

RESEARCH
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Distribution of Lymphoid Neoplasms in Northeast Turkey: A retrospective analysis of 1136 Cases According to the World Health Organization Classification

ABSTRACT

Objective: Malignant lymphoma is one of the most common cancer type around the world. In this study, the distribution and demographic characteristics of the histologic subgroups of mature lymphoid neoplasms in Northeast Turkey were investigated.

Methods: The study consists of 1136 patients diagnosed as mature lymphoid neoplasm between 2008 and 2014. The demographic data of the patients were analyzed and histological subgrouping was performed according to the World Health Organization classification.

Results: Mature B-cell neoplasms accounted for 79.2% (n=900) of all lymphoid neoplasms, Hodgkin lymphoma (HL) for 10.9% (n=124), mature T/natural killer-cell neoplasms for 9% (n=102), and histiocytic and dendritic cell neoplasms for 0.9% (n=10). In our study, the most common subtypes of lymphoid neoplasms were as follows: diffuse large B-cell lymphoma (n=261; 23%), plasma cell myeloma (n=252; 22.2%), chronic lymphocytic leukemia/small lymphocytic lymphoma (n=230; 20.2%), mycosis fungoides (MF) (n=66; 5.8%) and nodular sclerosing type classical HL (n=63; 5.5%). Only 2.9% of the cases of non-Hodgkin lymphoma (NHL) were follicular lymphoma. All patients with HL were diagnosed by a lymph node biopsy. However, 48.1% of the patients with NHL arose from extranodal sites.

Conclusions: This is the first study investigating the distribution of lymphoid neoplasms in Northeast Anatolia region with the review of the literature. The present study showed that the epidemiologic features similar to those reported in Western and Asian countries, whereas some subtypes showed distinct features. The high frequency of MF and the low frequency of follicular lymphoma are interesting findings of this study.

Keywords: Lymphoma, Lymphoid Neoplasms, WHO Classification, Subtype, Distribution

Türkiye'nin Kuzeydoğusundaki Lenfoid Neoplazm Vakalarının Dağılımı: 1136 Vakanın Dünya Sağlık Örgütü Sınıflamasına Göre Retrospektif İncelenmesi

ÖZET

Amaç: Malign lenfoma dünyada en sık görülen kanser tiplerinden biridir. Bu çalışmada, Türkiye'nin kuzeydoğusundaki matür lenfoid neoplazm vakalarının histolojik alt gruplarının dağılımları ve demografik özellikleri incelenmiştir.

Gereç ve Yöntem: Bu çalışmada 2008 ve 2014 yılları arasında matür lenfoid neoplazm tanısı almış 1136 hasta yer almaktadır. Hastaların demografik verileri araştırılıp Dünya Sağlık Örgütü sınıflamasına göre histolojik alt grupları tespit edilmiştir.

Bulgular: Tüm lenfoid neoplazilerin %79.2' si (n=900) matür B hücreli neoplaziler, %10.9' u (n=124) Hodgkin lenfoma (HL), %9' u (n=102) matür T/natural killer hücreli neoplaziler, %0.9' u (n=10) histiyositik ve dendritik hücreli neoplazilerden oluşmaktadır. Çalışmamızda lenfoid neoplazilerin en sık görülen alt tipleri şöyledir: diffüz büyük B hücreli lenfoma (n=261; %23), plazma hücreli miyelom (n=252; %22.2), kronik lenfositik lösemi/ küçük lenfositik lenfoma (n=230; %20.2), mikoziis fungoides (MF) (n=66; %5.8) ve nodular sklerozan tip HL (n=63; %5.5). Non-Hodgkin lymphoma (NHL) tanılı vakaların yalnızca %2.9' u folliküler lenfoma tanılıdır. HL hastalarının tümü lenf nodu biyopsisinden tanı almıştır. Bununla birlikte NHL vakalarının %48.1' i ektranodal bölge yerleşimlidir.

Sonuç: Bu çalışma Kuzeydoğu Anadolu' daki lenfoid neoplazilerin dağılımını literatür verileriyle karşılaştırarak inceleyen ilk çalışma niteliğindedir. Çalışmamızda batı ve Asya ülkeleri ile benzer epidemiyolojik veriler elde edilmesine rağmen bazı alt gruplarda farklılıklar dikkati çekmektedir. MF' in sıklıkla görülmesi ve folliküler lenfomanın nadir izlenmesi bu çalışmanın çarpıcı bulgularıdır.

Anahtar Kelimeler: Lenfoma, Lenfoid Neoplaziler, WHO Sınıflaması, Alt Tip, Dağılım

INTRODUCTION

Lymphoid neoplasms are a very diverse group of neoplasms with different clinical presentations, histology, and biologic behaviors. Major progression has been made in understanding the pathobiology of these diseases in the last two decades, leading to development of the internationally adopted The World Health Organization (WHO) classification system and its updated version. The WHO classification of neoplasms of the hematopoietic and lymphoid tissues published in 2008 and then it was updated in 2016 and revised in 2017. The WHO classification system incorporated morphology, immunophenotype, cytogenetic and molecular features, clinical behavior, and some known aspects of etiology and pathogenesis in the definition of each disease subtype. Many studies on the epidemiology of lymphoma using WHO classification were reported all over the world up to now. According to WHO classification, lymphoid neoplasms are divided into 6 main groups as follows: 1- Precursor B-cell and T/natural killer (T/NK)-cell neoplasms, 2- Mature B-cell neoplasms, 3- Mature T/NK-cell neoplasms, 4- Posttransplant lymphoproliferative diseases, 5- Hodgkin lymphoma (HL) and 6- Histiocytic and dendritic cell neoplasms (1,2).

Lymphoid neoplasms are representing as the sixth most common malignancy worldwide. Their highest incidence rates are found in South America and Australia, followed by Europe. However, incidence rates are much lower in Asia (3). The exact reasons of geographic variations remain unknown even though some risk factors have been documented recently, including immune system anomalies, genetic factors, lifestyle, environmental exposures, and infections (1,4).

According to the data of Turkey GLOBOCAN 2018 (New Global Cancer Data), non-Hodgkin lymphoma (NHL) is the 12th (2.7%) and HL is the 23rd (0.74%) most common type of cancer in Turkey. NHL is the 11th leading cause of cancer death. NHL patients showed 2.5 deaths and HL patients showed 0.2 deaths per 100,000 person-year. Five-year NHL and HL prevalence proportions are 19.34 and 6.85 (5).

In this study histological subgroups, incidence rates and demographic characteristics of cases with lymphoid neoplasm diagnosed between the years 2008 and 2014 in the Department of Pathology, Karadeniz Technical University in Northeast region of Turkey which provides health services for a large area were investigated. All patients were classified according to the WHO classification. As there are only limited revisions and no new definite entities in the 2016 new classification method compared with the previous version, and the data was collected before 2014, therefore, we still adopted the 2008 version as classification criteria. Despite the limitations of

using one single hospital-based data, this is the first comprehensive study of subtype, age, gender, and biopsy specimens and their distribution patterns in Northeast Turkey, which would provide strong theoretical basis for public health, clinical and basic research.

MATERIAL AND METHODS

The clinical and pathological data of patients diagnosed lymphoid neoplasms at the Department of Pathology in Karadeniz Technical University Faculty of Medicine from January 2008 to December 2014 was collected and analyzed. The present study followed the Declaration of Helsinki for medical protocols and ethics. The Karadeniz Technical University Institutional Review Board approved the study plan under protocol 2015/33. To determine the exact distribution, patients whose pathologic material was available for review were included. Patients morphologically suspected of having a mature lymphoid neoplasm, but with ambiguous immunostaining results or insufficient tissue for full characterization, were excluded. Precursor lymphoid neoplasms and duplicated data were excluded.

All cases reviewed by two pathologists, which included the first author. All histopathological diagnoses were reclassified according to the WHO 2008 classification. Additional immunohistochemical staining was performed when necessary. Tissue sections of 3-4 m thickness from paraffin-embedded tissue and decalcified bone marrow specimens (trephine biopsy) were examined by hematoxylin and eosin. The panel of antibodies used for immunohistochemistry included CD2, CD3, CD4, CD5, CD7, CD8, CD10, CD15, CD20, CD21, CD23, CD30, CD43, CD45, CD56, CD79a, CD38, CD138, ALK-1 (Anaplastic lymphoma kinase-1), EMA (epithelial membrane antigen), Pax-5, cyclin D1, bcl-1, bcl-2, bcl-6, MUM-1, Ki-67, Granzyme B, TIA-1 (T-cell intracellular antigen-1), kappa and lambda light chain. The existence of Epstein-Barr virus (EBV) was detected using the immunohistochemical stain for latent membrane protein 1. Clinical information was also collected, including basic characteristics (age, gender, and region) and the site of tissue sampling. To analyze the distribution of neoplasm primarily biopsied/resected, we divided the neoplasms into two main groups; nodal and extranodal.

The data were analyzed using SPSS 23.00 package program. The qualitative data were summarized using numbers and percentages and the quantitative data were summarized using median (minimum, maximum) and mean (\pm standard deviation) values. The chi-square test was used to compare the qualitative data and $p < 0.05$ was considered statistically significant.

RESULTS

Subtypes of lymphoid neoplasms: Our study included a total of 1136 lymphoid neoplasm cases which consisted of mature B-cell neoplasms (n=900; 79.2%), HL (n=124; 10.9%), mature T/NK-cell neoplasms (n=102; 9%), and histiocytic and dendritic cell neoplasms (n=10; 0.9%) (Table

1). Diffuse large B-cell lymphoma (DLBCL) (n=261; 23%) was the most common subgroup, followed by plasma cell myeloma (n=252; 22.2%), CLL/SLL (n=230; 20.2%), mycosis fungoides (MF) (n=66; 20.2%), nodular sclerosing type classical HL (n=63; 5.5%).

Table 1. Distribution of lymphoid neoplasms in four main groups

Lymphoid neoplasms	Mature B-cell neoplasms	Hodgkin lymphoma	Mature T/NK-cell neoplasms	Histiocytic and dendritic cell neoplasms
Number of cases (%)	900 (79.2%)	124 (10.9%)	102 (9%)	10 (0,9%)

Among mature B-cell neoplasm cases, the most common type was DLBCL (n=261; 29%), followed by plasma cell myeloma (n=252; 28%), CLL/SLL (n=230; 25.6%), mantle cell lymphoma (n=31; 3.4%), and FL (n=29; 3.2%). The most frequently seen subtypes of mature T/NK-cell neoplasms were MF (n=66; 64.7%), peripheral T-cell lymphoma, NOS (PTCLU) (n=13; 12.7%), and angioimmunoblastic T-cell lymphoma (n=8; 7.8%). Among the 124 cases of HL, 119 were classical HL and 5 were nodular lymphocyte predominant HL. Nodular sclerosing type classical HL was the commonest variant (n=63; 50.8%), followed by mixed cellular type (n=54; 43.5%) (Table 2).

Gender: All lymphoid neoplasm cases consisted of 706 (62.1%) male and 430 (37.9%) female patients. Male dominance was pronounced for all four major subgroups (Table 2). The male to female ratio was 1.6/1 in B-cell neoplasms, 1.1 /1 in T/NK-cell neoplasms and 2.6/1 in HL. In addition, male/female ratios were found to be statistically significant in these groups ($p < 0,05$).

Age: Most subgroups of lymphoid neoplasms were seen between 50-70 years. The patients with DLBCL had the widest age range (1-96 years). HL patients were diagnosed earlier (HL, median age, 36 years) than NHL patients. Burkitt lymphoma was diagnosed predominantly at a younger age (median age, 40 years) compared to other mature B-cell neoplasms. Furthermore, the patients with nodular sclerosing type classical HL were younger (median age, 28 years) than those with other HL variants (Table 2).

Anatomical region: All of plasma cell myeloma, CLL/SLL, and hairy cell leukemia cases

were diagnosed by bone marrow biopsy (504 cases, 50.3% of NHL cases). The diagnosis of primary cutaneous lymphoid neoplasms (primary cutaneous follicle center lymphoma, MF, and primary cutaneous CD30 (+) lymphoproliferative disease) were based on the histopathological examination of skin biopsies. When these cases (the cases diagnosed by bone marrow or skin biopsy) were excluded, 48.1% (n=207) of NHL cases occurred in extranodal sites and 51.9% (n=223) of them occurred in nodal sites. DLBCL was found to be the most common subtype of extranodal NHL cases (66%). Besides DLBCL, the following subtypes of extranodal lymphomas were extranodal marginal zone B-cell lymphoma, MALT type (11%), Burkitt lymphoma (6%), splenic marginal zone B-cell lymphoma (5%) and lymphoplasmacytic lymphoma (4%).

All of the HL cases have lymph node involvement. Nodal involvement was observed in 5 different regions; cervical, axillary, inguinal, mediastinal and intraabdominal. The most frequent site was cervical group lymph nodes (Table 3). 198 cases of mature B-cell neoplasms and 9 cases of mature T/NK-cell neoplasms cases occurred in extranodal sites. The extranodal cases were divided into 22 groups based on their anatomical sites. The most common extranodal site was the GIS in cases of mature B-cell neoplasms (n=53 cases; 26.8%). Majority of the 53 cases (n=39) occurred in GIS, diagnosed based on the histopathological examination of the gastric biopsy or gastrectomy materials. Waldeyer's ring was the second most common extranodal site (n=50; 25.3%) (Table 4).

Table 2. Demographics of each subtype of lymphoid neoplasms

Category	Number (n=1136)	Percent %	Age range (year)	Mean age (year)	Male/ Female
Mature B-cell neoplasms	900	79.2	1-96	62.8	555/345
Diffuse large B-cell lymphoma (DLBCL)	261	23			
DLBCL, NOS	239	21	1-96	61.8	128/103
Primary DLBCL of the CNS	12	1.1	43-81	57.1	6/6
T cell/histiocyte-rich DLBCL	4	0.4	43-73	62.2	2/2
Primary mediastinal (thymic) LBCL	2	0.2	26-32	29	0/2
Intravascular LBCL	2	0.2	57-85	71	1/1
ALK (+) LBCL	1	0.1	53	53	1/0
Plasmablastic lymphoma	1	0.1	54	54	1/0
Plasma cell myeloma	252	22.2	31-88	64.3	149/103
Chronic lymphocytic leukemia/ small lymphocytic lymphoma	230	20.2	34-90	66.1	157/73
Mantle cell lymphoma	31	2.7	44-89	63.5	26/5
Follicular lymphoma	29	2.6	31-80	57	16/13
Extranodal marginal zone B-cell lymphoma, MALT type	24	2.1	38-81	60	13/11
Hairy cell leukemia	22	1.9	33-79	58.6	19/3
Burkitt lymphoma	17	1.5	3-77	32.6	13/4
Splenic marginal zone B-cell lymphoma	10	0.9	48-71	62.5	3/7
Lymphoplasmacytic lymphoma	10	0.9	62-75	69.1	4/6
Nodal marginal zone B-cell lymphoma	8	0.7	50-84	61.5	5/3
Extramedullary plasmacytoma	4	0.4	44-81	66	4/0
Primary cutaneous follicle center lymphoma	1	0.1	46	46	1/0
Splenic lymphoma/leukemia, unclassifiable	1	0.1	74	74	1/0
Mature T/NK-cell neoplasms	102	9	7-87	53.1	53/49
Mycosis fungoides	66	5.8	20-87	51.7	34/32
Peripheral T-cell lymphoma, NOS	13	1.1	15-83	56.4	3/10
Angioimmunoblastic T-cell lymphoma	8	0.7	27-86	60.5	4/4
ALK (-) Anaplastic large cell lymphoma	5	0.4	47-73	60.4	4/1
Extranodal NK/T-cell lymphoma, nasal type	4	0.4	24-72	51.8	3/1
ALK (+) Anaplastic large cell lymphoma	3	0.3	7-80	39.7	2/1
Enteropathy type T-cell lymphoma	1	0.1	36	36	1/0
Primary cutaneous CD30 (+) lymphoproliferative disease	1	0.1	69	69	1/0
T-cell prolymphocytic leukemia	1	0.1	55	55	1/0
Hodgkin lymphoma (HL)	124	10.9	4-89	37	90/34
Nodular sclerosis HL	63	5.5	5-89	34	44/19
Mixed cellularity HL	54	4.8	4-83	39.3	40/14
Nodular lymphocyte-predominant HL	5	0.4	19-60	43.8	4/1
Lymphocyte-rich HL	1	0.1	54	54	1/0
Lymphocyte-depleted HL	1	0.1	48	48	1/0
Histiocytic and dendritic cell neoplasms	10	0.9	1-55	15.3	8/2
Langerhans cell histiocytosis	9	0.8	1-38	10.9	8/1
Histiocytic sarcoma	1	0.1	55	55	0/1

* DLBCL, NOS: Diffuse large B-cell lymphoma, not otherwise specified; CNS: Central nervous system; and LBCL, Large B-cell lymphoma

Table 3. Locations of lymph nodes involved in lymphoid neoplasms

Lymph nodes	Mature B-cell neoplasms	Mature T/NK-cell neoplasms	Hodgkin lymphoma
Cervical	82 (41.6%)	12 (46.2%)	66 (53.2%)
Inguinal	35 (17.8%)	8 (30.8%)	14 (11.3%)
Axillary	34 (17.3%)	5 (19.2%)	19 (15.3%)
Intraabdominal	28 (14.2%)	-	8 (6.5%)
Mediastinal	18 (9.1%)	1 (3.8%)	14 (11.3%)

Table 4. Extranodal sites involved in mature B-cell neoplasms

Ekstranodal sites	Mature B-cell
GIS	53 (26.8%)
Waldeyer's ring	50 (25.3%)
Spleen	16 (8.1%)
Brain	15 (7.6%)
Bone marrow	9 (4.6%)
Nasal cavity	7 (3.6%)
Lung	6 (3%)
Testis	6 (3%)
Skin	5 (2.5%)
Thyroid	5 (2.5%)
Intraabdominal region	5 (2.5%)
Soft tissue	5 (2.5%)
Salivary gland	4 (2%)
Liver	3 (1.5%)
Lacrimal gland	2 (1%)
Breast	1 (0.5%)
Ovary	1 (0.5%)
Cervix	1 (0.5%)
Conjunctiva	1 (0.5%)
Palate	1 (0.5%)
Kidney	1 (0.5%)
Cerebellum	1 (0.5%)

DISCUSSION

In the present study, most of the lymphoid neoplasms cases (n=1136) consisted of mature B-cell neoplasms (n=900, 79.2%), similar to other reports (6-8). Mature B-cell neoplasms comprise more than 90% of lymphoid neoplasms in the world. It is especially more frequently observed in developed countries such as US, Australia and Western Europe (1). Since our country is mostly located in Asia continent, the incidence of B-cell neoplasms is less than this rate (79.2%).

Many studies show that DLBCL is the most common subtype of lymphoid neoplasms (3,4,6-13). Isikdogan et al. performed a study on 490 cases with NHL in Southeastern Anatolia region of Turkey and most frequent histological subtype is DLBCL (41%) (14). In our study, DLBCL constituted 26% of NHL. This finding is consistent with the previously reported incidence rates in the USA and Europe (25-30%) (15).

The ratio of the most common subtypes of mature B-cell neoplasms changes in studies

performed in various regions. In our study, DLBCL, plasma cell myeloma, and CLL/SLL were the most common subtypes. DLBCL is the most common subtype according to the results of the studies in Turkey and Poland, and data from the US National Cancer Institute's Surveillance, Epidemiology, and Results (SEER) cancer registries (6,7,14). According to The European Cancer Registry-based project on hematologic malignancies (HAEMACARE), plasma cell myeloma ranks in the first place (16). In our study, plasma cell myeloma constituted 22.2% of all lymphoid neoplasms. This rate is close to the incidence of multiple myeloma reported in Europe and South America (25.43% and 21.98%, respectively) (17).

Higher incidence of FL is reported from the USA and Western Europe. In these countries, 35% of NHL cases were diagnosed as FL. They are less frequently observed in South America, Eastern Europe, Africa and Asia (1). Although its etiology and pathogenesis are not fully understood, some environmental risk factors are thought to affect the incidence of FL. Studies have detected the association between the pesticide exposure (insecticides, herbicides, and fumigants) and t(14;18) chromosomal translocation. This translocation has been identified in FL (70-90%) and DLBCL cases (20-30%) (18). Using of pesticide has been thought to be related with increased incidence of t(14;18) positive NHL cases (19). In another study, FL is the most frequent subtype of NHL in Argentina and South America (34.1% and 33.8%, respectively) (17). However, lower incidence of FL is reported from Egypt, Pakistan and Saudi Arabia (20,21). Naresh et al. reported that lower FL rates in developing countries may be due to many DLBCL that progressed from previously undiagnosed FL. Environmental and genetic factors might be associated with progression of FL to DLBCL (22). In our study, FL only diagnosed in 29 cases (2.9% of NHL cases). Lower incidence of FL might be because of small/fragmented samples or inadequate immunohistochemical marker for the diagnosis.

In our study, HL constituted 10.9% of all lymphoid neoplasms and this rate is almost similar to that in the USA (6,23). In the literature, incidence of HL is 23.7% in Eastern India, but the higher incidence is indicated (38.7%) in another study performed in India. However, lower rates are remarkable in some Asian countries: Japan 7%, Thailand 8.5%, China 6.6% (12,24). Nodular sclerosing subtype is the most common subtype of HL in our study, similar to that in Western countries (6,7,16). Mixed cellular classical HL is the most common subtype in Pakistan and India, contrary to Western countries (12,20,24). Increased incidence of mixed cellular type HL in Asian countries may be related to higher risk of childhood exposure to EBV infection (12).

Among lymphoid neoplasms, the incidence of T/NK-cell neoplasms in Asian countries is higher than Western countries and USA (China, 26.3%; Japan, 25%; India, 19.8%; Taiwan, 18.1%; USA, 6% and Poland, 5.7%) (4,6-8,12,25). In our study, 9% of all neoplasms were mature T/NK-cell neoplasms. The rate of T/NK-cell neoplasms is lower than that in Asian countries but similar to that in west.

Half of the T/NK-cell neoplasms consist of cutaneous T-cell lymphomas based on the results of HAEMACARE project in Europe (16). In our study, more than half of (65.7%) mature T/NK-cell neoplasms cases were cutaneous T-cell lymphoma (MF, n=66; primary cutaneous CD30 (+) lymphoproliferative disease, n=1). In another study, peripheral T-cell lymphoma is the most common subtype in Central and South America (23.7%), while the very small percentage of the cases are diagnosed as MF (3.4%) (17). In our study, MF is the most frequently seen subtype of mature T/NK-cell neoplasms (64.7%) which has a higher incidence when compared with the results of the studies performed in Europe, the USA, and Asian countries (4,6,8,12,16). Some etiologic factors, such as exposure to allergen and chronic dermatoses which are frequently seen in our region can cause this high incidence. Also, this might be due to the higher number of performing punch biopsy of the skin by dermatologists in our hospital.

In many studies, PTCLU is the most common subtype of mature T/NK-cell neoplasms (9,11,13,26). In a study performed in China by Yang et al. extranodal NK/T-cell lymphoma, nasal type (ENKTL-NT) is the most frequently seen subtype of mature T/NK-cell neoplasms as an interesting feature. Higher incidence rate of ENKTL-NT in Asian countries may be explained by EBV infection, using of pesticides and chemical substances which play important roles in its etiology (4). In our study, there were only 4 cases with ENKTL-NT.

In our study, male/female ratio was 1.64/1 in all lymphoid neoplasms. Male predominance was detected, similar to other studies (3,4,12,14,25). Also, the median age for classical HL with nodular sclerosing type (28 years) was younger than other variants of classical HL and NHL. Similar to

literature findings, nodular sclerosis HL is seen in relatively younger patients (1,3,4)

In our study, 48.1% of the cases occurred in the extranodal sites. Incidence rates of extranodal lymphomas in various countries are as follows: USA, 24%; Canada, 27%; India, 27%; Denmark, 37%; Netherlands, 41%; Italy, 48% and Turkey, 44.5% (12,14,17). Higher incidence rates were seen in Asian countries: Pakistan 42%; Japan, 46.6%; Korea 55% and Thailand, 58.7% (4). In our study, the frequency of extranodal NHL is similar to that reported in other Asian populations but higher than that of Western countries.

The GIS and Waldeyer's ring are the most commonly affected extranodal sites in the literature (27,28). The stomach is the most frequent site followed by small bowel and colon (29,30). In our study, the majority of patients with extranodal NHL had GIS (26.6%) and Waldeyer's ring (25.6%) involvement. Also, the rate of lymphoid neoplasm patients with Waldeyer's ring involvement is higher when compared with other countries (8,14,31-34). Interestingly, in a Japan study, Waldeyer's ring ranks first place among extranodal sites (40% of NHL cases) (35).

CONCLUSION

Histological subtype distribution of lymphomas in the current study is demonstrated and compared with reports all over the world. The importance of the current study is that it documents the various types of lymphoid neoplasms based on the WHO classification in a geographical area (Northeast Anatolia) that has not been previously investigated. It shows higher number of NHL cases (n=1002) than HL cases (n=124). DLBCL is the most common subtype of lymphoid neoplasms. The incidence of FL is very lower compared to that in Western studies. The nodular sclerosing type of HL is the most common subtype like in Western studies. In our study, the incidence of T/NK-cell neoplasms is lower than in Asian countries. MF constitutes more than half of the cases with T/NK-cell neoplasms and it is more common in our study when compared with Europe, the USA and, Asian countries. In the present study, the frequency of extranodal NHL is similar to that reported in Asian countries, but higher than that of Western countries.

REFERENCES

1. Swerdlow SH, Campo E, Harris NL, et al. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Lyon, France: IARC Press; 2008.
2. Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood*. 2016;127(20):2375-90.
3. Yoon SO, Suh C, Lee DH, et al. Distribution of lymphoid neoplasms in the Republic of Korea: analysis of 5318 cases according to the World Health Organization classification. *Am J Hematol* 2010;85(10):760-4.
4. Yang QP, Zhang WY, Yu JB, et al. Subtype distribution of lymphomas in Southwest China: analysis of 6,382 cases using WHO classification in a single institution. *Diagn Pathol* 2011;6:77.
5. World Health Organization, Global Health Observatory. Geneva: World Health Organization, 2018. Available from: <http://gco.iarc.fr/today/data/factsheets/populations/792-turkey-fact-sheets.pdf>

6. Morton LM, Turner JJ, Cerhan JR, et al. Proposed classification of lymphoid neoplasms for epidemiologic research from the Pathology Working Group of the International Lymphoma Epidemiology Consortium (InterLymph). *Blood* 2007;110(2):695-708.
7. Szumera-Cieckiewicz A, Galazka K, Szpor J, et al. Distribution of lymphomas in Poland according to World Health Organization classification: analysis of 11718 cases from National Histopathological Lymphoma Register project - the Polish Lymphoma Research Group study. *Int J Clin Exp Pathol* 2014;7(6):3280-6.
8. Chen WL, Tsai WC, Chao TY, et al. The clinicopathological analysis of 303 cases with malignant lymphoma classified according to the World Health Organization classification system in a single institute of Taiwan. *Ann Hematol* 2010;89(6):553-62.
9. Lee MY, Tan TD, Feng AC, et al. Clinicopathological analysis of 598 malignant lymphomas in Taiwan: seven-year experience in a single institution. *Am J Hematol* 2006;81(8):568-75.
10. Sharma M, Mannan R, Madhukar M, et al. Immunohistochemical (IHC) Analysis of Non-Hodgkin's Lymphoma (NHL) Spectrum According to WHO/REAL Classification: A Single Centre Experience from Punjab, India. *J Clin Diagn Res* 2014;8(1):46-9.
11. Gross SA, Zhu X, Bao L, et al. A prospective study of 728 cases of non-Hodgkin lymphoma from a single laboratory in Shanghai, China. *Int J Hematol* 2008;88(2):165-73.
12. Mondal SK, Mandal PK, Roy SD, et al. Malignant lymphoma in Eastern India: a retrospective analysis of 455 cases according to World Health Organisation classification. *J Cancer Res Ther* 2014;10(2):354-8.
13. Sukpanichnant S. Analysis of 1983 cases of malignant lymphoma in Thailand according to the World Health Organization classification. *Hum Pathol* 2004;35(2):224-30.
14. Isikdogan A, Ayyildiz O, Buyukcelik A, et al. Non-Hodgkin's lymphoma in southeast Turkey: clinicopathologic features of 490 cases. *Ann Hematol* 2004;83(5):265-9.
15. Anderson JR, Armitage JO, Weisenburger DD. Epidemiology of the non-Hodgkin's lymphomas: distributions of the major subtypes differ by geographic locations. Non-Hodgkin's Lymphoma Classification Project. *Ann Oncol* 1998;9(7):717-20.
16. Sant M, Allemani C, Tereanu C, et al. Incidence of hematologic malignancies in Europe by morphologic subtype: results of the HAEMACARE project. *Blood* 2010;116(19):3724-34.
17. Laurini JA, Perry AM, Boilesen E, et al. Classification of non-Hodgkin lymphoma in Central and South America: a review of 1028 cases. *Blood* 2012;120(24):4795-801.
18. Chiu BC, Dave BJ, Blair A, et al. Agricultural pesticide use and risk of t(14;18)-defined subtypes of non-Hodgkin lymphoma. *Blood* 2006;108(4):1363-9.
19. Schroeder JC, Olshan AF, Baric R, et al. Agricultural risk factors for t(14;18) subtypes of non-Hodgkin's lymphoma. *Epidemiology* 2001;12(6):701-9.
20. Mushtaq S, Akhtar N, Jamal S, et al. Malignant lymphomas in Pakistan according to the WHO classification of lymphoid neoplasms. *Asian Pac J Cancer Prev* 2008;9(2):229-32.
21. Yaqo RT, Hughson MD, Sulayvani FK, et al. Malignant lymphoma in northern Iraq: a retrospective analysis of 270 cases according to the World Health Organization classification. *Indian J Cancer* 2011;48(4):446-51.
22. Naresh KN, Srinivas V, Soman CS. Distribution of various subtypes of non-Hodgkin's lymphoma in India: a study of 2773 lymphomas using R.E.A.L. and WHO Classifications. *Ann Oncol* 2000;11 Suppl 1:63-7.
23. Jemal A, Siegel R, Xu J, et al. Cancer statistics, 2010. *CA Cancer J Clin* 2010;60(5):277-300.
24. Chakrabarti S, Sarkar S, Goswami BK, et al. Hodgkin's and Non-Hodgkin's lymphomas in an indian rural medical institution: comparative clinicopathologic analysis. *Asian Pac J Cancer Prev* 2010;11(6):1605-8.
25. Aoki R, Karube K, Sugita Y, et al. Distribution of malignant lymphoma in Japan: analysis of 2260 cases, 2001-2006. *Pathol Int* 2008;58(3):174-82.
26. Au WY, Gascoyne RD, Klasa RD, et al. Incidence and spectrum of non-Hodgkin lymphoma in Chinese migrants to British Columbia. *Br J Haematol* 2005;128(6):792-6.
27. Zucca E, Cavalli F. Extranodal lymphomas. *Ann Oncol* 2000;11 Suppl 3:219-22.
28. Di Leonardo G, Ginaldi L, De Martinis M, et al. [Extranodal localizations of lymphoma. Clinico-epidemiologic study of 353 cases]. *Recenti Prog Med* 2000;91(10):500-6.
29. Grogan TM, Jaramillo MA, Miller TP. Natural history, diagnosis, and staging of the non-Hodgkin's lymphomas. Haskell CM, editor. Philadelphia, WB Saunders, 2001.
30. Zucca E, Roggero E, Bertoni F, et al. Primary extranodal non-Hodgkin's lymphomas. Part 1: Gastrointestinal, cutaneous and genitourinary lymphomas. *Ann Oncol* 1997;8(8):727-37.
31. Economopoulos T, Papageorgiou S, Dimopoulos MA, et al. Non-Hodgkin's lymphomas in Greece according to the WHO classification of lymphoid neoplasms. A retrospective analysis of 810 cases. *Acta Haematol* 2005;113(2):97-103.
32. Chuang SS, Lin CN, Li CY. Malignant lymphoma in southern Taiwan according to the revised European-American classification of lymphoid neoplasms. *Cancer* 2000;89(7):1586-92.

33. Ho FC, Todd D, Loke SL, et al. Clinico-pathological features of malignant lymphomas in 294 Hong Kong Chinese patients, retrospective study covering an eight-year period. *Int J Cancer* 1984;34(2):143-8.
34. Freeman C, Berg JW, Cutler SJ. Occurrence and prognosis of extranodal lymphomas. *Cancer* 1972;29(1):252-60.
35. Kadin ME, Berard CW, Nanba K, et al. Lymphoproliferative diseases in Japan and Western countries: Proceedings of the United States--Japan Seminar, September 6 and 7, 1982, in Seattle, Washington. *Hum Pathol* 1983;14(9):745-72.