinical presentation, histopathology, immunophenotype, and prognosis (6).

Lymphoma types vary across geographic regions reflecting the impact of ethnicity, socioeconomic status and various environmental factors on lymphomagenesis(22).

In the United states of America, the incidence has increased by 4% annually since 1950, with a steady age-dependent increase from childhood through the eighth decade of life. Malignant lymphoma is the fifth common type of cancer. In Europe , the increase in the incidence rate is 4.8% per year (21).

Data from the International Agency for Research on Cancer indicated that at least 287,000 of Non-Hodgkin lymphoma (NHL) and 62,000 of Hodgkin lymphoma (HL) new cases were annually diagnosed worldwide. In the USA, NHL is already ranked fifth among white male cancers for both incidence and mortality, and sixth for female cancer (15).

Lymphomas are subdivided into Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL) (4).The Hodgkin lymphoma (HL) is also subclassified into four categories termed Nodular sclerosis (NS) Mixed cellularity(MC), Lymphocyte depletion(LD) and Lymphocyte-rich(LR). In addition , the working formulation classification has been adopted in the US. According to this system, NHL has been divided into low, intermediate, and high grades (10, 18).HLs involve the lymph nodes predominantly and only approximately 5% arise in extranodal sites , whereas 30% of NHL were present in extranodal sites (4).

It has been observed that, during the last two decades, the incidence of NHL has increased, and that of primary extranodal lymphoma (pENL) increased more rapidly than nodal type.(16) This trend is seen particularly in developing countries ,more so in the Middle East and the Far East, with an increase in diffuse histological pattern over nodular, and is more aggressive than indolent behavior(28,29).

Lymphoma can occur at any age; however, it has a bimodal presentation with one peak in early years of life and other after middle age. Patients with lymphoma usually present with constitutional symptoms of weight loss, fever and night sweats or because of enlarged lymph nodes.(12) Patients having B symptoms (fever, wt. loss, night sweat) show a more severe condition than asymptomatic patients with the same cancer stage, tumour location or size. Onset of B symptoms at the time of diagnosis suggests that lymphoma is progressing(23).

Symptoms may also develop due to pressure effects of lymph nodes on surrounding structures, or due to involvement of extranodal sites such as gastrointestinal tract (GIT), central nervous system (CNS), liver, or bone, thus leading to atypical presentations(12).

Due to the varied clinical picture, many patients were misdiagnosed and treated for diseases like tuberculosis, systemic lupus erythematosis, for a long time before coming to the correct diagnosis (2).

The aim of the study is to determine the main subtypes of lymphoma at the National Oncology Center in Aden and, to analyze the clinical parameters including age, gender, anatomic distribution (nodal and extra nodal), signs, symptoms, grading, and to compare our results with other geographic regions.

Patients and methods:

A retrospective study was done during two years (2013-2014). Out of a total of 167 cases of lymphoma were collected from the National Oncology Center at Al-Sadakha Teaching Hospital, Aden. The Patients whom their files were unavailable were excluded (succumbed patients) , some files contain no data also excluded. The available cases were 127 ,the diagnosis was based on histological morphology following the International Working Formulation Classification System (25). Data were subjected to statistical software; Statistical Package for Social Sciences SPSS version 19. Age, gender, type of lymphoma, anatomic location, B symptoms were computed in term of frequency.

Results:

A total of 127 cases of lymphoma were studied. The ratio of NHL to HL was 1.59: 1,age range was 15-80, and mean age for NHL was 51.08±19.1 and for HL 39.84± 16.9.

NHL was 61.4% (n=78), 38.6% (n=49) were males and 22.8% (n=29) were females with a male to female ratio of 1.68 :1. Hodgkin lymphoma was 38.6% (n=49); 22.0% (n=28) were males and 16.5% (n=21) were females with a male to female ratio 1.3:1 (Table 1)

Table 1: Distribution of Patients with Non-Hodgkin and Hodgkin lymphoma according to sex.

Sex	Diagnosis		Total	P-value
	Non-Hodgkin lymphoma	**Hodgkin lymphoma**		
Male	49 38.6 %	28 22.0 %	77 60.6%	0.524
Female	29 22.8 %	21 16.5 %	50 39.4%	
Total	78 61.4 %	49 38.6%	127 100.0 %	

The most common age group affected for NHL in both sexes was ≥ 60 & 45-59, 22.8% & 15.0%, respectively , together accounting for more than 50% of NHL , while the most common age group affected for HL was 30-44 & 15-29, 14.2%&10.2% respectively, together accounting for more than 50% of HL .(Table 2).

Table 2: Distribution of Patients of Non-Hodgkin lymphoma and Hodgkin lymphoma according to age.

Age group	Diagnosis		Total	P-value
	Non-Hodgkin lymphoma	**Hodgkin lymphoma**		
15-29	12 9.4 %	**13** 10.2 %	25 19.7%	0.124
30-44	18 14.2 %	**18** 14.2%	36 28.3%	0.096
45-59	**19** 15.0 %	11 8.7 %	30 23.6 %	0.805
≥ 60	**29** 22.8 %	7 5.5 %	36 28.3 %	0.005
Total	78 61.4 %	49 38.6 %	127 100.0 %	-

According to the grading of NHL , the high grade lymphoma was 14.1% (n=11) , intermediate grade was 48.7% (n=38), and low grade 37.2% (n=29) (Table 3) Regarding the subtypes of HL , the most common subtype was mixed cellularity 57.1% (n=28), followed by nodular sclerosis 38.8% (n=19). (Table 3)

Table 3: Distribution of Non-Hodgkin and Hodgkin lymphoma patients according to grade and subtype.

Grade NHL	**No**	**%**
High	11	14.1
Intermediate grade	38	48.7
Low grade	29	37.2
Total	78	100.0
Subtypes HL	**No**	**%**
Nodular sclerosis	19	38.8
Mixed cellularity	28	57.1
Lymphocyte Predominant	1	2.0
Lymphocyte Depletion	1	2.0
Total	49	100.0

Distribution of lymphoma according to site of primary presentation is illustrated in Table 4.

Table 4: Distribution of NHL and HL according to site of primary presentation

Site	**Diagnosis**		**Total %**
	Non-Hodgkin lymphoma %	**Hodgkin lymphoma%**	
Nodal	50 (39.37)	48 (37.79)	98 (77.16)
Extra nodal	28 (22.04)	1 (0.78)	29 (22.83)
Total	78 (61.41)	49 (38.58)	127 (100)
P= 0.0000			

NHL with nodal presentation was seen in 39.37% (n=50) of cases , and extra nodal 22.04% (n=28), while HL was mainly manifested as nodal in 37.79% (n=48) and only 0.78% (n=1) extra nodal. Cervical was the most common nodal presentation , while gastrointestinal was the most common extranodal presentation.

Swelling of neck, axilla, and groin were the most common symptoms for both NHL and HL 48.7% & 67.3%, respectively, followed by wt. loss (41.0%) for NHL and fever and wt. loss 46.9% & 36.7% for HL respectively (Table 5). Anemia was the most common sign 62.8% & 67.3% for both NHL and HL respectively, followed by hepatomegaly and splenomegaly for HL (38.8 %& 51.0% respectively) (Table 5).

Table 5: Symptoms and signs of Non-Hodgkin lymphoma and Hodgkin lymphoma.

Symptoms	**NHL %**	**HL%**	**Sign**	**NHL %**	**HL %**
Fever	29.5	46.9	Anemia	**62.8**	**67.3**
Weight loss	**41.0**	36.7	Hepatomegaly	11.5	**38.8**
Swelling neck,axilla groin	**48.7**	67.3	Splenomegaly	14.1	**51.0**
Abdominal pain	32.1	24.5	Ascites	11.5	0.0
Vomiting	7.7	6.1	Abdominal mass	3.8	0.0
Headache	0.0	2.0	Others	11.5	4.1
Joint pain	5.1	0.0			
B symptoms	20.5	24.5			
Others	7.7	0.0			

Discussion:

Lymphoma represents one of the major problems all over the world. Out of 127 cases of lymphoma, NHL was 61.4 % and HL was 38.6 %, the ratio of NHL to HL was 1.59 : 1.Ishtiaq et al.(13) found that NHL was 73 % and HL 27 % . Similarly,Hingorjo et al.(11), found 81.6 % for NHL and 18.3 % for HL and Kim et al.(19) found NHL 95.4 % and HL 4.6 %. In our study, NHL was more or less twice the HL cases, while in other studies NHL varies from 3- 20 times the HL (13,19).

In our current study, there was male predominant, with male to female ratio for NHL of 1.68:1 which is in agreement with all other studies of Hamid et al,(9) and Anunbi et al.(3) 1.6:1 and 1.8:1 respectively. The male to female ratio for HL was 1.3:1 which is in agreement with Sughayer et al.(26) in which the male to female ratio was 1.8:1.

The most common age groups affected for NHL in both sexes was ≥ 60& 45-59, 22.8 % & 15.0 % respectively, together accounting for more than 50 % of NHL.In a study done in Senegal , the

60-69 age group were the representative for NHL with the frequency of 25% followed by 20-29 age group with the frequency 18.2% (24). Other studies reported in West-Midland Regional Cancer Registery 1995 (UK),that the disease was more common in elderly and approximately half of the cases were above 65yrs (27), while it is completely different from a study done in Yemen in which the most common affected age group was 30-39 (32.2%) and above 50 yrs only (11.2%)(1).For HL, the most common age group affected was 30-44(14.2%) , followed by 15-29 (10.2 %) , together accounting for more than 50% of HL . Mansoor found that in another study done in Hungary, the most common age groups affected were 15-29 & 30-44, (40%&26% respectively) (20). We concluded that Hodgkin lymphoma affect mainly younger individuals, while Non-Hodgkin lymphoma affect most frequently elder individuals.

The study of Histological grading of NHL revealed the highest frequency of intermediate grade 48.7 %, this is agrees with Anunbi CC et al.(3) who found that 39% of the cases were intermediate grade. Echonomophos et al.(8), as well, found that 66.7 % of the cases were intermediate, Abdurrahman Isikogan et al. (14).likewise support our finding because they found the highest frequency of intermediate grade in 69.8 % of the cases. On the contrary,Keszeler A. et al. (17) found that the most frequent grade was high grade.

Regarding the subtypes of HL , the most common subtype was mixed cellularity 57.1 %, followed by nodular sclerosis 38.8 %, which is similar to the study of Dinand et al. (7). who found mixed cellularity 72.4% and Nodular sclerosis 22.8%; these two subtypes were also the most common in many different studies (21, 1).

Regarding the site of primary presentation, NHL with nodal presentation was seen in 39.37%, while the exra nodal was 22.04% . Similarly, Castella et al.(5) , found that nodal was 71% and extra nodal 29%. On the contrary Mansoor found that in one study done in Hungary, nodal presentation was seen in 39.2%, while extra nodal in 41.9% (20).

Swelling in neck, axilla, groin were the most common symptoms (48.7% for NHL, and 67.3% for HL) followed by wt. loss (41.0%) for NHL, and fever (46.9%) for HL, B symptoms only seen in 20.5% for NHL and 24.5% for HL. Similarly in a study done in Abbottabad, Pakistan(11), the most common symptoms were fever (67.3% for NHL and 90.9% for HL) , followed by swelling in neck, axilla, groin (61.2% for NHL and 90.9% for HL), B symptoms were also common in HL 90.9%.

Anemia was the most common sign (62.8% for NHL and 67.3% for HL) followed by hepatomegaly and splenomegaly for HL (38.8% & 51.0% respectively). Similarly, the most common sign was anemia (100% for both NHL and HL) , followed by hepatomegaly 83.6% for NHL and splenomegaly 81.8% for HL (11).

Conclusions:

Non-Hodgkin lymphoma was twice the Hodgkin lymphoma. NHL was the most common in elder age group, while HL in younger age group. Histological grade of NHL revealed the highest frequency of intermediate grade. Mixed cellularity was the most common subtype HL. Nodal presentation predominate than extranodal. Lymphoma presents commonly as lymphadenopathy, fever, wt. loss ,hepatomegaly,splenomegaly.

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الأنواع و المظاهر السريرية لسرطان الغدد الليمفاوية لدى البالغين في جنوب اليمن

نفيسة عوض منصور
قسم علم الأمراض/ كلية الطب والعلوم الصحية/ جامعة عدن
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ملخص

الاورام الليمفاوية هي نسيج تكاثري مستنسخ وهي غير متجانسة في العرض السريري، النسيج المرضي، المناعي، والتكهني.
هدفت الدراسة إلى تحديد الأنواع الفرعية من سرطان الغدد الليمفاوية في المركز الوطني للأورام، لتحليل المعلمات السريرية المشتملة على: العمر، الجنس، التوزيع التشريحي (العُقدي وغير العُقدي)، العلامات والأعراض، ودرجتها ومن ثم مقارنة نتائجنا مع المناطق الجغرافية الأخرى.
تم جمع إجمالي عدد 127 حالة من سرطان الغدد الليمفاوية خلال سنتين. كان عدد حالات سرطان الغدد الليمفاوية غير الهودجكن (NHL) 78 حالة وحالات سرطان الغدد الليمفاوية الهودجكن (HL) 49 حالة. استند التشخيص على التشكل النسيجي التابع لنظام التصنيف العالمي (Working Formulation) . تم معاملة النتائج في البرنامج الإحصائي (الحزمة الإحصائية للعلوم الاجتماعية) (SPSS)نسخة 19. وتم احتساب العمر, الجنس, نوع سرطان الغدد الليمفاوية، الموضع التشريحي، والعلامات والأعراض بحسب التكرار.
هذه دراسة استعادية لعدد 127 حالة من سرطان الغدد الليمفاوية خلال الاعوام 2013 - 2014 وكانت نسبة السرطان الليمفاوي غير الهودجكن الى السرطان الليمفاوي الهودجكن 1.59 : 1. وكانت نسبة سرطان الغدد الليمفاوية غير الهودجكن61.4%، منها 38.6 % نسبة الذكور و22.8 % نسبة الإناث. مع نسبة الذكر للأنثى 1.68: 1، وكانت نسبة سرطان الغدد الليمفاوية الهودجكن 38.6%، منها 22.0 % هي نسبة الذكور و16.5% هي نسبة الإناث مع نسبة الذكر إلى الأنثى 1.3: 1.وكانت الفئة العمرية الأكثر شيوعا المتأثرة بسرطان الغدد الليمفاوية غير الهودجكن في كلا الجنسين ≥ 60 و 45 – 59، بنسب 22.8% و 15.0% على التوالي. وهما معاً يمثلا اكثر من 50% من سرطان الغدد الليمفاوية غير الهودجكن(NHL).في حين أنَّ الفئة العمريةالأكثر شيوعا المتأثرة بسرطان الغدد الليمفاوية الهودجكن بين 30- 44 و 15-29، بنسب 14.2% و 10.2% على التوالي وهما معاً يمثلا أكثر من 50% من سرطان الغدد الليمفاوية الهودجكن(HL)، ووفقاً لتدرج سرطان الغدد الليمفاوية غير الهودجكن،جاء سرطان الغدد الليمفاوية عالية التدرج بنسبة 14.1% , و سرطان الغدد الليمفاوية متوسطة التدرج بنسبة 48.7%، وسرطان الغدد الليمفاوية بطيئة التدرج بنسبة 37.2%. وفيما يتعلق بالأنواع الفرعية لسرطان الغدد الليمفاوية الهودجكن, فإنَّ الأنواع الفرعية الأكثر شيوعاً هي الاختلاط الخلوي والتصلب العُقدي بنسب 57.1% و 38.8 % على التوالي. وتم ملاحظة سرطان الغدد الليمفاوية غير الهودجكن بالمظهر العُقدي في 39.37% من الحالات، وغير العقدي في 22.4% منها. في حين ظهر سرطان الغدد الليمفاوية الهودجكن بشكل رئيسي كعُقدي في 37.79% وفي 0.78% فقط غير عقدي.
وكان التورم في الرقبة,والإبط و الأربي هو علامة المرض الأكثر شيوعاً لسرطان الغدد الليمفاوية غير الهودجكن, وسرطان الغدد الليمفاوية الهودجكن، بنسب 48.7% و67.3% على التوالي. وكان فقر الدم هو السمة الأكثر شيوعاً لسرطان الغدد الليمفاوية غير الهودجكن وسرطان الغدد الليمفاوية الهودجكن، بنسب 62.8% و67.3% على التوالي، يليه تضخم الكبد وتضخم الطحال في سرطان الغدد الليمفاوية الهودجكن، بنسب 38.8% و 51% على التوالي.
كان سرطان الغدد الليمفاوية غير الهودجكن ضعف سرطان الغدد الليمفاوية الهودجكن، وهو الأكثر شيوعاً في الفئة العمرية الأكبر سناً غي حين كان سرطان الغدد الليمفاوية الهودجكن أكثر شيوعاً في الفئة العمرية الأصغر سناً. كشف التدرج النسيجي لسرطان الغدد الليمفاوية غير الهودجكن أعلى تردد من المتوسط التدرج. وكان الاختلاط الخلوي هوالنوع الفرعي الأكثر شيوعاً لسرطان الغدد الليمفاوية الهودجكن. وفاق عدد المظهر العُقدي عن عدد المظهر الغير العُقدي.
يتجلى سرطان الغدد الليمفاوية عموماً في تضخم عقد لمفية، حمى، فقدان الوزن، تضخم الكبد وتضخم الطحال.

الكلمات المفتاحية: سرطان الغدد الليمفاوية، غيرالهودجكن, الهودجكن، تدرج، المظاهر السريرية.