RESEARCH ARTICLE

Colorectal Cancer Risk Factors among the Population of South-East Siberia: A Case-Control Study

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Abstract

Colorectal cancer remains one of the most widespread malignancies in the world. However, there is a lack of comprehensive studies considering colorectal cancer risk factors among Russian populations, particularly in Siberia. The aim of this investigation was to determine the impact of various lifestyle, dietary, family, and socioeconomical factors on colorectal cancer risk in South-East Siberia. We recruited 185 Russian colorectal cancer cases and 210 gender-, age-, and ethnicity-matched asymptomatic controls with no history of any malignant tumor, using a specially designed questionnaire to obtain relevant information. After the statistical analysis, we defined several significant factors affecting colorectal cancer risk. Among these were smoking (OR=2.13, 95%CI=1.4-3.24, P=0.0004), being overweight (BMI between 25-30, OR=2.45, 95%CI=1.49-4.03, P=0.0004), alcohol drinking (OR=8.73, 95%CI=5.49-13.87, P<0.0001), beer drinking (OR=9.24, 95%CI=5.14-16.61, P<0.0001), consumption of hard liquor (OR=9.37, 95%CI=5.92-14.82, P<0.0001), excessive red meat consumption (P<0.0001), excessive intake of red meat products (P<0.0001), excessive intake of dairy products (P<0.0001), excessive sour cream and cheese consumption (P<0.0001 and 0.0002, respectively), spicy food consumption (OR=2.87, 95%CI=1.9-4.33, P<0.0001), family history of gastrointestinal malignant tumors (OR=3.99, 95%CI=2.09-7.59, P<0.0001), and income exceeding twice the subsistence minimum (OR=5.34, 95%CI=3.35-8.53, P<0.0001). Certain factors, such as high concentration of salt in the food and precancerous colonic lesions, demonstrated borderline significance (OR=3.45, 95%CI=1.68-7.1, P=0.0008, and OR=5.25, 95%CI=1.94-14.22, P=0.001, respectively). Some factors were established as protective, like consumption of rye bread and both rye and wheat bread (OR=0.32, 95%CI=0.21-0.5, P<0,0001, and OR=0.07, 95%CI=0.02-0.21, P<0.0001, respectively), and also low concentration of salt in the food, although this was of borderline significance (OR=0.43, 95%CI=0.26-0.69, P=0.0006). ABO and Rhesus blood antigens were not associated with increased colorectal cancer risk. These results should be definitely applied for elaboration of programs of colorectal cancer prevention in Russia, particularly in Siberia.

Keywords: Colorectal cancer - epidemiology - risk factors - Russian populations - blood group - South-East Siberia

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Introduction

Colorectal cancer remains one of the most widespread malignancies in the world. According to the last global oncoepidemiological analysis (Jemal et al., 2010; 2011; Ferlay et al., 2010), it is the second most common cancer among women, and the third most common cancer among men. In 2008, more than 1, 2 million of new colorectal cancer cases and about 609,000 deaths caused by colorectal cancer were registered (Ferlay et al., 2010). There is almost 10-fold difference in colorectal cancer incidence between distinct geographic regions (Jemal et al., 2010). The highest incidence was revealed in Europe (Germany, Czech Republic and Slovakia), North America, Japan, Australia, and New Zealand; the lowest incidence was noted in Africa, South and Central America, and South-Central Asia (India and Pakistan), and the incidence among men is significantly higher than among women (Jemal et al., 2010; 2011). There is a tendency to elevation of colorectal cancer incidence in certain regions where it was low before (Japan, Korea, China, Spain, Czech Republic, Slovakia, Slovenia), that has attracted the attention of cancer epidemiologists (Center et al., 2009a; 2009b). It may be caused by a combination of various factors, such as shift of dietary pattern, increase in average BMI, and increase in smoking prevalence (Garcia-Alvarez et al., 2007; de Kok et al., 2008; Martin et al., 2008 ;Center et al., 2009a; 2009b). According to the recent data, USA is the only country where a steady decline of colorectal cancer incidence among both men and women has been observed during the latest years (Center et al., 2009b; Edwards et al., 2010). Possibly, this may be due

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to implementation of wide-ranging screening measures in populations; consequently, it leads to considerable prevalence of early detection and adequate treatment of precancerous lesions (Center et al., 2009b; Edwards et al., 2010). Additionally, stabilizing of incidence has also been noticed in Canada and New Zealand (Center et al., 2009a, 2009b).

Unfortunately, colorectal cancer mortality still increases in the majority of countries due to limitation of allocated resources and to underdevelopment of medical infrastructure (Center et al., 2009b). This problem is particularly actual for Mexico, Brazil, and Romania (Center et al., 2009b). At the same time, in certain Western countries the trend to decline of colorectal cancer mortality has been observed (Center et al., 2009b), which is related to an increase in the share of early detected cases, and to a progress in treatment (Chu et al., 1994; Sant et al., 2001; Mitry et al., 2002; Edwards et al., 2010). 5-year-survival after the detection of colorectal cancer varies from 28-42% (Sankaranarayanan et al., 1999; Sankaranarayanan et al., 2009) to more than 60% in USA, Japan, and Switzerland (Coleman et al., 2008; Sant et al., 2009).

In Russia, colorectal cancer is the second most common cancer in men, and the third most common cancer in women (Zhivotovskiy et al., 2012). In 2009, 57, 363 new colorectal cancer cases were registered in Russia, that is 20,7% higher compared to 2000 (Zhivotovskiy et al., 2012). Standardized incidence rates increased from 11,44 to 13, 5 per 100,000 for colon cancer (mean year increment 1, 9%), and from 9, 6 to 10, 7 per 100,000 for rectal cancer (mean year increment 1, 2%), and the incidence raised higher in men than in women (Zhivotovskiy et al., 2012). The number of deaths from colorectal cancer in 2009 was 38,343, that is 10% higher in comparison with 2000 (Zhivotovskiy et al., 2012).

There is a number of well-known correctable colorectal cancer risk factors including smoking, low physical activity, overweight and obesity, excessive alcohol, red meat and processed meat consumption (Giovannucci and Wu, 2006; Ferrari et al., 2007; Boyle and Levin, 2008). The problem of wide implementation of relevant screening programs is particularly actual for the countries with increasing lifespan and gradually westernizing lifestyle (Mandel et al., 1993; Muller and Sonnenberg, 1995; Zauber et al., 2008; Lambert et al., 2009).

To date, there is a lack of comprehensive studies regarding colorectal cancer risk factors among Russian population, particularly Siberian population. Therefore, the present study was aimed to define the impact of various lifestyle, dietary, family, and socioeconomical factors on colorectal cancer risk in population of South-East Siberia.

Materials and Methods

The study was conducted at Kemerovo Regional Clinical Oncological Dispensary, which is the only cancer center in the city, and at primary Kemerovo healthcare centers from September 2011 to September 2012. Kemerovo Regional Clinical Oncological Dispensary is a referral center for all colorectal cancer patients throughout the North of Kemerovo Region. We recruited 185 Russian colorectal cancer cases and 210 gender-, age- (±4 years), and ethnicity-matched asymptomatic controls with no history of any malignant tumor. To collect relevant information about risk factors, special questionnaire, the same for cases and controls, was designed by all authors. In addition to classical colorectal cancer risk factors, such as smoking, high red and processed meat intake, low intake of fruits and vegetables, overweight/obesity, family history, we included certain additional risk factors, for instance, ABO and Rh blood groups, water supply features, storey of living, consumption of spicy and salt food, and dairy products. Interviews were carried out by trained nurses and surgeons. In addition, clinicopathological features of cancer patients were extracted from case histories and then documented by the surgeons. The study is in compliance with the Helsinki declaration, and it has been approved by the Medical Ethical Committee of Kemerovo State Medical Academy. All the study participants signed the informed consent prior to their inclusion in the study on their own accord.

For the collection of data about ABO and Rh blood groups, we used medical records from 2,063 cancer patients living in Kemerovo and neighboring settlements for ten-year period of time (2002-2012). Data were presented on 388 cases of cancer of the caecum, ascending, transversal, and descending colon, 397 cases of cancer of the sigmoid and 1278 cases of rectal cancer. All the cancer cases were histopathologically confirmed. The control group was formed from the database of blood donor records from Kemerovo Regional Blood Transfusion Station and included 22,581 individuals. The distribution of ABO and Rh blood groups in the control group is supposed to reflect the general population of Kemerovo Region and Southern Siberia. Determination of blood groups in both cases and controls was performed by conventional serological methods. Monoclonal anti-A, anti-B, and anti-AB antibodies were used to determine ABO blood groups, while Rhesus factor was identified by anti-D (IgM) monoclonal antibodies ("Gematolog", Moscow).

Statistical analysis was performed by utilizing the MedCalc v.9.6.4.0 (MedCalc Software, Belgium). Distribution of all numerical data were ascertained as non-parametric (rejection of normality was assessed by D'Agostino-Pearson test and Kolmogorov-Smirnov test), so all differences between continuous variables were evaluated by Mann-Whitney test. For categorical variables, χ^2 test was used. Odds ratio (OR) and 95% confidence intervals (95%CI) were also calculated where it was possible to define the referent group. All P values were two-tailed and those less than 0.05 were considered as statistically significant. In addition, for the avoiding of multiple comparisons effect, Bonferroni correction was applied. Since there were 95 comparisons, only P value less than 0,0005 were considered as statistically significant.

Results

Table 1 shows the colorectal cancer risk factors from the questionnaire. Of 79 general risk factors (all excluding ABO and Rh blood groups), 23 were statistically

significant (P<0,0005 after Bonferroni correction). These risk factors were smoking (OR=2.13, 95%CI=1.4-3.24, P=0.0004), overweight (BMI between 25-30, OR=2.45, 95%CI=1.49-4.03, P=0.0004), alcohol drinking (OR=8.73, 95%CI=5.49-13.87, P<0.0001), beer drinking (OR=9.24, 95%CI=5.14-16.61, P<0.0001), consumption of hard drinks (OR=9.37, 95%CI=5.92-14.82, P<0.0001), excessive red meat consumption (P<0.0001), excessive intake of red meat products (P<0.0001), excessive intake of dairy products (P<0.0001), excessive sour cream and cheese consumption (P<0.0001 and 0.0002, respectively), spicy food consumption (OR=2.87, 95%CI=1.9-4.33, P<0.0001), family history of gastrointestinal malignant tumors (OR=3.99, 95%CI=2.09-7.59, P<0.0001), and income exceeding 2 subsistence minimum (OR=5.34, 95%CI=3.35-8.53, P<0.0001). In addition, certain factors, such as high concentration of salt in the food and precancerous colonic lesions, were at borderline significance (OR=3.45, 95%CI=1.68-7.1, P=0.0008, and OR=5.25, 95%CI=1.94-14.22, P=0.001, respectively). Some factors were established as protective, for instance, consumption of rye bread and both rye and wheat bread

Table 1. Colorectal Cancer Risk Factors Among the Population of South-East Siberia

Characteristic		Case group		Control group		OR (95%CI)		P value
Smoking	Non-smokers	111/185	(54.6%)	155/210	(73.8%)	Ref.		0.0004*
	Smokers	84/185	(45.4%)	55/210	(26.2%)	2.13	(1.4-3.24)	
	Median of age of smoking beginning	18	(16-20)	18	(17-20)			0.77
Smoking index	<10	20/84	(23.8%)	11/42	(26.2%)	Ref.		
	10-25	25/84	(29.8%)	15/42	(35.7%)	0.91	(0.35-2.43)	0.86
	>25	39/84	(46.4%)	16/42	(38.1%)	1.34	(0.52-3.42)	0.54
Body mass index	Distrophy (<18)	3/180	(1.7%)	1/205	(0.5%)	5.25	(0.53-51.77)	0.16
(BMI)	Normal weight (18-25)	52/180	(28.9%)	91/205	(44.4%)	Ref.		
	Overweight (25-30)	70/180	(38.9%)	50/205	(24.4%)	2.45	(1.49-4.03)	0.0004*
	Grade 1 obesity (30-35)	40/180	(22.2%)	35/205	(17.1%)	2.00	(1.13-3.53)	0.02
	Grade 2 obesity (35-40)	11/180	(6.1%)	20/205	(9.8%)	0.96	(0.43-2,16)	0.93
	Grade 3 obesity (>40)	4/180	(2.2%)	8/205	(3.8%)	0.87	(0.25-3.04)	0.83
Diabetes	No diabetes	160/185	(86.5%)	168/210	(80%)	Ref.		
	Glucose intolerance	7/185	(3.8%)	2/210	(1%)	3.67	(0.75-17.9)	0.11
	Diabetes	18/185	(9.7%)	40	(19%)	0.47	(0.26-0.86)	0.01
Alcohol	Non-drinkers	37/185	(20%)	144/210	(68.6%)	Ref.		
	Drinkers	148/185	(80%)	66/210	(31.4%)	8.73	(5.49-13.87)	<0.0001*
Beer	Non-drinkers	105/185	(56.8%)	194/210	(92,4%)	Ref.		
	Drinkers	80/185	(43.2%)	16/210	(7.6%)	9.24	(5.14-16.61)	<0.0001*
	Less than 1 bottle per week	24/80	(30%)	6/14	(42.9%)	0.96	(0.27-3.39)	0.95
	1 bottle per week	25/80	(31.3%)	6/14	(42.9%)	Ref.		
	More than 1 bottle per week	31/80	(38.7%)	2/14	(14.2%)	3.72	(0.69-20.05)	0.13
Wein	Non-drinkers	156/185	(84.3%)	187/210	(89.5%)	Ref.		0.17
	Drinkers	29/185	(15.7%)	23/210	(10.5%)	1.51	(0.84-2.72)	
	Less than 1 glass per week	24/28	(85.7%)	13/23	(56.5%)	Ref.		
	1 glass per week	2/28	(7.15%)	10/23	(43.5%)	0.22	(0.06-0.83)	0.025
	More than 1 glass per week	2/28	(7.15%)					
Hard drinks	Non-drinkers	49/185	(26.5%)	162/210	(77.1%)	Ref.		<0.0001*
	Drinkers	136/185	(73.5%)	48/210	(22.9%)	9.37	(5.92-14.82)	
	Less than 1 drink per week	99/136	(72.8%)	35/48	(72.9%)	Ref.		
	1 drink per week	28/136	(20.6%)	8/48	(16.7%)	1.24	(0.52-2.97)	0.63
	More than 1 drink per week	9/136	(6.6%)	5/48	(10.4%)	0.64	(0.2-2.03)	0.44
Red meat	Median (intake/day)	100	(100-150) g	150	(150-200) g			<0.0001*
	Median (ingestions/week)	7	(7-7)	3	(3-4)			<0.0001*
	Median (intake/week)	700	(700-1050) g	450	(450-800) g			<0.0001*
Red meat products	Median (intake/day)	70	(70-100) g	100	(100-100) g			0.43
	Median (ingestions/week)	4	(3-5)	2	(2-3)			<0.0001*
	Median (intake/week)	280	(210-500) g	200	(200-300) g			<0.0001*
Fish	Median (ingestions/week)	1	(1-2)	1	(1-2)			0.4
Fruits and vegetables	Median (intake/day)	350	(300-350) g	300	(250-300) g			0.0002*
	Median (ingestions/week)	7	(6-7)	7	(7-7)			0.002
	Median (intake/week)	2450	(1800-2450) g	2100	(1750-2100) g			<0.0001*
Bakery products	Wheat bread	130	(70.2%)	77	(36.7%)	Ref.		
	Rye bread	51	(27.6%)	94	(44.8%)	0.32	(0.21-0.5)	<0.0001*
	Both rye and wheat bread	4	(2.2%)	33	(15.7%)	0.07	(0.02-0.21)	<0.0001*
	Not consumed	None		5	(2.4%)			
	Median (intake/day)	200	(150-200) g	175	(150-200) g			0.27
	Median (ingestions/week)	7	(7-7)	7	(7-7)			0.1
	Median (intake/week)	1400	(1050-1400) g	1225	(1050-1400) g			0.1
Dairy products	Median (intake/day)	500	(500-500) ml	300	(250-300) ml			<0.0001*
	Median (ingestions/week)	7	(5,77-7)	7	(7-7)			0.16
	Median (intake/week) (ml)	3500	(2885-3500)	2100	(1750-2100)			<0.0001*
Pattern of dairy products	Milk	119/185	(64.3%)	149/210	(71%)			Non-significant
	Yogurts	7/185	(3.8%)	57/210	(27.1%)			Non-significant
	Cottage cheese	162/185	(87.6%)	165/210	(78.6%)			0.0432
	Kefir	168/185	(90.8%)	165/210	(78.6%)			0.0032
Sour cream	174/185 (94%)	154/210	(73.3%)					<0.0001*
	Cheese	174/185	(94%)	168/210	(80%)			0.0002*

Table 1 (Con.). Colorectal Cancer Risk Factors Among the Population of South-East Siberia

Characteristic		Case group		Control group		OR (95%CI)		P value
Spicy food	No	74/185	(40%)	138/210	(65.7%)	Ref.		
	Yes	111/185	(60%)	72/210	(34.3%)	2.87	(1.9-4.33)	<0.0001
	Median (ingestions/week)	1	(0.25-2)	0	(0-0)			<0.0001
Salt	Low	32/185	(17.3%)	77/210	(37.6%)	0.43	(0.26-0.69)	0.0006
(concentration in the food)	Medium	113/185	(61.2%)	116/210	(56.6%)	Ref.		
	High	37/185	(20%)	11/210	(5.3%)	3.45	(1.68-7.1)	0.0008
	Food without salt	1/210	(0.5%)					
Diet and fasting	No diet	185/185	(100%)	165	(78.6%)	Ref.		
	Diet	None		45	(21.4%)	0.01	(0.0006-0.16)	0.0012
	No fasting	184/185	(99.5%)	195/210	(92.9%)	Ref.		
	Fasting	1/185	(0.5%)	15/210	(7.1%)	0.07	(0.009-0.54)	0.01
Water supply	Centralized	156/182	(85.8%)	172/193	(89.1%)	Ref.		
	Decentralized	24	(13.2%)	21	(10.9%)	0.79	(0.42-1.48)	0.47
Water consumption	Boiled water	96/185	(51.9%)	118/210	(56.2%)	Ref.		
	Unboiled water	36/185	(19.5%)	58/210	(27.6%)	0.76	(0.46-1.25)	0.28
	Bottled water	11/185	(5.9%)	37/210	(17.6%)	0.36	(0.18-0.75)	0.0065
	Filtered water	42/185	(22.7%)	76/210	(36.2%)	0.68	(0.43-1.08)	0.1
Storey of living	Cottage	44/175	(25.1%)	48/209	(23%)	Ref.		
	1st floor	30/175	(17.1%)	13/209	(6.2%)	2.52	(1.17-5.43)	0.02
	2nd floor	26/175	(14.9%)	27/209	(12.9%)	1.05	(0.53-2.07)	0.89
	3rd floor	26/175	(14.9%)	19/209	(9.1%)	1.49	(0.73-3.06)	0.27
	4th floor	20/175	(11.4%)	18/209	(8.6%)	1.21	(0.57-2.58)	0.62
	5th floor	17/175	(9.7%)	50/209	(23.9%)	0.37	(0.19-0.74)	0.005
	>5th floor	34/209	(16.2%)	0.38	(0.18-0.84)			0.016
Family history	Relatives without cancer of gastrointestinal tract							
		144/185	(77.8%)	196/210	(93.3%)	Ref.		
	Relatives with cancer of gastrointestinal tract	41/185	(22.2%)	14/210	(6.7%)	3.99	(2.09-7.59)	<0.0001
	First degree relatives with cancer of gastrointestinal tract							
		34/185	(18.2%)	11/210	(5.4%)	3.93	(1.92-8.02)	0.0002
	Second degree relatives with cancer of gastrointestinal tract							
		13/185	(6.9%)	3/210	(1.5%)	4.78	(1.33-17.23)	0.02
	Relatives with colorectal cancer	24/185	(12.9%)	7/210	(3.4%)	4.12	(1.72-9.84)	0.0014
	First degree relatives with colorectal cancer	18/185	(9.7%)	6/210	(2.9%)	3.66	(1.42-9.44)	0.007
	Second degree relatives with colorectal cancer	6/185	(3.2%)	1/210	(0.5%)	7	(0.83-58.74)	0.07
	Relatives with gastric cancer	19/185	(10.2%)	3/210	(1.5%)	6.98	(2.01-24.23)	0.002
	First degree relatives with gastric cancer	13/185	(7%)	2/210	(1%)	7.21	(1.59-32.67)	0.01
	Second degree relatives with gastric cancer	6/185	(3.2%)	1/210	(0.5%)	7	(0.83-58.74)	0.07
Precancerous lesions	No precancerous lesions	164/185	(88.7%)	205/210	(97.6%)	Ref.		
	Polyposis coli	20/185	(10.8%)	2/210	(1%)	5.25	(1.94-14.22)	0.001
	Ulcerative colitis	1/185	(0.5%)	2/210	(1%)			
	Crohn's disease	None	1/210	(0.5%)				
Stool frequency	Median of stool frequency	1	(1-1)	1	(1-1)			0.4
Constipation	No constipation	162/185	(87.6%)	174/210	(82.9%)	Ref.		
	Constipation	23/185	(12.4%)	36/210	(17.1%)	0.69	(0.39-1.2)	0.19
Occupation	Mainly related to brainwork	55/124	(44.3%)	57/195	(29.2%)	Ref.		
	Related to little physical activity	27/124	(21.8%)	59/195	(30.3%)	0.47	(0.26-0.85)	0.01
	Related to medium physical activity	38/124	(30.6%)	64/195	(32.8%)	0.61	(0.36-1.06)	0.08
	Related to hard physical activity	4/124	(3.3%)	14/195	(7.2%)	0.3	(0.09-0.95)	0.04
	Related to very hard physical activity	None		1/195	(0.5%)			
Income	Less than 1 subsistence minimum	1/183	(0.5%)	22/209	(10.5%)	0.09	(0.01-0.65)	0.02
	1-2 subsistence minimum	80/183	(43.7%)	151/209	(72.3%)	Ref.		
	More than 2 subsistence minimum	102/183	(55.8%)	36/209	(17.2%)	5.34	(3.35-8.53)	<0.0001

(OR=0.32, 95%CI=0.21-0.5, P<0,0001, and OR=0.07, 95%CI=0.02-0.21, P<0.0001, respectively), and also low concentration of salt in the food and diet, although it was at borderline significance (OR=0.43, 95%CI=0.26-0.69, P=0.0006, and OR=0.01, 95%CI=0.0006-0.16, P=0.0012, respectively).

As seen in Table 2, no statistically significant association of ABO and Rhesus blood antigens with colorectal cancer risk was revealed. In addition, no statistically significant correlation was found after stratification of this large group of malignant tumors into three separate ones, namely, cancer of the caecu, ascending, transversal, and descending colon, cancer of the sigmoid and rectal cancer

Discussion

Colorectal cancer still represents a global burden, particularly for the developed countries, and there is a number of risk factors which deserve attention and investigation. Our study sheds light on the pattern of colorectal cancer risk factors in Russia, particularly in the population of South-East Siberia. Yet in 1967, Wynder and Shigematsu (1967) were the first who proposed the role of smoking in colorectal cancer development. In this study, we approved this suggestion for Siberian population, revealing more than 2-fold colorectal cancer risk for smokers. In 1985, Garfinkel (1985) found a positive correlation between colorectal cancer risk and overweight, that was also demonstrated in our study

Table 2. Distribution of AB0 and Rh Blood Antigens between Cases and Controls

Blood group	Case group	Control group	OR(95%CI)	P value
Cancer of the colon (n = 388)				
O	136 (35.05%)	6702 (35.05%)	Ref.	
A	136 (35.05%)	6570 (34.37%)	1.02 (0.8-1.3)	0.87
B	79 (20.36%)	4248 (22.22%)	0.92 (0.69-1.21)	0.54
AB	37 (9.54%)	1599 (8.36%)	1.14 (0.79-1.65)	0.48
A+AB	173 (44.59%)	8169 (42.72%)	1.04 (0.83-1.3)	0.71
B+AB	116 (29.9%)	5847 (30.58%)	0.98 (0.76-1.26)	0.86
Rh+	336 (86.6%)	19032 (84.3%)	Ref.	
Rh-	52 (13.4%)	3549 (15.7%)	0.83 (0.62-1.11)	0.21
Cancer of the sigmoid colon (n = 397)				
O	140 (35.26%)	6702 (35.05%)	Ref.	
A	121 (30.48%)	6570 (34.37%)	0.88 (0.69-1.13)	0.31
B	95 (23.93%)	4248 (22.22%)	1.07 (0.83-1.39)	0.61
AB	41 (10.33%)	1599 (8.36%)	1.23 (0.86-1.75)	0.25
A+AB	162 (40.81%)	8169 (42.72%)	0.95 (0.75-1.19)	0.66
B+AB	136 (34.26%)	5847 (30.58%)	1.11 (0.88-1.41)	0.38
Rh+	332 (83.42%)	19032 (84.3%)	Ref.	
Rh-	66 (16.58%)	3549 (15.7%)	1.07 (0.812-1.39)	0.64
Cancer of the rectum (n = 1278)				
O	430 (33.65%)	6702 (35.05%)	Ref.	
A	465 (36.38%)	6570 (34.37%)	1.1 (0.96-1.26)	0.16
B	277 (21.67%)	4248 (22.22%)	1.02 (0.87-1.19)	0.84
AB	106 (8.29%)	1599 (8.36%)	1.03 (0.83-1.29)	0.77
A+AB	571 (44.97%)	8169 (42.72%)	1.09 (0.96-1.24)	0.19
B+AB	383 (29.96%)	5847 (30.58%)	1.02 (0.89-1.18)	0.77
Rh+	1075 (84.71%)	19032 (84.3%)	Ref.	
Rh-	194 (15.29%)	3549 (15.7%)	0.97 (0.83-1.13)	0.68

(almost 2.5-fold risk). However, our data suggest that obesity is not a risk factor. Possibly, this can be explained by insufficient sample size, and further investigations in nutritional epidemiology of colorectal cancer in Siberia may assist to solve this issue. Conversely, diet possessed a protective effect, although it seems to be exaggerated in our study. In 1974, increased colorectal cancer risk among alcohol abusers (particularly hard drinks abusers and beer abusers) was found in Finland (Hakulinen et al.) and in USA (Breslow and Enstrom), and excessive consumption of alcohol, beer and hard drinks was definitely established as a colorectal cancer risk factor in our investigation as well (about 9-fold risk for all three).

Regarding dietary factors, McKeown-Eyssen and Bright-See (1984) revealed a correlation between increased red meat intake and higher colorectal cancer risk, that was also clearly shown in our study (P<0.0001). Iscovich et al. (1992) found the association of excessive dairy products intake, particularly cheese intake, with elevated colorectal cancer risk. Although the data on this issue are contradictory (Larsson et al., 2005), in our study overconsumption of dairy products, particularly cheese and sour cream, was related to an increased colorectal cancer risk (P<0.0001, P=0.0002 for sour cream). Arole of spices in elevation of colorectal cancer risk was shown by Nayak et al. (2009) and it was confirmed in our study as well (almost 3-fold risk). We also found a correlation between high concentration of salt in the food and increased colorectal cancer risk (almost 3.5-fold risk), whilst low concentration of salt possessed a protective effect (0.43-fold risk), sustaining a hypothesis of Tuyns (1988). Rye bread may also possess an anti-cancerous effect (Gråsten et al., 2000), and it was associated with lower colorectal cancer risk in our study, particularly in combination with wheat bread (0.32- and 0.07-fold risk, respectively). Precancerous colonic lesions, as it was expected (Andersen et al., 2012), were associated with higher colorectal cancer risk as well (5.25-fold risk). According to recent fundamental, translational and clinical studies (Pinar et al., 2011; Ghosh et al., 2012), there is a great role of genetic predisposition in colorectal cancer development; therefore, we assessed family history of colorectal cancer and found positive correlation (4-fold risk increase). High socioeconomical status is associated with increased age, westernized lifestyle, and it is a reason why colorectal cancer is more significant problem for developed countries compared to developing (Doubeni et al., 2012). In our study, it was also affirmed (more than 5-fold risk). It is important to note that an association between the ABO and Rh blood antigens and colorectal cancer risk was not confirmed in series of studies across different populations and ethnicities (Halvorsen, 1986; Slater et al., 1993; Khalili et al., 2011), and in our study as well, despite the extension of the sample. A lack of statistically significant results was observed regarding other widely established colorectal cancer risk factors, such as constipation, physical activity, and quantity of consumed bakery products; possibly, this is due to insufficient sample size. Storey of living, as well as family history of gastric cancer and colorectal cancer apart also did not reach statistical significance as a risk factor, but were very close to it, and enlargement of sample size may precise this moment.

However, our study has several limitations. First of all, the number of study participants was relatively low (only 185 cases and 210 controls), and it is necessary to increase it for verification of our suggestions. In addition, it is not possible to define risk factors for colon cancer and rectal cancer separately due to insufficiency of the sample size. Secondly, risk factors for the population of South-East Siberia may not match with risk factors for Russian population, and a series of comparative studies in distinct Russian regions is needed. Anyway, these limitations can be overpassed in the following years, and this study may be only the preliminary one. Ideally, risk factors for cancer of every part of the gut (caecum, ascending colon, transverse colon, descending colon, sigmoid and rectum) should be defined separately; however, large-scale and multicenter studies involving large samples are required for achievement of this goal.

To summarize, we suggest that various family, dietary, lifestyle, and socioeconomical factors affect colorectal cancer incidence in the population of East-Siberia. The most significant are excessive alcohol consumption, high concentration of salt in the food, precancerous colonic lesions, family colorectal cancer history, and high socioeconomical status. Rye bread possessed a significant protective effect, particularly in combination with wheat bread. Further investigations in this field are necessary for more precision but our results should be definitely applied for elaboration of programs of colorectal cancer prevention in Russia, particularly in Siberia, and may be useful for the comparison of ways of colorectal cancer prevention in different countries.

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