RESEARCH ARTICLE

The Incidence of Malignant Tumors in Environmentally Disadvantaged Regions of Kazakhstan

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Abstract

Objective: To explore the prevalence of malignant tumors in the adult population through 2003-2014 in parts of the Aral Sea region: a zone of ecological disaster, a zone of ecological crisis and a zone of precritical conditions. **Methods:** The long-time average annual levels of cancer morbidity stratified by zones of the Aral Sea region and trends of long-time average annual incidence indicators of malignant tumors were identified. Leading cancer localizations in the adult population was established and associations between cancer incidence and environmental pollution were analyzed. In addition, associations between individual risk factors and cancer incidence in the adult population was established. Correlations between a hazard index and the cancer incidence in the adult population were calculated. **Results:** In all three Aral Sea regions, as well as in Zhanaarkinskii district, leading cancer in adult population was esophageal, stomach, tracheal, lung, hepatobiliary, and breast. Long-time average annual levels of cancer morbidity in adult population living in the Aral sea region is 1.5 times higher comparing to the control region. In particular, long-time average annual levels of cancer morbidity in adult population living in the zone of ecological disaster was 57.2% higher, in the zone of ecological crisis - 61.9% higher, and in the zone of precritical condition – 16.8% higher. Long-time average annual levels in the adult population of the Aral Sea region significantly exceeded control levels for brain and central nervous system cancer, cancer of bone and articular cartilage, and thyroid cancer. **Conclusion:** It has was established that the total cancer morbidity depended on the total hazard index associated with the inhalation of nickel and the combined cadmium intake (r=0.8).

Keywords: Cancer- prevalence- population of the Aral Sea region- adult population- environmental factors

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Introduction

Considering its consequences, the ecological crisis in the basin of Aral Sea is characterized as the biggest disaster covering the territories of five states of the Central Asia with nearly 50 million population. Environmental degradation caused by the Aral Sea shrinking led to extremely unfavorable living conditions for the population the region. Available scientific work conducted in the Aral Sea area is mainly devoted to ecological problems (Omirbaev et al., 2004; Slazhneva et al., 2007). Only few studied the prevalence of malignant neoplasm's in this region. Assessment of age-related features of the malignant neoplasms prevalence (Igissinov et al., 2011a; Igissinov et al., 2011b) in the Aral Sea region revealed that the average age of patients with esophageal cancer and lung cancer tended to increase due to age.

The issue of finding connections between impact of environmental factors and population health conditions, including the evaluation of ecological risk factors, is difficult but topical issue. The increasing pollution of air with emissions from industries and manufactures, of water and soil with heavy metals lead to increase of morbidity (Mamyrbayev et al., 2015; Mamyrbayev et al., 2016), including cancer morbidity. The studies held in Kazakhstan and Russia (Moore et al., 2010; Poirier, 2012) show high oncopathology incidence in industrially developed regions.

The objective of the research was to describe regional features of cancer morbidity among adults in Aral Sea region.

Materials and Methods

Shrinking of the Aral Sea and its influence on population health is a major problem for the Republic of Kazakhstan is an adverse impact on public health of the environmental disaster zone due to the. According to the

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Law of the Republic of Kazakhstan "On social protection of citizens affected by the environmental disaster in the Aral Sea region" three zones of ecological problem: 1 zone - ecological disaster, 2 zone - ecological crisis, 3 zone - precritical condition.

The datawas obtained from official reports on malignant neoplasms (Form 7) prepared by the regional oncology dispensaries. In addition, other statistical data were used (Form 7, 35, form 030-y, 025-y, 090-y) "Oncology service indicators of the Republic of Kazakhstan" and reports of regional oncology dispensaries "Analysis of annual statistical forms of oncology services".

Study population was living in three Aral Sea zones - disaster (Aral, Kazaly, and Shalkar districts), crisis (Zhalagash, Karmakshy, and Shiely districts), and zone in precritical condition (Irgiz, Arys, and Ulytau districts). Population from Zhanaarka district of Karaganda region was considered as a control group. Data were analyzed retrospectively for 10 years, from 2004 to 2013.

The main research method used was a retrospective study with descriptive and analytical methods of modern epidemiology. Extensive, crude, and age-adjusted morbidity indicators were calculated.

The impact of environmental pollution in the Aral Sea region on population health was evaluated by time series analysis. Time series is a sequence of observations ordered by time. Comparing with the analysis of random samples time-series analysis based on the assumption that the continuous data values are observed in an equal time intervals. Findings show regression relationship existed between the dependent variable - health indicator (variable Y (t)) and independent variables that describe the environment or living conditions (Xi (t)). Moreover, there is a connection between the two data sets tracked during similar time. As a time interval a year was chosen. Regular component of time series was the trend represented by the general systematic linear component that could be changed over time.

As a hypothesis, it has been assumed that the continuous variables in the database are observed in equal time intervals. Regression analysis of time series was conducted on the assumption that the variables are distributed normally or follow Poisson distribution. Dependency ofincidence on the level of environment contamination (air, soil, drinking water, open water reservoirs) was checked in the same year, the previous year (a single log) and two years (double lag), and multiple regression was applied. The consistency of the results and the normality of the error distribution was controlled.

Seasonal components of the time series were found using the correlogram which shows the autocorrelation function (ACF) both graphically and numerically, or the autocorrelation coefficients (and standard errors) for a sequence of lags of a certain range. Its reliability was determined in the range of two standard errors for each lag, and the power from the value of the autocorrelation.

Filtration procedures were carried out before application of the regression model. Both dependent and independent variables were filtered.

The study used computational procedures of mathematical statistics methods in the licensed integrated statistical package for the complex data processing – "Statistica-10".

Dependency of the cancer incidence among adult population from environmental factors (chemicals) was calculated using the module "Indepth analysis methods - Time series". The extent of the chemicals' impact on the incidence of the adult population was estimated at the level of the coefficient of determination –R^2, which can get a value from 0 to 1. The closer it is to 1, the higher is the degree of approximation to the reality.

In each settlement types of diseases were selected for the analysis by the relative riskcoefficient, ie the long-time annual average incidence rates that are significantly higher than the controls. The study also used commonly accepted methods of cancer risk assessment.

Results

Cancer incidence analysis was conducted in the adult population living in three Aral Sea zones – disaster (Aral, Kazaly, and Shalkar districts), crisis (Zhalagash, Karmakshy, and Shiely districts), and zone in precritical condition (Irgiz, Arys, and Ulytaudistricts) through 2004-2013. A control group was population from Zhanaarka district of Karaganda region and data for the Republic of Kazakhstan. Long-time annual average incidence ratesfor people living in different areas of the Aral Sea region are presented in Figure 1.

Cancer incidence of the adult population in the disaster and crisis zones of the Aral Sea region was significantly higher than in the control region and in the Republic of Kazakhstan. Long-time annual average level of the cancer incidence in the disaster zone is 205.4 per 100 thousand population, which is 57.2% higher than in the control region (130.7 per 100 thousand population). In the crisis zone cancer incidence is 211.6 per 100 thousand population, which is 61.9% higher than in the control region. In the zone of precritical condition cancer incidence is 152.7 per 100 thousand population, which is 16.8% higher comparing to control region but 18.8% lower than in Kazakhstan.

If to compare the malignant neoplasms morbidity rates in the Aral Sea region with the Western Kazakhstan, in particular with Atyrau region (with the developed oil and gas industry and possible environmental risks) in 2000-2008, where cancer incidence in 2000 was 148.5 per 100 thousand population and in 2008 - 134.1 per 100 thousand population, rates in all zones of the Aral Sea region were higher.

Dynamics of long-time annual average incidence of malignant neoplasms in the Aral Sea region (Figure 2) show a slight (9.4%) increase in the control area. In Kazakhstan cancer incidence in the adult population remained almost unchanged. In the disaster and crisis zones incidence of malignant neoplasms decreased by 3.4% and 3.9% over the period of observation. Incidence of malignant neoplasms increased by 27.8% in the precritical zone mainly due to the Arys and Ulytau districts, where the rate increased almost two-fold. The official statistical data on the trends of cancer incidence 2004 - 2013 is presented in Appendix A, Table 1.

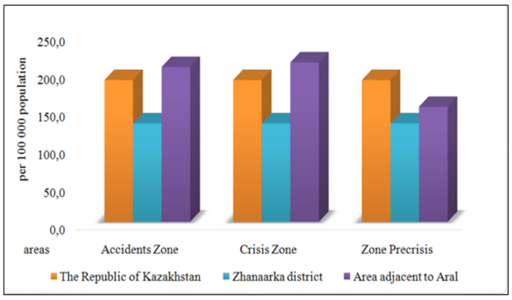

Figure 1. Long-Time Annual Average Incidence Rates by Zone of Aral Sea Region

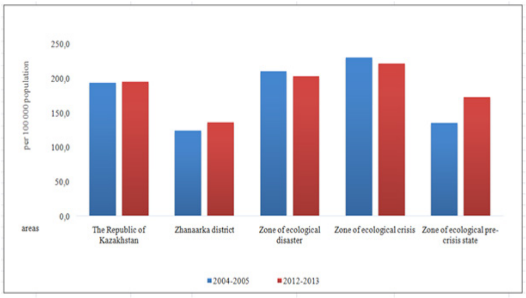

Figure 2. Long-Time Annual Average Malignant Neoplasms Incidence Trends in the Aral Sea Region

Long-time annual average cancer incidence rates in the Aral Sea region are shown in the Figure 3.

Long-time annual average incidence rates of malignant neoplasms in the disaster zone were higher comparing to the control region: the Aral district more than 1.7 times (225.8 per 100 thousand population, t = -10.0, p <0.001), Kazalinsk district 1.5 times higher (200.2 per 100 thousand population, t = -7.0, p <0.001), Shalkar district of Aktobe region 1.4 times higher (179.9 per 100 thousand population, t = -5.4, p <0.001). Long-time annual average cancer incidence rates in Kazakhstan was lower than in the studied areas, except Ulytau district.

Long-time annual average incidence rates of malignant neoplasms in the crisis zone were higher comparing to the control region: Zhalagash and Karmakshy districts 1.7 times (215.9 per 100 thousand population, t=-10.9, p<0.001 and 221.3 per 100 thousand population, t = -5.2, p <0.001 respectively), Shieli district 1.5 times (t = -8.0, p <0.001) comparing to Zhanaarka district (200.6 per 100 thousand population).

Table 1. Correlation between the Individual Cancer Risk and Incidence rate of Malignant Tumors in Adult Population Living in the Studied Areas of the Aral Sea Region

Localization of malignant tumor	Chemicals				
	Nickel CRi	Cadmium CRi	Cadmium CRo	Arsenic CRi	Arsenic CRo
Malignant tumors, including:	0,8*	0,7*	0,8*	0.5	-0.4
Lip	0.5	0.4	0.5	0.1	-0.4
Tongue, oral cavity and pharynx	0.6	0.4	0.6	0.4	-0.3
Esophageal	0,8*	0,7*	0,7*	0.5	-0.5
Stomach	0.3	0.2	0.2	0,7*	-0.1
Colon	0.3	0.4	0.3	-0.3	-0.1
Rectal, colorectal, anal	0.3	0.1	0.5	0.3	-0.1
Liver and intrahepatic bile ducts	0.6	0,6*	0.5	0.6	-0.3
Pancreatic	0	-0.2	-0.4	0.3	0.1
Laryngeal	-0.1	0	-0.1	0.4	-0.1
Tracheal, bronchial, lung	0.4	0.4	0,7*	0,7*	-0.1
Bone and articular cartilage	0,7*	0,6*	0.4	0.2	-0.6
Connective and other soft tissues	-0.1	-0.4	0.1	-0.1	0
melanoma, other skin neoplasms	0.3	0.2	-0.1	0.4	-0.1
Prostate	-0.3	-0.5	-0.4	0.2	0.1
Testicular	0.26	0.21	0.32	-0.22	-0.11
Female breast	0.51	0.2	0.26	-0.13	-0.3
Cervical	0.47	0.35	0.53	0.3	0.05
Uterine	0.36	0.07	0.01	0.2	-0.44
ovarian	0,69*	0.47	0.45	-0.02	-0.39
kidney	0,83*	0.7	0,78*	0.01	-0.61
Bladder	0.63	0.6	0.35	-0.02	-0,74*
Brain and central nervous system	0,80*	0,78*	0,70*	0.14	-0.56
thyroid	0.33	0.27	0.39	0,81*	-0.34
Lymphoid and hematopoietic	0.37	0.38	0.35	0.8	-0.21
Other malignant tumors	0,66*	0.54	0.42	0.33	-0,75*

*, marked correlation is significant at p<0.05; CRi, inhalation intake; CRo, peroral intake

Table 2. Correlation between the Hazard Index and Incidence Rate of Malignant Tumors in Adult Population Living in the Studied Areas of the Aral Sea Region

Localization of malignant tumor	Exposure route	
	Inhalation	Per oral
Malignant tumors, including:	0.4	0.4
Lip	0.76*	0.3
Tongue, oral cavity and pharynx	0.2	0.3
Esophageal	0.5	0.3
Stomach	0.0	-0.3
Colon	0.0	0.2
Rectal, colorectal, anal	-0.1	0.1
Liver and intrahepatic bile ducts	0.2	0.1
Pancreatic	-0.5	-0.5
Laryngeal	-0.2	0.1
Tracheal, bronchial, lung	0.3	0.4
Bone and articular cartilage	0.7*	0.0
Connective and other soft tissues	-0.1	0.4
melanoma, other skin neoplasms	-0.1	0.0
Prostate	-0.5	-0.1
Testicular	0.67*	0.2
Female breast	0.3	0.3
Cervical	-0.1	0.3
Uterine	0.3	0.3
ovarian	0.4	0.3
kidney	0.8*	0.4
Bladder	0.9*	0.5
Brain and central nervous system	0.8*	0.6
thyroid	0.4	0.1
Lymphoid and hematopoietic	0.3	0.2
Other malignant tumors	0.7*	0.4

*, marked correlation is significant at $p<0.05$

Long-time annual average incidence rates of malignant neoplasms in the precritical zone particularly in the Irgiz district was 1.5 times higher (202.2 per 100 thousand population) comparing to the control region, in Arys (153.3 per 100 thousand people) and Ulytau (102.6 per 100 thousand population) districts significant differences were not observed.

Analysis of the structure of oncological diseases allowed to rank the leading cancer sites in the control districts and in the three zones of the Aral Sea region. The official statistical data of leading malignancies localization, registered in the study area during 2004 - 2013 are presented in the Appendix A, Table 2.

In all three zones of the Aral Sea region, as well as in control Zhanaarka district, leading cancer localizations were esophageal; stomach; trachea, bronchus and lung; liver and intrahepatic bile ducts; breast. Data is presented in the Figure 4.

Analysis of correlation between cancer incidence in the adult population living in the Aral Sea region and environment pollution factors revealed a number of features listed below.

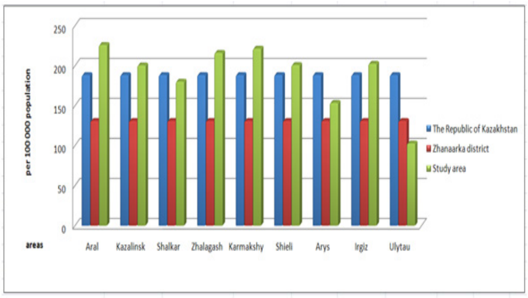

Figure 3. Long-Time Annual Average Cancer Incidence Rates in the Aral Sea Region

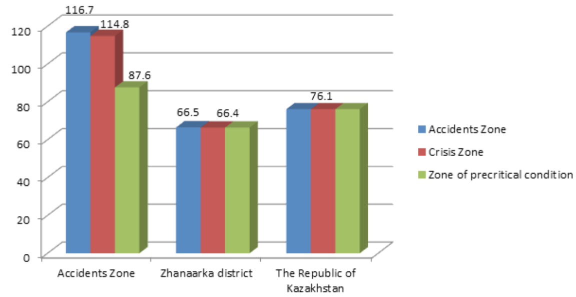

Figure 4. Long-TIme Annual Average Rates of Leading Cancer Sites in Adults (Stomach, Esophagus, Trachea, Bronchus, Lung, Liver and Bile Ducts, Breast)

It was found that the incidence rate of newly diagnosed malignancies in adults living in study districts of the Aral Sea region depends on the individual cancer risk associated with inhalation intake of nickel (r = 0.8), inhalation and per oral intake of cadmium (r = 0.7, r = 0.8, respectively). The data obtained in the rank correlations are presented in Tables 1 and 2.

Esophageal cancer was strongly correlated with the inhalation intake of nickel (r = 0.8), inhalation intake of cadmium (r = 0.7), the oral intake of cadmium (r = 0.7). Stomach cancer in adults living in the Aral Sea region correlated with the inhalation intake of arsenic (r = 0.7). The liver cancer is correlated with the inhalation intake of cadmium (r = 0.6).

Tracheal, bronchial and lung cancer is correlated with the oral intake of cadmium (r = 0.7) and inhalation intake of arsenic (r = 0.7).

Bone and articular cartilage or related with the inhalation intake of nickel (r = 0.8) and cadmium (r=0.6). Also, correlation of ovarian cancer in women with the inhalation intake of nickel (r = 0.7) was found. Kidney cancer correlated withthe inhalation intake of nickel (r = 0.8), inhalation intake of cadmium (r = 0.7), the oral intake of cadmium (r=0.8).

It was also found that cancer of brain and central nervous system is most strongly correlated with the inhalation intake of nickel (r = 0.8),inhalation intake of cadmium (r = 0.8), the oral intake of cadmium (r=0.7). Thyroid cancer and hemoblastoses correlated with the inhalation intake of arsenic (r=0.8 and r=0.8 respectively).

The hazard index associated with the inhalation intake of chemicals in the human bodyis correlated with bladder cancer (r = 0.9), lip cancer, kidney, brain and central nervous system (r = 0.8), bone and articular cartilage cancer (r = 0.7), testicular cancer in men (r = 0.6).

It was also found that the incidence rates of newly diagnosed malignant neoplasms among living in the Aral Sea region depende on the total hazard index associated with intake of nickel (r = 0.7), cadmium (r = 0.6), mercury (r = 0.8), nitrates (r = 0.7), selenium (r = 0.7).

Lip cancer depend on the total hazard index caused by intake of manganese (r = 0.7), nickel (r = 0.6), cobalt (r = 0.8), mercury and selenium (r = 0.7). Tongue cancer correlated with the total hazard index associated with mercury (r = 0.8), nitrates and selenium (r = 0.6).

Esophageal cancer depends on the total hazard index associated with intake of nickel, mercury (r = 0.8), cadmium, selenium, nitrates and phosphates (r = 0.7); inverse correlation was found with total hazard index associated with zinc (r = -0.8).

Tracheal, bronchial and lung cancer or related with the total hazard index, associated with intake of nitrates (r=0.6) and negatively correlated with the total hazard index, associated withplumbum (r=-0.7).

Bone and articular cartilage cancer correlated with the total hazard index, associated with nickel (r=0.7), chrome(r=0.6), mercury and selenium(r=0.8).

Testicular cancer in men correlated with the total hazard index, associated with cobalt (r = 0.7). It was found that breast cancer in women depend on the total hazard index associated with mercury (r = 0.6), ovarian cancer - with manganese (r = 0.6), chrome and selenium (r = 0.7), mercury (r = 0.8).

The strongest correlation with the total hazard index was found for kidney cancer: from nickel and selenium (r = 0.9), cobalt, manganese and mercury (r = 0.8), sulfates, phosphates, nitrates and cadmium (r = 0.7). Bladder cancer is also depend on the total hazard index, associated with manganese and cobalt (r = 0.8), nickel, cadmium, selenium, chrome and sulphates (r = 0.7).

Brain and central nervous system cancer correlated with the total hazard index, associated with intake of manganese and cobalt (r = 0.9), cadmium, mercury, selenium and nitrates (r = 0.8), nickel and chromium sulfate (r = 0.7).

Thus, analysis of rank correlation between the incidence of cancer in adults and environment pollution factors showed that the overall cancer incidence depended on the total index of hazard associated with the inhalation of nickel and combined intake of cadmium.

High rates of esophageal cancer was caused by inhalation of nickel, combined (inhaled and oral) intake of cadmium, as well as the total hazard index associated with mercury, selenium, nitrates and phosphates.

Cancer of the bone and articular cartilage on inhalation of nickel and cadmium, as well as the total hazard index associated with intake of copper, selenium, chromium and mercury.

In the occurrence of kidney cancer and bladder factors such as the inhalation of nickel and cadmium, the total index of hazard associated with manganese, cobalt, chromium, nickel, cadmium, selenium and sulfate played a major role.

Brain and central nervous system cancer depend on inhalation intake of nickel, cadmium combined intake and the total hazard index associated with manganese, nickel, cobalt, chromium, cadmium, selenium, sulfates and nitrates.

Discussion

Thus, epidemiological analysis of the frequency of Long-time annual average malignant neoplasms incidence trends showed that in all zones of the Aral Sea region (the disaster, crisis and precritical) cancer incidence in the adult population was significantly higher than in the control district. Long-time annual average cancer incidence rates among the adult population in the disaster zone of the Aral Sea region was 57.2% higher, in the crisis zone - 61.9%, and in precritical zone - 16.8% higher than in the control district.

Analysis of the trends in the cancer incidence showed that the overall rate of malignant tumors increased 1.4 times by the end of the observation period in comparison with 2004 in the control area. In almost all areas of the Aral Sea region, except Ulytau district, for the analyzed period cancer incidence rate was significantly higher than in the control area. In most of the studied districts it either did not change significantly, or tended to decrease by 15-30%. Only in Shalkar and Arys districts it increased up to 1.2-2.6 times, respectively by 2013. At the beginning of the analyzed period only in Ulytau district the rates were significantly lower. However, the increase of incidence among population by 2013 more than 4.6 times led to equalize its level with the control area.

It is proved that the correlations between individual cancer risk and malignancies incidence rate in the adult population in the studied districts of the Aral Sea region, as well as the correlations between the hazard index and the malignancies incidence rate in the adult population in the studied districts of the Aral Sea region depend on the presence of chemicals in the living environment.

Studies have shown that in all zones the Aral Sea region (the disaster, crisis and precritical) cancer incidence of the adult population was significantly higher than in the control district. Long-time annual average cancer incidence rates among the adult population in the disaster zone of the Aral Sea region was 57.2% was higher, in the crisis zone - 61.9%, in precritical zone - 16.8% higher than in the control district.

Analysis of the trends in the cancer incidence showed that the overall rate of malignant tumors increased 1.4 times by the end of the observation period in comparison with 2004 in the control area. In almost all areas of the Aral Sea region, except Ulytau district, for the analyzed period cancer incidence rate was significantly higher than in the control area. In most of the studied districts it either did not change significantly, or tended to decrease by 15-30%. Only in Shalkar and Arys districts it increased up to 1.2-2.6 times, respectively by 2013. At the beginning of the analyzed period only in Ulytau district the rates were significantly lower. However, the increase of incidence among population by 2013 more than 4.6 times led to equalize its level with the control area.

Analysis of the structure of cancer allowed to rank the leading cancer sites in the control area, as well as in the three zones of the Aral Sea region. In all three zones the Aral Sea region as that in control Zhanaarka district leading cancer localizations were esophageal, stomach, trachea, bronchus and lung, liver and intrahepatic duct cancer, breast. Esophageal cancer in all zones of the Aral Sea region was among the first in the structure of cancer pathology. It was diagnosed 3.3 times more often in the disaster zone than in the control, 3.2 times more often in the zone of crisis, by 1.9 times in precritical zone. Cancer the stomach in the area of the disaster was 40%, in the zone of crisis - 32.3%, in precritical zone - 22.4% higher than in Zhanaarka district. Lung cancer in the disaster zone exceeded control 1.5 times, the crisis zone–1.6 times, in precritical zone - was almost the control level. Liver cancer was 2 times more often in a disaster zone, 1.9 times in the crisis zone, 1.8 times in precritical zone comparing with the control. Breast cancer in the disaster zone did not exceed the reference level, but in the crisis zone it was diagnosed 1.4 times more frequently than in the control zone, in precritical zone this number was lower than in the control.

Attention was drawn to the excess of the long-time annual average cancer incidence rates, which was not included in leading pathology. For example, brain and central nervous system cancer in the adult population living in the disaster area was 7.5 times higher than in control, in the crisis zone - 10.1 times, precritical zone - 4.1 times. Cancer of bone and articular cartilage of the population living in the disaster zone, was diagnosed more often than in the control up to 6.8 times, in the area of crisis - 10 times, precritical zone - 4.2 times.

In our opinion this is due to excess levels of heavy metals in the environment, particularly of cadmium. The frequency of thyroid cancer exceeded the control in a disaster zone - 4.3 times, in the crisis zone - 3.4 times, in precritical zone - 2.2 times. This localization of cancer relates to the hormone-dependent forms of cancer that can occur under the influence of persistent organic pollutants (POPs) in the food in the crisis zone and in environment, which is not excluded in the Aral Sea region in connection with the use of pesticides in the cultivation of agricultural products. In the Aral Sea region bladder cancer diagnosed 2.6 times in the crisis zone more often than in the control and 2.4 times more often in the disaster zone.

Long-time annual average lip cancer incidence rates in the disaster zone was 2.5 times higher, in the crisis zone – 5.5 times higher, and in precritical zone – 1.3 times higher comparing with control district. It is known that lip cancer predisposing risk factors are lasting influence of adverse weather factors: solar radiation, wind, sharp temperature fluctuations, exposure to ionization. The results may indicate the presence of predisposing factors in residents of the Aral Sea region, as evidenced by the excess incidence of lip cancer comparing with the control district. Tongue, mouth and throat cancer happened 1.6 times more often in the disaster zone and 1.3 times - in the crisis area comparing with the control district. In the precritical zone the indicator did not exceed the reference level. Melanoma was diagnosed 18-25% more often in districts of the Aral Sea region than in the control district.

As known, the degree of expression of many risk factors is influenced by the local characteristics of the living conditions and way of life (Moore et al, 2009; Moore et al, 2010; Crouse, 2010; Magomedov, 2011). The complex of factors affecting the population determines the age patterns and sustainable structural relations of various cancer types. At the same time, the changing conditions of population existence and behavior patterns determine the development trends of cancer epidemiological processes, since morbidity and mortality trends are delayed (Cambra, 2011; Ibeanu et al. 2013; Aykan et al, 2015). Naturally, unfavorable environmental conditions and exposure to chemicals (Künzli et al., 2013; Sakiev et al., 2016) lead to the growth of not only the overall morbidity, but also tumors incidence. Chemical pollutants with long-term effects lead to the growth of malignant tumors among the urban and rural population (Meek et al, 2011, Laumbach et al., 2012; Demetriou et al., 2012; Johannson et al., 2015). Our own studies have shown that chromium, bromium and other chemicals have a direct impact on health (Bekmukhambetov et al, 2015a; Bekmukhambetov et al, 2015b) of population living in Aktobe region, where the southern districts are part of the zone of crisis of the Aral Sea region.

Our studies showed that the leading localization of cancer is the digestive system. This was followed by the diseases of the sexual, respiratory, nervous, endocrine, and hematopoietic systems. Furthermore, most study areas had high levels of diseases of skin, nervous system, haematopoietic and lymphoid tissues over the analyzed period. These data indicate a distinct effect of changes in climatic, physical, chemical, and social living conditions of population. The main reason for these changes is the environmental disaster that occurred as a result of human-induced reduction of water flow and shrinking of the Aral Sea. Undertaken measures to improve the Kazakh part of the Aral Sea bring some positive results in improving the living conditions and population health. However, they are not sufficient.

In the zones of ecological tension considered indicators were lower in the precritical zone and higher in disaster and crisis zones. Although data on the crisis zone are slightly higher than in the disaster zone for age groups 15-44 and 80 and elder.

The analysis of correlation between the cancer incidence and environment pollution showed that the incidence rate depend on individual carcinogenic risk associated with inhalation intake of nickel ($r = 0.8$), inhalation and oral intake of cadmium ($r = 0.7$ and $r=0.8$ respectively).It was also found that the incidence rate of malignant neoplasms in the AralSea region depend on the total hazard index associated with intake of nickel ($r = 0.7$), cadmium ($r = 0.6$), mercury ($r = 0.8$), nitrates ($r = 0.7$), selenium ($r = 0.7$).

Epidemiological research aimed at identification and measurement of the association between exposure to carcinogens and cancer risk takes the leading role in the risk assessment of harmful factorson population health. Availability of reliable epidemiological data allows to create an adequate risk models to make predictions and to develop targeted programs for the prevention of cancer.

Thus, analysis of rank correlation between the incidence of cancer in adults and environment pollution factors showed that the overall cancer incidence depended on the total index of hazard associated with the inhalation of nickel and combined intake of cadmium. High rates of esophageal cancer was caused by inhalation of nickel, combined (inhaled and oral) intake of cadmium, as well as the total hazard index associated with mercury, selenium, nitrates and phosphates.Cancer of the bone and articular cartilage on inhalation of nickel and cadmium, as well as the total hazard index associated with intake of copper, selenium, chromium and mercury.In the occurrence of kidney cancer and bladder factors such as the inhalation of nickel and cadmium, the total index of hazard associated with manganese, cobalt, chromium, nickel, cadmium, selenium and sulfate played a major role. Brain and central nervous system cancer depend on inhalation intake of nickel, cadmium combined intake and the total hazard index associated with manganese, nickel, cobalt, chromium, cadmium, selenium, sulfates and nitrates.

1. Long-time annual average cancer incidence rates among the adult populationin the Aral Sea region was 1.5 times higher than in the control area. In particular, long-time annual average cancer incidence rates among the adult population in the disaster zone of the Aral Sea region was 57.2% higher, in the crisis zone - 61.9%, and in precritical zone - 16.8% higher than in the control district.

2. In all three zones of the Aral Sea region, as well as in control Zhanaarka district, leading cancer localizations were esophageal; stomach; trachea, bronchus and lung; liver and intrahepatic bile ducts; breast.

3. Long-time average annual levels in the adult population of the Aral Sea region significantly exceded for brain and central nervous system cancer, cancer of bone and articular cartilage, thyroid cancer.

4. Overall cancer incidence depended on the total index of hazard associated with the inhalation of nickel and combined intake of cadmium (r=0.8).

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