Research Journal of Medical Sciences 11 (2): 114-118, 2017
ISSN: 1815-9346

Colorectal Cancer and Ethnic Groups in Kazakhstan. A Retrospective Study of 709 Cases

[1]Rassim A. Kerimov, [2]Bakhytzhan D. Seksenbayev, [3]Oleg V. Galimov,
[2]Bekaydar K. Nurmashev and [4]Murat E. Zhanteyev
[1]Department of Medicine, Khoja Akhmet Yassawi International Kazakh-Turkish University,
B. Sattarkhanov Avenue 29, 161200 Turkestan, Kazakhstan
[2]Department of Administration, South Kazakhstan State, Al-Farabi Square,
Pharmaceutical Academy 1, 160019 Shymkent, Kazakhstan
[3]Department of Surgical Diseases and New Technologies, Bashkortostan State Medical University,
Lenin St. 3, 450000 Ufa, Russia
[4]Department of Abdominal Surgery, South Kazakhstan Regional Oncology Dispensary,
Baitursynov St. 85a, 160021 Shymkent, Kazakhstan

Abstract: Colorectal cancer keeps an upward incidence trend worldwide. Many studies show that colon cancer is preventable disease in most cases: 70% of them might be avoided by lifestyle and diet changes. Despite the globalization processes, ethnic mode of life at a certain extent forms lifestyle and nutrition habits of the Kazakhstan population. Disparities in people traditions may be reflected in the features of colorectal cancer development among different ethnic groups of the studied areas. The aim of the study was to assess associations between colorectal cancer and major ethnic groups residing in Kazakhstan. This was a retrospective study in which we analyzed all primary cases of colorectal cancer registered in 2013 year. All records were provided by the regional oncology centers in 4 regions of the republic. Eventually, a cohort of 709 cases was formed. Each record of the disease was analyzed in terms of ethnicity, age, gender, disease stage and tumor location. A significant association between colorectal cancer and ethnicities was found in the patient group ($\chi^2_{(2)} = 213.5, p<0.001$): in Russians, the disease was registered 1.9 time as many as it was expected. No associations between colorectal cancer and tumor location were found for any ethnic group. The study suggests a significant association between the disease and the ethnic groups residing in Kazakhstan. Nutrition and lifestyle tendencies might play rather important role in this matter than any biological signs. We suggest a case-control study should be conducted for further investigation of revealed relationship.

Key words: Colorectal cancer, globalization, nutrition, ethnicity, tendencies

INTRODUCTION

In 2006, cancer of the colon and rectum took the 5th place among all malignancies in Kazakhstan (Ward *et al*., 2004). The disease rate gradually rose from year to year. And in 2014, it was the third most frequent malignant illness in the Republic (3086 cases) behind lung and breast cancers (Kamkhen and Turbekova, 2015). Increasing incidence of the disease is consistent with a prognosis of the International Agency for Research on Cancer (IARC), according to which global cancer rates could rise by 1.5 times by 2020 mainly at the expense of lung and colorectal cancer 14.

Growing incidence of the malignancies may be caused by the risk factors which unfortunately become a part of everyday life in many cases. Despite the fact that strong correlations between heredity and colorectal cancer have been found (Dragovich, 2016), according to IARC's report, genetic susceptibility involved in <5% of the cases 14. In addition, colon and rectum cancer was generally indicated as a preventable disease: 70% of the cases were caused by diet and lifestyle habits (Anand *et al*., 2008). In this regard, the World Cancer Report (released by IARC in 2003) described Western lifestyle and nutrition as being associated with some risk factors of cancer development: a highly caloric diet combined with low physical activity. Moreover, industrial societies of developed countries were characterized by the earlier onset of smoking and long exposure to occupational carcinogens. All these points might lead to

Corresponding Author: Rassim A. Kerimov, Department of Medicine,
Khoja Akhmet Yassawi International Kazakh-Turkish University, B. Sattarkhanov Avenue 29,
161200 Turkestan, Kazakhstan

the higher malignant morbidity in affluent countries. But at the same time, the report made reservations about the developing world: coming wealth and industrialization would result in the rapid lifestyle changes what might also lead to an increase of cancer incidence there.

Although, globalization processes influence the population of Kazakhstan, still there is no obvious unification of the peoples' lifestyles in different parts of the republic. Traditional patterns might play more essential role in this matter. It is commonly understood that they are closely related with any ethnic culture and at a certain extent may concern particular qualities of a diet which in turns, may cause or on contrary, mitigate some risk factors of colorectal cancer. Moreover, an attitude to medical care may also vary among the different people traditions what may delay or on the contrary, provide appropriate treatment of the disease.

Above listed points might result in cancer disparities in relation to ethnic and racial groups. It was shown in several studies performed in the USA what in turns, increased awareness among healthcare organizations of the country. For example, Ward *et al.* (2004) in their study showed that African Americans, American Indians, Asian and Pacific Islanders had lower 5 year survival than non-Hispanic Whites (Ward *et al*., 2004). A decade earlier, Jessup *et al.* (1996) indicated that above-mentioned race and ethnic groups had less access to medical care (Jessup *et al*., 1996). Yusup *et al.* (2013) found that Uygur patients were associated with younger age, more aggressive colorectal cancer and significantly worse prognosis than Chinese patients (Yusup *et al*., 2013). Koo *et al.* (2008) studying outcomes of colorectal cancer in Australia revealed that Asians were diagnosed at a younger age and had fewer poorly differentiated malignancies than Australians (Koo *et al*., 2008). Interesting findings concerning tumor location among different ethnicities were found by Le *et al.* (2008): in their study, sigmoid colon was the most common location for Filipinos and the least common for Caucasians (Le *et al*., 2008). Basing by sigmiodoscopy results, Theuer *et al.* (2001) reported that left-sided colorectal cancer (distal to the splenic flexure) had been more common among Asian patients followed by Latino ones.

If we take into account that the population of Kazakhstan is not homogeneous in its ethnic makeup and consists of two major groups (Kazakhs and Russians) with an essential influence of traditional mode of life, it becomes clear that there are several distinct lifestyle patterns in the republic. In this connection, we studied some features of the disease development in major ethnic groups residing in the studied areas.

MATERIALS AND METHODS

A retrospective survey included all cases of colorectal cancer registered in 2013. We excluded from the analysis the cases of follow-up patients and the histories with no data on studied variables. Eventually, a cohort of 709 cases of the disease was formed. All medical records were provided by the Regional Oncology Centers located in the cities of Shymkent (South Region of Kazakhstan), Karaganda (Central Region), Ust-Kamenogorsk (Eastern Region) and Aktau (Western Region). Each center was a governmental hospital providing diagnostic, treatment and consulting assistance for cancer patients residing in the corresponding regions. Their bed capacities were 50, 200, 215 and 342 for Aktau, Shymkent, Ust-Kamenogorsk and Karaganda centers accordingly.

Kazakhs, Russians and 'Others' were considered as ethnic groups. 'Others' included rest ethnicities which were too small in quantity to be considered as separate categories. 'Age' was only numerical data in the study. We calculated mean age and its standard deviation. Spearman's rank method was used for calculating a correlation coefficient between years old and the disease.

For all nominal data, we compared distributions of both groups: the 1st group included patients, the 2nd one included controls in an equal number. The latter were based on official data for the studied regions 1. Expected proportions of ABO blood types were calculated with considering the blood type distribution inherent for each ethnic group (Burkitbay, 2004). Control distributions of tumor location and stage were calculated on the basis of their frequencies in the entire patient group.

Null hypotheses were tested by comparing shares in tables. Comparisons for nominal data were made by a χ^2-test. A critical level of the test was assumed to be 3.84, 5.99 and 7.81 (for df = 1, 2 and 3 accordingly). The critical level of statistical significance was accepted to be 0.05. Effect size was calculated by means of Cramer's V; the strength of the relationship was estimated by recommendations of Rea and Parker. The tumors were grouped by anatomic subsites as follows: right colon (cecum and ascending colon), transverse colon (hepatic flexure, transverse colon, splenic flexure), left colon (descending colon, sigmoid) and rectum (rectosigmoid, rectum).

The tumor stages were sorted by a staging system of the American Joint Committee on Cancer (AJCC system): 1-a tumor within submucosa or muscularis propria, no metastasis; 2-a tumor invades subserosa, adjacent organs or perforates peritoneum, no any metastasis; 3-metastasis to 1-3 regional lymph nodes, extending of a tumor may be

any described above; 4-distant metastases. Selection bias was minimized due to the survey included all primary cases of colorectal cancer. There were not measurement and interpretation biases because of the nature of the study.

RESULTS AND DISCUSSION

About 709 disease cases were enrolled in this study (345 men and 364 women) Table 1. The distribution of ethnic groups in patients was Kazakhs 36.8%, Russians 45.7% and 'Others' 17.5% while their frequencies in the general population of the studied regions were 61.9, 24.1 and 14% accordingly. These differences were highly significant ($\chi^2_{(2)} = 213.5$, $p<0.001$). According to Rea and Parker recommendations, the relationship was considered as moderate (V = 0.32). Similar differences were revealed when entire patient group was divided into the studied regions of the republic ($p<0.001$, Cramer's V was >0.3).

Mean age was 59.7 for the whole group (for Kazakhs 59.9, Russians 63.7 and Others 62.2). Patient age ranged from 20-88 year. There was a direct correlation between the disease and age for all considered ethnicities. Gender proportions for Kazakhs and Others did not significantly differ from the expected ratio. However, there was a gender disparity in Russians with women being prevalent: 62.1% in patients vs. 51.2% in general population ($\chi^2_{(1)} = 15.1$, $p<0.001$, V = 0.12). The most common location of colorectal cancer was the rectum being prevalent across all ethnic groups. The less common tumors were located in the right and transverse colon. No associations between the tumor locations and the ethnic groups were found ($p>0.15$ for all groups).

Studied groups had slightly unequal proportions of the disease stages. Shares of 1 and 2 stages were more common than expected in Russians and less frequent in Kazakhs (13.2 and 46.2% vs 8.8 and 33.7% accordingly). On contrary, shares of 3 and 4 stages were more common in Kazakhs than in Russians (38.7 and 18.8% vs 29 and 11.4%). Revealed differences were significant, however associations between the stages and the ethnic groups had no strong effect size (V = 0.12 for Kazakhs and V = 0.09 for Russians).

Jessup *et al.* (1996) showed that right-sided colon cancer was more than half of all cases (54.7%) in the US (Jessup *et al.*, 1996) while, in our cohort, it was only 13.4% for all patients. In contrast to Le *et al.* (2008) and Theuer *et al.* (2001) studies, we did not find significant associations between tumor locations and any ethnic group.

The share of Russians in the patient group significantly exceeded prevalence of this ethnicity in the studied regions of Kazakhstan (45.7% vs. 24.1%, $p<0.001$). On the contrary, Kazakhs in the studied groups were less common than expected shares (36.8% vs. 61.9%, $p<0.001$). Revealed associations between the tumor and the ethnic groups might be explained by the following possible causes: genetic susceptibility, nutritional factors and a level of seeking the medical care which might vary in the studied groups. According to IARC, heredity resulted only in 5% of the disease cases 14. Hence, the rest possible causes deserve more detailed consideration.

Table 1: ABO blood types, gender, tumor location, stages, living places and ethnic groups

	Ethnic groups						
	Kazakhs		Russians		Others		
Variabls	1st group (95% CI)	2nd group	1st group (95% CI)	2nd group	1st group (95% CI)	2nd group	Total
No. of cases	261 (235.8-286.2)	439	324 (298-350)	171	124 (104.2-143.8)	99	709
Gender							
Men	127 (111.2-142.8)	127	123 (105.9-140.1)	158	63 (52.1-73.9)	60	345
Women	134 (118.2-149.8)	134	201 (183.9-218.1)	166	61 (50.1-71.9)	64	364
Tumor location							
Right	43 (33.5-52.5)	35	41 (31.5-50.5)	42	11 (4.9-17.1)	17	95
Transverse	19 (12.1-25.9)	20	24 (16.8-31.2)	25	12 (6-18)	9	55
Left	50 (38.3-61.7)	64	96 (83.2-108.8)	79	26 (16.8-35.2)	30	172
Rectum	149 (130.2-167.8)	142	163 (144-182)	178	75 (59.8-90.2)	68	387
Stages							
1	23 (15.2-30.8)	28	43 (34.6-51.4)	34	9 (3.5-14.5)	13	75
2	88 (72.6-103.4)	109	150 (133.1-166.9)	136	60 (46.4-73.6)	52	298
3	101 (86.2-115.8)	85	94 (79.4-108.6)	106	36 (25.2-46.8)	41	124
4	49 (39-59)	39	37 (27.4-46.6)	48	19 (11.3-26.7)	19	105
Living places							
South Region	149 (133.3-164.7)	190 (72.93%)	47 (34.8-59.2)	12 (4.6%)	65 (51.3-78.7)	59 (22.47%)	261
Karaganda Region	51 (38.6-63.4)	117 (55.35%)	138 (123.3-152.7)	85 (36.52%)	44 (32.3-55.7)	31 (13.13%)	233
Eastern Region	35 (24.6-45.4)	105 (59.37%)	133 (121.8-144.2)	65 (37.11%)	8 (2.6-13.4)	6 (3.52%)	176
Mangystau Region	26 (20.2-31.8)	35 (90.26%)	6 (1.6-10.4)	2 (6.1%)	7 (2.3-11.7)	2 (3.64%)	39

*1st group-patients; 2nd group-controls

As mentioned before, in the studied regions, ethnic traditions play a significant role in peoples' lifestyle. Notoriously, many of them have been closely attributed with any religion. In this regard, it might be assumed that ethnic groups confessing Islam (Kazakhs) were under more rigorous restrictions on lard and alcohol consumption that among others were listed as the disease risk factors (Watson and Collins, 2011). In addition, Russians, probably might have been more prone to the Western lifestyle. The latter was described in the World Cancer Report as closely associated with risk factors increasing probability of cancer development.

From the other hand, our results suggest that patients of any ethnic group might face with some barriers to seek medical assistance. We found, for example, some differences in the stage distribution between ethnic groups: initial stages of the disease were more frequent in Russians while advanced stages were more common in Kazakhs. However, small value of these differences might indicate that unequal access to a medical care might have not been main reason of such a significant ethnic disparity; this, in turns may point that the revealed patterns of the disease distribution among the peoples might be caused mainly by the primary risk factors. It might also be assumed that in other settings where these ethnic groups lived under the same lifestyle and traditional factor played a negligible role, we would not find such a disparity.

Nevertheless, for further research of the revealed association between ethnicities and the disease, we suppose, it may be appropriate to carry out a case-control study for analyzing all possible risk factors with traditional lifestyle being considered. We suggest that comprehensive knowledge of colorectal cancer development in diverse populations would provide necessary information for health policy makers to enhance prophylactic measures. For instance, colorectal screening programs may include any cultural features of the ethnic groups. In turns, this may produce advances in prevention of the disease development in the population scale.

CONCLUSION

The results suggest an association between the ethnic group and colorectal cancer in Kazakhstan. This cancer disparity may be caused by different lifestyles and nutrition among ethnicities residing in the studied regions. Causes that result in this relationship require further research which would help to develop strategies mitigating the disease risk factors in the population.

LIMITATIONS

Results of the study should be carefully applied to the same ethnic groups in other populations since it should be considered that revealed patterns unlikely resulted from any biological features but rather connected with the local disparities in modes of life.

ACKNOWLEDGEMENTS

For informational support authors of the article are grateful to Dr. Nurgali Ormanov (Oncology Dispensary of Shymkent), Dr. Zhomart Kenzhalin (Oncology Dispensary of Ust-Kamenogorsk), Dr. Nurlan Dzhariev (Oncology Dispensary of Aktau), Dr. Muratbek Zhumakayev (Oncology Dispensary of Karaganda).

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