

RESEARCH ARTICLE

Epidemiological Assessment of Leukemia in Kazakhstan, 2003-2012

Nurbek Igissinov^{1,2*}, Dariyana Kulmirzayeva^{2,3}, Malcolm A Moore⁴, Saginbek Igissinov², Gulnara Baidosova⁵, Gulnur Akpolatova³, Zhanar Bukeyeva³, Yelvira Omralina³

Abstract

Cancer is a major health problem facing the entire world, and Kazakhstan is not the exception. The aim of this study was to present an epidemiological assessment of leukemia in the population of Kazakhstan during 2003-2012. This descriptive and retrospective study was based on data obtained from all oncological organizations of the whole country. Age standardized incidence rates per 100,000 population for leukemia were calculated. Totally, 6,741 new cases of leukemia were registered in Kazakhstan during the 10 year period. The mean age of patients with leukemia was 48.5. The ASRs for leukemia among men and women were 5.3 and 3.6, respectively ($p < 0.001$). In conclusion, our results showed a high incidence rate of leukemia in Kazakhstan, especially in the north of the country. The incidence of leukemia was significantly higher in males and increased with age. Determining and controlling important risk factors of leukemia may lead to decrease in its burden.

Keywords: Leukemia - epidemiology - time trends - geographical distribution - Kazakhstan

Asian Pac J Cancer Prev, 15 (16), 6969-6972

Introduction

Epidemiology as a science plays an important role in prevention of diseases. Interpretation of the findings of epidemiologic studies, identifying populations at increased risk, ascertaining the cause of their risk, and analyzing the ways of eliminating or reducing exposure to the causal factors all require an understanding of basic epidemiologic concepts (Gordis, 2008; Modak et al., 2011). Today cancer is an eminent health problem (Xie et al., 2012), which is responsible for a leading cause of death in developed countries and a second leading cause of death in developing countries (Jemal et al., 2011; Siegel et al., 2012). About 12.7 million cancer cases and 7.6 million cancer deaths are estimated to have occurred in 2008 (Rajabli et al., 2013). According to Globocan 2008, the age-standardized incidence rates (ASR) of all cancers were 202.8 in men and 164.4 in women per 100,000 population. In Kazakhstan, malignancies also have remarkable incidence (www.stat.kz - the Republic of Kazakhstan Statistic Agency).

.ASR of all cancers were 225.4 and 166.5, respectively (Ferlay et al., 2010).

Leukemia is the general term for hematological cancers occurring in the tissues responsible for blood formation, with various clinical and pathological presentation (Goldman et al., 2012; Tahmasby et al.,

2013), which plays an emotive role in the modern society, as a result of its relatively high incidence and often poor survival (Modak et al., 2011). In children leukemia is the most common form of cancer, accounting for one-quarter to one-third of childhood malignancy cases (Campana et al., 2008). In adults, leukemia is included in the top 15 of the most common forms of cancer according to the WHO (Kampen, 2012). Leukemia may arise from lymphoid or from myeloid cells and are generally classified as acute if the cells are arrested early in differentiation (blasts or early progenitors), or as chronic if the cells are mature. Risk factors for leukemia include genetic factors, physical and chemical exposures, infectious agents and other environmental factors (Goldman et al., 2012).

The ASRs of leukemia worldwide were 5.8 in men and 4.3 in women per 100,000 inhabitants (Rajabli et al., 2013). The highest rates for men have been registered in such countries as New Zealand (14.3), Israel (13.4), USA (12.1), Australia (11.9), for women in New Zealand (9.8), Italy (8.6), French Polynesia (8.3), Israel (8.1). Worldwide, age standardized mortality rate from leukemia in males is high (>6) in Lebanon, Iraq, Iran, Uruguay, for female (>5) in Kuwait, Vanuatu, Albania, Qatar. According to Globocan 2008, in Kazakhstan the ASRs of leukemia per 100,000 population were 6.8 (men) and 5.0 (women), mortality rates were 5.0 in male and 3.7 in female (Ferlay et al., 2010).

¹National Center for Neurosurgery, ²Central Asian Cancer Institute, ³Astana Medical University, Astana, ⁴APJCP Editorial Office, Bangkok, Thailand, ⁵West Kazakhstan Marat Ospanov State Medical University, Aktobe, Kazakhstan *For correspondence: n.igissinov@gmail.com

Study the epidemiological features, geographical variation, changes in incidence of leukemia allow to monitoring its trends and assess the impact of possible causal factors of risk. Thus, epidemiological studies of malignant tumors plays a vital role in learning about the cancer. The aim of this paper was to present epidemiological assessment of leukemia in the Kazakhstan population during 2003-2012 with a focus on age and sex characteristics.

Materials and Methods

This study is descriptive and retrospective. Data on leukemia (C91-96) were collected from all cancer institutions of the whole country (form N7). Incidence data discussed in this paper were based on cases of first diagnosed leukemia among Kazakhstan population during 2003-2012. Data from the Agency of Statistics of the Republic of Kazakhstan on the entire, male and female populations, age structure were used (www.stat.kz).

In the study extensive and intensive indexes, crude, age-specific and age-standardized incidence rates per 100,000 population, average values, mean error, 95% confidence interval and the average annual growth/decline rate (T, %) were calculated (Glantz, 2001). Trends were calculated using least squares method, age-standardized rates by the direct method. The method of map compiling was used, based on the calculation of the standard deviation (σ) from the mean (x) (Igissinov, 1974).

Results

During the period 2003-2012 in Kazakhstan were registered 6,741 new cases of leukemia, of which 3,578 (53.1%) were men and 3,163 (46.9%) women. The ratio of male and female patients was 1.13:1. The average age at diagnosing patients with leukemia was 48.5±0.3 (95% CI=47.9-49.1). The average age among men was 46.9±0.4 (95% CI=46.1-47.7), women 50.2±0.5 (95% CI=49.3-51.2) (p<0.05) (T=+0.1% and T=+0.7%, respectively). Average annual trend of change in age was T=+0.4%. In dynamics, the average crude incidence rate of leukemia per 100,000 population during 10 years period in total over the republic decreased (Table 1). Average annual trends of decline were T=-3.3% (both sexes), T=-3.9 (men) and T=-2.5% (women).

During the study period, the ASR for leukemia in Kazakhstan per 100,000 population decreased (Table 1). In average the ASR for leukemia equaled to 4.4±0.2 (95% CI=4.0-4.7). T=-3.3%. Average annual trends of decline among male and female population were T=-3.7 and T=-2.9%, respectively.

In dynamics, a high proportion of patients with leukemia (both sexes) were found in 65-69 years

Table 1. Crude and Age-standardized Leukemia Incidence Rates in Male and Female Populations per 100,000 in Kazakhstan, 2003-2012

	2003			2012			Average		
	Both sexes	Men	Women	Both sexes	Men	Women	Both sexes	Men	Women
Crude rate	4.3	4.9	3.7	3.2	3.5	2.9	4.3	4.8	3.9
ASR	4.3	5.5	3.5	3.2	3.9	2.7	4.4	5.3	3.6

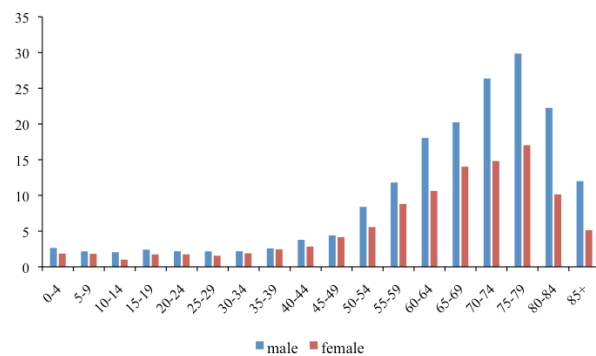
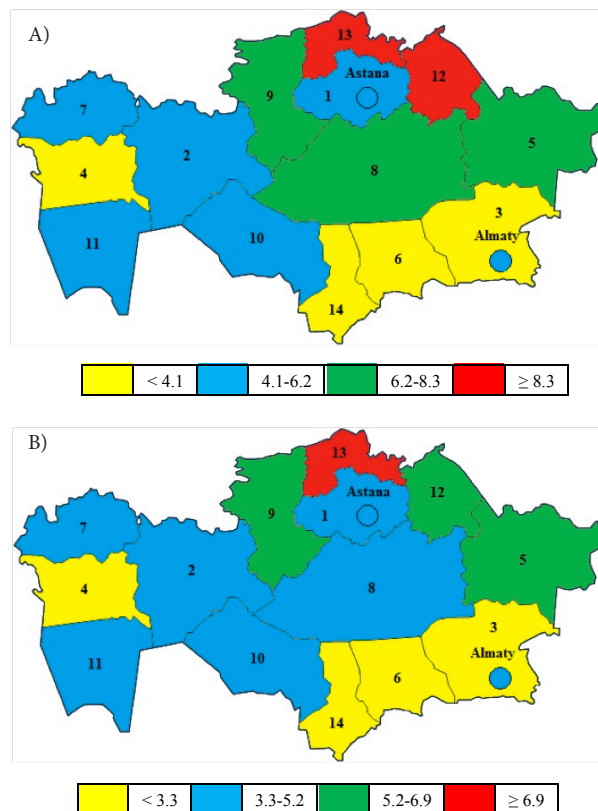


Figure 1. Average Age-specific Incidence Rates of Leukemia in Male and Female Populations per 100,000 Inhabitants in Different Age Groups in Kazakhstan for 2003-2012



Regions: 1. Akmola, 2. Aktobe, 3. Almaty, 4. Atyrau, 5. East Kazakhstan, 6. Zhambyl, 7. West Kazakhstan, 8. Karaganda, 9. Kostanai, 10. Kyzylorda, 11. Mangystau, 12. Pavlodar, 13. North Kazakhstan, 14. South Kazakhstan

Figure 2. Cartograms of Leukemia Incidence per 100,000 among A) Males and B) Females in Kazakhstan for the Years 2003-2012

(10.8%), a similar pattern was for men (9.9%) and women (11.9%). The distribution of age-specific incidence rates of leukemia per 100,000 population over the republic showed the higher rates in age group 75-79 (21.1%, 29.9% in men, 17.0% in women). The age distributions in men and women had similar patterns (Figure 1).

Regional distribution of leukemia incidence rates per 100,000 inhabitants in men and women are illustrated in a maps (Figure 2). Four groups were determined. The highest rates of leukemia over 10-years period were found for men in North-Kazakhstan (9.0) and Pavlodar (8.5) regions, for women in North-Kazakhstan region (8.2), the lowest rates both for men and women in the Almaty region (2.1 and 1.6, respectively).

Discussion

Our study showed that incidence rate of leukemia was higher in males than females. Overall incidence ratio of leukemia in male to female was 1.13:1. The gender distribution pattern of leukemia in Kazakhstan was in line with those found in other studies (Rajabli et al., 2013; Peter et al., 2013; Novak et al., 2012; Thygesen et al., 2009). It may be proposed that gender has the possible impact on the incidence of leukemia and men are at higher risk of leukemia due to genetic or environmental factors (Peter et al., 2013).

In this study, the ASRs for leukemia among men and women were 5.3 and 3.6 per 100,000 population, respectively ($p < 0.001$). These rates were higher than those reported for Oman (4.8 for men and 3.3 for women per 100,000 population) and approximately equal to Kuwait (4.9 and 3.8) (Salim et al., 2009). But these rates were lower reported for Hong Kong (5.9 and 4.6) (Xie et al., 2012), Jordan (7.2 and 5.4) (Ismail et al., 2013), Egypt (5.4 and 4.1) (Salim et al., 2009) and the world (5.8 and 4.3) (Ferlay et al., 2010).

In dynamics, the lowest age-specific incidence rate of leukemia was at age group 10-14 years, the highest at age group 75-79 years, which showed a relationship between patient's age and morbidity of leukemia, which also was found by other researchers (Tahmasby et al., 2013; Longo et al., 2011; Robert et al., 2011, Sanoff, 2009).

As in the present study clear differences in incidence rates based on age, gender, residence have been reported (Tahmasby et al., 2013), indicative of environmental influences. High exposure to pesticides and other agricultural related products have been implicated in some studies (Rajabli et al., 2013; Zheng et al., 2013), but not others (Balasubramaniam et al., 2013). Tobacco appears to be a risk factor (Balasubramaniam et al., 2013), and null genotypes of both GSTM1 and GSTT1 genes may confer elevated risk of chronic myeloid leukaemia (Bhat et al., 2012), implying carcinogen involvement. It is of clear interest that earlier studies of breast cancer showed highest incidences where pollution was highest, including Pavlodar (Bilyalova et al., 2012). Similarly laryngeal cancer demonstrates highest incidences in North Kazakhstan and Pavlodar (Igissinov 2013a), like leukemia here. This might be partly due to the prevalence of Russian ethnicity in these provinces, given the ethnic differential in incidence rates (Igissinov et al., 2013). In contrast, esophageal cancer appears most frequent in the West of the country (Igissinov et al., 2012a) and cervical cancer in the northern half (Igissinov et al., 2012b).

Among the environmental factors affecting the health of the northern regions inhabitants, one could be

high content of sulphate and ammonia in water, which are risk factors in the occurrence and development of the blood and blood circulation diseases (Lihodumova, 2009). It is also important to pay attention on aspects of radiation exposure on human health. According to scientists approximately 90% of leukemia with an unclear etiology, ionizing radiation is recognized as the main environmental risk factor (Belson et al., 2007). In Kazakhstan from 1949 to 1989 in the areas adjacent to the nuclear test site, which was located on the border of the Semipalatinsk (now the East Kazakhstan), Pavlodar and Karaganda regions, residents were hundreds of times exposed to ionizing radiation (Baimukhanov et al., 2002). As a consequence increase of cancer cases, cardiovascular diseases, leukemia, central nervous system disorders among the population was noted (Baimukhanov et al., 2002; Hirabayashi et al., 2008).

In conclusion, the present results indicated differences of incidence rate based on age and sex and geographical location. The ASRs for leukemia both in men and women are lower than world rates but remain high. Our results showed the higher incidence rate of leukemia in men compared to women, the leukemia morbidity increase with age and inhabitants of north and east regions of Kazakhstan are more predisposed to disease. These results can serve as a basis for detailed study of the causes of high and low levels of leukemia in different regions of Kazakhstan. Determining and controlling important exogenous and endogenous risk factors may decrease its burden in the Kazakhstan population.

References

- Belson M, Kingsley B, Holmes A (2007). Risk factors for acute leukemia in children: a review. *Environ Health Persp*, **115**, 138-145.
- Baimukhanov SB, Gusev BI, Baimukhanov TS (2002). Radioactivity and Population Health Status around Semipalatinsk Nuclear Test Site. Almaty, part 1, chapter 1, pp. 1-10.
- Balasubramaniam G, Saoba SL, Sarhade MN, Kolekar SA (2013). Lifestyle factors including diet and leukemia development: a case-control study from Mumbai, India. *Asian Pac J Cancer Prev*, **14**, 5657-61.
- Bhat G, Bhat A, Wani A, et al (2012). Polymorphic variation in glutathione-S-transferase genes and risk of chronic myeloid leukaemia in the Kashmiri population. *Asian Pac J Cancer Prev*, **13**, 69-73.
- Bilyalova Z, Igissinov N, Moore M, et al (2012). Epidemiological evaluation of breast cancer in ecological areas of Kazakhstan - association with pollution emissions. *Asian Pac J Cancer Prev*, **13**, 2341-4.
- Campana D, Pui CH (2008). Childhood Leukemia. In 'Abeloff's Clinical Oncology', Abeloff MD, Armitage JO, Niederhuber JE, et al. Churchill Livingstone, 4th Edition, Chapter 96, pp. 1850-72.
- Ferlay J, Shin HR, Bray F, et al (2010). GLOBOCAN 2008 v1.2, Cancer Incidence and Mortality Worldwide: IARC Cancer Base No. 10 [Internet]. Lyon, France: International Agency for Research on Cancer; 2010. Available from: <http://globocan.iarc.fr>, accessed on 22.10.2013.
- Glantz SA (2001). Primer of Statistics. 5th edition, McGraw-Hill, New York.
- Goldman L, Andrew IS (2012). Goldman's Cecil Medicine: 24th

- Edition. Section 15, pp. 1203-33.
- Gordis L (2008). Epidemiology. 4th edition, Elsevier. Chapter 19, 333-347.
- Hirabayashi K, Kawano N, Ohtaki M, et al (2008). Health status of radiation exposed residents living near the Semipalatinsk Nuclear Test Site based on health assessment by interview. *Hiroshima J Med Sci*, **57**, 27-35.
- Igissinov SI (1974). Method of production and use of maps in oncological practice. *Kazakhstan Health*, **2**, 69-71.
- Igissinov S, Igissinov N, Moore MA, Kalieva Z, Kozhakhmetov S (2012a). Epidemiology of esophageal cancer in Kazakhstan. *Asian Pac J Cancer Prev*, **13**, 833-6.
- Igissinov N, Nuralina I, Igissinova G, et al (2012b). Epidemiological aspects of morbidity and mortality from cervical cancer in Kazakhstan. *Asian Pac J Cancer Prev*, **13**, 2345-8.
- Igissinov N, Zatoskikh V, Moore MA, et al (2013a). Epidemiological evaluation of laryngeal cancer incidence in Kazakhstan for the years 1999-2009. *Asian Pac J Cancer Prev*, **14**, 3969-74.
- Igissinov N, Zatoskikh V, Moore MA, et al (2013b). Laryngeal cancer in Kazakhstan - ethnic, age and gender differences over time variation. *Asian Pac J Cancer Prev*, **14**, 7033-8.
- Ismail SI, Soubani M, Nimri JM, Al-Zeer AH. (2013). Cancer incidence in Jordan from 1996 to 2009 – a comprehensive study. *Asian Pacific J Cancer Prev*, **14**, 3527-34.
- Jemal A, Bray F, Center MM, et al (2011). Global cancer statistics. *CA Cancer J Clin*, **61**, 69-90.
- Kampen KR (2012). The discovery and early understanding of leukemia. *Leukemia Res*, **36**, 6-13.
- Lihodumova IN (2009). Environmental risk assessment of morbidity of North-Kazakhstan region. Barnaul, 18 p.
- Longo D, Anthony F, Dennis K, et al (2011). Harrison's Principles of Internal Medicine: 18th Edition. Part 7, pp. 435-70.
- Modak H, Kulkarni SS, Kadakol GS, et al (2011). Prevalence and risk of leukemia in the multi-ethnic population of North Karnataka. *Asian Pac J Cancer Prev*, **12**, 671-5.
- Novak I, Jaksic O, Kulis T, Batinjan K, Znaor A (2012). Incidence and mortality trends of leukemia and lymphoma in Croatia, 1988-2009. *Croat Med J*, **53**, 115-23.
- Peter HW, John MG, Janice PD, Robert AK (2013). Neoplastic Diseases of the Blood, 5th Edition, 2013.
- Rajabli N, Naeimi-Tabaei M, Jahangirrad A, et al (2013). Epidemiology of leukemia and multiple myeloma in Golestan, Iran. *Asian Pacific J Cancer Prev*, **14**, 2333-6.
- Robert MK, Bonita MD S, Joseph SG, et al (2011). Nelson Textbook of Pediatrics: 19th Edition. Part 22, pp. 489-490.
- Salim EI, Moore MA, Bener A, et al (2010). Cancer epidemiology in South-West Asia - past, present and future. *Asian Pacific J Cancer Prev*, **11 Suppl 2**, 33-48.
- Sanoff HK, Mitchell BS (2009). Leukemias. In 'Netter's Internal Medicine (2ND)', Runge MS and Greganti AM. W.B. Saunders Elsevier, Health Sciences, p.1332.
- Sant M, Allemani C, Tereanu C, et al (2010). Incidence of hematologic malignancies in Europe by morphologic subtype. *J Am Soc Hematol*, **116**, 3724-34.
- Siegel R, Naishadham D, Jemal A (2012). Cancer statistics, 2012. *CA Cancer J Clin*, **62**, 10-29.
- Tahmasby B, Marnani AB, Maleki M, et al (2013). Blood malignancies in Mazandaran Province of Iran. *Asian Pacific J Cancer Prev*, **14**, 1053-6.
- Thygesen LC, Nielsen OJ, Johansen C (2009). Trends in adult leukemia incidence and survival in Denmark, 1943-2003. *Cancer Causes Control*, **20**, 1671-80.
- Xie WC, Chan MH, Mak KC, Chan WT, He M (2012). Trends in the incidence of 15 common cancers in Hong Kong, 1983-2008. *Asian Pac J Cancer Prev*, **13**, 3911-6.
- Zheng RZ, Zhang QH, He YX, et al (2013). Historical long-term exposure to pentachlorophenol causing risk of cancer—a community study. *Asian Pac J Cancer Prev*, **14**, 811-6.