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The association between colorectal cancer and index of nutritional quality (INQ); a case-control study

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HIGLIGHTS

- Is the Index of Nutritional Quality (INQ) associated with colon cancer?
- This study compared the INQ of various dietary components between colorectal cancer patients and healthy controls. A total of 480 participants were enrolled in the study (160 patients with colorectal cancer as a case group and 320 healthy control). The results showed that CRC is significantly associated with INQ for some micronutrients. INQ can be considered as an indicator to assess clinical nutritional problems.

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ABSTRACT – Background – The nutritional quality of diet may influence the risk of colorectal cancer (CRC). This study compared the Index of Nutritional Quality (INQ) of various dietary components between colorectal cancer patients and healthy controls. **Methods –** A total of 480 participants were enrolled in the study (160 patients with colorectal cancer as a case group and 320 healthy control). An analysis was conducted on the general characteristics of the participants, their medical histories, anthropometric indicators, physical activity, alcohol consumption, reproductive history, smoking and food intake. A valid food frequency questionnaire was used to assess nutrient intake and INQ was calculated from daily nutrient intake. **Results –** A Significant inverse association was found between CRC and INQ for vitamins A (OR=0.01, CI: 0.01–0.01), K (OR=0.04, CI: 0.01–0.15), and B12 (OR=0.71, CI: 0.51–0.98), B5 (OR=0.43, CI: 0.00–0.01), zinc (OR=0.35, CI: 0.13–0.95), and phosphorus (OR=0.17, 0.19–0.94). The association between the INQ of vitamin B12 and zinc with colorectal cancer was disappeared after age adjustment. There was a significant negative association between CRC with the INQ of vitamins A, K, B5, phosphorus, and calcium after further adjustments for gender, BMI, menopausal status, and total energy intake. **Conclusion –** CRC is significantly associated with INQ for some micronutrients. INQ can be considered as an indicator to assess clinical nutritional problems.

Keywords – Colorectal cancer; dietary intake; the Index of Nutritional Quality.

INTRODUCTION

Among cancers diagnosed worldwide in 2018, colorectal cancer (CRC)s are the fourth most frequent, followed by cancer of the rectum and colon. Together CRCs account for 11% of all cancer diagnosis worldwide[1-3]. CRC morbidity and mortality rates differ greatly between countries, with the highest rates in developed countries and the lowest in developing countries, including Asian, African, and most Latin American countries[4]. CRC was responsible for 881,000 deaths in 2018 and the number will increase to about 2.5 million cases in 2035[5]. Many researchers believe that environmental factors such as smoking, weight gain, sedentary lifestyle, and poor diet are leading causes of CRC incidence[6,7].

Numerous investigations have shown genetic and environmental factors such as age, family history, dietary components, alcohol intake, obesity, and smoking are causes of CRC development[8-10]. Among them, dietary factors play a key role in the etiology of CRC[11,12]. Epidemiological studies demonstrated higher intake of red and processed meat with pro-inflammatory properties, and lower fiber consumption, dairy products, calcium supplement, and whole grains with anti-inflammatory properties, were associated with increased CRC risk[13-16].

For assessment of diet quality, there are many reliable and efficient methods available, including the Index of Nutritional Quality (INQ) which is specifically designed for assessing the qualitative and quantitative quality of food, diet and diet- related issues[17-19]. The INQ is calculated by dividing the percentage of each nutrient consumed by the average calorie requirement provided by the diet. Revealing the potential content of some nutrients in foods[18,20].

Numerous studies have assessed the relationship between the INQ of dietary components and variety of diseases, including breast cancer[21], ulcerative colitis[22], gastric cancer[23], glioma[24] as well as non-alcoholic fatty liver disease[17]. This study evaluated the association between the INQ and CRC in the Iranian people in light of the high prevalence of CRC in this population and the lack of investigation on the association between the INQ and CRC.

METHODS

Study population

The case control study conducted on 480 participants who were referred to Firoozgar Hospital in Tehran, Iran between January and June 2021 (160 patients with colorectal cancer as the case group and 320 healthy individuals as a control group). The participants were selected using a simple randomization method. Inclusion criteria of the case group included histological confirmation of CRC, newly diagnosed CRC patients (within 2 months of the diagnosis of CRC), and age range 35 to 70 years. Inclusion criteria for the healthy control group included an age range of 35 to 70 years, no malignancy, Exclusion criteria included non-adherence to the study protocol, total energy intake <800 kcal/day or >4200 kcal/day for men, and <600 kcal/day or >3500 kcal/day for women, and the patient's inability to respond to the questions. All patients and healthy individuals in the case and control groups were matched in terms of age, sex and ethnicity. A previously validated Iranian version of the International Physical Activity Questionnaire was used to assess PA data[25].

Ethical statement

The Institutional Review Board of the Shahid Behesti Medical University approved the research protocol of this study (code: IR.SBMU.CRC.REC.1398.028), Date: 2019/11/12. Data collection was conducted with the written consent of all participants.

Dietary intake and INQ assessment

In this study, patients were asked to provide information about their diet before colorectal cancer. Therefore, the collected data were not affected by the disease or the treatments received. The food intake of participants was assessed using a validated 168 semi-quantitative food frequency questionnaire (FFQ). The validity and reliability of the questionnaire have already been evaluated in the Iranian population[26]. In our study, we analyzed the frequency of eating each food during the past year, over daily, weekly, monthly, and yearly periods. We changed the daily intake frequency of each reported food to the daily intake frequency, and calculated each food's daily intake based on one serving.

Nutritionist IV software (First Database; Hearst, San Bruno, CA, USA) was used to extract energy and nutrient content from the foods that make up the USDA food composition data. The Iran Food Composition Chart (IFCT) was used for traditional Iran food analysis that was not included in this database[27]. INQ is an indicator of the ratio of nutrients to food calories. Analyzing parameters that may vary for each clinical condition requires the calculated number of nutrients and standard amounts[17,23,28]. An INQ is the amount of nutrients per 1000 calories divided by its Recommended Dietary Allowance per 1000 calories[18].

Statistical analysis

The dietary data obtained from FFQ was used to calculate the INQ scores for all participants. Nutrients used for INQ measurements include vitamin A, vitamin C, iron, vitamin D, vitamin E, thiamine, riboflavin, niacin, pantothenic acid, vitamin B6, folic acid, vitamin B12, copper, magnesium, zinc, calcium, and Contains selenium. Statistical analysis was used to compare qualitative variables between groups using a chi-square test or Fisher's exact test. For quantitative variables, the Kolmogorov-Smirnov test was used to examine the normality of the distribution of the quantitative variables. Next, we used an independent test procedure for the quantitative variables of the normal distribution between the groups and the Mann Whitney U test for the quantitative variables of the anomalous distribution. Logistic regression was used to calculate the multivariate adjusted odds ratio (OR) and 95% confidence interval. IBM SPSS software (version 21) was used for statistical analysis of the data and $P<0.05$ was considered significant. Benjamini-Hochberg correction is used for multiple comparisons and all *P*-values are displayed after this correction.

RESULTS

The cases had higher body mass index (BMI) (27.58±3.25 vs 28.76±3.97, $P<0.01$) and smoking (7.6% vs 0.9%, $P<0.01$) compared to the controls (TABLE 1). No significant difference was found on age, sex, weight, physical activity, smoking, and alcohol use among two groups.

TABLE 1. Distribution of characteristics of the participants (N=480).

Variables	Mean±SD or N (%)		*P*-value*
	Cases (n=160)	Controls (n=320)	
Age (year)	52.36±17.06	51.8±10.82	0.06
Males (n, %)	81 (54.7%)	163 (51.1%)	0.11
Weight (kg)	69.39±8.64	70.12±10.59	0.44
Height (cm)	158.49±7.59	156.11±5.31	<0.01
BMI (kg/m^2)	27.58±3.25	28.76±3.97	<0.01
Physical activity (hrs/wk)	7.51±1.95	7.31±1.58	0.28
Smoking (n, %)	12 (7.6%)	3 (0.9%)	<0.01
Alcohol use (n, %)	0 (0.0%)	3 (1.2%)	0.73

BMI: body mass index. * Independent sample *t*-test was used for comparing variables; Benjamini–Hochberg correction was applied to all *P*-values; all *P*-values are displayed after this correction

As presented in TABLE 2, the INQ of vitamin A (0.58±0.34 vs 0.67±0.13 µg/d, $P<0.01$), vitamin E (0.53±0.21 vs. 0.68±0.24 mg/d, $P<0.01$), magnesium (0.71±0.07 vs 0.73±0.06 mg/d, $P=0.04$), selenium (0.73±0.37 vs 0.97±0.23 mg/d, $P<0.01$), and folate (1.02±0.16 vs 1.11±0.13 mg/d, $P<0.01$) were higher in controls group. However, the INQ of calcium (0.88±0.09 vs 0.86±0.11 mg/d, $P=0.05$), phosphorus (1.60±0.18 vs 1.55±0.14 mg/d, $P<0.01$), zinc (0.90±0.19 vs 0.86±0.20 mg/d, $P=0.04$), vitamin K (1.13±0.35 vs 0.98±0.17 µg/d, $P<0.01$), vitamin B12(1.50±0.65 vs 1.36±0.61 µg/d, $P=0.04$) and vitamin B5 (0.88±0.28 vs 0.83±0.24 mg/d, $P=0.03$) are higher in cases.

There was a significant negative association between the CRC and INQ of vitamin A (OR<0.01, CI: 0.00–0.01, $P<0.01$), K (OR=0.04, CI: 0.01–0.15, $P<0.01$), B12 (OR=0.71, CI: .51–0.98, $P=0.04$), B5 (OR=0.43, CI: 0.00–0.01, $P=0.03$), zinc (OR=0.35, CI: 0.13–0.95, $P=0.04$), phosphorus (OR=0.17, 0.19–0.94, $P=0.02$). A significant negative association between vitamin B12 INQ and zinc and colorectal cancer disappeared after age adjustment. There was also a significant negative association between CRC and INQ of calcium, and another result remained the same after adjusting for age, gender, BMI, and menopause (TABLE 3).

DISCUSSION

In the crude model analysis, vitamin A, K, B12, B5, zinc, phosphorus, and calcium were inversely related to CRC. Due to the proven role of demographic, ge-

TABLE 2. Comparison of the Index of Nutritional Quality (INQ) of the participants.

Mean±SD	Mean±SD			*P*-value*
	Cases (n=160)	Controls (n=320)	Total (n= 480)	
Vitamin A (µg)	0.58±0.34	0.67±0.13	0.73±0.23	<0.01
*Iron (mg)	1.87±0.30	1.82±0.26	1.84±0.27	0.09
Calcium (mg)	0.88±0.09	0.86±0.11	0.86±0.10	0.05
Magnésium (mg)	0.71±0.07	0.73±0.06	0.72±0.07	0.04
Phosphorus (mg)	1.60±0.18	1.55±0.14	1.57±0.16	<0.01
Zinc (mg)	0.90±0.19	0.86±0.20	0.87±0.20	0.04
Copper (mg)	1.39±0.57	1.46±0.59	1.44±0.58	0.24
Manganese (mg)	1.93±0.67	2.05±0.70	2.02±0.69	0.09
Selenium (mg)	0.73±0.37	0.97±0.23	0.90±0.30	<0.01
Vitamin E (mg)	0.53±0.21	0.68±0.24	0.63±0.24	<0.01
Thiamine (mg)	1.46±0.57	1.55±0.56	1.52±0.56	0.11
Riboflavine (mg)	1.49±0.64	1.51±0.66	1.50±0.65	0.73
Niacine (mg)	1.14±0.10	1.13±0.15	1.14±0.14	0.58
Vitamin B6 (mg)	1.19±0.48	1.14±0.47	1.16±0.47	0.35
Folate (µg)	1.02±0.16	1.11±0.13	1.09±0.15	<0.01
Vitamin B12 (µg)	1.50±0.65	1.36±0.61	1.41±0.62	0.04
Vitamin B5 (mg)	0.88±0.28	0.83±0.24	0.85±0.25	0.03
Biotin (µg)	0.71±0.11	0.74±0.14	0.73±0.13	0.06
Vitamin C (mg)	1.37±0.20	1.38±0.42	1.38±0.37	0.68
Vitamin D (µg)	0.56±0.44	0.52±0.39	0.53±0.41	0.41
Vitamin K (µg)	1.13±0.35	0.98±0.17	1.02±0.25	<0.01

*Independent sample *t*-test was used for comparing variables; Benjamini–Hochberg correction was applied to all p-values; all *P*-values are displayed after this correction.

TABLE 3. ORs and confidence intervals for the association between INQ and colorectal cancer.

	ORs (95%CI)	*P*-value [a*]	ORs (95%CI)	*P*-value [b*]	ORs (95%CI)	*P*-value [f*]
INQ vitamin A	0.01 (0.01–0.01)	<0.01	0.00 (0.00–0.01)	<0.01	0.00 (0.00–0.02)	<0.01
INQ iron	0.53 (0.26–1.11)	0.09	0.55 (0.26–1.14)	0.11	0.55 (0.23–1.31)	0.17
INQ calcium	0.14 (0.01–1.22)	0.07	0.13 (0.01–1.27)	0.08	0.04 (0.00–0.75)	0.03
INQ phosphorus	0.17 (0.04–0.75)	0.02	0.20 (0.05–0.83)	0.03	0.09 (0.01–0.57)	0.01
INQ thiamine	1.33 (0.93–1.93)	0.12	1.36 (0.94–1.98)	0.09	1.23 (0.81–1.90)	0.33
INQ vitamin B6	0.82 (0.54–1.25)	0.35	0.78 (0.51–1.20)	0.27	0.82 (0.50–1.35)	0.44
INQ riboflavin	1.05 (0.77–1.43)	0.73	1.07 (0.78–1.45)	0.67	1.11 (0.77–1.60)	0.57
INQ vitamin K	0.04 (0.01–0.15)	<0.01	0.04 (0.01–0.16)	<0.01	0.07 (0.02–0.30)	<0.01
INQ vitamin D	0.82 (0.50–1.32)	0.41	0.83 (0.51–1.35)	0.47	0.97 (0.55–1.70)	0.92
INQ vitamin B12	0.71 (0.51–0.98)	0.04	0.73 (0.52–1.01)	0.06	0.76 (0.52–1.11)	0.17
INQ vitamin C	1.12 (0.62–2.03)	0.68	1.12 (0.61–2.03)	0.70	1.24 (0.53–2.90)	0.61
INQ zinc	0.35 (0.13–0.95)	0.04	0.37 (0.13–1.00)	0.051	0.40 (0.12–1.26)	0.11
INQ niacin	0.67 (0.16–2.75)	0.58	0.65 (0.15–2.72)	0.56	1.56 (0.27–8.90)	0.61
INQ copper	1.23 (0.87–1.73)	0.24	1.23 (0.87–1.75)	0.23	1.37 (0.91–2.07)	0.12
INQ manganese	1.30 (0.95–1.75)	0.09	1.30 (0.95–1.77)	0.09	1.34 (0.93–1.94)	0.11
INQ pantothenic acid	0.43 (0.19–0.94)	0.03	0.44 (0.20–0.98)	0.04	0.38 (0.15–0.97)	0.05

[a]Crude model; [b]Age-adjusted model; [f]Age, gender, BMI, menopausal status, and total energy intake adjusted. *Benjamini–Hochberg correction was applied to all *P*-values; all *P*-values are displayed after this correction.

netic, and environmental factors in the development of CRC[21,29], the effects of age, menstrual status, obesity, gender, and nutritional factors were adjusted. A contrary relationship between CRC risk and intake of vitamin A, vitamin K, pantothenic acid, and phosphorus was observed after adjusting for the confounding factors. Diet quality indices such as INQ allow groups assess the effects of various components of the overall dietary pattern. Using nutritional value scores, researchers can evaluate a diet as a whole and understand it in the context of other dietary interactions[21,29]. Some studies in Iran that examined the relationship between cancer and INQ, have shown that there is a contrary relationship between vitamin A intake and gastric cancer and calcium intake with colorectal cancer, which is similar to our findings. However, in Bahrami et al.'s study, there was an inverse relationship between vitamin C and B2 with CRC, which was not found in this research[23,30]. Inconsistent with our results in two studies that had even more samples, there was no association between vitamin C and B2 intake with CRC[31,32]. It was suggested that inclusive results may be due to the presence of differences in samples of each study including smoking, physical activity, and supplement analysis[33,34].

The mechanism of action of nutrients in colorectal cancer is not exactly known. In line with the present study, results from a meta-analysis review identified that the growth and differentiation of colonic epithelial cells are tightly regulated by retinoid activation genes; as a result, vitamin A can decline may have a role through The important pathways that sell CRC progressions such as decreased levels of matrix metalloproteinases (MMP), cyclin D1, and other factors that induce cell infiltration or proliferation[35]. Results from another review study demonstrated vitamin A nutritional management is effective in the prevention of cancer[36].

Dahlberg et al.'s study indicated that Vitamin K is involved in anticancer responses through multiple mechanisms of action, including suppression of inflammation and oncogene expression, reduction of apoptosis, proliferation signaling, and reactive oxygen species production[37]. In line with our findings, dietary vitamin K was reported to cause an inhibition of cell proliferation and an induction of apoptosis in the human colon carcinoma cell line[38].

In addition to being essential for carrying out critical cellular functions, B vitamins serve as key intermediates in pathways that generate cofactors such as B5 and Coenzyme A (CoA)[39]. According to Penet et al. (2016) study, pantothenic acid, a precursor to vitamin B5, is a promising new drug to treat ovarian cancer. The compound targets both tumor progression and the development of metastasis and ascites[40]. Furthermore, a large prospective cohort study of 27,853 women over 45 years showed that taking pantothenic acid supplements reduced the risk of breast cancer among moderate drinkers[41].

Regarding vitamin B roles, Vitamin B12 also assists as a cofactor for methionine synthase, which remethylates homocysteine to methionine. Methionine is an essential amino acid that is used for DNA methylation, so its deficiency can interfere with the regulation of gene expression, which could promote colorectal carcinogenesis. Recent case-control studies have shown that high vitamin B12 intake is inversely associated with CRC risk in the Chinese population[42].

Consistent with our findings in the European Positive Dietary Whole Association Study (DWAS), after assessing 386,792 participants, the low risk of CRC is phosphorus, magnesium, potassium, riboflavin, beta-carotene. It was suggested that it was related to the high dietary intake of total protein for duration[43]. Calcium consumption was also found to significantly reduce men's and women's CRC risk in a study of 922 Korean cases[44]. According to a study, calcium may enhance the function of T cells in order to prevent colorectal cancer. calcium-sensing receptor (CASR), a Ca2 + channel and calcium-binding G protein-coupled receptor, plays a key role in T cell and immunity function[45].

Similar to our study, some studies found a beneficial impact of zinc on CRC. Zinc is a potent antioxidant that defends DNA synthesis, and immune functions. Therefore, the defect may contribute to single-stranded and double-stranded DNA breaks and oxidative modification of DNA that increases the risk of cancer[46,47].

Authors' contribution

Gholamalizadeh M, Doaei S, and Akbari ME designed the study, Shekari S, Hassanpour N, Vahid F,

and Hossinzadeh P were involved in the data collection, analysis, and drafting of the manuscript. Aslani Z, Asbaghi O, Lavasani A, Hajipour A, Rajabi MA, and Doaei S were involved in the design of the study. All authors contributed to the article and approved the submitted version.

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RESUMO – Contexto – A qualidade nutricional da dieta pode influenciar o risco de câncer colorretal (CCR). Este estudo comparou o Índice de Valor Nutricional (INQ) de vários componentes dietéticos entre pacientes com CCR e controles saudáveis. **Métodos –** Um total de 480 participantes foram inscritos no estudo (160 pacientes com CCR como um grupo de casos e 320 controles saudáveis). Uma análise foi conduzida sobre as características gerais dos participantes, seus históricos médicos, indicadores antropométricos, atividade física, consumo de álcool, histórico reprodutivo, tabagismo e ingestão de alimentos. Um questionário de frequência alimentar válido foi usado para avaliar a ingestão de nutrientes e o INQ foi calculado a partir da ingestão diária de nutrientes. **Resultados** – Associação significativa entre CCR e INQ para as vitaminas A (OR=0,00, IC: 0,00-0,01), K (OR=0,04, IC: 0,01-0,15), B12 (OR=0,71, IC: 0,51-0,98) houve uma associação negativa), B5 (OR=0,43, IC: 0,00-0,01), zinco (OR=0,35, IC: 0,13-0,95), fósforo (OR=0,17, IC: 0,19-0,94). A associação entre o INQ da vitamina B12, zinco e CCR desapareceu após o ajuste pela idade. Houve uma associação negativa significativa entre CCR e INQ de cálcio, e outros resultados não mudaram após ajustes adicionais para idade, gênero, Índice de Massa Corporal, estado de menopausa e ingestão total de energia. **Conclusão –** CCR está significativamente associado ao INQ para alguns micronutrientes. O INQ pode ser usado como um indicador para avaliar problemas nutricionais clínicos.

Palavras-chave – Câncer colorretal, ingestão dietética, Índice de Qualidade Nutricional.

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