RESEARCH ARTICLE

Trends in Breast Cancer Epidemiology in Chelyabinsk Region, 2006-2015

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Abstract

Breast cancer among women occupies a leading position in the profile of cancer incidence in most parts of the world. The present study of the incidence and prevalence of breast cancer was carried out using data from the Chelyabinsk population cancer registry for 2006-2015. A stable growth trend in the incidence over time was noted overall, as well as major differences in the figures for women of different ethnicities (Russian, Tatar, Bashkir), by far the highest incidences being observed for Russian women. Urban rates were generally higher than in rural sites and a shift towards older age at presentation was seen between 2006 and 2015. At the same time a slight decrease in mortality was noted, from 42.4% to 33.5% relative to incidence, with a decrease in the proportion of stage IV cancers. This might have been related to increasing use of mammography screening.The data have obvious connotations for primary prevention and particularly for measures adopted for secondary prevention in detection of the disease in its early stages, facilitating reduction in associated mortality. Improvement in screening rates is thus a high priority for more effective management of breast cancer in the region.

Keywords: Breast cancer - incidence - trends - age dependence - ethnic variation - Chelyabinsk

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Introduction

Breast cancer is of great importance throughout Europe, generally being the most prevalent cancer in females, as evidenced by data from GLOBOCAN (Ferlay et al., 2015) and recent issues of Cancer Incidence in Five Continents (Parkin et al., 2002; Curado et al., 2007; Forman et al, 2014). Generally speaking, continuing increase in rates has been observed, although in the most developed countries of the world a recent slow down has been noted with even negative change evident in North American whites.

For the country members of the former Soviet Union the situation is equivocal. While it is clear that breast cancer is the commonest cancer in females, whether in data published by IARC or by specific research groups, there is considerable variation. While findings in Cancer Incidences in Five Continents 8, 9 and 10 demonstrated increases from 33.0 to 41.0/100,000 over ten years in Belarus, 41.5 to 48.9 in Estonia, 39.4 to 48.4 in Latvia and 37.7 to 46.4 in Lithuania, the St Petersburg registry showed only a very slight increment from 46.1 to 47.4 . In neighbouring Kazakhstan also, the incidence rate has been found to be increasing over time (Bilyalova et al., 2011; Igissinov et al., 2011; 2012; Beysebayev et al., 2015).

Since only limited data for time trends are available for the Russian Federation (Starinsky et al., 2005; Poddubnaya et al., 2007; Kutikhin et al., 2012 ; Dudarev et al., 2013) the present study using data from the population-based cancer registry of Chelyabinsk region was conducted, focusing on both incidence and survival. According to the Local Agency of Federal State Statistics Service of the Chelyabinsk region in 2015, the death rate from cancer in the Chelyabinsk Region II is second only to that from cardiovascular disease. Given reports of higher rates in Russians than Turkic inhabitants, for example in Kyrgyzstan (Igisinov et al., 2004; 2005), particular attention was here given to Tatar and Bashkir, in comparison with Russian, ethnic populations, as well as to variation between urban and rural sites, the latter often having lower rates (Dey et al., 2010). The numbers of other minor groups, like Ukrainians and Kazaks, were too low for effective inclusion in this analysis. The time period from 2006-2015 was selected to allow tracking of changes in indicators with standardized registration practices throughout.

Given the well established finding of younger age at presentation for Asians as compared to Caucasians (Moore and Sobue, 2010) another focus was on the age distribution. Since breast cancer screening could have a major influence on both incidence, because of lead time bias, as well as age at diagnosis and outcome in terms of survival (Beckman et al., 2014), recent screening rates were also taken into consideration, with attention to the

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Table 1. Dynamics of Incidence and Mortality Data for Chelyabinsk Females with Breast Cancer (C50) 2006-2015

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Crude incidence rate	67.8	73.9	75.7	75.9	80.6	82.5	79.9	78.5	88.1	93.9
Standardized incidence rate	42.7	46.2	46.2	45.8	48.4	47.0	46.8	46.1	50.1	54.2
Crude mortality rate	31.9	31.9	29.2	30.5	31.2	32.0	32.6	33.1	33.2	31.3
Standardized mortality rate	18.1	17.7	16.4	16.7	17.6	17.2	16.8	16.5	16.8	16.0

Table 2. Incidences of Female Breast Cancer, Depending on Ethnicity and Residence (Urban and Rural), 2006-2015

Ethnicity %			2006		2007		2008		2009		2010		2011		2012		2013		2014		2015	
			No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
Russian	81.4	Urban	1017	77.7	1067	81.5	1090	83.2	1106	84.5	1188	90.7	1141	87.1	1145	87.4	1126	86.0	1275	97.4	1306	99.7
		Rural	144	60.6	162	68.1	163	68.6	160	67.3	177	74.4	161	67.7	186	78.2	166	69.8	172	72.3	249	104.7
Tartar	5.2	Urban	46	59.2	60	77.2	72	92.6	50	64.3	27	34.7	42	54.0	36	46.3	50	64.3	47	60.5	37	47.6
		Rural	12	57.9	21	101.3	21	101.3	21	101.3	11	53.0	15	72.3	20	96.4	9	43.4	14	67.5	9	43.4
Bashkir	4.7	Urban	11	22.6	9	18.5	15	30.9	7	14.4	10	20.6	6	12.3	12	24.7	5	10.3	19	39.1	12	24.7
		Rural	5	13.0	9	23.4	7	18.2	7	18.2	8	20.8	12	31.3	7	18.2	6	15.6	10	26.1	11	28.7

Rate per 100,000 population

Table 3. Statistics on Breast Cancer Characteristics in 2006-2015

Variable	Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Case Numbers		1209	1321	1350	1346	1394	1369	1404	1366	1544	1612
Stage											
I-II		61.4	60.7	61.3	57.9	63.7	63.5	61.9	60.7	63.2	67.0
III		25.7	27.9	27.8	29.9	26.5	27.7	28.6	29.9	27.8	26.0
IV		12.7	11.1	10.7	12.0	9.6	8.5	9.3	9.3	8.5	6.6
Unknown		0.2	0.3	0.2	0.1	0.1	0.2	0.1	0.1	0.7	0.3
Morphological confirm %		95.7	95.8	96.2	96.3	96.4	95.3	96.0	95.6	96.8	97.1
One-year mortality %		10.9	13.8	11.4	9.8	10.0	9.5	9.9	7.5	7.5	8.3
Five-year survival %		55.0	54.0	56.0	57.1	55.8	57.7	58.5	58.1	59.7	56.8
Active detection %		27.5	31.6	32.6	31.9	33.8	29.7	41.0	45.8	50.6	55.8
Treatment:											
Surgery only %		16.0	18.7	24.5	17.7	19.1	23.7	23.1	25.1	23.5	27.2
Combined %		84.0	80.6	74.6	80.6	78.6	75.8	76.9	74.9	76.5	72.8

stage distribution of the breast cancers diagnosed.

The aim was to provide a first detailed appraisal of the situation with regard to breast cancer incidence and mortality in the Chelyabinsk region.

Materials and Methods

The subjects for this study were females diagnosed with a malignant neoplasm of the breast for the first time in their lives, residing in the territory of the Chelyabinsk region in the period from 2006 to 2015. All information about the female population morbidity and mortality from malignant neoplasms were verified and analyzed on the basis of the organizational-methodological department "Chelyabinsk Regional Clinical Oncology Center". In addition to age and ethnicity, data on tumour stage, morphological confirmation, treatment and outcome interms of one year mortality and five year survival were obtained by active follow-up. This information is routinely entered into the population register of cancer of the Chelyabinsk region. For the calculation of standardized indicators the basic standard age distribution of the population, adopted by the World Health Organization, was applied.

Since 2010, a set of measures for secondary prevention through breast examination of women over 20 years of age visiting clinics, as well as population-based mammography screening of the female population over 40 years for the purpose of early detection of breast cancer, have been introduced.

All information on the results of these activities were accumulated and analyzed in the Organizational and Methodical Department of Chelyabinsk Regional Clinical Oncology Center.

Results

Malignant cancer of the breast in females of the Chelyabinsk region occupied the leading position in 2015 accounting for 23.4% of the total neoplasms in women. Analysis of the incidence of cancer of breast in the Chelyabinsk region in the period from 2006 to 2015 showed a statistically significant increase in the standardized rate from 42.7 to 54.2 per 100,000 population ($p < 0.05$) (see Table 1). During the same period a decrease in mortality was noted (18.1 to 16.0/100.000, relative to incidence this reduction from 42.4% to 29.5% was more marked).

Regarding the three major ethnic groups, incidence rates were highest in the Russians, followed by the Tatars and Bashkiris, only the former demonstrating a clear increase over time (see Table 2 and Figure 1). Similarly, only the Russian group exhibited consistent differences between urban and rural populations, except in the year

Table 4. Dynamics of Screening Coverage for the Chelyabinsk Female Population over 40 Years Old

	2010	2011	2012	2013	2014	2015
Population >40 years	810,004	843,492	843,504	804,874	827,399	948,011
No. of women subjects	277,124	164,000	164,000	173,000	173,000	444,595
No. screened	79168	110765	119747	158479	168996	225994
% Implementation	28.6%	67.5%	73.0%	91.6%	97.7%	50.8%
Number of mammogram machines	55	55	55	58	58	64
*Load	1439.4	2013.9	2177.2	2732.4	2913.7	3531.2
No of cancers confirmed	265 (100)	740 (100)	603 (100)	520 (100)	390 (100)	471 (100)
Stage I	29 (9.5)	138 (18.6)	98 (16.3)	118 (12.3)	116 (29.7)	137 (29.1)
Stage II	141 (53.2)	360 (48.6)	297 (49.3)	239 (46.0)	179 (45.9)	210 (44.6)
Stage III	67 (25.3)	189 (25.5)	166 (27.5)	144 (27.7)	79 (20.3)	112 (23.8)
Stage IV	14 (5.3)	53 (7.2)	42 (7.0)	19 (3.6)	16 (4.1)	12 (2.5)
Unknown	14 (5.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Screening Effectiveness	0.33%	0.67%	0.50%	0.33%	0.23%	0.21%

*Mammography work in 2 shifts at 12 women a day, 250 days = 6000 women studied

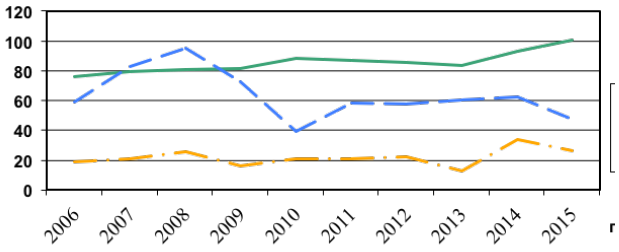

Figure 1. Ethnic Distribution of Breast Cancer Cases Over Time

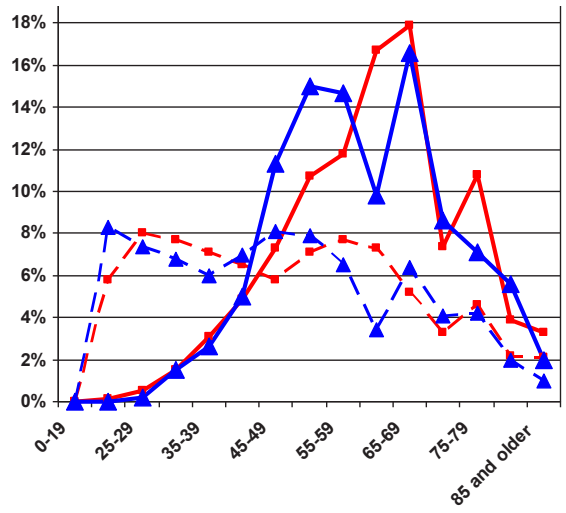

Figure 2. Age Distribution of Breast Cancer and General Female Populations. Solid lines, cases; dotted lines, general population; grey, 2006; red 2015

2015 (see Table 2).

Taking into account the present demographic situation in the region, characterized by a gradual aging of the female population and the uneven distribution of women in the age structure, there is a shift from the peak incidence age group 55-59 years in the older age groups. By 2015, the peak incidence (Figure 2) was recorded in the age group 50-70 years in 2006 and 65-80 in 2015. What appear to be twin peaks might be explained by the troughs in numbers of women aged 60-65 in 2006 and 70-75 in 2015, possibly related to decrease in the birth cohort during and immediately after world war II. However, the shift towards older age in 2015 as compared to 2006 is likely to be real.

During the period from 2006 to 2015, Chelyabinsk region among the female population has seen an increase share of I-II breast cancer stages from 60.7% to 67%, while stage IV decreased by 4.5% from 11.1 to 6.6%, stage III not appreciably changing (see Table 3). There has been a slight increase in surgery only treatment. In line with these data, although mortality within the first year has decreased, there has been no significant improvement in 5 year survival. During the period from 2010 to 2015, the coverage of mammography screening of women increased from 19.5% to 47.7% of the subject population (see Table 4). Detection of breast cancer in stage I-II reached 73.7% by 2015, but this was only slightly greater than the figure for those diagnosed in general. However, the percentage of screened cancers at stage IV has become very low.

The level of histological confirmation of diagnosis reached 97.1% at the end of 2015 (Table 3), with difficulties mainly related to the lack of morphological verification capabilities in some areas of the Chelyabinsk region, as well as the refusal of older women to accept further examination and treatment.

Discussion

The present results demonstrated a clear increase in the overall incidence rate of breast cancer in Chelyabinsk Oblast over the time period from 2006-2015 with only limited change in mortality. Much lower rates were evident in Tatar and especially Bashkir populations than in Russians and there was a general tendency for lower rural than urban rates, at least until the most recent data.

The 17.1 % increase in 10 years observed here, from 42.7 to 54.2 per 100,000, giving an annual increment of approximately 1.7%, is in line with results found elsewhere, for example in the former states of the USSR, with the notable exception of the St Petersburg Russian Federation registry, and also neighbouring Eastern European countries (see Table 5). Similarly, in Kazakhstan as a whole the increase in incidence was 1.9% a year from 1999-2014 (Beysebayev et al., 2015a) and in the Aral sea area a rise from 13.4-26.1/100,000 was noted from 1999-2010 (Igissinov et al., 2011a). In the Kemerova region also gradual increase was observed from 1999-2009 (Kutikhin et al., 2012), although there was no discernible trend in

Table 5. Change in Breast Cancer Incidence in Five Continents Data Over Time

Region/Country	Incidence			Change	%
	CIV8[1]	CIV9[2]	CIV10[3]	in No.	Change
Austria (Tyrol)	68.9	72.3	70.7	1.8	2.6
Belgium (Flanders)	88.1	101.3	110.8	22.7	25.7
Germany (Saar)	71.4	76.6	81.9	10.5	14.7
Ireland	69.6	78.1	83.1	13.5	19.4
Netherlands	85.6	90.3	93.4	7.8	9.1
UK (England)	79.4	80.4	82.6	3.2	4.0
(N. Ireland)	73.5	76.5	80.2	6.7	9.1
(Scotland)	75.6	79.2	82.8	7.0	9.3
Denmark	81.3	83.7	86.1	4.8	5.9
Finland	72.4	80.6	83.2	10.8	14.9
Iceland	76.1	84.6	86.7	10.6	13.9
Norway	63.2	71.0	75.9	12.7	20.1
Sweden	76.5	78.9	81.1	4.6	6.0
Belarus	33.0	35.6	41.0	7.0	21.2
Estonia	41.5	47.2	48.9	7.4	17.8
Latvia	39.4	44.1	48.4	9.0	22.8
Lithuania	37.7	43.7	46.4	8.7	23.1
Russia	46.1	47.7	47.4	1.3	2.8
Croatia	47.3	57.4	59.4	12.1	25.6
Czech	52.9	55.9	64.6	11.7	22.1
Slovakia	42.4	46.9	51.7	9.3	21.9
Slovenia	51.3	58.8	63.6	12.3	24.0
Israel Jew	89.5	96.8	89.4	-0.1	-0.1
Arab	27.7	38.5	56.1	28.4	102.5
India Mumbai	28.9	26.9	30.4	1.5	5.2
Karunagapally	15.0	16.0	16.6	1.6	10.7
Thailand Bangkok	25.5		34.3	8.8	34.5
Chiang Mai	16.1	21.6	25.6	9.5	59.0
Songkhlaa	11.7	18.2	21.6	9.9	84.6
Philippines	54.2	55.2	60.1	5.9	10.9
Singapore C	44.7	56.4	59.2	15.5	34.7
I	36.7	45.0	49.0	12.3	33.5
M	37.1	43.5	53.6	16.5	44.5
China Hong Kong	36.2	41.3	45.2	9.0	24.9
Jiashan	9.1	14.7	22.4	13.3	146.2
Korea Seoul	20.8	28.8	37.3	16.5	79.3
Japan Miyagi	33.1	42.5	54.0	20.9	63.1
Osaka	27.9	32.0	37.3	9.4	33.7

[1]Parkin et al., 2002; [2]Curado et al., 2007; [3]Forman et al., 2014

the Aktobe region, 2004-2008 (incidence range 6.0-10.1), mortality (5.9-8.8) (Bekmukhambetov et al., 2015a; 2015b). Regarding the St Petersburg apparent anomaly, we must wait for CIV 11 to appear since increase from an incidence of 19 in 1970 to 75 in 2010 was reported in a recent Russian overview document (Merabishvili, 2015). Presumably within each population there is a stable level which is achieved, at least looking at data from a number of registries in Europe, Australia and Northern America where rates have not appreciably changed over the last decade. Why relatively stable rates may greatly vary, for example from 30 in India Mumbai to 70 in Austria and almost 90 in Israeli Jews (Table 5), must reflect variation in overall exposure to risk factors. Explanation of explosive increase from very low levels as in Israeli Arabs and rural China might depend at least partly on quality of registration but continued rapid increase from a high level in Belgium points to other factors. Clearly more emphasis needs to be placed on impact at the country or local regional level on risk factors like those from the Korean breast cancer risk assessment tool: family history of breast cancer, age at menarche, menopausal status, age at menopause, experience of pregnancy, age at first full-term pregnancy, number of pregnancies, duration of breastfeeding, oral contraceptive usage, hormone replacement therapy, exercise, body mass index (BMI), smoking, alcohol drinking, and number of screening breast examinations (Park et al., 2013).

Reported risk factors in nearby Kazakhstan include unfavorable living conditions, chronic stress, unilateral breastfeeding, breastfeeding less than 3 months and over 2 years, abortions, and hereditary predisposition (Toleutay et al., 2013). In addition, 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 has been described (Bilyalova et al., 2012). Whether these are also influences in Chelyabinsk remains to be determined.

Our findings for ethnicity are in line with earlier reports for Kyrgyzstan (Igisinov, 2004; Igisinov et al., 2005) with standardized rates in 1995-2002 of 39.1 for Russian but only 10.6 for Kyrgyz. Particularly low rates have also been described for Mongolians (Sandagdorj et al., 2010; Troisi et al. 2012). Ethnic differences have also in been documented in Israel, rates for Israelis being much higher than for Arabs (Salim et al., 2010), and in Pakistan, where Baluchis from the rural north have much lower incidences than in Punjabis and immigrants from India (Bhurgri et al., 2007). Also in Guam (Haddock et al., 2009) and in Australia where Aborigines are less affected than whites (Roder, 2005), while the opposite is true in New Zealand, Maoris having higher rates than Caucasians (Forman et al., 2014). There is evidence for environment not genotype as the predominating influence. For example in Singapore, Indians had higher rates than Malays and Chinese in the 1960s but more recently Chinese have higher incidences, looking at CIV data (Moore et al., 2010e). In our specific Tatar and Baskiri populations the lower rates than in Russians might be linked to religious and cultural differences in terms of reproductive factors like age at marriage and parity, and exposure to environmental lifestyle factors like alcohol (Brooks and Zakhari., 2013).

Regarding age dependence, our findings indicate increase to a plateau at ages 55 and now 65, compared with the 50 and above reported for the Aral sea area (Igissinov et al., 2011b). Age effects were earlier found to level off after 40s in Japan (Ito et al., 2011). Whether the shift in age that we noted reflects a cohort influence requires further investigation.

Our findings for influence of mammography do not point to a major role in increasing the incidence, in contrast to earlier reports for the Western world (Duffy and Parmar, 2013; Beckmann et al., 2014) although minor effects on numbers of stage I and II cancers can not be ruled out. Detection of breast cancer in stage I-II reached 73.7% by 2015, but this was only slightly greater than the figure for those diagnosed in general. However, the percentage of screened cancers at stage IV has become very low. In general, there has been a significant increase in the active

detection of breast cancer among the female population of the Chelyabinsk region is almost 2 times the 10-year period from 2006 to 2015. from 27.5% to 55.8%, while the nationwide rate in 2015 was 37.2%.

While only very slight decrease in overall mortality was evident, contrasting to the 0.8% decrease per year reported by Beysebayev et al. (2015a) the present study indicated an improvement of the mortality to incidence ratio from 42.4% to 29.5%. While much higher than the 15-20% evident in most Western European countries, this compares well with data for Eastern Europe and country members of the ex-Soviet Union (Ferlay et al., 2015). While short term survival for one year appears to have considerably improved the same is not the case for five year data and compared to other regions of the world the observed 57% is very low.

In conclusion, at the population level, increase in breast cancer incidence in the Chelyabinsk region was identified, primarily affecting Russians. The lower levels in other ethnic groups presumably reflect lifestyle and religious influences. From the literature, the relatively poor survival might be linked to the distribution of molecular subtypes (Jia et al., 2014; Kongsiang et al., 2014), which were not determined in the present study. This should be a focus of attention in the future, along with any age dependence of subtypes, as described earlier (Thapa et al., 2013; Tichy et al., 2013; Elkablawy et al., 2015). Use an arsenal of measures to optimise secondary prevention (Cherenkov et al 2013;; Beysebayev et al 2015b) and provision of the most effective clinical therapies clearly need emphasis, with an ongoing focus on accurate accounting of cases of morbidity and mortality, within the context of development of a network of specialized oncology institutions in the Russian Federation.

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