RESEARCH COMMUNICATION

Dietary and Lifestyle Characteristics of Colorectal Cancer in Jordan: a Case-control Study

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Abstract

Objectives: We evaluated dietary pattern and lifestyle characteristics of patients with colorectal cancer (CRC) in Jordan. Design: The case-control study included 220 recently diagnosed CRC cases and 220 age and gender matched healthy subjects as a control group. Results: The participating CRC cases had lower dietary intake of fibre, folate, vitamin B12, β-carotene, vitamin C and selenium as compared to controls (P<0.05). The frequency of consumption of fruits and vegetables was also lower among CRC cases, while the frequency of consumption of red meat and saturated fat was higher and positively associated with CRC risk. Furthermore, family history for CRC played a positive role and the majority of CRC cases and controls had a low physical activity level. Conclusions: A sedentary lifestyle and a diet low in fruits and vegetables, and high in animal red meat and saturated fat, appeared associated with CRC among the studied Jordanian subjects. This is consistent with the reported CRC studies in developed nations indicating global causal effects for this tumour type.

Keywords: Colorectal cancer - diet - lifestyle - case-control - Jordan

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Introduction

Cancer is considered a leading cause of death worldwide, accounting for 7.6 million of all deaths from a total of 58 million deaths reported in year 2005 and the world health organization (WHO) estimates that there will be 20 million new cases and 12 million deaths from cancer alone by the year 2020 (WHO, 2006; Stewart & Kleihues, 2003). The prevalence of cancer is higher in developed nations, yet 70% of all cancer deaths in 2005 occurred in developing countries (WHO, 2005).Recent reports indicating that migrant populations moved from countries of low cancer incidence to the west adopted the high cancer incidence trend of the new country (Hardling et al., 2009; Ronellenfistch et al., 2009; Sung et al., 2005). The international experts from the recent World Cancer Research Fund Report, 2007, concluded that CRC is a major public health problem worldwide 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 (WCRF, 2008).

There are several established dietary risk factors for CRC, largely related to folate deficiency (Choi and Mason, 2000), diets from animal sources that are low in fibre and high in fat (Willett et al., 1990, Slattery et al., 1997). In addition experimental evidence from animal studies suggests that reactive oxygen species production alter DNA and lipid membrane structures in proliferated cells, suggesting a protective effect of antioxidants nutrients against different types of cancer, including CRC (Greenberg et al., 1994; La Vecchia et al., 2001).

Non dietary risk factors for CRC include, decreased physical activity (Friedenreich and Orenstein, 2002), obesity, a body mass index (BMI) of greater than or equal to 30 kg/m2 (Calle et al., 2003; Jass, 2005), type 2 diabetes mellitus (Campbell et al., 2010), genetic susceptibility (Heavy et al., 2004; Frezza et al., 2006), alcohol drinking (Wu et al., 1987; Shimizu et al., 2003), smoking (Uldrich et al., 2001) and exposure to environmental carcinogens that may lead to proliferation and malignant transformation of colorectal cells (IARC 1993; Irigaray et al., 2007).

In spite of considerable public health significance of CRC, a recent study in Jordan revealed that most study participants are not well informed about CRC and early screening (Omran and Ismail, 2010). Dietary studies, pertinent to colorectal cancer, in our region are limited, where life style related factors, mainly the diet and physical activity, are much different than developed countries. In Jordan there was no reported

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studies conducted to investigate the association between diet, lifestyle factors and CRC risk. Therefore this case-control study was planned to evaluate the dietary pattern, sociodemographic and other lifestyle risk factors of CRC patients as compared to control subjects in Jordan.

Materials and Methods

Study participants

A case-control approach was used to conduct this study between the period of February 2008 and through January 2009 at Al-Bashir Hospital, a national referral hospital and the principal governmental center for CRC registry and therapy in Jordan. This study included all recently diagnosed and histologically confirmed CRC cases within the specified period of the study and they were 118 males and 102 females. The controls were selected from those attending the outpatient departments at the same hospital and they were a total of 600 controls sampled, 417 of whom were eligible to participate based on the study inclusion criteria; being free of gastrointestinal diseases and have no previous diagnosis of CRC or other types of cancers. Of the 417 eligible controls, 220 were interviewed based on age and gender matching criteria to CRC cases. All female cases and controls were not currently pregnant or lactating.

Ethical approval

This study was approved by the Institution Research Board (IRB) of the High Institute of Public Health, Alexandria University, Egypt and Research Ethics Committee of the Ministry of Health in Jordan. All patients and controls gave informed, written consent for enrollment in the study.

Data collection

In-person interviews were scheduled for study participants (cases and controls). They were asked to complete the study questionnaire included questions related to: (I) Sociodemographic data, smoking, alcohol drinking, family, history of CRC, vitamins supplement use, monthly income and physical activity (II) Dietary intake using a food frequency questionnaire (FFQ). Appetite problems (poor, good or excellent) were also reported. (III) Anthropometric measurements of cases and controls.

Anthropometric measurements

For all participants; height was measured to the nearest 0.5 cm and weight was recorded to the nearest 0.5 kg using a precision sale. Body mass index (BMI) for every subject was calculated as weight in kilograms divided by height in meters squared (kg/m^2) and categorized as normal (BMI=18-25), overweight and obese (BMI>25).

Clinical presentation for cases with colorectal cancer

Cases were inquired about date of first complaint and the interval of time between the appearance of first sign and/or symptom and visit to health provider confirming diagnosis. Basis of confirmed diagnosis, staging and diagnostic facility information (hospitals and laboratories) were collected from medical records. Clinical data were collected and coded by following of the International Classification of Diseases for Oncology (ICD-O-3) as a dual classification with coding system for both topography and morphology.

Dietary assessment

To overcome the problem of reverse causality, that cancer patients might change their dietary habits after the diagnosis, we included only newly diagnosed cases in which diagnosis was confirmed 10-14 days prior to dietary intake questionnaire. 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 12-months prior CRC diagnosis for cases and prior being interviewed for controls, this period was chosen to take into account seasonal variation in food consumption. Also, all study subjects were inquired if they have changed their diet than the usual routine in the last 12 months. The FFQ was adapted according to portion sizes based on commonly used household serving units/utensils in Jordan, 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 Jordanians 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 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. (d) The percentage of kilocalories (Kcal) contribution to the total energy intake from protein, carbohydrate and fat were calculated for each participant.

Physical activity assessment

Physical activity was expressed as either low, moderate or high and calculated according to World Health Organization (Global Physical Activity Questionnaire) (WHO, Physical activity/GPAQ v2.0) as detailed below: Total Physical Activity = [(P2 * P3 * 8) + (P5 * P6 * 4) + (P8 * P9 * 4) + (P11 * P12 * 8) + (P14 * P15* 4)].

In the equation; constant 8: means vigorous metabolic equivalents (MET) in both domains (work and recreational). Constant 4: means moderate MET in both domains (work and recreational). One MET is defined as 1 kcal/kg/hour and is equivalent to the energy cost of sitting quietly.

The three physical activities suggested for classifying populations were low, moderate, and high. The criteria for

these are shown below:

High: If (P2 + P11) ≥ 3 days & total physical activity MET minutes per week is ≥ 1500 . OR. IF: (P2 + P5 + P8 + P11 + P14) ≥7 days & total physical activity MET minutes per week is ≥ 3000.

Moderate: If: (P2 + P11) ≥ 3 days & ((P2 * P3) + (P11 * P12)) ≥ 60 minutes. OR IF: (P5 + P8 + P14) ≥ 5 days & ((P5 * P6) + (P8 * P9) + (P14 * P15) ≥ 150 minutes OR • IF: (P2 + P5 + P8 + P11 + P14) ≥ 5 days & total physical activity MET minutes per week ≥ 600..

Low: If the value does not reach the criteria for either high or moderate levels of physical activity.

Statistical analysis

Data analysis was done using The Statistical Package for Social Sciences, for personal computer, (SPSS-PC) version 17. The chi-squared test was used to analyze categorical variables and the unpaired Student's t-test for analyzing continuous variables. P-value <0.05 was considered statistically significant. The Logistic Regression Analysis, stepwise method was used as a multivariate analysis, where the dependent variable was being either cases or controls. The procedure began by selecting a group of variables that were associated with the disease status. First variable was selected for regression model, and then coupled with the next variable and so on. The procedure continued until all variables were selected or no additional variables provided an improvement in the model.

Results

There were 220 (118 males and 102 females) CRC cases and 220 matched controls for age and gender. The CRC cases and controls were similar in age (56.3 ± 12.3 years for males and 53.7 ± 6.8 years for females) and gender (53.6 % males & 46.4% females). As presented on table 1; the CRC female cases and controls had no significant difference with regards to BMI (t=1.33, P>0.05), mean while, BMI for males of controls group was higher than that of CRC cases, t=2.78, P<0.05.

CRC cases and controls had comparable monthly income, educational level, marital status, and residence status. None of the study participants consumed either multi-vitamin supplements or alcoholic beverages and the majority (67.7% for CRC cases and 71.8% for controls) never smoke, table 1. The assessment of physical activity levels (low, moderate and high) and routine exercise practice were comparable among CRC cases and controls group, table 1.

Table 2 shows the common dietary habits of the study participants, the majority of the study sample consumed fresh green salad on daily basis 80% and 85% for CRC cases and controls group respectively compared to 20% of cases and 15% of control group who consumed fresh green salads 1-2 times/week, the difference was not significantly different, P>0.05. CRC cases and controls had a similar dietary pattern with regard; adding olive oil to foods, adding lemon to beans and salads, type of bread eaten, and citrus fruits consumption, Table 2. All study participants reported a good appetite for eating and consuming foods without any preference.

Table 1. Lifestyle Characteristics of CRC Cases and Controls

Characteristic	Cases**		Controls**		Test of
	No.	%	No.	%	significance
Physical Activity Level					$\chi2$= 1.98,
Low	170	77.3	166	75.5	P=0.372
Moderate	40	18.2	37	16.8	
High	10	4.5	17	7.7	
Routine Exercise Practice					$\chi2$= 21.74,
Yes	40	18.2	84	38.2	P =0.000*
No 1	80	81.8	136	61.8	
Smoking History					$\chi2$= 19.24,
Current Smoker	48	21.8	60	27.3	P=0.000*
Ex-Smoker	23	10.5	2	0.9	
Never Smoke	149	67.7	158	71.8	
First Degree Family History of CRC					COR=2.34
Yes	20	9.1	9	4.1	1.04 -5.27
No	200	90.9	211	95.9	
Body mass index (kg/m^2) Mean ± S.D					
Male	23.9 ± 3.6		25.3 ± 4.1		P =0.006*
Female	27.3 ± 5.8		28.5 ± 7.05		P =0.185

*Significant (P<0.05); **n=220; COR, Crude Odds Ratio

Table 2. Dietary Habits of CRC Cases and Controls

Characteristic	Cases**		Controls**		Test of
	No.	%	No.	%	significance
Drinking Tea					$\chi2$=3.96,
After meal	209	95.0	198	90.0	P=0.046*
Not drinking	11	5.0	22	10.0	
Adding lemon to beans and salads					$\chi2$=1.13,
Yes	132	60.0	121	55.0	P=0.288
No	88	40.0	99	45.0	
Fresh green vegetables consumption					$\chi2$=1.90,
Daily	176	80.0	187	85.0	P=0.17
1-2 times/week	44	20.0	33	15.0	
Adding olive oil to foods					$\chi2$=0.18,
Yes	209	95.0	207	94.0	P=0.67
No	11	5.0	13	6.0	
Type of bread eaten					$\chi2$=0.87,
White bread	202	92.0	207	94.0	P=0.35
With Zatar	18	8.0	13	6.0	
Citrus fruits					$\chi2$= 0.48,
Daily	143	65.0	136	62.0	P= 0.49
1-2 times/week	77	35.0	84	38.0	

*Significant (P<0.05); **n=220

Foods group analysis (number of daily servings as compared to USDA Food Guide Pyramid) is represented in Table 3. It shows that the daily intake of servings from various food groups based on the USDA Food Guide Pyramid. Highly significant differences were observed from the vegetables, fruits and meat groups between CRC cases and controls (P<0.05), where for CRC cases, 30 % consumed than 3 servings vegetables/day, 43% consumed less than 2 fruits servings/day, and 43.6% consumed more than 3 servings of meat/day. On the other hand, no significant differences were observed in the daily intake of servings from the cereals and milk groups (P>0.05).

The percentage of energy from different macronutrients analysis revealed that for CRC cases, approximately 30% of dietary calories in the standard diet consists of fat, that is statistically higher than controls (P<0.05). The

Table 3. Frequency of Food Consumption of CRC Cases as Compared to Controls

Food group[1]	Cases** No.	%	Controls** No.	%	Test of significance
Bread, Cereal, Rice& Pasta Group					$\chi2$= 1.66
<6	1	0.45	2	0.91	P =0.44
6-11	217	98.6	213	96.8	
≥11	2	0.91	5	2.27	
Vegetables Group					$\chi2$=48.63
<3	65	29.6	10	4.54	P = 0.000*
3-5	81	36.8	109	49.5	
≥5	74	33.6	101	45.9	
Fruits Group					$\chi2$= 37.09
<2	94	42.7	36	16.4	P= 0.000*
2-4	97	44.1	136	61.8	
>4	29	13.2	48	21.8	
Milk, Yogurt & Cheese Group					$\chi2$=2.34
<2	17	7.7	26	11.8	P =0.31
2-3	196	89.1	189	85.9	
≥3	7	3.18	5	2.27	
Meat, Poultry, Fish, Dry Beans, Egg & Nuts Group					
<2	17	7.73	40	18.2	$\chi2$=33.18
2-3	107	48.6	137	62.3	P = 0.000*
≥3	96	43.6	43	19.6	

[1]number of servings/day; *Significant (P<0.05); **n=220

Table 4. Energy from Different Macronutrients and Mean Daily Intake of Different Fat Types

Variable	Cases**	Controls**	Statistical Analysis
Percentage of energy			
% protein	23.7±0.16	22.3±0.15	t=94.0, P=0.000*
% fat	26.9±0.52	24.4±0.72	t= 40.8, P=0.000*
% carbohydrate	49.4±2.15	53.2±1.61	t=21.2, P=0.000*
Fat Types (g/day or mg)			
Saturated	18.0± 9.80	13.3±7.28	t-test=5.67, P=0.000*
Monounsaturated	16.5±12.3	13.9±9.83	t-test=2.46, P =0.014*
Polyunsaturated	8.5±6.2	5.8±5.1	t-test=4.98, P=0.000*
Cholesterol	159±153	111±170	t-test=3.07, P=0.002*

Data presented as Mean ± S.D, *Significant (P<0.05); **n=220

same pattern was observed for the percentage of energy derived from protein and carbohydrate among CRC cases as compared to controls, P<0.05, Table 4. The different types of fats consumed daily and contributing to total daily fat amount is also presented in Table 4, and it is observed that the daily intake from saturated , mono and polyunsaturated fats and cholesterol is significantly higher among CRC cases as compared to controls, (P<0.05).

The mean daily intake of fibre for CRC patients (4.63 ± 5.46 g/day) was significantly lower than the control (18.8 ± 3.1 g/day), t= 33.47, (P<0.05), and lower than the RDA for fibre (25 g/day). The mean daily intake of vitamins and minerals for CRC patients was comparable to controls and within RDA values with the exception to the folate and vitamin B12 for CRC patients (189.2 ± 11.7 μg/day and 1.09 ± 1.1 μg/day respectively) was significantly lower than the controls group (212.5 ± 13.1 μg/day and 1.49 ± 1.3 μg/day respectively), (t = 19.68 and t = 3.48 respectively), (P<0.05). Furthermore, β-carotenes (1946.96 ± 1485.18 mg/day for CRC cases and 2257.23 ± 1561.90 mg/day for controls), vitamin C (45.48 ± 16.81 μg/day for CRC cases and 64.78 ± 13.74 μg/day for controls), and selenium (38.75 ± 11.42 μg/day for CRC cases and 59.26 ± 8.91 μg/day for controls), were significantly lower, (t= 2.13, t= 13.19 and t = 21.00 respectively), (P<0.05).

The association between nutrients intake as independent predictors for CRC risk was determined using the multivariate analysis, stepwise method for logistic regression analysis, where the dependent variables were either CRC cases or controls. The model showed that: total fat: OR=1.46 (1.15– 1.84), potato: OR =1.77 (1.18 – 2.66), sweets and cakes: OR= 2.33 (1.67– 3.25), fruits: OR =1.80 (1.26 – 2.58), red meat: OR=2.66 (1.83 – 3.88), saturated fat: OR=1.03 (1.01– 1.05), were the higher independent predictors for CRC among the interviewed groups. Meanwhile, calcium: OR = 0.99 (0.99 – 1.00), green leafy vegetables: OR = 0.99 (0.99 – 1.00), vegetables: OR = 0.99 (0.99 – 0.99) and eggs: OR =0.89 (0.84 – 0.94), were marginally independent predictors for CRC among interviewed groups.

Discussion

Diet represents the most significant environmental factor to which humans are exposed on a regular basis over prolonged periods of time and its impact in the etiology or primary prevention of CRC had been extensively studied in developed nations. Few dietary population-based studies were conducted at the Middle East, yet reported high consumption of red meat, fast foods and saturated dietary fats and a decreased consumption of fresh vegetables and fruits, a typical high risk dietary profile for CRC (Musaiger and Miladi, 2001; Galal, 2003). In Jordan, CRC cases accounted for 12.1% of all newly diagnosed cancer cases in 2007, and ranked the first among all new cancers among males and second among females (Tarawenh and Nimri, 2007).The results of our study suggested three associations regarding the modifiable risk factors associated with CRC risk in Jordan:

A family history of CRC is recognized as an important risk factor for the CRC incidence (Fuchs et al., 1994) and our data showed a significant high risk for CRC among those of first degree of family history for CRC. In previous reports physical activity have been related to risk of CRC (Byers et al., 2002, Giovannucci et al., 1997), our data support this link where it was observed a trend of decreased physical activity among CRC cases, that is similar to the recent published meta-analysis report (Harriss et al., 2009). Unlike the published results at developed nations with regard to positive association between obesity and CRC risk (Calle et al., 2003, Adami and Trichopoulos, 2003), obesity was not prevalent among the study male groups for both CRC cases and controls, meanwhile female subjects for both groups had higher mean BMI, < 30, with no statistical differences.

Fruits and vegetables are good sources for different mineral, vitamins and dietary fiber. We observed that the daily fiber intake of the studied subjects was lower than the recommended dietary allowances (RDA) of fiber (25 g/day). This is in accordance with numerous epidemiological studies suggested that populations with diets low in fiber have higher CRC rates (Sheila et al., 2003; Timothy et al, 2009). On the other hand, the recent WCRF report did not support this relation (WCRF, 2008), in addition to

two large prospective studies, the Iwo Women's Health Study (Negri et al., 1998), and the Health Professionals Follow-Up Study (Steinmetz et al., 1994) have shown no significant protective effect of dietary fiber against CRC. In addition controlled clinical studies had revealed that high consumption of dietary fiber did not reduce polyp recurrence among patients with recently detected colorectal adenomas (Giovannucci et al., 1994).

The CRC patients had lower daily intake than the RDA for dietary antioxidants; vitamin C (60 mg/day) and selenium (55-70 μg/day). This increases the risk of oxidative stress and subsequent cellular damage by reactive oxygen species; this has been involved in the pathology of many non communicable diseases including cancer (Baron, 2005; Schrauzer et al., 1977; Johnson, 2001). Dietary folic acid and vitamin B12 levels for CRC cases were lower than the RDA (400 and 2.4 μg/day respectively) this increase the risk of CRC as reported by a recent meta-analysis of prospective cohort studies indicated a significant reduction in CRC risk for subjects in the highest quintile of dietary folate and vitamin B12 intake compared with the lowest (Sanjoaquin et al., 2005).

Few prospective studies showed a positive association between animal protein intake and colorectal cancer risk (Cross et al., 2010; Alexander et al., 2009). Likewise our study shows that the consumption of red meat among CRC patients was higher than controls and associated with high risk for CRC. It is quiet interested that the methods of cooking of meat in Jordan is mainly charring and boiling and it is the same for CRC patients and controls with no significant differences, attributed that cooking methods are not associated with CRC incidence unlike some Western studies that reported a positive association (Gunter et al., 2005).

Among the studied subjects, contribution of saturated fat to the daily intake and total energy intake was higher in CRC patients as compared to controls and increases their total energy intake which is positively correlated with CRC incidence as indicated by previous reports (Schatzkin et al., 2000; Giovannucci et al., 1994).

In conclusion, our results indicated that the CRC cases enrolled in this study, were adopting a sedentary lifestyle and their dietary pattern was high frequency of red meat and saturated fat consumption and low consumption of fruits and vegetables. In addition they had inadequate daily intake of four key nutrients that protect against CRC risk, vitamin C, selenium folate and B12. These findings are similar to risk factors associated with increased CRC incidence at developed nations. Further prospective population-based studies are needed to establish a base line dietary intake data for the Jordanian population.

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