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Iranian Dietary Patterns and Risk of Colorectal Cancer

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ABSTRACT

Background: Role of diet on colorectal cancer (CRC) has been considered in terms of single foods and nutrients, but less frequently in terms of dietary patterns in Iran. The objective of this study was to determine the association between Iranian dietary patterns and CRC.

Methods: This case–control study was conducted in four hospitals in Tabriz City of Iran including 414 participants aged 35–75 years:207 cases with CRC confirmed by pathology and colonoscopy findings were selected and 207 controls free of neoplastic conditions and diet-related chronic diseases (from the same hospital at the same period for the cases). Dietary data were assessed using a 123-item semi-quantitative food frequency questionnaire. Two dietary patterns were found by using of Principal Component Analysis (PCA) method;"*Healthy pattern"*and "*Iranian pattern"*. Multivariate logistic regression analysis was used to estimate adjusted odds ratios (OR) for relationship between dietary patterns and colorectal cancer.

Results: After adjusting for confounding factors, the Iranian dietary pattern was significantly associated with an increased odds of colorectal cancer (OR= 1.46; 95% Confidenec Interval (CI)=1.05–2.19) while a reduced odds of colorectal cancer was observed with the Healthy dietary pattern (OR=0.18; 95% CI= 0.091-0.47).

Conclusion: Iranian dietary pattern (IDP) seems to increase the odds of colorectal cancer and protective effect of Healthy dietary pattern.

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Introduction

Several studies have indicated a role of diet in the etiology of colorectal cancer (CRC).[1,2] Most studies[3-5] have investigated the effect of specific foods, food groups, or nutrients. Consumption of vegetables and dairy products has been related to a decreased colorectal cancer risk, whereas consumption of red and processed meat has been associated with an increased Risk.[6] Although many studies (World Cancer Research, Hu and Safari studies)[6-8] have demonstrated a relationship between diet and CRC, it is difficult to detect the food specific effects because confounding by other food components. The use of dietary patterns has thus been proposed to analyze the association

between diet and cancer, given their ability to capture the variations in overall food intake.[9] In particular, a few case–control[10-16] and cohort[17-21] studies have investigated the effect of diet on colorectal cancer identifying dietary patterns through factor analysis.

The incidence rate of CRC in Asia is lower than Europe, Australia, New Zealand and NorthAmerica.[22] Japan and China have the highest incidence rates of colorectal cancer in Asia[23] among Iranians, CRC is the third and fourth most commonly diagnosed malignancy in males and females, respectively. In the last few decades, the incidence and mortality rates of CRC have increased markedly in Iran.[24,25] Most of the studies[26-28] on the association between colorectal cancer and dietary patterns were conducted in developed countries. The role of diet on CRC has been considered in terms of single foods and nutrients, but less frequently in terms of dietary patterns in Iran as a developing country. On the other hand, dietary culture in Iran is fundamentally different from Western societies and no studies have been devoted specifically to the Iranian dietary pattern.

The aim of this study was to identify Iranian dietary patterns and its association with the odds of CRC in Tabriz, Iran.

Methods

Study design

The present study was a case–control study and conducted from April 2012 through March 2014 in Colonoscopy Unit of the Cancer Institute of Imam Reza Hospital Complex and three general hospitals (Shahid Madani, Sina and Alinasab) in Tabriz City, northwestern Iran. The sample size was determined based on Magalhãesstudy.[29] Considering a confidence level of 95%, α=0.05%, β=0.2, OR= 2, P_0=0.3 and by considering a 18% decrease due to random error, the sample size was for each group was 207 subjects. Inclusion criteria were age35-75years old, CRC confirmed for the cases, being free of CRC for the controls and informed consent. Exclusion criteria were age above 75 years and lower than 30 years old, being free of neoplastic conditions and diet-related chronic diseases for the controls.

Participants

The study population was patients referred to colonoscopy units. A total of 414 participant aged 35–75 years including 207 cases with CRC (confirmed by pathology and colonoscopy findings, diagnosed no longer than six months before the interview) and 207 controls free of neoplastic conditions and diet-related chronic diseases (from the same hospital at the same period the cases selected) and matched by age (within 10-years categories) and sex.

Dietary assessment

The semi-quantitative Food Frequency Questionnaire (FFQ) was used to assess dietary intake. This questionnaire consisted of a validated[30] 123 foods and beverages (with standard serving sizes) commonly consumed by Iranians. This Food Frequency Questionnaire (FFQ) has a good validity and reproducibility. The reliability of the questionnaire using Cronbach's Alpha coefficient was α=0.78.A validated food album[31] and a set of household measurements (e.g., cup, tablespoon, teaspoon plate, glass, small bowl, and spatula) were used to assist respondents to estimate the portion size and type of food items.

Respondents were asked to report the frequency of consumption of a given serving of each food item on a daily, weekly, monthly and yearly basis and data were then converted to daily intake frequency. Portion size of each food item consumed was converted to grams and milliliter based on Nutritionist 4 software. Intake of each food item in grams was then determined by multiplying the portion size by daily intake frequency. Consumption of seasonal food items (e.g., watermelon, melon, and persimmon) was taken into account based on the period of the year the food items were available. The edible fraction of foods was also considered using household measurement guidelines.[32] Dietary data were asked during the year prior to cancer diagnosis.

To identify two dietary patterns (Iranian dietary pattern and Healthy dietary pattern), the 123 food items were categorized into 29 food groups (Table 1) based on their similarity of nutrient content and culinary usage (Common ways of cooking and preparing foods) or their relationship with cancer[33] Food items that were not fit to be included in a certain food group or were assumed to represent individual dietary behaviors were left as unique food groups (e.g. French fries, egg, tea and doogh or Iranian yogurt drink).

Data collection

The questionnaires were completed by trained interviewers for cases and controls. This questionnaire included information on socio-demographic characteristics, family history of CRC, physical activity, smoking habit, cooking techniques and dietary intake. Weight was measured to the nearest to 0.1 kg with respondents wearing minimal clothes and without shoes. For patients who had undergone surgery or a long stay in the hospital, the weight at the time of admission was used as current weight. Height was measured using a SECA body meter with a precision of 0.1cm with respondents stand erect, without shoes, their feet together and eyes in a parallax state. For bedridden patients, the recumbent length was obtained in a supine position. Body mass index (BMI) was then calculated as weight (kg) divided by height (meters) squared and was classified according to WHO standard for adults.

Physical activity was assessed using a validated self-report questionnaire, Standard metabolic energy equivalent task (MET) times/week, based on reported time spent on different activities which were weighted according to intensity level was applied. Physical activity was completed based on activities during the year before CRC diagnosis (cases) or during the year before interview (controls). Alcohol intake information was not sought from respondents as during the pre-testing of questionnaire, they refused to respond to the item due to cultural and religious beliefs. Iran is an Islamic country where sale and consumption of alcoholic beverages are prohibited.

Statistical analysis

Data were analyzed with SPSS (version 16.0, Chicago, IL, USA). For check of data normality, Kolmogorov-Smirnov test was used. Square root data transformation was applied for data not normally distributed.

Dietary patterns were derived using factor analysis by extraction method of Principal Component Analysis (PCA) based on the 123 food items. Prior to extracting factors (patterns), suitability of using factor analysis for this study was assessed using two criteria tests, namely Kaiser-Meyer-Olkin (KMO-test) and Bartlett's test of Sphericity. Sampling adequacy and inter-correlation of variables were supported by KMO value > 0.647 and Bartlett's test of Sphericity < 0.05, respectively. Food groups (e.g. chicken, egg, boiled potato and high fat dairy) with communality value < 6% indicated low and insufficient degree of correlation with other food groups and were thus dropped from subsequent analysis. Scree plot was assessed to determine the number of factors with an Eigen value of > 1.0, and direct Oblimin rotation was applied to review the correlations between variables and factors, because calculated correlations by direct Oblimin method was more than 0.3. Post-rotated factor loadings showed two dietary patterns described the sample and these patterns were called based on each food group having the highest loading on each pattern. Food groups with positive loadings in each pattern indicate the direct relationship with that pattern and food groups with negative loadings shows the inverse relationship with that pattern. The factor score for each pattern was calculated by summing the consumption of each food group that were weighted by factor loading and each person received an individual factor score for each identified pattern. Factor scores were then categorized into two groups based on the mean of factor score (0) and used as the outcome variable.

Chi-square ($\chi 2$) test was used to assess the associations between variables and study groups. Independent t-test was applied for comparing means between two groups. Univariate and multivariate logistic regression were used to estimate the odds ratio with a 95% confidence interval (CI) for the

risk factors of CRC. A *P*-value less than 0.05 were considered as statistically significant.

Ethical considerations

The present study was approved by the Medical Research and Ethics Committee of Ilam University, Iran, and Treatment Vice Chancellor of Tabriz University of Medical Science, Iran. Written informed consents were obtained from all respondent prior to the interviews.

Table 1: Food groups used in the dietary pattern analysis[8]

Food group	Food items
Processed Meat	Sausages, hamburger, salami
Red Meat	Beef, mutton, ground meat ,Visceral meat
Fish	Tuna, any type of fish
Poultry	Fried chicken
Egg	Fried eggs, boiled eggs
Low fat Dairies	Low fat milk, Low fat yogurt, ordinary yogurt,
High fat Dairies	Whole milk, yogurt(high fat, drained and cream),cream cheese, cream, ice cream
Yogurt drink	Yogurt drink
Tea	Black tea, green tea
Coffee	Coffee
Fruits	Cantaloupe, watermelon, melon, sloe, apple, apricot, cherry, sour cherry, fig, nectarine, peach, pear, Citrus fruit, date, kiwi, grape, pomegranate, strawberry, banana, grape fruit, plum, persimmon, raisin, mulberry, compotes, other fruits
Artificial juice	Lemon juice and packed juice
Tomato	Tomato
Carrot	Carrot
Vegetables	Spinach, lettuce, mixed vegetable, stew vegetables, eggplant, green squash, local vegetables, pepper, mushroom, cucumber, garlic, kinds of cabbage, root, vegetables, other vegetables
Legumes	Bean, chickpea, split pea, soybean, lentil, other cereals
Fried potato	Fried potato
Boiled potato	Boiled potato
Whole grains	Barbary bread, Sangak bread, Taftoon bread, local bread
Refined grains	Lavash bread, baguette, rice, macaroni
Snacks	Biscuits, puff, chips
Nuts	Peanut, almond, walnut, pistachio, hazelnut, roasted seeds
Sweets and desert	Cakes, cookies, chocolate, pastry, dry sweet, honey, jam, halvah
Sugar	Sugar, sugar cube, candy, sugar candy, tahini
Pickles	pickle, cucumber Pickle
Animal butter	Animal butter
Solid oil	Solid vegetable oil, animal fat, rump
Liquid oil	Liquid oil
Olive	Olive and olive oil

Results

Of 414 patients studied, 47% were female. Table 2 shows the socio -demographic and lifestyle characteristics of the 207 cases and 207 controls. By group-matched design, age and gender were similar in controls and cases. The mean age of respondents at diagnosis of colorectal cancer (CRC)

was 60.54 years for men and 58.96 years for women. There were no statistically significant differences between case and control groups by educational level, Residence**,** occupation, history of hypertension**,** cooking methods and smoking status. However, cases were more likely than controls to have a family history of CRC in the first-degree relative (*P*=0.001) and history of diabetes (*P*=0.006). The mean body mass index (BMI) was higher in the case than in the control group, and was statistically significant differences (*P*=0.034). Controls had statistically significantly higher physical activity than the cases (*P*=039) (Table 2).

Table 2: Characteristics of case and control groups with the odds of colorectal cancer (N=414)

Variables		**Control(N=207) n %**	**Case (N=207) n %**	****P- value**
Age (years)	Male (M±SD)	59.51±13.73	60.54±13.23	*
	Female (M±SD)	57.48±12.8	58.96±12.36	
Gender	Male	52(108)	112 (54)	*
	Female	99 (48)	95 (46)	
Body Mass Index(BMI) (Kg/m^2)	≥ 24.9	75(36)	66(31.8)	
	25-2939	93(45)	103(50)	0.034
	≤ 30	39(19)	38(18)	
Residence	Urban	144(69.5)	158(76)	0.250
	Rural	63(30.5)	49(24)	
Level of education	No education/ Elementary	131 (67.6)	140 (67.6)	
	Junior/ Senior or high school	57 (27.5)	36 (17.4)	0.721
	Diploma/College/ University	19 (9.2)	31 (15)	
Occupation	Self- employed	24 (11.6)	24 (11.6)	
	Housewife	109 (52.650	71 (34.3)	
	Employed/ Government	24 (11.6)	28 (13.5)	0.304
	Employed/ Private	38 (18.4)	55 (26.5)	
	Retired	12 (5.8)	29 (14)	
Family history of CRC in first degree		28 (13.5)	58 (28)	0.001
History of Diabetes		21 (10.2)	48 (23.2)	0.006
History of Hypertension		77 (37)	76 (36.7)	0.811
Smoking status(times/week)	Never	142 (68.5)	169 (81.6)	
	Former smoker	23 (11)	32 (15.45)	0.142
	Current smoker (times/week) <20	13 (6.3)	16 (7.7)	
	Current smoker (times/week) ≥20	17 (8.2)	2 (1)	
Smoking hookah	Yes	8 (3.8)	10 (4.8)	0.410
	No	199 (96)	197 (95.2)	
Physical activity (times/week)	Never	70 (33.8)	88 (42.5)	
	1-2 times/week	118 (57)	113 (45.5)	0.039
	≤ 3 times/week	19 (9.2)	6 (3)	
Common ways of cooking meat	Fried	39 (18.8)	59 (28.5)	
	Fried /Boiling	107 (51.6)	99 (47.8)	0.244
	Smoking/Grilling	61 (29.5)	49 (23.6)	
Common ways of preparing vegetable	Raw/ fresh	121 (58.45)	81 (39)	
	Boiled	27 (13)	21 (10.14)	0.127
	Fried, Fried / Freezed	59 (28.5)	105 (50.7)	

* Matched variables/** Using chi-square, t-test was used difference between case and control groups.

Table 3 shows the two dietary patterns (Healthy pattern and Iranian pattern**)** and the factor loadings for each dietary pattern by Factor analysis. Food groups with absolute factor load-

ings > 0.20 were considered as having significant contribution to the pattern. These two dietary patterns explained 38% of the total variance in food intake. The first pattern with high loadings for fruits, vegetables, liquid oil, olive, fish, yoghurt drink, carrot, low-fat dairy products and nuts was labeled "Healthy dietary pattern". This pattern was significantly related to respondents who were non-married, had diploma or higher degree, self-employed, with higher income, use acetaminophen, vitamins and commonly consume raw/ fresh vegetable. The second pattern with high loadings for refined grain (rice and lavash bread particularly), Fried chicken, processed and red meat, Black tea, carbonated beverage sand different levels of other food items was named "Iranian dietary pattern". This dietary pattern was usual and common Foods that were consumed by Iranian.

Table 4 shows the ORs and corresponding CIs for colorectal cancer (CRC) by the mean of dietary pattern scores. We found significantly association between Iranian dietary pattern and colorectal cancer after adjusting for history of CRC in first degree relative, history of diabetes and physical activity, so that consumption of Iranian dietary pattern around 1.5 times increases the odds of CRC compared with that of the controls (OR= 1.46; 95% CI=1.05-2.19) while having healthy dietary pattern decreased CRC odds (OR=0.18; 95% CI= 0.091-0.47).

Table 3: Factor loading* matrix of food groups for Healthy and Iranian dietary patterns

Food group	Healthy pattern	Iranian pattern
Fruits	0.76	
Vegetables	0.69	
liquid oils	0.67	
Low fat Dairy	0.55	
Olives	0.51	
All Fish	0.48	
Carrot	0.46	
Nuts	0.42	
Yogurt Drink	0.35	
Sugars		0.28
Poultry		0.685
Red meat		0.22
Black tea		0.43
Pickles		0.21
Sweets and desert		0.28
Snacks		0.24
Processed Meat		0.295
Refined Grains		0.725
Solid Oil		0.23
Animal butter		
Total variance	19%	26%

Absolute factor loading values < 0.20 for both patterns were excluded for simplicity

Table 4: Odds ratios and 95% confidence intervals for colorectal cancer by dietary patterns

Dietary pattern	Controls n (%)	Cases n (%)	Crud OR (95% CI)	Adjusted OR* (95% CI)
Healthy pattern				
**Low	89 (43)	154 (74.4)		
High	118 (57)	53 (25.6)	0.25(0.15-0.62)	0.18(0.091-0.47)
P-value			0.001	0.002
Iranian pattern				
Low	117 (56.52)	93 (44.9)		
High	90 (43.48)	114 (55.1)	1.59(1.08-2.39)	1.46(1.05-2.19)
P-value			0.0183	0.021

*Adjusted for history of diabetes, family history of CRC in first-degree relative, physical activity and other confounding factors**Cutoff points were, Low: score <0; High: score > 0 (mean factor score = 0).

Discussion

In this study, after adjustment the socio-demographic and lifestyle confounders, an Iranian dietary pattern (IDP) was associated increased odds of CRC; in contrast, healthy dietary pattern (HDP) conferred a protective effect against CRC odds. Our findings indicate that routines dietary intake by Iranians (in studied area) is approximately susceptible to risk of colorectal cancer. Perhaps, a change in dietary pattern is one of the factors that increase the rate of colorectal cancer in recent

decades. A dietary pattern characterized by low intake of fried foods, alcohol and processed meat or high intake of fruits, vegetables, yams, cereals, legumes and low fat dairy products lowered the risk of CRC [34,35] and also, our findings confirm it.

Healthy dietary pattern (HDP) are good sources of various micronutrients and other compounds including minerals, vitamins A, C, E, arytenoids, selenium, flavonoids and fibers, which display overlapping and complementary mechanisms of action, such as binding and dilution of carcinogens and anti-oxidant effects.[36,37] In US population, prudent diet- characterized by a high consumption of vegetables, fruits, whole grains, poultry, fish, and legumes has shown to be protective against CRC, while the Western pattern (high intake of sweets and desserts, red and processed meats, refined grains and French fries) was shown to increase the risk of CRC.[11] In case control studies in Iran, the adoption of a Western dietary pattern- characterized by a higher intake of red and processed meat, butter, high-fat dairy products, sweets and desserts, hydrogenated fats and soft drinks was positively associated with to CRC while or whereas fruits, vegetables, high physical activity and low energy intake was a protective effect against CRC risk.[38,39] Generally,15 to 25 percent of CRC are attributed to fat intake in human and animal studies.[40,16]

It has been hypothesized that high fat intake because of high energy density and its association to obesity, may potentially cause hormonal changes that can over motivate the re-generation of colonic endothelial cells and persuade the growth of polyps and adenomas. It may also promote CRC risk through alterations in immunologic responses and insulin resistance.[11, 40]

In the present study, tea had a high factor loading for the IDP. In Iran and particularly in Tabriz, black tea is the most popular drink commonly served with sugar or cube sugar. We found that sugars (e.g. sugar, sugar cube, candy, sugar candy, and tahini) had the highest factor loading for the IDP as compared to other food groups in this pattern. Hence, in some studies, tea consumption is a risk factor for CRC [41,42] while an inverse association was observed between tea intake and CRC risk in other studies.[11,40] This findings inconsistency might be related to constipation and the inverse association with secretion of bile acids.[43]

We also found, an inverse association between fish consumption and CRC odds similar toother studies.[11,16] This protective effect could be due to high content of n-3 polyunsaturated fatty acids and vitamins D and A in fish. In this study, fish was a component in the HDP. The traditional Iranian diet does not usually entail high consumption of fish due to the higher prices and/or lower availability than red meat.[44] Intake of milk and dairy products has also shown to decrease the risk of CRC, [43,45] which possibly is due to their micronutrient contents such asriboflavin, calcium, vitamin B12 and vitamin D.

Limitations

Although in this case-control study we could found the association between dietary pattern and CRC risk after adjusting for the possible confounders, however there are some limitations. Although we tried to reduce recall biases by choosing those who were not diagnosed CRC more than last 6 months of cancer diagnosis. Interviewers were not aware of case and control groups categorized and carefully trained. Another imitation was selection bias; to minimize this problem by selection of cases and controls with a common referral basis (colonoscopy units) and matching the cases and controls by age and sex.

Conclusion

After adjusting for the confounders, IDP seems to increase the odds of colorectal cancer while healthy dietary pattern (HDP) was associated with lower odds of colorectal cancer.

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