Original Article

Colorectal Cancer Nutritional Risk Factors: A Population Based Case-Control Study

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Abstract

Background: Colorectal cancer (CRC) is the third common malignancy all over the world. Modern life styles affecting nutritional habits have been providing a potential impact on CRC. This study aims to assess the nutritional characteristics in CRC patients of Golestan province, Northeast of Iran.

Methods: All incident CRC cases (N=47) in northeast of Iran (2004-2005) and a matched number of healthy persons were selected as cases and controls respectively. The subjects filled the Questionnaires containing socio-demographic and nutritional characteristics (FFQ).

Results: Data analysis showed that Total Energy Expenditure (TEE) higher than 1837.5 Kcal/ day (first quartile of TEE) was significantly related to CRC risk (OR= 3.8; 95% CI:1.2 - 11.3); no other relationship was reported.

Conclusions: Findings suggested that higher levels of total energy expenditure may increase the risk of CRC about 4-fold. We also found that there are relationships between CRC and high fat diets or cooking methods. Nutritional interventions should be considered as an important part in colorectal cancer prevention programs.

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Introduction

Colorectal cancer (CRC) is the third common malignancy in the world. The age-adjusted incidence rate of colorectal cancer was reported to be higher in prosperous industrialized countries. In the USA and Western Europe, Australia and New Zealand, the age-standardized incidence rates of colorectal cancer among males are currently around 50 per 100000 people- per year. Overall, the average rate of colorectal cancer amongst males in the "less developed" countries (defined by the World Health Organization) is around 20% of that of the industrialized ones [1]. Data on incidence and prevalence of cancers in Iran show an increase in colorectal cancer rates ,and now this cancer is the fifth common cancer in Iran, and the 4th most common cancer in both sexes [2].

While Genetic factors and inflammatory bowel diseases are among the proposed etiologies, nutritional status and life style have a close relationship with CRC [3]. Dietary factors may account for 75% of sporadic colorectal cancer in the west, but the mechanisms remain obscure [4].

The major challenge facing those who seek to harness nutrition as a strategy for colorectal cancer prevention is the development of mechanistic hypotheses to account for interactions between diet and the disease process. In general, such hypotheses tend to be based on the concept of "high-risk" diets, which may contain high levels of either carcinogens or promoters or lack of one or more anti-carcinogenic protective factors. A third possibility currently gaining credence is that high-risk diets exert their effects on the development of colorectal cancer indirectly; for example, by causing obesity and thus modifying an individual's overall metabolic status in such a way that the colorectal mucosa becomes more vulnerable to carcinogenesis [5]. Given the complexity of f human diets and the mechanisms regulating epithelial integrity in the

alimentary tract, all the three possibilities must be taken into account [4].

The investigation field of the role of nutrition in cancer process is very broad. As research continues, it is becoming clearer that nutrition plays a major role in cancer.

Due to increasing prevalence of CRC and recent changes in dietary and behavioral habits in developing countries like Iran, we designed this study to evaluate nutritional and some other risk factors of CRC in Golestan province, Northeast of Iran.

This study will focus on those dietary factors, which have been shown to contribute to increased risk of cancer as well as those additional protective dietary factors, which reduce cancer risk.

Materials and Methods

In this population based case-control study, all new CRC patients registered in Golestan population-based Cancer Registry during 2004 to 2005 were recruited. Controls were the patients' neighbors who were matched by age and sex by means of caliper matching method [6] .In this method, each case and control was classified in a 5-year subgroup. The number of controls was the same as the cases.

After obtaining informed consents, face-to-face interviews were performed at the subjects' homes.

A two–part questionnaire was completed for each participant. The first part was about the demographic data and the second was a nutritional questionnaire.

Nutritional questionnaire was designed in the frame of semi quantitative FFQ (Food Frequency Questionnaire) and was completed by trained staffs. Data were entered in SPSS software, and matched analysis was done in STATA/ version 8 by conditional logistic regression.

Odds ratio was used to evaluate the relationship between risk factors or probable protective factors and the disease occurrence (CI=95%). Quantitative nutritional indices (Total Energy Expenditure = TEE) were classified to four groups based on the quartiles, and were entered into the analysis model. P-value <0.05 was considered as significant.

Results

Alive available CRC patients (N=47) and 47 healthy persons were included in the study. Most of the participants were males (59.6%). The age distribution of the participants is shown in figure 1.

The mean (± SD) and median age for cases were 52.36 (±13.19) and 48 years respectively. In the control group, these values were 52.15 (±13.1) and 49 years respectively (P-value>0.05).

A significant relationship was observed between the total energy intake and CRC risk. Increase in total energy intake resulted in increase in CRC risk [CI 95percentage: 1.1-2.7, OR=1.71, P-value<0.01]. CRC risk in patients with total energy intake in the fourth quartile was higher than the first one (Table1).

Those in the higher quartile of protein consumption had a higher risk (P-value>0.05) (Table 2).

We found that CRC risk was higher in individuals with Total Energy Expenditure of higher than 1837.5 Kcal/day (first quartile of TEE) than the participants in other quartiles of TEE (OR =3.8, CI 95%: 1.2-11.3). Odds Ratio was three in females and six in males for TEE.

Present findings showed that fat consumption of higher than 118.5 gr/day (i.e. 4th quartile of fat consumption) could lead to increase in CRC risk in comparison with other quartiles (OR=6.5, CI 95%: 1.5-28.8) (Table 3).

No difference was observed between the cases and controls in terms of vegetable consumption (OR=1.3, CI 95%: 0.9-1.7), milk intake (OR=1.2, CI 95%:0.9-1.6), low physical activity, increased carbohydrate intake and different fruit usage.

Subjects who did not consume fruits showed higher risk of CRC in comparison to others (OR=1.8, CI 95%: 0.6-5%).

Cooking methods (frying or barbecued) increase CRC risk (OR=3, CI 95%: 0.8-11.1) (Table 4).

Discussion

Interest in the relation between underfeeding and reduced mortality from cancer is long standing. Most of the research on nutrition and cancer has been reductionism; that is, a particular food or a nutrient has been studied in relation to its impact on tumor formation/regression or some other end points of cancer at a particular site in the body

The relationship between nutritional factors and CRC have been evaluated and it is estimated that any correction in life style and obesity, no alcohol usage and low red meat intake can prevent 30-50% of the cancer cases.

Eating too much food is one of the main risk factors for cancer. This can be best expressed in two ways: 1- by the additional risk of malignancies caused by obesity and 2- by the protective effect of eating less food.

In the present study, total energy intake of more than 1877.5 kcal/day lead to 4-fold increase in CRC risk, a matter confirmed in other studies as well [7-8].

Because accurate separation of fat content of red meat is impossible, the exact effect of protein on the

disease could not be evaluated. Red meat has been implicated in colon and rectal cancer [7].

In this study, the mean protein consumption was much lower than other studies in CRC cases and controls; and white meat was the main protein consistent not considered as a risk factor. Further studies on the relationship between red and white meat consumption and CRC risk are suggested.

No significant relationship was observed between different levels of carbohydrate intake and CRC. This result was in contrast with other studies that introduced carbohydrates as a risk factor for CRC [3, 9].

Although in other studies effective carbohydrate was measured, in the present study total carbohydrate was compared between cases and controls. Since carbohydrates are rich in fiber, it is suggested to omit the fiber amounts from carbohydrate sources.

Levi et al. found a reverse relation between simple lump sugar and CRC, and explained that fruits are the main source of simple lump sugar, which acts as the protective factor for CRC [9]. In this study, total fat consumption more than 118.5 gr/daily was associated with increased CRC risk of up to 3.8-fold. Unfortunately, due to sample size limitation, multivariable logistic regression analysis was not carried out. Conversely, in most studies , after adjusting the energy intake, no relationship was found and this suggested an indirect role of fat on unusual life style and high-energy intake

[11-12].

In this study, higher vegetable consumption was not protective but did not increase the disease rate significantly. Unpublished data showed that manure and fertilizing supplements in agricultural industry and toxins (herbicide, insecticide, etc) are used frequently in Iran; especially in Golestan province. Complementary studies on residual toxins and CRC risk are suggested. There were controversies about the relationship between vegetable and fruit consumption and CRC [13-15].

One of the most important messages of modern nutrition research is that a diet rich in fruits and vegetables protects against cancer. There are many mechanisms by which fruits and vegetables are protective and an enormous body of research supports the recommendation for people to eat more fruits and vegetables.

Many substances are protective in fruits and vegetables, so that the entire effect is not very likely to be due to any single nutrient or phytochemical [16-17].

Folic acid is the dark green leafy vegetable vitamin. It has an integral role in DNA methylation and DNA synthesis. Folic acid works in conjunction with vitamin B-6 and vitamin B-12 in the single carbon methyl cycle. Folate may be more important for rapidly dividing tissue such as the colonic mucosa. Therefore, the cancer risk associated with low folate intake is probably higher for colon cancer [9].

Dairy products had shown no significant relationship with CRC. This result was similar to that of other studies [20].

It seems that in the present study, increasing dairy products consumption resulted in increase in CRC prevalence. However, this finding cannot be judged due to small sample size.

Fatty dairy products and their confounding role can explain this result. Abouta satia et al, reported that frequent use of milk in African – Americans increases CRC risk up to 2-folds [3]. In this study, total dairy product consumption was evaluated; further studies should be conducted in detail in this regard.

A joint report by the World Cancer Research Fund and the American Institute for Cancer Research found convincing evidence that a high fruit and vegetable diet would reduce cancers of the colon and rectum [20]. Results of this report are compared with the present results in Table 5.

A non–significant relationship was reported between physical activity and CRC. Heavy exercise leads to increase in CRC prevalence [22-23]. It is suggested to study the duration and severity of physical activities in relation with CRC prevalence in a larger sample size.

Several biological mechanisms are mentioned; all of which show a relationship between immobility and CRC. For example, obesity and inactive life cause insulin surges and stimulates tumor cell growth. Another mechanism is bowel transition, which can be more rapid with physical activity, thus carcinogens contact with intestinal mucosa decreases [23-24].

Generally, exercise can reverse the risk of CRC indirectly due to weight, insulin and BMI control. However, heavy physical activity produces free radicals that result in higher CRC risk [26-28].

In the present study, every cooking method except for meals boiled in water increased the CRC risk up to 1.8-folds, although it was not meaningful due to the small sample size. This result was similar to results of other studies [7-8].

Mutagens like heterocyclic amines, aromatic hydrocarbons and other probable factors can be produced in cooking methods with high temperature and are responsible for causing CRC [29-31].

Conclusions

The increasing prevalence of CRC can be related to two main factors: 1)A true change in the incidence of colon cancer which can result from the changes in disease risk factors such as life style and personal habits; and 2)a false change in the incidence of disease which is a consequence of improvement in cancer data gathering (cancer registry system).

Although these two etiologies could not be separated carefully, life style and personal habits would be considered as the two notable factors.

Diet low in fiber and high in fat (like western countries), increasing obesity, and fast food consumption are the probable risk factors of CRC among Iranians. Machinery life (immobility) and low exercise are other risk factors [21].

Risk of cancer can be reduced as much as 30% to 40% by making healthier food choices [2-3]. In fact, some foods can actually help protect against certain cancers. Eating a plant-based diet (fruits, vegetables, whole grains and beans) and being physically active reduce the risk of cancer as well as heart disease and diabetes [2].

Obesity, nutrient sparse foods such as concentrated sugars and refined flour products that contribute to impaired glucose metabolism (which leads to diabetes), low fiber intake, consumption of red meat, and imbalance of omega 3 and omega 6 fats all contribute to excess cancer risk. Intake of flax seed, especially its lignin fraction, and abundant portions of fruits and vegetables will lower cancer risk [3].

Such a diet would be conducive to prevent cancer and would favor recovery from cancer as well [3].

It was previously reported that higher levels of energy intake in childhood increase the risk of the later development of cancer [18]. Therefore, it will be important to collect morbidity and mortality data from other cohorts for which data on childhood diet were gathered.

In summary, our results showed a relationship between high total energy intake, high fat intake, and cooking methods like frying, and occurrence of CRC.

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Conflict of Interest

The authors declare that they have no conflict of interest in this article.

Authors' Contribution

AK and SS designed the project and analyzed data, SB wrote and proof the article, MA and NA contributed in literature review and data process, GR and other colleagues in Golestan Research Center of Gastroenterology and Hepatology contributed in data entry and data process.

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