

RESEARCH ARTICLE

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## Factors Associated with Colorectal Cancer Among Jordanians: a Case- Control Study

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### Abstract

**Objective:** In recent years, the incidence of colorectal cancer (CRC) in Jordan has been on the rise. We aimed to determine associations with lifestyle factors, demographic and clinical variables. **Methods:** This case-control study included 102 patients diagnosed with CRC and 198 age and gender matched healthy subjects as controls. Cases were purposefully sampled; however, the control group were selected by simple random sampling of a cross-section of the population in Northern Jordan. Participating cases and controls completed an anonymous questionnaire inquiring about their demographic characteristics, lifestyle factors, and clinical variables. Data about the medical history and diagnosis of participating cases were obtained from the cases themselves and confirmed by reviewing their medical records. **Results:** In the cross tabulation analysis, the Chi square test showed that diabetes and hypertension were significantly associated with CRC ( $P < 0.05$ ). Additionally, regression modeling revealed that age  $\geq 45$  years (OR=10.93), positive family history for CRC (OR=5.53), physical inactivity (OR=7.4), cigarette smoking (OR=3.71), and having other types of cancer (OR=13.61) were all associated with increased risk of CRC. **Conclusions:** Physical inactivity and cigarette smoking are among the top modifiable risk factors for CRC among Jordanians. Moreover, diabetes and hypertension were found to be statistically significant risk factors in univariate, but not multivariate analysis. More effective strategies for elevating awareness and prevention are required at both national and international levels. Improving screening strategies is needed for early detection of CRC in Jordan.

**Keywords:** Case-control-colorectal cancer- Jordan- lifestyle

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### Introduction

According to World Health Organization (WHO), during the year 2015 nearly 1 in 6 of all 8.8 million global deaths is attributed to cancer (WHO, 2017). Lung, prostate, colorectal, stomach and liver cancers are the most common types of cancer in men, while breast, colorectal, lung, cervix and stomach cancer are the most common among women (WHO, 2017). In Jordan, cancer is the second leading cause of death after heart diseases with colorectal cancer (CRC) comprising about 11 per cent of all registered cancer cases (King Hussein Cancer Center (KHCC)-unpublished data, 2017). Based on 2010 Jordan's National Cancer Registry report, CRC is the second most common cancer among both genders comprising 15 % and 9.4 % of all males and females cancer cases, respectively (Tarawneh et al., 2010). In 2012, cancer incidence report indicated that CRC ranked the second most common cancer among all cancers in both genders in Jordan. However, in 2017, CRC was the most common

cancer among males and the second most common cancer among females (KHCC, 2017).

Despite Jordanians were mostly aware of CRC as a major cause of mortality as reported by Omran (2015), the incidence of CRC is increasing. In the literature, little is known about the factors associated with CRC in Jordan. Essentially, few published studies were found, among which only one study investigated the association between CRC and life style factors (Ahmad and Al-Gama, 2014; Arafa et al., 2011; Sharkas et al., 2017; Taha et al., 2015). Therefore, we aimed to determine the lifestyle, demographic, and clinical factors associated with CRC in Jordanians, with the ultimate goal of identifying preventive strategies and improve early diagnosis of CRC.

### Materials and Methods

#### *Study design and participants*

The study was implemented over two main stages. In the first stage, a purposeful sampling of cases was

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conducted at the largest two public hospitals in Northern Jordan (King Abdullah University Hospital and Princess Basma Teaching Hospital) between August 2016 and July 2017. These two institutions are tertiary and referral hospitals treating almost all types of illnesses, including cancer. Participants were recruited in the oncology and gastroenterology clinics. The survey was carried out by using a semi-structured questionnaire developed by the research team based on literature review. After that, it was validated after refinement by 3 expert panel reviewers. The questionnaire collected information about socio-demographic characteristics, lifestyle behaviours, and clinical variables. Inclusion criteria for participation were being older than 18 years, diagnosis of CRC, and being a Jordanian citizen. Data about the medical history and diagnosis of participating cases were obtained from the cases themselves and confirmed by reviewing their medical records.

In the second stage, a cross-section of the general public using simple random sampling was implemented using the same semi-structured questionnaire. Inclusion criteria for participation were: age older than 18 years, free of gastrointestinal diseases, have no history of CRC or other types of cancers, and being a Jordanian citizen. Participant was considered physically active if he was involved in any activity that required energy expenditure at least for 30 minutes per day.

#### Data collection procedure

The data were collected via face-to-face interviews. Four experienced interviewers and 2 field supervisors were recruited to collect the data. To eliminate any kind of researcher's bias, the data collections teams attended two training sessions to make sure that all are at similar level of understanding the questionnaire items and perform similar procedure of data collection. The supervisors monitored data collection in the field, did quality checks on the data and provided assistance. Participants in both data collection stages were given special ID number to prevent duplication.

All data collection procedures were implemented according to Helsinki declaration. Privacy and confidentiality were taken into consideration throughout the research period.

#### Ethical Approval

Ethical approval was obtained from the Research Committee, Faculty of Medicine at Yarmouk University. Informed and signed written consent was obtained from each participant.

#### Data analysis

All data were analyzed using SPSS (Version 20 for Windows). Frequency distribution and descriptive statistics were calculated. Questionnaire responses were compared using chi-square test. Binary logistic regression analysis was performed to estimate and predict the impact of independent variables on the dependent variable. A  $p$  value of  $<0.05$  was considered to indicate statistical significance in all cases. To identify factors associated with colorectal cancer, all risk factors

with a  $p$  value  $\leq 0.25$  in the univariate analysis were included in a stepwise binary logistic regression analysis.

## Results

The results are based on the questionnaire responses of 300 participants (102 cases and 198 controls). Our study population age ranged from 18 to 70 years with the majority being 55 years and older (36.3%). As illustrated in Table 1, both genders were almost equally represented in the study (49% males and 51% females).

Table 1. Demographic and Clinical Characteristics of Study Population (n=300)

| Characteristic                                     | n (%)      |
|--|------------|
| Gender   |            |
| Male   | 147 (49.0) |
| Female   | 153 (51.0) |
| Age/year   |            |
| 18-24  | 29 (9.7)   |
| 25-34  | 29 (9.7)   |
| 35-44  | 49 (16.3)  |
| 45-54  | 84 (28.0)  |
| $\geq 55$  | 109 (36.3) |
| BMI  |            |
| Underweight  | 8 (2.7)    |
| Normal   | 95 (31.7)  |
| Overweight   | 122 (40.7) |
| Obese  | 75 (25.0)  |
| Has colorectal cancer                              |            |
| No   | 198 (66.0) |
| Yes  | 102 (34.0) |
| Positive family history of CRC                     |            |
| No   | 268 (89.3) |
| Yes  | 32 (10.7)  |
| History of diabetes                                |            |
| No   | 241 (80.3) |
| Yes  | 59 (19.7)  |
| History of hypertension                            |            |
| No   | 231 (77.0) |
| Yes  | 69 (23.0)  |
| Physically active                                  |            |
| No   | 192 (64.0) |
| Yes  | 108 (36.0) |
| History of IBD                                     |            |
| No   | 277 (92.3) |
| Yes  | 23 (7.7)   |
| Smoking status (if the participant smokes)         |            |
| No   | 220 (73.3) |
| Yes  | 80 (26.7)  |
| Passive smoking (if a member in the family smokes) |            |
| No   | 146 (48.7) |
| Yes  | 154 (51.3) |

BMI, Body mass index; IBD, Inflammatory bowel disease

Table 2. Cross Tabulation of Demographic and Life Style Factors Associated with CRC\* in Northern Jordan (n=300)

| Variable          | Colorectal Cancer |            | P value |
|-------------------|-------------------|------------|---------|
|                   | Cases             | Controls   |         |
|                   | n (%)             | n (%)      |         |
| Gender            |                   |            | 0.327   |
| Female            | 48 (47.1)         | 105 (53.0) |         |
| Male              | 54 (52.9)         | 93 (47.0)  |         |
| Age               |                   |            | 0.000   |
| 18-24             | 0 (0.0)           | 29 (14.6)  |         |
| 25-34             | 2 (2.0)           | 27 (13.6)  |         |
| 35-44             | 7 (6.9)           | 42 (21.2)  |         |
| 45-54             | 28 (27.5)         | 56 (28.3)  |         |
| 55 or older       | 65 (63.7)         | 44 (22.2)  |         |
| BMI               |                   |            | 0.192   |
| Underweight       | 4 (3.9)           | 4 (2.0)    |         |
| Normal            | 28 (27.5)         | 67 (33.8)  |         |
| Overweight        | 38 (37.3)         | 84 (42.4)  |         |
| Obese             | 32 (31.4)         | 43 (21.7)  |         |
| Physical Activity |                   |            | 0.000   |
| No                | 42 (41.2)         | 48 (24.2)  |         |
| Yes               | 60 (58.8)         | 150 (75.8) |         |
| Smoking status    |                   |            | 0.000   |
| No                | 72 (70.6)         | 173 (87.4) |         |
| Yes               | 30 (29.4)         | 25 (12.6)  |         |
| Passive smoking   |                   |            | 0.876   |
| No                | 49 (48.0)         | 97 (49.0)  |         |
| Yes               | 53 (52.0)         | 101 (51.0) |         |
| Job               |                   |            | 0.117   |
| Housewife         | 36 (35.3)         | 59 (29.8)  |         |
| Worker            | 44 (43.1)         | 96 (48.5)  |         |
| Retired           | 17 (16.7)         | 21 (10.6)  |         |
| Others            | 5 (4.9)           | 22 (11.1)  |         |

\*CRC, Colorectal cancer; BMI, Body mass index

A cross-tabulation analysis using chi-square test was performed to assess factors associated with increased risk for having colorectal cancer. Table 2 shows the association between demographic characteristics and life style factors with CRC, and Table 3 shows the relationships between CRC and participants' clinical variables.

As illustrated in Table 2, only 3 items (age, smoking status and physical inactivity) were found to have significant statistical differences. Noticeably, BMI of participants was not significantly associated with CRC.

Interestingly, all factors related to participants' clinical medical characteristics were significantly associated with CRC except the presence of inflammatory bowel disease, and cases had almost doubled percentages in having diabetes and hypertension compared to controls) as shown in Table 3.

To identify factors associated with colorectal cancer, all risk factors with a p value  $\leq 0.25$  in the univariate analysis were included in a stepwise binary logistic

Table 3. Cross Tabulation of Association Between CRC\* and Participants' Clinical Characteristics (n=300)

| Variable                    | Colorectal Cancer |            | P. value |
|-----------------------------|-------------------|------------|----------|
|                             | Cases             | Controls   |          |
|                             | n (%)             | n (%)      |          |
| Diabetes                    |                   |            | 0.015    |
| No                          | 74 (72.5)         | 167 (84.3) |          |
| Yes                         | 28 (27.5)         | 31 (15.7)  |          |
| Hypertension                |                   |            | 0.001    |
| No                          | 67 (65.7)         | 164 (82.8) |          |
| Yes                         | 35 (34.3)         | 34 (17.2)  |          |
| Family history of CRC       |                   |            | 0.001    |
| No                          | 83 (81.4)         | 185 (93.4) |          |
| Yes                         | 19 (18.6)         | 13 (6.6)   |          |
| Inflammatory bowel diseases |                   |            | 0.934    |
| No                          | 94 (92.2)         | 183 (92.4) |          |
| Yes                         | 8 (7.8)           | 15 (7.6)   |          |
| Previous other cancers      |                   |            | 0.029    |
| No                          | 98 (96.1)         | 197 (99.5) |          |
| Yes                         | 4 (3.9)           | 1 (0.5)    |          |

\*CRC, Colorectal cancer

regression analysis. Table 4 illustrates the statistically significant risk factors in the last regression model.

Table 4 illustrates the binary logistic regression analysis. Most interestingly, participants aged 45 years and older were about 11 times more likely to have CRC compared to their younger counterparts. Moreover, physical inactivity was a predictor of having CRC with an odd of more than 7 times compared to those who were physically active.

Table 4. The Binary Logistic Regression Analysis of Factors Associated with CRC\* (n=300)

| Variable                     | OR    | 95% Conf. Interval |        | p.value |
|------------------------------|-------|--------------------|--------|---------|
|                              |       | Lower              | Upper  |         |
| Age/year                     |       |                    |        |         |
| < 45                         | 1**   |                    |        |         |
| $\geq 45$ years              | 10.93 | 4.63               | 25.77  | 0.001   |
| Family history of CRC        |       |                    |        |         |
| No                           | 1**   |                    |        |         |
| Yes                          | 3.53  | 1.40               | 8.88   | 0.007   |
| Practicing physical activity |       |                    |        |         |
| Yes                          | 1**   |                    |        |         |
| No                           | 7.4   | 3.80               | 14.39  | 0.001   |
| Smoking cigarettes           |       |                    |        |         |
| No                           | 1**   |                    |        |         |
| Yes                          | 3.71  | 1.64               | 8.39   | 0.002   |
| Previous other cancers       |       |                    |        |         |
| No                           | 1**   |                    |        |         |
| Yes                          | 13.61 | 0.89               | 207.55 | 0.006   |

\*, Colorectal cancer, \*\*, Reference for other categories within each variable.

## Discussion

Results of this study showed that physical inactivity and cigarette smoking were among the top modifiable risk factors for CRC among Jordanians. On the other hand, age older than 45 years, family history of CRC and presence of previous other cancers were predictive non modifiable risk factors. Moreover, diabetes and hypertension were found statistically significant risk factors for CRC in the univariate analysis, but not in the multivariate analysis.

Participants' age was significantly associated with greater risk of having CRC with an OR of about 11 for those aged 45 years and older compared to their younger counterparts. This result is in agreement with previous results about median age of diagnosis of CRC in Jordan as reported by Tarawneh et al., (2010) who reported that median age of diagnosing CRC was 61 years for both genders. Age can unquestionably be regarded as the strongest non modifiable risk factor for the development of CRC (Rasool et al., 2013). Previous studies suggested that the majority of patients with CRC are above the age of 65 (Curado et al., 2007; Muhandas and Desai, 1999). CRC occurring before age of 40 years accounted for less than 10 % of the total CRC cases in India (Zafar et al., 2008).

In our study, physical inactivity was strongly associated with increased odds for having CRC. Participants who were physically inactive were 7 times more likely to have CRC compared to their counterparts who were physically active. Adoption of a sedentary life style together with a habit of having physically inactive life style can be considered as active players to some extent. Results from the only study conducted by Arafa et al., (2011) about the effect of life style factors on CRC in Jordan have revealed similar trend. Other studies have reported around the world have reported similar findings (Moghaddam et al., 2007; Moskal et al., 2007; Botteri et al., 2008; Renehan et al., 2008; Theodoratou et al., 2014). For that reason, practicing physical activity is vital for decreasing CRC risk and is strongly recommended, especially for those 45 years and older.

Expectedly, smokers were about 4 times more likely to develop CRC compared to non smokers. Several studies have reported smoking to be associated with increased CRC risk (Barrow et al., 2017; Moghaddam et al., 2007; Moskal et al., 2007; Renehan et al., 2008; Siegel et al., 2017; Theodoratou et al., 2014). The International Agency for Research on Cancer concluded in 2009 that tobacco smoking is the cause of CRC (American Cancer Society, 2011). A number of studies have reported similar trend about the strong association between smoking and CRC (Secretan et al., 2009; Paskett et al., 2007; Liang et al., 2009). Moreover, a meta-analysis conducted by Botteri et al. (2008) based on 42 observational studies reported that smokers were at a greater risk of developing adenomatous polyps than non smokers (OR=2.14). Consequently, preventive and counter marketing strategies for smoking are urgently needed to tackle its associated risks.

In agreement with previous results as reported by Rasool et al., (2013), participants who had other types of cancers in our study were about 14 times at greater risk for having CRC compared to those without any other cancers.

Literature indicates that genetic instability and mutations may be critical for the development of colorectal cancers (Lengauer, 1997; Hartwell, 1992).

Not surprisingly, family history of CRC increased the risk of having the disease by 3.5 times compared to those who had no family history of the disease. This result is in agreement with results reported by a study from Jordan (Arafa et al., 2011), and results from Scotland as reported by Theodoratou et al., (2014). According to Center for Disease Control and Prevention, people with a history of CRC in one or more relatives are at an increased risk (Hagggar and Boushey, 2009). Previous studies have reported similar results of the association between presence of family history and CRC (Boardman et al., 2007; Jasperson et al., 2010).

Results of the current study were in agreement with other studies which reported diabetes mellitus as independent risk factor of CRC (Yuhara et al., 2011; Deng et al., 2012). However, this result was significant in the univariate analysis, but not in the multivariate. Our results are similar to results of the study conducted by Will et al., (1998) which revealed moderate association between diabetes and CRC. Similar results were found concerning the associations of hypertension and CRC. These results suggest that diabetes and hypertension could have resulted from the CRC as a secondary complication of psychological stress or medications and not the vice-versa as reported by Scartozzi et al., (2008).

With respect to the association between increased BMI and CRC, it has been reported that general and central obesity were positively associated with an increased risk of CRC (Ma et al., 2013). However, the association between obesity and rectal cancer is weaker than that with colon cancer (Gribovskaja-Rupp, 2011). Therefore, studying colon cancer and rectal cancer independently may reveal more accurate results and can eliminate any confounding effect of such results. Furthermore, obesity might be associated with poor prognosis and outcomes of CRC as suggested by Bardou et al., (2013).

In conclusion, in recent years, the incidence of CRC in Jordan has been increasing. Several socio-demographic, lifestyle, and clinical factors were found associated with CRC in Jordan. Age  $\geq 45$  years, physical inactivity, cigarette smoking, family history of CRC, having other types of cancers, diabetes and hypertension were all found to be significantly associated with CRC in our population. More effective strategies of awareness and prevention are needed at both national and international levels. Moreover, we need to untangle the complex effect of different environmental and lifestyle factors. Targeted preventive strategies should be implemented to decrease the effect of the modifiable risk factors associated with CRC in Jordan.

In order to explore the associated risks and highlight preventive strategies, more studies are needed to increase public awareness about the disease, and hence, decreasing its incidence. Longitudinal research studying environmental and lifestyle factors is also needed.

### *Statement of conflict of interest*

All authors declare that they have no conflict of

interest.

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