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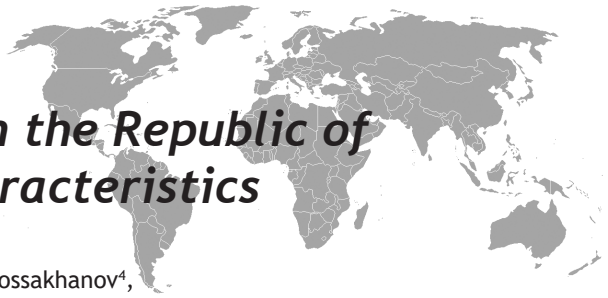

Stomach cancer morbidity in the Republic of Kazakhstan: Trends and characteristics

Galiya Orazova[1,2,] Leonid Karp[1], Keun-Young Yoo[3], Alikhan Dossakhanov[4], Gulnar Rakhimbekova[5], Abduzhappar Gaipov[6]

ABSTRACT

Objective: *Within oncological diseases, stomach cancer is ranked fourth in Kazakhstan, following breast cancer, cancer of the trachea, bronchi and lungs, and skin cancer. In males, stomach cancer is ranked second, following cancer of the trachea, bronchi and lungs, and amounting to 11.8% from all the localizations.*

Methods: *Descriptive methods of modern oncological epidemiology were used in the present study, which was performed on the total population of Kazakhstan. The calculation of the unadjusted and adjusted rates, and the morbidity structure rates was performed according to all age-gender groups over a 10-year period (between 2004 and 2013).*

Results: *2013, the stomach cancer morbidity frequency in Kazakhstan was 16.4/100,000 of the population (21.8 in males and 11.6 in females). In the structure of malignant growths, the proportion of stomach cancer was 8.5%. There was a tendency in morbidity reduction between 2004 and 2013 (growth rate, -18.0%). A significant predominance of the prevalence rate of this localization was observed among males. The morbidity peak was indicated in the 75-79 years old group (225.8 and 90.3/100,000 of the relevant population in males and females, respectively).*

Conclusion: *In spite of the progress made in oncology worldwide, stomach cancer in Kazakhstan remains one of the most prevailing malignant growths. Identification of the features of stomach cancer morbidity in Kazakhstan may reduce its prevalence in the future by tailoring research into preventing the incidence and improving treatment..*

Key words: *Stomach cancer, morbidity characteristics, Kazakhstan*

Kazakistan' da mide kanseri morbidite' si: Trendler ve özellikleri

ÖZET

Amaç: *Onkolojik hastalıkların içinde, meme kanseri, trakea, bronş ve akciğer, cilt kanseri sonrasında mide kanseri Kazakistan'ın dördüncü sırasında yer almaktadır. Erkeklerde, trakea, bronş ve akciğer kanserleri takiben, mide kanseri ikinci sırada ve genelde % 11.8 tutarında yer alıyor.*

Yöntem: *Bu çalışma Kazakistan nüfusunda modern onkolojik epidemiyoloji tanımlayıcı yöntemler kullanılarak yapıldı. Düzeltilmemiş ve düzeltilmiş oranlarının hesaplanması ve morbidite oranları yapısı 10 yıllık dönemde tüm yaş-cinsiyet gruplarına göre gerçekleştirilmiştir (2004 ve 2013 yıllar arası).*

Bulgular: *2013 yılında, Kazakistan'da mide kanseri morbidite sıklığı 16.4/100.000 nüfus idi (kadınlarda 21.8 ve erkeklerde 11.6). Malign büyümeleri yapısında, mide kanseri oranı % 8.5 idi. 2004 ve 2013 yıllar arasındaki morbiditede azalma eğilimi vardı (büyüme hızı, - %18.0). Bu yerelleştirme yaygınlık oranı önemli bir üstünlüğü erkeklerde gözlendi. Morbidite zirvesi 75-79 yaş grubunda belirtilmiştir (erkeklerde 225.8/100.000 ve kadınlarda 90.3/100.000).*

Sonuç: *Dünya çapında onkoloji kaydedilen ilerlemeye rağmen, Kazakistan'da mide kanseri en yaygın malign büyümelerinden biridir. Kazakistan'da mide kanseri morbidite özelliklerinin tanımlanması, insidansının önlenmesi ve kanser araştırma ve tedavisini geliştirerek gelecekte mide kanseri yaygınlığı azaltılabilirdir*

Anahtar kelimeler: *Mide kanseri, morbidite özellikleri, Kazakistan*

Astana Medical University, Departments of Public Health[1] and Internal Medicine[5], Astana, Kazakhstan. National Scientific Medical Research Center, Departments of Management Science and Evidence-based medicine[2], Strategic Development[4], Extracorporeal Hemocorrection[6] Astana, Kazakhstan. Seoul National University College of Medicine Seoul, Korea[3].

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Correspondence: *Galiya Orazova*
Astana Medical University, Department of Public Health, Str Beibitshilik 41, 010000, Astana, Kazakhstan.
E-mail: galiyaorazova@gmail.com

INTRODUCTION

MIn recent decades, regardless of the significant reduction in morbidity and with consideration of population ageing, stomach cancer (SC) remains one of the most prominent malignant diseases worldwide (1-4). In morbidity patterns, SC is the second most common among the organs of the gastro-intestinal tract (GIT), with 952,000 new cases each year (5-6). By 2020, the occurrence of these diseases is expected to increase to 1.3 million and according to the prognosis of malignant growths of the GIT organs by specialists, SC will be the leading disease for morbidity and mortality in the 21st century (7-8). Approximately 71% of SC cases occur in less developed countries. The highest SC morbidities have been identified in countries of Eastern Asia (including Japan and China), Eastern Europe, Latin America and the Caribbean, with a relatively low SC morbidity in South America, Southern Asia, and Northern and Eastern Africa (9). SC most frequently occurs among senior citizens. Worldwide, SC is predominantly diagnosed at 69 years old. On the average 1 person of 111 is undergone the risk of suffering from the SC (10).

According to the adjusted incidence rate for SC, Kazakhstan is seventh in the world, yielding to the Republic of Korea, Mongolia, Japan, Guatemala, China and Tajikistan (11). In 2012, the adjusted incidence rate was 21.6/100,000 of the population. The rate of SC among males in Kazakhstan is higher (fifth following the Republic of Korea, Mongolia, Japan and Kyrgyzstan) with a rate of 35.2/100,000 of the relevant population. Specifically in Kazakhstan, there is one of the highest rates of SC among males and females (2.75 per 100,000 population). In the structure of oncological diseases, SC is fourth in Kazakhstan, and in particular, it is second in males (8.5%). Regardless of the significance of the SC complications, an in-depth study of this topic remains to be performed in Kazakhstan.

The aim of the present study was to investigate the age, gender and regional features of SC morbidity in Kazakhstan, with an estimation of the changing frequency over time.

MATERIAL AND METHODS

Study design. The present study was a retrospective epidemiological study involving descriptive evaluation and approved by Local Ethics Committee. Statistical data were received from the Ministry of Healthcare and Social Development of the Republic of Kazakhstan (Astana, Kazakhstan). Descriptive methods of modern oncological epidemiology were used (12). The present study was performed on the whole population of the Republic of Kazakhstan. The calculation of the rates was performed according to all age-gender groups over a 10-year period (between 2004 and 2013), with new cases of SC, which were not previously registered. The data for the whole population of Kazakhstan and for certain regions with regards to the age-gender composition per year were used according to the data of the Agency of Statistics of the Republic of Kazakhstan (Astana, Kazakhstan).

Calculation of incidence and morbidity rates. The calculation of the oncological morbidity structure was performed using the association of the SC primary disease incidence cases of a certain population to the total amount of malignant growths in this population, expressed as a percentage. The unadjusted rates were calculated through the association of the number of primary disease incidences to the number of relevant population (per 100,000 of relevant population). To obtain more detailed characteristics, the age-specific rates of SC morbidity were calculated. The analysis of the SC morbidity rate dynamics was performed in the 2004 to 2013 time frame. The 2012 world standards were applied for the calculation of the adjusted rates (13). All the rates were calculated with the standard errors and confidence intervals. The statistical series rates in the form of growth rate were applied to the characteristics for processing the rate of change.

Statistical analysis. Student t test was used to determine the significance of the rates. $P<0.05$ was considered to indicate a statistically significant difference. Correlation analysis of the morbidity rate, in association with the mortality rate, was performed by Spearman's method. The cumulative rates were calculated using the method by Petrova et al (14) (sums of age-related SC morbidity rates in Kazakhstan for 2013) and cumulative risk of SC development (risk of developing of the certain malignant growth which would be suffered by a person during his lifetime if there are no other mortality causes) by the exponential formula: 100x[1-exp(-cumulative rate/100)]. The method by S.Igissinov (15) which is based on the determination of the mean-square deviation from the arithmetic average, was used to generate cartograms of the prevalence proportion.

Table 1. The prevalence and rank place of stomach cancer in the structure of oncological morbidity of the Kazakhstan population between 2004 and 2013.

Gender		Year									
		2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Males and females	Share, %	10.3	9.8	10.1	10.2	9.6	10.6	9.0	8.8	8.5	8.5
	Rank no.	4	4	4	4	4	3	4	4	4	4
Males	Share, %	13.3	12.7	13.2	13.7	12.9	12.4	12.1	12.0	12.0	11.8
	Rank no.	2	2	2	2	2	2	2	2	2	2
Females	Share, %	7.6	7.2	7.4	7.1	6.7	6.5	6.3	6.2	5.7	5.7
	Rank no.	3	4	4	4	4	4	4	4	4	5

RESULTS

Structure of SC primary disease incidence in Kazakhstan. The prevalence and rank place of SC in the structure of oncological morbidity in the population of Kazakhstan between 2004 and 2013 are represented in Table 1.

In the structure of oncopathology, the relative density and rank place of SC changed over the 10 years (between 2004 and 2013). The general share of SC in the population was reduced from 10.3 to 8.5%, maintaining a fourth place ranking. The share of SC morbidity among males changed from 13.3 to 11.8%, and maintained a second place ranking following cancer of the trachea, bronchi and lungs. There was a significant reduction among females (from 7.6 to 5.7%), and the SC rank moved from third to fifth place, following breast, skin, cervix uteri and uterine cancer (Table 2).

Analysis of unadjusted rates of SC morbidity. The most representative depiction of SC morbidity dynamics among the population is provided by the raw rates. The dynamics of the general and average annual rate of growth are represented in Table 2. In 2013, SC morbidity was 16.4/100,000 of the population (confidence interval, 15.6-17.0). For 10 years a statistically significant SC morbidity rate reduction occurred ($p<0.001$). The average annual rate of SC morbidity growth between 2004 and 2013 was -1.8. SC morbidity among males was 1.9-fold higher compared with females, while the primary disease incidence for all types of cancer among females was 1.2-fold higher compared with males.

The proportion of morbidity in males and females increased from 1.7 in 2004 to 1.9/100,000 of the population in 2013 (Table 2).

There was a correlation for the association of the medium coefficient between SC morbidity in males and females (Spearmen's $\rho=0.56$, $P<0.05$).

The dynamics of age-related SC morbidity rates in males and females in Kazakhstan between 2004 and 2013 are represented in Tables 3 and 4. Therefore, the SC morbidity rate in males aged 70-79 years old was higher compared with the analogous morbidity rate at the age of 40-49 years old by 16.3-fold, and among females this was 14.6-fold. The rate analysis of the 10-year SC morbidity growth in each age-related group among males and females demonstrated that growth rates in the male population (Table 3) were reduced with age, from -56.3 (20-29 years old) to -3.2% (70-79 years old). An exception is the ≥80 year's old group, in which the growth rate was -46.9% (Table 3).

Different results were apparent for the female population, as apart from the oldest age-related group, the growth rates varied from -12.5 to -28.7%, with no significance. Of note, the growth rates in females aged between 30 and 69 years old were similar (Table 4). A more detailed frequency of morbidity with a 5-year age range is represented in Figure 1.

By comparison of the age-related SC morbidity rates among males and females in Kazakhstan, there was a growth of the general rates for the age category of 75-79 years for both; subsequently a reduction was observed. A comparison of morbidity frequency on the basis of gender among all the malignant growths was predominant in females aged ≤55 years old, following which there was a significant morbidity level among males. When assessing the age-related SC morbidity rate, there was a different outcome. From 45 years old in each age-related group,

Table 2. *Dynamics of the unadjusted rates of stomach cancer morbidity among males and females in Kazakhstan between 2004 and 2013.*

	Unadjusted rates/100,000 of the population				
Years	Overall population	Confidence interval	Males	Females	Proportion of males/females
2004	20.1	19.2-20.8	25.6	15.1	1.7
2005	18.9	18.2-19.6	24.3	14.1	1.7
2006	18.9	18.2-19.6	24.3	14.2	1.7
2007	18.8	18.1-19.5	24.9	13.4	1.9
2008	17.4	16.8-18.0	22.7	12.7	1.8
2009	16.9	16.3-17.5	22.0	12.4	1.8
2010	16.3	15.7-16.9	21.0	12.1	1.7
2011	16.2	15.6-16.8	21.0	11.9	1.8
2012	16.3	15.7-16.9	21.4	11.8	1.8
2013	16.4	15.6-17.0	21.8	11.6	1.9
Growth rate from 2004 to 2013, %	-18.0		-13.9	-22.8	
Average annual rate of growth from 2004 to 2013, %	-1.8		-1.4	-2.3	

the SC morbidity among males was higher compared with the females (by at least double), and for the group aged 65-69 years old this was more than triple (183 and 56.9 per 100,000 population). Reduction of the morbidity frequency at ≥80 years can be explained by the insufficient availability of medical assistance for this population category.

Adjusted SC incidence rates. The calculated adjusted incidence rates of SC among males and females in each section of the country demonstrated that if there is a pattern for age in the Kazakhstan population, this is close to the world distribution. The level of adjusted morbidity rates in males and females were higher and lower, respectively (25.58 and 9.77/100,000 of the relevant population). The dynamics of the adjusted incidence rates demonstrated a relative stability in males (growth rate, -2.4%), which is

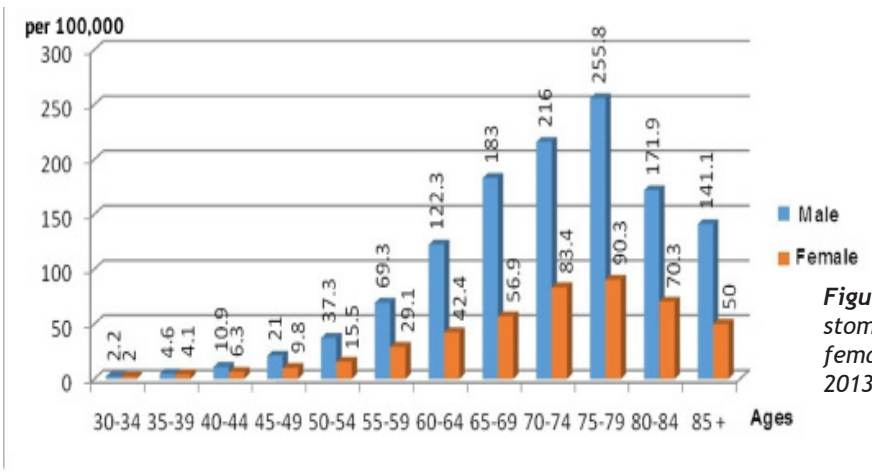

Figure 1. *Age-related morbidity of stomach cancer among the male and female populations of Kazakhstan in 2013 (per 100,000 of the population).*

Table 3. *Dynamics of the age-related stomach cancer morbidity rate among males in Kazakhstan between 2004 and 2013.*

Years	*Age groups, years*								
	0-19	***20-29***	***30-39***	***40-49***	***50-59***	***60-69***	***70-79***	***≥80***	***Total/100,000 of the population***
2004	*0.00*	*0.87*	*4.4*	*21.6*	*72.5*	*172.3*	*225.6*	*283.2*	*25.6*
2005	*0.00*	*0.77*	*5.3*	*20.7*	*72.8*	*158.9*	*225.8*	*186.2*	*24.3*
2006	*0.04*	*0.75*	*4.8*	*21.1*	*63.6*	*169.4*	*245.1*	*172.5*	*24.3*
2007	*0.11*	*1.16*	*6.9*	*21.6*	*73.1*	*156.8*	*229.3*	*194.8*	*24.9*
2008	*0.04*	*0.63*	*4.8*	*18.6*	*67.3*	*152.5*	*202.8*	*176.2*	*22.7*
2009	*0.07*	*0.34*	*3.9*	*18.8*	*63.2*	*142.6*	*201.4*	*173.3*	*22.0*
2010	*0.07*	*0.60*	*4.2*	*16.5*	*57.3*	*139.8*	*198.5*	*192.9*	*21.0*
2011	*0.07*	*0.26*	*3.7*	*15.7*	*55.6*	*140.5*	*209.4*	*153.5*	*21.0*
2012	*0.00*	*0.71*	*3.3*	*15.8*	*50.7*	*141.6*	*228.9*	*162.5*	*21.4*
2013	*0.00*	*0.38*	*3.6*	*13.4*	*58.0*	*145.7*	*218.4*	*150.4*	*21.8*
Growth rate	*0.0*	*-56.3*	*-17.9*	*-37.9*	*-20.1*	*-15.4*	*-3.2*	*-46.9*	*-14.9*

another confirmation of the hypothesis that the influence of risk factors in the male population remains unchanged. However, there was a significant reduction in the adjusted rates in females (growth rate, -31.4%; Table 5).

Cumulative risk of SC development. The cumulative factor and cumulative risk of SC development among males and females of Kazakhstan are represented in Table 6. In general, the cumulative factors were 5,865.4/100,000 males (5.87%) and 2,265.8/100,000 females (2.27%).

The cumulative risk was 100x[1-exp(-5.87/100)]=5.72% for males and 100x[1-exp(-2.27/100)]=2.24% for females. As a result, without other reasons for the risk of SC development in males from Kazakhstan was 5.72%, and in females this was 2.24% (Table 6).

Regional-specific features of SC in Kazakhstan. Visualization of the geographical distribution of SC is

Table 4. *Dynamics of the age-related SC morbidity rate among females in Kazakhstan between 2004 and 2013.*

Years	*Age groups, years*								
	0-19	***20-29***	***30-39***	***40-49***	***50-59***	***60-69***	***70-79***	***≥80***	***Total/100,000 of the population***
2004	*0.00*	*0.80*	*3.2*	*8.6*	*26.9*	*68.0*	*107.0*	*94.5*	*15.1*
2005	*0.00*	*0.86*	*3.0*	*11.1*	*24.8*	*68.9*	*91.6*	*68.8*	*14.1*
2006	*0.04*	*0.38*	*4.0*	*9.2*	*26.7*	*68.4*	*97.8*	*64.0*	*14.2*
2007	*0.12*	*1.11*	*4.4*	*9.7*	*25.1*	*60.1*	*85.8*	*68.2*	*13.4*
2008	*0.00*	*0.79*	*3.7*	*8.1*	*21.6*	*58.3*	*84.6*	*76.0*	*12.7*
2009	*0.04*	*0.56*	*2.9*	*7.8*	*21.3*	*53.6*	*94.4*	*58.6*	*12.4*
2010	*0.04*	*0.99*	*3.3*	*8.0*	*21.2*	*55.0*	*87.1*	*67.0*	*12.1*
2011	*0.04*	*0.45*	*2.3*	*9.0*	*18.9*	*52.4*	*92.9*	*63.3*	*11.9*
2012	*0.04*	*0.96*	*3.1*	*8.0*	*21.5*	*47.3*	*85.8*	*62.9*	*11.8*
2013	*0.04*	*0.70*	*2.4*	*6.2*	*20.3*	*50.2*	*90.3*	*56.4*	*11.6*
Growth rate	*0*	*-12.5*	*-26.8*	*-28.7*	*-24.6*	*-26.1*	*-15.6*	*-40.3*	*-22.8*

shown in Fig.2. The levels of population morbidity with SC (high, medium and low) were determined for each region in 2013.

There were three regions, which were referred to as low level with factors <11.0/100,000 of the population. Six regions were classed as medium level, in which the morbidity was 11.0-14.8/100,000. A high level of morbidity was identified in five regions of the country, where the morbidity was >14.8/100,000 of the population. As a result, the high level of morbidity covered the entire north-east section of the country, while the medium level was typical for the west and north-west regions, and the regions with a low level were located in the south, south-west and south-east sections of the country. A significant difference between the maximum and minimum rates was apparent when studying SC prevalence. The fluctuation amplitude of the frequency between the end rate was 2.3 in certain regions of the country in 2004 and in 2013. When calculated from a perspective of each region, the growth rates revealed that there is also an increase regardless of the SC morbidity reduction covering a 10-year period in certain regions.

Taken together, these provided evidence of territorial inequality of the SC prevalence in Kazakhstan.

DISCUSSION

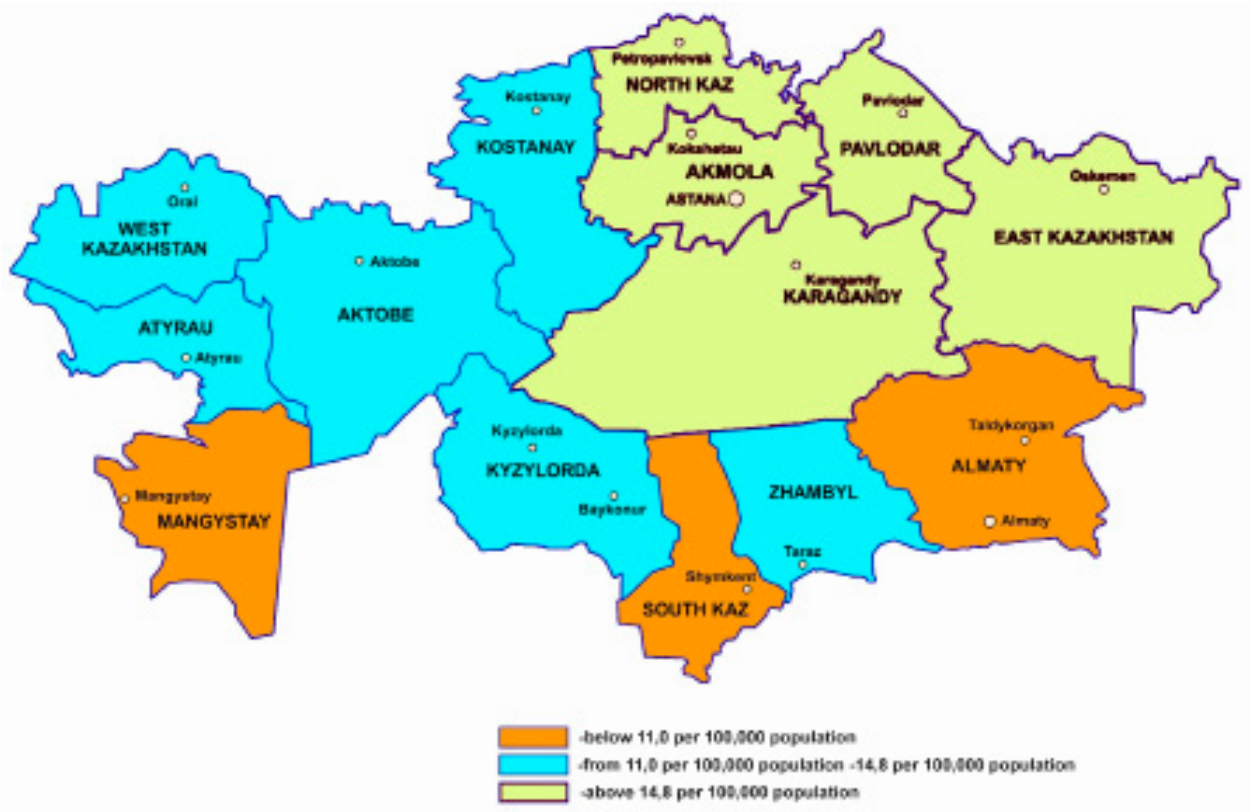

***Figure 2**. Stomach cancer morbidity in certain regions of Kazakhstan in 2013.*

A total of 27,955 patients with a first-time diagnosis of SC were registered over a 10-year period (2004-2013) in the Republic of Kazakhstan (63.6% of males and 36.4% of females) and 22,152 patients died. Regardless of the progression in SC treatment, the 5-year survival rate is only 45.3%, which is lower compared with all the malignant growths as a whole (50.0%). For a number of years, SC has been second place among all malignant growths in the structure of mortality (12.5% in 2013), yielding to mortality from cancer of the trachea, bronchi and lungs. A previous study revealed that the preventive measures

Table 5. Dynamics of the adjusted incidence rates of stomach cancer among males and females in Kazakhstan between 2004 and 2013 (world standard of 2012).

Years	Adjusted rates/100,000 of the population (world standard)	
	Males	Females
2004	26.21	14.24
2005	24.40	13.13
2006	29.90	12.43
2007	30.04	11.64
2008	27.50	10.86
2009	26.26	10.48
2010	25.44	10.57
2011	25.06	10.22
2012	25.38	9.94
2013	25.58	9.77

of malignant growth is possible only on the basis of epidemiological study, which includes studying the mechanisms of pathology prevalence and the risk factors influencing the incidence rate (16). The significance of the present study included not only the establishment of the specific features of SC morbidity in Kazakhstan and its dynamics, but attempts to identify and detect common factors, allowing a focus on certain age-gender groups of the population, residing at certain territories.

The study by Abdrakhimov (16) investigated the morbidity from SC in Kazakhstan; however, the submitted data were valid prior to 1991. Furthermore, prior to the end of the 1980s there was an increased morbidity from SC, i.e. the tendencies of SC morbidity were different.

Until the 1990s, SC morbidity in the country was the most prominent in the structure of cancer morbidity. However, over the past decade certain changes have occurred in the country, which affected the levels and nature of the incidence rate. Currently, SC is ranked fourth in the structure of cancer morbidity in Kazakhstan, and in males is ranked second (8.5%). The submitted data provide no evidence for the reduction of morbidity, and only provide evidence for the reduction of the SC proportion in the total number of malignant growths.

Previous data for the Soviet Union, which included Russia and Kazakhstan, allows for the comparison of numerous factors, including morbidity from SC. Therefore, a variety of studies concerned with the epidemiology of SC have been published in the Russian Federation (8, 17-18). Russian investigators suggested that trends of territorial distinctions of SC morbidity can reflect the distribution of risk factors and their associations with processes occurring in the surrounding environment and lifestyle for a population (19-20).

One of the most important aspects in studying the reasons and factors that contribute to the malignant growth prevalence is examining the regional-specific features of this pathology. The prevalence of SC in countries located

Table 6. Cumulative factor and cumulative risk of stomach cancer development among males and females of Kazakhstan.

Age-related groups, years	Years of life in age-related group	World standard, % (t_i)	Age-related rate of morbidity in males (a_i)	Males ($a_i t_i$)	Age-related rate of morbidity in females (a)	Females ($a_i t_i$)
0-19	20	40	0.00	0.0	0.04	0.8
20-29	10	16	0.38	3.8	0.70	7.0
30-39	10	12	3.62	36.2	2.38	23.8
40-49	10	12	13.45	134.5	6.15	61.5
50-59	10	9	57.96	579.6	20.30	203.0
60-69	10	7	145.70	1457.0	50.24	502.4
70-79	10	3	218.40	2184.0	90.29	902.9
80-90	10	1	150.43	1504.3	56.44	564.4
Total	10	100	21.78	5895.4	11.64	2265.8

in close proximity to Kazakhstan is of interest. In Iran, similar to in Kazakhstan, there is a geographical variability of morbidity frequency; SC morbidity is more prevalent in north and north-west sections of the country (21). In Turkey, as in Kazakhstan, SC ranks second in the structure of morbidity in males (following lung cancer) with almost an equal share (8.7%); however, the level of morbidity in Turkey (9.6 cases/100,000 of population per year) is lower compared with in Kazakhstan (22-23). As identified in the present study, the significant fluctuation amplitude of the frequency between ends rates in certain regions can be explained with various reasons, including different levels of access to medical services, and volume and quality of its rendering in different regions of Kazakhstan. Emphasis on the regions with a high SC morbidity level may provide an opportunity to understand how to reduce the incidence of SC.

Numerous studies have reported that the prevalence of SC in males occurs more frequently compared with females, and that this proportion increases with an increase of age (9, 24-25). In Russia, during recent years the proportion of unadjusted factors has reduced and the adjusted ones increased (18). In spite of a previous report regarding the growth rate of morbidity with an increase of age, the growth rates in Kazakhstan overwhelm According to the data of a Russian study, the peak of the morbidity rate for cancer is the 70-74 years old group (in the present study this is the 75-79 years old group); however, a certain section of these patients succumb prior to this age and prior to cancer onset. Specific previous studies have shown that the maximum morbidity rate is accounted for by ≥85 years in the general population and among females (8, 17-18).

The submitted data revealed a clear trend of SC morbidity reduction in females, compared with in males, as evidenced by the dynamics of not only the unadjusted factors, but also the adjusted ones. The reasons for the SC morbidity reduction in Kazakhstan do not have sufficient scientific clarification. However, there is controversy regarding the leading role of dietary factors. Factors including smoking, alcohol abuse and stresses may also be observed among the other factors (5, 26-27). However, studying the risk factors of SC morbidity is one of the focus areas for future research.

The present study had a number of strengths. All the SC cases in Kazakhstan during a 10-year period were included in the present study. The 10-year time period is generally accepted as sufficient for the evaluation of the epidemiological situation. However, there was a limitation to the study, which was that it was not designed to assess the risk factors leading to morbidity in cancer. The tendency of SC morbidity reduction was registered in Kazakhstan between 2004 and 2013.

In conclusion, there was a significant predominance of SC prevalence among males. The peak of morbidity was revealed in the 75-79 years old group. The highest SC morbidity was registered in the northern regions, and additionally, the nature of the reduction of cancer morbidity was different. The calculation of the cumulative risk for SC development showed that among males it is more than twice as high compared with females. Identification of the particular aspects of SC morbidity and prognosis in Kazakhstan should aid in reducing its prevalence.

Ethical considerations

Ethical issues (including plagiarism, data fabrication and/or falsification, double publication and/or submission, and redundancy) have been completely observed by the authors.

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