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Lifestyle, Occupational, and Reproductive Factors and Risk of Colorectal Cancer

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Abstract

PURPOSE—Lifestyle factors and environmental exposures might help explain the risk of colorectal carcinoma in countries where the incidence is low but unique patterns of young onset, and a high proportion of rectal cancer exist.

METHODS—We obtained detailed lifestyle information from 421 colorectal cancer patients and 439 hospital-controls from Egypt. Logistic regression models were computed to evaluate the risk factors of colorectal carcinoma.

RESULTS—History of pesticide exposure and more frequent eating food directly from farms were significantly associated with a higher risk of colorectal carcinoma [odds ratio= 2.6, 95% confidence interval= 1.1-5.9; odds ratio= 4.6, 95% confidence interval= 1.5-14.6, respectively]. Parous women who reported 7 or more live births or breastfed for 19 months or longer per live birth had a significantly lower risk for colorectal carcinoma (odds ratio= 0.3, 95% confidence interval= 0.2-0.7; odds ratio= 0.2, 95% confidence interval= 0.1-0.4, respectively). Compared to patients aged 40 years or older, industrial exposures were more common in younger patients (P =0.05).

CONCLUSIONS—Agricultural and industrial exposures were associated with increased risk of colorectal carcinoma, while prolonged lactation and increased parity were inversely associated with colorectal carcinoma in women. Further research to elucidate the biological role of intense environmental and industrial exposures and reproductive factors including lactation may further clarify the etiology of colorectal cancer.

Keywords

Colorectal Cancer; Lifestyle; Occupation; Reproductive Factors; Risk Factors

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Introduction

Colorectal carcinoma is a major contributor to cancer burden worldwide. A rapid increase in colorectal cancer incidence has been observed in developing countries where the occurrence was formerly low.[1] Some of these countries have also experienced special patterns of young onset, low prevalence of colorectal adenomas and/or and high proportion of cancer in the rectum when compared to colorectal carcinoma seen in developed countries.[2-3]

Although such patterns have been suspected to be attributable to distinct life styles and/or possible environmental exposures in developing countries, no specific factors have been explored comprehensively. We have conducted a series of studies in Egypt revealing an unusually high rate of colorectal carcinoma under age 40 (36%), low prevalence of colorectal polyps in cancer patients (4%-8%), and a predominant cancer subsite in the rectum (45%-68%).[4-7] We reported that colorectal tumors from Egypt show distinct molecular characteristics compared to tumors from the U.S. and other countries,[6-7] suggesting a different etiology of the disease in this population.[8-9] Different from developed countries, Egypt would be a unique setting for epidemiologic research on colorectal carcinoma given the high fertility and prolonged breast feeding prevalent in women, the common use of noncigarette tobacco products (i.e. water pipe, cigar), and the extensive environmental and industrial pollutions.[8,10-11] These features reasonably led us to investigate environmental, occupational, and life style factors in relation to colorectal carcinoma risk in Egypt.

Materials and Methods

Study Population and Data Collection

We recruited 421 colorectal carcinoma patients and 439 hospital-based controls during 2001-2005. Participants were from two major hospitals in Egypt: 301 (72%) patients and 359 (82%) controls from the National Cancer Institute (NCI-Cairo) and University Hospital of Cairo University; 120 (28%) patients and 80 (18%) controls from the Gastrointestinal Surgery Center (GSC) and University Hospital of Mansoura University.

All cancer patients were consecutive newly diagnosed with primary malignancy in the colon or rectum. Two patients with Crohn's disease and 13 anal cancer patients were excluded. Although not an exclusion factor, we did not find any patients with hereditary nonpolyposis colorectal cancer (HNPCC).[12] The study included 167 (41%) patients with colon cancer (from cecum to descending colon, and non-specific subsite in the colon), 242 (59%) rectal cancers (rectosigmoid junction and rectum), and 12 colorectal cancers with unknown defined site. The most common histologic type was adenocarcinoma (99.7%), followed by undifferentiated carcinoma (1%), and carcinoma in situ (0.3%).

From the same hospitals where the colorectal cancer patients were recruited, we invited patients admitted to the Department of Ear/Nose/Throat, Ophthalmology, or Orthopedics for acute illnesses to participate as the comparison group. Patients with prior history of colorectal cancer were considered ineligible, while eligible controls were chosen by systematic random sample and frequency-matched to patients on age (± 5-years) and sex.

Study participants were interviewed by well-trained interviewers using a Health and Risk Assessment Questionnaire used in our previous studies.[6,10-11] The questionnaire elicited detailed information on demographic characteristics, tobacco consumption, lifetime occupational exposures, medical and reproductive histories, and family history of cancers.

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This study was approved by the institutional review boards of the University of Michigan and recruitment hospitals and universities in Egypt.

Occupational History and Exposures

To explore lifetime exposures to agricultural substances, we identified study participants who reported jobs of farming for the longest duration in their lifetime. We collected information on whether farmers applied and used pesticides, insecticides, herbicides, or fertilizers directly or hired applicators to do such jobs. Additionally, we collected information on exposure methods and intensities by accessing frequency of eating food items directly from the farm, and frequency of working on the farm soon after pesticides were applied (never or seldom vs. about half of the time or more).

Exposure to industrial materials was defined as being in contact with any of following substances for at least 8 hours a week for a year (yes vs. no): solvents, paint thinners, printer's inks or dyes, paints, lacquer, pigments, motor oils, gasoline, petroleum, car exhaust, diesel fuel, fumes, natural gas, tar, mineral oil, hydrochloric acid, bleach or cleansers, dry cleaning fluids, leather, tanning solutions, rubber products, glues, plastics, resins, sawdust, wood dust, coal dust, soot, metals, metal dust or fumes, radioactive materials, or asbestos.

Medical History

We asked each participant about medical conditions (i.e. rectal bleeding and Schistosomiasis) diagnosed by physicians at least one year prior to the recruitment date. The self-reported weight and height at one year prior to the diagnosis or interview were used to calculate the body mass index (BMI, kg/m^2).

Reproductive History

Information on menstrual and reproductive factors was obtained from 200 female colorectal cancer patients and 203 female controls. Nulliparity was reported by 15 (8%) of the patients and 27 (13%) of the controls. Oral contraceptive use, number of pregnancies, number of live births, and duration of breast feeding were analyzed for parous women only. Use of hormone replacement therapy in postmenopausal women was rare in the study population and not evaluated here.

Tobacco Consumption

Cigarette smokers were subjects who had ever smoked 100 or more cigarettes during their lifetime or ever smoked cigarettes regularly for at least a year.[11] Use of non-cigarette tobacco products, such as water pipes, cigars, and pipes, at least once/week for 6 months or longer was considered as non-cigarette smoking.[11] Our preliminary results showed similar effects of cigarette and non-cigarette smoking on colorectal carcinoma risk. Therefore, subjects who smoked any tobacco products were classified as active smokers, compared with subjects who reported negative exposure to both active and passive smoking.

Statistical Analysis

Differences in frequencies between the patients and controls were evaluated by simple contingency table analyses (Fisher exact test and Chi-square test) using the SAS package (version 9.1; SAS Institute, Cary, NC). Unconditional and multivariate logistic regression models were used to test associations between cancer status and smoking, medical, occupational, and reproductive factors, yielding odds ratio (OR) and 95% confidence intervals (95% CI). The Cochran-Armitage trend test was performed to determine the linearity of parity, lactation, and BMI in related to colorectal carcinoma risk.

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Results

The mean age of patients was 46.7 years [standard deviation (SD)=14.7, range 14-82], and the mean age of controls was 46.0 years (SD=16.9, range 12-84). About one third (34%) of patients were diagnosed with colorectal carcinoma before age 40 (Table 1). Urban residency ($P<0.0001$), non-farming occupation ($P=0.004$), exposure to industrial materials ($P<0.0001$), and family history of colorectal carcinoma ($P=0.02$) were more frequently reported in patients than in controls (Table 1).

We further compared younger colorectal cancer patients (<age 40) to older patients (age 40+). The male/female ratio was 1.41 in younger patients and 0.98 in older patients ($P=0.08$, Table 2). Younger patients were more likely to have rectal cancer ($P=0.01$), poorly- or undifferentiated tumors ($P=0.01$), and cancer at a more advanced stage ($P=0.08$, Table 2). Industrial exposure was more common in the younger group ($P=0.05$), while obesity was more prevalent in older patients ($P=0.02$, Table 2).

Regarding differences in subsites, rectal cancer patients (49.1±15.1 years) were on average 4 years younger than colon cancer patients (45.0±14.1 years, $P=0.005$), and more likely to have family history of cancers ($P=0.03$, data not shown).

Other lifestyle factors were evaluated but none showed significant difference by the age groups and subsites (Data not shown). We then combined all patients as one group compared to the controls in the following analyses. Among subjects who reported farming as the longest lifetime occupation, 70% of the patients and 63% of the controls had ever handled or been exposed to pesticides. History of pesticide exposures was significantly correlated with an elevated risk of colorectal carcinoma (OR=2.6, 95% CI=1.1-5.9, Table 3). Exposure to insecticides or herbicides was associated with increased risk for colorectal cancer same as pesticides (Table 3). Agricultural workers who ate food items from the field for half of the time or more had significantly higher risk of colorectal carcinoma (OR=4.6, 95% CI=1.5-14.6, Table 3).

We did not find significant association between oral contraceptive use and large bowel cancers in women after adjusting for cofactors (OR=1.4, 95% CI=0.8-2.3, Table 4). Nevertheless, we observed that increased parity and prolonged lactation were both associated with a reduced risk of colorectal carcinoma among parous women in Egypt (both $P_{trend}<0.0001$). Compared with women who reported 1-3 live births, women who had 4-6 and 7 or more live births demonstrated an inverse correlation with colorectal cancer risk (OR=0.9, 95% CI=0.5-1.6 and OR=0.3, 95% CI=0.2-0.7, respectively, Table 4). Parous women who breastfed for 73 months or more in lifetime (OR=0.3, 95% CI=0.2-0.8) and parous women who breastfed each child for 19 months or more in average (OR=0.2, 95% CI=0.1-0.4) had a significantly lower risk for colorectal carcinoma (Table 4).

We also noticed gender effects in relation to colorectal cancer risk. Active smokers accounted for 15% of female patients and 2% of female controls. When compared to nonsmokers, female smokers had a significantly increased risk for colorectal carcinoma (OR=9.4, 95% CI=2.8-31.8) after adjusting for age, residence, industrial exposure, and BMI levels. History of active smoking was reported in 58% of male patients and 70% of male controls. Interestingly, smoking in men showed a decreased risk for colorectal carcinoma (OR=0.4, 95% CI=0.3-0.7) after controlling for the same cofactors. Increased duration and intensity of active smoking were not correlated with colorectal cancer risk in both men and women (Data not shown). We observed a similar gender difference for passive smoking. There were 54% of male patients, 56% of male controls, 52% of female patients, and 10% of female controls reporting history of passive smoking. Compared to nonsmokers, the adjusted OR for passive smokers was 0.8 (95% CI=0.5-1.2) in men and 7.1 (95% CI=3.5-14.1) in

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women, after controlling for age, residence, industrial exposure, BMI levels, and reproductive factors for women (Data not shown).

Finally, our data suggest that increased BMI might be associated with colorectal carcinoma in men, but not in women. Compared to male subjects who had BMI below 25.0, men at risk of obesity (BMI 25.0-29.9) had a non-significant OR (OR=1.0, 95% CI=0.6-1.5), and obese men (BMI 30.0+) had 2.2 times higher risk of colorectal carcinoma (OR=2.2, 95% CI=1.1-4.3, P_{trend}=0.045), after controlling for age, residence, industrial exposure and active smoking (Data not shown).

Discussion

This study illustrated the possible role of lifestyle factors in colorectal carcinoma etiology in a developing country with a unique pattern in epidemiology – early onset, high proportion of rectal cancer, and low presence of adenomas.[4-5,7] We observed that agricultural and industrial exposures were significantly associated with a higher risk of colorectal carcinoma. In women, parity and breastfeeding were inversely associated with colorectal cancer risk.

Our findings are in agreement with previous research regarding the impact of occupational exposures in colorectal cancer risk. Being exposed to industrial materials was associated with 2-4 times higher risk for large bowel cancer in Canada and China.[13-14] Working in dusty environment for 10 years or longer was significantly associated with colorectal carcinoma in early adulthood (OR=2.0, 95% CI=1.0-4.0).[15] Consistently, we observed that history of industrial exposures was more frequent in younger patients than older patients.

Rural residency and farming occupations have been associated with a lower risk of colorectal carcinoma when compared to urban residency and non-farming occupation.[16-17] However, intense pesticide exposure may increase cancer risk among rural residents and farmers. Geographical distribution of high colorectal carcinoma incidence tends to be parallel with regions of high agricultural activity in the U.S.[18-19] In China, villages with higher contents of polychlorinated biphenyl (PCB) and dichlorodiphenyltrichloroethane (DDT) in rice and soil samples were found with significantly higher incidence of colorectal carcinoma.[20]

The high consumption of fresh vegetables in the general population and the widespread use of pesticides in Egypt might alter colorectal cancer risk through dietary intake starting from early childhood.[21-22] We have reported higher serum organochlorine pesticide levels in colorectal cancer patients from Egypt.[8] Consistently, we observed that being exposed to pesticides and eating fresh food items from farm were significantly associated with a higher risk of colorectal carcinoma among Egyptian farmers in this study. Although no difference was found in agricultural exposures between the young and old patients, we think that intense environmental pollution and pesticide exposures may help to explain the unique pattern of early onset of colorectal carcinoma in Egypt.[22]

Our research have shown that colorectal tumors from younger Egyptian patients illustrated distinct molecular characteristics when compared to tumors from older Egyptian, HNPCC, and sporadic colorectal carcinoma patients in the U.S. and other countries.[6-7,23-24] Future studies should be conducted to investigate the interaction between pesticide exposures and genes on altering colorectal carcinogenesis.

We also observed that higher fertility and prolonged lactation were inversely correlated with colorectal carcinoma, and the protective effects were not different by anatomic subsites. It has been hypothesized that hormonal changes correlated with pregnancy might interact with bile-acid or estrogen receptors, resulting in a reduced risk for colon cancer.[25] However,

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conflicting results were showed in previous studies.[25-28] Compared to women who had 1-2 live births, women who had 5 or more live births showed a significantly lower risk of colon cancer in the U.S. (OR=0.6, 95% CI=0.3-0.9), but this protective effect was found only in women under age 65, not in the older group.[26] A more recent study in the U.S. found an inverse correlation between parity and rectal cancer (P_{trend}=0.05), but not for colon cancer (P_{trend}=0.3).[27]

Only a study evaluated the possible correlation between breastfeeding and risk of colorectal carcinoma.[28] Lifetime duration of lactation for 19 months or more was not associated with colorectal carcinoma when compared to never lactation.[28]

In addition to hormonal changes, the reduced risk of colorectal carcinoma in Egyptian women might also be correlated with environmental exposures. We have reported that Egyptian women who breastfed for 23.5 months or longer per live birth in average had lower levels of serum dichlorodiphenyldichloroethylene (DDE, P=0.04).[10] This finding suggests that breastfeeding might protect women from the accumulation of environmental carcinogens by excreting these components to infants within the breast milk.[10] In contrast to Egyptian women, women in Costa Rica have common use of contraceptives, low fertility rate, and short-term breastfeeding.[29] Interestingly, significantly increased risks of rectal cancer (RR=1.9, 95% CI=1.1-3.3) and female hormone-related cancers (RR between 1.3 and 1.8) were associated with high pesticide exposure levels in Costa Rica women from rural counties.[16]

The connection between tobacco consumption and colorectal carcinoma remains inconclusive. We observed a null association between active smoking and overall colorectal carcinoma risk when compared with nonsmoking, and the association was in opposite direction by gender. Some factors may help explain these findings. First, there might be a 40-year induction period of cigarette smoking in colorectal carcinoma development.[30-31] Ji et al. (2002) found no association between cigarette smoking and colorectal carcinoma in China, with relatively shorter duration (mean 32 years) and intensity (16 cigarettes per day) for cigarette smoking in their study population.[32] However, a later study in Hong Kong observed an increased risk of rectal cancer in current regular smokers (OR=1.4, 95% CI=1.0-2.1), whose average duration of cigarette smoking was 40 years.[33] Egyptian smokers in our study reported a mean 25 years of cigarette smoking (SD=15.1 years, range 0.5-66.0 years, median=23.0 years) and smoked 0.9 pack of cigarettes per day on average (SD=0.6 pack, range 0.1-3.0 packs, median=1.0 pack), which were lower than observations in studies showing significant association.[31,33] Little is known for smoking water pipes in relation to colorectal carcinoma risk, although water pipe smoking dominates non-cigarette tobacco consumption in Egypt and is emerging in western countries.[11,34] Our data suggest that cigarette and non-cigarette smoking have similar impacts on colorectal carcinoma in Egypt.

Colorectal adenomas have been recognized as an important predictor of colorectal carcinoma, but more consistently associated with cigarette smoking across studies.[30,35] Synchronous adenomas was only found in 6% of colorectal carcinoma patients in Egypt,[5] and the prevalence of polypoid colorectal carcinoma tends to be much lower in Asia and Africa than that in the U.S.[2,36] If cigarette smoking acts at the early stage of polypoid colorectal carcinoma, it might be less influential in colorectal carcinogenesis without preceding adenomas.

The excess risk of colorectal carcinoma in female smokers reported in this study should be considered with caution, given the low counts of female smokers present. However, with over half of female patients exposed to passive smoking compared to only 10% of controls and the statistically significant difference between the 2 groups, it might be reasonable to

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consider that both active and passive smoking have similar biological effect on the etiology of colorectal cancer in this study.

Nevertheless, the difference in gender might reflect uncontrolled confounding factors such as physical activity, social-economical status, and nutrition intake. Additionally, genetic susceptibility may alter risk of colorectal carcinoma in conjunction with gender and residence as we reported earlier.[37] Alcohol consumption was less likely to modify our results, because rates of alcohol drinking are very low in Egypt.

Our data also suggest that obesity was significantly associated with colorectal carcinoma in men, but not in women. Similar findings were recently reported in a meta-analysis.[38] Excess risks of large bowel cancer in men was found with every 5-unit increase in BMI (RR=1.3, 95% CI=1.3-1.4 for colon cancer; RR=1.1, 95% CI=1.1-1.2 for rectal cancer). In women, higher BMI was only correlated with colon cancer (RR=1.1, 95% CI=1.1-1.2), but not with rectal cancer (RR=1.0, 95% CI=0.99-1.1).[38]

The major strengths of this study include the relatively large sample size and detailed lifestyle information from a developing country. Although many developing countries have observed a tendency of early onset and a rapid increase in colorectal cancer occurrence,[1-3] not many studies were reported from these countries to explore risk factors for colorectal carcinoma. The intense exposure to industrial materials and pesticides, high parity and prolonged lactation in Egypt are distinct from factors seen in most developed countries, providing a unique setting for epidemiological studies. Although food frequency questionnaires and dietary assessments have been criticized in case-control studies,[39-40] including dietary assessment could have added knowledge to this study. In summary, this study illustrated the possible role of lifestyle factors in colorectal carcinoma etiology in Egypt. Agricultural and industrial exposures were significantly associated with a higher risk of colorectal carcinoma in this population. In women, parity and breastfeeding were inversely associated with colorectal cancer risk. Future large-scale laboratory studies are needed to assess the dose-response relationship and the actual levels in exposed and non-exposed individuals in this population. Future studies should focus on investigating the biological mechanisms of environmental, industrial, and reproductive factors in colorectal carcinogenesis.

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References

1. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin. 2005; 55:74–108. [PubMed: 15761078]
2. Sung JJ, Lau JY, Goh KL, Leung WK. Asia Pacific Working Group on Colorectal Cancer. Increasing incidence of colorectal cancer in Asia: implications for screening. Lancet Oncol. 2005; 6:871–6. [PubMed: 16257795]
3. El Mistiri M, Verdecchia A, Rashid I, El Sahli N, El Mangush M, Federico M. Cancer incidence in eastern Libya: the first report from the Benghazi Cancer Registry, 2003. Int J Cancer. 2007; 120:392–7. [PubMed: 17066425]
4. Soliman AS, Bondy ML, Levin B, et al. Colorectal cancer in Egyptian patients under 40 years of age. Int J Cancer. 1997; 71:26–30. [PubMed: 9096661]

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5. Abou-Zeid AA, Khafagy W, Marzouk DM, Alaa A, Mostafa I, Ela MA. Colorectal cancer in Egypt. Dis Colon Rectum. 2002; 45:1255–60. [PubMed: 12352245]
6. Soliman AS, Bondy ML, El-Badawy SA, et al. Contrasting molecular pathology of colorectal carcinoma in Egyptian and Western patients. Br J Cancer. 2001; 85:1037–46. [PubMed: 11592777]
7. Chan AO, Soliman AS, Zhang Q, et al. Differing DNA methylation patterns and gene mutation frequencies in colorectal carcinomas from Middle Eastern countries. Clin Cancer Res. 2005; 11:8281–7. [PubMed: 16322286]
8. Soliman AS, Smith MA, Cooper SP, et al. Serum organochlorine pesticide levels in patients with colorectal cancer in Egypt. Arch Environ Health. 1997; 52:409–15. [PubMed: 9541361]
9. Soliman AS, Bondy ML, Levin B, et al. Familial aggregation of colorectal cancer in Egypt. Int J Cancer. 1998; 77:811–6. [PubMed: 9714045]
10. Soliman AS, Wang X, DiGiovanni J, et al. Serum organochlorine levels and history of lactation in Egypt. Environ Res. 2003; 92:110–117. [PubMed: 12854690]
11. Lo AC, Soliman AS, El-Ghawalby N, et al. Lifestyle, occupational, and reproductive factors in relation to pancreatic cancer risk. Pancreas. 2007; 35:120–9. [PubMed: 17632317]
12. Vasen HF, Watson P, Mecklin JP, Lynch HT, ICG-NHPCC. New clinical criteria for hereditary nonpolyposis colorectal cancer (HNPCC, Lynch syndrome) proposed by the International Collaborative group on HNPCC. Gastroenterology. 1999; 116:1453–6. [PubMed: 10348829]
13. Dumas S, Parent ME, Siemiatycki J, Brisson J. Rectal cancer and occupational risk factors: a hypothesis-generating, exposure-based case-control study. Int J Cancer. 2000; 87:874–9. [PubMed: 10956400]
14. De Roos AJ, Ray RM, Gao DL, et al. Colorectal cancer incidence among female textile workers in Shanghai, China: a case-cohort analysis of occupational exposures. Cancer Causes Control. 2005; 16:1177–88. [PubMed: 16215868]
15. Peters RK, Garabrant DH, Yu MC, Mack TM. A case-control study of occupational and dietary factors in colorectal cancer in young men by subsite. Cancer Res. 1989; 49:5459–68. [PubMed: 2766308]
16. Wesseling C, Antich D, Hogstedt C, Rodríguez AC, Ahlbom A. Geographical differences of cancer incidence in Costa Rica in relation to environmental and occupational pesticide exposure. Int J Epidemiol. 1999; 28:365–74. [PubMed: 10405835]
17. Wang Y, Lewis-Michl EL, Hwang SA, Fitzgerald EF, Stark AD. Cancer incidence among a cohort of female farm residents in New York State. Arch Environ Health. 2002; 57:561–7. [PubMed: 12696654]
18. Lai SM, Zhang KB, Uhler RJ, Harrison JN, Clutter GG, Williams MA. Geographic variation in the incidence of colorectal cancer in the United States, 1998-2001. Cancer. 2006; 107(5 Suppl):1172–80. [PubMed: 16838315]
19. Carozza SE, Li B, Elgethun K, Whitworth R. Risk of childhood cancers associated with residence in agriculturally intense areas in the United States. Environ Health Perspect. 2008; 116:559–65. [PubMed: 18414643]
20. Chen K, Zhao YW, Ma XY, Zhang LJ, Zheng S. Relationship between organochlorine pollution in soil and rice and the incidence of colorectal cancer in Jiashan county, Zhejiang province. Zhonghua Liu Xing Bing Xue Za Zhi. 2004; 25:479–83. [PubMed: 15231121]
21. Galal OM. The nutrition transition in Egypt: obesity, undernutrition and the food consumption context. Public Health Nutr. 2002; 5:141–8. [PubMed: 12027277]
22. Soliman AS, Bondy ML, Hamilton SR, Levin B. Colon cancer in young Egyptian patients. Am J Gastroenterol. 1999; 94:1114. [PubMed: 10201503]
23. Soliman AS, Bondy ML, Guan Y, et al. Reduced expression of mismatch repair genes in colorectal cancer patients in Egypt. Int J Oncol. 1998; 12:1315–9. [PubMed: 9592192]
24. Abdel-Rahman SZ, Soliman AS, Bondy ML, et al. Inheritance of the 194Trp and the 399Gln variant alleles of the DNA repair gene XRCC1 are associated with increased risk of early-onset colorectal carcinoma in Egypt. Cancer Lett. 2000; 159:79–86. [PubMed: 10974409]
25. Potter JD. Hormones and colon cancer. J Natl Cancer Inst. 1995; 87:1039–40. [PubMed: 7616590]

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26. Slattery ML, Mineau GP, Kerber RA. Reproductive factors and colon cancer: the influences of age, tumor site, and family history on risk (Utah, United States). Cancer Causes Control. 1995; 6:332–8. [PubMed: 7548720]
27. Nichols HB, Trentham-Dietz A, Hampton JM, Newcomb PA. Oral contraceptive use, reproductive factors, and colorectal cancer risk: findings from Wisconsin. Cancer *Epidemiol Biomarkers Prev*. 2005; 14:1212–8. [PubMed: 15894674]
28. de Verdier, M Gerhardsson; London, S. Reproductive factors, exogenous female hormones, and colorectal cancer by subsite. Cancer Causes Control. 1992; 3:355–60. [PubMed: 1617123]
29. United Nations Children's Fund (UNICEF). [Accessed Aug 05, 2008] Available at: http://www.unicef.org/infobycountry/costarica_statistics.html
30. Giovannucci E, Martínez ME. Tobacco, colorectal cancer, and adenomas: a review of the evidence. J Natl Cancer Inst. 1996; 88:1717–30. [PubMed: 8944002]
31. Mizoue T, Inoue M, Tanaka K, et al. Tobacco smoking and colorectal cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2006; 36:25–39. [PubMed: 16423841]
32. Ji BT, Dai Q, Gao YT, et al. Cigarette and alcohol consumption and the risk of colorectal cancer in Shanghai, China. Eur J Cancer Prev. 2002; 11:237–44. [PubMed: 12131657]
33. Ho JW, Lam TH, Tse CW, et al. Smoking, drinking and colorectal cancer in Hong Kong Chinese: a case-control study. Int J Cancer. 2004; 109:587–97. [PubMed: 14991582]
34. Maziak W, Ward KD, Soweid RA Afifi, Eissenberg T. Tobacco smoking using a waterpipe: a re-emerging strain in a global epidemic. Tob Control. 2004; 13:327–33. [PubMed: 15564614]
35. Sarebø M, Skjelbred CF, Breistein R, et al. Association between cigarette smoking, APC mutations and the risk of developing sporadic colorectal adenomas and carcinomas. BMC Cancer. 2006; 6:71. [PubMed: 16545110]
36. Segal I, Edwards CA, Walker AR. Continuing low colon cancer incidence in African populations. Am J Gastroenterol. 2000; 95:859–60. [PubMed: 10763922]
37. Abdel-Rahman SZ, Soliman AS, Bondy ML, et al. Polymorphism of glutathione S-transferase loci GSTM1 and GSTT1 and susceptibility to colorectal cancer in Egypt. Cancer Lett. 1999; 142:97–104. [PubMed: 10424787]
38. Larsson SC, Wolk A. Obesity and colon and rectal cancer risk: a meta-analysis of prospective studies. Am J Clin Nutr. 2007; 86:556–65. [PubMed: 17823417]
39. Kristal AR, Peters U, Potter JD. Is it time to abandon the food frequency questionnaire? Cancer Epidemiol Biomarkers Prev. 2005; 14:2826–8. [PubMed: 16364996]
40. Potter JD. Pancreas cancer--we know about smoking, but do we know anything else? Am J Epidemiol. 2002; 155:793–5. [PubMed: 11978581]

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Table 1

Demographic Characteristics and Medical Histories of the Study Population [a]

	Patients n= 421 No. (%)	Controls n= 439 No. (%)	*P*-value
Age (years)			
< 40	142 (33.7)	160 (36.5)	
40-49	99 (23.5)	80 (18.2)	
50-59	82 (19.5)	81 (18.4)	
60 +	98 (23.3)	118 (26.9)	0.206 [b]
Gender			
Male	221 (52.5)	236 (53.8)	
Female	200 (47.5)	203 (46.2)	0.710 [b]
Menopausal status[c]			
Pre-menopausal	98 (50.8)	92 (45.3)	
Post-menopausal	95 (49.2)	111 (54.7)	0.277 [b]
Residence			
Rural	216 (51.7)	294 (67.0)	
Urban	202 (48.3)	145 (33.0)	<0.0001 [b]
Occupation			
Farming-related	73 (17.3)	112 (25.5)	
Non-farming	348 (82.7)	327 (74.5)	0.004 [b]
Industrial exposure			
No	301 (71.5)	376 (85.7)	
Yes	120 (28.5)	63 (14.3)	<0.0001 [b]
Family history of any cancer			
No	378 (89.8)	368 (88.9)	
Yes	43 (10.2)	46 (11.1)	0.674[b]
Family history of colorectal cancer			
No	410 (97.4)	412 (99.5)	
Yes	11 (2.6)	2 (0.5)	0.022 [d]
Rectal bleeding			
No	395 (97.3)	424 (96.6)	
Yes	11 (2.7)	15 (3.4)	0.552 [b]
Schistosomiasis			
No	345 (82.1)	342 (78.1)	
Yes	75 (17.9)	96 (21.9)	0.137 [b]

[a] Column total may be different due to missing data;

[b] Chi-square test;

[c] Only female study participants were included in the analysis;

[d] Fisher's exact test

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Table 2

Demographic, Pathological, and Medical Characteristics in Colorectal Carcinoma Patients by Age[a]

	<40 n= 142 No. (%)	40+ n= 279 No. (%)	*P*-value
Gender			
Male	83 (58.5)	138 (49.5)	
Female	59 (41.5)	141 (50.5)	0.081 [b]
Industrial exposure			
No	93 (65.5)	208 (74.6)	
Yes	49 (34.5)	71 (25.4)	0.052 [b]
Family history of any cancer			
No	125 (88.0)	253 (90.7)	
Yes	17 (12.0)	26 (9.3)	0.395 [b]
Family history of colorectal cancer			
No	136 (95.8)	274 (98.2)	
Yes	6 (4.2)	5 (1.8)	0.194 [c]
Cancer site			
Colon	49 (35.2)	118 (46.2)	
Rectum	90 (64.8)	152 (56.3)	0.099 [b]
Grade			
1, 2	73 (67.6)	177 (80.1)	
3, 4	35 (32.4)	44 (19.9)	0.013 [b]
Stage			
I, II	37 (40.7)	104 (51.7)	
III, IV	54 (59.3)	97 (48.3)	0.079 [b]
Mucin producing			
None	86 (65.7)	175 (69.2)	
Focal or Diffused	45 (34.3)	78 (30.8)	0.483 [b]
BMI			
<25.0	67 (53.2)	90 (40.7)	
25.0-29.9	39 (30.9)	69 (31.2)	
30.0+	20 (15.9)	62 (28.1)	0.020 [b]

[a] Column total may be different due to missing data;

[b] Chi-square test;

[c] Fisher's exact test

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Table 3

Logistic Regression Analysis for Colorectal Carcinoma Associated with Agricultural and Farming-related Exposures[a]

	Patients n= 73 No. (%)	Controls n= 112 No. (%)	Crude OR (95% CI)	Adjusted[b] OR (95% CI)
Exposed to pesticides				
No	22 (30.1)	42 (37.5)	1.0	1.0
Yes	51 (69.9)	70 (62.5)	1.4 (0.7-2.6)	2.6 (1.1-5.9)
Exposed to insecticides				
No	30 (41.1)	82 (73.2)	1.0	1.0
Yes	43 (58.9)	30 (26.8)	3.9 (2.1-7.3)	3.2 (1.5-6.5)
Exposed to herbicides				
No	34 (46.6)	83 (74.1)	1.0	1.0
Yes	39 (53.4)	29 (25.9)	3.3 (1.8-6.1)	5.5 (2.4-12.3)
Exposed to fertilizers				
No	32 (43.8)	42 (37.5)	1.0	1.0
Yes	41 (56.2)	70 (62.5)	0.8 (0.4-1.4)	1.8 (0.8-4.0)
Frequency of eating food from the field[c,d]				
Never or seldom	5 (10.6)	37 (41.6)	1.0	1.0
Half of the time or more	42 (89.4)	52 (58.4)	6.0 (2.2-16.6)	4.6 (1.5-14.6)
Frequency of working soon after pesticides were applied [d]				
Never or seldom	7 (16.7)	29 (31.2)	1.0	1.0
Half of the time or more	35 (83.3)	64 (68.8)	2.3 (0.9-5.7)	2.1 (0.7-5.9)

[a] Only study participants who reported jobs of farming for the longest duration in their lifetime were included in the analyses;

[b] Adjusted for age (continuous), gender (male, female), residence (rural, urban), industrial exposure (yes, no), and active smoking (yes, no);

[c] Excluded 1 patient and 4 controls whose major farming products were not food items;

[d] Column total was different due to missing data

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Table 4

Logistic Regression Analysis for Colorectal Carcinoma Associated with Menstrual and Reproductive Factors[a]

	Patients n= 200 No. (%)	Controls n= 203 No. (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
Age at menarche				
=<12	66 (34.4)	107 (60.5)	1.0	1.0
13+	126 (65.6)	70 (39.5)	2.9 (1.9-4.5)	3.5 (2.2-5.7)[b]
Oral Contraceptive use				
Never	96 (54.2)	118 (67.1)	1.0	1.0
Ever	81 (45.8)	58 (32.9)	1.7 (1.1-2.6)	1.4 (0.8-2.3) [c]
Number of pregnancies				
1 – 3	69 (39.0)	46 (26.1)	1.0	1.0
4 – 6	80 (45.2)	52 (29.6)	1.0 (0.6-1.7)	1.0 (0.5-1.7) [c]
7+	28 (15.8)	78 (44.3)	0.2 (0.1-0.4)	0.3 (0.1-0.5) [c]
Number of live births				
1 – 3	77 (43.5)	53 (30.1)	1.0	1.0
4 – 6	77 (43.5)	64 (36.4)	0.8 (0.5-1.3)	0.9 (0.5-1.6) [c]
7+	23 (13.0)	59 (33.5)	0.3 (0.1-0.5)	0.3 (0.2-0.7) [c]
Lifetime duration of lactation (months)				
0 – 20	32 (18.7)	20 (11.5)	1.0	1.0
21 – 72	87 (50.9)	60 (34.7)	0.9 (0.5-1.7)	0.7 (0.4-1.5) [d]
73 +	52 (30.4)	93 (53.8)	0.3 (0.2-0.7)	0.3 (0.2-0.8) [d]
Average duration of lactation (months/child)				
0 – 7	38 (22.2)	19 (11.0)	1.0	1.0
8 – 18	90 (52.6)	59 (34.1)	0.8 (0.4-1.4)	0.7 (0.4-1.4) [d]
19 +	43 (25.2)	95 (54.9)	0.2 (0.1-0.4)	0.2 (0.1-0.4) [d]

[a] Only female study participants were included in the analyses, and column total may be different due to missing data;

[b] Adjusted for age (continuous), residence (rural, urban), industrial exposure (yes, no), and active smoking (yes, no);

[c] Adjusted for age (continuous), residence (rural, urban), industrial exposure (yes, no), active smoking (yes, no), oral contraceptive use (yes, no), number of live births (1-3, 4-6, 7+), and average duration of lactation per birth (0-7, 8-18, 19+ months) among parous women only;

[d] Adjusted for age (continuous), residence (rural, urban), industrial exposure (yes, no), active smoking (yes, no), oral contraceptive use (yes, no), and number of live births (1-3, 4-6, 7+) among parous women only