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

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 neoplasms 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
The study used computational procedures 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 risk coefficient, 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 Shely 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 of incidence 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”.

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 data was 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-й, 025-й, 090-й) “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 Shely 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.
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The long-time annual average cancer incidence rates in the studied areas were higher compared 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 Aral Sea region are shown in the Figure 3.

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 | 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 tumors | 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
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.

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 \( r = 0.0 \). Also, correlation of ovarian cancer in women with the inhalation intake of nickel \( r = 0.7 \) was found. Kidney cancer correlated with the inhalation intake of nickel \( r = 0.8 \), inhalation intake of cadmium \( r = 0.7 \), the oral intake of cadmium \( r = 0.6 \).

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 \( r = 0.7 \)

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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 body is correlated with bladder cancer \( r = 0.9 \), lip cancer, kidney, brain and central nervous system \( r = 0.8 \), bone and articular cartilage

| 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 \( p<0.05 \)
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 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 \((r = 0.7)\).

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 with plumbum \((r = -0.7)\).

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 depend 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 of 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. 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 Aral Sea 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 factor on 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 the 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 Zhaanarka 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 exceeded 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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