Original Article

Risk factors of colorectal cancer among Saudi Population: Case-control study

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Abstract

Background: Colorectal cancer (CRC) incidence and related mortalities have been steadily increasing in KSA over the past 20 years. CRC in the Kingdom of Saudi Arabia (KSA) population presents in younger ages and in more advanced disease states as compared to other countries. This study was aimed to determine factors (demographic, habitual, environmental, nutritional, and genetic) associated with CRC in Riyadh, KSA. **Materials and Methods:** A matched case-control study conducted in the major hospitals in Riyadh (King Khalid university Hospital, King Faisal Specialist Hospital, Riyadh Military Hospital, Security Force Hospital, King Fahd Medical City). Here most of CRC cases are managed. The cases (n = 121) group included all recently diagnosed and pathologically confirmed Saudi cases of CRC identified during the period 1st of January 2017 till 31st of December 2018 who agreed to participate and fulfilled the inclusion criteria. A similar number of controls attending the study settings were selected consecutively from the clinics where cases were managed and matched on a 1:1 basis with cases based on age (+/-3 years) and gender. Data were collected using a structured questionnaire. Conditional logistic regression models were fitted to determine factors associated with risk of CRC. **Result:** This study included similar number of males and females in both groups: males 69 (57%) and females 52 (43%) in each group (Chi-square test P = 1.0). The mean (S.D) age in the cases group was 53.6 (S.D = 12.9) and 53.3 (S.D = 12.9) in the controls group (Student test P = 0.86). In the final multivariate conditional logistic regression model, variables independently associated with risk of colorectal cancer were body mass index (OR = 0.93; 95% CI 0.87–0.98; P = 0.011) employment status (inverse relation: OR = 0.33; 95% CI 0.14–0.77; P = 0.010), colon polyps (OR = 4.09; 95% CI 1.06–15.82; P = 0.041), and constipation (OR = 4.98; 95% CI 1.91–15.99; P = 0.001). **Conclusion:** Factors associated with CRC in the major referral hospitals in KSA were colon polyps, chronic constipation, and unemployment. These factors should be considered when screening for patients at risk for CRC.

Keywords: Cases, colorectal carcinoma, risk factors, Saudi population awareness

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Introduction

Worldwide, colorectal cancer (CRC) emerges as the third most frequent human cancer and the second most important cause of cancer-related death.[1] According to the World Health

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Organization cancer is considered a leading cause of death worldwide; accounting for 7.6 million, or 13%, of all deaths from a total of 58 million deaths reported in year 2005. Although the overall prevalence of cancer is higher in developed nations, about 70% of all cancer deaths in 2005 occurred in low- and middle-income countries.[2] In Saudi Arabia, the age-standardized rate (ASR) of CRC increased from 5.0 per 100,000 persons to 9.6 per 100,000 persons during period of 2001–20015.[3] Most of the CRC cases are diagnosed during clinical evaluations rather than through screening programs in Saudi Arabia.[4]

Regarding gender distribution, it is the third most commonly diagnosed cancer among males and the fourth most common among females worldwide.[5]

An international study found colorectal cancer incidence rates for both males and females increased in 27 of 51 countries worldwide between 1983 and 2002, and points to increasing Westernization as being a likely culprit. That rise was seen primarily in economically transitioning countries in many parts of the world.[6] In terms of occurrence, it is more common in males than in females.[7] The Kingdom of Saudi Arabia (KSA) is considered to be a country with a low CRC incidence. However, CRC incidence and related mortalities have been steadily increasing in the country over the past 20 years.[8-10] The Saudi Cancer Registry (SCR) is a definitive guide to the population-based incidence of cancer in KSA.[11] The 2007 SCR report indicates that CRC is the second most common malignancy in the country and the most common malignancy among Saudi males between the ages of 45 and 74 years. The report also found CRC to be the second most common malignancy in the Makah region, with the highest incidence present among males. There are few reports that describe the epidemiology of CRC in Jeddah[10] or KSA.[8,12,13] A recent research found that CRC incidence, morbidity and mortality in KSA have been increasing steadily for more than twenty years.[14,15]

The global geographic variations in the incidence of colorectal adenoma and cancer are thought to be due to multiple factors, particularly diet and genetics. Hereditary factors play a definite role, but gene–environment interactions are also more important in the pathogenesis of colorectal cancer.[9,16] Other risk factors for colorectal cancer include age over 50,[17] hereditary poly- and non-polyposis colorectal family syndromes,[18] ulcerative colitis or Crohn's disease,[19] a diet low in fiber and high in fat and from animal sources,[20] hypertriglyceridemia, physical inactivity,[21] and obesity and high body mass index and body size,[21] type II diabetes mellitus, alcohol, and smoking and others.[22]

The risk factors may differ from region to the other even within the same country as many of the reported risk factors are related to lifestyle and eating habits. So, the current study aimed to assess the different risk factors for CRC in Saudi Arabia.

Materials and Methods

A case-control study design was conducted including all new cases of colorectal cancer from King Khalid university hospital, King Faisal specialist hospital, Riyadh Military hospital, and Security force hospital and King Fahd medical city after getting approval from ethical committee 16-04-2013. It was planned to include King Saud and King Abdulaziz medical cities in the research but because of administrative issues and time limit these two medical cities were excluded. Cases were defined as All Saudi patients, recently diagnosed and pathologically confirmed cases of colorectal cancer identified during the period from 1st of January 2011 till 31st of December 2013 and attending the study settings were included in the study. Controls were selected from healthy individuals from the same hospitals who did not diagnosed with CRC and agree to participate and fulfilled the inclusion criteria.: Using Epi Info software hypothesizing odds ratio for CRC for those with positive family history of 3 (personal communication with Prof in the clinics), using 1:1 matching with a power of 80% and a confidence level of 95%. A total of 121 cases and 121 controls required to achieve the study objective. Data were collected using a pre-structured questionnaire which included sociodemographic data, risk factors of colorectal cancer including family history, comorbidity, life style and habits, dietary habits, drug use, and surgical history.

Data analysis

Analysis was conducted using the IBM SPSS software (version 22; Chicago, USA). Categorical variables were described as proportions while continuous variables summarized as means (standard deviation; S.D). Pearson Chi-square with crude odds ration was used for univariate relation of different risk factors with CRC. Multivariate conditional logistic regression model was fitted to identify adjusted factors associated with the risk of having colorectal cancer. Variables found significant in univariate analysis were included in the final regression model. Strength of association was expressed as an adjusted odds ratio (OR) along with its 95% confidence interval (CI) and a Wald test *P* value. All tests were two-sided and *P* value less than 0.05 was considered significant.

Results

Table 1 showing his case-control study included similar number of male and female in both groups; males 69 (57%) and females 52 (43%) (Chi-square test *P* value = 1.0). The mean age (S.D) in the cases group was 53.6 (S.D = 12.9) and 53.3 (S.D = 12.9) in the controls group (Student test *P* value = 0.86). Education level and marital status were not significantly different in the two groups. However, more controls were employed (74.4%) than cases (55.4%); OR = 0.40; 95% CI 0.22–0.72; *P* = 0.002), body mass index was significantly higher in controls compared with cases (OR = 0.96; 95%CI 0.94–0.99; *P* = 0.011). However, no significant differences were found in life style between cases and controls. More than two thirds of the patients in both groups physically exercised at least 30 min weekly; however, few patients reported practicing a sport. A high proportion in the two groups led sedentary life and are not involved in carrying heavy work at home. The greater proportion

of patients in both groups was non-smokers. Nonalcoholic predominate in the two groups [Table 2].

Patients in the two groups were mostly similar in terms of dietary profile. A high proportion of fruit and vegetable intake was reported in both groups. A similar result was observed when red meat intake was compared. However, a significantly higher proportion of camel meat intake was observed in cases compared with control (OR = 1.75; 95% CI 1.01–3.03; $P = 0.046$). Frequent cooking method did not differ significantly between the two groups. Although overall proportion is low in both groups, cases were significantly more likely to have a family member with a history of colon/rectal cancer (OR = 2.43; 95% CI 1.01–5.86; $P = 0.048$), Table 2.

Cases had significantly higher proportions of patients with polyps (OR = 4.25; 95% CI 1.54–12.6; $P = 0.009$), colon chronic disease (OR = 3.00; 95% CI 1.09–8.25; $P = 0.033$), chronic constipation (OR = 3.78; 95% CI 1.81–7.88; $P < 0.0001$). However, proportion of patients with hypertension, diabetes, surgical operation history, appendectomy, anal fissure, hemorrhoid, and other surgical operations in the two groups was not significantly different [Table 3].

In the multivariate condition logistic regression model, variables independently associated with risk of colorectal cancer were body mass index (OR = 0.93; 95% CI 0.87–0.98; $P = 0.011$), employment status (inverse relation: OR = 0.33; 95% CI 0.14–0.77; $P = 0.010$), colon polyps (OR = 4.09; 95% CI 1.06–15.82; $P = 0.041$), and constipation (OR = 4.98; 95% CI 1.91–15.99; $P = 0.001$), Table 4.

Discussion

This was a case-control study done to determine risk factors for CRC done during the period from 1st of January 2011 till 31st of December 2013. The colorectal cancer cases were recruited from the main hospitals in Riyadh, where most of cases were managed.

There was equal number of males 69 (57%) and females 52 (43%) in each group, with mean age (S.D) in the cases group was 53.6 (S.D = 12.9) and 53.3 (S.D = 12.9) in the controls group [$P = 0.86$]. The preponderance of males in this study is in agreement with a study by Ibrahim *et al.*, 2008[8] who reported that CRC now ranks first among all cancers in males and third among females in Saudi Arabia. The mean age of 53.6 (SD = 12.9) concurs with the fact that CRC is a disease of elderly people (≥50 years). In addition, age distribution of CRC cases in this study is similarly to those included in local CRC Registry[11] which reported age distribution between the ages of 45 and 74 years. However, the disease tends to be more frequent in late middle-age populations in both sexes compared to other age categories.

No significant difference was observed by educational level but increased OR = 3.49 among illiterate when compared with higher educated may come from non-commitment about healthy life habits and other disadvantage of poor education is that the patients are usually seen at an advanced stage of colorectal cancer in Saudi Arabia, and this epidemiological trend is attributed to poor patient awareness of the disease, this is matched with Almurshed, K. S., 2009[23] at Riyadh KSA who noticed OR = 2.4 among illiterates.

No significant difference with marital status ($P = 0.356$) this is matched with Almurshed, K. S., 2009[21] at Riyadh KSA who noticed no difference among married and singles but OR = 1.42 may come from sedentary life and type of feeding habits among married.

There is significant difference ($P = 0.002$) when comparing employment status with OR = 0.4, so unemployment carry more risk and this may be due to more sedentary life style among unemployed this is matched with Almurshed, K. S., 2009[23] at Riyadh KSA who noticed less risk among employed with OR = 0.29.

The difference in BMI gave significant difference ($P = 0.011$) with lower BMI among cases. There is converging evidence that markers of obesity have been associated with higher risk of colorectal cancer (Frezza EE *et al.*, 2006).[21] The findings of this study were not consistent with this: BMI was significantly higher among the control group. The explanation may be that, although cases were newly diagnosed, they were in the advanced stages of carcinoma and this would reduce their weight, and therefore BMI.

Physical exercise (30 min weekly at least) nor practicing sport gave a significant different although lower OR among those who practicing sport or exercises, this may explained by lower practicing of exercises among elderly age group especially in our community this is opposite to what Belza B and Warms C, 2004[24] said as physical exercise play a significant risk reduction in CRC, the difference may come from cultural difference.

Carry heavy works at home showed no significant difference with lower OR among active workers this explained by the effect of sedentary life effect.

Smoking status also gave no significant difference with almost equal risk and this is matched with Giovannucci E., 2001,[25] who reported no association between cigarette smoking with an increased risk of colorectal cancer.

Table 1. Sociodemographic characteristics of study groups

Characteristic	Cases=121 *n* (%)	Controls=121 *n* (%)	*P*
Education			0.062
Illiterate	38 (31.4)	27 (22.3)	
Elementary/Secondary	64 (52.9)	66 (54.5)	
University and above	19 (15.7)	28 (23.1)	
Marital status			0.356
Married	100 (82.6)	95 (78.5)	
Single	21 (14.4)	26 (21.5)	
Employment status			0.002
Employed	67 (55.4)	90 (74.4)	
Unemployed	54 (44.6)	31 (25.6)	

Table 2. Life style, eating habits and family history among study cases and controls

Lifestyle and eating habits	Cases=121 *n* (%)	Controls=121 *n* (%)	OR (95%CI)	*P*
Physical exercise (at least 30 minutes)	83 (68.6)	82 (67.8)	0.96 (0.56-1.65)	0.890
Practicing a sport	18 (14.9)	20 (16.5)	0.81 (0.39-1.69)	0.578
Carry heavy works at home	38 (31.4)	29 (24)	0.81 (0.56-1.21)	0.308
Tobacco use	28 (23.1)	27 (22.3)	1.06 (0.55-2.01)	0.868
Alcohol use	6 (5)	9 (7.4)	0.79 (0.35-1.79)	0.570
Fruits intake	107 (88.4)	115 (95)	0.69 (0.39-1.20)	0.189
Vegetables	116 (95.9)	117 (96.7)	0.89 (0.37-2.20)	0.810
Red meat intake	112 (92.6)	105 (86.8)	1.43 (0.73-2.83)	0.298
Camel meat intake	82 (67.8)	67 (55.4)	1.75 (1.01-3.03)	0.046
Frequent cooking method				
Boiled	62 (51.2)	69 (57)	1	0.474
Mandi	20 (16.5)	17 (14)	1.14 (096-1.90)	
Mathbi	3 (2.5)	4 (3.3)	0.91 (0.28-2.89)	
Grilled	16 (13.2)	23 (19)	0.87 (0.50-1.50)	
Other	20 (16.5)	8 (6.6)	1.51 (0.91-2.50)	
Family history of CRC	19 (15.7)	9 (7.4)	2.43 (1.01-5.86)	0.048

Table 3. Comorbidity and surgical history among cases and controls

Characteristic	Cases=121 *n* (%)	Controls=121 *n* (%)	OR (95%CI)	*P*
Colon polyps	18 (14.9)	5 (4.1)	4.25 (1.54-12.63)	0.009
Colon chronic disease	18 (14.9)	8 (6.6)	3.00 (1.09-8.25)	0.033
Hypertension	34 (28.1)	46 (38)	0.60 (0.33-1.08)	0.087
Diabetes	44 (36.4)	52 (43)	0.72 (0.41-1.27)	0.260
Chronic constipation	49 (40.5)	24 (19.8)	3.78 (1.81-7.88)	0.001
Surgical operation history	60 (49.6)	64 (52.9)	0.87 (0.51-1.47)	0.953
Appendectomy	11 (9.1)	6 (5)	1.83 (0.68-4.96)	0.232
Anal fistula	1 (0.8)	1 (0.8)	1.00 (0.06-15.99)	1.000
Cholecystectomy	10 (8.3)	12 (9.9)	0.82 (0.34-1.97)	0.655
Anal fissure	1 (0.8)	1 (0.8)	1.00 (0.06-15.99)	1.000
Hemorrhoid	2 (1.7)	6 (5)	0.33 (0.07-1.65)	0.178
Other surgical operation	37 (30.6)	45 (37.2)	0.74 (0.43-1.27)	0.277

Table 4. Multivariate stepwise conditional logistic regression analysis of factors associated with colorectal cancer

Factor	Adjusted Odds ratio (95% CI)	*P*
Body Mass Index	0.93 (0.87-0.98)	0.011
Employment status	0.33 (0.14-0.77)	0.011
Family history of colorectal cancer	1.67 (1.1-5.63)	0.047
Colon polyp	4.09 (1.06-15.82)	0.041
Colon chronic disease	2.16 (1.0-7.88)	0.049
Constipation	4.98 (1.91-15.99)	0.001

Alcohol status gave no significant difference that is because the nonalcoholic predominates in the two groups because of cultural, religious factors.

About dietary habits and colorectal cancer, the fruit intake showed no significant difference with lower risk for CRC among frequently fruit intakers, this may explained by protective effect of fibers and vitamins present in fruits, this is in agreement with Chan, A. T., and Giovannucci, E. L., 2010[25,26] who noticed the protective effect of fruit intake regarding CRC.

The vegetable intake gave no significant difference with lower risk for CRC among frequently vegetables users, this may be explained by protective effect of fibers and minerals present in vegetables, this is in agreement with Chan, A. T., and Giovannucci, E. L., 2010[26,25] who noticed the protective effect of vegetables intake regarding CRC.

Red meat intake gave no significant difference with higher risk for CRC among frequently red meat intakers, this may explained by Norat T, *et al.*, 2005[27] who said "Red meat might stimulate secretion of endogenous insulin, which is a mitogen. Other relevant hypotheses include red meat as a major source of total or saturated fat, heme iron, or carcinogenic heterocyclic amines."

The camel meat intake showed a statistically significant difference with higher risk (OR = 1.75) the explanation is the same as with red meat but the significant relation explained by increased consumption of camel meat in our area.

Frequent cooking method showed no significant difference with CRC with almost same OR between the different methods, this indicate that the method of cooking doesn't affect CRC incidence but the type of food affects most.

The relation between positive family history of colorectal cancer and colorectal cancer occurrence which gave significant relation with increased risk among positively family history for (OR = 2.73) this may explained by genetic predisposition or sharing same life habits and social characters, which is in agreement with other research showing that a family history of colorectal cancer increases the risk of having this disease (Jass JR, 2005)[28] and in agreement with Heavy PM. *et al.*, 2004[9] who reported hereditary factors play a definite role in CRC occurrence. The relation between various possible comorbidities and surgical history with colorectal cancer, colonic polyps history had significant association with CRC occurrence with OR = 4.25, this is because the possibility of malignant transformation of such polyps this is in agreement with (Jass JR, 2005)[28] who reported that hereditary poly- and non-polyposis colorectal family syndromes are risk factors for CRC.

Chronic colon diseases also gave significant association with CRC with OR = 3; this is explained by inflammatory process and disturbance in digestive mechanisms and absorption this is in agreement with Jarvinen HJ, 2003[29] who reported association between ulcerative colitis or Crohn's disease and CRC.

Hypertension nor diabetic gave significant association with CRC this may be due to large proportion of hypertension and diabetes in both cases and control.

None of all surgical history either (Surgical operation history, Appendectomy, Anal fistula, Anal fissure, Cholecystectomy, Hemorrhoid or Other surgical operation) gave significant association with CRC, this may be due to small numbers in both cases and control.

Chronic constipation showed highly significant association with OR = 3.78; the possible explanation is retention of carcinogenic and aromatic amines inside colon and this is in agreement with Watanabe, T. *et al.*, 2004[30] who reported that constipation or laxative use increases the risk of colon cancer.

In the multivariate logistic regression model, variables independently associated with risk of colorectal cancer were body mass index (OR = 0.93; 95% CI 0.87–0.98; P = 0.011) employment status (inverse relation: OR = 0.33; 95% CI 0.14–0.77; P = 0.010), colon polyps (OR = 4.09; 95% CI 1.06–15.82; P = 0.041), and constipation (OR = 4.98; 95% CI 1.91–15.99; P = 0.001).

The limitations of this study come mainly from exclusion of King Saud and King Abdul-Aziz medical cities in the research because of administrative issue and time limit. This may introduce an element of selection bias for both cases and controls.

Also, the use of waist circumference and waist–hip ratio would be a better measure than BMI because these are more indicative of visceral obesity and are sex-specific.

Conclusion

In conclusion, being unemployed, colon polyps, and chronic constipation were risk factors for colon cancer in these referral hospitals in Saudi Arabia. Although the risk of colorectal cancer was higher in the patient who had family history of CRC, however this risk was not statically significant. More emphasis to be given on improvement of standardized system for screening for those at risk and elderly >50 for early detection of colorectal cancer and provision of health educational information either by community approach or high risk approach for possible risk and protective factors to enhance their awareness.

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Conflicts of interest

There are no conflicts of interest.

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