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Full Length Research Paper

Dietary and other risk factors for Colo-Rectal cancer in Saudi Arabia

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Abstract

The study was carried out in the MOH hospitals in four different regions in Saudi Arabia. The target population comprised all recently diagnosed colorectal cancer cases admitted to Saudi hospitals in four different regions during a period 6 months. For each case one control was selected from the same hospital, and matched for age and sex. All cases were subjected to a questionnaire interview, dietary assessment using the food frequency questionnaire (FFQ), physical exercise and anthropometric measurements assessment. Results: Family history of colon cancer, physical activity and the use of Non steroidal anti-inflammatory drugs (NSAIDs) were the most significant variable that independently associated with the risk of colorectal cancer. It was observed that, although CRC Cases had consumed higher daily intake of total calories than the controls, (P <0.05), yet their intake was lower than the RDA. On the other hand there was no significant difference, between CRC cases and controls regarding their daily intake of protein, and dietary fiber, which was also adequate to their corresponding RDA, P >0.05. There was a trend of low intake of dietary antioxidants among CRC cases as compared to controls. Conclusions: A modification of diet and lifestyle could reduce morbidity and mortality from CRC, In Saudi Arabia, primary prevention of CRC is feasible through multidisciplinary intervention programs such as; long-term behavior modifications in food choices, dietary pattern and physical activity. Addressing the daily intake of dietary antioxidants is an asset to develop a dietary approach for the primary prevention of CRC among high risk population of the Saudi adults.

Keywords: Colorectal cancer, dietary factors, physical activity, risk factor, KSA.

INTRODUCTION

Colorectal cancer is a major cause of morbidity and mortality throughout the world (Jemal et al., 2011). It accounts for over 9% of all cancer incidences (Siegel et al., 2013; Boyle et al., 2005). It is the third most common cancer worldwide and the fourth most common cause of death (Siegel et al., 2013). It affects men and women almost equally. Countries with the highest incidence rates include Australia, New Zealand, Canada, the United States, and parts of Europe. The countries with the lowest risk include China, India, and parts of Africa and South America (Boyle et al., 2005).

Worldwide, colorectal cancer represents 9.4% of all incident cancer in men and 10.1% in women. Colorectal cancer, however, is not uniformly common throughout the world (Boyle et al., 2005). There is a large geographic difference in the global distribution of colorectal cancer. Colorectal cancer is mainly a disease of developed countries with a Western culture (Boyle et al., 2005). In fact, the developed world accounts for over 63% of all cases (Janout et al., 2001). The incidence rate varies up to 10-fold between countries with the highest rates and those with the lowest rates (Jemal et al., 2011; Wilmink 1997). It ranges from more than 40 per 100,000 people in the United States, Australia, New Zealand, and Western Europe to less than 5 per 100,000 in Africa and some parts of Asia (Siegel et al., 2013). However, these incidence rates may be susceptible to ascertainment bias; there may be a high degree of underreporting in developing countries.

Worldwide mortality attributable to colorectal cancer is approximately half that of the incidence. Colorectal cancer survival is highly dependent upon stage of

disease at diagnosis, and typically ranges from a 90% 5-year survival rate for cancers detected at the localized stage; 70% for regional; to 10% for people diagnosed for distant metastatic cancer (Jemal et al., 2004; Ries et al., 2008). In general, the earlier the stage at diagnosis, the higher the chance of survival. Since the 1960s, survival for colorectal cancer at all stages has increased substantially (Jemal et al., 2004). The relative improvement in 5-year survival over this period and survival has been better in countries with high life-expectancy and good access to modern specialized health care. However, enormous disparities in colorectal cancer survival exist globally and even within regions (Boyle et al., 2005; Parkin et al., 2005; Jackson-Thompson et al., 2006). This variation is not easily explained, but most of the marked global and regional disparity in survival is likely due to differences in access to diagnostic and treatment services (Boyle et al., 2005) .

In Saudi Arabia There is an increase in the incidence of CRC between 2001 and 2006, the age at the time of diagnosis is low when compared with reports from developed countries (Mosli and Al-Ahwal, 2012). The overall ASR was 7.3/100,000. ASR for males was 8.3/100,000 and for females 6.3/100,000 (Saudi Cancer registry 2007).

Several factors have been incriminated as risk factors for CRC e.g. genetic or familial polyposis, alcohol, smoking, ulcerative colitis. Low socioeconomic status (SES) is also associated with an increased risk for the development of colorectal cancer; one study estimated the CRC risk to be about 30 percent increase in the lowest as compared to the highest SES quintile. Unhealthy but potentially modifiable behaviors such as physical inactivity, unhealthy diet, smoking, and obesity are thought to account for a substantial proportion (estimates of one-third to one-half) of the socioeconomic disparity in risk of new onset colorectal cancer. Other factors, including lower rates of CRC screening, also contribute substantively to SES differences in CRC risk (Ahnen and Macrae, 2013).

A large number of factors have been reported by at least some studies to be associated with a decreased risk of CRC. These include regular physical activity, a variety of dietary factors, the regular use of aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs), and hormone replacement therapy in postmenopausal women (Ahnen and Macrae, 2013; Chan AT and Giovannucci, 2010).

Knowing the risk factors in Saudi population could be a significant aid for prevention and early detection of cancer. Hence the aim of the current study was to study and determines the different risk factors related to colorectal cancer in Saudi population.

SUBJECTS AND METHODS

The study was carried out in the Saudi hospitals in four different regions in Saudi Arabia, East, Middle, West and South. A case-control approach was used to study the risk factors related to colorectal cancer. The target population comprised all recently diagnosed colorectal cancer cases admitted to governmental hospitals during a period 6 months and all cases of cancer that are managed in the radiotherapy or chemotherapy department during the same period of study. For each case one control was selected from the same hospital, and matched for age and sex. All controls were free of gastrointestinal disease and other types of cancer.

Procedures of data collection

A- Interview Questionnaire

A pre coded designed questionnaire was used to collect relevant information from cases and controls. Participants were interviewed by trained interviewers. Filled questionnaires were checked for completeness and consistency. The questionnaire includes the following:- Personal data, risk factors related to colorectal cancer, family history of colorectal cancer, Physical Activity: the General Practice Physical Activity Questionnaire GPPAQ (Heron et al., 2014) is a validated screening tool for use in primary care that can be used to assess adult (16-74 years) physical activity levels. It generates simple, 4-level Physical Activity Index (PAI) categorizing patients as: Active, Moderately Active, Moderately Inactive, and Inactive. Diabetes Mellitus and using vitamins and/or food supplements were inquired about.

Dietary assessment: To overcome the problem of reverse causality, that CRC patients might change their dietary habits after the diagnosis, we included only newly diagnosed cases. The retrospective dietary intake of the study participants was estimated using a semi-quantitative FFQ (Block et al., 1990) where, cases and controls were asked to report the frequency (how often) and portion size for each food item consumed during a period of 6 months prior to CRC diagnosis for cases and prior

The FFQ was adapted according to portion sizes based on commonly used household serving units/utensils in Saudi Arabia, and was tested for its validity, reliability and reproducibility before conducting the study (Pietinen et al., 1988).

The different food groups included in the questionnaire were 9 groups as follow: Breads/cereals, vegetables, fruits, meat/meat substitutes, milk/dairy products, deserts, beverages, sandwiches, and traditional Jordanian dishes. The collected dietary data were categorized into: (a) Dietary habits of CRC Saudi subjects as compared to their matched controls, (b) Food groups' analysis: The numbers of daily servings of food groups, based on the frequency of consumption, for all respondents were subsequently grouped according to the Food Guide Pyramid from US Department of Agriculture (USDA, 2005). (c) Daily intake of nutrients: The Food Processor

Table 1. General characteristics of study sample

Variable	Cases N0=174	Controls No=185
BMI	Mean, SD	Mean , SD
	28.3+5.3	27.2±5
Smoking: - never smoke	123(70.7%)	127 (68.6%)
- smokers	51 (29.3%)	58 (31.4%)
Use of anti-inflammatory drugs	No 111 (63.8%)	52 (28.1%)
	Yes 63 (36.2%)	133(71.9%)
Diabetes Mellitus		
Yes	34 (19.5%)	33 (17.8%)
Physical exercise		
Inactive	120(69%)	94(51%)
Moderately inactive	34(19.5%)	29(15.7%)
Moderately active	14(8%)	28(15.1%)
Active	6(3.4%)	34(18.4%)
Family history of colo-rectal cancer	22(12.7%)	19(10.3%)

software version 10.2 (ESHA Research, Salem, OR, USA) was used to calculate means of daily nutrient intakes of macronutrients, fiber, and specific micronutrients as estimated from the frequency of consumption, reported portion size, and nutrient content for all foods reported by each participant.

B- Anthropometric measurements

The conventional methods to measure the different anthropometric indices was followed, they included, standing height, body weight.

C- Data procedure

Data was managed through SPSS software; it was cleaned and revised before data entry. Statistical analysis: Data is expressed as mean ± SD (standard deviation). Chi-square ($\chi 2$) test was used for comparing the categorical variables. Student's unpaired t-test was used for comparing the continuous variables. The $P < 0.05$ was considered as statistically significant. Logistic regression analysis was adopted for determining risk factors related to CRC.

RESULTS

Our sample comprised 359 subjects 174 Cases and 185 healthy controls, their age ranged from 20 to 85 years; there were 200 (55.7%) males and 159 (44.3%) females. Nearly one third (32.2%) of the cases and over half of the controls (58.8%) were having a university degree, while those had secondary education constituted 29.9% and 18.4% of case and controls respectively. Table 1 illustrates the general characteristics of case and controls. The Mean Body Mass Index (BMI) for cases is slightly higher than that for controls, the difference between the two groups is statistically significant; t=2.1, p=0.03. Most of our sample didn't smoke (70.1% of cases and 68.6% of controls) while those who are currently or ex smokers were 29.3% and 31.4% for both groups respectively.

With regards to physical activity; most of the cases were inactive (88.5%), in comparison to two thirds of the controls (66.5%), active cases and controls constituted 3.4% and 18.7% of our sample respectively. The difference between both groups was significant; chi square = 27.5 & p=0.00. Less than two thirds of cases (63.8%) and 28.1% of controls never used non-steroidal anti-inflammatory drugs (NSAIDs), P=0.0001. Regarding Family history of disease, only 12.7% of cases had a history of one or more relative who complained from colorectal cancer in comparison to 10.3% of controls. No significant difference was detected between cases and controls regarding diabetes; p=0.68

Logistic regression was used to explore the effect of different factor on colorectal cancer and to adjust for confounding. All factors which were included in the model were dichotomized, except for BMI which was categorized into three categories; normal weight (referent category), over weight and obese. Family history of colon cancer, physical activity and the use of NSAIDs were the most significant variable that independently associated with the risk of colorectal cancer; while family history and physical in-activity has a risky effect, NSAIDs use has a protective significant effect on colorectal cancer. The risk is increased with increasing weight particularly with obese and very obese persons, table 2.

Nutritional data

Table 3 presented the daily servings from different food groups by the study participants, according to USDA

Table 2. Logistic regression results for factors associated with colorectal cancer

Factors	Beta	Odds Ratio	95% CI
Family history	1.17	1.23	1.1 – 4.7
Physical activity	1.16	3.21	1.7 – 5.8
BMI			
Overweight	0.17	0.84	0.45-1.5
Obese	0.46	1.6	1.03 – 2.7
NSAIDs	1.39	0.24	0.15 – 0.4
Smoking	0.32	1.37	0.82 – 2.3
Diabetes Mellitus	0.14	1.16	0.46 – 2.1

Table 3. Food consumption frequency of CRC cases and controls

Food group (servings/ day)	CRC Cases (n= 174) N (%)	Controls (n=185) N= 185	Statistical Analysis	*P*-value
Bread, Cereal, Rice & Pasta				
<6				
6-11	36 (20.68)	90 (48.65)		
>11	70 (40.23)	60 (32.43)	χ^2= 17.57, df=2	0.0002*
	68 (39.09)	35 (18.92)		
Meat, Poultry & Fish				
<2	25 (14.37)	18 (9.73)		
2-3	110 (63.22)	120 (64.86)	χ^2= 0.8844, df=2	0.6426
>3	39 (22.41)	47 (25.41)		
Milk, Yogurt & Cheese				
<2	18 (10.35)	20 (10.81)		
2-3	122 (70.11)	135 (72.97)	χ^2= 0.2802, df=2	0.8693
>3	34 (19.54)	30 (16.22)		
Vegetables				
<3	64 (36.78)	16 (8.65)		
3-5	100 (57.47)	132 (71.35)	χ^2= 26.11, df=2	<0.0001#
>5	10 (5.75)	37 (20)		
Fruits				
<2	51 (29.31)	10 (5.41)		
2-4	118 (67.82)	171 (92.43)	χ^2= 21.07, df=2	<0.0001#
>4	5 (2.87)	4 (2.16)		

*Significantly less than CRC cases group, #significantly higher than CRC cases group, $P<0.05$.

Food Guide Pyramid, and data showed no significant (P > 0.05) differences with regard the consumption of foods from meat, meat alternatives and dairy products groups between the CRC cases and controls. The consumption of fruits and vegetables was however significantly (P < 0.05) higher in controls as compared to CRC cases. The majority of CRC cases consumed more (6-11 & >11) daily servings of bread and cereals as compared to controls (P < 0.05).

Daily intakes of energy, macronutrients, and dietary antioxidants (β-carotene, α-tocopherol, vitamin C, and selenium) of the study subjects as compared to the recommended dietary allowances (RDA) are presented in Table 2. It was observed that, although CRC Cases had consumed higher daily intake of total calories than the controls, (P <0.05), yet their intake was lower than the RDA. On the other hand there was no significant difference, between CRC cases and controls regarding their daily intake of protein, and dietary fiber, which was also adequate to their corresponding RDA, P >0.05. There was a trend of low intake of dietary antioxidants among CRC cases as compared to controls (Table 4).

Table 4. Daily Dietary Characteristics of the Study Subjects

Nutrient	CRC Cases N= 174	Controls N= 185	Statistical Analysis	*P*-value
Calories (kcal)	2222.16 ± 491.10	1980.42±225.43	*t*= 6.067, df=361	<0.001*
Carbohydrates (g)	178.40± 29.81	125.8± 25.36	*t*= 18.52, df=362	<0.001*
Saturated Fat (g)	138.09± 49.37	136.90±43.01	*t*= 0.246, df=362	0.805
Protein (g)	64.58± 14.95	62.62±13.55	*t*=1.385, df=362	0.167
Fiber (g)	25.41 ± 11.39	24.65±8.36	*t*= 0.7562, df=362	0.45
β-Carotene (µg)	3185 ± 1108	4948 ± 2163	*t*= 9.722, df=362	< 0.001#
α-Tocopherol (mg)	8 ± 3	16 ± 4	*t*= 21.51, df=362	< 0.001#
Vitamin C (mg)	32.38±6.42	64.84±12.37	*t*= 31.26, df=362	< 0.001#
Selenium (µg)	21.40±6.37	39 ± 14.45	*t*= 15.32, df=362	< 0.001#

*Significantly less than CRC cases group, #significantly higher than CRC cases group, *P*<0.05. Estimated average requirements (EARs); (Energy intake: 2300.00 kcal/day), (Carbohydrate requirements: 275-375 g/day), (Fat energy ratio: 20-25 %/total caloric), (Protein requirements: 40-55 g/day), (Fiber requirements: 16-40 g/day), (β-Carotene, and α-Tocopherol: non-detectable , respectively), (vitamin C requirements: 50 mg/day), (Selenium requirements: 40 µg/day).

DISCUSSION

The risk of developing colorectal cancer (CRC) is influenced by several acquired risk factors, including environmental exposures and comorbid medical conditions that are partially genetic in nature. These risk factors are based on data almost exclusively derived from observational studies. Because of the possibility of bias due to confounding, these acquired risk factors should not be automatically assumed to be causative, and in fact some may not be truly independent risk factors. Modifiable risk factors of CRC include smoking, physical inactivity, being overweight and obesity, eating processed meat, and drinking alcohol excessively (Tárraga López et al., 2014)

The current study revealed that obesity, lack of physical activity and family history were considered as risk factors for CRC, while the use of NSAIDs act a protective element against CRC incidence .

NSAID use was associated with a reduced colorectal cancer risk; the magnitude of this association differed between aspirin and non-aspirin NSAIDs. Daily aspirin and non-aspirin NSAID use by individuals with a family history of colon cancer significantly reduced the risk of rectal and colon cancer, respectively (Ruder et al., 2011, www.uspreventiveservicestaskforce.org)

Substantial observational data suggest that regular physical activity, either occupational or leisure time, appears to be associated with protection from colorectal cancer. In a meta-analysis of 21 studies, there was a significant 27 percent reduced risk of proximal colon cancer when comparing the most versus the least active individuals.

The mechanism underlying the apparent protective association of physical activity is not known and no intervention trials of physical activity for CRC prevention have been reported. It is not known whether weight loss alone in the absence of increased physical activity would decrease CRC risk in adults (Wolin et al., 2009; Boyle et al., 2012).

Family members share genes, behaviors, lifestyles, and environments that together may influence their health and their risk of chronic disease. Most people have a family health history of some chronic diseases (e.g., cancer, coronary heart disease, and diabetes) and health conditions (e.g., high blood pressure and hypercholesterolemia). People who have a close family member with a chronic disease may have a higher risk of developing that disease than those without such a family member.

With regards to nutrition data it was observed that, the consumption frequencies of food items rich in antioxidants were less among the enrolled CRC cases, indicating their low daily intake of dietary antioxidants which might be a trigger for cancer pathogenesis, including CRC, suggesting that CRC carcinogenesis is modifiable in accordance to antioxidant dietary factors with potential anticancer properties.

In comparison with the average requirement (AR), the intake of CRC cases and controls of protein exceeded the daily requirements and this might be explained by the fact that a high frequency of red meat consumption was reported among all study participants. The majority of correlation and case-control studies suggest a positive association between meat intake and CRC (Magalhães et al., 2011; Arafa et al., 2011; Zhivotovskiy et al., 2012). However, the evidence from large prospective studies is conflicting, and our study results is contradicting and this is might be attributed to the cooking methods and fat content might be removed before cooking. Also, in support for our findings; two large prospective studies (Giovannucci et al., 1994; Larsson et al., 2006; Egeberg

et al., 2013) do not support a positive association between animal protein intake and CRC risk as suggested by observations from some case-control studies (Potter, 1999; Zhivotovskiy et al., 2012).

Regarding fiber intake, our results are in line with the findings from observational epidemiological, animal, and intervention studies which does not unequivocally support a protective role of fiber against the development of CRC (Bingham, 2006). Three large prospective studies; the Nurses 'Health study (n=121,700), the Iowa Women's Health Study (n=98,030), and the Health Professionals Follow-up study (n=51,529) have shown no significant association between dietary fiber intake and CRC in both genders (Fuchs et al., 1999; Steinmetz et al., 1994; Giovannucci et al., 1994). In addition, larger placebo-controlled, randomized trials have generally no beneficial effect associated with dietary fiber supplementation on adenoma recurrence (Alberts et al., 2000; Schatzkin et al., 2000). In the trial reported by the Toronto Polyp Prevention Group from Canada, for 2 years of follow-up with colonoscopy, 201 subjects with colorectal adenomas were randomized after polypectomy either to receive intense counselling on either a diet high in fiber (50 g/day), or to follow a diet low in fiber showed no significant difference between the dietary groups with regard to adenoma recurrence.

During the past years, the regular consumption of traditional foods in Saudi Arabia is being replaced with more Western-style and ready-made foods, in addition to adopting a sedentary life style in daily life and other related activities (Almurshed, 2009; Elbasmi et al., 2010). There is dearth of research exploring the relationship between diet and CRC risk in Saudi Arabia, although the recent flourishing scientific research studies from other parts of the world concluded that CRC is a major public health problem and modernization in food choices, sedentary life style and increased life expectancy are the major factors that might synergize with genetics for the epidemic of CRC worldwide (World Cancer Research Fund, 2008).

There are several established dietary risk factors for CRC, largely related to diets from animal sources that are low in fibre and high in fat (Arafa et al., 2011). Meanwhile, allium vegetables, fruits, pulses and foods containing selenium protect against cancer (Zhou et al., 2011). Non dietary risk factors for CRC include decreased physical activity and obesity (Friedenreich et al., 2002; Frezza et al., 2006). Adopting healthy diets and regular physical activity are two effective strategies in the primary prevention of CRC, among different populations worldwide (Norat et al., 2014; Uddin et al., 2009).

The complexity of the human diet represents a daunting challenge to researchers contemplating a study of its relation to CRC, and very few national studies have tackled the role of Westernization of diet in association with CRC (Arafa et al., 2011; Waly et al., 2012). Meeting energy and nutrients needs, and preventing nutritional-related disorders while establishing healthy eating habits among adolescents is the main challenge for primary prevention of CRC (Arafa, 2014). The establishments of healthy eating behavior are essential to reduce the risk to develop CRC (Xu et al., 2013).

Adequate intake of dietary antioxidants continues to play an important in the primary prevention of oxidative stress-mediated chronic diseases, including CRC (Leenders et al., 2014). Adequate intake of dietary antioxidants attenuates the progression of CRC among vulnerable population (Stone et al., 2014). Oxidative stress is a condition under which the intracellular antioxidant glutathione and dietary antioxidants (vitamin C, selenium, β-carotene and vitamin E) are not counterbalancing the reactive oxygen species, and subsequently induce cellular damage which is involved in the pathogenesis of cancer (La Vecchia et al., 2001). Vegetables and fruits are good sources of antioxidants that provide a protective effect against the ROS-mediated DNA and lipids cell membrane structures damage in proliferated cells (Greenberg et al., 1994).

CONCLUSIONS

The results of this study acted as an attempt to establish a base line data for daily intake of dietary antioxidants, in relation to health and wellbeing of CRC and their first degree relatives who are considered as vulnerable group for CRC among the Saudi population.

A modification of diet and lifestyle could reduce morbidity and mortality from CRC, In Saudi Arabia, primary prevention of CRC is feasible through multidisciplinary intervention programs such as; long-term behavior modifications in food choices, dietary pattern and physical activity. Addressing the daily intake of dietary antioxidants is an asset to develop a dietary approach for the primary prevention of CRC among high risk population of the Saudi adults.

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