

Global Diet Quality Score and odds of colorectal cancer in adults: a multicenter case-control study

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Abstract

Background

Colorectal cancer (CRC), as one of the most common malignancies, poses many threats to the public health system. Although the association between dietary intake and CRC has been studied in numerous prior studies, no study has examined the association between the global diet quality score (GDQS) and CRC. Therefore, this study was conducted to examine the association among Iranian adults.

Method

This multicenter case-control study was conducted across three provinces of Iran, including 402 CRC patients and 825 cancer-free controls. CRC was diagnosed through colonoscopy findings. The majority of patients in this study were new cases of CRC with ≤ 3 months' diagnosis-to-enrollment interval. A validated 130-item food frequency questionnaire (FFQ) was used to assess participants' dietary intake. We constructed GDQS using the protocol suggested by Bromage et al.

Results

In total, 385 CRC cases and 791 controls had complete and valid data for the analysis. In the fully adjusted model, participants in the highest tertile of GDQS had 34% lower odds of CRC than those in the lowest tertile (OR: 0.66; 95% CI: 0.45–0.96). Also, this inverse association became stronger when the analysis was limited to CRC cases with a diagnosis-to-enrollment interval of ≤ 3 months (OR: 0.58, 95% CI: 0.37–0.91). In terms of CRC subtypes, high diet quality based on GDQS was associated with decreased odds of colon cancer (OR: 0.60; 95% CI: 0.38–0.95), while no significant association was observed for rectal cancer after adjusting for potential covariates (OR: 0.62; 95% CI: 0.3–1.27).

Conclusion

We found that GDQS is inversely associated with CRC and colon cancer, but not rectal cancer, in Iranian adults.

INTRODUCTION

Colorectal cancer (CRC) is one of the most common malignancies worldwide, ranking as the third most frequent cause of cancer-related mortality [1, 2]. Approximately 41% of CRC cases arise in the proximal colon, 22% in the distal colon, and about 28% in the rectum [3]. Epidemiological studies in Western nations, particularly in the United States, reported the age-standardized incidence rate of > 40 cases per 100,000 individuals [4, 5]. It has been shown that CRC incidence has declined in many Western countries, largely due to the implementation of population-based screening programs [6–8]. However, a rising trend

in CRC incidence has been observed in developing countries, including Iran, largely due to rapid lifestyle changes such as Westernized diets, physical inactivity, and obesity[9, 10].

Dietary intakes represent a key modifiable risk factor for CRC [11]. Evidence indicates that adherence to the DASH or Mediterranean diet, lower Empirical Dietary Index for Hyperinsulinemia (EDIH) and Empirical Dietary Inflammatory Pattern (EDIP) scores, and avoidance of Western dietary patterns may reduce CRC risk [12–15]. These dietary patterns have been designed for a specific population or health condition. Therefore, capturing overall diet quality in a comprehensive and standardized manner remains a methodological challenge. Recently, the Global Diet Quality Score (GDQS) was developed as a novel, globally applicable metric to evaluate overall diet quality [16]. The GDQS incorporates 25 food groups, including 16 healthy, seven unhealthy, and two conditionally unhealthy categories (such as high-fat dairy and red meat), and is designed to reflect both beneficial and adverse dietary components. Higher GDQS values reflect greater adherence to a healthy dietary pattern and facilitate comparisons of diet quality across populations [16].

Despite the growing use of GDQS in nutritional research, we still lack evidence linking this index to CRC. So far, most studies have focused on the associations of GDQS with non-fatal cardiovascular events and all-cause mortality in diverse populations, and in most of them, GDQS has a protective effect [17–19]. In contrast, some established diet quality scores, such as the healthy eating index (HEI), have been widely studied in relation to CRC risk [20–22]. In the Women's Health Initiative Observational Study of postmenopausal women, greater adherence to the HEI-2010 and DASH dietary guidelines was associated with a lower risk of CRC [20]. Findings from a systematic review showed that higher diet quality, assessed using the HEI, Mediterranean diet, and other indices, is consistently associated with lower CRC risk [23]. Together, these findings highlight that overall diet quality plays a key role in CRC risk. However, the relation between GDQS and CRC has not yet been examined. Assessing the association is more important in Iran, where the incidence of CRC is increasing at an alarming rate. Therefore, the present study aimed to investigate the association between GDQS and the odds of CRC among Iranian adults.

METHODS

Participants

This multicenter case-control study was conducted between 2024 and 2025 across three provinces in Iran (Isfahan, Khuzestan, and Lorestan). A total of 402 incident CRC cases and 825 controls were enrolled from the provinces. Cases were identified through the cancer registry systems maintained by the Health Offices of Isfahan University of Medical Sciences and Khuzestan University of Medical Sciences, which serve as the primary regional cancer registries. In Lorestan, due to the absence of a comprehensive provincial cancer registry, cases were recruited from Shohada Rahimi Hospital and the Baran Radiotherapy Center, both major referral centers for cancer diagnosis and treatment affiliated with Lorestan University of Medical Sciences. At all 3 centers, cases were selected based on predefined

inclusion criteria. Eligible cases were individuals 30 years of age or older with a diagnosis of CRC confirmed by colonoscopy findings and without a prior history of malignancy in other organs. Controls were randomly selected from among individuals referring to health centers affiliated with Isfahan and Khuzestan Universities of Medical Sciences. Medical records at each center were reviewed to identify eligible controls who met the inclusion criteria. At the Isfahan center, we selected controls with a negative result on the fecal immunochemical test (FIT), a screening test for CRC. In addition, companions of eligible patients in hospitals affiliated with Lorestan University of Medical Sciences were selected as controls. Control participants were 30 years of age or older, had no history of any cancer, and were free of acute illnesses that could potentially affect dietary patterns. Participants who refused to participate or who followed special or medically restricted diets were excluded. Both case and control groups were contacted by telephone and invited to designated health centers or hospitals. Written informed consent was obtained from all participants before data collection. Detailed information was subsequently collected on demographic factors, dietary intake, physical activity, anthropometric measurements, medical history, supplement use, and exposure to environmental toxins. In Khuzestan and Lorestan, the questionnaires were completed through face-to-face interviews. However, in Isfahan province, the questionnaires were self-administered by adults under 65 years with basic literacy skills, while data from participants aged 65 and older or those who were illiterate were collected through interviews. This manuscript was drafted according to the STROBE reporting guidelines, and the completed STROBE checklist is presented in the supplementary files [24]. The study protocol received ethical approval from the Ethics Committee of Isfahan University of Medical Sciences, Isfahan, Iran (IR.MUI.REC.1401.031), Khuzestan University of Medical Sciences, Ahvaz, Iran (IR.ABADANUMS.REC.1402.096), and Lorestan University of Medical Sciences, Khorramabad, Iran (IR.LUMS.REC.1404.014).

Sample size calculation

Sample size was calculated using the standard formula for comparing two proportions in an unmatched case-control design. Since the study was conducted across multiple centers with varying case-to-control ratios, we adopted a conservative approach by calculating the sample size based on a 1:1 ratio to ensure adequate statistical power across all centers. Assuming a two-sided α of 0.05, 80% power, an exposure prevalence of 40% among cases and 20% among controls, the minimum required sample was 78 cases and 78 controls per center. Notably, sample size estimation using a 2:1 ratio yielded a smaller required number of cases (approximately 60 cases per center), confirming that our conservative 1:1-based calculation provided more than sufficient power. To further enhance statistical power and enable subgroup analyses, we recruited larger participants: Isfahan (172 cases, 516 controls), Khuzestan (151 cases, 151 controls), and Lorestan (79 cases, 158 controls). This resulted in 402 cases and 791 controls, with an overall control-to-case ratio of approximately 2:1, providing ample power to detect the anticipated associations.

Dietary intakes

A 130-item, dish-based, semi-quantitative food frequency questionnaire (DS-FFQ) with a validated Willett format was used to assess participants' dietary intake. This questionnaire was developed specifically for Iranian adults and includes 40 mixed foods along with 90 individual food items. These items were grouped into different categories: bread and cereal group (10 items), dairy products (8 items), fruits and natural fruit juices (14 items), dried fruits (3 items), vegetables (7 items), nuts (4 items), sweets and deserts (11 items), caffeinated beverages (3 items), fats (3 items), spices (6 items), sugar-sweetened beverages (SSBs) (5 items), meat and processed meat (5 items), herbal infusion (3 items), and miscellaneous (8 items). Participants reported the frequency of consumption of each item using a 9-point scale ranging from “never or less than once a month” to “six or more times a day”. For some commonly consumed items in Iranian diets, such as tea and sugar, additional frequency options were included, extending to “sixteen or more times per day.” Respondents were asked to recall their food intake over the past year. Daily intake of each food item was estimated using standard home portion sizes and converted to grams per day [25]. Nutrient intake was then calculated using the Nutralyze platform (<https://nutralyze.ir>), which extracts nutrient content based on the USDA National Nutrient Database [26].

A validation study was conducted among 122 Iranian adults to assess the validity and reliability of the 130-item DS-FFQ. They were asked to complete the FFQ questionnaire at baseline and 12 months after the baseline. In addition, 18 detailed dietary recalls, which served as the gold standard, were collected from subjects over 12 months. The findings of this study showed an acceptable correlation between FFQ results and dietary recalls, indicating high validity of dietary data obtained from the FFQ. For instance, the correlation coefficient for fiber intake was 0.55, indicating that the FFQ has high validity for assessing high-quality diets. Also, previous studies using the FFQ yielded reasonable results regarding diet-disease associations [27].

Global diet quality score

The primary exposure in this study was overall diet quality, assessed using the GDQS, which includes 25 food groups. The GDQS was calculated according to the standardized scoring system developed by the Global Diet Quality Project [28]. The GDQS points are assigned according to three or four categories of consumed amounts (in grams) of each group. This categories are including 16 healthy food groups (citrus fruits, deep orange fruits, other fruits, dark green leafy vegetables, cruciferous vegetables, deep orange vegetables, other vegetables, legumes, deep orange tubers, nuts and seeds, whole grains, liquid oils, fish and shellfish, poultry and game meats, low-fat dairy, and eggs) which higher intakes result in higher points, seven unhealthy food groups (processed meats, refined grains and baked goods, sweets and ice creams, sugar-sweetened beverages, juices, white roots and tubers, and fried foods) with more points by lower intake, and two food groups (high-fat dairy and red meats) that take higher points before

reaching excessive amounts, after that no points are given. The total GDQS is calculated by summing each group's points and ranges from 0 to 49, with higher scores indicating better overall diet quality [16].

Colorectal cancer evaluation

Case patients were identified from medical records, and their CRC diagnoses were confirmed by both colonoscopy and histopathological examination. For each case included in the study, the interval from diagnosis to enrollment and the CRC subtype (colon or rectal cancer) were extracted. For controls in Isfahan, the absence of CRC was confirmed using a negative FIT result. However, for controls from other centers, we were unable to perform this test. To minimize the effect of reverse causality, we restricted a substantial proportion (approximately 72%) of our case group to newly diagnosed patients with a diagnosis-to-enrollment interval of ≤ 3 months. Additionally, we performed a sensitivity analysis excluding these patients to assess the robustness of our findings.

Evaluation of other variables

Anthropometric measurements, including body weight and height, were recorded for each participant. Weight was measured using a digital scale with an accuracy of 0.1 kg, while participants were wearing minimal clothing and no shoes. Standing height was measured with a tape measure while participants stood upright and barefoot. Body mass index (BMI) was calculated using the standard formula: weight in kilograms divided by height in meters squared. Obesity was defined as a BMI ≥ 30 kg/m². In addition, data were collected on several variables such as age (years), gender (male or female), marital status (single or married), occupation, education levels (college education, no college education, or illiterate), household size (≥ 4 or < 4 people), and history of exposure to chemicals and toxins (yes/no). Other variables included smoking status (i.e., cigarettes, hookah, and secondhand smoke) (yes/no), history of exposure to radiographic X-rays (yes/no), opium use (yes/no), alcohol consumption (categorized as sometimes/always or never), duration of daily mobile phone use (≥ 2 or < 2 hours per day), history of colon related diseases (yes/no), breakfast skipping (defined as fewer than three times per week), frequent intake of grilled food (≥ 3 times/week), and family history of colorectal or other cancers (yes/no).

Socioeconomic status (SES) scores were calculated based on five variables, each scored from 1 to 3: education (university educated = 3, not university educated = 2, illiterate = 1), house ownership (owner = 3, organizational housing = 2, rental housing = 1), car ownership (foreign car = 3, national car = 2, no car = 1), and international travel (non-pilgrimage travel = 3, pilgrimage travel = 2, no travel = 1), and occupation (employed or self-employed = 3, other job = 2, and unemployed = 1). The total SES score for each participant was obtained by summing these values, yielding a score ranging from 5 to 15. Participants were classified as exposed to chemicals and toxins if they had occupational exposure to such substances, lived near agricultural areas, used insecticides or pesticides at least once a month, or lived near industrial plants. Both current and former cigarette and hookah smokers, as well as those exposed

to secondhand smoke, were included in the exposed group. The use of dietary supplements (e.g., multivitamins and minerals, vitamin D, iron, calcium, omega-3 fatty acids, probiotics, folate, zinc) for at least one month during the past year was also recorded. Physical activity was assessed using the International Physical Activity Questionnaire (IPAQ), validated among Iranian adults [29]. Total physical activity was calculated as metabolic equivalent of task (MET) minutes per week based on the frequency and duration of walking, and moderate-, and vigorous-intensity activities. It was categorized into three levels: low (< 600 MET-min/week), moderate (600–3000 MET-min/week), and high (> 3000 MET-min/week), according to the IPAQ scoring protocol.

Statistical analysis

To compare general characteristics and dietary intakes between CRC cases and controls, an independent-samples t-test was used for continuous variables and a chi-square test for categorical variables. Participants were categorized into tertiles of GDQS. Then, differences in demographic, lifestyle, and dietary variables across GDQS tertiles were assessed using one-way ANOVA for continuous variables and a chi-square test for categorical variables. To examine the association between GDQS and the odds of CRC while accounting for potential confounders, a binary logistic regression with adjustment for potential confounders was conducted. Model 1 was adjusted for age, sex, and total energy intake. In model 2, we further adjusted for marital status, SES, household size, family history of CRC or other cancers, exposure to toxins and chemicals, history of chronic diseases, radiographic exposure, duration of daily mobile phone use, smoking status (including cigarette, hookah, and secondhand smoke), opium use, alcohol consumption, dietary supplement intake, breakfast skipping, frequent intake of grilled foods, and physical activity. Model 3 included BMI in addition to prior confounders. GDQS scores were categorized into tertiles for each center. The first and second tertile cut points were 28.25 and 31.58 in Khuzestan, 26.75 and 30.33 in Lorestan, and 26.50 and 30.50 in Isfahan, respectively. In all models, the lowest tertile of GDQS was considered the reference category. Linear trends of odds ratios (ORs) across GDQS tertiles were examined by entering the tertiles as a continuous variable in the regression models. Sensitivity analyses were conducted by: (1) restricting to cases with a diagnosis-to-enrollment interval $\leq$ 3 months to minimize recall bias; (2) performing separate analyses for colon and rectal cancer subsites; and (3) excluding participants with extreme energy intake (< 800 or > 4200 kcal/day) in all analyses. Multicollinearity was assessed using the variance inflation factor (VIF), with values > 10 considered indicative of collinearity. Missing data were handled using listwise deletion, as the proportion of missing values was < 5% for all variables. The statistical analyses were conducted using SPSS (version 26; SPSS Inc., Chicago, IL), and results with p-values < 0.05 were considered statistically significant.

RESULTS

Of the 1227 participants at baseline, 1176 were included in the analysis, of whom 385 were in the case group and 791 in the control group. Fifty-one individuals were excluded due to under- or over-reporting of energy intake, based on the optimal range of 800–4200 kcal/day, or due to incomplete data. The participant flowchart of is shown in Fig. 1. The mean age of the participants was 59.41 ± 11.52 years,

and 45.5% were female. Demographic characteristics and dietary intakes of cases and controls are summarized in Table 1. Compared with the control group, participants with CRC had significantly lower BMI, SES, and physical activity. They were less likely to use nutritional supplements and to be exposed to radiographic X-rays. Also, family size, exposure to toxins and chemicals, family history of cancer and CRC, opium consumption, and frequent intake of grilled food were higher in the case group compared to controls. In terms of dietary intake, CRC cases had lower consumption of vegetables, nuts, fiber, calcium, and vitamin C, and higher consumption of meats, refined grains, and vitamin E compared with the control group. No other significant differences were observed for demographic variables and dietary intakes between the case and control groups.

Table 1
General characteristics and dietary intakes of cases and controls

Variables	Cases (n = 385)	Controls (n = 791)	P-value*
Demographic variables			
Age (year)	60.03 ± 12.71	59.11 ± 10.89	0.22
Female (%)	44.2	46.1	0.52
BMI (> 30 kg/m ²) (%)	9.6	23.0	< 0.001
Married (%)	83.4	82.3	0.65
Family size (≥ 4) (%)	41.6	27.6	< 0.001
Exposure to toxins/chemicals (%)	51.9	36.7	< 0.001
SES	9.74 ± 1.99	10.75 ± 2.10	< 0.001
FH of CRC (%)	21.6	6.3	< 0.001
FH of cancer (%)	50.6	25.9	< 0.001
Cell phone use duration (> 2 h/d)	35.8	39.6	0.22
Physically active ^a	2.1	8.8	< 0.001
History of chronic diseases (%)	56.4	57.4	0.74
Exposure to smoke (%) ^b	43.1	37.8	0.08
Alcohol consumption (%)	7.3	8.0	0.68
Supplement use (%)	41.3	76.0	< 0.001
Opium consumption (yes) (%)	13.0	2.9	< 0.001
Exposure to radiographic X-ray (%)	12.5	17.7	0.02
Breakfast skipping (%)	9.4	12.9	0.08
Frequent use of grilled food (≥ 3 times/wk) (%)	35.3	19.6	< 0.001
Dietary intakes			
Whole grains (g/d)	36.41 ± 59.12	40.29 ± 51.17	0.25
Refined grains (g/d)	322.88 ± 146.61	296.15 ± 184.54	0.01
Meats (g/d)	131.24 ± 67.11	122.40 ± 73.40	0.05
Data are presented as mean (SD) or percent.			

Variables	Cases (n = 385)	Controls (n = 791)	P-value*
Demographic variables			
Dairy (g/d)	277.29 ± 189.27	272.76 ± 190.30	0.70
Fruits (g/d)	284.47 ± 210.27	285.08 ± 179.23	0.96
Vegetables (g/d)	400.89 ± 179.34	456.17 ± 239.37	< 0.001
Legumes (g/d)	53.59 ± 28.66	54.37 ± 32.23	0.68
Nuts (g/d)	7.05 ± 7.46	9.64 ± 9.44	< 0.001
Energy (kcal/d)	2059.30 ± 784.90	2058.24 ± 856.52	0.98
Protein (g/d)	82.25 ± 30.12	82.90 ± 35.59	0.74
Carbohydrate (g/d)	250.26 ± 101.49	255.22 ± 103.99	0.44
Fat (g/d)	85.19 ± 38.90	83.37 ± 42.22	0.46
Fiber (g/d)	22.48 ± 9.21	24.13 ± 9.83	0.006
Calcium (mg/d)	658.24 ± 282.91	712.18 ± 346.17	0.005
Iron (mg/d)	14.92 ± 6.52	14.96 ± 6.75	0.93
Vitamin C (mg/d)	130.36 ± 96.28	141.01 ± 79.52	0.04
Vitamin E (mg/d)	13.09 ± 6.68	11.83 ± 7.08	0.004
Selenium (µg/d)	75.82 ± 31.16	78.57 ± 39.66	0.19
Data are presented as mean (SD) or percent.			

A summary of demographic information and dietary intakes across the different GDQS tertiles is presented in Table 2. BMI and exposure to smoke differed significantly across GDQS tertiles. Moreover, those subjects in the third GDQS tertile were more likely to be female and had higher SES than those in the first tertile. Regarding dietary intakes, those with higher GDQS had higher intakes of whole grains, meats, dairy, fruits, vegetables, legumes, nuts, protein, carbohydrates, fiber, fat, calcium, iron, vitamin C, vitamin E, selenium, and energy. No significant associations were found for other demographic variables or dietary intakes across the GDQS tertiles.

Table 2
General characteristics and dietary intakes of participants across GDQS tertiles

Variables	Tertiles of GDQS scores			
	T1	T2	T3	P-value*
Demographic variables				
Age (year)	59.0 ± 12.29	60.6 ± 12.22	59.22 ± 9.93	0.40
Female (%)	42.6	42.7	51.0	0.03
BMI (> 30 kg/m ²) (%)	23.0	15.0	17.5	< 0.001
Married (%)	82.5	85.0	80.6	0.27
Family size (≥ 4) (%)	31.7	32.7	29.0	0.60
SES score	10.20 ± 2.13	10.39 ± 2.10	10.68 ± 2.04	0.005
Exposure to toxins and chemicals (%)	36.7	36.9	41.7	0.24
FH of CRC (%)	8.5	8.4	10.1	0.49
FH of cancer (%)	24.7	24.0	27.8	0.49
Cell phone use duration (> 2 h/d)	22.9	23.4	24.5	0.86
Physically active ^a	29.7	28.8	31.3	0.78
History of chronic diseases (%)	46.4	49.3	49.1	0.57
Exposure to smoke (%) ^b	29.6	26.9	35.3	0.04
Alcohol consumption (%)	1.5	2.6	3.3	0.11
Supplement use (%)	19.7	18.2	19.7	0.81
Exposure to radiographic X-ray (%)	64.1	64.9	65.0	0.96
Data are presented as mean ± SD or percent.				
Abbreviations: BMI: body mass index, SES: socioeconomic status, MET: metabolic equivalent of task, FH: family history, SD: standard deviation				
*Obtained from one-way analysis of variance (ANOVA) or Chi-square test, where appropriate				
^a People with MET-min/week above 3000				
^b Current or ex-user of cigarettes or hookah, or secondhand smoker				

Variables	Tertiles of GDQS scores			
	T1	T2	T3	P-value*
Opium consumption (%)	7.2	7.1	8.1	0.88
Breakfast skipping (%)	19.0	18.5	18.4	0.97
Grilled food (≥ 3 times/wk) (%)	8.5	9.0	12.6	0.08
Dietary intakes				
Whole grains (g/d)	25.61 $\pm$ 46.33	39.71 $\pm$ 52.10	51.94 $\pm$ 59.35	< 0.001
Refined grains (g/d)	298.42 $\pm$ 171.85	310.10 $\pm$ 186.34	306.48 $\pm$ 162.08	0.63
Meat (g/d)	104.07 $\pm$ 63.56	127.59 $\pm$ 68.94	144.58 $\pm$ 75.69	< 0.001
Dairy (g/d)	227.95 $\pm$ 176.57	271.02 $\pm$ 190.76	324.20 $\pm$ 190.24	< 0.001
Fruits (g/d)	191.96 $\pm$ 173.68	298.18 $\pm$ 166.08	366.23 $\pm$ 186.32	< 0.001
Vegetables (g/d)	330.44 $\pm$ 178.44	448.63 $\pm$ 219.19	536.95 $\pm$ 219.04	< 0.001
Legumes (g/d)	44.88 $\pm$ 26.34	56.20 $\pm$ 33.24	61.47 $\pm$ 31.18	< 0.001
Nuts (g/d)	4.82 $\pm$ 5.07	8.98 $\pm$ 9.70	12.62 $\pm$ 9.49	< 0.001
Energy (kcal)	1805.56 $\pm$ 780.21	2086.40 $\pm$ 837.23	2288.18 $\pm$ 812.62	< 0.001
Protein (g/d)	69.18 $\pm$ 29.06	84.41 $\pm$ 33.44	94.71 $\pm$ 34.02	< 0.001
Carbohydrate (g/d)	227.40 $\pm$ 102.10	255.52 $\pm$ 103.29	278.29 $\pm$ 97.87	< 0.001
Fat (g/d)	72.36 $\pm$ 38.38	85.52 $\pm$ 40.74	94.23 $\pm$ 41.41	< 0.001
Fiber (g/d)	18.48 $\pm$ 7.97	24.17 $\pm$ 9.33	28.21 $\pm$ 9.03	< 0.001
Data are presented as mean $\pm$ SD or percent.				
Abbreviations: BMI: body mass index, SES: socioeconomic status, MET: metabolic equivalent of task, FH: family history, SD: standard deviation				
*Obtained from one-way analysis of variance (ANOVA) or Chi-square test, where appropriate				
^a People with MET-min/week above 3000				
^b Current or ex-user of cigarettes or hookah, or secondhand smoker				

Variables	Tertiles of GDQS scores			
	T1	T2	T3	P-value*
Calcium (mg/d)	576.92 ± 293.23	699.07 ± 333.72	809.26 ± 313.81	< 0.001
Iron (mg/d)	12.91 ± 6.43	15.29 ± 6.84	16.68 ± 6.21	< 0.001
Vitamin C (mg/d)	100.05 ± 73.71	141.25 ± 75.17	171.91 ± 90.56	< 0.001
Vitamin E (mg/d)	10.25 ± 6.23	12.66 ± 6.94	13.87 ± 7.24	< 0.001
Selenium (µg/d)	66.29 ± 35.15	78.83 ± 36.23	88.07 ± 36.69	< 0.001
Data are presented as mean ± SD or percent.				
Abbreviations: BMI: body mass index, SES: socioeconomic status, MET: metabolic equivalent of task, FH: family history, SD: standard deviation				
*Obtained from one-way analysis of variance (ANOVA) or Chi-square test, where appropriate				
^a People with MET-min/week above 3000				
^b Current or ex-user of cigarettes or hookah, or secondhand smoker				

Multivariable adjusted ORs with 95% CIs for the association between GDQS and CRC are reported in Table 3. Accordingly, higher GDQS were associated with a 44% reduction in the odds of CRC (OR: 0.52; 95% CI: 0.38–0.72) in the unadjusted model. The inverse association persisted even after adjusting for potential confounders: individuals in the top tertile of GDQS had 34% lower odds of CRC compared with those in the bottom tertile (OR: 0.66; 95% CI: 0.45–0.96). After restricting the analysis to CRC cases with a diagnosis-to-enrollment interval of ≤ 3 months, the significant inverse association strengthened (OR: 0.58, 95% CI: 0.37–0.91). In the subgroup analysis, we observed a significant inverse association between GDQS and colon cancer in both the crude and fully adjusted models (OR: 0.60; 95% CI: 0.38–0.95). For rectal cancer, although we found a significant inverse association with GDQS in the unadjusted model and in the model controlled for age, gender, and energy intake (OR: 0.43; 95% CI: 0.23–0.81), further adjustment for potential confounders resulted in a non-significant association between GDQS and rectal cancer.

Table 3
Odds ratio (95% CIs) of colorectal cancer across the tertiles of GDQS scores in Iranian adults

Variable	Tertiles of GDQS scores			
	T1	T2	T3	P-value*
Colorectal cancer (n = 385)				
Cases	156	125	104	
Crude	1.00	0.77 (0.58–1.04)	0.56 (0.41–0.76)	0.001
Model 1	1.00	0.74 (0.55–0.99)	0.52 (0.38–0.72)	< 0.001
Model 2	1.00	0.67 (0.46–0.95)	0.66 (0.46–0.97)	0.04
Model 3	1.00	0.65 (0.45–0.93)	0.66 (0.45–0.96)	0.03
Cases with ≤ 3 months diagnosis-to-enrollment interval (n = 277)				
Cases	111	92	74	
Crude	1.00	0.80 (0.58–1.11)	0.56 (0.40–0.79)	0.004
Model 1	1.00	0.71 (0.51-1.00)	0.47 (0.33–0.67)	< 0.001
Model 2	1.00	0.65 (0.43–0.98)	0.60 (0.39–0.93)	0.04
Model 3	1.00	0.62 (0.41–0.94)	0.58 (0.37–0.91)	0.02
Colon cancer (n = 260)				
Cases	105	85	70	
Crude	1.00	0.78 (0.56–1.09)	0.56 (0.39–0.79)	0.005
Model 1	1.00	0.71 (0.51-1.00)	0.48 (0.34–0.70)	< 0.001
Model 2	1.00	0.64 (0.42–0.97)	0.62 (0.40–0.97)	0.05
Model 3	1.00	0.61 (0.40–0.94)	0.60 (0.38–0.95)	0.03
Rectal cancer (n = 79)				
Cases	37	24	18	
Crude	1.00	0.63 (0.36–1.08)	0.41 (0.23–0.73)	0.001
Model 1	1.00	0.60 (0.34–1.05)	0.43 (0.23–0.81)	0.02
Model 2	1.00	0.60 (0.31–1.13)	0.62 (0.30–1.24)	0.21
Model 3	1.00	0.61 (0.32–1.16)	0.62 (0.30–1.27)	0.24

Variable	Tertiles of GDQS scores			
	T1	T2	T3	P-value*
Data are presented as OR (95% CI)				
Abbreviations: BMI: body mass index, CI: confidence interval				
*Obtained from the binary logistic regression				
Model 1: adjusted for age, gender, and energy intake				
Model 2: Model 1 + adjusted for marital status, socioeconomic status, family size, family history of cancer or colorectal cancer, exposure to toxins and chemicals, history of chronic diseases, exposure to radiographic X-rays, exposure to smoke, opium use, alcohol consumption, supplement use, breakfast skipping, cell phone use duration, consumption of grilled food, and physical activity.				
Model 3: model 2 + adjusted for BMI				

DISCUSSION

The results showed that adherence to a high-quality diet based on GDQS was associated with decreased odds of CRC and colon cancer in adults. The inverse associations were obtained after controlling for a wide range of confounding variables. Similarly, an inverse association was also observed for GDQS and rectal cancer; however, in the fully adjusted model, the association became non-significant. Accordingly, these findings highlight the potential role of diet quality in CRC prevention and support public health strategies that promote the consumption of healthful plant-based foods, particularly among the Iranian population.

The association between diet quality indices and CRC risk has long been studied. Previous studies have mainly focused on HEI, dietary diversity score, and DASH/Mediterranean diet [12–15]. We are aware of no study that examined the relationship between GDQS and CRC in adults. This index is a novel diet quality index and appears more comprehensive than previously introduced diet quality indices [16]. In the current study, higher adherence to a high-quality diet, as assessed by the GDQS, was associated with lower odds of CRC. Our findings were consistent with previous studies on healthy and unhealthy dietary patterns. A 2025 meta-analysis showed that adherence to a low-quality diet, as assessed by the dietary inflammatory index (DII), can increase the risk of CRC in adults, with the increase stronger in males [30]. Moreover, another meta-analysis of observational studies concluded that adherence to a healthy, nutrient-rich diet, such as the DASH dietary pattern, was inversely associated with CRC risk [31]. In addition, a meta-analysis indicates that plant-based dietary patterns can decrease the risk of CRC and colon cancer [32]. Consumption of plant-based products such as fruits, vegetables, whole grains, legumes, and nuts is also emphasized in GDQS. Nevertheless, some studies have reported different results. Findings from the Netherlands Cohort Study showed a null and non-significant association between the Mediterranean diet, as a high-quality diet, and colorectal, rectal, and colon cancers [33]. The different results for the cohort, compared to our findings, might be due to a lower quality of the

Mediterranean diet than that of GDQS. In GDQS, 25 food groups, including 16 healthy, seven unhealthy, and two conditionally unhealthy categories, are considered in scoring. At the same time, the Mediterranean diet is constructed based on 9 items, all of which are covered in GDQS [34]. Therefore, GDQS is more comprehensive than other dietary quality indices. However, differences in populations studied, adjustments for potential confounders, and study designs are other reasons for the inconsistency.

In the current study, a significant association was observed between higher GDQS adherence and lower odds of colon cancer. The inverse association was also observed for rectal cancer; however, it was no longer significant in the fully adjusted model. In a large case-control study among the Moroccan population, Kinany et al. reported that adherence to the Mediterranean diet, considered a healthy diet, was associated with lower odds of colorectal, colon, and rectal cancers [35]. Also, in a meta-analysis conducted by Abbasi et al. [31], adherence to a healthy DASH-based diet pattern was associated with 25% and 17% lower risks of colon and rectal cancers, respectively. In that meta-analysis, although a significant association was reported for both sites, the protective association at the colon site was stronger than at the rectal site. Differences in gut microbiome composition and anatomical size might explain the different effects of diet on the two gut sites. The colon is bigger than the rectum, and this might be a reason for the higher prevalence of colon than rectal cancer. This was the case in our study, in which more than 67% of CRC patients had a tumor in the colon, while the prevalence of rectal cancer was 20%. If more patients with rectal cancer were included in the present study, the inverse association observed in the fully adjusted model might have been significant.

GDQS can be linked to CRC risk by many mechanisms. Diets with high GDQS are rich in fiber and antioxidants, and contain a low amount of carcinogenic N-nitroso compounds, such as those found in red and processed meats [16]. For example, carotenoids in orange fruits and vegetables exhibit anticancer activities, including immune modulation, cell differentiation, hormone and growth factor signaling, apoptosis, and regulation of cell cycle progression [36]. GDQS focuses on lycopene-rich foods. Lycopene decreases Akt activation and nonphosphorylated β -catenin expression in CRC cells, and increases levels of phosphorylated β -catenin, which is inversely associated with cyclin D1 expression and with reduced CRC growth and proliferation [37]. Fiber plays an important role in the anticancer effect of GDQS [38, 39]. Carcinogens in the colon can readily bind to dietary fiber and pass out of the alimentary tract in stools, thereby reducing their interaction with colonic mucosal cells. Whole-grain fibers can increase fecal bulk, resulting in a shorter transit time in the gut [40]. In addition, dietary fiber increases the production of short-chain fatty acids (SCFAs) in the gut, which can lower pH in the colon. This process leads to preventing the conversion of metabolites of bile acids into more toxic forms [41, 42].

Interestingly, participants in the highest tertile of GDQS had a significantly higher total energy intake than to those in the lowest tertile. This seemingly paradoxical finding may be explained by the fact that a higher GDQS in this population was driven by increased consumption of energy-dense healthy food groups, such as meats, dairy, and fruits, rather than refined grains or sweets. Crucially, all multivariable

models were adjusted for total energy intake using the residual method, thereby isolating the effect of diet quality from that of total energy consumption.

The present study has both strengths and weaknesses. To the best of our understanding, this is the first study to examine the association between GDQS, a comprehensive dietary quality index, and CRC in adults. Also, the use of valid and reliable FFQs, specifically developed for the Iranian population, ensures the reliability and accuracy of the measurements. Moreover, the large sample size and recruitment from multiple centers enhance the statistical power and generalizability of our results. Also, we controlled for several potential confounders to estimate an independent association between GDQS and CRC. Nevertheless, certain limitations should be considered when interpreting our results. The observational studies limit the ability to show a causal association between GDQS and CRC risk. The influence of disease on dietary intakes among case-control studies is unavoidable. Patients with CRC might adhere to a healthy diet high in fiber and antioxidants and low in unhealthy fats and processed meats. Such residual confounding may attenuate the risk estimates; therefore, the actual results might be even stronger than those seen in this study. Also, although reverse causality is an inherent concern in case-control designs, we made concerted efforts to mitigate it. The robustness of the association in the subgroup of patients with a diagnosis-to-enrollment interval of ≤ 3 months (OR: 0.58) not only suggests that our primary findings are not merely a consequence of post-diagnosis dietary changes but also reinforces the validity of the observed inverse association. Furthermore, evaluating dietary intake using the FFQ is prone to misreporting (over- or underestimation) and misclassification. Although we tried to include a wide variety of people in this multicenter case-control study, it included only Iranian adults, so we cannot generalize the results to other populations with different dietary behaviors or genetic makeup.

CONCLUSION

This study showed a significant inverse association between adherence to GDQS and lower odds of CRC among Iranian adults. The inverse association was also observed for colon cancer, but not for rectal cancer. These findings underscore the need to adopt healthy diets rich in fruits, vegetables, whole grains, dietary fiber, and antioxidants and to avoid red and processed meats to prevent adverse conditions such as cancer. To support this claim, further studies with varied populations are required. Future research using long-term observational approaches and clear biological indicators may provide a greater understanding of these connections, helping determine whether they are truly cause-and-effect relationships.

Abbreviations

BMI

body mass index

SES

socioeconomic status

MET

metabolic equivalent of task

FH

family history

SD

standard deviation

Declarations

Clinical trial number

not applicable.

Ethics approval and consent to participate:

The study protocol received ethical approval from the Ethics Committee of Isfahan University of Medical Sciences, Isfahan, Iran (IR.MUI.REC.1401.031), Khuzestan University of Medical Sciences, Ahvaz, Iran (IR.ABADANUMS.REC.1402.096), and Lorestan University of Medical Sciences, Khorramabad, Iran (IR.LUMS.REC.1404.014). All participants signed informed permission before the beginning of the study. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and relevant ethical guidelines. All participants were aged 18 years or older, therefore parental or legal guardian consent was not required. For illiterate participants and those aged over 65 years, the informed consent form was read aloud and explained by the interviewer before consent was obtained. This study was based on questionnaire data, and no human biological samples or tissues were collected or used.

Consent for publication:

Not applicable.

Competing interests:

The authors declare no known competing financial interests or personal affiliations that could have influenced the findings reported in this paper.

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Author Contribution

OS and AH conceived and designed the study. OS, MZ, BH, and NH were responsible for data acquisition and field management across the three provinces. MaM performed the statistical analyses and verified the underlying data. AH, TK, and FS contributed to data interpretation and drafted the initial manuscript. OS and MaM critically reviewed and substantially revised the manuscript for important intellectual content. All authors had full access to the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. The final manuscript was read, critically revised, and approved by all authors. All authors agree to be accountable for all aspects of the work and to ensure that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. OS is the guarantor of the study.

Data Availability

The datasets are not publicly available due to privacy or ethical restrictions. Datasets of the study are available from the corresponding author upon reasonable request and with permission from the relevant institutional ethics committees.

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Figures

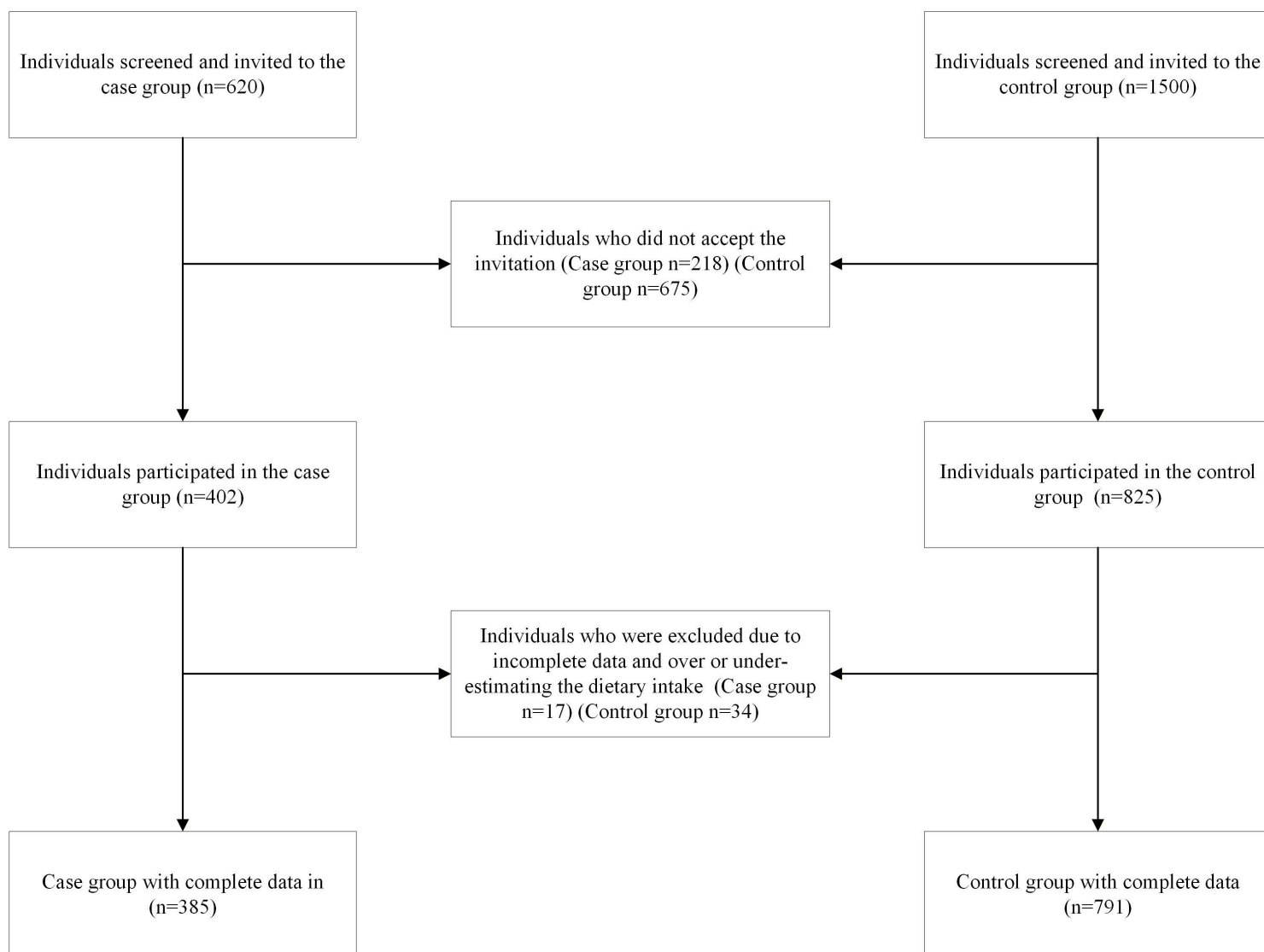


Figure 1

Flowchart of participants