Genetic, Environmental, and Dietary Risk Factors of Colorectal Cancer: A Case–Control Study in the Algerian East

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Abstract Colorectal cancer (CRC) is the second most common cancer diagnosed in Algeria. Incidence and mortality rate of CRC has increased to rank Algeria in third place on the African scale. Environmental and genetic factors have an important role in CRC pathogenesis; for this reason, this study aimed to clarify the role of some risk factors (RF) of CRC in the east of Algeria region. We performed a case–control study in five Medical Oncology Services in the Algerian East: Tebessa, Batna, Annaba, Setif, and Constantine, between 2016 and 2019. A total of 200 patients diagnosed with CRC and 200 age-matched controls were included in this study. They were interviewed about environmental, dietary, and genetic RF (family history of cancer) using a questionnaire. Results showed a significant link between high educational level and an increased risk of CRC (OR = 0.39; CI: 0.24–0.64; $p < 0.001$). Cancer and CRC in 1st degree (mother, father, brother, sister, or child) relatives were significantly associated with CRC risk (OR = 2.23; CI: 1.35–3.69; $p = 0.002$ and OR = 4.94; CI: 1.39–17.47; $p = 0.013$, respectively). Occupational exposures showed a significant connection to an increased risk of CRC (OR = 3.37; CI: 1.73–6.55; $p < 0.001$); also obesity and alcohol consumption were significantly associated ($p = 0.038$; $p < 0.001$, respectively). Yogurt (OR = 0.63; CI: 10.41–0.96) and cereals (OR = 0.34; CI: 0.22–0.51) consumption were significant protective factors, while red meat and fizzy drink were associated with an increased risk; OR of 1.67 (CI: 1.11–2.51) and 2.66 (CI: 1.78–3.99), respectively. This study suggests enhancing the awareness about CRC, adopting healthy dietary choices, and avoiding exposure to risk factors.

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1 Introduction

Colorectal cancer (CRC) is the third most common cancer in the world, and the second in terms of mortality. CRC rate ranks Algeria in the third place in Africa, and in the first place on the North African scale. In 2018, it was the most common cancer after breast cancer. In terms of mortality, it comes in the third position after lung and breast cancers [7]. The risk of developing colorectal cancer is influenced by age, genetic factors (family history of CRC) and environmental factors (diet, sedentary lifestyle, obesity…) [23].

Due to the increase of CRC rates among the Algerian population, especially for young adults (less than 50 years) and due to the lack of epidemiological studies in Algeria on colorectal cancer risk factors, a case–control study was conducted in the East of the country to clarify the role of some environmental and genetic risk factors.

2 Materials and Methods

The case–control study was conducted in five Medical Oncology Services in the Algerian East: Tebessa, Batna, Annaba, Setif, and Constantine, between April 2016 and April 2019. The study was carried out using data from 400 subjects: 200 patients (106 males and 94 females) from the mentioned services and who had been diagnosed with colorectal cancer, and 200 age-matched controls (100 males and 100 females) who are healthy subjects without any diagnosis of any type of cancer or any other chronical diseases.

The necessary data were derived from personal interviews using a standardized questionnaire about age, sex, and educational level; family history of cancer; environmental risk factors: tobacco, alcohol, nonsteroidal anti-inflammatory drugs (NSAIDs) use; and occupational risks (occupational exposures to heavy metals in cement, paint, pesticides, materials treatment products, industrial dust, and smoke). Subjects were also asked about the consumption frequency of cereals, yogurt, fruits, vegetables, red meat, and fizzy drinks. Consumption criteria were frequently = one or more times a week, and rarely = three times a month or less. Obesity was determined when body mass index BMI $\geq 30\,kg/m^2$, and was calculated using the weight in kilograms divided by the square of height in meters [8]. Patients were interviewed about their weight before cancer diagnosis and their BMI was calculated using this weight, while controls' BMI was calculated using their actual weight which was measured using a mechanical scale. Height was measured for both cases and controls using a toise.

The statistical analysis was carried out using SPSS software (version 25). Continuous variables were expressed as means ± SD and calculated using the Student's

t-test, while categorical variables were expressed as percentages and numbers, using Pearson's Chi-square test. Binary logistic regression analysis was performed to estimate the association of various risk factors with the risk of colorectal cancer, displayed as odds ratios (OR) with 95% confidence intervals (CI). The level of $p < 0.05$ was considered statistically significant. Informed consent was obtained from all participants in the study, and all procedures performed were in accordance with the 1964 Helsinki declaration.

3 Results

A total of 400 subjects were included in the study: 200 CRC patients (106 males and 94 females) and 200 controls (100 males and 100 females). The mean age of the patients was 55.6 ± 13.0 years and 55.2 ± 15.7 years in controls.

Results showed a significant association of high educational level (OR = 0.39; CI: 0.24–0.64; $p < 0.001$) with decreased risk of CRC (see Table 1). Cancer and CRC

Table 1 Genetic, environmental, and dietary risk factors associated to colorectal cancer

	Variables	Cases N = 200 n (%)	Controls N = 200 n (%)	OR	95% CI	*P* value
Cancer in 1st degree relatives	Yes	55 (27.50)	29 (14.50)	2.23	1.35–3.69	0.002
	No	145 (72.50)	171 (85.50)			
CRC in 1st degree relatives	Yes	14 (7.00)	3 (1.50)	4.94	1.39–17.47	0.013
	No	186 (93.00)	197 (98.50)			
Education	Low	86 (43.00)	72 (36.00)	1.34	0.9–2	1.34
	Medium	86 (43.00)	69 (34.50)	1.43	0.95–2.14	0.082
	High	28 (14.00)	59 (29.50)	0.39	0.24–0.64	$p < 0.001$
Obesity	Yes	59 (29.50)	41 (20.50)	1.62	1.02–2.56	0.038
	No	141 (70.50)	159 (79.50)			
Alcohol	Yes	29 (14.50)	6 (3.00)	5.48	2.22–13.52	$p < 0.001$
	No	171 (85.50)	194 (97.00)			
Tobacco	Yes	80 (40.00)	65 (32.50)	1.38	0.92–2.08	0.119
	No	120 (60.00)	135 (67.50)			
NSAIDs use	No	131 (65.50)	140 (70.00)	0.81	0.53–1.23	0.336
	Occasionally	67 (33.50)	49 (24.50)	1.55	1–2.4	0.048
	Daily	2 (1.00)	11 (5.50)	0.17	0.04–0.79	0.024
Occupational risks	Yes	38 (19.00)	13 (6.50)	3.37	1.73–6.55	$p < 0.001$
	No	162 (81.00)	187 (93.50)			

Table 2 Dietary risk factors associated to colorectal cancer

	Variables	Cases N = 200 n (%)	Controls N = 200 n (%)	OR	95% CI	*P* value
Cereals	Frequently	53 (26.50)	103 (51.50)	0.34	0.22–0.51	$p < 0.001$
	Rarely	147 (73.50)	97 (48.50)			
Yogurt	Frequently	127 (63.50)	147 (73.50)	0.63	0.41–0.96	0.032
	Rarely	73 (36.50)	53 (26.50)			
Fruit	Frequently	180 (90.00)	183 (91.50)	0.83	0.42–1.65	0.605
	Rarely	20 (10.00)	17 (8.50)			
Vegetables	Frequently	193 (96.50)	198 (99.00)	0.28	0.057–1.35	0.114
	Rarely	7 (3.50)	2 (1.00)			
Red meat	Frequently	88 (44.00)	64 (32.00)	1.67	1.11–2.51	0.014
	Rarely	112 (56.00)	136 (68.00)			
Fizzy drink	Frequently	123 (61.50)	75 (37.50)	2.66	1.78–3.99	$p < 0.001$
	Rarely	77 (38.50)	125 (62.50)			

in 1st degree relatives (mother, father, brother, sister, or child) were significantly associated with CRC risk (OR = 2.23; CI: 1.35–3.69; $p = 0.002$ and OR = 4.94; CI: 1.39–17.47; $p = 0.013$, respectively). Obesity ($p = 0.038$) and alcohol consumption ($p < 0.001$) were significantly associated with a higher risk of CRC, while tobacco use was not associated with risk of CRC in the study (see Table 1). Daily and occasionally use of NSAIDs were significant protective factors for CRC (OR = 0.17; CI: 0.04–0.79; $p = 0.024$ and OR = 1.55; CI: 1–2.4; $p = 0.048$, respectively). Exposures to carcinogenesis in the workplace as heavy metals in construction materials, pesticides, industrial dust, and smoke showed a significant association with an increased risk of CRC (OR = 3.37; CI: 1.73–6.55; $p < 0.001$).

An elevated risk was found for red meat and fizzy drink with an OR of 1.67 (CI: 1.11–2.51) and 2.66 (CI: 1.78–3.99), respectively, for daily and weekly consumption. While the consumption of cereals and yogurt on a daily and weekly basis appeared to exert a protective effect ($p < 0.001$ and 0.032, respectively). No significant associations were found for fruit and vegetable consumption (see Table 2).

4 Discussion

In this study, we examined the relationship between different risk factors and the risk of CRC. A high educational level was associated with a decreased risk of CRC, which was found in a Moroccan case–control study [20] and in previous others studies [11, 16]. People with a high educational level have a higher awareness of cancer risk factors and symptoms [14]. In our study, colorectal cancer and any cancer in 1st degree relatives were associated with an increased risk of CRC. Data from several

studies showed that a higher prevalence of CRC was found in subjects with a positive family history (of cancer and CRC) compared to subjects with no family history [10, 12, 22]. Obesity is a known risk factor for several diseases. A case–control study with about 1800 subjects found a positive association of obesity with risk of CRC for men and women combined [4]. In this study, obesity was also associated to CRC risk, which may be caused by a metabolic syndrome, insulin resistance, and modifications in the levels of adipocytokines [1]. A large number of epidemiological studies found an increased risk of colorectal cancer with higher alcohol consumption, which was found in this study too [27]. Alcohol consumption has been designed to increase the risk of CRC through alteration of bile acid composition, DNA methylation, abnormal DNA repair, and induce cytochrome P450 enzymes to increase carcinogen production [5, 13]. Tobacco use was not associated with colorectal cancer in this study, which is similar to Katsidziraa study [12], while, in Cross study and in Sidi Deoula study, tobacco was associated with an elevated risk of CRC [6, 20].

NSAIDs use was a significant protective factor for CRC in this study, which was not found in a study realized in a Moroccan case–control study and in Katsidziraa study [12, 20]; other epidemiological and experimental studies have proven that NSAIDs reduce the risk of CRC by inhibiting the cancer cell proliferation, reducing inflammation, and inducing apoptosis of colon cancer cells [9, 19]. Several epidemiological studies have shown that some occupational exposures such as industries, firefight, agriculture, and construction… expose workers to chemical compounds considered as carcinogenesis (heavy metals, nanoparticles, pesticides, dusts, smoke…), and because of which, cancer risk was significantly elevated for several localizations, including colorectum [26] [15, 17]. This study has shown also a significant correlation between CRC incidence and these occupational exposures in workplaces.

Another correlation between red meat, fizzy drink consumption (western diet) and CRC risk was found in this study, while cereals seem to have the opposite effect. Despite the proven protective effect of fruits and vegetables, no significant association with CRC was found in the current work. In Vogtmann study, vegetable consumption was largely unrelated to this risk [24]. Several epidemiological studies showed the protective role of cereals, fruit and vegetables (high levels of anticarcinogenic compounds) while considered the high consumption of meat and high-sugar drinks responsible for an increased risk of CRC and promoting its development [3, 18, 25]. The Tunisian population has similar habits to our study population; Ben Othman et al. found that obesity and the high consumption of red meat were significant risk factors while the consumption of fruits, vegetables, and cereals was higher in controls [2]. Song et al. suggested that yogurt consumption has a potential anti-CRC effect by reducing absorption of mutagens and inactivating the intestinal carcinogens [21]. In this study, yogurt consumption has a similar effect against colorectal cancer.

5 Conclusions

This study suggests spreading awareness about CRC risk factors and the importance of the early screening of CRC, especially among people whose relatives have cancer history. In addition, people have to be motivated to adopt healthy dietary choices and reduce their exposure to carcinogens.

References

1. Bardou, M., Barkun, A.N., Martel, M.: Obesity and colorectal cancer. Gut **62**(6), 933–947 (2013)
2. Ben Othman, R., Ksira, I., Smida, A., et al.: Malnutrition and risk factors in Tunisian patients with colorectal cancer. Ibnosina J. Med. Biomed. Sci. **10**(3), 88–93 (2018)
3. Bouvard, V., Loomis, D., Guyton, K.Z., et al.: Carcinogenicity of consumption of red and processed meat: International Agency for research on cancer monograph working group. Lancet Oncol. **16**, 1599–1600 (2015)
4. Campbell, P.T., Jacobs, E.T., Cornelia, M., et al.: Case–control study of overweight, obesity, and colorectal cancer risk, overall and by tumor microsatellite instability status. J. Natl. Cancer Inst. 17 **102**(6), 391–400 (2010)
5. Choi, S.W., Stickel, F., Baik, H.W., et al.: Chronic alcohol consumption induces genomic but not p53-specific DNA hypomethylation in rat colon. J. Nutr. **129**, 1945–1950 (1999)
6. Cross, A.J., Boca, S., Freedman, N.D., et al.: Metabolites of tobacco smoking and colorectal cancer risk. Carcinogenesis **35**(7), 1516–1522 (2014)
7. Ferlay, J., Colombet, M., Soerjomataram, I., et al.: Global and Regional Estimates of the Incidence and Mortality for 38 Cancers: GLOBOCAN 2018. International Agency for Research on Cancer/World Health Organization, Lyon (2018). https://gco.iarc.fr/today/online-analysis-table. Accessed 06 April 2019
8. Ferrera LA (2005) Body mass index. Nova Publishers, pp 7
9. Hamoya, T., Fujii, G., Miyamoto, S.: Effects of NSAIDs on the risk factors of colorectal cancer: a mini review. Genes Environ. **38**, 6 (2016)
10. Henrikson, N.B., Webber, E.M., Goddard, K.A., et al.: Family history and the natural history of colorectal cancer: systematic review. Genet. Med. **17**(9), 702–712 (2015)
11. Hvidberg, L., Pedersen, A.F., Wulff, C.N., Vedsted, P.: Cancer awareness and socio-economic position: results from a population-based study in Denmark. BMC Cancer **14**, 581 (2014)
12. Katsidziraa, L., Gangaidzo, I.T., Makunike-Mutasa, R., et al.: A case–control study of risk factors for colorectal cancer in an African population. Eur. J. Cancer Prev. **28**(3), 145–150 (2019)
13. Kune, G.A., Vitetta, L.: Alcohol consumption and the etiology of colorectal cancer: a review of the scientific evidence from 1957 to 1991. Nutr. Cancer **18**, 97–111 (1992)
14. Lagerlund, M., Hvidberg, L., Hajdarevic, S., et al.: Awareness of risk factors for cancer: a comparative study of Sweden and Denmark. BMC Public Health **15**, 1156 (2015)
15. LeMasters, G.K., Genaidy, A.M., Succop, P., et al.: Cancer risk among firefighters: a review and meta-analysis of 32 studies. J. Occup. Environ. Med. **48**, 1189–1202 (2006)
16. Mouw, T., Koster, K., Margaret, E., et al.: Education and risk of cancer in a large cohort of men and women in the United States. PLoS ONE **3**(11), e3639 (2008)
17. Oddone, E., Modonesi, C., Gatta, G.: Occupational exposures and colorectal cancers: a quantitative overview of epidemiological evidence. World J. Gastroenterol. 21 **20**(35), 12431–12444 (2014)

18. Pou, S.A., Díaz, MdP, Osella, A.R.: Applying multilevel model to the relationship of dietary patterns and colorectal cancer: an ongoing case-control study in Córdoba, Argentina. Eur. J. Nutr. **51**, 755–764 (2012)
19. Rothwell, P.M., Wilson, M., Elwin, C.E., et al.: Long-term effect of aspirin on colorectal cancer incidence and mortality: 20-year follow-up of five randomisedtrials. Lancet **376**(9754), 1741–1750 (2010)
20. Sidi Deoula, M., Huybrechts, I., Elkinany, K., et al.: Behavioural, nutritional and genetic risk factors of colorectal cancers in Morocco: protocol for a multi-centre case-control study. J. Glob. Oncol. (2019). https://doi.org/10.2196/preprints.13998
21. Song, M., Garrett, W.S., Chan, A.T.: Colorectal cancer prevention. Gastroenterology **148**(6), 1244–1260.e16 (2015)
22. Taylor, D.P., Burt, R.W., Williams, M.S., et al.: Population-based family history-specific risks for colorectal cancer: a constellation approach. Gastroenterology **138**(3), 877–885 (2010)
23. Thanikachalam, K., Khan, G.: Colorectal cancer and nutrition. Nutrients **11**(1), 164 (2019)
24. Vogtmann, E., Xiang, Y.B., Li, H.L., et al.: Fruit and vegetable intake and the risk of colorectal cancer: results from the Shanghai Men's Health Study. Cancer Causes Control **24**(11), 193545 (2013)
25. Wada, K., Oba, S., Tsuji, M., et al.: Meat consumption and colorectal cancer risk in Japan: The Takayama study. Cancer Sci. **108**(5), 1065–1070 (2017)
26. Won, J.L., Dale, P., Sandler, et al.: Pesticide use and colorectal cancer risk in the Agricultural Health Study. Int. J. Cancer **121**(2), 339–346 (2007)
27. World Cancer Research Fund/American Institute for Cancer Research: Food, Nutrition, Physical Activity, and the Prevention of Cancer a Global Perspective. AICR, Washington DC (2007)