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Hodgkin's lymphoma: epidemiological features, the current epidemiological situation in the regions of Kazakhstan

Relevance: *The diseases of the lymphoid and hematopoietic systems, including lymphomas, are among the top ten in the overall structure of oncopathologies. In Kazakhstan, they rank 4th accounting for about 5% of the total number of cancers; at that, hemoblastoses rank 8th in the structure of mortality.*

Hodgkin's lymphoma (HL) is one of the most common malignant lymphoid tumors. HL makes up no more than 0.5% of the total cancer burden worldwide; however, its unusual biology, epidemiology, and response to treatment attract close attention. The epidemiology of malignant lymphomas varies within and between geographic regions.

Purpose of the study: *to reflect the specifics of HL epidemiology in Kazakhstan.*

Results: *In 2018, 4611 patients were on file with malignant lymphoma. The absolute incidence of lymphoma was 794 cases per year (4.3‰), with an increase of 7.1% vs. 2017.*

The epidemiology of malignant lymphomas varied within and between geographic regions. The highest incidence of lymphoma was registered in Akmola, Karaganda, Qostanai, Pavlodar, East Kazakhstan, West Kazakhstan, and North Kazakhstan regions, and Nur-Sultan. It was partially associated with the ethnic structure of the population and might be associated with access to diagnostics.

The average national mortality rate was 1.8%000. The highest mortality rate from malignant lymphomas was registered in Pavlodar, East Kazakhstan, North Kazakhstan, Qostanai, and Karaganda regions.

Conclusion: *Certain regional dependence is traced both in incidence and, as a result, in mortality from lymphomas.*

Keywords: *Hodgkin's lymphoma, epidemiology, incidence, mortality, region, neoplasm.*

Introduction: Hodgkin's lymphoma (HL) is a malignant neoplasm from lymphoid tissue of B-cell origin. Its morphological substrate is composed of giant multinuclear Berezovsky-Reed-Sternberg cells and mononuclear Hodgkin cells. These types of cells are located in a kind of cell cluster – a "granuloma" formed by a mixture of tumor and non-tumor reactive cells such as lymphocytes, neutrophils, and plasma cells, sometimes surrounded by collagen fibers. The Berezovsky-Reed-Sternberg cells are derived from the B-cells of germinal centers of lymphatic tissue. They make up only about 1% of the entire tumor mass.

HL is a rare neoplasm. Its frequency varies greatly depending on age, gender, ethnicity, geographical location, and socio-economic status.

Although HLs make approximately 0.67% of the total cancer incidence, they account for about 30% of all lymphoma cases. It is important to note that every sixth oncologic diagnosis at the age of 15 to 24 is HL [1].

LH incidence is higher in more developed regions of the world, and lower in Asia; it is higher in men than in women. In the United States in 2013, about 9 300 new LH cases were registered; the annual incidence was 2.8 per 100,000 people [2].

A distinctive feature of HL epidemiology is its age variability at diagnosis. In industrialized countries, this is represented by a well-known bimodal curve having two peaks: the biggest one refers to young people (15–34 years old), and the second one observed at a later age (over 50 years old). These peaks represent mainly different subtypes of the disease: the nodular sclerosis variant is predominant at earlier peak age, and the mixed cell variant prevails at a later peak age [3].

Despite the relatively low incidence and low risk throughout life, HL accounts for 15% of all cancer cases in young people and has a significant impact on their quality of life.

Various epidemiological studies of HL conducted these days shall provide a better understanding of the nature of this disease and allow revealing the geographical, ethnic, socio-demographic, and economic factors influencing the development of this pathology.

Purpose of this work was to reflect the epidemiological features of HL in Kazakhstan.

Materials and methods: Global epidemiology of HL was analyzed based on data from the International Agency for Research on Cancer (IARC), GLOBOCAN 2012 [4], and the European Mediterranean Mediterranean Research Group [13]. Data on HL mortality and temporal trends for the covered Mediterranean countries were obtained from the World Health Organization (WHO) online mortality database [5]. The statistical data of the oncological service of the Republic of Kazakhstan for recent years was used to analyze the incidence, mortality, late detection, distribution by regions of Kazakhstan, and the dynamics of HL incidence. From now on we refer to the classic version of HL.

Results and Discussion

Hodgkin lymphoma epidemiology, global data

The WHO classification of lymphoid neoplasms is still evolving to account various variants of lymphoproliferative diseases which include not only HL, non-Hodgkin lymphomas (NHL) but also plasma cell neoplasms and lymphoid leukemias [6]. In 2012, nearly 566,000 new cases of lymphoma were registered worldwide, and about 305,000 deaths from this disease were reported [7]. Each variant of lymph-

oproliferative disease in principle does not matter much in the overall picture of the incidence of malignant neoplasms, but in the aggregate lymphomas rank 7th among oncopathologies detected all over the world [7].

According to GLOBOCAN, more than 385,000 new NHL cases and almost 66,000 HL cases were registered in 2012, and about 200,000 deaths from NHL and more than 25,000 deaths from HL [8]. New cases of NHL are equally often detected in regions with high, medium, and low incomes; however, the mortality rate was higher in middle-income and low-income countries (62%). In the same year, the vast majority of new cases and deaths from HL (56% and 75%, respectively) were registered in low-income regions. Projections show that both incidence and mortality rates for NHL and HL will increase by 2035, possibly due to improved diagnostic methods, industrialization, population aging, and an increase in HIV infection in some regions [8–9].

In 2012, HL cases accounted for no more than 0.5% of the total cancer burden worldwide; however, unusual biology and epidemiology and the response of HL to treatment attract close attention [8]. The overall frequency of HL varies considerably in the whole world. The pathogenesis of this geographical discrepancy is unknown; however, environmental and lifestyle factors were theorized as potential factors.

Unlike NHL, which shows an exponential increase in age-related incidence, age-related incidence indices of HL are bimodal, with the first peak in the European, American, Latin American and Australian populations occurring between the ages of 15 and 34, and the second after 60 years. In middle-income countries, the incidence of HL is high in early childhood and among the oldest age groups. A high incidence in childhood is associated with an increased risk of a young adult HL variant which indicates a delay in contact with the common infectious agent, whereas children living in less favorable conditions have a high incidence of lymphomas.

Progress in treatment, the improvement of diagnostic capabilities, and the access to medical care made HL largely curable in many parts of the world. Reported mortality has declined by more than 75% in North America, Western Europe, and Japan [9]. A noticeable decrease in HL mortality was also observed in most countries of Latin America, except for Cuba, Costa Rica, Mexico, and Venezuela.

In 1971, an international survey on HL showed that the distribution of bimodal age in the Western world correlated with the level of socio-economic development of the population. In developing countries, the HL incidence was relatively high in boys but low y young adult men, while in the developed regions, the incidence of HL was low in children, but high – in young people. Other evidence suggested that a mixed cell or lymphocyte subtype prevailed in developing regions, and a nodular sclerosis subtype dominated in developed regions. The ecological correlation between the socioeconomic level and the HL incidence has shown the opposite role of the child's environment in relation to the risk of HL in children and young people. One model suggested that HL was a rare consequence of a common infection, the risk of which increased when the age of infection was delayed, for example, through the improvement of living conditions.

Evidence confirming that the socioeconomic environment of childhood affects the risk of HL at a young age has been provided in several studies. For example, in a study that took into account such criteria as the level of socio-economic security in childhood, type of housing, mother's education and paternal social class, an association of an increased risk of HL incidence with a low level of socio-economic security was found, and this trend was traced more in young adults than in childhood [10].

Thus, these results confirm the multifactorial model of the pathogenesis of HL. This model accounts for both genetic factors and environmental risk factors [11].

The epidemiological situation on lymphomas in the Republic of Kazakhstan (RK)

The existing cancer registry of Kazakhstan provides information on the leading epidemiological indicators related to lymphoproliferative diseases. Unfortunately, it does not yet offer complete information on single variants of lymphoma but knowing that HL makes about 30% of all lymphomas, we can get an idea of the HL epidemiology in the Republic of Kazakhstan. In 2018, 4,611 patients were on file with malignant lymphomas. The annual incidence was 794 cases per year (4.3‰), with the growth rate of 7.1% to the previous year.

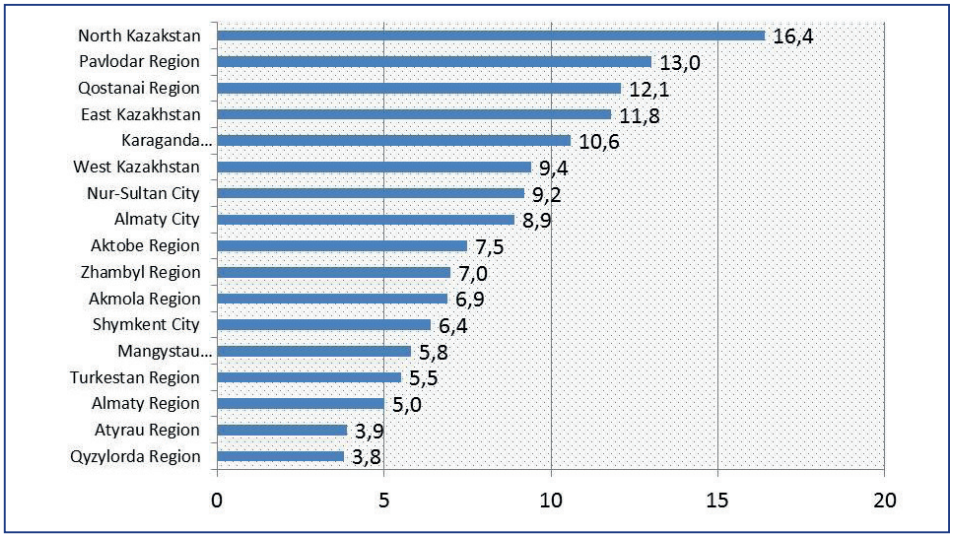

Figure 1 – Incidence of lymphomas in the regions of Kazakhstan, 2018 (‰)

The highest incidence (above the Republican average of 8.1 per 100 000 population) was registered in Akmola, Karaganda, Qostanai, Pavlodar, East Kazakhstan, West Kazakhstan, and North Kazakhstan regions and the city of Nur-Sultan. That might be partly due to the ethnic composition of the population; perhaps there was a connection with the access to diagnostics.

Some prevalence of men over women is observed in the structure of incidence, approximately 2.3 per 100 000 male population to 2.1 per 100 000 female population.

Of great importance is the possibility of morphological verification. Histological and immunological test methods have become a standard for diagnosing lymphoproliferative diseases in the past decade. According to the Diagnostic and Treatment Protocols of the Republic of Kazakhstan, these methods are mandatory for lymphoma verification. What is the situation with the morphological diagnostics of lymphomas in the Republic of Kazakhstan?

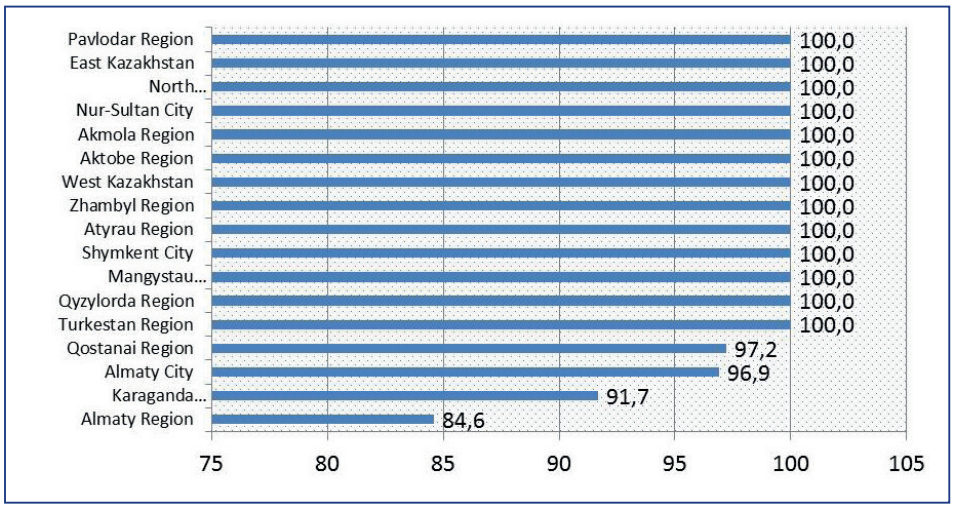

Figure 2 – Morphological verification of lymphomas in the regions of Kazakhstan, 2018 (%)

96% of all lymphomas pass morphological verification in Kazakhstan, with the lowest levels in Almaty and Karaganda regions.

The stage of the disease at detection is of great importance in terms of prognosis. What is the share of early detection in Kazakhstan?

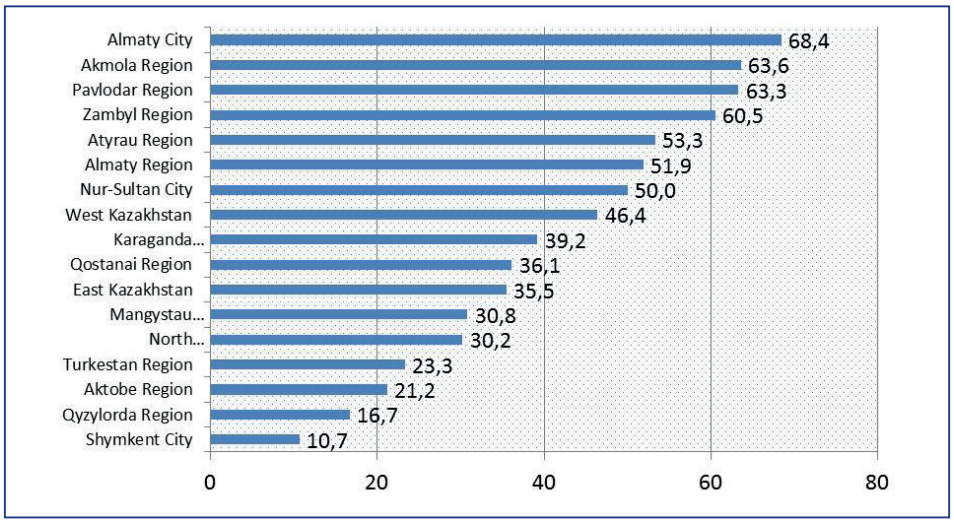

Figure 3 – The proportion of lymphoma stages 1 and 2 in the regions of Kazakhstan, 2018 (%)

On average, in the Republic of Kazakhstan in 2018, the percentage of early detection of lymphomas was 44.4%. The highest percentage of stages I and II at detection was recorded in Almaty, Akmola, Pavlodar, and Zhambyl regions, the lowest – in the city of Shymkent, as well as in Kyzylorda, Aktobe, and Turkestan regions.

As for the late detection (advanced stages of the disease), the average national detection rate for stage IV lymphomas in 2018 was 7.1%. At the same time, the highest percentage of late detection was noted in Karaganda, East Kazakhstan, Akmola and Turkestan regions, and the least high – in the cities of Almaty and Shymkent, and the Almaty region.

Currently, chemotherapy is the primary method of therapy for lymphoproliferative diseases. 85-88% of patients with newly diagnosed lymphoma receive specialized treatment, and in 65% of cases, they receive drug therapy (chemotherapy).

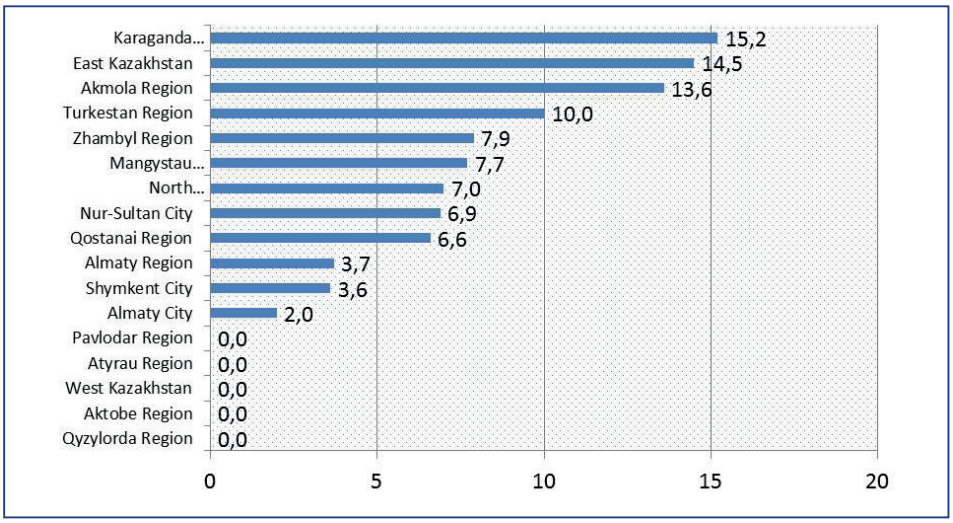

Figure 4 – The proportion of lymphoma stage IV in the regions of Kazakhstan, 2018 (%)

One-year mortality in patients with lymphoma is quite high – 22.4%, indicating a high aggressiveness of the tumor process. For reference, the annual mortality rate for breast cancer is 4.5%, for endometrial cancer – 7.5%, for prostate cancer – 8.1%.

The five-year survival of patients with lymphoma amounted to 54.8% in 2017, and 55.4% in 2018.

Mortality from lymphoma has amounted to 8.4% in 2017, and 7.0% in 2018 (322 people died of lymphomas in 2018). The mortality from lymphoma is reducing over time.

In the general structure of cancer pathologies in the Republic of Kazakhstan, the diseases of the lymphoid and hematopoietic systems, including lymphomas, ranked 8th in 2016, 6th in 2017, and 4th in 2018 making up to 5% of the total number of cancer diseases. In the structure of mortality, hematological cancer ranked 6th in 2017, and 8th in 2018 [12].

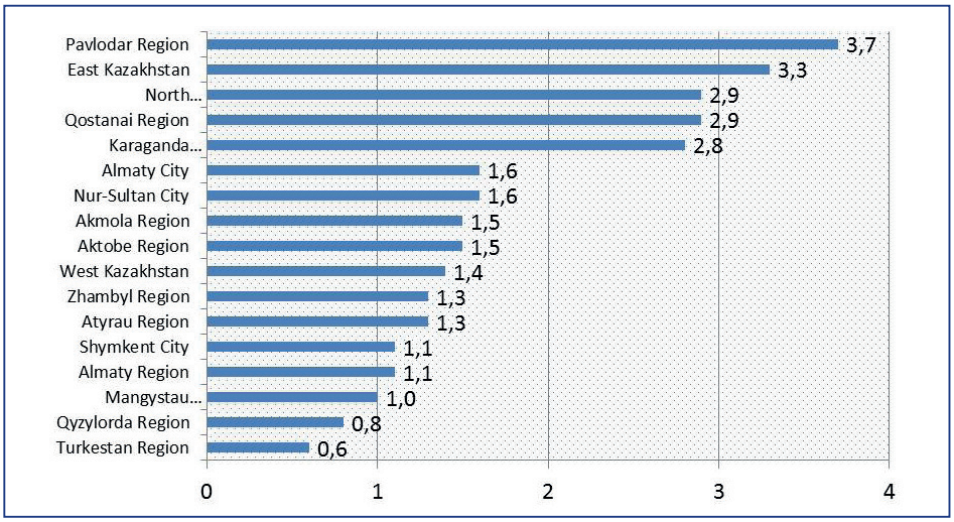

Figure 5 – Mortality from lymphomas in the regions of Kazakhstan, 2018 (‰)

The average national mortality rate is 1.8 per 100 000 population. The highest mortality rate from malignant lymphomas is noted in Pavlodar, East Kazakhstan, North Kazakhstan, Qostanai, and Karaganda regions.

Conclusions

The epidemiology of malignant lymphomas varies within and between geographic regions. Several studies show that the characteristics, incidence, and survival rates of different lymphoma subtypes for some racial groups differ from others. A better understanding of these factors will be required to identify the changing treatment barriers and improve outcomes for all patients. The incidence of lymphomas has a bimodal distribution with an increase in rates in young people, as well as in patients 55 years and older.

In the general structure of cancer pathologies, the diseases of the lymphoid and hematopoietic systems, including lymphomas, are among the Top 10. In Kazakhstan, they occupy the 4th rank position making up about 5% of the total number of cancer diseases, while in the structure of mortality, they hold the 8th place. The highest incidence of lymphoma is noted in Akmola, Karaganda, Qostanai, Pavlodar, East Kazakhstan, West Kazakhstan, and North Kazakhstan regions, and the city of Nur-Sultan. This might be partly due to the ethnic composition of the population;

perhaps there is a connection with the availability of diagnostics. The highest mortality rates from malignant lymphomas are recorded in Pavlodar, East Kazakhstan, North Kazakhstan, Qostanai, and Karaganda regions.

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