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Epidemiology and histological subtypes of Hodgkin lymphoma in the south-west of Turkey

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SUMMARY

Lymphomas are solid tumors of the immune system, and are diseases characterized by interrupted differentiation of lymphocytes, which are major components of the system, at various phases and their clonal proliferation. In this article, the epidemiology of Hodgkin's lymphoma and the factors influencing the frequency of its histological subtypes, with the population-based data of 1994 to 2010 from Antalya Cancer Registration Center are discussed. The study covered patients who were histopathologically diagnosed to have Hodgkin's lymphoma from 1994 to 2010. The study involved 454 patients, 284 (62.6%) males and 170 (37.4%) females. Male/female ratio was found as 1.67. The average age of all patients was identified as 36.6±18.9 years and their median age was 34 (range 2-88) years. Changes in histological subtypes were studied with respect to years. Nodular sclerosis subtype predominated over time. In conclusion, the epidemiological findings on Hodgkin's lymphoma in Turkey are similar in general to those reported in the Western literature. The frequency of histological subtypes is associated with sex, age and the occurence of EBV infection. Further studies are required to determine the factors that play role in the etiology of this disease, which is frequent in Turkey, and to shed light on its pathogenesis.

Key words: *Epidemiology, histological subtype, Hodgkin's lymphoma*

ÖZET

Türkiye'nin güneybatı bölgesinde Hodgkin lenfomanın epidemiyolojisi ve histolojik alt tipleri

Lenfomalar, immün sistemin solid tümörleridir ve bu sistemin önemli bir bileşeni olan lenfositlerin farklılaşmasının çeşitli aşamalarda durması ve klonal proliferasyonu ile karakterize bir hastalık grubudur. Bu yazıda Antalya Kanser Kayıt Merkezinin nüfus tabanlı 1994-2010 verileri eşliğinde Hodgkin lenfoma epidemiyolojisi ve histolojik alt tiplerinin sıklığına etki eden faktörler tartışılmıştır. Çalışmaya 1994 ile 2010 yılları arasında histopatolojik olarak Hodgkin lenfoma tanısı konulan hastalar alınmıştır. Çalışmaya 284'ü (%62.6) erkek, 170'i (%37.4) kadın toplam 454 hasta alındı. Erkek/kadın oranı 1.67 olarak bulundu. Hastaların ortalama yaşı 36.6±18.9 yıl ve mediyan yaşı 34 (2-88) yıl olarak saptandı. Histolojik alt tiplerin yıllara göre değişimi incelendi. Nodüler sklerozan tipin zaman içinde giderek daha baskın duruma geldiği saptandı. Sonuç olarak Türkiye'de Hodgkin lenfomanın epidemiyolojik bulguları genel olarak batı literatürü ile benzerlik göstermektedir. Histolojik alt tiplerin görülme sıklığı cinsiyet, yaş ve EBV enfeksiyonu görülmesi ile ilişkilidir. Ülkemizde sık görülen bu hastalığın etiyolojisinde rol oynayan faktörlerin belirlenmesi ve patogenezinin aydılatılması için daha fazla sayıda çalışma yapılmasına ihtiyaç vardır.

Anahtar kelimeler: *Epidemiyoloji, histolojik alt tip, Hodgkin lenfoma*

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Introduction

Lymphomas are solid tumours of the immune system, and are diseases characterized by interrupted differentiation of lymphocytes, which are major components of the system, at various phases and their clonal proliferation. Their clinical manifestations vary in terms of morphological and immunological properties depending on the stage of differentiation. Hodgkin's lymphoma (HL), which is a subtype of lymphomas, originates from germinal center and post-germinal center B-cells. HL, which was first defined by Thomas Hodgkin in 1832, comprises 10% of all lymphomas. Its proportion among all cancers is 0.6% (1).

The frequency of lymphoma varies depending on the age, sex, exposure to viral factors such as EBV and geography. In the USA, 8220 new cases are diagnosed each year (2). In Turkey, the estimated number of cases per year is 2000 (3). The incidence in Europe is approximately 2,4 in 100.000 (4). The age of onset of the HL and its histological subtypes may vary depending on the level of development of the countries and regions concerned (5).

In this article, the epidemiology of Hodgkin's lymphoma and factors influencing the frequency of its histological subtypes, are discussed using the population-based data of the years between 1994 to 2010 obtained from Antalya Cancer Registration Center.

Material and Methods

The present study involved patients who were histopathologically diagnosed to have HL from 1994 to 2010. The data of the patients belonging to the years from 1994 to 2010 were gathered from the databank of the Turkish Ministry of Health, Antalya Provincial Health Directorate, Cancer Registration Center. The

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data were screened to exclude the duplicated ones. The cases without data on the subtype of lymphoma were not evaluated. The patient data recorded outside of the province were included in the evaluation.

The cases who were pathologically classified according to 2001 classification of the World Health Organization (WHO) of HL as well as according to the subsequently updated 2008 classification were included in the study. The histological subgroups were evaluated in terms of sex. The patients were divided into groups as follows: 0-20 yr, 20-40 yr, 40-65 yr and older than 65 years old, and the distribution of histological subtypes among these groups were studied. The patients were grouped by age into 5-year intervals in order to determine the age distribution besides the distribution of histological subtypes. The temporal changes in the frequencies of HL subtypes were investigated within three intervals, namely 1994-2000, 2001-2005 and 2006-2011.

Statistical analyses were conducted by SPSS 13.0. Inter-group differences were evaluated with chi-square test. A p value <0.05 was considered as statistically significant.

Results

The study involved 454 patients, including 284 (62.6%) males and 170 (37.4%) females. Male/female ratio was found as 1.67. The average age of all patients was identified as 36.6±18.9 yr and their median age was 34 (Range 2-88) yr. The patients were grouped into 5-year age intervals, and as the age distribution demonstrates, the patients center around the age intervals of 20-30 yr and 50-60 yr (Figure 1).

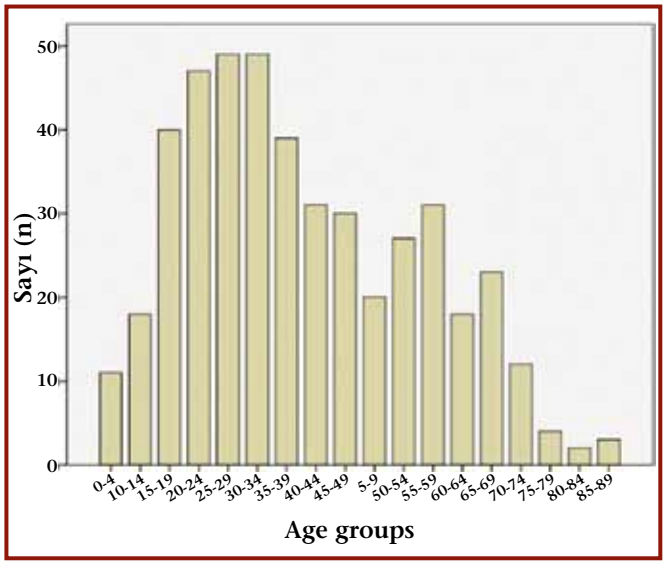


Figure 1. Age distribution of patients

The most common registry address of the patients was Antalya with a percentage of 74.9%. Most of the other patients were registered in Isparta and Burdur, the nearest provinces to Antalya.

The patients were most commonly diagnosed by lymph node biopsy with 90.3%. Six patients (1.3%) were diagnosed by cytological examination. HL was accompanied by lymphatic involvement in 438 patients, and the head and neck were the most common sites of lymphatic involvement. Information on the localization of lymph nodes was unavailable for 82 patients (Table I).

Extra-lymphatic involvement was 3.5%, and was most commonly identified in the stomach with 7 patients. Other extra-lymphatic localizations were identified as nasopharynx, pancreas, parotid gland, tonsil, lung, colon and small intestine.

Nodular sclerosis was the most common histological subtype with 173 patients (52.7%). Nodular lymphocyte predominant HL was identified in 7 patients. While nodular sclerosis type HL was more common among female patients, the mixed cellularity type HL was more common among male patients as compared to female patients (Table II). The differences were not

Table I. Involved lymph node sites in patients

Lymph node site	*Number of patients*	*Percentage (%)*
Head and neck	200	56
Intrathoracic	23	6.4
Intraabdominal	13	3.7
Axillary	39	11
Inguinal	36	10.2
Pelvic	5	1.5
Multiple sites	40	11.2
Total	356	100

Table II. Gender distribution of histological subgroups

Histological Subtype	*Female n (Row percentage)*	*Male n (Row percentage)*	*Whole patients group n (Row percentage)*
Nodular lymphocyte predominant	1 (0.1%)	6 (2.9%)	7 (2.1%)
Nodular sclerosis	71 (58.8%)	102 (49.3%)	173 (52.7%)
Mixed cellularity	34 (27.9%)	73 (35.2%)	107 (32.5%)
Lymphocyte-rich	8 (6.6%)	20 (9.7%)	28 (8.5%)
Lymphocyte-deprived	8 (6.6%)	6 (2.9%)	14 (4.2%)
Total	122 (100%)	207 (100%)	329 (100%)

statistically significant (p=0.580). A study of histological subtypes by patient age groups demonstrated that nodular sclerosis type was more common in the age group of 20-40 years old, and the mixed cellularity type was more common among patients over 65 years old (Table III). The differences in histological subtypes among the age groups were not statistically significant (p=0.726).

Changes in histological subtypes were studied with respect to years. Nodular sclerosis type predominated over time (Table IV).

Discussion

HL age distribution exhibits a bimodal distribution in developed countries. Its first peak occurs at about 20 years of age, and its second peak around 65 years of age. Sant et al. demonstrated bimodal distribution among HL patients in a study on European hematological malignity incidence (4-6). It is known that the distribution moves towards earlier ages at young ages, and towards older ages among elders in developed countries (7). Our study has evaluated the data of 454 patients who were diagnosed with HL from 1994 to 2010, and a bimodal distribution was also identified in our patient group. The patients were grouped in the ages of 20-30 and 50-60, which was consistent with the findings of developed countries.

In HL, the female-male ratio varies between 1.6-1.8 in Asia and Africa, and between 1.1–1.2 in Europe and North America (8). We determined this ratio as 1.67 in our patient group, resembling to the ratio in the Asian countries. Mani et al. demonstrated that HL incidence peak was slightly earlier in women than in men (9). However, our study did not reveal any difference in age distribution between female and male patients. We found that the disease peak was at similar ages in both genders.

HL has less extranodal involvement as compared to non-Hodgkin lymphoma. Our study has identified the percentage as 3.5%, and the most common extranodal involvement site was the gastrointestinal system, primarily the stomach. The most common nodal involvement site was the head and neck. These findings are consistent with the literature.

Seven patients were diagnosed with nodular lymphocyte predominant HL which was brought to agenda by the WHO 2008 classification. Nodular sclerosis HL, which is the most common classical subtype of HL, was encountered in all patient groups. A study of differences of histological subtypes with respect to genders has demonstrated that the nodular sclerosis type was more common in female patients with 58.8% as compared to the male patients. In their study, Cozen et al. also identified that nodular sclerosis histology was more dominant in female patients (10).

Table III. Distribution of histological subtypes with respect to age groups

Histological subtype	*0-20 years old n (Row percentage)*	*20-40 years old n (Row percentage)*	*40-65 years old n (Row percentage)*	*Over 65 years old n (Row percentage)*
Nodular lymphocyte predominant	2 (2.6%)	3 (2.3%)	2 (2.6%)	0 (0%)
Nodular sclerosis	45 (60%)	71 (56%)	44 (58.7%)	13 (40.6%)
Mixed cellularity	20 (26.6%)	41 (32.2%)	32 (33.7%)	14 (43.7%)
Lymphocyte-rich	4 (5.3%)	9 (7%)	12 (12.6%)	3 (9.3%)
Lymphocyte-deprived	4 (5.3%)	3 (2.3%)	5 (5.2%)	2 (6.2%)

Table IV. Differences in histological subtype percentages with respect to years

Histological subtype	*1994-2000 n (Row percentage)*	*2001-2005 n (Row percentage)*	*2005-2010 n (Row percentage)*
Nodular lymphocyte predominant	0	0	7 (4.4%)
Nodular sclerosis	32 (39%)	50 (55.5%)	94 (58.9%)
Mixed cellularity	34 (41.5%)	28 (31.4%)	45 (28.2%)
Lymphocyte-rich	11 (13.4%)	6 (6.7%)	11 (6.8%)
Lymphocyte-deprived	5 (6.1%)	6 (6.7%)	3 (1.7%)
Total	82 (100%)	90 (100%)	160 (100%)

The incidence of nodular sclerosis increases (11). We also found that the incidence of nodular sclerosis type gradually increased over time in our patient group. On the other hand, the mixed cellularity type did not change in general. The mixed cellular type is more common in cases of HL where HIV plays a role in the etiology (12). In our population, we believe that the HIV does not have a determining role in the etiology since there was not any relevant increase in the mixed cellularity type of HL (Table III).

Engert et al. also identified a lower incidence of nodular sclerosis HL among elderly patients in the German patient population (13). They also found that the mixed cellularity type increases in the elderly population. These findings were consistent with previous studies (14-16). We also found that the cellularity type was the most common type and increasing in the patients over 65 years old. This is associated with the infection pattern of EBV (17). EBV-related HL is rather a mixed cellularity histological subtype and it usually occurs in patients under 10 years old as well as in elder patients (18-20).

In conclusion, the epidemiological findings on HL in Turkey are similar to the Western literature in general. The frequency of histological subtypes is associated with sex, age and the occurence of EBV infection. Further studies are required to determine the factors that play role in the etiology of this disease, which is frequent in Turkey, and to shed light on its pathogenesis.

References

1. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics, 2009. CA Cancer J Clin 2009; 59: 225-249.
2. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2008. CA Cancer J Clin 2008; 58: 71-96.
3. Eser S, Yakut C, Özdemir R, et al. Cancer incidence rates in Turkey in 2006: a detailed registry based estimation. Asian Pac J Cancer Prev 2010; 11: 1731-1739.
4. Sant M, Allemani C, Tereanu C, et al.; HAEMACARE Working Group. Incidence of hematologic malignancies in Europe by morphologic subtype: results of the HAEMACARE project. Blood 2010; 116: 3724-3734.
5. Glaser SL. Regional variation in Hodgkin's disease incidence by histologic subtype in the US. Cancer 1987; 60: 2841-2847.
6. Smith A, Roman E, Howell D, Jones R, Patmore R, Jack A; Haematological Malignancy Research Network. The Haematological Malignancy Research Network (HMRN): a new information strategy for population based epidemiology and health service research. Br J Haematol 2010; 148: 739-753.
7. Correa P, O'Conor GT. Epidemiologic patterns of Hodgkin's disease. Int J Cancer 1971; 8: 192-201.
8. Roman E, Smith AG. Epidemiology of lymphomas. Histopathology 2011; 58: 4-14.
9. Mani H, Jaffe ES. Hodgkin lymphoma: an update on its biology with new insights into classification. Clin Lymphoma Myeloma 2009; 9: 206-216.
10. Cozen W, Katz J, Mack TM. Risk patterns of Hodgkin's disease in Los Angeles vary by cell type. Cancer Epidemiol Biomarkers Prev 1992; 1: 261-268.
11. Clavel J, Steliarova-Foucher E, Berger C, Danon S, Valerianova Z. Hodgkin's disease incidence and survival in European children and adolescents (1978-1997): report from the Automated Cancer Information System project. Eur J Cancer 2006; 42: 2037-2049.
12. Biggar RJ, Jaffe ES, Goedert JJ, Chaturvedi A, Pfeiffer R, Engels EA. Hodgkin lymphoma and immunodeficiency in persons with HIV/AIDS. Blood 2006; 108: 3786-3791.
13. Engert A, Ballova V, Haverkamp H, et al.; German Hodgkin's Study Group. Hodgkin's lymphoma in elderly patients: a comprehensive retrospective analysis from the German Hodgkin's Study Group. J Clin Oncol 2005; 23: 5052-5060.
14. Erdkamp FL, Breed WP, Bosch LJ, Wijnen JT, Blijham GB. Hodgkin's disease in the elderly. A registry-based analysis. Cancer 1992; 70: 830-834.
15. Weekes CD, Vose JM, Lynch JC, et al.; Nebraska Lymphoma Study Group. Hodgkin's disease in the elderly: improved treatment outcome with a doxorubicin-containing regimen. J Clin Oncol 2002; 20: 1087-1093.
16. Mir R, Anderson J, Strauchen J, et al. Hodgkin's disease in patients 60 years of age or older. Histologic and clinical features of advanced-stage disease-The Cancer and Leukemia Group B. Cancer 1993; 71: 1857-1866.
17. Armstrong AA, Alexander FE, Cartwright R, et al. Epstein-Barr virus and Hodgkin's disease: further evidence for the three disease hypothesis. Leukemia 1998; 12: 1272-1276.
18. Kapatai G, Murray P. Contribution of the Epstein Barr virus to the molecular pathogenesis of Hodgkin lymphoma. J Clin Pathol 2007; 60: 1342-1349.
19. Glaser SL, Lin RJ, Stewart SL, et al. Epstein-Barr virus-associated Hodgkin's disease: epidemiologic characteristics in international data. Int J Cancer 1997; 70: 375-382.
20. Jarrett RF, Gallagher A, Jones DB, et al. Detection of Epstein-Barr virus genomes in Hodgkin's disease: relation to age. J Clin Pathol 1991; 44: 844-848.