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Trends in colorectal cancer incidence in western Kazakhstan through the first decade of the screening implementation, 2009–2018

Saule Balmagambetova [a,*], *Sajad Ahmad Bhat* [b], *Arip Koyshybaev* [c], *Zhanna Gumarova* [b], *Olzhas Urazayev* [a], *Anar Tulyaeva* [a], *Ainel Urazova* [a], *Arzhan Taumova* [b]

[a] *West Kazakhstan Marat Ospanov Medical University, Department of Oncology, Aktobe, Kazakhstan*
[b] *West Kazakhstan Marat Ospanov Medical University, Chemical Sciences Department, Aktobe, Kazakhstan*
[c] *West Kazakhstan Marat Ospanov Medical University, Oncology Department, Aktobe, Kazakhstan*

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ABSTRACT

Introduction: The study is aimed to outline the vector of colorectal cancer incidence in the industrial Aktobe province of western Kazakhstan through the first decade of the screening implementation, 2009–2018.

Methods: Rough incidence rates and annual percent changes were estimated for each age group at diagnosis, ethnicities, gender, residences, the disease stages and anatomic subsites (total N 1128) via regression analysis.

Results: Within 2009–2018 colorectal cancer rates increased from 14.74 to 23.19, with annual percent changes of 4.69%. The most significant growth was traced in men compared to women, up to 28.39 by 2018, with annual percent changes 6.64% vs. 2.64% ($p = 0.0009$). Annual percent changes in Kazakhs reached 8.7%, whereas Slavic groups showed decline in the incidence, annual percent changes −4.3% ($p = 0.002$). Declining in rates was also observed in urban population compared to rural one, annual percent changes −3.3% vs. 17.6%, respectively. Patients aged 60–69 made 31% of all cases and showed the largest annual percent changes 9.37% ($p = 0.002$). Patients at Stage II made 61% of all observations, but general trend evidenced sharp growth in the group of Stage I (annual percent changes 28.91%, $p < 0.0001$).

Conclusion: Overall, during the last decade colorectal cancer incidence increased 1.5 fold with expected further rise. However, the increment of Stage I portion by 2018 vs. advanced stages at diagnosis and the trend to decrease in rates among urban population inspire a definite assurance in potential efficiency of the screening program in long run. The next researches on colorectal cancer should include scenarios to reveal the role of disadvantaged environment in the region and consuming unhealthy ultra-processed food.

* *Corresponding author.*
E-mails: sau3567@gmail.com, info@zkgmu.kz (S. Balmagambetova).

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Tendências na incidência do câncer colorretal no Cazaquistão ocidental durante a primeira década da implementação do rastreamento, 2009–2018

Palavras-chave:
Carcinoma colorretal
Cazaquistão
Taxas de incidência
Prognóstico

RESUMO

Introdução: O objetivo do estudo é delinear o vetor da incidência do câncer colorretal na província industrial de Aktobe, no oeste do Cazaquistão, durante a primeira década da implementação do rastreamento, 2009–2018.

Métodos: Taxas de incidência brutas e alterações percentuais anuais foram estimadas para cada faixa etária ao diagnóstico, etnias, sexo, residências, estágios da doença e localizações anatômicas (N total de 1.128) através da análise de regressão.

Resultados: Entre 2009–2018, as taxas de câncer colorretal aumentaram de 14,74 para 23,19, com alteração percentual anual de 4,69%. O crescimento mais significativo foi evidenciado em homens em comparação com as mulheres, até 28,39 em 2018, com alterações percentuais anuais de 6,64% contra 2,64% (p = 0,0009). Alterações percentuais anuais nos cazaques atingiu 8,7%, enquanto os grupos eslavos mostraram declínio na incidência, alterações percentuais anuais -4,3% (p = 0.002). O declínio nas taxas também foi observado na população urbana em comparação com a rural, alterações percentuais anuais -3,3% vs. 17,6%, respectivamente. Pacientes com idade entre 60–69 anos eram 31% de todos os casos e apresentaram as maiores alterações percentuais anuais 9,37% (p = 0,002). Os pacientes no Estágio II eram 61% de todas as observações, mas a tendência geral evidenciou crescimento acentuado no grupo do Estágio I (alterações percentuais anuais 28.91%; p < 0,0001).

Conclusão: No geral, durante a última década, a incidência de câncer colorretal aumentou 1,5 vezes com expectativa de maior aumento. No entanto, o incremento da porção do Estágio I em 2018 em comparação com os estágios avançados no momento do diagnóstico e a tendência de diminuição nas taxas entre a população urbana inspira uma garantia definitiva de eficiência potencial do programa de rastreamento em longo prazo. As próximas pesquisas sobre o câncer colorretal devem incluir cenários para revelar o papel do ambiente desfavorecido na região e o consumo de alimentos ultraprocessados não saudáveis.

Introduction

According to GLOBOCAN 2018 estimates, Colorectal Cancer (CRC) ranks fourth in worldwide scale in both sexes combined, accounting for 6.1% of all first diagnosed cancer cases.[1] There are commonly known risk factors for CRC occurrence: the presence of chronic inflammatory bowel disease, adenomatous polyps; family history; age of men and women over 50, given that more than 90% of patients with CRC are made up of people of this age; consuming unhealthy food and etc.[2–4]

Among the risk factors for CRC development, environmental pollution with chemical compounds is not mentioned as top-ranked, however the Aktobe province of western Kazakhstan is known by its large chromium producing facilities. To our knowledge, an increased level of the chromosomal aberrations was found in peripheral blood leukocytes in workers exposed to the chromium.[5,6] On assessing the dynamics of cancer morbidity and mortality in the Aktobe province, local researchers had found out almost threefold increase in the rectum cancer incidence in tenths.[7] Environmental pollution is also related to the fact that the Aktobe province is partially located in the vast Aral Sea ecological disaster region. According to data, long-time average annual levels of cancer morbidity for 2004–2013 in adult population living in the Aral Sea environs was up to 2.6 times higher, comparing to ecologically intact terrains. In particular, long-time average annual levels of cancer morbidity in adult population living in that zone was up to 57.2% higher, and the total cancer morbidity depended on the hazard coefficient (HQ) associated mostly with the inhalation of nickel and the combined cadmium intake (r = 0.8).[7]

Given the rising rates of CRC, the nationwide screening program launched in Kazakhstan since 2009. Design of the program was developed according to the principles of the "European guidelines for quality assurance in CRC screening and diagnosis" and included iFOBT (immune analysis of fecal occult blood, FIT) and total colonoscopy at positive iFOBT in target groups of both genders 50–70 years aged with 2 year interval.[8]

Commonly, the 10 years period of the screening implementation serves as first milestone in evaluation of some key indices of the disease.

Hence, the study is aimed to outline the vector of colorectal cancer incidence in the environmentally disadvantaged Aktobe province of western Kazakhstan through the specifying rates and trends in all age groups, as well as by gender, ethnicities, residences, stages and tumor sites.

Methods

This retrospective database research was approved by the University's IREC (Protocol n° 21, 24.01.2019). Informed consent was not required because the individually identifiable data of patients were not involved.

Study setting

Territory of the Aktobe province is the largest in western Kazakhstan (Central Asia) and featured by chromium mining, presence of Oil industry and gas condensate works. Indigenous inhabitants are Kazakhs, of turcic ethnic group, followed by Slavs representing about 20% of entire population. Traditional diet of Kazakhs is of nomadic nature and consists mostly of meat and dairy.

Study population

Data on the province' total population within 2009–2018 (857,711 as of January 2018) were requested from the Aktobe Statistical Committee.

All incident cases of first diagnosed colorectal cancer since 2009 through 2018 in adults aged 20 years and older were obtained from the Cancer registry of the Aktobe regional Oncologic Center. Rough incidence rates (per 100,000) and Annual Percent Changes (APCs), as well as the ratios were estimated for each age group at diagnosis (20–39, 40–49, 50–59, 60–69, 70+ years), by gender, ethinicities, residence (urban or rural area), the disease stages (The 8th edition of the UICC TNM Classification, 2016) and anatomic subsites.

This analysis operated with the ethinicities of patients as it was presented in the Cancer registry (Kazakhs, Slavs and Others). As to the anatomic subsites, the entire CRC was presented as C18.0–C18.4 (ascending colon), C18.5–C18.7 (descending colon), C19 (rectosigmoid junction) and C20–C21 (rectum), respectively (according to International Classification of Diseases, X version, 2016).

Statistical analysis

All calculations were carried out in Statistica.10 (Dell Technologies, Round Rock, Texas, USA), as well as in the software SPSS.v.25. For all tests a two-side type I error of $p < 0.05$ at 95% Confidence Interval (CI) was assumed statistically significant. Incidence trends and corresponding 95% CIs were determined by the least squares method of regression analysis and expressed as the number of cases per 100,000 individuals. Changes in the incidence rates over time were calculated using the Student's criterium and expressed as APCs. Ratios for the examined population's gender, age, stages, CRC anatomic subsites, residences and ethnic groups were presented. The prognostic index of the CRC incidence was obtained by the method of moving averages, based on the smoothing procedure with an interval $m = 1$.

Table 1 – Characteristics of individuals first diagnosed with CRC in the Aktobe province within 2009–2018.

Population groups	N total, 1128	%
Gender		
Males	600	53.2
Females	528	46.8
Ethnicity		
Kazakhs	667	59.2
Slavic diasporas	413	36.6
Others	48	4.2
Residence		
Urban area	732	64.9
Rural area	396	35.1
Age		
20–39	60	5.3
40–49	121	7.3
50–59	279	24.7
60–69	350	31.0
70+	318	28.2
Stage		
I	62	5.5
II	688	61.0
III	203	18.0
IV	175	15.5
Tumor site		
C18.0–C18.4	209	18.6
C18.5–C18.7	324	28.7
C19	195	17.3
C20–C.21	398	35.3

Results

In the Aktobe Cancer registry, within 2009–2018 a total of 1128 records were found on patients first diagnosed with CRC. General description of the study population is presented in Table 1.

A slight disproportion in favor of men is traced, while the rest items of the profile are featured with substantial differences (Table 1). Affected by CRC are mostly Kazakhs living in urban area, of 60–69 age, registered mostly with Stage II at presentation and having the predominant tumor location either at descending colon, or at rectum (left-sided CRC). Table 2 presents overall crude CRC rates by years, gender, stage (I/II – resectable, III/IV – advanced) and age groups.

The dynamics by years evidences the boosted growth in incidence in men compared to women, up to 2 times and higher. The incidence rates in young patients (20–39 years old), as well as in 40–49 and 70+ aged have showed insignificant positive dynamics throughout a decade, in patients of 50–59 years slightly have grown up, whereas in 60–69 aged patients the rate soared up to 2.5 times. Age-specific trends with APCs are also presented in Fig. 1.

Though the present profile of patients diagnosed with CRC is featured by prevailing of Kazakhs, mostly men of 60–69 year's old living in urban area, APCs dynamics allows for supposing the boomed growth in incidence among other population groups in the nearest years. We should expect significant CRC affecting in men representing the ethnic minorities (Coreans, Azerbajanians, Dagestanians, Tatars, Germans), living in overwhelming majority in rural area (APC 17.6%) and having conventional distal location of CRC. Definitely, these individuals should be allocated into a special

Table 2 – CRC incidence rates by years: gender, stages and age groups.

Years	CRC rate	St. error	95% CI	Men	Women	I–II st.	III–IV st.	20–39 yrs	40–49 yrs	50–59 yrs	60–69 yrs	70+ yrs
2009	14.74	1.68	11.45;18.03	13.33	15.02	8.90	6.79	0.80	1.71	4.33	3.54	5.30
2010	16.68	1.77	13.21;20.15	16.78	16.49	9.56	7.07	0.85	1.81	4.46	4.12	5.39
2011	18.31	1.82	14.74;21.88	18.23	16.96	10.21	7.34	0.89	1.90	4.59	4.59	5.47
2012	19.56	1.87	15.88;23.22	19.68	17.44	10.87	7.62	0.94	1.99	4.73	5.27	5.56
2013	19.11	1.84	15.51;22.71	21.13	17.91	11.53	7.90	0.98	2.09	4.86	5.84	5.65
2014	19.22	1.83	15.63;22.81	22.58	18.38	12.18	8.17	1.03	2.18	4.99	6.41	5.74
2015	21.44	1.92	17.67;25.21	24.04	18.85	12.84	8.45	1.07	2.27	5.13	6.99	5.82
2016	23.02	1.99	19.12;26.91	25.49	19.33	13.49	8.73	1.12	2.36	5.26	7.56	5.91
2017	23.60	2.00	19.67;27.54	26.94	19.80	14.15	9.00	1.16	2.46	5.39	8.14	6.00
2018	23.19	1.97	19.32;27.06	28.39	20.27	14.80	9.28	1.21	2.55	5.52	8.71	6.09

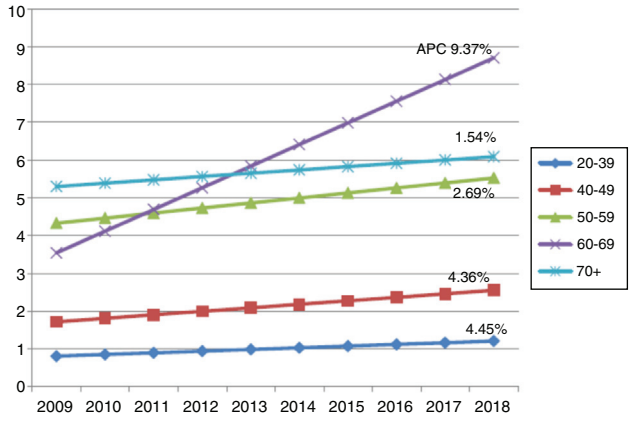

Fig. 1 – Age-specific trend in CRC incidence with APCs*. *Group aged 20–39 labelling in blue; aged 40–49 labelling in red; aged 50–59 labelling in green; aged 60–69 labelling in violet; and aged 70+ in turquoise, respectively.

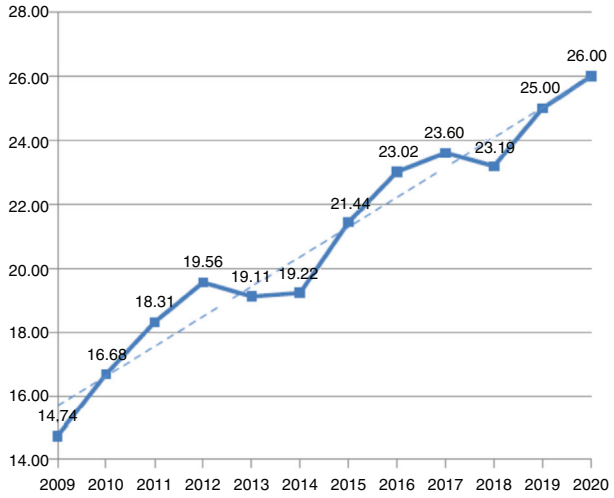

Fig. 2 – Overall CRC incidence rates by years, including prognostic indices for 2019–2020.

group at risk, and specialists responsible for population to be screened in countryside, should take this consideration into account.

It is appropriate to assume that impressive dynamics in stages at presentation - positive APC of Stage I (28.91%) and negative annual growth for Stage III (−7.62%) are provided by the launched screening program which significantly impacted the disease revealing.

Further prognosis on CRC incidence for 2019–2020 was performed. Prognostic rates evidence its continuing growth to 25.01 by 2019 (95% CI 23.69–26.34) and up to 25.94 by 2020 (95% CI 24.43–27.46), respectively.

Data on the overall CRC incidence rates by years, including prognostic indices for 2019–2020 are also presented graphically (Fig. 2).

Discussion

This retrospective study provided summarized information on the rates and trends of CRC in the province within first decade of the screening implementation. As it is presented in Table 3, the averaged crude incidence rate between 2009 and 2018 has been found substantially high (19.88 per 100,000), besides, further tendency to rise with positive APC of 4.69% is traced.

While in western Kazakhstan the screening uptake for the time being is accompanied with continuing rise in CRC incidence, the U.S. authors recorded negative APC (−2.7%) at incidence rate of 45.9 within 14 years, 2000–2014.[9] Reportedly, until the late 1980s colorectal cancer was the second leading cause of cancer-related deaths for both men and women in the United States.[10] At a later date the overall age-adjusted CRC incidence rate decreased steadily between 1975 and 2010 in patients aged 50+ years owing to the screening program introducing since late 1980s.[11] The U.S. authors clarified that the overall incidence in whites as being 75.5/100,000 and up to 83.6/100,000 in black persons then decreased since 1980s until 2010–2013, but only among the screening-age population (ages 50 years or older).[12–14]

Overall, the role of nationwide screening programs based on iFOBTs (FITs), followed by colonoscopy to reduce the CRC mortality rates currently is proven persuasively. The USPSTF research group reported that the "biennial screening with the guaiac-based FOBT compared to no screening resulted in reduction of CRC-specific mortality at 11–30 years of follow-up, ranging 9%–22% after 2–9 rounds of screening" (based on 5 RCTs, n = 404,396).[15] Based on data from 59,389 screenees age 50 to 69 years, researchers from Taiwan found that after a positive FIT-based screening, colonoscopy can reduce by about half the number of deaths from CRC.[16]

There is an accompanying effective measure to prevent growing incidence of CRC through increasing of public

Table 3 – Pivotal table on some key CRC indices within 2009–2018 in the Aktobe province.

Population groups	Rate	St. error	95% CI, lower	95% CI, upper	Rate ratio, RR	APC, %	p-value
Total	19.88	1.91	15.76	21.05		4.69	
Gender							
Female	10.6	1.36	7.93	13.23	ref.	2.61	
Male	9.3	1.27	6.80	11.80	0.88	6.64	0.0009
Ethnicity							
Others	0.8	0.37	0.07	1.53	ref.	11.4	
Kazakhs	11.8	1.44	8.99	14.61	14.75	8.7	0.0003
Slavs	7.3	1.13	5.09	9.51	9.13	−4.3	0.002
Residence							
Urban area	12.9	1.5	9.96	15.84	ref.	3.3	
Rural area	6.9	1.1	4.75	9.05	0.53	17.6	0.011
Age							
20–39	0.92	0.4	0.13	1.71	ref.	4.45	
40–49	1.89	0.57	0.76	3.02	2.05	4.36	0.006
50–59	4.56	0.89	2.81	6.31	4.96	2.69	0.0002
60–69	6.48	1.06	4.39	8.57	7.04	9.37	0.002
70+	6.01	1.02	4.00	8.02	6.53	1.54	0.0004
Stage							
I	1.09	0.44	0.23	1.95	ref.	28.91	
II	12.11	1.45	9.26	11.11	4.7	3.24	0.00016
III	3.58	0.79	2.03	5.13	3.28	−7.62	0.0069
IV	3.08	0.73	1.64	4.52	2.86	11.75	0.0052
Tumor site							
C18.0–C18.4	3.7	0.8	2.12	5.28	ref.	1.86	
C18.5–C18.7	5.7	1.0	3.74	7.66	1.55	5.08	0.0023
C19	3.4	0.77	1.89	4.91	1.03	6.26	0.057
C20–C21	7.1	1.11	4.83	9.17	1.89	2.27	0.0044

awareness on the disease which could arise a willingness to undergo a screening. According to mentioned US authors, not only the screening uptake, but arranging of nation-scale public health campaigns such as “Screen for Life”, allowed for significant decline in the CRC incidence rates.[9] The findings of Saudi authors (Zubaidi et al.) who have explored the level of public awareness and possible ways to raise a willingness to undergo CRC screening, are of great interest as being universal in respect to population of any countries.[17] Almadi et al. upon studying the effect of public knowledge concluded that “neither gender, level of education, occupation, income, marital status, nor general knowledge about CRC was found to be associated with the willingness to undergo CRC screening”.[18] As much as a majority of people are mostly negative about CRC screening, likely, only nationwide media campaigns may run as quite an effective tool to change their perception.

According to our data, although the highest proportion and annual growth were recorded in patients aged 60–69 (31.0%, APC 9.37%), the younger groups of age 20–39 and 40–49 (5.3% and 7.3%, respectively) also demonstrated quite sizable annual growth (APCs within 4.5%). Analysts from the USA noted that “the lifestyle behaviors, such as consuming unhealthy diets and physical inactivity, with the resultant increase in the prevalence of overweight and obesity were possible factors contributing to the increased rates of CRC among people younger than 50 years”.[11] Such environmental factors as cultural and economic relations play in this context considerable role, as low- and middle income countries have adopted diet and lifestyle practices similar to high-income countries. In regard to CRC, across Sub-Saharan Africa (SSA), reportedly, the significant affecting of younger patients under 40 years has been observed, compared to 3%–7% in high-income countries, which is related mostly to nutrition transition made by native Africans in favor of western food.[19] The issues of consuming unhealthy, particularly processed food leading to obesity have widely been studying the latest years.[20,21] Recently presented data on associations between ultra-processed food consumption and risk of cancer statistically proved a global trend: a 10% increase in the proportion of such a food is linked to a more than 10% in the risks of overall cancer.[22,23]

Based on our Registry, data on rates and APCs by CRC tumor subsites (Table 3) partly vary from the USA’s indices within 2000–2014,[9], as the ascending colon (20.0 per 100,000 in the USA, 42.9%) is not a predominant location of the neoplasm in western Kazakhstan, unlike the descending part (28.7%) and, particularly, rectum (35.3%), though the most sharp growth (APC 6.26%) is recorded in C19, recto sigmoid junction. Saudi authors, who also marked the growing CRC incidence in the country last years, reported almost similar data on the tumor sites distribution: rectum 28.1% and sigmoid 37.7% with a negligible proportion of the ascending colon.[24]

In order to get an overall idea on our current situation with CRC incidence rates, the same indices throughout other countries from different world regions were being compared. Reportedly, as of 2016 across the European high-income countries, CRC incidence rates were 38.9 in Norway and 29.2 in Sweden, whereas in Finland, where a national organized program was available, they were 23.5, respectively.[25] The most populated country of Latin America, Brazil, has also faced high incidence and mortality from CRC, and both indices imminently tended to grow. Until the year 2025, mortality rates are expected at the level of 75.8% in men and 67.5% in women in Brazil.[26] From the other hand, in Mediterranean countries, adhered to a Mediterranean dietary pattern, noticeably low

incidence of cancers linked to dietary factors, including CRC has been observed comparing to Scandinavian countries, the United Kingdom, and the United States.[27]

Thus, our region with the actual incidence rate of 19.88 per 100,000 currently takes the mid position among the listed countries, but overall trends in incidence predict further worsening that can be prevented through the national screening program.

Strengths and limitations of the study

Overall, the incidence rates analysis among various population groups may be referred to strengths of this epidemiological study. In fact, identifying the group at risk on CRC development in the region was the most important value of the research performed. Meanwhile, data on the trends in CRC precancerous conditions diagnosis were not analyzed and discussed in frames of this study, as well as other key indices, such as mortality and survival rates. This shortness may be considered undoubtful limitation.

Conclusions

The overall vector of CRC incidence through the first decade of the screening implementation in western Kazakhstan evidenced its 1.5 fold growth with further expected rise. However, the increment of stage I portion vs. advanced stages at diagnosis by 2018, as well as the trend to decrease in rates among urban population inspires, to a definite extent, assurance in unconditional efficiency of the screening programmed in long run.

Data obtained must contribute to changing a current state of things, such as fast growing CRC rates among rural people, for whom timely medical examination is far less available. Public awareness to prevent CRC diagnosis at advanced stages should be straightened through the nationwide media campaigns.

The next researches on CRC should include scenarios to highlight and differentiate as much as possible the role of disadvantaged environment in the region and consuming unhealthy, in particular ultra-processed food.

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Conflicts of interest

The authors declare no conflicts of interest.

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