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#### ORIGINAL ARTICLE

# Association between the Quality and Diversity of Diet and the Risk of Colorectal Cancer

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# ABSTRACT

**Background:** Colorectal cancer is the third-most common cancer in the world. Diet is one of the most important factors in colorectal cancer prevention. This study examined the association between the diet quality and diversity and the risk of colorectal cancer.

**Methods:** In a case-control study, 213 participants comprising 71 cases and 142 controls were enrolled. A semi-quantitative, 125-item frequency questionnaire was used to collect dietary information. The Food Quality Score (FQS) and Dietary Diversity Score (DDS) were employed to check the diet quality and variety. Logistic regression determined the relationship between the quality and diversity of diet and the risk of colorectal cancer.

**Results:** Between the highest and lowest tertiles of the FQS, the risk of colorectal cancer dropped significantly (OR=0.28, 95% confidence interval (95%CI): 0.13-0.61, p=0.001). This trend continued when all confounders were considered in the adjusted model (OR=0.07, 95%CI: 0.02–0.22, p<0.001). For the DDS in the crude model, the last tertile when compared to the first tertile, a decreasing trend was observed for the risk of colorectal cancer (OR=0.37, 95%CI: 0.18–0.79, p=0.001). After adjusting for confounding factors in the adjusted model, the odds of colorectal cancer decreased with a more diversified diet (OR=0.30, 95%CI: 0.11-0.82, p=0.019).

**Conclusion:** The results revealed that a diet with high quality and diversity had a preventive role in reducing the risk of colorectal cancer.

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#### Introduction

Colorectal cancer (CRC) is one of the most common types of cancers (1). According to the Global Cancer Observatory (GCO), CRC is the third most common cancer worldwide after female breast cancer and lung cancer. CRC with 916 thousand deaths in 2020 is the second cancer after lung cancer in terms of mortality rate among cancers (2). In Iran, CRC is the third and fourth most common cancer in males and females, respectively. The incidence and mortality of this cancer in Iran have increased significantly during the last few decades (3). CRC is a major concern, with a notable rise in occurrence in developed/developing countries. Nowadays, some

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risk factors including sedentary lifestyle, obesity, smoking, alcohol consumption, and unhealthy dietary patterns are considered primary targets to be modified to decrease the risk of cancer. These factors significantly raise the chance of developing CRC (4). Research studies have indicated that 40 to 70 percent of the occurrence of CRC may be attributed to unhealthy dietary choices (5). Overall, the impact of food/nutrients on the risk of CRC has been investigated for decades to clarify this issue (6).

Previous studies have shown the association between overall/whole dietary composition and CRC that has been more consistent and reliable than the relationship between individual food/nutrients and cancer (7, 8). Diet quality indices have been developed to assess overall dietary patterns, rather than a single nutrient or food (9). Furthermore, foodbased indices are more practical for clinical use. The food quality score (FQS) is an index that consists of a total of 14 food items or food groups, which are divided into two groups (healthy and unhealthy foods) (10). The association between FQS and metabolic syndrome, coronary heart disease, cardiovascular disease, and breast cancer has been studied before (11). Another index as the Dietary Diversity Score (DDS) has also been used in this relation. The DDS is a useful method for evaluating the diversity of food consumed and the overall diet quality (12). It was shown that high-quality and diversified diets can protect against chronic diseases and promote the health status and the lifespan (13). Therefore, the current case-control study was designed to investigate the association of FQS and DDS with CRC risk, since previous researches have revealed contradictory findings and there is a shortage of published data on this topic in Iran.

# **Materials and Methods**

In a hospital-based case-control study in Tehran, Iran between September 2008 and January 2010, the study involved 19 CRC surgical units from the Cancer Institute of Imam Khomeini Hospital Complex and three other large hospitals (Shariati, Imam Hussein, and Ayatollah Taleghani). The inclusion criteria were pathology-confirmed CRC that was diagnosed within six months prior to the interview; age of patients to be 40-75 years; absence of additional cancers, absence of inflammatory bowel disease (IBD) or familial adenomatous polyposis; and lack of other medical conditions. The control group consisted of randomly chosen noncancerous individuals without chronic disorders admitted to the same hospitals as the cases. The controls had various medical conditions (38% for fractures and sprains, 14% for osteoarticular disorders, 11.5% for disk disorders, 9.5% for acute surgical conditions; e.g., hernia inguinalis, appendicitis and kidney stone, 7.0% for trauma and injuries, 7.0% for skin diseases, and 13.0% for other illnesses; e.g., eye or nose disorders, debridement, removal of plates, pins, screws, and wires). Each case was matched with two controls by age (within 5-year categories) and sex.

Out of a total of 267 patients (89 cases and 178 controls) who were screened according to the inclusion criteria, 16 controls and 8 cases were excluded from the study due to their unwillingness to proceed. During the analysis of dietary patterns, 30 more patients (10 cases and 20 controls) were excluded, since they had incomplete food frequency questionnaire (FFQ) (more than 40% of food items were not assessed) and their total energy intake was outside the range of  $\pm$ 3 standard deviations from the mean (<716 and >3,764 Kcal/d for men and <541 and >3,397 Kcal/d for women). Finally, the final sample size included 71 cases and 142 controls.

Dietary intake was evaluated using a semiquantitative FFQ. The questionnaire included 125 food and beverage items (with standard serving sizes). Previous studies have shown the validity and reliability of this 125-semi-quantitative FFQ (14, 15). Dietary intake of participants was estimated based on what they consumed in the year prior to their cancer diagnosis (cases) or interview (controls). The participants were asked to report the consumption frequency of a given serving of each food item on a daily, weekly, monthly, and yearly basis. Then, the data were converted to daily intake frequency. The portion size of each food item was converted to grams and energy, and nutrient intake was calculated using the Nutritionist IV software (version 7.0; N-Squared Computing, Salem, OR, USA).

Trained interviewers used pre-tested questionnaires to gather information from cases and controls. The obtained information were sociodemographic characteristics, dietary intake, family history of CRC, physical activity, smoking habits, and medication information (use of non-steroidal anti-inflammatory drugs (NSAIDs) and vitamin/ mineral supplements). Alcohol intake information was not obtained from respondents due to cultural and religious beliefs. Weight was measured with a precision of 0.1 kg (with minimal clothes and without shoes). A SECA body meter measured height with a precision of 0.1 (standing barefoot with his/her back to the wall). Body mass index (BMI) was calculated by weight (kg)/height (m)<sup>2</sup> formula. A validated self-report questionnaire, weighted according to intensity level, measured the physical activity level of participants in the metabolic equivalent task (MET) hours/day (16). Activities of the year before CRC diagnosis were considered for case patients, while activities of the year before the interview were considered for control subjects.

Fung et al.'s method was used to calculate the FQS (17). This scale consists of a total of 14 food items or food groups, divided into two groups (healthy and unhealthy food). The healthy group of FQS included vegetables, fruits, whole grains, nuts, legumes, yogurt, and coffee. On the other hand, the unhealthy group consisted of refined carbohydrates, sugary drinks, sweets, ice cream, red meat, processed meats, potatoes, chips, and fried meals. For each food group, participants' intake was categorized in quintiles, assigning scores of 1-5 to the healthiest food groups. A reverse quintile rating (scores of 5 to 1) was also assigned for unhealthy food groups. Finally, each food group's ranking was summed up to generate an overall score, ranging from 14 to 70, where a higher score signified a healthier diet.

To score dietary diversity, the method described

by Kant et al. was used (18). This method consisted of five groups, including grains, vegetables, fruits, meats, and dairy products. This approach was based on food groups introduced by the Food Guide Pyramid of the United States Department of Agriculture (USDA). These 5 groups were divided into 23 subgroups. Bread and grains group was divided into seven subgroups (refined bread, biscuits, pasta, whole grain bread, corn flakes, rice, and refined flour), fruits into two subgroups (fruit/fruit juice and berries/citrus fruits), vegetables into seven subgroups (vegetables, potatoes, tomatoes, other starchy vegetables, legumes, yellow vegetables, and green vegetables), meat into four subgroups (red meat, chicken, fish, and eggs), and also dairy products group that was divided into three subgroups (milk, yogurt, and cheese). The minimum and maximum diversity scores for each food group were defined as 0 and 2, respectively. Each of the five food categories received a maximum diversity score of 2 out of a possible 10 points. The total score was the sum of the five main groups' scores.

Table 1: Basic characteristics of the study participants in the case and control groups.						
Variable	Case group (n=71)	Control group (n=142)	*P value			
Age (year)	58.2±10.46	57.7±10.44	0.78			
Weight (kg)	72.78±12.55	72.16±11.59	0.71			
Height (cm)	163.44±9.83	$164.44 \pm 9.56$	0.47			
Body mass index (kg/m <sup>2</sup> )	27.6±4.18	26.67±4.23	0.36			
Income (Dollars)	393.0 (253.0)	402.0 (302.0)	0.14			
Physical activity (MET-h/day)	36.81±3.60	36.75±4.85	0.93			
Gender (number)			0.45			
Male	35	70				
Female	36	72				
Education level (number)			0.15			
No formal education	28	36				
Elementary	22	45				
Junior. Senior High School	7	19				
Diploma. College. University	14	42				
Family history of CRC (number)			0.017			
Yes	7	3				
No	64	139				
Smoking (number)			0.95			
Never smoker	57	101				
Former smoker	8	15				
Current smoker	6	26				
Non-steroidal anti-inflammatory drugs			0.08			
(NSAIDs) use (number)			0.01			
Ibuprofen	5	22	0.05			
Aspirin	1	17	0.15			
Acetaminophen	4	24				
Baby aspirin	15	19				
Vitamins and minerals supplements use (number)			0.015			
Yes	8	35				
No	63	107				

BMI: Body mass index, MET.h: Metabolic equivalent of task per hour, CRC: Colorectal cancer. The chi-square test for categorical variables and Mann-Whitney/independent samples t-test for continuous variables were used. <sup>1</sup>Values were numbers (percent). <sup>2</sup>Values were mean±standard deviation (SD). <sup>3</sup>Values were median (IQR).

The maximum and minimum total food diversity scores were between 0 and 10.

The distribution normality of the variables in the DDS and FQS was evaluated using a histogram chart and Kolmogorov-Smirnov test. At first, all food items were adjusted by the residual method for energy. For the analysis of continuous variables with normal distribution, independent s a m p l e t-test was utilized. On the other hand, for nonnormal distribution, we employed Mann-Whitney test. As for categorical variables, Chi-square test was used. The study participants were classified into tertiles in terms of DDS and FQS. Dietary intake was compared using a one-way analysis of variance among tertiles, and for the qualitative variables; Chisquared test was applied. Logistic regression was used to determine the relationship between DDS and FQS with the risk of CRC, in the crude and adjusted models. In the adjusted model, the confounders including BMI, income, smoking status, education, physical activity, vitamin and mineral supplement usage, NSAIDs intake, and family history of CRC were adjusted. However, age and sex were not considered as confounding factors in the adjusted model, since the participants were already matched in both groups by age and sex. In all models, the first tertile was considered as the reference group. SPSS software (Version 26, Chicago, IL, USA) was used to perform the statistical analysis. The significance level of the p value was considered less than 0.05.

#### Results

The anthropometric demographic and characteristics of the participants in the study were shown in Table 1. Both groups had no significant differences in terms of age, weight, height, BMI, income, smoking, physical activity, gender, and educational level. However, a significant difference was observed in distribution of family history of CRC, NSAIDs intake, and vitamin/mineral supplements usage between the both groups. The comparison of the average intake of macronutrients and micronutrients based on the FQS was shown in Table 2. The results indicate that individuals in the third tertile of the FQS had a higher intake of thiamin, pyridoxine, vitamin K, and potassium

Table 2: Intake of macronutrients and micronutrients based on the FQS tertiles.							
Item	ſ	<b>[1</b>	Τ2		Т3		<i>P</i> -value*
	Mean	SD	Mean	SD	Mean	SD	
Energy (kcal/day)	2216.90	365.71	2319.44	397.62	2226.30	368.88	0.19
Carbohydrates (g/day)	346.84	75.135	365.33	79.44	343.19	78.08	0.17
Protein (g/day)	80.12	14.77	84.21	15.99	81.98	15.37	0.29
Fat (g/day)	61.02	8.33	62.59	9.14	63.10	8.35	0.35
Fiber (g/day)	19.59	2.85	20.26	3.03	19.76	2.93	0.36
Saturated fatty acid (g/day)	17.76	3.55	18.69	4.17	18.78	4.81	0.31
Cholesterol (mg/day)	209.27	62.57	219.36	53.58	223.09	42.12	0.13
PUFA (g/day)	11.50	1.85	11.25	1.82	11.94	1.68	0.06
MUFA (g/day)	20.25	2.99	20.59	3.26	21.35	3.49	0.30
Thiamine (mg/day)	2.20	0.50	2.31	0.56	2.10	0.47	0.049
Riboflavin (mg/day)	1.97	0.46	2.19	0.54	2.12	0.50	0.050
Niacin (mg/day)	22.10	5.06	23.20	5.72	21.27	5.15	0.08
Pyridoxine (mg/day)	1.47	0.22	1.61	0.21	1.59	0.25	0.002
Folate (µg/day)	471.79	102.67	499.49	103.00	471.46	94.90	0.15
Vitamin B12 (µg/day)	8.95	6.52	10.35	6.57	8.71	5.13	0.21
Vitamin C (mg/day)	124.11	38.28	135.85	43.87	130.13	32.13	0.20
Vitamin A (RAE/day)	1699.40	672.75	1904.96	678.08	1724.50	701.40	0.14
Vitamin D (µg/day)	0.75	0.13	0.80	0.14	0.80	0.17	0.21
Vitamin E (mg/day)	12.83	2.02	13.11	1.68	12.90	1.60	0.60
Vitamin K (µg/day)	110.27	31.25	133.39	36.43	122.17	34.83	0.001
Sodium (mg/day)	2663.47	335.80	2700.29	416.21	2636.13	290.73	0.53
Potassium (mg/day)	3167.07	479.98	3459.74	539.22	3472.86	678.54	0.003
Calcium (mg/day)	860.15	197.02	940.02	276.53	962.57	337.19	0.08
Phosphorus (mg/day)	1375.57	263.80	1477.70	296.62	1453.71	318.09	0.11
Magnesium (mg/day)	333.32	62.31	355.28	65.15	344.93	66.18	0.13
Iron (mg/day)	18.23	3.40	18.21	3.75	17.68	4.47	0.63
Zinc (mg/day)	9.71	1.89	10.35	1.95	10.04	2.06	0.16
Copper (mg/day)	2.26	0.80	2.44	0.81	2.15	0.66	0.06

<sup>a</sup>Data were expressed as mean±standard deviation (SD). Analysis of variance test was used. PUFA: Polyunsaturated fatty acids. MUFA: Monounsaturated fatty acids.

when compared to the first tertile. Moreover, the subjects who were in the third tertile of the DDS, they had a higher intake of energy, carbohydrate, protein, fat, fiber, saturated fatty acids, cholesterol, monounsaturated fatty acids (MUFA), thiamine, riboflavin, niacin, pyridoxine, folate, vitamin C, vitamin K, potassium, calcium, phosphorus, magnesium and zinc in comparison to individuals in the first tertile (Table 3).

Odds ratios in crude and adjusted models for CRC among tertiles of FQS and DDS were demonstrated in Table 4. In the crude model, the odds of CRC were significantly lower in the third tertile of the FQS when compared to the first tertile [Odds Ratio (OR)=0.28, 95% Confidence Interval (95%CI): 0.13-0.61, p=0.001]. This association remained significant after adjusting confounding factors (BMI, income, smoking status, education, physical activity, vitamin and mineral supplement usage, NSAIDs intake, and family history of CRC) in the adjusted model (OR=0.07, 95%CI: 0.02-0.22, p<0.001). Furthermore, in the crude model, individuals in the third tertile

of the DDS in comparison to the first tertile had a lower odd of CRC (OR=0.37, 95%CI: 0.18-0.79, p=0.010). After adjusting for the confounders, the association remained statistically significant and results showed a decreased chance of CRC for those who consumed a diversified diet (OR=0.30, 95%CI: 0.11- 0.82, p=0.019).

#### Discussion

The findings of this study showed that higher FQS was associated with lower odds of CRC and a higher DDS was significantly associated with a reduced chance of CRC. According to the results, it can be concluded that the non-dietary factors affecting the chance of CRC in this study had the same distribution between the case and control groups. This is the first research investigating the association of FQS and DDS with CRC. As mentioned earlier, the FQS consisted of 14 food groups which were categorized into healthy and unhealthy groups. The healthy food group included vegetables, fruits, whole grains, nuts, legumes,

Table 3: Intake of macronutrients and micronutrients based on the DDS tertiles.							
Item	Т	<u>`1</u>	Т2		Т3		P value*
	Mean	SD	Mean	SD	Mean	SD	
Energy (kcal/day)	2121.81	327.35	2281.70	374.29	2367.12	397.77	< 0.001
Carbohydrates (g/day)	330.40	67.71	351.93	75.17	374.48	85.01	0.003
Protein (g/day)	75.88	13.57	84.35	14.92	86.39	15.91	< 0.001
Fat (g/day)	59.76	7.28	64.28	9.27	62.78	8.73	0.006
Fiber (g/day)	19.06	2.24	19.89	3.06	20.72	3.23	0.003
Saturated fatty acid (g/day)	16.89	3.37	19.07	4.29	19.35	4.57	0.001
Cholesterol (mg/day)	203.40	56.04	232.81	56.24	216.28	42.15	0.004
PUFA (g/day)	11.67	1.94	11.50	1.73	11.50	1.73	0.79
MUFA (g/day)	19.90	2.80	21.54	3.50	20.76	3.33	0.01
Thiamine (mg/day)	2.06	0.43	2.19	0.46	2.37	0.60	0.001
Riboflavin (mg/day)	1.92	0.48	2.14	0.47	2.23	0.54	0.001
Niacin (mg/day)	21.10	4.97	22.33	5.06	23.22	5.91	0.06
Pyridoxine (mg/day)	1.49	0.24	1.57	0.19	1.63	0.25	0.002
Folate (µg/day)	455.37	105.43	490.06	98.93	499.54	93.37	0.02
Vitamin B12 (µg/day)	8.81	6.75	10.03	6.07	9.28	5.53	0.49
Vitamin C (mg/day)	120.43	29.44	133.19	41.94	137.54	41.63	0.02
Vitamin A (RAE/day)	1704.97	662.53	1806.65	659.62	1836.67	740.57	0.49
Vitamin D (µg/day)	0.80	0.12	0.78	0.16	0.77	0.17	0.49
Vitamin E (mg/day)	12.66	1.85	13.27	1.94	12.93	1.41	0.11
Vitamin K (µg/day)	111.53	31.41	129.18	38.82	127.32	33.63	0.005
Sodium (mg/day)	2661.05	306.63	2642.94	332.40	2699.40	414.66	0.62
Potassium (mg/day)	3119.95	487.90	3398.13	565.57	3610.83	605.43	< 0.001
Calcium (mg/day)	806.06	220.38	931.41	280.42	1032.82	292.74	< 0.001
Phosphorus (mg/day)	1306.48	249.83	1466.31	294.64	1543.11	296.08	< 0.001
Magnesium (mg/day)	319.37	56.19	348.47	63.13	337.24	66.70	< 0.001
Iron (mg/day)	17.22	3.94	18.07	3.33	18.81	4.29	0.054
Zinc (mg/day)	9.25	1.74	10.28	1.88	10.62	2.06	< 0.001
Copper (mg/day)	2.18	0.84	2.36	0.72	2.32	0.72	0.34

<sup>a</sup>Data were expressed as mean±standard deviation (SD). <sup>b</sup>Analysis of variance test was used. DDS: Dietary diversity score. PUFA: Polyunsaturated fatty acids. MUFA: Monounsaturated fatty acids.

R) and 95% cc	onfidence interval (95%CI)	) of colorectal	cancer (CRC) accordin	g to the tertile of
T1	Τ2	P value*	T3	<i>P</i> value <sup>¥</sup>
5)				
Ref	0.55 (0.27, 1.08)	0.086	0.28 (0.13, 0.61)	0.001
Ref	0.29 (0.11, 0.77)	0.014	0.07 (0.02, 0.22)	< 0.001
(DDS)				
Ref	0.84 (0.43, 1.66)	0.63	0.37 (0.18, 0.79)	0.010
Ref	0.73 (0.31, 1.70)	0.46	0.30 (0.11, 0.82)	0.019
(	() and 95% co T1 S) Ref Ref (DDS) Ref Ref	T1 T2   5) Ref 0.55 (0.27, 1.08)   Ref 0.29 (0.11, 0.77)   (DDS) Ref 0.84 (0.43, 1.66)   Ref 0.73 (0.31, 1.70)	T1 T2 P value*   5) Ref 0.55 (0.27, 1.08) 0.086   Ref 0.29 (0.11, 0.77) 0.014   (DDS) Ref 0.84 (0.43, 1.66) 0.63   Ref 0.73 (0.31, 1.70) 0.46	T1 T2 P value* T3   S) Ref 0.55 (0.27, 1.08) 0.086 0.28 (0.13, 0.61)   Ref 0.29 (0.11, 0.77) 0.014 0.07 (0.02, 0.22)   (DDS) Ref 0.84 (0.43, 1.66) 0.63 0.37 (0.18, 0.79)   Ref 0.73 (0.31, 1.70) 0.46 0.30 (0.11, 0.82)

Data were expressed as odds ratio (95% CI). <sup>a</sup>Adjusted for body mass index (BMI), income, smoking status, education, physical activity, vitamin and mineral supplement usage, non-steroidal anti-inflammatory drugs (NSAIDs) intake, and family history of colorectal cancer (CRC). \**P* value for the T2 vs. T1, obtained by logistic regression. \**P* value for the T3 vs. T1, obtained by logistic regression.

yogurt, and coffee. Except for yogurt, all items in the healthy category were plant-based and previous studies have also defined a plant-based diet as a diet in which some or all animal food have been eliminated (19, 20). Many other studies have shown that plant-based diets have been associated with a reduced risk of chronic diseases (21-23).

In a cohort research, Orlich et al. found that plant-based diets lowered cancer risk. This study evaluated diet as an exposure factor using a validated quantitative FFQ, then classified participants into four vegetarian dietary patterns (vegan, lacto-ovo vegetarian, pesco-vegetarians, and semi-vegetarian) and a non-vegetarian pattern. All vegetarians had 23% lower colon cancer risk and 29% lower rectal cancer risk than non-vegetarians after 7 years of follow-up (24). In another study, Fung et al. investigated the effect of dietary patterns on women's risk of CRC during a 12-year follow-up. Their study's results demonstrated that the risk of CRC was not correlated with a healthy eating pattern, emphasizing the consumption of more fruits, vegetables, legumes, fish, chicken, and whole grains. Also, in this study, the western dietary pattern (more consumption of red and processed meat, sweets and desserts, fried potatoes, and refined grains) caused a non-significant increase in the risk of CRC (25), which is not in line with the present study findings. One of the reasons for this discrepancy is different food patterns between healthy and unhealthy food groups in the current study.

In a case-control study, Safari *et al.* investigated the relationship between dietary patterns and the risk of developing CRC. They examined two main food patterns including healthy dietary pattern and Western dietary pattern. A healthy dietary pattern could significantly reduce the risk of CRC by 80%, while a Western dietary pattern increased the risk of colon cancer by 75% (26). In many ways, this study had the same methodology as the current study, but exposure factors, type of analysis, and different adjusted confounding factors resulted in different findings in relation to the two mentioned studies.

Some mechanisms can explain the observed relationship between FQS and CRC, although the exact mechanism is still unknown. Firstly, an anti-inflammatory diet, such as a healthy highquality pattern, which is known as rich sources of antioxidants and polyphenols by consuming more fruits, vegetables, legumes, and nuts can reduce stress and chronic inflammation and is effective in reducing the risk of cancer, especially CRC (27). Secondly, healthy dietary patterns are good sources of micronutrients such as folic acid and magnesium (28, 29). Folate plays an important role in methylation and correct cell divisions and is also an inhibitory factor against cellular disorders and acts as inhibitory factors against cellular disorders (30), and magnesium deficiency is also associated with chronic inflammation and insulin resistance (31). Thirdly, increasing beneficial gut bacteria in a healthy diet may contribute to reducing CRC risk by preventing chronic inflammation, protecting intestinal cells, and improving insulin sensitivity and cell division (32, 33).

The results demonstrated a significant inverse relationship between DDS and CRC, suggesting that a more diverse diet or a higher DDS may lower the risk of CRC. Contrary to our findings, Slattery et al. did not notice any relationship between DDS and CRC. In their study, higher consumption of meat, fish, chicken, eggs, and refined grains was associated with an increased risk of CRC in men; however, women who had a higher consumption of plant food (fruits, vegetables, or whole grains) were at a lower risk of CRC (34). DDS is based on the American Food Guide Pyramid; therefore, adherence to this guideline is associated with higher diet quality and adequate nutrient intake (35). Previous studies have demonstrated an inverse relationship between micronutrient deficiency and higher DDS as a valid indicator of vitamin and mineral adequacy. Any diet with a lower diversity score can raise the risk of nutrient deficiency, particularly in vulnerable populations like children, the elderly, and women (36).

In a cross-sectional study, Mirmiran et al. showed that a higher DDS was associated with a higher intake of calcium, vitamin C, magnesium, zinc, vitamin B6, copper, and vitamin B12 (37). Acham et al. conducted another cross-sectional study that revealed a higher intake of minerals and vitamins; while better nutrient adequacy was associated with a high dietary diversity (38). Moreover, various studies have investigated the relationship between micronutrients and CRC. A diet rich in micronutrients with antioxidant capabilities (selenium, vitamins E and C), as well as those with roles in DNA methylation (folate, methionine, vitamins B6, and B12), may contribute to a decreased risk of CRC (39). Moreover, the current findings suggest the correlation between DDS and CRC that may be attributed to the consumption of more nutritious food groups. Individuals who had a more varied diet tend to incorporate a greater amount of vegetables and fruits into their meals. This type of diet has been found to have a positive impact on preventing CRC by helping to manage body weight, promoting the production of beneficial short-chain fatty acids, reducing inflammation, and regulating blood sugar levels (40).

The present study had some limitations too. Given that dietary intake was assessed by an FFQ, it is important to acknowledge that there may have been some measurement errors, potentially resulting in the underestimation of certain associations. Nevertheless, we addressed this limitation by utilizing a validated FFQ and excluding individuals who either over- or under-reported their energy intake. Additionally, the controls were chosen from patients with different diseases (hospital-based casecontrol design), which may not accurately reflect the exposure of individuals who were at risk of developing the condition being studied. Additionally, it is important to consider the possibility of residual confounding resulted from imprecise measurement of key covariates. As a case-control study, it is important to consider the potential for recall bias. Patients may remember their diets differently after a cancer diagnosis, and there is a chance that those who were aware of any potential links between diet and CRC may recall their exposure more than those who were not. Nevertheless, we made efforts to minimize any potential bias by selecting hospital controls with medical conditions that were not linked to diet or other significant risk factors for CRC. Furthermore, cases were recorded at a median of 6 months after diagnosis, and all FFQs were conducted by trained dietitians to minimize any potential recall bias.

### Conclusion

The findings suggested an inverse association of a higher-quality and diversified diet with a lower risk of CRC. However, to reach precise and conclusive findings in this field, additional comprehensive studies are required to uncover a stronger correlation and the fundamental mechanisms behind these relationships.

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# Authors' Contribution

SKD and MA contributed the statistical analysis. BR and AA conducted the study design. MA and SKD interpreted data and wrote the manuscript. All authors read and approved the final manuscript.

# **Conflict of Interest**

The authors declared no conflicts of interest.

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