RESEARCH COMMUNICATION

Impacts of Family History and Lifestyle Habits on Colorectal Cancer Risk: A Case-Control Study in Qatar

Abdulbari Bener[1, 2*], Malcolm A Moore[3], Raghib Ali[4], Hanadi R El Ayoubi[5]

Abstract

Background: Associations between family history of colorectal cancer (CRC) in first degree relatives and risk of developing cancer have been well defined, but interactions with environmental, lifestyle and dietary factors are much less clear. Aim: The aim of this study was to evaluate family history, lifestyle and dietary factors associated with developing colorectal cancer in an Arab population. Design: This matched case-control study was conducted from August 2008 to February 2009 in Al-Amal Hospital and Primary Health Care Centers in Qatar. Subjects and Methods: The study covered 146 colorectal cancer patients from Al-Amal hospital and 282 healthy subjects matched by age and gender as controls from primary health care centers. The questionnaire included socio-demographic information, type of consanguinity, medical history, lifestyle habits, and dietary intake. Of the selected 185 colorectal cancer cases, 146 (78.9%) agreed to participate in the study, whereas from the 350 selected controls, 282 (80.6%) gave consent. Results: The mean age of cases was 54.1±12.4 and of controls 53.1±13.1. Among the life style factors, being overweight and obese (60.2%; 30.1% p=0.006), having a smoking habit (26.7%, p=0.025), and consuming bakery items (78.8% p<0.001) and soft drinks (28.7% p<0.02), were positively associated with CRC. The majority of the studied cases and controls were consuming fresh fruits (87.7% vs 85.5%), fresh vegetables (95.2% vs 95%) and green salad (91.1% vs 89.4%) regularly. Family history of CRC (41.8%) was significantly higher in colorectal patients than in controls (29.1%) (p<0.01). Parental consanguinity was observed more frequently in colorectal cancer patients (35.6%). Multivariate stepwise logistic regression analysis showed that smoking, BMI, family history, consuming bakery and soft drinks were significant predictors of development of colorectal cancer. Conclusion: The present study revealed family history and parental consanguinity to be strongly associated with the development of colorectal cancer. Age, gender, a sedentary lifestyle, and being overweight were also positively linked with CRC risk.

Keywords: Epidemiology - case-control - colorectal cancer - BMI - dietary - family history - Qatar

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Introduction

Colorectal carcinoma is the third most common malignant tumour in the world and in the USA, it is the second leading cause of cancer related deaths (American Cancer Society, 2006). The Colorectal cancer is the third most common cancer among both men and women in the US. Each year, approximately 150,000 people are diagnosed with the disease (Haiman et al., 2007). In Europe (Bray et al., 2002), an estimation of cancer incidence and mortality using WHO and National Cancer Registry data shows that colorectal cancer is the second most common neoplasia after lung cancer in males and breast cancer in females. The number of new cases is approximately equal for men and women annually (Correa et al., 2005).

Epidemiological, experimental and genetic studies suggest that colorectal cancer results from a complex interaction between inherited susceptibility and environmental or lifestyle factors (Fearon and Vogelstein 1990; Winawer et al., 1993). In a population-based prospective study, it was found that the children of colorectal cancer patients had a 75% increased risk of developing the disease, in comparison with the general population (Sondergaard et al., 1991). It has also been observed that when people move from a low incidence country to a high incidence country, they quickly adopt the pattern of incidence of the disease of the new place. This suggests that environmental risk factors can lead to the development of carcinomas and increasing evidence suggests that diet may be a major factor. High red meat, processed meat and fat intake increase the risk, while a high intake of fiber from whole grains, fruits and vegetables appears to protect against colorectal cancer (Kerber et al., 1998; Slattery, 2003; Martinez, 2005).

Colorectal cancer has traditionally been seen as a

*[1]Dept of Medical Statistics & Epidemiology, Hamad General Hospital, Hamad Medical Corporation, Weill Cornell Medical College, Qatar, [2]Department of Evidence for Population Health Unit, School of Epidemiology and Health Sciences, The University of Manchester, Manchester, United Kingdom, [3]UICC Asian Regional Office for Cancer Control, Thailand, [4]Cancer Epidemiology Unit, University of Oxford, United Kingdom, [5]Dept. of Oncology & Hematology, Al Amal Hospital, Hamad Medical Corporation, Qatar.[b]*For correspondence : abener@hmc.org.qa, abb2007@qatar-med.cornell.edu*

disease of the West where it is one of the most common cancers in the developed countries whereas it is less common in developing countries (Bener et al., 2007). In the developed parts of the world, the age standardized rate (ASR) is 40 in males and 26.6 in females, in less developed areas, the rates are 10.2 and 7.7 respectively. The highest incidence rates occurred in North America, Australia, Western Europe and Japan. Freedman et al., (2006) reported that Jordanians and Egyptians presented the lowest rates 11.3 and 6.0 per 100,000 population respectively. Cyprus had a lower incidence rate (17.3/100,000 population) similar to that of Israeli Arabs (15.2). In Jordan, colorectal cancer was the second most common cancer among both males and females (Boyle and Langman, 2000). The overall incidence rate of colorectal cancer in the Gulf countries is lower than most of the industrial countries. In the Kingdom of Saudi Arabia12, colorectal cancer ranks second after breast cancer, constituting almost 9% of the newly diagnosed cases. Also, in the State of Qatar, Colorectal cancer ranked second after the breast cancer with 9% of total cancer cases. Salim et al., (2009) reported in a review of cancer epidemiology in Arab region that age standardized incidence rate for colon and rectum was higher in Kuwait (8.4 & 5.2) and Bahrain (7.9 & 4.4) compared to other arab countries.

Incidence rates are increasing in countries that are undergoing rapid industrialization because of the lifestyle risk factors including diet, physical activity, obesity which play a pivotal role in the aetiology of the disease. Qatar, like many other developing countries, has witnessed rapid change in many aspects of life during the last two decades. The discovery of oil in the 1950s has contributed to significant social change, and Qatar has experienced a rapid transition in its socioeconomic status. This rapid growth and changing environmental and social conditions in the State of Qatar affected the prevalence and patterns of cancer. The increasing incidence of colorectal cancer during the past decade coincides with several changes in lifestyle habits in the Arab population. It is thus important to evaluate to what extent familial predisposition is involved in both the early and late stages of colorectal carcinoma.

This case-control study was designed to evaluate the impact of family history, life style and dietary factors on colorectal cancer in an Arab population.

Subjects and Methods

The study was carried out at Al-Amal Cancer hospital and primary health care centers in Qatar from August 2008 to February 2009. The Al Amal hospital is the only cancer center in the State of Qatar and it is affiliated with the Weill Cornell Medical College in the United States and Heidelberg University in Germany. The Al Amal hospital provides tertiary care to its cancer patients and is a referral center for all such patients throughout the country. This study was conducted to identify the familial genetic and life style factors associated with developing colorectal cancer. For each case, two controls were selected and matched by age and gender. The controls are matched by gender, race and age by allowing the year of birth to be different by ±5 years.

Colorectal cancer cases were recruited from the national cancer disease registry of the Al Amal cancer hospital registering all the reported cancer cases in Qatar. A total of 185 colorectal cases were selected from the registered cases during the period (January 2003-Decmber 2008) and 146 cancer patients (78.9%) gave consent to participate in this study. 39 colorectal cancer cases were excluded from the study due to their refusal to participate or incomplete records. Whereas 350 controls were identified from the primary heath care centers as healthy with no history of any malignant tumour and 282 agreed to take part in the study (80.6%). 68 subjects were excluded from the study sample for having any acute or chronic diseases or incomplete records. In order to have a homogeneous sample, the study recruited subjects from Arab nationals.

A questionnaire was designed by the principal investigator to collect information on socio-demographicvariables, family history, parental consanguinity, medical history, lifestyle habits, and dietary intake. Any person smoking at least 10 cigarettes a day was labeled as a smoker. Dietary habits were classified into regular and irregular. Regular dietary habit means that subjects take the respective food at least once daily, while irregular dietary habit means that they take the respective food only once in a week or month. The questionnaire was translated in Arabic and translated back into English by a blinded translator to check the validity of the first translation. Face-to-face interviews were conducted by trained nurses, whose mother tongue was Arabic, using the same standardized questionnaire for the cases and the controls. The survey instrument was then tested on 50 randomly selected cancer patients and 50 randomly selected control subjects from the health centers to test reliability. Family history of cancer information was collected as part of the interviewer-administered questionnaire. Study participants were asked to list first names of all first-degree blood relatives, including parents, brothers, sisters, uncles and aunts. The pathology and clinical data were extracted by the investigators and nurses from the hospital records and documented in standardized form. The coefficient of inbreeding (F) of patients and controls was determined from their responses as outlined below:

Measuring Consanguinity:

Consanguinity was evaluated based upon the coefficient of inbreeding (F) which is the probability of homozygosity by descent and was determined in the offspring of six types of consanguineous unions as follows (Bener et al., 2009):

Consanguinity type	Coefficient of inbreeding (F)
Double first cousins	0.125
First cousin	0.0625
First cousin once removed	0.03125
Second cousin	0.0015625
Second cousin once removed	0.0078125

All other types of unions were considered non consanguineous with coefficient of inbreeding set to 0.

The study was approved by the Research Ethics Committee of Hamad General Hospital, Hamad Medical Corporation. All the persons who agreed to participate in this study gave their informed consent prior to their inclusion in the study.

Students t-test was used to ascertain differences between the mean values of two continuous variables and confirmed by non-parametric Mann-Whitney test. χ^2 was utilized to establish the association between categorical variables. Where the sample size was small, the Fisher exact test was used instead of χ^2. The level of inbreeding was assessed in terms of coefficient of kinship values for each population. Multiple stepwise logistic regression analysis was used to asses the relationship between dependent and independent variables and to adjust for potential confounders and order the importance of risk factors (determinant) for colorectal cancer. All p values are two-tailed and those less than 0.05 were considered statistically significant.

Results

Table 1 shows the socio-demographic characteristics of the colorectal caner patients and controls. The mean ages of cases and controls did not significantly differ. Also no variation was observed between cases and healthy subjects in terms of socio-demographic variables.

Table 2 examines the life style and dietary habits of colorectal cancer patients and controls. Having a BMI between 25 and 30 was significantly higher in colorectal cancer patients compared to controls (60.2% vs. 47.2%, p=0.006). Smoking was also associated with an increased risk of colorectal cancer (26.7% vs, 17.0%), p=0.025). Consuming bakery items was also associated with colorectal cancer (78.8% vs. 52.8%, p<0.001) as were soft drinks (28.7% vs. 18.8%; p=0.015) There were no siginificant differences between cases and controls in the intake of fresh fruits (87.7% vs 85.5%), fresh vegetables (95.2% vs 95%) and green salad (91.1% vs 89.4%).

Table 3 compares the consanguinity and family history of colorectal cancer between cases and controls. Overall, the parental consanguinity was higher in colorectal patients (35.6%) with a higher inbreeding coefficient (0.019), compared to healthy subjects (29.4%; 0.016) but this was not statistically significant. In younger patients below 50 years of age, the parental consanguinity was less frequent in colorectal cancer cases (29.1%) than in elder cancer cases above 50 years of age (39.6%). Family

Table 1. Socio-Demographic Characteristics of the Studied Arab Population According to Cases and Controls (N=428)

Variables	Case N=146	Control N=282	p value
Age [Mean±SD] Range	54.1±12.4 18-82	53.1±13.1 19-80	0.440
Age groups			
<40	14 (9.6)	43(15.2)	0.172
40-49	41(28.1)	57(20.2)	
50-59	42(28.8)	83(29.4)	
≥ 60	49(33.6)	99(35.1)	
Gender			
Male	93(63.7)	156(55.3)	0.096
Female	53(36.3)	126(44.7)	
Nationality			
Qatari	49(33.6)	107(37.9)	0.372
Other Arabs	97(66.4)	175(62.1)	
Education level			
Illiterate	20(13.7)	55(19.5)	0.234
Primary	30(20.5)	54(19.1)	
Intermediate	37(25.3)	63(22.3)	
Secondary	41(28.1)	61(21.6)	
University or higher	18(12.3)	49(17.4)	
Household income			
<5000 QR	13 (8.9)	35(12.4)	0.202
5000 -10000 QR	43(29.5)	59(20.9)	
10000-15000 QR	34(23.3)	77(27.3)	
>15000 QR	56(38.4)	111(39.4)	
Occupation			
Not Working	33(22.6)	99(35.1)	0.069
Sedentary / Professional	57(39.0)	98(34.8)	
Manual	23(15.8)	27 (9.6)	
Business	20(13.7)	35(12.4)	
Police / Army	13 (8.9)	23 (8.2)	
Consanguinous Parents			
Yes	52(35.6)	83(29.4)	0.192
No	94(64.4)	199(70.6)	

Table 2. Life Style and Dietary Habits of Colorectal Cancer Patients and Controls (N=428)

Variables	Case N=146	Control N=282	p Value
Lifestyle habits			
Body mass index (Kg/M²)			
<25	14 (9.6)	57(20.2)	0.006
25-30	88(60.2)	133(47.2)	
>30	44(30.1)	92(32.6)	
Smoking			
Non smoker	107(73.3)	234 (83)	0.025
Smoker	39(26.7)	48 (17)	
Smoking of Sheesha			
Non smoker	116(79.5)	225(79.8)	0.964
Smoker	30(20.5)	57(20.2)	
Dietary habits			
Fresh fruits			
Regular	128(87.7)	241(85.5)	0.630
Irregular	18(12.3)	41(14.5)	
Fresh Vegetables			
Regular	139(95.2)	268(95.0)	0.938
Irregular	7 (4.8)	14 (5.0)	
Green Salad			
Regular	133(91.1)	252(89.4)	0.691
Irregular	13 (8.9)	30(10.6)	
Frozen Meat/Chicken			
Regular	107(73.3)	196(69.5)	0.481
Irregular	39(26.7)	86(30.5)	
Fast Food			
Regular	21(14.4)	45(16.0)	0.669
Irregular	125(85.6)	237(84.0)	
Bakery items			
Regular	115(78.8)	149(52.8)	<0.001
Irregular	31(21.2)	133(47.2)	
Soft drinks			
Regular	42(28.7)	53(18.8)	0.015
Irregular	104(71.3)	229(81.2)	
Processed Food			
Regular	25(17.1)	59(20.9)	0.418
Irregular	121(82.9)	223(79.1)	

Table 3. Characteristics of Consanguinity and Family History of Colorectal Cancer Among Patients and controls (N=428)

Variables	Cases	Controls	p value
Overall Frequency	146	282	
Parents consanguineous			
Yes	52(35.6)	83(29.4)	0.231
No	94(64.4)	199(70.6)	
Mean coefficient of inbreeding	0.019	0.016	0.440
Age <50 years Frequency	55	100	
Parents consanguineous			
Yes	16(29.1)	31(31.0)	0.948
No	39(70.9)	69(69.0)	
Mean coefficient of inbreeding	0.016	0.019	0.464
Age ≥50 years Frequency	91	182	
Parents consanguineous			
Yes	36(39.6)	52(28.6)	0.090
No	55(60.4)	130(71.4)	
Mean coefficient of inbreeding	0.020	0.015	0.112
Family history of cancer			
Yes	61(41.8)	82(29.1)	<0.011
No	85(58.2)	200(70.9)	
Cancer in type of relatives			
1st Degree	33(22.6)	39(13.8)	0.030
2nd Degree	17(11.6)	9(3.2)	0.001
3rd Degree	11(7.5)	4(1.4)	0.002

Table 4. Predictors for Colorectal Cancer Using Multivariate Stepwise Logistic Regression Analysis

Independent Variables	Odds Ratio	95% Confidence Interval	P - value Significance
Family History	2.65	(1.55 - 4.72)	<0.0001
Bakery products	2.52	(2.30 - 2.88)	<0.0001
BMI	2.30	(1.38 - 3.83)	<0.0001
Smoking	2.12	(1.12 - 3.85)	0.017
Soft drinks	1.62	(1.19 - 2.17)	0.020

history of CRC was significantly higher in cases than in the control group (41.8% vs. 29.1%, p<0.011), particularly in the first degree (22.6% vs. 13.8%; p=0.03) and second degree relatives (11.6%; vs. 3.2%, p=0.001).

Table 4 shows predictors for the colorectal cancer using stepwise logistic regression analysis. As can be seen from this table, family history, consuming bakery items, BMI, smoking, and soft drink use were found to be significant predictors for colorectal cancer.

Figure 1 shows the distribution of the studied colorectal cancer cases according to gender and age group. The frequency of CRC among men and women has been increasing with the age with a highest peak in men and women in the age group above 60 years. Frequency of CRC remains relatively low in both men and women under 40 years of age.

Discussion

Cancers of the colon and rectum constitute a significant proportion of the global burden of cancer morbidity and mortality, particularly in highly industrialized countries. Colorectal cancer is a consequence of multiple risk factors,

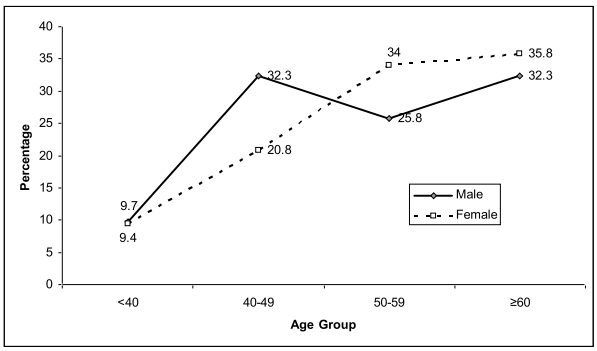

Figure 1. Distribution of the Studied Colorectal Cancer Cases According to Gender and Age Group

among which the interaction between environmental and genetic factors is of particular interest. In this case-control study, we investigated whether family history, lifestyle and dietary factors were associated with risk of developing colorectal carcinoma. Parkin et al., (2005) reported that more than 90% of the newly diagnosed colorectal cancers occurred among individuals older than 50 years of age. A similar situation is found in the present study too that the colorectal cancer was more frequent in patients above 40 years (90.5%). Few studies (O'Connel et al., 2003; Minardi et al., 1998) reported that the incidence of colorectal cancer remains relatively low under 40 years of age. It was suggested CRC can be defined as a disease of elderly people. In the studied patients, sedentary life style has been associated with an increased risk of colorectal cancer which is similar to some other studies (White et al., 1996; Friedenreich, 2001). Also, Whittemore et al., (1990) observed a high risk for colon and rectal cancer with increasing time spent sitting and for those reporting an overall sedentary life style. Colorectal cancer risk was more among the studied men (63.7%) than in women (36.3%). These socio-demographic factors associated with the development of colorectal cancer in our study is in agreement with a previous study by Okamoto et al (2002) reported that the tumor distribution throughout the large intestine depends on the sex, race and the age of the patient in addition to the genetic and environmental factors.

Various studies have suggested that a healthy life style may be protective and prevent initiation of the premalignant stages of CRC. Being overweight was significantly higher in the CRC patients (60.2%) than in healthy subjects (47.2%) which could be due to the lack of physical activity or diet pattern in their life. Friedenreich (2001) stated that physical inactivity, excess body weight, and a central disposition of adiposity have a major influence on the risk of CRC. It is reported (Terry et al., 2001) that cigarette smoking is associated with an increased tendency to form adenomas that develop into colorectal cancer and our study findings also found a positive association between the smoking habit and the CRC risk.

The risk of colorectal cancer is mainly associated with lifestyle factors, particularly dietary factors. A higher risk of CRC was found in subjects consuming a diet poor in fiber and rich in meat and fat (Mckeown-Eyssen, 1994). The majority of the cases consumed fresh fruits (87.7%), fresh vegetables (95.2%), and green salad

(91.1%) regularly. It was reported (Tiemersma et al. 2002) that intakes of red meat and processed food were associated with the risk of cancer in the colon and rectum respectively. However, in our studied patients, intakes of unhealthy food like fast food (14.4%), soft drinks (18.5%) and processed food (17.1%) were very low. The present study revealed a healthy dietary pattern in Arab population with high intake of fruits and vegetables which is in line with the observation of the research team that the low incidence of colorectal cancer in the Arab countries is due to the dietary factors (Salim et al., 2009). It is commonly agreed that the risk of colorectal cancer can be modified by food and dietary habits.

In our study population, family history of CRC was significantly higher in cases (41.8%) than in the healthy subjects (29.1%), particularly in the first degree (22.6%) and second-degree (11.6%) relatives. Our study findings suggest that a family history of colorectal cancer is an important risk factor for the development of CRC in this population and confirms the observation reported by others that a family history of colorectal cancer increases the risk of CRC (Slattery, 2000; Slattery et al., 2003; Martinez, 2005). The proportion of studied patients with a family history of colorectal cancer within 1st degree relatives was 22.6% which is appreciably higher than the figure previously reported in another study (12.4%) (Kotake et al., 1995). First degree relative of individuals with CRC are known to have an approximately two fold increased risk of sporadic CRC (Kerber et al., 1998). Furthermore, parental consanguinity was higher in colorectal patients with a higher inbreeding coefficient (35.6%; 0.019), compared to healthy subjects (29.4%; 0.016) but this was not statistically significant. Stepwise logistic regression analysis of the present data supported the findings that a positive family history is positively associated with the risk of CRC which supports a genetic contribution to colorectal cancer risk. This is in line with the study of Schoen et al., (2000) showed that increased evidence of colorectal cancer is among persons with a family history of CRC and families in which multiple family members affected with CRC. In the studied Arab population, family history and parental consanguinity were the important associated factors for the development of CRC. This shows that inheritance plays a special role in CRC development.

In the studied Arab population, although the CRC patients had a healthy dietary pattern, other factors like gender, age, sedentary life style, being overweight, family history and consanguinity were the main risk factors in the studied population. This study suggests that since lifestyle factors influence the development of cancer among those with a family history of the disease, there appears to be a practical approach for individuals with a family history of CRC to reduce their cancer risk.

In Conclusion the study findings revealed that the incidence of colorectal cancer increased with increasing age and it occurred mostly among individuals older than 50 years of age. Men were more victims of colorectal cancer than women. Although the colorectal cancer patients had a healthy dietary habbit, their age, gender, sedentary life style, being overweight, family history and parental consanguinity were positively associated with the development of colorectal cancer. Among the life style factors, being overweight was a significant associated factor for CRC risk. The risk of colorectal cancer in Arab population is highly influenced by family history and parental consanguinity. The study results indicate a genetic contribution to colorectal cancer risk.

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