

## RESEARCH ARTICLE

# Type Distribution of Lymphomas in Lebanon: Five-Year Single Institution Experience

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### Abstract

**Background:** Lymphomas represent the fifth most frequent cancer in Lebanon. However, little is known concerning epidemiologic characteristics and distribution of lymphoid neoplasms according to the 2008 WHO classification. **Materials and Methods:** We conducted a retrospective study of lymphoma cases diagnosed from 2008 till 2012 at Hôtel-Dieu de France University Hospital. **Results:** A total of 502 new cases of lymphoma were diagnosed at our institution during a five year period: 119 cases (24%) were Hodgkin lymphomas (HL) and 383 cases (76%) were non-Hodgkin lymphomas (NHL). HLs were equally distributed in both sexes with a mean age at diagnosis of 30 years. Among NHL, 87% (332 cases) were B cell lymphomas, 9% (34 cases) were T cell lymphomas and 4% (17 cases) were classified as precursor lymphoid neoplasms. Among B cell lymphomas, 44% (147 cases) were diffuse large B cell lymphomas (DLBCL), 20% (65 cases) follicular lymphomas and 8% (27 cases) mantle cell lymphomas. DLBCL were equally distributed in both sexes with a mean age of 58 years. Follicular lymphomas were characterized by a male predominance (57%) and a mean age of 60 years. Mantle cell lymphomas showed a pronounced male predominance (85%) with a mean age of 60 years in men and 70 years in women. Some 72% of patients having T cell lymphomas were men, with a mean age of 57 years in men and 45 years in women, while 65% of patients having precursor lymphoid neoplasms were women with a mean age of 22 years in women and 30 years in men. **Conclusions:** The lymphoma subtype distribution in Lebanon is unique when compared to other countries from around the world. In fact, Hodgkin and follicular lymphomas are more frequent than in most Far Eastern, European and American countries, while T-cell lymphomas and DLBCL are less frequent.

**Keywords:** Lymphoma - WHO 2008 classification - epidemiology - Lebanon - eastern Mediterranean area

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### Introduction

Lymphomas represent the fifth most frequent cancer in Lebanon. Every year, between 600 to 700 new cases of Hodgkin lymphoma and non-Hodgkin lymphoma (NHL) are diagnosed in the country (2004). The last WHO classification of tumors of hematopoietic and lymphoid tissues was adopted in 2008 and distinguishes 5 main subtypes of the lymphoid neoplasms: precursor lymphoid neoplasms, mature B-cell neoplasms, mature T- and NK-cell neoplasms, Hodgkin lymphoma and immunodeficiency-associated lympho-proliferative disorders (Swerdlow et al., 2008).

Many epidemiologic studies have been conducted in the Asian continent, to explain different subtype distribution among different countries. The association between lymphomas and viral infections has been discussed, especially regarding Epstein Barr Virus

infection in Hodgkin lymphoma patients (Fatima et al., 2011; Li et al., 2012) and Hepatitis B Virus infection in patients diagnosed with any lymphoma (Tang et al., 2013). Patients diagnosed of NHL have been the subject of many more epidemiologic studies. Risk factors has been detected such as a higher consumption of carbohydrate in Oman (Ali et al., 2013) and an increase in pesticides usage in Turkey (Yildirim et al., 2013). The latter has been previously estimated as a 3-fold excess risk in India, among other risk factors: cigarette smoking, consumption of mutton and consumption of milk (Balasubramaniam et al., 2013). On the other hand, a reduced risk of NHL was associated with coffee consumption in India (50% reduction) (Balasubramaniam et al., 2013) and with a higher educational level and a higher intake of vegetables in Oman (Ali et al., 2013). Finally, the gene expression profiling of NHL has been the main interest of recent studies. New differentially expressed genes may be

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**Table 1. Distribution of Lymphoma Subtypes according to Mean Age (with Extremes) and Gender**

Lymphomas	Number of Cases	Proportion	Mean Age	Sex Ratio M/F	Number of Male Cases	Mean Age in Male	Number of Female Cases(years)	Mean Age in Female (years)
Hodgkin lymphoma	119	24%	30 (6-75)	1.02	60	29	59	31
Non-Hodgkin lymphoma	383	76%	44 (5-95)	1.27	214	48	169	40
B-cell lymphoma	332	87%	57 (10-95)	1.24	184	58	148	56
T-cell lymphoma	34	9%	53 (7-77)	2.4	24	57	10	45
Precursor lymphoid neoplasms B-cell lymphoma	17	4%	25 (6-65)	0.55	6	30	11	22
Diffuse large B-cell lymphoma	147	44%	58 (15-95)	1.1	77	58	70	57
Follicular lymphoma	65	20%	60 (32-89)	1.32	37	61	28	59
Mantle cell lymphoma	27	8%	61 (12-86)	5.75	23	60	4	70
Other B lymphoma subtypes	93	28%	52 (10-85)	1.02	47	53	46	51

markers for NHL patients and individuals at high risk of cancer development (Zekri et al., 2013). Among NHL subtypes, DLBCL patients have been further studied for epidemiologic characteristics. Indeed, DLBCL has even been reported as the most frequent lympho-proliferative disorder detected in multiple primary cancers (Demirci et al., 2012). A Chinese study identified a direct or indirect protective effect of traditional Chinese medicine against DLBCL. It also revealed a possible predisposition for DLBCL in TB patients and farmers (Fan et al., 2012).

To our knowledge, the literature is poor regarding the distribution of lymphoid neoplasm subtypes in the Lebanese population especially according to the 2008 WHO Classification of tumors of hematopoietic and lymphoid tissues.

The aim of this study is to determine the epidemiologic characteristics of lymphomas in Hôtel-Dieu de France University Hospital, knowing that approximately 20% of all newly Lebanese cancer cases are diagnosed in this tertiary hospital (unpublished data). Moreover, the distribution of these lymphoma cases according to WHO classification of 2008 will be reported.

## Materials and Methods

A search for the diagnosis of lymphoid neoplasms in the computerized database of the pathology department of Hôtel-Dieu de France, Saint Joseph University hospital was conducted. From January 2008 to December 2012, 502 patients newly diagnosed with lymphomas at any site were included after eliminating all the duplicated cases. Two different pathologists established the diagnosis. Discordant cases were reviewed by expert hematopathologists. The age, the gender and the lymphoma subtype according to the 2008 WHO Classification of Hematopoietic and Lymphoid Tissues of patients were attributed and analyzed using the SPSS version 20 statistics program.

## Results

Of the 502 cases of lymphomas diagnosed during five years in our institution, HL accounted for 119 cases (24% of all lymphomas), NHL for 383 cases (76% of all lymphomas), mature B cell neoplasms for 332 cases (87% of all NHL), mature T cell neoplasms for 34 cases (9% of all NHL) and precursor lymphoid neoplasms for 17 cases

(4% of all NHL).

Hodgkin lymphomas (HL) were equally distributed in both sexes with a mean age at diagnosis of 30 years (age ranged from 6 to 75) (Table 1). More than 50% (62 cases) of HL were diagnosed between the ages of 10 to 30. Another peak incidence was detected within the 6th decade of age.

Concerning non-Hodgkin lymphomas (NHL), the mean age of patients was 44 years old (age ranged from 6 to 95). Among those, 44% (169 cases) were women with a mean age of 40 years and 56% (214 cases) were men with a mean age of 48 years (Table 1). 60% of patients diagnosed with NHL were aged between 50 and 80 years.

Of all NHL cases, mature B-cell neoplasms represented 87% (332 cases) with a mean age of 57 years (age ranged from 10 to 95). Regarding gender repartition, 45% (148 cases) were women and 55% (184 cases) were men. Most common subtypes of mature B-cell neoplasms were DLBCL (44%, 147 cases), follicular lymphoma (20%, 65 cases) and mantle cell lymphoma (8%, 27 cases). Each of the remaining mature B-cell neoplasm subtype accounted for less than 3% of all B lymphoid neoplasms (Table 1).

The mean age of patients diagnosed with DLBCL was 57 years (age ranged from 15 to 95); 48% (70 cases) were women and 52% (77 cases) were men. The peak incidence of patients with DLBCL was between 60 and 80 years. The mean age of patients diagnosed with follicular lymphoma was 60 (age ranged from 32 to 89); 43% (27 cases) were women and 57% (38 cases) were men. The peak incidence of these patients was between 50 and 70. The mean age of patients diagnosed with mantle cell lymphoma was 61 years (age ranged from 12 to 86 years); 15% (4 cases) were women with a median age of 70 and 85% (23 cases) were men with a median age of 60 years (Table 1).

Only 9% of NHL (34 cases) were mature T- and NK-cell neoplasms with a mean age of 53 years (age ranged from 7 to 77). 29% were women with a mean age of 45 years and 71% were men with a mean age of 57 years (Table 1). Approximately 50% of these lymphomas were diagnosed in patients aged more than 60 years.

At last, 4% of NHL (17 cases) were precursor lymphoid neoplasms with a mean age of 25 years (extremes 6 to 65). 65% were women with a median age of 22 and 35% were men with a median age of 30 (Table 1). The three quarter of these patients were aged less than 30 years.

Table 2. Comparison of Lymphoma Subtypes Frequencies in Different Countries

	Middle East												Far East Asia				North America			Europe	
	HDF	Lebanon (Otrock et al., 2013)	Turkey (Kileksiz et al., 2011)	Saudi Arabia (Akhtar et al., 2009)	China (Yang et al., 2011)	Japan (Aoki et al., 2008)	Korea (Yoon et al., 2010)	Thailand (Sukpanichnant, 2004)	Taiwan (Chen et al., 2010)	USA (Wu et al., 2009)	USA (Morton et al., 2006)	USA (Wu et al., 2009)	USA (Morton et al., 2006)	England (Lowry and Linch, 2013)	France (Troussard et al., 2009)						
Year	2008-2012	2007	1992-2005	1988-2007	2000-2008	2001-2006	1989-2008	1993-2002	1995-2007	1999-2003	1992-2001	1992-2001	2009	1997-2004							
Number of lymphoma cases	502	272	1394	385	6382	2260	5318	1983	303	30444	114548	114548	-	2672							
HL	24%	33%	17%	32%	13%	7%	4%	8%	9%	9%	9%	9%	13%	16%							
NHL	76%	67%	83%	68%	87%	93%	96%	92%	91%	78%	91%	91%	87%	84%							
B-NHL	87%	88%	77%	82%	64%	70%	70%	75%	80%	78%	88%	88%	94%	89%							
T-NHL	9%	9%	8%	18%	30%	27%	13%	25%	20%	16%	6%	6%	6%	11%							
P	4%		15%		6%	1%	17%				6%										
NC		3%				2%															
B-NHL																					
DLBCL	44%	46%		51%	64%	51%	46%	67%	61%	51%			54%	41%							
FL	20%	23%		7%	9%	28%	3%	11%	11%	10%			22%	20%							
MCL	8%	7%		2%	5%	4%	3%	1%	6%	3%			-	4%							
MZL	1%	8%		5%	10%	7%	19%	6%	5%	16%			-	7%							

\*H = Hodgkin Lymphoma; NHL = Non-Hodgkin Lymphoma; B-NHL = B-cell Non-Hodgkin Lymphoma; p = Precursor lymphoid neoplasms; NC = Not Classified; DLBCL = Diffuse Large B-cell Lymphoma; FL = Follicular Lymphoma; MCL = Mantle Cell Lymphoma; MZL = Marginal Zone Lymphoma

## Discussion

To our knowledge, this study is the largest in Lebanon analyzing more than 500 cases of lymphomas in a single institution over a five-year period. It describes the epidemiologic characteristics and subtypes of lymphomas according to the WHO classification of 2008. A one-year national study of 227 cases of lymphomas classified according to the 2001 WHO classification of malignant lymphomas has recently been published (Otrock et al., 2013).

HL represents 24% of all lymphomas in our study, a high percentage when compared to the literature. In Asia, HL incidence doesn't exceed the 5% in Korea (Yoon et al., 2010) and in China 13% (Yang et al., 2011). In developed countries, HL represents 9% of all lymphoma cases in the US (Morton et al., 2006), 13% in England (Lowry and Linch, 2013) and 16% in France (Troussard et al., 2009). Our results concerning HL proportion are not far from the results mentioned in the Lebanese cancer registry where the HL represents 22% of all lymphomas (2004). HL constitutes 32% of all lymphoid neoplasm in Saudi Arabia (Akhtar et al., 2009) and 17% in Turkey [10] (Table 2).

The proportion of T-cell lymphomas is less than 10% of all NHLs in our study. Those data are comparable to the results in developed countries such as in US, France and England where T cell lymphomas proportion doesn't exceed respectively 6% (Morton et al., 2006), 16% (Wu et al., 2009), 12% (Troussard et al., 2009) and 6% (Lowry and Linch, 2013). In Turkey as well, it only reaches 8% [10]. However, this percentage of T lymphomas is very low when compared to China (30% of all NHL) (Yang et al., 2011), Japan (27%) (Aoki et al., 2008), Thailand (25%) (Sukpanichnant, 2004) and Saudi Arabia (18%) (Akhtar et al., 2009) (Table 2).

In our study, B cell lymphomas represent 87% of all our NHL cases. These results are similar to those found in developed countries (Morton et al., 2006; Troussard et al., 2009; Lowry and Linch, 2013) and discordant with most Far East Asian countries (Sukpanichnant, 2004; Aoki et al., 2008; Yang et al., 2011), where T cell lymphomas are more frequent (Table 2).

When discussing the subtypes of B cell lymphomas, many characteristics are detected. Follicular lymphomas (FL) represent nearly 20% of all NHL in our study. This is a relatively high percentage when compared to the FL percentage in China (9%) (Yang et al., 2011), Korea (3%) (Yoon et al., 2010) and US (10%) (Wu et al., 2009), where FL represents less than 10% of all NHL. Similarly a high proportion of FL is described in the French population (20%) (Troussard et al., 2009) (Table 2).

DLCBL accounts for 45% of all B-cell neoplasms in our study, while it represents more than 60% of all B-cell neoplasms in China (Yang et al., 2011) and Taiwan (Chen et al., 2010). Mantle cell lymphoma (MCL) represents 8% of all B-cell neoplasms, which exceeds by far the percentage of MCL in Saudi Arabia (2%) (Akhtar et al., 2009), Korea (3%) (Yoon et al., 2010), Thailand (1%) (Sukpanichnant, 2004), USA (3%) (Wu et al., 2009) and France (4%) (Troussard et al., 2009) (Table 2).

The distribution of different lymphoma subtypes in the Lebanese population shows similarities to that reported in the French and Turkish populations. A hypothesis should be highlighted when comparing these results: Is there any specific subtype distribution for the lymphomas in the Mediterranean region? Mediterranean multi centric studies can help investigating the presence of possible distinct epidemiologic features characterizing the Mediterranean population.

In conclusion, the distribution of the different lymphoma subtypes in Lebanon is unique when compared to other countries from around the world. Indeed, Hodgkin and follicular lymphomas are more frequent than in most Far Eastern, European and American countries, while T-cell lymphomas and DLBCL are less frequent.

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