Original Research Article

Nutritional, Epidemiological and Pathological Profiles of Colorectal Cancer in Jijel Province: A Case Control Study

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ABSTRACT

Colorectal cancer or CRC is one of the most prevalent cancers worldwide; its incidence rate in Algeria has been incrementally and steadily increased because of socio-economic transition during the last decades. Diet has been reported to play a major role in the CRC etiology. The present study aimed to gain a better understanding of the relationship between some lifestyle factors such as the food groups' frequency consumption and CRC in Jijel Wilaya (Algeria). We conducted a case control study among the CRC patientssupported by the Jijel Hospital. The comparison of 34 cases with their controls revealed that the high educational level (OR= 0.0578, p-value= 0.0075), the low household income (OR=7.8386, p value=0.0374), the smoking (OR=0.0751, p-value=0.0174) and the familial history of CRC (OR=5.2500, p-value=0.0034) may be associated with the CRC occurrence in this population. A protective effect of consumption of dairy products (OR=0.9808, p-value=0.0437) and cereals (OR=0.9865, p-value= 0.0100) was observed, while the fish consumption appeared be positively associated with CRC (OR=1.0665, p-value=0.0392). We showed that of the proximal colon tumors were associated with a low consumption of fruits, vegetables and cereals and a consumption of dairy products. By contrast, the distal and rectal colon tumors seemed to be dependent to the excessive consumption of fruits, vegetables and cereals. Unexpectedly, the red meat consumption did not exerciseany effect on the sub-sites of the tumors occurrence. *Key words:* colorectal cancer, Diet, cancer incidence, protective effect.

INTRODUCTION

The colorectal cancer (CRC) is an important public health problem throughout the world. ^[1,2] It is the third most common cancer in men, after prostate cancer and lung cancer and the second in women, after breast cancer and lung cancer, worldwide. ^[3] The increases in the number of both the newly diagnosed cases and the death are respectively estimated at 77% and 80% by 2030. The CRC is a very heterogeneous disease, which is caused by the interaction of genetic and environmental factors. ^[4] The western life style and the dietary habits characterized by higher intake of meat, fat and total calories, along with increasing life

expectancy and population growth, are beyond the remarkable increase in the burden of CRC.

Algeria is an example of real epidemiological transition, marked by a structural change in the population profile. ^[5] The demographic transition resulted in a gradual aging of the population importantly towards people over 60 years in the age pyramid. ^[5] However, the environment transformation, an acute change in the individual and collective life (increased smoking, stress, sedentary lifestyle, and urbanization) and life style change are the cause of emergence of non-communicable diseases, including cancer, which is often a

multifactorial disease and its causes are difficult to study.

In order to better understanding of the CRC progression in the Jijel population, we sought to explore the possible associations between lifestyle and colorectal cancer. The lifestyle indicators include obesity, overweight, physical activity lack, medical history and socioeconomic status. Thus, we assessed the impact of diet and eating habits (meals composition, their daily distribution and frequency) on the risk of CRC.

MATERIALS AND METHODS Population and Study Design

То assess the effect of some environmental factors, mainly diet, on the CRC incidence in Jijel (Wilaya of North east, Algeria), we choose a model of case control study. According to this model, the risk factors were determined by comparing the exposure of the CRC cases and the corresponding controls to these factors, and then their effects were estimated by calculating an algebraic value: the odds ratio (OR) who represented the strength of the association between the exposure and the outcome. All cases included in our study were resident in Jijel and recruited in the oncology service of Mohamed Seddik Ben Yahia hospital. The CRC diagnosis was histologically confirmed. The control group was randomly chosen by sampling control subjects from the population and the control subjects were unmatched.

Pathoclinical and lifestyle data

The pathoclinical data of CRC cases were obtained from patient files archived in the oncology department of the Mohamed Seddik Benyahia Hospital. They mainly included date and method of diagnosis; cancer site; tumor histological type, cancer biomarkers. То and collect stage information on the general lifestyle (cases and controls), we used a questionnaire for each patient during the period April-June 2016, using a face-to-face interview. The study covered the period before diagnosis, (patients) or the year 20016 (controls).

We focused on socio-demographic variables (age, gender, matrimonial status, educational level, resident location and household outcome). anthropometric weight), measures (height and and comorbidity history, personal and family history of colorectal cancer, medicine intakes and lifestyle factors (smoking, consumption physical alcohol and activities).

Food frequency questionnaire

^[6]A frequency questionnaire, which consisted of a list of foods with associated consumption frequency categories such as day frequency was used to ask our interlocutors to verify, for each food on the list and the frequency closest to its usual consumption. The food frequency questionnaires (FFQs) are widely used in epidemiological studies to assess dietary intake and to explore diet and chronic disease associations in specific populations. ^[6] This instrument is inexpensive, relatively easy to administer and can measure dietary intake over a long time.^[7] It is critical that a FFQ is culturally appropriate for the population being studied.

We used a semi quantitative food frequency questionnaire to assess dietary intake. The FFQ is designed to assess usual food intake pattern during the past one year for controls and during the period before diagnosis for cases- Response options for most food items had 7 levels: none or little, once a month, 2-3 times a month, 1-3 times a week, 3-6 time a week, once a day, 2-4 times a day.

The FFQ consisted in 100 food items divided into five groups and thirteen food subgroups: cereal products (Rice, frick, semolina, wheat flour, couscous, tlitli, vermicelli, chakhchoukha, pasta, spaghetti pasta, vermicelli flood, bread, gheraif, kesra, biscuit, puff brioche, pastry, and millefeuilles); vegetables and fruits (Tomato, cucumber, zucchini, sweet pepper, green salad, cauliflower, parsley, carrot, cabbage, onion, garlic, beetroot flood, concentrated fennel, tomato, orange. mandarin, apple, perry, apricot, plum,

melon, watermelon, grapes, medlar, banana, date, pitted green olives and black olive); meat and derivatives (Beef, sheep meat, processed meat, liver and sausages), poultry and eggs (Poultry, eggs and pisces); fish (Sardine, tuna in oil, whiting and shrimp) and airy products (Milk, l'ben, processed cheese portion and yogurt). In order to quantify the food consumption, we attributed a numeric value to each frequency, and then calculated the sum of these values for each participant.

Data analysis

The data analysis, including the frequency distribution and the descriptive statistics was done for each variable using EPI INFO 3.5.4.0 version. The odds ratio (OR), which is the odds of cases exposure divided by the odds of controls exposure and t-test were used to determine the significance of the differences between cases and controls. A p-value less than 0.05 were considered statistically significant.

RESULTS AND DISCUSSION

Comparison of general characteristics between cases and controls

Evidence on a possible effect of life style factors on CRC incidence came from studies done on Japanese immigrants in the USA, Asian Jewish immigrants in Israel and East European immigrants in Australia.^[8] These immigrants acquire the common CRC rates in the country of their adoption. Thus, no doubt remains that some environmental factors, probably diet, may account for these cancer rates. In order to evaluate the effect of some life style factors and food frequency consumption on the CRC incidence in Jijel, we conducted a case control study. Among 108 CRC cases, we succeeded in interviewing 34patients. In parallel, we investigated the life style and the dietetic characteristics of 34 controls among the general population (healthy persons).

The Table 1 summarized the main characteristics of the CRC patients and their controls. No significant differences have been registered between the two groups in terms of sex (p-value=0.2261), age (pvalue=0.1730), physical activity (p-value= 0.8177), occupation (p-value= 0.7298) and matrimonial status (p-value=0.6014). We demonstrated that the CRC familial history (OR=5.2500, p-value=0.0034) was related to the CRC incidence. ^[9] It has been reported that up to 20% CRC patients are descendants of families affected by the disease. The reasons for the increased CRC risk are not clear, but they are very likely inherited due to genes, shared environmental factors or some combination of them.

The low levels of education and household income appeared to be risk factors in the study population. These two variables have been somewhat associated with the disease, as the graduate degree level often allowed more lucrative occupations. The household income was disease significantly related to the (OR=7.8386, value=0.0374, after р adjustment for age, physical activity and smoking). Indeed, the families with a low household income were often exposed to the environmental factors risks (worse quality of water and foods, pollution) and had less accessibility to medical care.

By contrast, the high educational level was related to the CRC reduction (OR=0.0578, p-value=0.0075, after adjustment for age and smoking). It enabled the population to have better access to information about diseases, their etiology, their symptoms and the associated risk factors, and therefore, contribute to reducing the impact of this public health burden. Moreover, well-educated people tended to accept diagnosis more easily, while many diseases still represent a taboo for low education level subjects.

In addition, smoking was considered as a risk factor to develop CRC, since a protective effect was observed when comparing never smokers to ex-smokers (OR=0.0751, p-value= 0.0174, after adjustment for educational level, household income and familial history). ^[4] It is well known that tobacco smoking is associated

with a higher risk for colonic adenoma formation as well as increased of CRC incidence. Tobacco smoke includes manypro-carcinogens substances such as aromatic amines, nitrosamines, heterocyclic polycyclic and aromatic amines hydrocarbons. ^[10] These substances undergo metabolism through cytochromes P450, leading to the formation of aberrant DNA and further gene mutation.

Table 1: Comparison of general characteristics between the cases and controls groups

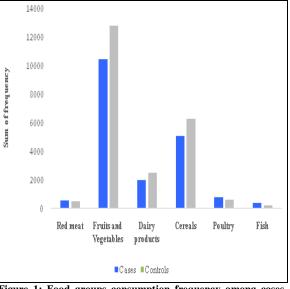
cases and controls groups	Cases	Controls	p-value
Sex	34	34	
Male	19	20	0.2261
Female	15	14	
Age group (years)			
<40	6	7	0.1730
40-60	13	13	
≥ 60	15	14	
Smoking status			
Never	20	26	0.0174
Former	11	7	
Current	3	1	
Physical activity			
Low	4	4	0.8177
Medium	12	13	
High	18	17	
Education			
Illiterate	8	4	
Middle classes	11	4	0.0075
Secondary	2	9	
Superior	2	11	
Family history of colorectal cancer			
Yes	19	6	0.0034
No	15	28	
Household income	-		
<18 000,00 AD	19	9	
18 000,00-50 000,00 AD	12	15	0.0374
50 000,00-100 000,00 AD	2	8	
≥100 000 AD	1	2	
Occupation	10		
Active	12	14	0.7200
House Keeping	12	9	0.7298
Retired	10	11	
Matrimonial status	- 20	20	0 (01)
Married	30	29	0.6014
Single	4	4	
Widow	0	1	

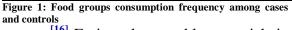
Association between Food groups frequency intake and CRC incidence

^[11] Dietary factors play an important role in the occurrence of CRC and differences in these factors seem to contribute to the variation of cancer incidence between countries. We evaluated the association between the frequency consumption of some food groups (red meat, fruits and vegetables, cereals, dairy products, poultry, fish) and the incidence of

CRC in the JijelWilaya. Figure 1 represents the results of the frequency consumption of some food groups among cases and controls. The frequency of red meat consumption appeared to be higher in cases group. However, we failed to find a significant association between CRC incidence and red meat consumption frequency (crude Odds Ratio=1.0050, pvalue=0.8003, after adjustment for covariates including age group and household income level), this no significant association did not change (OR=1.0392 and p-value of 0.1210). ^[ĭ2] The red meat consumption more than 2-3 times a month is an independent risk factor in multivariate regression analysis and increases the odds of developing CRC by 5.41 times compared to those never or hardly consume.

Many studies showed that high red meat intake increased odds for CRC incidence. ^[11,13] Elevated risks of CRC have been among high consumers of total meat, red meat and processed meat. ^[14] The consumption of fresh red meat was associated with moderately increased risks of rectal cancer but had little association with risk of colon cancer. ^[15] Summarv association (null or just above the null value) between the red meat and CRC has been reported in virtually all models.





and controls ^[16] Fruit and vegetables are rich in dietary fibers and, although there are other

important sources such as unrefined cereals, it might be expected, if dietary fibers reduce the CRC risk, that this risk reduction would be observed in association with high intakes of fruit and vegetables. We observed a more frequent consumption of these diets among the controls. This difference was not statistically significant (Crud OR=0.9978, pvalue=0.1525) and did not change after adjustment of age, sex, physical activity, household and income smoking [17] This (OR=0.9971, p-value=0.1288). finding was in agreement with that found in a prospective cohort study, in which the authors have evaluated the association between fruit and vegetable intakes and CRC. ^[18] Indeed, Fruit and vegetable intakes were not strongly correlated with colon cancer risk overall but may be associated with a lower risk of distal colon cancer. ^[19] The association between fruit and vegetable consumption and CRC risk is inconclusive. [20] Fruit consumption was inversely associated with the CRC risk, whereas vegetable intake was not significantly ^[21] Thus, EPIC associated with risk. (European Prospective Investigation into Cancer and Nutrition) study suggested that a high consumption of fruit and vegetables is associated with a reduced CRC risk, especially of colon cancer; however, their effect may depend on smoking status.

Obviously, it has been noted that dairy consumption frequency was more decisive in controls, essentially among the older ones (> 60 years). We showed no significant protective effect of dairy consumption (Crud OR=0.9808, pvalue=0.0580), which became significant (OR=0.9808, p-value=0.0437), after adjustment of the consumption frequency of the different dairy groups (red meat, fruits and vegetables, fish and cereal). ^[22] It has been reported that high intake of dairy food decrease the CRC risk with a food for both men and women.

Elsewhere, the high intake of dietary fibers, particularly from cereal and whole grains is associated with a reduced CRC risk. A protective effect of consumption of dietary fibers and whole grain against the CRC risk is biologically plausible. Indeed, whole grain foods are important sources of dietary fibers and may decrease the CRC risk by increasing stool bulk, diluting fecal carcinogens and decreasing transit time.^[23] In addition, fibers bacterial fermentation results in the production of short chain fatty acids, which may have protective effects against CRC.As shown in Figure 1, consumption frequency of cereals is more important in controls, we demonstrated a significant protective effect of cereals consumption 0.9865, (OR =p-value= 0.0100).

In addition, we showed that poultry frequency consumption is greater in cases group specifically. However, this result is statistically significant (crud not OR=1.0375, p-value=0.1255) even when we adjusted the OR for age, sex, and household income (OR=1.0402, p-value=0.1564). ^[24] It has been reported that there was no association between poultry-rich diets and CRC risk. ^[25] Several cohort studies have reported an inverse association between poultry and CRC, while a number of others have suggested a positive association. Like for red meat, the amount of poultry consumed and the cooking method play a role in these disparities in results.

Finally, as we can see in Figure 1, the cases consume fish more frequently than the controls, but this result failed to rich statistical significance (crud OR=1.0426, pvalue=0.1138). After adjustment for other group covariates, а significant food association is obtained (OR=1.0665, p-value =0.0392). ^[26] The association between fish intake and CRC risk among Guangdong Chinese population showed that higher intake of fresh fish including freshwater fish and sea fish was associated with a lower CRC risk.

Association between Food groups intake frequency and tumor sub site location

^[27] CRC was previously categorized as either proximal or distal (descending colon, sigmoid colon, recto sigmoid, and rectum). ^[28] Since then, rectal cancer was

addressed specifically as a unique type of CRC. There are many differences between the three sub sites, such as embryologic, morphologic and biochemical differences. ^[28] In addition, tumors of the proximal and distal colon differ in their genetic nature. Comparisons have shown that proximal colon tumors tend to have different molecular characteristics, with a higher proportion of microsatellite instability, and are more likely to have CpG island methylator phenotype and K-ras mutations than distal colon and rectal tumors. However, the right-sided (proximal) colon cancer is more aggressive type tumor compared to left-sided (distal) colon cancer, and patients with proximal colon cancer are more often females than males. ^[29] The advanced proximal colonic tumors are more often flat, while the distal ones are polypoid-type.

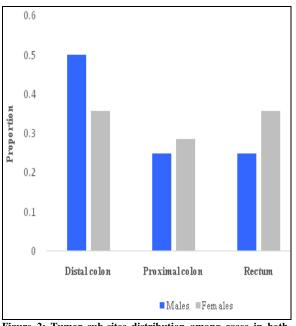


Figure 2: Tumor sub-sites distribution among cases in both males and females.

Distal colon tumors are more predominantly present in males than in females, whereas proximal colon and rectum tumors are just the opposite with more proportion value among females. Our results suggested that women have a higher risk then men for developing proximal colon cancer, and that is associated with poor prognosis, especially among older women. ^[27,30] These results are in harmony with some previous studies. ^[28] Also, the environmental factors such as diet and alcohol intake differ in their role in the tumors development in the three segments. We tried to assess such effect by measuring means of consumption frequency of some food groups between cases with respect to the tumor sub site. As shown in Figure 03, we observed that the proximal colon tumors were related to high level of dairy products consumption and little consumption of fruits, vegetables, and cereals. By contrast, both distal and rectal colon tumors seemed to be associated with high consumption fruits, vegetables and cereals.

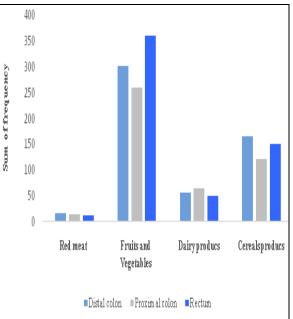


Figure 3: Relation between some food groups consumption frequency and tumor sub-sites distribution

Red meat consumption appeared to no effect on sub site tumors have occurrence.^[31] Previous studies have reported a significant implication of processed red meat consumption in increased cancer risk of distal colon, and not the proximal colon cancer. We stated that a more proximal shift tumors was registered by consumption of roast meat (OR=3.0, 95% CI=1.14~9.23) at least once a week. ^[32] So, It is primordial to determine the coking mode and the amount of consumption to achieve relevant results about the exact risk inherent to red meat consumption.^[29] The

levels of carcinogenic N-nitro so compounds, products of the red meat metabolism appear to be higher in distal colon and rectum than in colon. ^[33,34,35] The total consumption of fruits and vegetables is inversely associated with colon and rectal cancers, and relation is stronger for distal tumors than for the proximal ones. Our results may be explained by the fibers fermentation effect, which occurs mainly in the proximal colon, leading to the formation of short-chain fatty acids. These latter have been shown to promote cell differentiation, apoptosis cell-cycle arrest and of transformed colonocytes. ^[29]The fibers may dilute the concentration of carcinogenic substances in the distal colon. ^[36] Moreover, others environmental factor such as the nonrational pesticide use in agriculture may increase the colorectal cancer risk. [31,37] Finally, Swedish studies have reported the influence of the nature of milk and its frequency of consumption on the different locations of CRC.

To conclude we can say that the interpretation of our results should consider different particular characteristics of our society. The nutritional quality of different food groups may differ considerably from that of other countries notably due to the non-respect of the standards inherent to picking, transformation and conservation of fruits, vegetables, and cereal sand milk and meat products. The use of chemical additives complicates more the problem. In addition, the pollution due to the excessive use of pesticides and to the human industrial activity could be another factor, explaining our non-canonical results.

CONCLUSION

The present study was carried out to assess the nutritional status of CRC patients. The food habits should always be under check and the nutrition education can help to promote nutritional awareness and good eating habits.In conclusion, our results seemed to indicate no major impact of diet on CRC incidence in the population of Jijel Province. This may be explained by the low number of the cases implicated in the study and the presence of a potential problem of recall bias, as the study draw on recalling of nutritional habits of the last years. The health behavior change is likely playing key roles in these results as majority of patients change their nutritional regimen after being CRC diagnosed.

This work represents an introduction to the study of the effect of environmental factors, mainly diet, on the occurrence of CRC between Algerians. These current results should be complemented by other studies that take into account other factors such as pollution and the nutritional quality of foods. Such studies should make it possible to adopt relevant approaches to a best primary prevention.

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Conflict of interest: The authors declare that they have no conflict of interest.

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