RESEARCH ARTICLE

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Cancer Incidence in a Population Living Near Radioactive Waste Storage of Uranium Mining in Stepnogorsk Area, Northern Kazakhstan

Kuralay Ilbekova[1]*, Danara Ibrayeva[1], Polat Kazymbet[1], Meirat Bakhtin[1], Yerbol Dogalbayev[2]

Abstract

Objective: This study evaluates the impact of radioactive uranium waste storage facilities on cancer occurrence in nearby areas. **Methods:** Current research evaluates the effect of radioactive uranium waste storage facilities on cancer epidemiology in nearby areas. The critical area had Aqsu, Kvartsitka, Zavodskoy and Stepnogorsk cities, which are located at a less than 5 km distance to the south of the Hydrometallurgical Plant tailings dump while the control group had Akkol region in 90 km from the source. The majority of population had lived in this territory more than the 30 years. Data were obtained from the Electronic Register of Cancer Patients of the Republic of Kazakhstan from 2001-2015, and 2,271 incident cases of cancer were registered. **Results:** The most frequent malignancies were observed in the digestive organs (646 cases, 28%) and respiratory and intrathoracic organs (376 cases, 17%). The proportion of digestive organ cancers was higher in the critical group (560 cases out of 1913, 29%) than in the control group (86 cases out of 358, 24%). Additionally, respiratory organ cancers were more common in men, but the cancer incidence rate ratio was higher in the critical area. Notably, the study found that the cancer incidence rate ratios decreased over time, specifically for digestive, respiratory and female genital organs and breast cancer. **Conclusion:** In conclusion, while our study highlights significant differences in cancer incidence rates and frequencies between the critical and control groups, further analytical research, incorporating age-adjustment, is needed to provide a more conclusive evaluation of the potential impact of residence in proximity to the uranium mining waste storage on cancer occurrence in the study area.

Keywords: Cancer incidence- radioactive waste- cancer risk factors

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Introduction

The potential health effects associated with uranium mining and other types of non-radiation-related mining activities do not differ significantly [1]. Kazakhstan has the second largest (14% of world reserves) uranium reserves in the world, 67% of which are suitable for mining by the in-situ leaching method, which is the most environmentally friendly and lowest-cost method of uranium mining [2]. According to the World Nuclear Association, in 2021, Kazakhstan became the world's leading uranium producer, accounting for almost 45% of global production, which is equivalent to 21,819 tonnes uranium (U) [3].

Scientists started studies on the radiation safety of Kazakhstani land in the 1990s because of possible uranium deposits. The research on radiation safety is carried out in accordance with the Laws "On the use of atomic energy" [4] and "On the protection of the population from ionizing radiation" [5]. The largest regions enriched in uranium deposits are located within Northern Kazakhstan, where about 16.4% of the republic's uranium resources are concentrated [6]. In addition, there are also large storage facilities for radioactive waste in Northern and Western Kazakhstan. The total area exposed to radioactive waste from the uranium industry is approximately 100,000 ha with a total activity of 250,000 Curie [7]

The growth in uranium production, the increase in the number, and the expansion of existing storage facilities for radioactive waste at uranium mining enterprises have an unfavorable impact on the environment and population. The study of Ibrayeva et al. (2020) showed that gamma radiation, radon exposure, and uranium concentration in soil are contaminating the environment of Northern Kazakhstan. The outdoor gamma dose rates (0.13-2.87 μSv h-1) were found to be higher than the indoor gamma dose rates (0.15-0.3 μSv h-1) [8]. Moreover, the indoor radon concentrations (313-858 Bq m-3) were recorded to be higher than the outdoor ones (23-39 Bq m-3) [8]. The values of outdoor gamma dose rates and indoor and

[1]Institute of Radiobiology and Radiation Protection, JSC Astana Medical University, Astana, Kazakhstan. [2]CF University Medical Center, Kazakhstan.*For Correspondence: ilbekova.kb@gmail.com

outdoor radon concentrations are considerably higher than worldwide range for corresponding values [9]. The previous investigations of the radiation situation showed that the buildings and territories with high local contamination have been identified in Stepnogorsk area. According to these studies the annual effective dose of the population living near radioactively contaminated territories in Northern Kazakhstan was very high. For example, these doses were about 1 and 3.5 mSv y-1 in the Aqsu settlement and from radon exposure was 120 mSv y-1 [10]. Some studies investigated the effect of chronic exposure to low-level radiation on human health in Stepnogorsk, Northern Kazakhstan [11]. Results showed the pathology of the cardiovascular system among residents of the observed area. In addition, depleted uranium is a risk factor for another major noncommunicable disease – cancer [12, 13]. The literatures showed that the low doses of ionizing radiation could have an effect on initiation, promotion and proliferation of malignant neoplasms [14, 15]. This study aims to evaluate for the first time the cancer burden in the population living in the zone of influence of radioactive waste storage facilities in Kazakhstan.

Materials and Methods

Study population

The mining sites in Northern Kazakhstan are associated with 12 uranium deposits, and one of them is the Stepnogorsk Hydrometallurgical Plant (HMP) tailings disposal dump. HMP tailings dump is the biggest waste storage of uranium ores with 44.17 million tons of waste, which gives 5.42 GBq activity [16]. This study evaluates the effect of low-level uranium radiation and also chemo toxic-related on the cancer burden by comparison of tumor incidence in the critical and control areas between 2001 and 2015. The critical group includes residents from four residential areas of Northern Kazakhstan: Aqsu, Kvartsitka, Zavodskoy and Stepnogorsk, all located within a 5 km radius south of the HMP tailings dump (Figure 1). These areas have been identified due to their proximity to significant sources of uranium-related waste and their potential high exposure to both radioactive and chemical contaminants.

Conversely, the control group comprises residents of Akkol city, which is situated approximately 90 km away from the HMP tailings dump. This group was selected as a comparative baseline because the residents there share similar socioeconomic and demographic characteristics with the critical group but are significantly less exposed to the industrial contaminants.

Rationale for Group Selection

The definition and selection of these groups are crucial for analyzing the differential impacts of environmental exposure on cancer incidence. By comparing these two distinctly positioned groups, this study aims to isolate the effects of low-level radiation and chemotoxicity from other confounding variables. According to local executive bodies the population of Stepnogorsk area of the beginning of 2015 is 58.1 thousand 58100 people, where including:

Stepnogorsk city – 35.917 thousand people (17.872 male and 18.045 female); Aqsu – 4.027 thousand people (1989 male and 2038 female); Zavodskoy – 3.964 thousand people (2012 male and 1952 female) and others settlements – 14.144 thousand people [17,18]. The majority of population had lived in this territory more than the 30 years. The control group includes the population of Akkol city, who live for a long time in this territory and which is 90 km from the source of contamination. This population group had same lifestyle as in a critical area [18].

Throughout our research period, the numbers of men and women in both the critical and the control areas were comparable, even concerning individuals of European and Asian descent. The number of inhabitants in the areas under study minor fluctuated due to natural population movement and migration.

Cancer incidence data were retrospectively collected

Figure 1. Map of Critical and Control Group Location

for the abovementioned cities from the Electronic Register of Cancer Patients of the Republic of Kazakhstan. The database had deidentified information on the living area, the ICD-10 code of disease, the admission date when the tumor was first diagnosed, date of birth, gender, and the cancer stage, and cancer localization. Demographic data on population number and gender distribution were derived from the Statistics Committee of the Ministry of National Economy of the Republic of Kazakhstan [19].

Environmental radiation measurement

Environmental Dose Rates: Measurements were taken using NaI (TI) scintillation survey meters. Specifically, we used the DKS-AT-1123 meters from ATOMTEX Scientific Production Unitary Enterprise, Republic of Belarus, and the RKS-01-SOLO meters from SOLO LLP, Republic of Kazakhstan [20].

Indoor Measurements

In each settlement, indoor gamma exposure doses were assessed in main living spaces such as bedrooms, sitting rooms, and kitchens. Measurements were conducted at the center of these rooms, at a height of 1 meter above the ground. The mean of three readings was recorded for each measurement.

Statistical analyses

All statistical analyses were performed using STATA 16.0 software. The continuous variables were reported as arithmetic means and standard deviations. Only age was presented in continuous form. The categorical variables were presented as absolute and relative frequencies. Age was categorized as following: (1) younger than 18 years old (y.o.), (2) 18-34 y.o., (3) 35-50 y.o., (4) 51-70 y.o., and (5) older than 70 years of age. Gender, localization of malignant neoplasms and stage of cancer were categorical variables. The living area was chosen as an independent variable. For continuous variables, the student t-test was used to determine if the differences between means of variables in patients' groups are significant. If the data did not meet criteria for parametric test, Mann-Whitney U test was used. For categorical variables, Pearson's chi-square test was used for determining if the association with the outcome in two groups was significant. If the assumptions for Pearson's chi did not meet, Fisher's exact test was used. The significance level was set at $\alpha = 0.05$.

To investigate the dynamics of the cancer incidence, data were compared at three-time intervals: 2001-2005, 2006-2010, and 2011-2015. To calculate the incidence rate (IR) in this study, we divided the number of incident cases by the average population size of the respective groups over the period of interest. Rates were presented as number of cases per 1,000 and 10,000 persons of the population. The rate ratio was derived from the IRs to evaluate the burden of cancer in the critical area compared to the control area.

Results

During the observation period, 2,271 incident cancer cases were registered to hospitals in the critical and control areas. The socio-demographic and medical characteristics of patients by gender are presented in Table 1.

As it can be seen in Table 1 the average age of females at the first diagnosis of malignant disease was 61 years, while for males, the mean age was 63 years which differed statistically significantly ($p<0.001$). The gender distribution between critical and control groups did not differ significantly ($p=0.652$). In total, the most frequent cancer sites were digestive organs (28%), respiratory and intrathoracic organs (17%), followed by breast (12%), skin (11%), and female genital organs (11%). Among cancer patients 63% of men and 47% of women were diagnosed with 3rd or 4th stage of the disease ($p<0.001$).

Socio-demographic and medical characteristics of patients by areas of interest are presented in Table 2. Age distribution of cancer patients in the critical and control areas was similar (p for heterogeneity = 0.118). Digestive organs cancers were more frequent in the critical than in control group, 29% and 24%, respectively. As for the stage, the critical group had a higher rate of 2nd stage (641, 34%) in contrast to the control group (93, 25%). The results indicate the statistically significant difference in cancer stage frequency in percentage in the two groups ($p=0.031$).

The number of cancer cases per 10,000 persons of the population of areas of interest and rate ratios (RR) by the tumor site were summarized in Table 3. The RR of all registered cancer cases during 2001-2015 between critical and control groups decrease over the observation period, starting from 17,9 to 11,1 (Table 3). The result is not statistically significant as the low bound of 95% confidence interval is less than 1. Tumors of digestive organs were observed 2.6 times more in the critical area in 2001-2005. The difference was diminished by 2011-2015, showing a RR of 1.2 between groups. Although the burden of the cancer of female genital organs and breast was higher in the critical group (RR=1.71) at the beginning of the observation period, by the end the RR was 1.02 (Table 3). As for the tumor of the respiratory and intrathoracic organs, RR fluctuated from 1.75 to 1.47 over follow-up time.

Gender

Specific rate of cancer cases per 10,000 persons of the population in the critical and control groups by years are evaluated in Figure 2. The number of cancer cases are presented in Table 4. The higher tumor incidence tendency for both groups among both genders in 2006-2010 is shown in Figure 2a. In both areas, females have higher cancer rates than males. By the end of the observation period (2011-2015), cancer rates among females and males in the critical group, and women in the control group were similar.

The majority of respiratory and intrathoracic organs tumor are observed in males in both groups (Figure 2b). Although the tumor of digestive organs is more frequent in the population of the critical group, a sharp increase in incidence is detected in both females and males of the control group after 2001-2005 years (Figure 2c).

Table 1. Socio-Demographic and Medical Characteristics of Cancer Patients by Gender (n=2,271)

Characteristics	Total (n = 2 271)	Female (n = 1 173, 52%)	Male (n = 1 098, 48%)	p-value
Age at diagnosis, years (mean ± SD)	61 (±13)	61 (±14)	63 (±12)	<0.001
Age, at diagnosis n (%)				<0.001
<18 years	27 (1)	15 (1)	12 (1)	
18 - 34 years	56 (2)	36 (3)	20 (2)	
35 - 50 years	322 (15)	216 (19)	106 (10)	
51 - 70 years	1 248 (55)	586 (50)	662 (60)	
>70 years	618 (27)	320 (27)	298 (27)	
Living area				0.652
Critical group	1 913 (84)	992 (85)	921 (84)	
Control group	358 (16)	181 (15)	177 (16)	
Localization of malignant neoplasms, n (%)				
Lip, oral cavity, and pharynx	69 (3)	13 (1)	56 (5)	
Digestive organs	646 (28)	289 (25)	357 (33)	
Respiratory and intrathoracic organs	376 (17)	69 (6)	307 (28)	
Bone and articular cartilage	14 (0.6)	6 (0.5)	8 (0.7)	
Skin	246 (11)	148 (13)	98 (9)	
Mesothelial and soft tissue	32 (1.4)	12 (1)	20 (2)	
Breast	256 (12)	256 (22)	0	
Female genital organs	246 (11)	246 (21)	0	
Male genital organs	70 (3)	0	70 (6)	
Urinary tract	146 (6)	35 (3)	111 (10)	
Eye, brain, and other parts of the central nervous system	31 (1)	16 (1.5)	15 (1)	
Thyroid and other endocrine glands	27 (1)	24 (2)	3 (0.3)	
Ill-defined, secondary, and unspecified sites	33 (1)	15 (1)	18 (2)	
Stated or presumed to be primary, of lymphoid, hematopoietic, and related tissue	79 (4)	44 (3)	35 (3)	

Discussion

This is the first study to explore the association between the presence of radioactive uranium waste storage facilities and the incidence of cancer in the population of Northern Kazakhstan, using data from the Electronic Register of Cancer Patients of the Republic of Kazakhstan for 2001-2015. However, it should be noted that the study design did not specifically evaluate the potential health effects of the uranium storage facilities in isolation from other potential risk factors, such as smoking and alcohol consumption, which may contribute to the incidence of cancer in the study population. Major tumor sites were the digestive system, respiratory and intrathoracic organs, breast, and female genital organs. The majority of patients from the critical area had the 2nd or 3rd stage of cancer at the moment of diagnosis.

The results of this study show that the average age at cancer diagnosis was more than 60 years. However, women are diagnosed with the malignant disease at an earlier age. Taking into account the high proportion of cancer in female genital organs, the younger age of females at the onset of cancer can be explained by an increased risk of endometrial cancer after menopause, which takes place after 45 years [21, 22]. At the time of diagnosis, the majority of men had a terminal tumor stage. Late onset of symptoms, low awareness about cancer, less self-examination, and rare cancer screening are the possible explanations for the tendency [23].

The incidence rates of cancer of respiratory and intrathoracic organs were found to be higher in men compared to women in both the potentially contaminated and non-contaminated areas. Moreover, the rates of cancer in males living in the potentially contaminated area were found to be consistently higher during all observation periods, compared to those living in the non-contaminated area. The presented rates were not adjusted for age, and the age distribution of the population in the areas was not taken into account. Additionally, statistical tests were not conducted to assess the significance of the observed differences in incidence rates between the groups. The indirect decay product of uranium is radioactive gas radon, which concentration exceeds the permissible range in Northern Kazakhstan [24]. The literature demonstrates a direct correlation between radon and gene mutations and chromosome aberrations that lead to the formation of neoplasms [25]. The epidemiological studies show that radon is one of the leading causes of lung cancer [26]. According to Mozzoni et al. (2021), the limited number and heterogeneity of existing studies do not support a

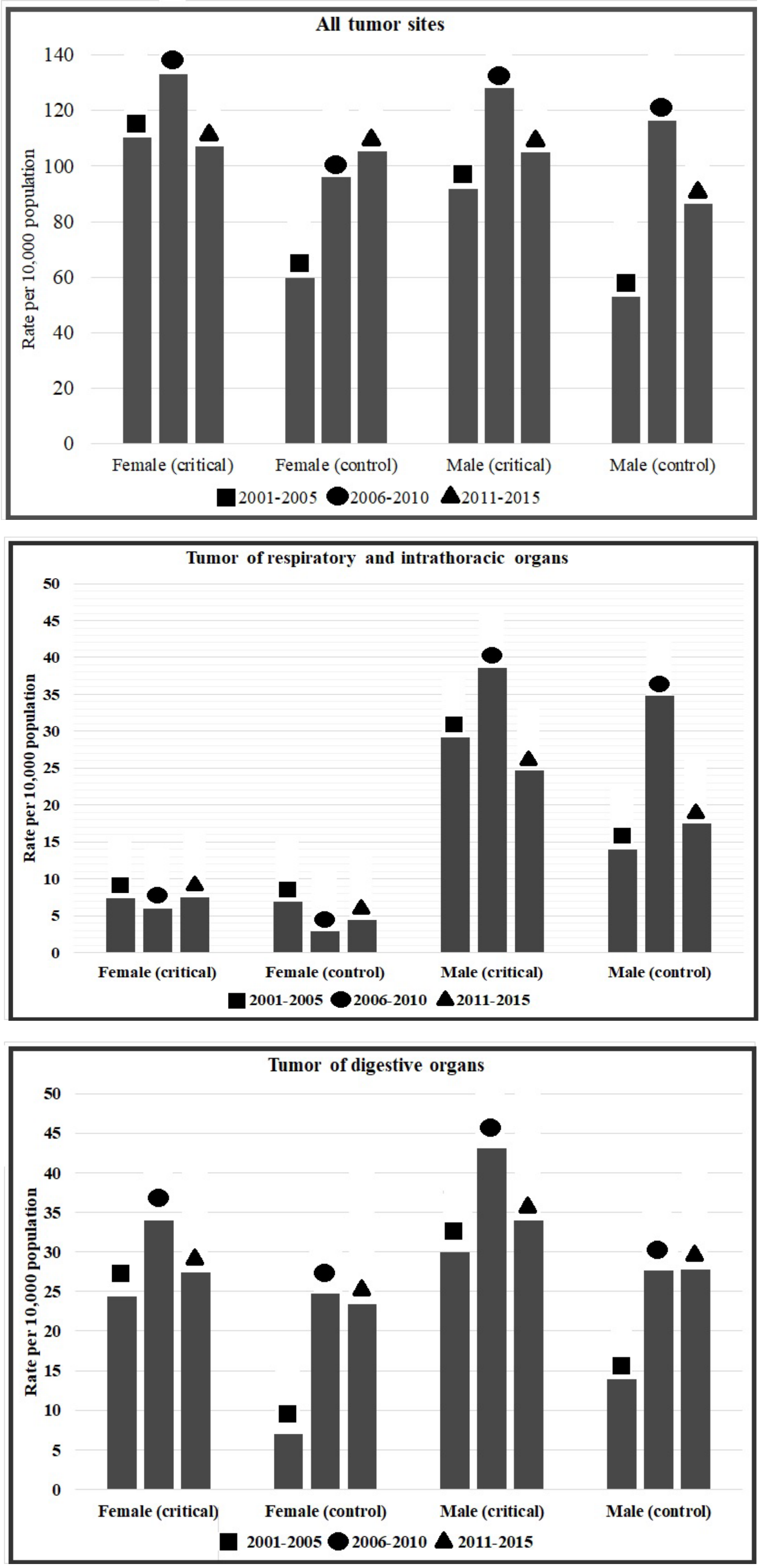
a)
b)
c)


Figure 2. Gender- Specific Crude Rates of Cancer Cases Per 10,000 Persons of the Population in the Critical and Control Groups by Years.

Table 2. Socio-Demographic and Medical Characteristics of Cancer Patients by Residence Area (n = 2,271)

Characteristics	Total (n = 2 271)	Critical group (n = 1 913, 84%)	Control group (n = 358, 16%)	p-value
Age, years (mean, SD)	61 (±13)	62 (±13)	60 (±15)	0.025
Age, n (%)				0.118
<18 years	27 (1)	19 (1)	8 (2)	
18 - 34 years	56 (2)	44 (2)	12 (3)	
35 - 50 years	322 (15)	264 (14)	58 (16)	
51 - 70 years	1 248 (55)	1 059 (55)	189 (53)	
>70 years	618 (27)	527 (28)	91 (26)	
Localization of malignant neoplasms, n (%)				
Lip, oral cavity, and pharynx	69 (3)	56 (3)	13 (4)	
Digestive organs	646 (28)	560 (29)	86 (24)	
Respiratory and intrathoracic organs	376 (17)	320 (17)	56 (16)	
Bone and articular cartilage	14 (0.6)	12 (1)	2 (0.6)	
Skin	246 (11)	204 (11)	42 (12)	
Mesothelial and soft tissue	32 (1.4)	23 (1)	9 (3)	
Breast	256 (12)	217 (11)	39 (10)	
Female genital organs	246 (11)	210 (11)	36 (10)	
Male genital organs	70 (3)	63 (3)	7 (2)	
Urinary tract	146 (6)	125 (7)	21 (6)	
Eye, brain, and other parts of the central nervous system	31 (1)	23 (1)	8 (2)	
Thyroid and other endocrine glands	27 (1)	22 (1)	5 (1.4)	
Ill-defined, secondary, and unspecified sites	33 (1)	23 (1)	10 (3)	
Stated or presumed to be primary, of lymphoid, hematopoietic, and related tissue	79 (4)	55 (3)	24 (6)	

causal association between Rn exposure and the risk of non-pulmonary neoplasms [27]. Even if the concentrations of radon in Northern Kazakhstan areas are low, they may enhance the effect of smoking, dust, and other factory gases. An extremely large gap in the incidence of the tumor of respiratory organs between males and females in both areas may be related to the fact that most men work in uranium mining facilities, and consequently, are more susceptible to disease. Another possible factor is smoking that is more frequent among males. However, non-smoking females have experienced an elevated incidence of lung cancer in recent years, according to research [28].

Table 3. Crude Cancer Incidence Rates (Number of Cases per 10,000 Persons of the Population), RR, and P Values for Selected Cancer Sites in Critical and Control Areas by Year of Investigation

Tumor sites	Group	2001-2005	2006 - 2010	2011 - 2015
All tumor sites	Critical	101.1	130.75	106.17
	Control	56.32	106.04	95.82
	RR [95% CI]	1,79 [0,63; 5,05]	1,23 [0,55; 2,77]	1,11 [0,46; 2,66]
Digestive organs	Critical	27.2	38.6	30.7
	Control	10.4	26.1	25.6
	RR [95% CI]	2,60 [0,27; 24,9]	1,47 [0,31; 7,07]	1,20 [0,22; 6,30]
	p-value	0.109	0.238	0.62
Respiratory and intrathoracic organs	Critical	18.3	22.3	16.1
	Control	10.4	18.9	11
	RR [95% CI]	1,75 [0,16; 19,4]	1,18 [0,17; 8,19]	1,47 [0,13; 16,6]
	p-value	0.927	0.818	0.273
Female genital organs and breast	Critical	22.5	30	22.4
	Control	13.2	18.9	21.9
	RR [95% CI]	1,71 [0,19; 14,7]	1,59 [0,26; 9,82]	1,02 [0,16; 6,57]
	p-value	0.816	0.173	0.653

* p-values were obtained using either Pearson's chi-squared test or Fisher's exact test, adjusted for the year of interest.

Table 4. Gender-Specific Absolute Frequencies of Cancer Cases in the Critical and Control Groups by Years

a) all tumor sites

	Female (critical)	Female (control)	p-value	Male (critical)	Male (control)	p-value
2001-2005	299	43	0.066	248	38	0.248
2006-2010	380	66		366	80	
2011-2015	313	72		307	59	

b) cancer of respiratory and intrathoracic organs

	Female (critical)	Female (control)	p-value	Male (critical)	Male (control)	p-value
2001-2005	20	5	0.754	79	10	0.348
2006-2010	17	2		110	24	
2011-2015	22	3		72	12	

c) cancer of digestive organs

	Female (critical)	Female (control)	p-value	Male (critical)	Male (control)	p-value
2001-2005	66	5	0.161	81	10	0.579
2006-2010	97	17		123	19	
2011-2015	80	16		99	19	

The incidence of digestive system cancer was higher in men and women of critical areas compared to control one. Increased risk of this tumor type can be associated with the uranium mining facilities nearby. However, the literature has controversial results on this issue. Turner et al. [29] evaluated in their study that radon does not seem to have a relationship with non-respiratory disease and mortality [29]. However, a study from Spain shows a statistically significant association between indoor radon and stomach cancer in women [30]. More profound research on the connection between radon and tumor of digestive organs is needed. As for the incidence rates, and rate ratios between critical and control groups, there is a direct tendency that RRs decrease over the observation period. The risk of cancer of female genital organs diminished significantly, and by the end of follow-up time, it is approximately equal for both areas. Perhaps, the work carried out on the conservation and liquidation of uranium deposits in the Northern Kazakhstan region by 2008 showed its effect [31]. However, the burden of cancer remains high in the critical area.

In our study, the critical and control groups reported a total of 2,271 incident cases of cancer. The most frequent malignancies were in the digestive (28%) and respiratory and intrathoracic organs (17%). The incidence in the critical group for digestive organ cancers (29%) was higher than in the control group (24%), which aligns with the national pattern where digestive cancers are a significant concern. The incidence rate of respiratory cancers, more prevalent among men, was also notably higher in the critical area, reflecting regional disparities possibly linked to environmental factors specific to those areas.

Comparison of these findings with the national data shows that while the national rates of breast and colorectal cancers are significant, our study highlighted digestive and respiratory cancers, suggesting localized environmental impacts might influence these discrepancies. Additionally, the high neglect rate and lower early diagnosis rates in regions like Akmola may correlate with the increased incidence and severity observed in our critical group, suggesting regional variations in healthcare access and cancer screening efficacy.

By aligning our local data with these national trends, we can better understand the environmental and healthcare factors contributing to regional cancer disparities. This comparison not only validates the heightened cancer risks in the critical areas identified in our study but also emphasizes the need for targeted healthcare interventions in these regions. It is important to acknowledge the limitation of not performing age-adjustment in our study. Due to resource constraints and the unavailability of age-specific cancer incidence rates for a standard population closely resembling the study cohort, we were unable to control for the potential confounding effect of age differences between the exposed and control groups. As a result, the observed differences in crude rates of cancer incidence may have been influenced by variations in age distribution, and caution should be exercised when interpreting and generalizing the study's findings. All the statistical tests performed in the study are of descriptive nature. Future research endeavors should aim to address this limitation to provide a more comprehensive understanding of the impact of low-level uranium radiation on cancer burden in the study region.

In conclusion, the findings of this study suggest the possibility of an unfavorable impact of the Stepnogorsk HMP on potentially increase the risk of some oncological diseases. However, it is important to acknowledge that this study has some limitations, including the lack of information on other potential risk factors, such as smoking and occupational hazards. Additionally, statistical evidence was not found to support the observed differences in incidence rates between the potentially contaminated and non-contaminated areas. Therefore, further research is needed to confirm and elucidate the impact of the Stepnogorsk HMP on the environment and the health of local residents.

Author Contribution Statement

Conceptualization Ilbekova K.; data curation Ilbekova K.; formal analysis Ilbekova K..; funding acquisition Bakhtin M. and Kazymbet P.; methodology Ilbekova K., Ibrayeva D., Bakhtin M., Kazymbet P., Dogalbayev Ye.; writing-original draft preparation Ilbekova K., Ibrayeva D.; writing-review and editing Ilbekova K., Ibrayeva D.; All authors have read and agreed to the published version of the manuscript.

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Approval

It is part of an approved student thesis.

Ethical Declaration

The data were retrospectively analyzed, and all ethical principles of the Helsinki Declaration have been followed. The Electronic Register of Cancer Patients of the Republic of Kazakhstan gave researchers the data blinded on personal information such as name, identity card number, or address. The Ethical Committee of the JSC Astana Medical University (No. 4 dated 7 September 2017) approved the study.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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