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Analysis of epidemiological characteristics of leukemia in Kazakhstan using unified nationwide electronic healthcare data

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ABSTRACT

Background: Leukemia is the fifth leading cause of cancer mortality worldwide. Based on the rate of cellular division, leukemia is classified into acute or chronic myeloid or lymphoid types. Previous studies have highlighted rising leukemia cases in Kazakhstan; however, no study has described the epidemiology of leukemia and its subtypes.

Methods: This retrospective cohort study uses the unified nationwide electronic healthcare system to characterize the epidemiology of leukemia and its subtypes in patients treated in any clinical setting in Kazakhstan from 2014 to 2019. The Chi-square test was used for categorical variables, the independent t-tests for continuous numeric variables between two groups, and ANOVA for comparing means across multiple groups. A cox proportional hazards regression model calculates crude and adjusted hazard ratios for all-cause mortality risk.

Results: Of 9,561 patients, 4,783 (50.1%) were male and 4,778 (49.9%) were female. Median survival was 12 years (4,508 days). Mortality rates varied, with a slight increase in unspecified leukemia (C95) diagnoses in 2018-2019. Males (HR = 1.15, [95% CI: 1.07-1.23]), urban residents (HR = 1.52, [95% CI: 1.40-1.65]), and older individuals had higher mortality risks. Russians (HR = 1.42, [95% CI: 1.28-1.57]) and patients with hypertension (HR = 1.58, [95% CI: 1.53-1.64]) or chronic kidney disease (HR = 1.84, [95% CI: 1.60-2.10]) faced higher risk of death.

Conclusion: Leukemia incidence and mortality in Kazakhstan are higher among males, urban residents, older individuals, and patients with comorbidities. These findings highlight the need for targeted healthcare policies and clinical management strategies to address disparities and improve outcomes in Kazakhstan.

Keywords: leukemia, diagnosis, subtype, comorbidity, epidemiology, burden, registry, database, Kazakhstan

INTRODUCTION

Leukemia is a group of malignant disorders characterized by the uncontrolled proliferation of abnormal white blood cells in the bone marrow and peripheral blood, leading to impaired hematopoiesis and immune dysfunction. Globally, leukemia is the fifth most common cause of cancer-related deaths [1]. In 2020, leukemia was responsible for over 310,000 cancer deaths worldwide [2], thus presents a significant global health concern. The pathophysiology involves genetic mutations leading to dysregulated proliferation and impaired apoptosis of hematopoietic progenitor cells [3]. This results in bone marrow failure and systemic complications, driven by distinct biological mechanisms across leukemia subtypes. Leukemia is broadly classified into myeloid or lymphoid based on the rate of cellular division and categorized into acute and chronic subtypes based on the level of cellular maturity (chronic myeloid, acute lymphoblastic, acute myeloid, and chronic lymphocytic leukemia) [3]. The etiology of leukemia is not yet well comprehended and remains a multifactorial disease cause with interplay between genetic and environmental factors [4]. The most common risk factors linked to leukemia include chemical and radiation exposure (occupational or residential), family history of leukemia, and smoking [5].

Although higher prevalence of leukemia was noted among developed countries compared to developing countries, the incidence rates of leukemia are relatively high in South American, Caribbean, Asian, and African populations [6]. In Kazakhstan, with an age-standardized incidence rate estimated at approximately 5.3 cases per 100,000 population among men and 3.6 per 100,000 among women, based on data collected between 2003 and 2012. During a 10-year period, 6,741 new leukemia cases were registered in Kazakhstan, with higher incidence observed particularly in northern regions such as North-Kazakhstan and Pavlodar [7]. Leukemia incidence varies by age, sex, and population, with a notably higher occurrence in males than females, a mean patient age of 48.5 years, and older adults exhibiting more diverse subtypes and variable survival rates, especially in advanced stages, making it a significant global health issue [8-12].

According to research by the International Agency for Research on Cancer [13] , leukemia is one of the most prevalent cancers in Kazakhstan and is influenced by several risk factors, including genetic predispositions, exposure to environmental contaminants, smoking, dietary and lifestyle factors [14, 15]. A prior retrospective study found that new leukemia cases were more prevalent in the eastern and western regions of Kazakhstan, with mean annual incidence increasing with age [16, 17]. An epidemiological assessment conducted between 2003 and 2012 further identified high incidence rates in the northern part of Kazakhstan, predominantly affecting the male population [7]. Both studies consistently noted that the disease incidence is greater in males and escalates with advancing age [7, 17]. Additionally, a recent study that investigated the epidemiology and socio-demographic characteristics of pediatric leukemia in Kazakhstan found that the incidence and all-cause mortality rates were highest among children aged 0-5 years, highlighting an increased risk of fatality for children diagnosed with acute myeloid leukemia (AML) [18]. Despite Kazakhstan's central position in Asia, there is a paucity of comprehensive epidemiological research on leukemia and its subtypes. Some reports have suggested an increase in leukemia cases in the region, but these insights remain limited [19]. This study aims to characterize the epidemiological features of leukemia and its subtypes in Kazakhstan from 2014 to 2019, using the unified nationwide electronic healthcare database, to inform healthcare policy and planning.

METHODS

Study Design and Population

This retrospective cohort study examined adult patients diagnosed with leukemia and its subtypes who received treatment in various clinical settings across the Republic of Kazakhstan from 2014 to 2019. The dataset was sourced from the "electronic registry of inpatients," maintained by the Kazakhstan Ministry of Health. This registry is a component of the unified nationwide electronic healthcare system (UNEHS), which was implemented in late 2013 to centralize healthcare data across the country. Further details on the UNEHS data have been described in the study by [20].

Exposure and Covariates

The variables abstracted from the database included personal information such as the population registry identification (RPN ID), date of birth, date of death, age, gender, region, ethnicity, place of residence, type of leukemia diagnosed (using ICD-10 codes: C77, C91, C92, C93, C94, and C95), date of diagnosis, comorbidities, and date of discharge. Additionally, the data contained details on censored events, specifying the subtype diagnosis and date of death. All data were anonymized, ensuring that no personal identifiers were disclosed. For patients whose first appointments were recorded before 2014, the UNEHS might have sourced their data from previous electronic systems and older records. Data regarding the date of birth and diagnosis were directly obtained from the UNEHS, while information on the date of death was linked through the population registry using the RPN number. The same database facilitated the collection of comorbidity information, including conditions such as diabetes, hypertension, and stroke.

Statistical Approaches

Descriptive statistics were used to summarize the study data. For categorical variables, absolute numbers and their corresponding percentages were calculated. To explore associations in bivariate analyses, appropriate statistical tests were applied depending on the variable type: Chi-square tests for categorical variables, independent t-tests for continuous numeric variables between two groups, and ANOVA for comparing means across multiple groups.

The study reports incidence, and mortality rates for the period 2014 to 2019, expressed as both crude and adjusted estimates, stratified by sex, age, residence and comorbidity status using the 2014 population as baseline reference year [21-23]. Additionally, incidence and mortality among leukemia patients were expressed as rates per 1,000 patient-years (per 1,000 PY) across different subgroups.

To evaluate the risk factors for all-cause mortality among leukemia patients, the cox proportional hazards regression model was employed. Both crude and adjusted hazard ratios with 95% confidence intervals (CIs) were estimated. Potential confounders, including age and sex, were controlled through adjustments based on theoretical frameworks and tests for model assumptions. Statistical significance was determined at a two-sided p-value of less than 0.05. The follow-up extended from the date of diagnosis until death or loss to follow-up, up to December 31, 2019. Data management and statistical analyses were performed using R-Studio (Version 4.3.1).

RESULTS

Patient Demographic Information

Table 1 shows the demographic information of the patient cohort. Of the 9,561 patients analyzed, 50.1% were male and 49.9% female. The mean (M) age of the patients was 54.1

Table 1. Demographic and clinical characteristics of leukemia patients at baseline

Variable	All	C77	C91	C92	C93	C94	C95	p-value
Cohort N (%)	9,561 (100)	664 (6.9)	2,990 (31.3)	4,422 (46.3)	41 (0.4)	1,307 (13.7)	137 (1.4)	
Age, M ± SD	54.1 (16.6)	58.512.8)	57.1 (17.7)	51.71 (16.6)	54.2 (16.4)	59.6 (13.0)	53.4 (18.1)	< 0.001
Age group, N (%)								
18-34	1,445 (15.1)	40 (6.0)	464 (15.5)	847 (18.2)	5 (12.2)	61 (4.7)	28 (20.4)	< 0.001

Table 1 (Continued). Demographic and clinical characteristics of leukemia patients at baseline

Variable	All	C77	C91	C92	C93	C94	C95	p-value
35-44	1,043 (11.0)	55 (8.3)	204 (6.8)	652 (14.7)	9 (22.0)	107 (8.2)	16 (11.7)	
45-54	1,524 (15.9)	104 (15.7)	337 (11.3)	815 (18.4)	8 (19.5)	237 (18.1)	23 (16.8)	
55-64	2,507 (26.2)	257 (38.7)	801 (26.8)	1,000 (22.6)	3 (7.3)	419 (32.1)	27 (19.7)	
65-74	1,935 (20.2)	158 (23.8)	715 (23.9)	719 (16.3)	13 (31.7)	308 (23.5)	22 (16.1)	
75-84	1,017 (10.7)	43 (6.4)	433 (14.5)	354 (8.0)	2 (4.8)	170 (13.0)	15 (10.9)	
85+	90 (0.9)	7 (1.1)	36 (1.2)	35 (0.8)	1 (2.4)	5 (0.4)	6 (4.4)	
Sex, N (%)								
Female	4,778 (49.9)	274 (41.3)	1,307 (43.7)	2,457 (55.6)	22 (53.7)	644 (49.3)	74 (54.0)	< 0.001
Male	4,783 (50.1)	390 (58.7)	1,683 (56.3)	1,965 (44.4)	19 (46.3)	663 (50.7)	63 (46.0)	
Ethnicity, N (%)								
Kazakh	4,358 (45.8)	319 (48.1)	1,157 (38.9)	2,200 (50.0)	19 (46.4)	599 (46.0)	64 (47.1)	< 0.001
Russian	689 (28.2)	158 (23.8)	1,094 (36.8)	1,056 (24.0)	11 (26.8)	337 (25.8)	33 (24.3)	
Other	2,473 (26.0)	186 (28.1)	725 (24.3)	1,145 (26.0)	11 (26.8)	367 (28.2)	39 (28.6)	
Residency, N (%)								
Rural	2,211 (23.1)	149 (22.4)	674 (22.5)	1,130 (25.6)	6 (14.6)	219 (16.8)	33 (24.1)	< 0.001
Urban	7,350 (76.9)	515 (77.6)	2,316 (77.5)	3,292 (74.4)	35 (85.4)	1,088 (83.2)	104 (75.9)	
Hypertension, N (%)								
Yes	2,210 (23.1)	132 (1.4)	621 (6.5)	839 (8.8)	8 (0.08)	588 (6.1)	22 (0.20)	< 0.001
No	7,351 (76.9)	532 (5.6)	2,369 (24.8)	3,583 (37.5)	33 (0.3)	719 (7.5)	115 (1.2)	
Diabetes, N (%)								
Yes	608 (6.4)	39 (0.5)	222 (2.3)	225 (2.4)	1 (0.01)	117 (1.2)	4 (0.04)	< 0.001
No	8,953 (93.6)	625 (6.5)	2,768 (2.9)	4,197 (43.9)	40 (0.4)	1,190 (12.4)	133 (1.4)	
Stroke, N (%)								
Yes	181 (1.9)	10 (0.1)	33 (0.3)	55 (0.6)	NA	82 (0.9)	1 (0.01)	< 0.001
No	9,380 (98.1)	654 (6.8)	2,957 (30.9)	4,367 (45.7)	41 (0.4)	1,225 (12.8)	136 (1.4)	
CKD, N (%)								
Yes	523 (5.5)	24 (0.3)	152 (1.6)	256 (2.7)	2 (0.02)	80 (0.8)	9 (0.09)	0.018
No	9,038 (94.5)	640 (6.7)	2,838 (29.7)	4,166 (43.6)	39 (0.4)	1,227 (12.8)	128 (1.3)	
Death, N (%)	3,362 (35.2)	267 (7.9)	1,094 (32.5)	1,674 (49.8)	20 (0.6)	233 (7.0)	74 (2.0)	< 0.001

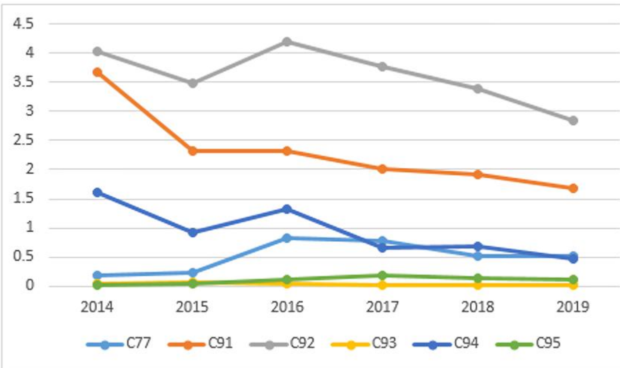

Figure 1. Incidence rate of leukemia diagnoses per 100,000 population (Source: Authors' own elaboration)

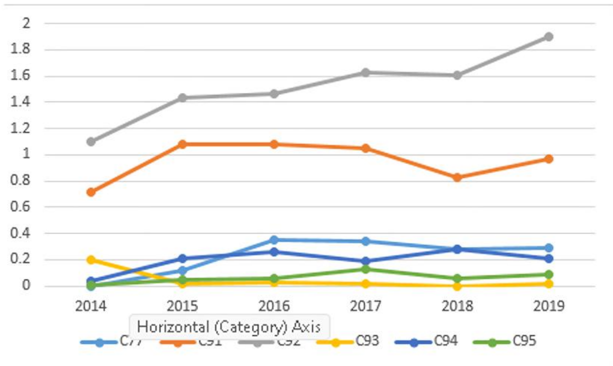

Figure 2. Mortality rate of leukemia diagnoses per 100,000 population (Source: Authors' own elaboration)

(standard deviation [SD] ± 16.6 years). Most of the patient population belongs to the Kazakh ethnicity (45.8%), while the remaining belonged to the Russian (28.2%) ethnic group, and others (26.0%). The age category between 55 and 64 years had the highest frequency of leukemia. A significant proportion (77%) of the patients were urban. The incidence of comorbidities such as diabetes, stroke, hypertension, and chronic kidney disease (CKD) were found to be 6.4%, 1.9%, 23.1%, and 5.5%, respectively. Patients diagnosed with myeloid (C92) leukemia experienced a higher percentage of death compared to other diagnoses.

Incidence and Mortality Rate

Figure 1 and **Figure 2** show the incidence and mortality rates of patients diagnosed with leukemia and its subtypes throughout the country. There was fluctuation in both incidence and mortality rates of the cases from 2014 to 2019. Among the different subtypes, myeloid leukemia (C92) was the most common subtype, followed by lymphoid leukemia (C91), other leukemia of specified cell types (C94), secondary and unspecified cell types (C77), leukemia of unspecified cell type (C95), and monocytic leukemia, respectively. But there was an observed rise in the mortality rate for each subtype of the disease per 100,000 population during the follow-up period.

The Overall Mortality

The median survival time for the whole cohort was 4,508 days, with 3,362 deaths recorded (35.2% of the total cohort). The mortality rate shows variation over time, with a slight increase in the number of patients diagnosed with leukemia of unspecified cell type (C95) toward the end of the study period in 2018 and 2019, as depicted in part B in **Figure 3**.

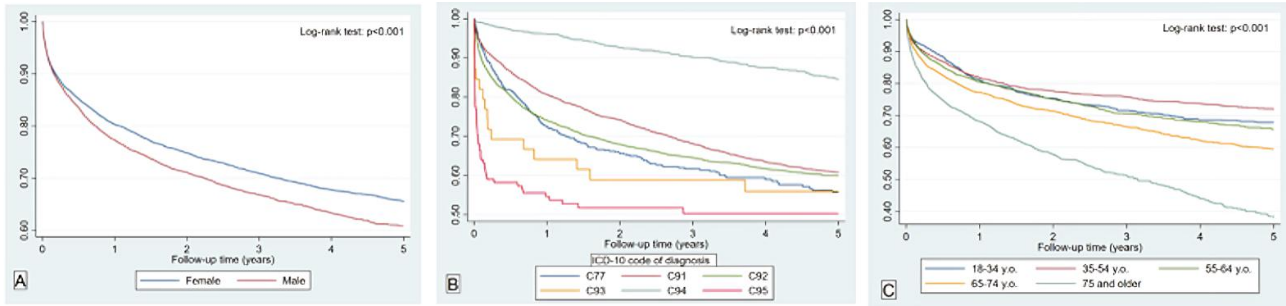

Figure 3. Patients' 5-year period survival function with leukemia with different sex (A), ICD-10 code of diagnosis (B), & age categories (C) (Source: Authors' own elaboration)

Table 2. Death rate and frequencies per 1,000 person-years stratified by leukemia subtype diagnosis

Variable	SU C77		Lymphoid C91		Myeloid C92		Leukaemia of unspecified cell type - C95	
	Death N (%)	Mortality rate per percentage 95% CI	Death N (%)	Mortality rate per percentage 95% CI	Death N (%)	Mortality rate per percentage 95% CI	Death N (%)	Mortality rate per percentage 95% CI
Age-group								
18-34	7 (2.6)	23.6 (11.3-49.5)	149 (13.5)	78.8 (67.0-92.6)	254 (15.2)	85.5 (75.4-96.9)	4 (1.7)	7.5 (2.8-20.1)
35-44	24 (9.1)	64.4 (41.1-101.0)	64 (5.9)	78.2 (60.3-101.3)	181 (10.7)	71.8 (61.4-83.9)	5 (2.1)	8.0 (3.3-19.2)
45-54	35 (13.1)	91.2 (62.5-132.9)	110 (10.1)	74.7 (60.7-91.9)	236 (14.1)	79.1 (68.8-90.9)	28 (12.0)	18.5 (12.2-28.1)
55-64	89 (33.3)	130.5 (104.8-162.5)	275 (25.1)	93.0 (81.9-106.7)	386 (23.1)	125.3 (112.5-139.6)	60 (25.8)	29.4 (22.4-38.5)
65-74	77 (28.8)	181.2 (143.1-229.4)	256 (23.4)	93.4 (81.7-106.7)	352 (21.0)	210.8 (188.7-235.5)	74 (31.8)	49.0 (38.5-62.4)
75-84	29 (10.9)	332.2 (227.8-484.4)	213 (19.5)	173.1 (150.6-198.9)	234 (14.0)	364.3 (319.1-415.9)	59 (25.3)	107.2 (82.7-139.0)
85+	6 (2.2)	1337.4 (618.8-3006.0)	27 (2.5)	368.7 (252.8-537.6)	31 (1.9)	1,176.5 (817.6-1693.0)	3 (1.3)	571.9 (184.4-1,773.2)
Sex								
Female	89 (3.3)	77.3 (62.8-95.4)	481 (44.0)	94.8 (86.6-103.8)	872 (52.1)	107.6 (100.6-115.1)	106 (45.5)	32.7 (27.0-39.7)
Male	178 (66.7)	157.4 (135.7-182.6)	613 (56.0)	103.7 (95.7-112.3)	802 (47.9)	143.1 (133.4-153.6)	127 (54.5)	36.3 (30.5-43.3)
Ethnicity								
Kazakh	124 (46.4)	122.2 (102.3-145.9)	414 (38.1)	88.1 (79.9-97.2)	816 (13.2)	124.8 (116.4-133.9)	109 (47.0)	33.9 (28.1-40.9)
Russian	67 (25.1)	123.8 (97.3-157.6)	428 (39.4)	122.3 (11.1-134.5)	5004 (81.2)	183.5 (167.9-200.5)	64 (27.6)	42.6 (33.3-54.5)
Other	76 (28.5)	105.3 (83.9-132.3)	244 (22.5)	88.8 (78.1-100.9)	342 (5.6)	78.8 (70.4-87.3)	59 (25.4)	29.3 (22.6-37.9)
Residence								
Rural	55 (20.6)	206.6 (158.2-269.8)	278 (25.4)	166.9 (148.2-188.0)	472 (28.2)	184.8 (168.8-2026)	50 (21.5)	63.7 (48.2-84.3)
Urban	212 (79.4)	105.3 (91.9-120z.6)	816 (74.6)	87.5 (81.7-93.8)	1202 (71.8)	107.5 (101.4-113.8)	183 (78.5)	30.7 (26.6-35.6)
Region								
Aqmola	9 (5.7)	418.4 (217.7-804.2)	50 (5.6)	188.7 (139.9-254.4)	41 (2.8)	309.2 (214.9-445.0)	2 (1.6)	16.6 (4.2-66.5)
Aktobe	11 (7.0)	183.8 (98.9-341.7)	24 (2.7)	193.9 (130.0-289.3)	35 (2.4)	221.2 (158.9-308.1)	11 (8.7)	47.7 (26.4-86.2)
Almaty Reg.	21 (13.3)	737.3 (480.7-1130.8)	47 (5.2)	251.9 (189.3-335.2)	53 (3.6)	170.3 (130.1-222.9)	9 (7.1)	42.8 (22.3-82.4)
Almaty	21 (13.3)	294.1 (189.7-455.8)	193 (21.5)	194.0 (168.1-223.6)	316 (21.6)	293.6 (262.5-328.3)	23 (18.3)	100.6 (66.8-151.3)
Atyrau	3 (2.0)	356.5 (89.2-1425.8)	12 (1.3)	166.7 (94.7-293.6)	35 (2.4)	238.7 (170.6-334.1)	3 (2.4)	24.8 (8.0-76.9)
East Kazakh	30 (19.0)	529.9 (368.2-762.5)	86 (9.6)	238.8 (193.3-295.0)	169 (11.5)	317.0 (272.2-369.3)	17 (13.5)	81.2 (50.5-130/6)
Zhambyl	4 (2.5)	703.1 (263.9-1873.3)	25 (2.8)	219.0 (148.5-325.3)	44 (3.0)	346.7 (558.0-465.9)	3 (2.4)	154.9 (50.0-480.3)
West Kazak	10 (6.3)	683.6 (367.8-1270.5)	35 (3.9)	183.4 (131.0-256.7)	59 (4.0)	270.5 (201.3-363.5)	5 (4.0)	53.3 (20.0-141.9)
Central Kazak	10 (6.3)	462.1 (240.4-888.1)	86 (9.6)	215.2 (174.2-265.7)	128 (8.7)	306.1 (257.0-364.5)	13 (10.3)	57.8 (33.6-99.6)
Kostanay	13 (8.2)	259.0 (150.4-446.0)	50 (5.6)	144.4 (109.2-191.1)	61 (4.2)	531.3 (412.5-684.2)	9 (7.1)	68.5 (34.2-136.9)
Kyzylorda	NA	NA	13 (1.5)	347.6 (201.8-598.5)	44 (3.0)	316.5 (234.7-584.2)	4 (3.2)	83.4 (31.3-222.1)
Mangystau	1 (0.6)	262.6 (37.0-1864.1)	1 (0.1)	22.3 (3.1-158.2)	11 (0.8)	230.7 (127.8-416.6)	1 (0.8)	20.9 (2.9-184.6)
Pavloda	6 (3.8)	576.4 (259.0-1283.0)	28 (3.1)	56.3 (38.3-82.7)	55 (3.8)	114.3 (87.5-146.2)	7 (5.6)	14.4 (6.5-32.0)
North Kazak	3 (1.9)	252.2 (81.4-782.1)	50 (5.6)	93.6 (71.0-123.5)	65 (4.4)	134.7 (105.2-172.4)	10 (7.9)	51.8 (27.9-96.4)
Turkestan	1 (0.6)	274.2 (38.6-1946.6)	58 (6.5)	86.8 (67.1-112.3)	88 (6.0)	50.4 (40.9-62.1)	1 (0.8)	40,583.3 (5,716.1-28,810.4)
Astana	8 (5.1)	102.0 (51.0-203.9)	136 (15.2)	148.0 (124.7175.6)	260 (17.8)	179.8 (159.0-203.4)	8 (6.3)	15.5 (7.7-30.9)
Shimkent	7 (4.4)	34.9 (16.6-73.1)	2 (0.2)	94.7 (23.7-378.7)	NA	NA	NA	NA
Comorbidity								
Hypertension	50 (52.1)	96.5 (73.1-127.3)	187 (50.0)	71.1 (61.6-82.0)	311 (54.4)	112.2 (100.4-125.4)	86 (52.1)	28.5 (23.0-35.2)
Diabetes	23 (23.9)	149.4 (99.3-225.0)	84 (22.5)	87.1 (70.3-107.9)	96 (16.8)	112.1 (100.0-149.1)	30 (18.2)	46.1 (32.2-65.9)
Stroke	7 (7.3)	235.1 (112.1493.1)	30 (8.0)	197.5 (138.1-282.5)	30 (5.2)	197.5 (138.1-282.5)	24 (14.5)	68.4 (45.8-102.0)
CKD	16 (16.7)	419.2 (256.8-684.3)	73 (19.5)	191.6 (152.4-241.1)	135 (23.6)	238.6 (201.6-282.5)	25 (15.2)	67.0 (45.3-99.2)

The data in **Table 2** shows the crude mortality rate per 1,000 patient years, and mortality due to leukemia was higher in males for all leukemia subtypes compared to females. It was also higher in patients of Russian ancestry compared to Kazakhs and other ethnic groups, except for C77 and C94 diagnoses. Additionally, the mortality rate was higher in older patients aged 34-84 years compared to younger patients, except for those aged 85 and above. Moreover, patients with leukemia who also have hypertension had higher mortality rates in all leukemia subtypes (C77, C91, C92, and C94) compared to patients with diabetes, CKD, and strokes, respectively. The mortality rates were reported as [per 100,000 PY]. These findings are depicted in **Figure 1** and **Figure 2**.

In this study, male patients exhibited a higher risk of mortality from leukemia compared to females (Hazard Ratio = [HR] = 1.15, [95% CI: 1.07-1.23], $p < 0.001$). Additionally, individuals residing in urban areas faced a greater risk of death (HR = 1.52, [95% CI: 1.40-1.65], $p < 0.001$) compared to those in rural regions. Mortality risk increased with age, using the 18-34 age group as the reference category. Among ethnic groups, Russians showed a higher mortality risk (HR = 1.42, [95% CI:

Table 3. All-cause mortality of crude and adjusted hazard model with 95% CI among leukemia patients

Risk factors	Crude HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
Age category				
18-34	Ref		Ref.	
35-44	1.01 (0.83-1.14)	0.76	0.90 (0.77-1.06)	0.200
45-54	1.03 (0.89-1.19)	0.68	0.93 (0.81-1.07)	0.330
55-64	1.30 (1.15-1.48)	< 0.001	1.19 (1.05-1.34)	0.005
65-74	1.75 (1.54-1.98)	< 0.001	1.50 (1.33-1.70)	< 0.001
75-84	2.73 (2.83-3.12)	< 0.001	2.30 (2.02-2.63)	< 0.001
85+	5.93 (4.57-7.70)	< 0.001	4.75 (3.67-6.14)	< 0.001
Gender				
Female	Ref		Ref.	
Male	1.15 (1.07-1.23)	< 0.001	1.16 (1.08-1.24)	< 0.001
Ethnicity				
Other	Ref		Ref.	
Kazakh	1.22 (1.11-1.34)	< 0.001	1.25 (1.14-1.36)	< 0.001
Russian	1.42 (1.28-1.57)	< 0.001	1.55 (1.41-1.71)	< 0.001
Residence				
Rural	Ref		Ref.	
Urban	1.52 (1.40-1.65)	< 0.001	1.48 (1.37-1.60)	< 0.001
Comorbidity				
Hypertension				
No	Ref.		Ref.	
Yes	1.58 (1.53-1.64)	< 0.001	1.74 (1.67-1.81)	< 0.001
Diabetes				
No	Ref.		Ref.	
Yes	1.13 (0.98-1.31)	0.100	1.07 (0.94-1.22)	0.320
Stroke				
No	Ref.		Ref.	
Yes	1.09 (0.85-1.39)	0.510	1.15 (0.92-1.45)	0.220
CKD				
No	Ref.		Ref.	
Yes	1.84 (1.60-2.10)	< 0.001	1.72 (1.52-1.196)	< 0.001

1.28-1.57], p < 0.001) compared to Kazakhs and other ethnicities. Furthermore, patients with hypertension and CKD had higher risk of death (HR = 1.58, [95% CI: 1.53-1.64] and HR = 1.84, [95% CI: 1.60-2.10], respectively, p < 0.001) compared to individuals with diabetes and stroke.

Table 3 shows all-cause mortality of crude and adjusted hazard model with 95% CI among leukemia patients.

DISCUSSION

We examined current epidemiological trends of leukemia in Kazakhstan across subtype diagnoses using a large-scale unified national healthcare database of the Republic of Kazakhstan. Our findings showed variation in the incidence and mortality rates of leukemia over the follow-up period from 2014 to 2019. Notably, after accounting for universal confounders such as age and sex, there was a significantly higher survival advantage among leukemia patients with hypertension among various ethnicities, as well as those of Russian descent, compared to unadjusted results. The higher survival probability noted among patients with hypertension may be related to closer medical monitoring, as supported by [24], which emphasize the benefits of targeted lifestyle interventions and supportive care in chronic conditions, which could translate into improved leukemia management outcomes. However, a decrease in survival probability was noted among older leukemia patients with CKD and those living in urban areas compared to rural areas, also compared to unadjusted results. The urban-rural discrepancies in survival and incidence underscore healthcare access inequities, consistent with environmental and genetic risk factors discussed in earlier epidemiological studies [25-31]. This is further supported by rehabilitation and lifestyle intervention findings [32] that suggest quality of life improvements can positively impact disease trajectories in blood disorders. The median survival time for the cohort was 4,864 days, with a survival advantage observed for females (4,864 days) compared to males (4,054 days). In examining differences in median survival times among subtypes of diagnosed cases, we observed that the C94 subtype had a notable survival advantage, with a median survival time of 6,994 days. This contrasts with other subtypes, which generally display lower survival rates. Age also emerged as a critical factor, with median survival times declining as age increased. This trend contradicts a previous study on the epidemiology and sociodemographic characteristics of pediatric leukemia in Kazakhstan [18], which showed that incidence and all-cause mortality rates were not significant among children aged 0-5 years for acute lymphoblastic leukemia and lymphomas. However, increased risks of death were found specifically in children diagnosed with AML. These suggest that both subtype specifics and age play crucial roles in survival outcomes.

The increased mortality noted among older urban leukemia patients with CKD aligns with the documented role of oxidative stress and comorbid conditions exacerbating disease severity, as described by [33] emphasizing the need to address oxidative stress and comorbidities in treatment planning [33]. Previous studies have demonstrated disparities in leukemia incidence between individuals living in urban and rural areas, which aligns with international findings [34, 35]. Our analysis revealed similar findings of higher leukemia cases in older adults. This may be associated with environmental factors such as increasing exposure to toxic chemicals, and/or that more people residing in urban areas have better access to healthcare facilities and are screened more frequently compared to those in rural areas. Furthermore, although the correlation between age, sex, and blood cancer occurrence has been long established, our study highlights a rise in leukemia incidence as patient age increases among men. These findings are consistent with earlier studies examining the relationship between age, sex, and leukemia incidence rates [24-28]. Leukemia is more prevalent among men than women, and incidence rises with increasing age [29, 30], similar to our study findings. Factors contributing to higher leukemia incidence in certain populations include lifestyle choices such as smoking and alcohol consumption, inequality in accessing primary healthcare services, the type of work individuals perform, place of residence, and genetic susceptibility [15, 31].

Leukemia mortality rates are consistently rising in developing countries, including Kazakhstan, and our findings are consistent with prior studies reporting increases in leukemia-related mortality in the People's Republic of China between 2003 to 2017 [6, 33]. The rise in leukemia incidence in Kazakhstan is comparable between urban and rural areas, consistent with previously conducted studies [36]. Historically, environmental factors likely impacting health in northern Kazakhstan include proximity to the former Semipalatinsk nuclear test site, which experienced heavy ionizing radiation during Soviet era [37]. Studies show that residents of the Karaganda and Pavlodar regions, in particular, were exposed to radiation hundreds of times higher than normal [38]. Consequently, the incidence of various health problems such as cancer (including leukemia), central nervous system disorders, cardiovascular diseases, and CKD has increased in these populations [39-42].

CONCLUSION

This study represents the first comprehensive nationwide analysis of leukemia incidence and all-cause mortality in Kazakhstan using a unified electronic healthcare database from 2014 to 2019. Our findings demonstrate higher leukemia diagnosis and mortality risks among males, older adults, urban residents, and patients with hypertension or CKD. The variation in survival across leukemia subtypes and demographic groups underscores the multifaceted nature of leukemia epidemiology in Kazakhstan. Environmental, genetic, healthcare access, and lifestyle factors likely contribute to observed disparities. These results emphasize the urgent need for improved healthcare infrastructure, equitable access to diagnostic and treatment services, and tailored public health strategies focusing on primary prevention and management of comorbid conditions. Future research should explore urban-rural differences, age-specific risks, and intervention impacts to further optimize leukemia care and reduce disease burden in Kazakhstan.

Strengths and Limitations

Our study has limitations, including potential underreporting and misdiagnosis due to variable diagnostic criteria, particularly in rural areas with limited access to medical facilities. Despite gradual improvements in the unified database since 2013, these factors may affect incidence and mortality estimates. Additionally, the retrospective design and reliance on administrative data contribute to possible misclassification. Nevertheless, this study's use of a comprehensive, standardized nationwide electronic healthcare database provides robust epidemiological insights with broad population coverage and longitudinal follow-up, offering valuable information to inform future research and national health policymaking in Central Asia.

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