

Research Article

Association Between Smoking and Colorectal Cancer: Case Control Study in El-Mania Governorate.

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Abstract

Background: CRC is a worldwide problem; its absolute number of cases will increase over the next two decades as a result of the aging and expansion of populations in both the developed and developing countries. Smoking is considered as one of lifestyle factors which significantly associated with colorectal cancer (CRC) incidence and mortality; smoking increases the risk of developing CRC by about 18% and the risk of dying by about 20%. Aim of the study: To determine the relation between smoking as a lifestyle factor and development of CRC among CRC patients attending El-Minia oncology center comparing them with their control. **Methods:** This is case control study, which carried out in El-Minia governorate during the period from October 2010 to August 2011. It was conducted among 100 CRC patients (attending El-Minia oncology center during the period from October 2010 to June 2011) and 300 age and sex matched controls selected randomly from community where the cases are belonging to during the period from June 2011 to August 2011. Data were collected using an interview-administered questionnaire included socio demographic data, medical data concerning CRC and its treatment, smoking history detailed smoking history and smoking index. **Results:** There was a significant difference ($p=0.000$) between CRC cases and controls regarding history of smoking, about one third (33%) of cases were smokers compared to 18.7% of controls and smoking index was significantly higher (769.8 ± 763.3) among CRC cases than controls (463.8 ± 423.2). there was statistically significant positive associations were observed between smoking and risk of CRC (OR= 4.4, 90% CI = 2.9 to 6.6). **Conclusion:** There was a strong relation between smoking and development of CRC. Recommendation: Increase awareness about CRC among general population and the role that could be played by smoking as an important risk factors in its occurrence, Prevention by educational programs can be applied in the form of mass media campaigns and public lectures and intervention program can be carried out to motivate population to quit smoking.

Key words: Colorectal cancer, Smoking and Case-control study.

Introduction

Colorectal cancer (CRC) is the third most common cancer worldwide after lung and breast⁽¹⁾. About three quarters of CRC cases are associated with the population lifestyle⁽²⁾.

The global annual incidence of CRC approximately one million cases and its annual mortality is more than five hundred thousand⁽³⁾. In Egypt the relative frequency of CRC is about 9-12% with high male predominance 3:1⁽⁴⁾. According to National cancer registry, 2011 Age-specific incidence rates of CRC per 100,000 was 3.6 for males and 3.2 for females in 2009.

A positive association between tobacco and CRC has been suggested, smoking is, also associated with "poor" dietary habits, which in turn may be related to the risk of adenomas⁽⁵⁾.

Tobacco smoking is a risk factor for development of CRC, burning of tobacco produces numerous genotoxic compounds, including PAHs (Polycyclic aromatic Hydrocarbons), HCAs (Heterocyclic amines), and NOCs (N-nitroso compounds), these tobacco carcinogens cause irreversible damage to the colorectal mucosa via the circulation after broncho alveolar absorption

into the blood stream or by direct contact after ingestion with saliva^(3,9).

The risk differed according to smoking status, daily consumption, and duration of smoking. Regarding smoking status: compared to never smokers, current smokers had a 17% higher risk of developing CRC and a 4% higher risk of its mortality, for former smokers, the relative risk for CRC was 1.20 and 1.10 for CRC mortality in comparison to never smokers⁽⁴⁾. Regarding daily cigarette consumption: intake of 20 cigarettes/day (1 pack/day) lead to 17.0% increase in risk for CRC incidence and 4.7% for CRC mortality, and this risk increase with the increased daily cigarette⁽⁴⁾ and regarding duration of smoking: the increased risk began after about 10 years of smoking and increased until it reached statistical significance after 20 years, that doesn't mean that there is no increased risk for people who smoked less than 20 years, it just means that there is a strong evidence that exposure of 20 years or more increases the risk of CRC^(1,7).

Against the above background, it was decided to undertake a study with the aim of determining the relation between smoking as a lifestyle factor and development of CRC among CRC patients attending El-Minia oncology center comparing them with their control.

Subjects and Methods

Study design: This is case control study, which carried out in El-Minia governorate during the period from October 2010 to August 2011.

Administrative and ethical consideration:

An approval was taken from the Ministry of Health and from the manager of El-Minia oncology center to obtain data about number of CRC patients attending the center during the previous years and to facilitate the communication with personnel working in the center. Following the ethical guidelines of epidemiological research, a written informed consent was taken from each participant.

Results

Study population:

1. **Selection of cases: Inclusion criteria:** 100 primary CRC cases receiving treatment (ie, surgery, chemotherapy, radiotherapy, or combination of these therapies) in El-Minia oncology center during the period from October 2010 to June 2011) from both sex with no restriction was made with regard to age. **Exclusion criteria:** Cases with family history of CRC, Patients with a primary cancer rather than CRC and severely ill cases.
2. **Selection of control: Inclusion criteria** 200 age and sex matched controls were selected randomly from community where the cases are belonging. during the period from June 2011 to August 2011 **Exclusion criteria:** Individuals who are relatives for cases and individuals with family history of colorectal cancer.

Collection of data: Data were collected by a designed well-structured questionnaire including socio demographic data: age, gender, residence, educational level, occupation and marital status. medical data concerning disease: its duration and site and the received therapy. Smoking history includes type of smoking, duration of smoking, number of cigarette per day and smoking index (= total number of cigarette (other types as shish was converted into cigarette unit) per day multiplied by the duration of smoking), exposure to passive smoking.

Statistical analysis

Data entry and analysis were all done with I.B.M. compatible computer using software called SPSS for windows version 12. Graphics were done by Microsoft office Excel 2002. Quantitative data were presented by mean and standard deviation, while qualitative data were presented by frequency distribution. Chi square test, and fisher exact tests were used to compare between proportions. Student t-test was used to compare two means. Odds ratio was calculated for the smoking to predict its risk. The probability of less than 0.05 was used as a cut off point for all significant tests.

Table ١: Frequency distribution of the studied CRC cases and controls according to their age and sex, El-Minia governorate, October ٢٠١٠ to August ٢٠١١.

Data		CRC cases		Control		P
		No	%	No	%	
Age groups	<٢٠ year	٤	٢.٧	٦	٢.٠	٠.٣*
	٢٠-٤٠ year	٤٥	٣٠	١٠٢	٣٤	
	٤٠-٦٠ year	٨٠	٥٣.٣	١٣٦	٤٥.٣	
	>٦٠ year	٢١	١٤	٥٦	١٨.٧	
Sex	Male	٧٢	٤٨	١٤٤	٤٨	١**
	Female	٧٨	٥٢	١٥٦	٥٢	
Residence	Urban	٥٨	٣٨.٧	١١٦	٣٨.٧	١**
	Rural	٩٢	٦١.٣	١٨٤	٦١.٣	
Marital status	Single	١٦	١٠.٧	٢٧	٩	٠.٢*
	Married	١١٧	٧٨	٢٥٠	٨٣.٨	
	Widow	١٦	١٠.٧	٢٣	٧.٧	
	Divorced	١	٠.٧	٠.٠	٠.٠	
Education level	Illiterate	٨٧	٥٨	١٦٢	٥٤	٠.١**
	Read and write	١٧	١١.٤	٥٠	١٦.٧	
	Secondary	٣٨	٢٥.٣	٨٢	٢٧.٣	
	University and above	٨	٥.٣	٦	٢.٠	
Occupation	Unemployed	١١٠	٧٣.٣	٢٤٦	٨٢	٠.٠٩**
	Clerical	٦	٤.٠	٩	٣.٠	
	Manual	٢٥	١٦.٧	٢٧	٩.٠	
	Professional	٩	٦.٠	١٨	٦.٠	
Total		١٥٠	١٠٠	٣٠٠	١٠٠	

- Fisher exact=٣.٢ and ٣.٦, DF=٣ and ٣, $\chi^2 = ٠.٠٠٠, ٠.٠٠٠, ٠.٩$ and ٦.٣, DF = ١, ١, ٣ and ٣.

It was found that more than half (٥٣.٣%) of CRC patients lied in the age group ٤٠-٦٠ years and ٤٥.٣% of controls lied in the same age group. Regarding sex ٥٢% of colorectal cancer occurs in females comparing to ٤٨% of males, the same percentages were found among controls, these differences were not statistically significant (p=٠.٣ for age and ١ for sex). Regarding other

socio- demographic data, ٦١.٣% of CRC patients from rural areas, ٧٨% were married, ٥٨% were illiterate and ٧٣.٣% were unemployed. In comparison to their controls there were no significant differences regarding these socio-demographic data (p=١, ٠.٢, ٠.١ and ٠.٠٩) for residence, marital status, educational level and occupation respectively (Table ١).

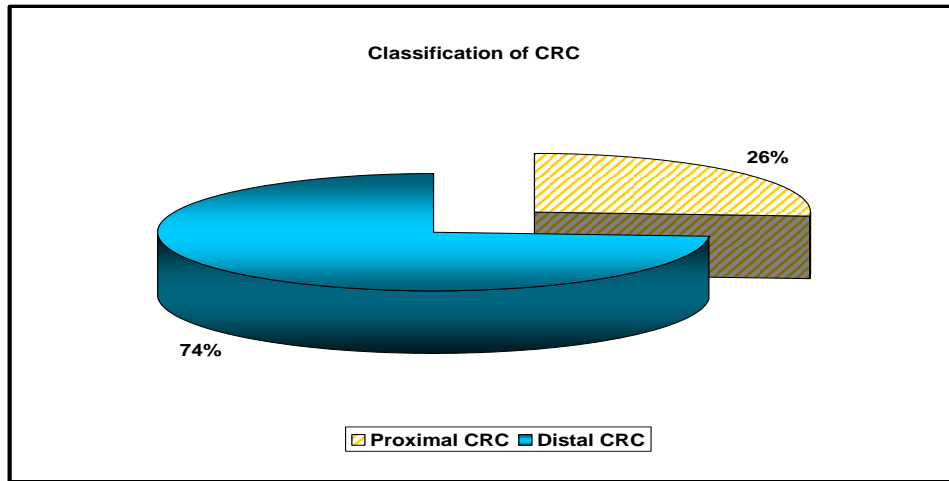


Figure ١: Frequency distribution of the studied CRC cases according to classification and distribution of cancer, El-Minia Oncology Center, October ٢٠١٠ to June ٢٠١١.

Table ٢: Frequency distribution of the studied CRC cases according to classification and distribution of cancer, El-Minia Oncology Center, October ٢٠١٠ to June ٢٠١١

Classification and distribution of CRC		NO	Percent
Colon	Total	٧٨	٥٢
	Ascending colon	١٥	١٩.٢
	Transverse colon	٤	٥.١
	Ascending colon and transverse colon	١	١.٣
	cecum	١٩	٢٤.٤
	Descending	٦	٧.٧
	Sigmoid	٣٣	٤٢.٤
Rectum	Total	٤٤	٢٩.٣
	Upper rectum	١١	٢٥
	Lower rectum	٣٣	٧٥
Colorectal	Recto sigmoid	٢٨	١٨.٧
Total		١٥٠	١٠٠

Regarding site of cancer, ٧٤% of patients had distal CRC and ٢٦% had proximal CRC (figure ١). Colon cancer accounted for ٥٢%, rectal cancer accounted for ٢٩.٩% and ١٨.٧% was recto sigmoid.

٤٢.٤% of colon cancer was in sigmoid region followed by ceacum (٢٤.٤%) then other sites, majority (٧٥%) of rectal cancer was lower rectum and ٢٥% in the upper rectum (Table٢).

Table (٣): Relation between smoking history and CRC among cases and controls, El-Minia governorate, October ٢٠١٠ to August ٢٠١١

Smoking		CRC cases Total=١٥٠		Control Total=٣٠٠		p
		NO	%	NO	%	
Smoking history	Non smokers	٦٢	٤١.٣	٢٢٨	٧٦	٠.٠٠٥**
	Smokers	٥١	٣٤	٥٦	١٨.٧	
	Passive smoker	٣٧	٢٤.٧	١٦	٥.٣	
Type of smoking	Cigarette	٦٨	٧٧.٢	٦٥	٩٠.٣	٠.١*
	Shish or goza	١٤	١٦	٦	٨.٣	
	Both	٦	٦.٨	١	١.٤	
	Total	٨٨	١٠٠	٧٢	١٠٠	

** $\chi^2 = ٥٢.٠٥$, DF = ٢, * Fisher exact = ١٠.٥ and ٥.٦, DF = ٢ and ٣.

The smoking history was higher (٣٤%) among CRC patients compared to only ١٨.٧% of controls, ٧٦% of control were non smokers comparing to ٤١.٣% of CRC patients and history of passive

smoking was higher among patients (٢٤.٧%) than controls (٥.٣%). These differences were statistically significant ($p=٠.٠٠٥$), (Table ٣).

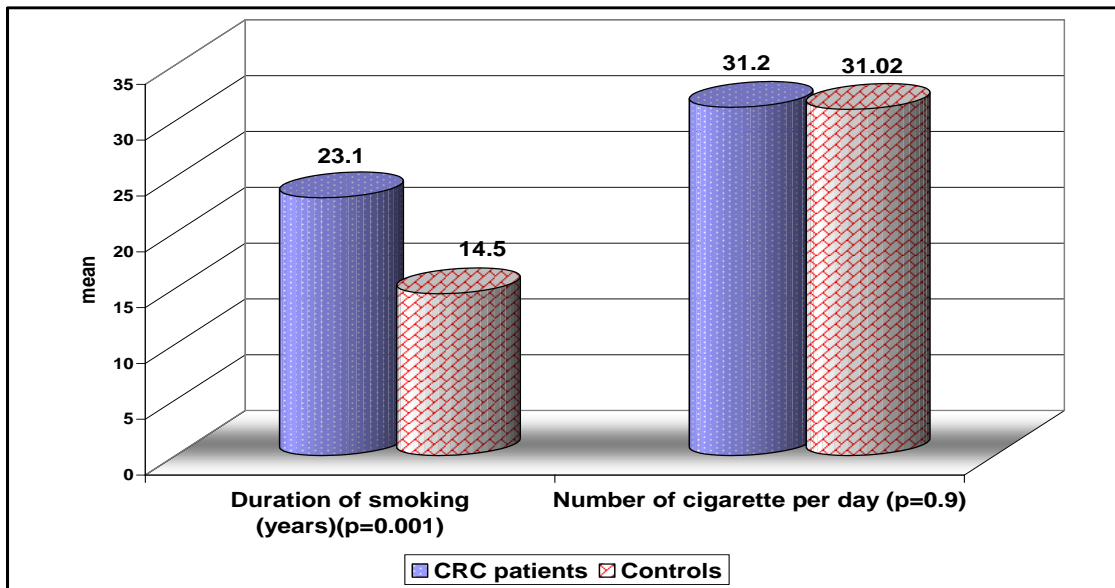


Figure ٢: Comparison between CRC cases and controls regarding duration of smoking and number of cigarettes per day, El-Minia governorate, October ٢٠١٠ to August ٢٠١١.

The mean duration of smoking was higher among patients (٢٣.١ ± ١٣.٣ years) than that of controls (١٤.٥ ± ١١.٢ years) and this difference was statistically significant ($P=٠.٠٠١$) but no signi-

ficant differences between patients and controls regarding number of cigarettes per day ($p=٠.٩$) (Figure٢).

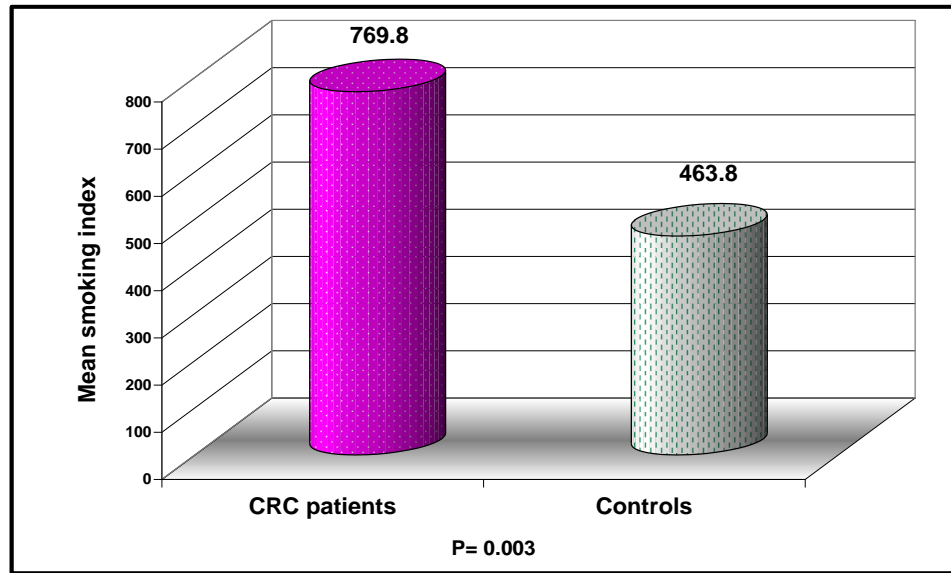


Figure ٣: Comparison between CRC cases and controls regarding smoking index, El-Minia governorate, October ٢٠١٠ to August ٢٠١١.

The mean of smoking index among patients was (٤٦٣.٨ ± ٤٢٣.٢) and this difference was statistically higher (٧٦٩.٨ ± ٧٦٣.٣) than that of controls (٤٦٣.٨ ± ٤٢٣.٢) and this difference was statistically significant ($P= ٠.٠٠٣$), (Figure ٣).

Table ٤: Relation between smoking history and cancer location among CRC cases attending El-Minia oncology center, October ٢٠١٠ to June ٢٠١١

	Colon		Rectum		Recto sigmoid		P
	NO	%	NO	%	NO	%	
Smoker	٢٠	٢٥.٦	٢٠	٤٥.٥	١١	٣٩.٣	٠.٢
Non smoker	٣٥	٤٤.٩	١٥	٣٤.١	١٢	٤٢.٢	
Passive smoker	٢٣	٢٩.٥	٩	٢٠.٥	٥	١٧.٩	
Total	٧٨	١٠٠	٤٤	١٠٠	٣٧	١٠٠	

$$**\chi^2 = ٥.٩, DF=٤$$

N.B. proximal CRC including cecum, ascending colon, hepatic flexure and transverse colon while distal CRC including splenic flexure, descending colon, sigmoid and recto sigmoid colon and rectum.

The history of smoking was higher among rectal cancer case (٤٥.٥%) and recto sigmoid cases (٣٩.٣%) than cases with colon cancer (٢٥.٦%) , but this difference was not statistically significant ($p=٠.٢$), (Table ٤).

Table 2: Odds ratio of smoking in prediction of CRC among cases attending El-Minia oncology center, October 2010 to June 2011.

Variables	CRC cases Total=100	Control Total=300	Odds ratio (OR)	95% CI	p value
Smoker	51	56	4.4	2.9-6.8	0.001
Non smoker	49	244			

There was a statistically significant positive associations between smoking and risk of CRC (OR= 4.4, 95% CI = 2.9 to 6.8), (Table 2).

Discussion

CRC is cancer of the colon and rectum arising from the mucosal lining of them, worldwide it is the third most commonly diagnosed cancer after lung and breast⁽¹⁾ and smoking is believed to play a large role in the incidence of it⁽¹⁾.

The age and sex were matched between cases and controls, their age was ranged between 16-80 years with mean 46.1±13.9 and 46.7±17.0 for cases and control respectively, the majority of them were in the age groups 40-60 years (53.3% for cases and 40.3% for controls) which was in agreement with Almurshed, (2009)⁽¹⁷⁾ who studied socio-demographic, life style and anthropometric parameters and CRC in a case control study in Riyadh and found that 54% of cases lie in the age groups 40-60 years and 46% of controls lie in the same age group. About half the cases (52%) and controls were females and 48% were male. Regarding other socio-demographic data, 71.3% of cases from rural areas, 70% were married, 58% were illiterate and 73.3% were unemployed (Table 1) which nearly similar to what reported by Almurshed, (2009)⁽¹⁷⁾ who found that 86% of cases were married, 44% were illiterate and 54% were unemployed.

It was observed from the study that the most common site of CRC was distal CRC (74%), followed by proximal CRC (26%) as shown from figure 1, these findings approximate what reported by Duijnhoven et al., (2009)⁽¹⁵⁾ who studied fruit, vegetables and CRC risk and found that 27.1% of cases were proximal cancer and

72.9% were distal cancer. About 60% of CRC cases arise in the distal part of colon in countries where colonic cancer incidence is high⁽¹⁾. This study revealed that 42.4% of colon cancer occurs in the sigmoid region, 70% of rectal cancer was in the lower rectum and 18.7% was recto sigmoid (Table 2).

From the study, it was found that there was a significant difference between CRC cases and controls regarding history of smoking, as 34% of cases versus 18.7% of controls were smokers and 24.7% of cases were passive smokers compared to only 0.3% of controls (Table 3), this was in agreement with Limsui et al., (2010)⁽¹²⁾ who studied the relation between cigarette smoking and CRC risk in prospective study and found that 34% of those who develop CRC were smokers and in agreement with Lu' chtenborg et al.⁽⁹⁾ who studied cigarettes smoking and CRC in case control study and found that history of smoking was higher among CRC cases (34%) than controls (28%) and also approximate what reported by Abdulbari et al., (2010)⁽¹³⁾ who studied lifestyle habits and CRC risk in a case control study in Qatar and found that 26.7% of cases and 17% of controls were smokers.

There was a significant difference regarding duration of smoking between cases and controls but no significant difference regarding number of cigarettes per day (Figure 2) which in agreement with Lu' chtenborg et al.⁽⁹⁾ who found that duration conferred a clearer risk of CRC than smoking intensity.

Smoking index was significantly higher (769.8±763.2) among CRC cases than controls (463.8±423.2) (Figure 3) which also

approximated what reported by Lichtenberg et al.⁽¹⁾ who found that smoking index was higher among cases (22.0 cigarette per year) than controls (0.6 cigarette per year).

From the study it was found that smoking history was higher among rectal cancer cases (40.0%) and recto sigmoid cases (39.3%) than cases with colon cancer (20.6%) (table 4), which approximate what reported by Shin et al, (2011)⁽¹⁵⁾ who studied site specific risk factors for colorectal cancer and found that smoking history was slightly higher among rectal cancer cases (69.1%) than colon cancer cases (78.7%).

It was observed from the study that smoking (OR=4.4) was significant risk for CRC (Table 5) which was in agreement with Abdulbari et al., (2010)⁽¹⁷⁾ who found that smoking (OR=2.12) increase the risk of CRC.

Possible confounding factors as socio-demographic factors were controlled by matching of age and sex between cases and controls, there were no significant differences between cases and controls regarding educational level, marital status and occupation and by multivariate analysis.

Conclusion

Smoking is considered a significant risk of CRC and it is a modifiable life style factor that can be modified by health education. Therefore motivating population to quit smoking by creating smoke free areas in public places and work places, increasing awareness about the presence of smoking quitting clinics and increasing its activities and enforcement of laws that forbid the sales of tobacco for children are very important to be applied.

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