

## RESEARCH COMMUNICATION

# Epidemiological Evaluation of Breast Cancer in Ecological areas of Kazakhstan - Association with Pollution Emissions

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### Abstract

The aim of the research was to evaluate the incidence of breast cancer in the ecological areas of Kazakhstan and assess the potential. A retrospective study of 11 years (1999 to 2009) was conducted using descriptive and analytical methods. The incidence of breast cancer was the lowest in the Aral-Syr Darya area ( $18.6 \pm 0.80/100,000$ ), and highest in the Irtysh area ( $48.9 \pm 1.90/100,000$ ), with an increasing trends over time in almost all areas. A direct strong correlation between the degree of contamination with high pollution emissions in the atmosphere from stationary sources and the incidence of breast cancer ( $r=0.77 \pm 0.15$ ;  $p=0.026$ ). The results indicate an increasing importance of breast cancer in Kazakhstan and an etiological role for environmental pollution.

**Keywords:** Breast cancer - incidence data - time trends - geographical variation - pollution - Kazakhstan

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### Introduction

Most of the earlier conducted epidemiological studies were directed at identifying the links between cancer and a wide range of population characteristics such as socio-economic characteristics and living habits, including in Asian countries (Sisikov and Vyprintsev, 1988; Katz et al., 2000, Robert et al., 2004; Moore and Sobue, 2010). However, within these categories, it was possible to identify some specific etiological factors, so it is now possible to put forward some hypotheses that can be tested in various studies to identify their role in the epidemiological distribution of various malignant tumors, including breast cancer.

Breast cancer is prevalent in North America, Australia, Western and Northern Europe. The lowest incidence of breast cancer in countries of Asia and Africa, and Latin America, Eastern and Southern European countries occupy an intermediate position. In most countries there is an increased incidence of breast cancer, the most pronounced growth among the population with initially low rates of morbidity, such as in Japan and other countries in Southeast Asia. Breast cancer is one of the most common diseases in developed countries but also in Central Asia (Zaridze and Yakovlev, 1989; Igissinov et al., 2002; Parkin et al., 2005; Davydov and Aksel, 2007; American Cancer Society, 2009; Moore et al., 2009; 2010; Ferlay et al., 2010; Igissinov et al., 2010; 2011; MEPs against cancer, 2011; WHO, 2011).

Geographical differences in incidence have helped to discover the role of different etiological factors in the

pathogenesis of disease, also in Central Asia (Moore et al., 2009; 2010; Moore and Sobue, 2010). During the period from birth to 80 years of age every ninth inhabitant of North America has breast cancer disease. Inhabitants of Asia are taken ill of the disease 5-10 times less than residents of North America and Western Europe. At the same time, women living in Asia, characterized by significantly lower levels of estrogen and progesterone. These differences cannot be explained by genetic factors, because the risk of breast cancer among the natives of Asia, living in developed countries, the same as that of the indigenous people of the same countries. But the natives of Asia, living in developed countries differ significantly from the residents of Asia on height and weight - indicators, from which depend heavily on the age of menarche, and estrogen levels in the blood (Bala et al., 2001; Moore and Sobue, 2010; Liao et al., 2011). Dietary factors are therefore clearly of importance. In addition, environmental conditions, including contamination levels may be important, as evidenced by clustering of disease (Lorenzo-Luaces Alvarez et al., 2009; Luginaah et al., 2012).

In various parts of the world, including a large country like Kazakhstan, the incidence of breast cancer varies with the locality. Existing risk factors may be both cultural and environmental, and in this regard, Kazakhstan has a complex ecosystem, in particular being characterized by significant climatic and geographical features of high-altitude zones (lowland, foothill and mountain areas), as well as northern, central and southern regions, which have fundamental differences in natural and anthropogenic

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environmental factors: temperature, partial pressure of oxygen, solar radiation intensity, type and intensity of economic activity of population, lifestyle, ethnicity, social factors.

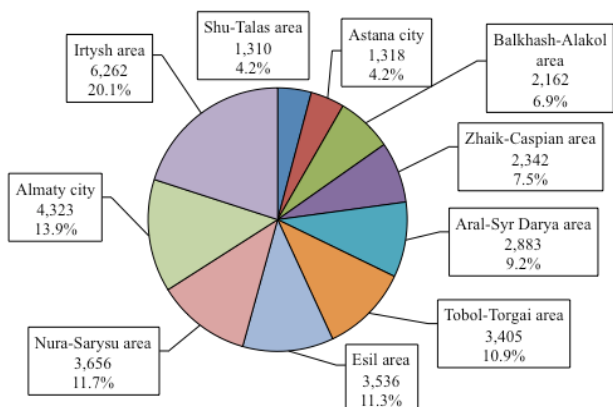
Studies in incidence in general of malignant neoplasms in ecological zones of Kazakhstan showed that the regions with low rates (up to 160.90/0000) Shu-Talas (106.1±1.8), Balkhash-Alakol (135.3±3.0) and the Aral-Syr Darya (153.8±3.5) zones. Averages (from 160.9 to 219.80/0000) identified Zhaik-Caspian (166.0±3.4) and the Tobol-Torgai (207.5±2.6) zones. Regions with high rates (over 219.80/0000) were Nur-Sarysu (239.7±3.4), Esil (240.8±3.3) and Irtysh (273.9±3.4) areas (Igissinov et al., 2011).

In Kazakhstan, eco-epidemiological studies of breast cancer have hitherto not been conducted. Spatial assessment of the incidence of female population with breast cancer in different climatic regions is one of the most important aspects that help analyze the propagation of disease, i.e., to establish the effect of various medical and social conditions and environmental factors. In this epidemiological assessment was made taking into account the division of the republic to the environmental area. In Kazakhstan, eight ecological zones are distinguished: the Aral-Syr Darya, Balkhash-Alakol, Esil, Zhaik-Caspian, Irtysh, Nur-Sarysu, Tobol-Torgai and Shu-Talas zone.

**Materials and Methods**

The sources of the study was compiled from the Cancer Registry of the Kazakh Research Institute of Oncology and Radiology about the patients who had established the first time in their life with breast cancer. The study period was 11 years (1999-2009). Data on the female population of the Agency of the Republic of Kazakhstan from 1999 to 2009 (Demography Yearbook of Kazakhstan regions, 2007, 2010). By conventional methods of biomedical statistics (Sepetliev, 1968) were calculated. Review and processing of the material performed by computer-program package of Microsoft Office 2010 (Excel, Word); BIOSTAT (Version 4.03 by Stanton Glantz).

Data on the pollution emissions were also obtained from Demography Yearbook of Kazakhstan regions, 2007, 2010.



**Figure 1. Distribution of Breast Cancer Patients in Kazakhstan among Ecological Zones for 1999-2009**

**Results**

In Kazakhstan, over the studied period, there were 31,197 new cases of breast cancer. The distribution of breast cancer patients by ecological zones showed that the lowest index of an extensive indicator was registered in Shu-Talas area 2.1% (1,310 patients), and the highest proportion was found in the Irtysh area – 20.1% (6,262 patients) (Figure 1). In the major cities over the study period, there were 5,641 cases of breast cancer patients. (18.1% of all cancers).

The average age of patients with breast cancer was the «youngest» in the Aral-Syr Darya district – 53.2 ± 0.3 years (95% CI = 52.7-53.7 years) and was significantly lower (p <0.05) compared to other ecological zones. The highest average age was established in the Irtysh area – 57.8±0.3 years (95% CI=57.2-58.3 years). Analysis of the 95% CI, middle age has shown that rates in the Aral-Syr Darya, Balkhash-Alakol Zhaik and Caspian were significantly lower (p <0.05) than in the Tobol-Torgai, Esil, Nur-Sarysu and Irtysh ecological zones of the country. The difference in the average age of patients is clearly related to the ethnic composition of the population of the ecozones and the contingent of patients, as we wrote above in the analysis of ethnic and age characteristics of breast cancer morbidity in Kazakhstan (Igissinov et al., 2010).

In the dynamics the most pronounced trends to growth were observed in Tobol-Torgai. Aral-Syr Darya and Esil zones (see Table 1).

Next, we consider the incidence of breast cancer in the ecological zones of the republic with age-related characteristics and emissions in air of pollutants from stationary sources (per capita in kilograms) (see Table 2). With growth of emissions per capita in the zones increased and incidence of breast cancer among women 30-39 years old in these ecozones. Thus, detected a direct strong correlation  $r=+0.74\pm0.16$  ( $t=2.677$ ,  $p=0.036$ ). In those aged 40-49 years, a direct moderate correlation  $r=+0.69\pm0.19$  ( $t=2.329$ ,  $p=0.058$ ) was established with pollution. In the 50-59 years clearly higher rates were evident in the Irtysh zone, Esil and Nura-Sarysu. Basically these also demonstrated highest rates in all the older groups.

In 60-69 years pollution in the ecological zones also increased the incidence in this age group –  $r=+0.83\pm0.11$  ( $t=3.627$ ,  $p=0.011$ ). Correlation coefficient was much more significant in comparison with other groups. In age group 70 years and older also was established strong direct

**Table 1. Average Annual Change in Incidence Rates of Breast Cancer by Region in Kazakhstan (1999-2008)**

Ecological Zone	Incidence %		T %
	M±m	95% CI	
Shu-Talas	2.68±0.12	2.45-2.91	+0.2
Aral-Syr Darya	2.46±0.08	2.30-2.63	+2.6
Balkhash-Alakol	2.59±0.19	2.21-2.96	-0.6
Esil	3.73±0.14	3.45-4.01	+2.6
Zhaik-Caspian	3.19±0.10	2.99-3.39	+1.9
Tobol-Torgai	3.41±0.13	3.16-3.65	+3.2
Irtysh	4.21±0.14	3.94-4.48	+2.6
Nura-Sarysu	4.16±0.12	3.92-4.39	+1.5

**Table 2. Average Annual Incidence Rates of Breast Cancer by Age and Region in Kazakhstan (1999-2008)**

Ecological Zone	Emissions per capita, kg	Incidence (M±m)/100,000						All
		<30	30-39	40-49	50-59	60-69	≥70	
Shu-Talas	17.4	0.20±0.08	13.5±1.6	53.0±3.5	83.4±6.3	72.9±4.4	76.4±7.6	23.2±1.1
Aral-Syr Darya	34.4	0.60±0.05	14.5±0.8	51.8±2.5	68.7±4.1	70.2±3.9	71.6±5.5	18.6±0.8
Balkhash-Alakol	41.4	0.61±0.11	15.3±1.5	51.5±4.4	78.9±6.6	74.3±8.0	64.4±4.8	24.3±1.7
Esil	84.0	0.78±0.17	17.8±2.0	73.5±5.1	113.2±5.0	112.5±6.2	107.1±6.9	43.1±1.9
Zhaik-Caspian	164.8	0.59±0.15	16.7±1.0	62.0±2.9	93.4±3.9	95.0±4.7	93.1±6.8	29.0±1.0
Tobol-Torgai	169.7	0.80±0.12	17.1±1.1	66.9±1.2	97.7±4.6	102.7±6.1	104.8±7.5	36.9±1.7
Irtys	416.7	0.67±0.17	21.7±1.0	74.7±2.0	123.2±5.9	133.8±8.3	136.8±4.2	48.9±1.9
Nura-Sarysu	885.0	0.62±0.15	19.8±1.6	75.1±2.6	116.2±4.8	139.0±5.8	121.1±4.3	46.6±1.4

correlation  $r=+0.71\pm 0.18$  ( $t=2.451$ ,  $p=0.049$ ) between pollution factor and incidence of breast cancer.

## Discussion

The present study identified clear differences in regional features of distribution of breast cancer in the territories of Kazakhstan, in line with earlier findings in Central Asia for breast (Igissinov et al., 2010), oesophagus (Igissinov et al., 2011a), cervix (Igissinov et al., 2012) and other cancers (Igissinov and Umaralieva, 2008; Igissinov et al., 2011b). The observed variation clearly points to differences in exposure to risk factors. Most importantly however, there appears to be a significant trend for increase, independent of the area. This appears to be the case for all of Asia, whether it be the North-west and Central (Moore et al., 2010a), South-West (Salim et al., 2010); Southern (Moore et al., 2010b); South-Eastern (Moore et al., 2010c; 2010d), Pacific (Moore et al., 2010e) or North-Eastern (Long et al., 2010) regions.

One possibility is that ethnic differences may be present, as indicated in earlier research in Kyrgyzstan and Kazakhstan (Igissinov, 2004; Igissinov et al., 2010). Racial disparities are well established in the United States (Keller et al., 2011) and in Australia (Roder and Currow, 2009). This area clearly warrants further attention. Similarly, the effects of altitude need to be taken into account (Igissinov et al., 2002).

Smoking may be of importance, including second hand or side-stream smoke (Luo et al., 2011) although findings have been inconclusive and possibly modified by genotype (Anderson et al., 2012). An ecologic analysis in North America revealed that the prevalence of rules prohibiting home and workplace smoking correlates with state-specific breast cancer outcomes (Piazza and Hyland, 2011).

Of greater interest, in light of the present finding of a correlation between breast cancer incidence and emissions, is the possibility of air pollution as an aetiological factor. In the US a higher incidence rate of breast cancer was found in high emission regions and metropolitan areas (Wei et al., 2012). Because both the time trend and geographic pattern of motor vehicles as a major source of NOx emissions are associated with breast cancer incidence rates, it has been stressed that further studies on the relationship between breast cancer and air pollution are needed (Chen and Bina, 2012). In Canada, evidence of an association between the incidence of postmenopausal breast cancer and exposure to ambient concentrations of NO2 has been presented

(Crouse et al., 2010). Women living close to incinerators may be at increased risk (Ranzi et al., 2011) and a positive association has been reported with metal-processing and energy-producing plants in Spain (Cambra et al., 2011). The probability of adverse effects from exposure to dioxin has also been stressed (Argo, 2010). Aromatic and heterocyclic amines have also been a focus of attention although in this case complex mixtures might be expected to be involved (Rabstein et al., 2010). Lastly, household cleaning and pesticide products may contribute to breast cancer, possibly through included endocrine disrupting chemicals or mammary gland carcinogens (Zota et al., 2010).

In conclusion, the present study provided clear evidence that breast cancer is increasing in Kazakhstan, while demonstrating great variation across ecological regions, with a strong correlation with air emissions suggestive of an aetiological role. Further research to clarify this and other underlying risk factors is a high priority.

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