Journal of Health, Population and Nutrition

RESEARCH

Open Access

A healthful plant-based diet can reduce the risk of developing colorectal cancer: case-control study

Sazin Yarmand[1], Bahram Rashidkhani[2], Arezoo Alimohammadi[3], Zainab Shateri[4], Mahboobeh Shakeri[5], Zahra Sohrabi[1,6*] and Mehran Nouri[7,8*]

Abstract

Introduction The benefit of adherence to a plant-based diet concerning colorectal cancer (CRC) has not been investigated among Middle Eastern population. This study aimed to investigate how adherence to a plant-based diet influences the risk of CRC in this understudied population.

Methods This case-control study was conducted in the CRC surgery departments of general hospitals in Tehran, Iran. A total of 71 individuals with newly diagnosed CRC (cases) and 142 controls subjects free of cancer and acute illness were concurrently recruited from the same hospital. Dietary information was collected using a semi-quantitative 168-item food frequency questionnaire. Dietary patterns were characterized using the plant-based diet index (PDI), unhealthy plant-based diet index (uPDI) and healthy plant-based diet index (hPDI). Multivariate logistic regression was employed to assess the association between these dietary patterns and the risk of CRC.

Results After adjusting the potential confounders, the risk of CRC was significantly lower in the highest tertile of hPDI compared to the lowest tertile (odds ratio (OR) = 0.21; 95% confidence interval (CI): 0.07–0.56, representing 79% risk reduction). Conversely, the risk of CRC was significantly higher in the highest tertile of uPDI compared to the lowest tertile (OR = 6.76; 95% CI: 2.41–18.94). PDI was no significant associated with the risk of CRC.

Conclusions This study found that higher scores on the hPDI was significantly associated with a decrease risk of CRC, while greater adherence to the uPDI contributed to a significantly increase risk.

Keywords Diets, Plant-based, Plant-based diet, Colorectal cancer, Colorectal neoplasms

*Correspondence:
Zahra Sohrabi
zahra_2043@yahoo.com
Mehran Nouri
mehran_nouri71@yahoo.com
[1]Department of Community Nutrition, School of Nutrition and Food Sciences, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Department of Community Nutrition, Faculty of Nutrition and Food Technology, National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[3]Department of Food Hygiene and Quality Control, School of Nutrition and Food Sciences, Shiraz University of Medical Sciences, Shiraz, Iran
[4]Department of Nutrition and Biochemistry, School of Medicine, Ilam University of Medical Sciences, Ilam, Iran
[5]Endoocrine and Metabolism Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
[6]Nutrition Research Center, School of Nutrition and Food Sciences, Shiraz University of Medical Sciences, Shiraz, Iran
[7]Cancer Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran
[8]Health Policy Research Center, Institute of Health, Shiraz University of Medical Sciences, Shiraz, Iran

Introduction

Colorectal cancer (CRC) ranks as the most common cancers globally, placing third and second in terms of prevalence and mortality, respectively [1–3]. Reflecting this global trend, the prevalence of CRC is increasing in Western and Asian countries [4]. While the historical incidence rate of CRC in Iran was lower compared to Western countries [5], it has been continuously increasing in recent years [5]. CRC now ranks as the fifth most prevalent cancer among Iranian men and the third most prevalent among Iranian women [6]. This highlights the growing public health burden of CRC in Iran, with over 90,000 new cancer cases diagnosed annually [7].

Diet is a recognized and influential factor in CRC occurrence, with the potential for both harmful and protective effects on its prevalence [8]. A plant-based diet, in particular, has been shown to modulate several CRC risk factors, potentially leading to a reduced risk of developing the disease [9]. Fruits and vegetables are rich in fiber, folate, vitamins, and antioxidant compounds, which have been linked to a protective effect against CRC [10]. In contrast to refined grains, whole grains contain the germ and bran, rich sources of fiber, antioxidants, and potentially other anticarcinogenic phytochemicals [11].

Several observational studies have reported an association between adherence to a plant-based diet and reduced risk of CRC. For instance, one study showed following a plant-based diet was linked to a 46% reduced risk of colon cancer and a 73% reduced risk of rectal cancer [12]. Similarly, another study noted a decrease in the risk of CRC with a plant-based dietary pattern [13].

Recently, novel measures of plant-based diets have been developed (plant-based diet index (PDI), unhealthful PDI (uPDI), and healthful PDI (hPDI)), to evaluate consumption of both animal and plant-based foods, while also considering the quality of plant-based options [14].

While limited research has investigated the association between these indices and CRC risk [14, 15], to our knowledge, no studies has explored this correlation within Middle Eastern populations. Notably, the dietary habits of Middle Eastern population differ significantly, with large portion sizes and a preference for refined grains like bread and white rice, leading to a higher carbohydrates intake compared to other regions [16]. Therefore, this study aimed to investigate the association between PDI, uPDI, hPDI, and the risk of CRC in Iranian adults, contribution to a deeper understanding of the link between diet and CRC risk.

Materials and methods

Study population

This hospital-based case-control study was conducted in three general hospitals and their associated CRC surgery departments of Tehran, Iran. The sample size was calculated considering a $\beta=0.2$, $\alpha=0.05$, and anticipated odds ratio (OR) of 0.45 based on a previous study investigating the association between a similar dietary factor and CRC risk [17].

Cases were individuals aged 40 to 75 years who were diagnosed with CRC, and had no prior history of cancer by convenient sampling method. The control group was randomly selected from the same hospitals, and free of chronic diseases or acute illness that could influence dietary pattern. The diseases of the patients in the control group include 14.1% osteoarticular disorders, 38% sprains and fractures, 11.3% disk disorders, 9.8% acute surgical conditions, 7.0% trauma, 7.0% skin diseases, and 12.0% other diseases.

Each CRC patient was paired with two control patients. A total of 267 patients were selected (89 cases and 178 controls). Twenty-four patients did not participate, and 30 were excluded due to dietary reporting error (total energy intake outside the defined range of ±3 standard deviations from the mean or incomplete food frequency questionnaire (FFQ)). Statistical analysis was performed on the remaining 71 cases and 142 controls. This study received approval from the Medical Research and Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.SCHEANUT.REC.1401.011). Some details of this study have been published previously [18–20].

Socio-demographic and anthropometric evaluations were conducted

Skilled interviewers administered valid questionnaires to all participants, collecting data on socio-demographic characteristics, family history of CRC, typical vegetable consumption methods, physical activity levels, medication use, smoking habits, and dietary intake. A nutritionist assessed participants' body measurements (weight with a precision of 0.1 kg; for hospitalized patients, weight at admission was used).

The dietary assessment included the calculation of plant-based diet scores

To assess usual food intake, a face-to-face interview was conducted with all participants using a validated 168-item FFQ [21]. Food intake data was then converted to grams per day using Nutritionist IV software (version 7.0; N-Squared Computing, Salem, OR, USA). This software computed mean energy intake and nutrient intake for all participants.

The Satije et al. method [22–24] was employed to create three variants of the plant-based diet index: PDI, uPDI, and hPDI. The FFQ was classified into 18 food groups within three main categories: animal foods (dairy, egg, meat, seafood, animal fat, and other animal-based foods), healthy plant foods (whole grains, nuts, vegetables, fruits, tea or coffee, vegetable oils, and legumes), and unhealthy

plant foods (sugar-sweetened beverages, potatoes, sweets or desserts, refined grains, and fruit juices). The scoring system assigned a score of 10 to the highest consumption and 1 to the lowest consumption for PDI and hPDI. Conversely, uPDI received a score of 1 was given for the highest consumption and 10 for the lowest consumption. The final score for each index ranged from 18 to 180, with a higher total score indicating greater adherence to that specific plant-based dietary pattern.

Table 1 Baseline features of the study population

Variables	Cases (71)	Controls (142)	*P*-value
Gender, % [1]	49.3/50.7	49.3/50.7	1.000
Male/Female			
BMI (kg/m^2) [2]	27.6 ± 4.2	26.6 ± 4.2	0.362
Age (year) [2]	58.2 ± 10.4	57.7 ± 10.4	0.746
Physical activity (MET-h/day) [2]	36.8 ± 3.6	36.7 ± 4.8	0.932
Income (dollar per month) [3]	393.0 (253.0)	402.0 (302.0)	0.206
Energy (kcal/day) [2]	2262.3 ± 450.1	2255.2 ± 341.2	0.908
PDI [2]	98.95 ± 11.61	99.04 ± 11.87	0.961
hPDI [2]	95.22 ± 10.27	101.36 ± 13.21	0.001
uPDI [2]	105.16 ± 12.72	99.38 ± 13.39	0.003
Fiber (g/day) [2]	18.9 ± 2.3	20.4 ± 3.1	<0.001
Education, % [1]	28 (39.3)	36 (25.4)	0.147
No formal education	22 (31.0)	45 (31.6)	
Elementary	7 (9.9)	19 (13.4)	
Junior/Senior high school	14 (19.7)	42 (29.6)	
Diploma/College/University			
common method of vegetable consumption, % [1]	29 (40.8)	78 (54.9)	0.083
	8 (11.3)	18 (12.7)	
Raw / Fresh	34 (47.9)	46 (32.4)	
Boiled			
Fried, Fried / Freezed			
Family history of CRC, % [1]	7 (9.9)	3 (2.1)	0.017
Yes	64 (90.1)	139 (97.9)	
No			
Smoking, % [1]	57 (80.2)	101 (70.1)	0.164
Never	8 (11.3)	15 (10.6)	
Former	6 (8.5)	26 (18.3)	
Current			
Mineral supplement use, % [1]	8 (11.3)	35 (24.6)	0.015
Yes	63 (88.7)	107 (75.4)	
No			
Aspirin, % [1]	1 (1.4)	14 (9.9)	0.016
Yes	70 (98.6)	128 (90.1)	
No			
Acetaminophen, % [1]	4 (5.6)	28 (19.7)	0.004
Yes	67 (94.4)	114 (80.3)	
No			

BMI, body mass index, MET, metabolic equivalent of task, PDI, plant-based diet index; hPDI, healthful plant-based diet index; uPDI, unhealthful plant-based diet index, CRC, colorectal cancer

Values are mean ± SD for continuous and frequency (percentage) for categorical variables

[1] Using chi-square test for categorical variables

[2] Using independent samples T-test for normal continuous variables

[3] Using Mann-Whitney U test for abnormal continuous variable

Statistical analysis

Data were analyzed using SPSS software (version 23.0), SPSS Inc, Chicago IL. The normality of the data was assessed using the Kolmogorov-Smirnov test. Quantitative variables were compared between the case and control groups using either the Mann-Whitney U test or the independent samples t-test, while qualitative variables were compared using the chi-square test. To evaluate the association between PDI, hPDI, and uPDI scores and CRC, both crude and adjusted logistic regression models were utilized (adjusted for confounder variables: physical activity, smoking, common method of vegetable consumption, energy and fiber intake, family history of CRC, taking the mineral supplement, acetaminophen, and aspirin). Also, all figures were depicted by R software.

Results

The baseline characteristics of the study participants are presented in Table 1. Notably, cases had significantly higher uPDI scores compared to controls ($p=0.003$). Conversely, hPDI score was significantly more in the control group ($p=0.001$). Cases were less likely to report a. Fiber intake (p<0.001), family history of CRC ($p=0.017$), use of mineral supplements ($p=0.015$), aspirin ($p=0.016$), and acetaminophen ($p=0.004$) also showed significant differences between the groups.

The participants' food group intakes are shown in Figs. 1, 2 and 3. The participants' food group intakes based on PDI tertiles are reported in Fig. 1. In the last tertile of PDI, the mean intake of whole grains (p<0.001), fruits (p<0.001), vegetables (p<0.001), nuts (p<0.001), legumes ($p=0.001$), vegetable oils ($p=0.002$), tea and coffee (p<0.001), refined grains ($p=0.015$), potatoes (p<0.001), and sweets and desserts ($p=0.001$) were significantly more.

The participants' food group intakes based on hPDI tertiles are reported in Fig. 2. The mean intake of refined grains ($p=0.009$), potatoes ($p=0.042$), sugar and sweetened beverages (p<0.001), sweets and desserts (p<0.001), animal fat (p<0.001), eggs ($p=0.024$), fish and seafoods (p<0.001), meats (p<0.001) and animal based foods (p<0.001) were significantly lower, but vegetables ($p=0.002$), intake was more in the last tertile of hPDI.

The participants' food group intakes based on uPDI tertiles are reported in Fig. 3. The mean intake of In the last tertile of uPDI, the mean intake of whole grains (p<0.001), fruits (p<0.001), vegetables (p<0.001), nuts ($p=0.006$), legumes ($p=0.004$), vegetables oils ($p=0.002$), animal fat ($p=0.003$), dairy products (p<0.001), eggs ($p=0.012$), fish and sea foods (p<0.001) and meats (p<0.001) were significantly lower in the last tertile of uPDI.

Table 2 presents the crude and multivariable-adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for CRC risk according to tertiles of PDI, hPDI, and uPDI

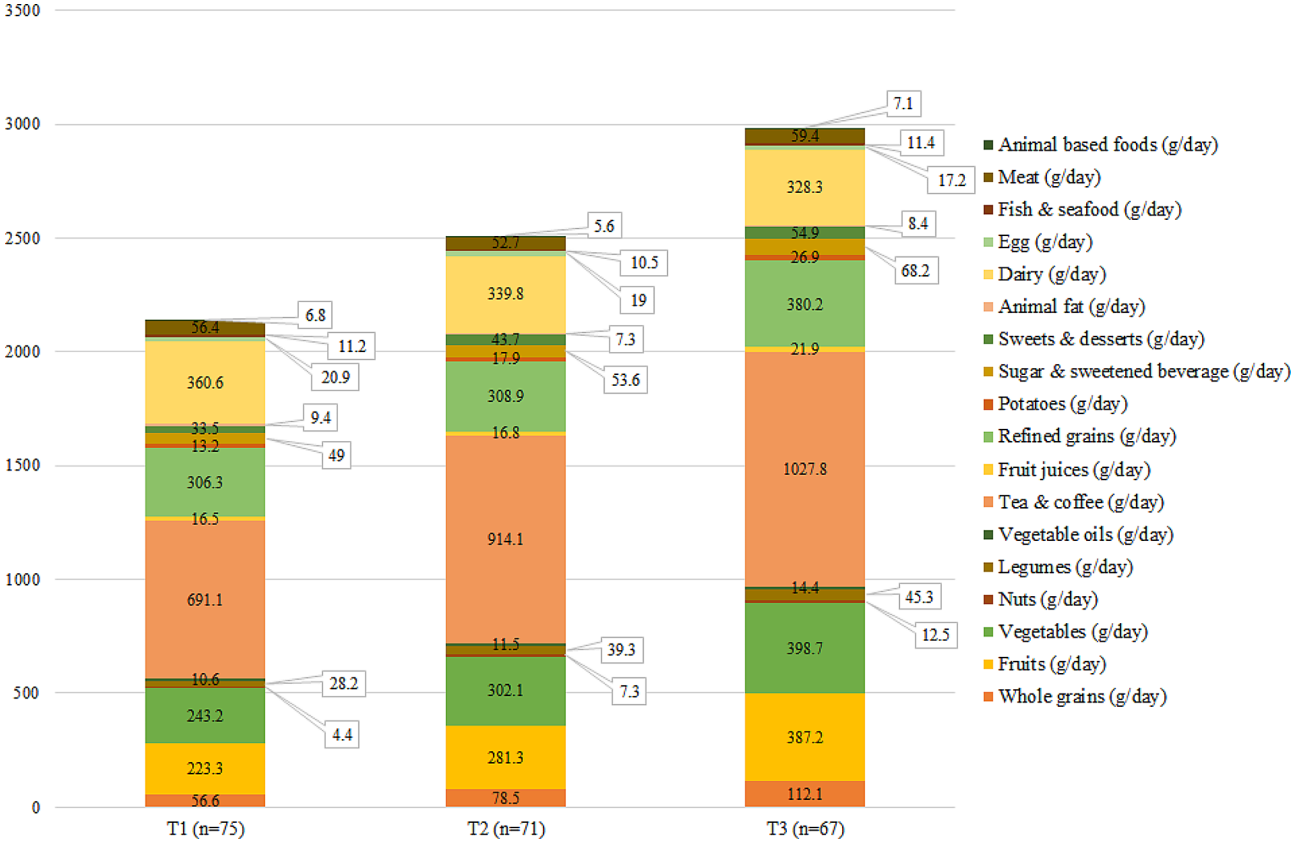

Fig. 1 Participants' food group intake across tertiles of PDI

scores. No significant association was observed between PDI and CRC (P_{trend}=0.609). In contrast, higher adherence to the hPDI was associated with a significantly lower risk of CRC in the highest tertile (79% reduction) compared to the lowest tertile. There was also a non-significant trend towards a lower risk in the second tertile (43% reduction). For the uPDI, participants in the second and highest tertiles had a higher risk of CRC compared to those in the first tertile (tertile $(T)_2$: OR=2.99; 95% CI: 1.12–7.96 - and T_3: OR=6.76; 95% CI: 2.41–18.94). No significant association was found between the highest tertile of PDI and CRC risk compared to the lowest tertile.

Discussion

Our study suggests that following a healthy plant-based diet (higher hPDI scores) may be associated with a lower risk of CRC, while a diet high in unhealthy plant-based diet (higher uPDI scores) might be linked to an increased risk. No significant association was found with overall plant-based diet index (PDI).

The current study's findings demonstrated an inverse relationship between higher hPDI tertiles and CRC risk. The aligns with previous research by Kim et al. [14] who reported a 20% reduction in CRC risk. Additionally, a study by Wang et al. [15] indicated that higher hPDI scores were associated with a reduced risk of CRC. These findings collectively support the potential protective role of healthy plant-based dietary patterns against CRC.

The inverse association between high hPDI scores and CRC risk observed in the present study and previous research can be explained by several potential mechanisms. Notably, hPDI emphasizes consuming a greater quantity of nutrient-dense plant-based foods, rich in fiber and antioxidants [25]. In contract, red meat consumption has been linked to an increased risk of CRC [26]. A meta-analysis study suggests that a daily increase of 150 g of red meat could increase elevate CRC risk by 20% [27]. The potential mechanisms for red meats carcinogenicity include the generation of N-nitroso compounds, heme iron, sulfur-containing amino acids, and saturated fatty acids [28]. Furthermore, fermentation of fiber in the colon by gut microbiota products short-chain fatty acids, such as butyrate, which can induce apoptosis and inhibit cancer cell proliferation. Additionally, dietary antioxidants neutralize free radicals that cause DNA damage and impede cancer cell formation [29–31].

A healthy gut microbiome, compared to a disrupted one, is associated with various health benefits, and a strong link has been established between its composition

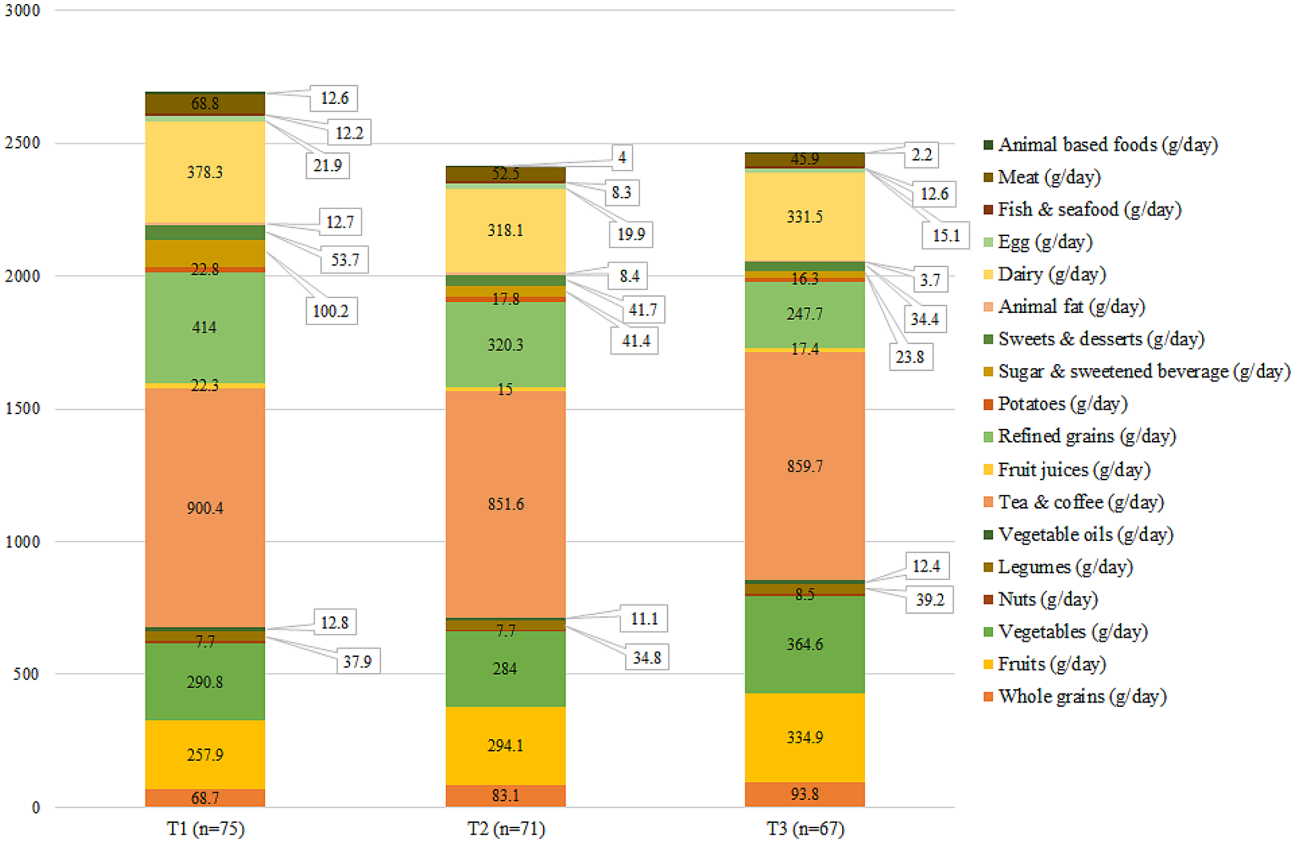

Fig. 2 Participants' food group intake across tertiles of hPDI

and cancer risk, particularly CRC [32, 33]. Certain plant foods rich in fructo-oligosaccharides and galacto–oligosaccharides (e.g., onions, garlic, artichokes) promote the growth of beneficial bacteria that can reduce CRC risk through multiple mechanism, including preventing chronic inflammation, protecting intestinal cells, improving insulin sensitivity, and promoting healthy cell division [34].

Furthermore, dietary polyphenols, such as Flavonols and anthocyanins, found abundantly in plant-based foods characteristics of high hPDI scores, can improve gut microflora composition [35, 36]. The cyclooxygenase-2 (COX-2) pathway plays a role in inflammation and cancer development. Its activation, induced by inflammatory cytokines like interleukin-6 (IL-6), can lead to cell proliferation, angiogenesis, and other changes that promote tumorigenesis. Conversely, anti-inflammatory diets, characterized by high hPDI scores, have been shown to suppress COX-2 pathway activation [31]. This suggests that hPDI may exert protective effects against CRC by modulating inflammatory processes. In conclusion, study suggests that adherence to an anti-inflammatory dietary pattern, reflected by high hPDI scores, rich in antioxidants, polyphenols, fruits, vegetables, legumes, nuts, and olive oil, may contribute to reduced chronic inflammation and potentially lower colorectal cancer risk [31].

Consistent with our finding, previous studies have reported a positive association between high uPDI scores and increased risk of CRC [14, 15]. A case-control study by Wu et al. involving 2799 CRC cases and 2799 age- and sex-matched controls further supports this observation, demonstrating that the odds of developing CRC increased with higher uPDI scores [37].

In contrast to hPDI, uPDI emphasizes high glycemic index (GI) foods like refined grains and sugar-sweetened beverages, which are typically lower in fiber [38]. This dietary pattern (uPDI) may contribute to CRC development through several mechanisms, including the stimulation of insulin secretion and hyperinsulinemia via the phosphatidylinositol 3kinase (PI3K)/ protein kinase B (AKT) signaling pathway [39]. Hyperinsulinemia, a condition of elevated blood insulin levels, can contribute to insulin resistance [39]. Insulin resistance can further promote CRC by stimulating growth-promoting effects in colon cells [40].

Our study found no significant association between overall adherence to the PDI and CRC risk. In contrast, higher adherence to the PDI was associated with a lower risk of CRC in Chinese women [37]. A meta-analysis

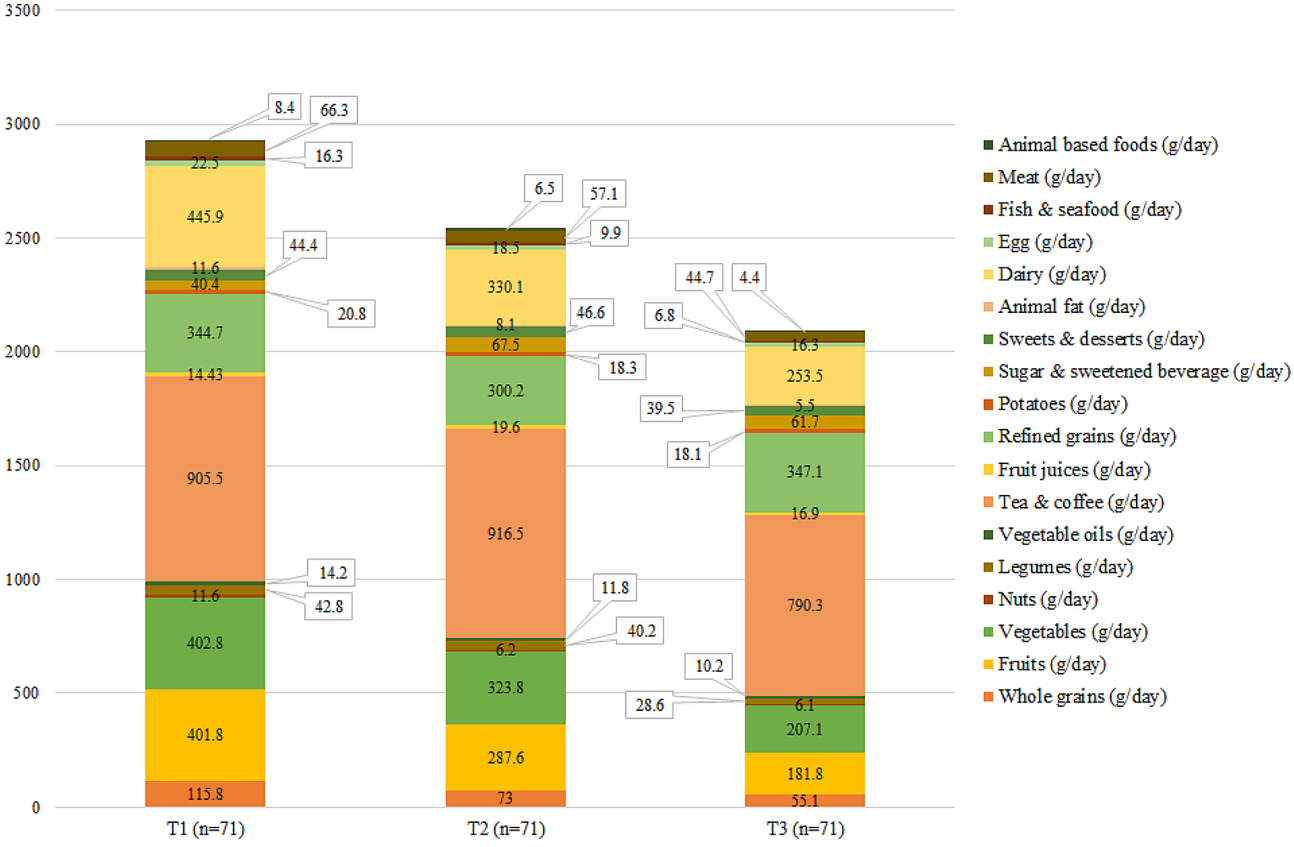

Fig. 3 Participants' food group intake across tertiles of uPDI

Table 2 Association between PDI, hPDI, and uPDI with CRC

Tertiles of indices	Case/Control	Crude Model		Adjusted Model	
		OR	95% CI	OR	95% CI
PDI					
T_1 (≤ 94)	29/46	1.00	Ref.	1.00	Ref.
T_2 (95–104)	19/52	0.58	0.28–1.16	0.34	0.14–0.85
T_3(≥ 105)	23/44	0.82	0.41–1.64	0.92	0.37–2.29
P_{trend}		0.553		0.609	
hPDI					
T_1 (≤ 93)	34/41	1.00	Ref.	1.00	Ref.
T_2 (94–104)	25/47	0.69	0.35–1.35	0.57	0.24–1.33
T_3 (≥ 105)	33/37	0.23	0.10–0.52	0.21	0.07–0.56
P_{trend}		< 0.001		0.002	
uPDI					
T_1 (≤ 94)	13/58	1.00	Ref.	1.00	Ref.
T_2 (95–108)	25/47	2.37	1.09–5.14	2.99	1.12–7.96
T_3 (≥ 109)	33/37	3.97	1.85–8.53	6.76	2.41–18.94
P_{trend}		< 0.001		< 0.001	

PDI, plant-based diet index; hPDI, healthful plant-based diet index; uPDI, unhealthful plant-based diet index; CRC, colorectal cancer

These values are odds ratio (95% CIs).

Obtained from logistic regression

Adjusted model: adjusted for physical activity, smoking, common method of vegetable consumption, energy and fiber intake, family history of CRC, taking mineral supplement, acetaminophen, and aspirin

study also reported no significant association between a vegetarian diet and CRC risk compared to a non-vegetarian diet [41]. Although no significant relationship was indicated between PDI and CRC risk, plant-based diets are good sources of certain nutrients, including folate, magnesium, and B vitamins [42, 43]. Folate plays a fundamental role in cellular deoxyribonucleic acid (DNA) methylation and cellular epigenetic changes. This function of folate introduces it as an essential factor in the correction of cell divisions as well as an inhibitory factor against cellular disorders [44].

To our knowledge, this is the first study to investigate the association between plant-based dietary indices and CRC risk in a Middle Eastern population. We employed a reliable and valid FFQ to minimize measurement error. Also, using valid instruments and controlling for multiple potential confounders were other strengths of this study. However, selection bias is inevitable in case-control studies. To mitigate this, we recruited cases and controls from the same referring hospital. Additionally, recall bias is inherent to the case-control design.

Conclusions

Our study found that greater adherence to the hPDI was significantly linked to a reduced risk of CRC, while higher uPDI scores were associated with an increased risk. This suggests that the quality, not just the quantity, of plant-based foods plays a significant role in CRC risk. Future studies with larger, diverse populations and prospective designs are warranted to confirm these findings and elucidate the underlying mechanisms by which hPDI and uPDI influence colorectal cancer risk.

Author contributions

Sazin Yarmand, Zainab Shateri, Mahboobeh Shakeri, Arezoo Alimohammadi and Mehran Nouri; Contributed to writing the first draft. Mehran Nouri and Bahram Rashidkhani; Contributed to all data and statistical analysis, and interpretation of data. Zahra Sohrabi and Bahram Rashidkhani.; Contributed to the research concept, supervised the work and revised the manuscript. All authors read and approved the final manuscript.

Funding

Not applicable.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study was approved by the Medical Research and Ethics Committee of Shiraz University of Medical Science (IR.SUMS.SCHEANUT.REC.1401.011). All study participants read and signed the informed consent. The present study was performed based on the amended Helsinki Declaration.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 22 April 2024 / Accepted: 26 July 2024
Published online: 31 July 2024

References

1. Mármol I, Sánchez-de-Diego C, Pradilla Dieste A, Cerrada E, Rodriguez Yoldi MJ. Colorectal carcinoma: a general overview and future perspectives in colorectal cancer. Int J Mol Sci. 2017;18(1):197.
2. Rafiemanesh HPR, Abedi M, Kor Y, Moludi J, Towhidi F, et al. Colorectal cancer in Iran: epidemiology and morphology trends. EXCLI J. 2016;15:738–44.
3. Siegel RL, Miller KD, Goding Sauer A, Fedewa SA, Butterly LF, Anderson JC. ea. Colorectal cancer statistics, CA: A Cancer Journal for Clinicians. 2020;70(3):145–164.
4. Tahmasbi B, Abedi G, Moosazadeh M, Janbabai G, Farshidi F, Mansori K, Moradi Y, Shadmani FK, Parang S, Khazaei Z. Determining the survival rate of colorectal cancer in Iran: a systematic review and meta-analysis. Asian Pac J cancer Prevention: APJCP. 2018;19(11):3009.
5. Dolatkhah R, Somi MH, Kermani IA, Ghojazadeh M, Jafarabadi MA, Farassati F, Dastgiri S. Increased colorectal cancer incidence in Iran: a systematic review and meta-analysis. BMC Public Health. 2015;15(1):1–14.
6. Ghalkhani F, Ghojavand M, Kashfi SMH, Jalaeikhoo H, Mojarad EN, Aghdaei HA. Clinico-pathological patterns of colorectal cancer patients in Tehran, Iran. Arvand J Health Med Sci. 2016;1:9–16.
7. Farhood B, Raei B, Malekzadeh R, Shirvani M, Najafi M, Mortezazadeh T. A review of incidence and mortality of colorectal, lung, liver, thyroid, and bladder cancers in Iran and compared to other countries. Contemp Oncology/Współczesna Onkologia. 2019;23(1):7–15.
8. Song MGW, Chan AT. Nutrients, foods, and colorectal cancer prevention. Gastroenterology. 2015;148(6):1244–e6016.
9. Rose S, Strombom A. Colorectal cancer prevention with a plant-based diet. Cancer Therapy Oncol Int J. 2019;15(2):50–67.
10. Michels KB, Giovannucci E, Chan AT, Singhania R, Fuchs CS. Fruit and vegetable consumption and colorectal adenomas in the nurses'health study. Cancer Res. 2006;66:3942.
11. Vogtmann E, Xiang YB, Li HL, Levitan EB, Yang G, Waterbor JW. ea. Fruit and vegetable intake and the risk of colorectal cancer: results from the Shanghai Men's health study. Cancer causes & control: CCC 2013. 24(11):1935–1945.
12. Chen Z, Wang PP, Woodrow J, Zhu Y, Roebothan B, Mclaughlin JR, Parfrey PS. Dietary patterns and colorectal cancer: results from a Canadian population-based study. Nutr J. 2015;14(1):1–9.
13. Orlich MJ, Singh PN, Sabaté J, Fan J, Sveen L, Bennett H, Knutsen SF, Beeson WL, Jaceldo-Siegl K, Butler TL. Vegetarian dietary patterns and the risk of colorectal cancers. JAMA Intern Med. 2015;175(5):767–76.
14. Kim J, Boushey CJ, Wilkens LR, Haiman CA, Le Marchand L, Park S-Y. Plant-based dietary patterns defined by a priori indices and colorectal cancer risk by sex and race/ethnicity: the multiethnic cohort study. BMC Med. 2022;20(1):1–14.
15. Wang F, Ugai T, Haruki K, Wan Y, Akimoto N, Arima K, Zhong R, Twombly TS, Wu K, Yin K. Healthy and unhealthy plant-based diets in relation to the incidence of colorectal cancer overall and by molecular subtypes. Clin Translational Med. 2022;12(8):e893.
16. Esmaillzadeh A, Azadbakht L. Major dietary patterns in relation to general obesity and central adiposity among Iranian women. J Nutr. 2008;138(2):358–63.
17. Terry P, Giovannucci E, Michels KB, Bergkvist L, Hansen H, Holmberg L, Wolk A. Fruit, vegetables, dietary fiber, and risk of colorectal cancer. J Natl Cancer Inst. 2001;93(7):525–33.
18. Shateri Z, Makhtoomi M, Mansouri F, Rajabzadeh-dehkordi M, Nouri M, Rashidkhani B. The association between empirical dietary inflammatory pattern and colorectal cancer risk: a case-control study. BMC Nutr. 2023;9(1):136.
19. Sicahni PH, Makhtoomi M, Leilami K, Shateri Z, Mohammadi F, Nouri M, Omidbeigi N, Mehrabani S, Rashidkhani B. Dietary and lifestyle indices for hyperinsulinemia and colorectal cancer risk: a case-control study. BMC Gastroenterol. 2023;23(1):434.
20. Nejad ET, Moslemi E, Souni F, Mahmoodi M, Vali M, Vatanpour M, Nouri M, Ramezani A, Shateri Z, Rashidkhani B. The association between pro-vegetarian dietary pattern and risk of colorectal cancer: a matched case-control study. BMC Res Notes. 2023;16(1):326.
21. Mirmiran P, Esfahani FH, Mehrabi Y, Hedayati M, Azizi F. Reliability and relative validity of an FFQ for nutrients in the Tehran lipid and glucose study. Public Health Nutr. 2010;13(5):654–62.
22. Satija A, Bhupathiraju SN, Rimm EB, Spiegelman D, Chiuve SE, Borgi L, Willett WC, Manson JE, Sun Q, Hu FB. Plant-based dietary patterns and incidence of type 2 diabetes in US men and women: results from three prospective cohort studies. PLoS Med. 2016;13(6):e1002039.
23. Borazjani M, Nouri M, Venkatakrishnane K, Najafi M, Faghih S. Association of plant-based diets with lipid profile and anthropometric indices: a cross-sectional study. Nutrition & Food Science; 2021.
24. Nouri M, Abdollahi N, Leilami K, Shirani M. The relationship between plant-based diet index and semen parameters of men with infertility: a cross-sectional study. Int J Fertility Steril. 2022;16(4):310–9.
25. Kim H, Caulfield LE, Garcia-Larsen V, Steffen LM, Coresh J, Rebholz CM. Plant-based diets are associated with a lower risk of incident cardiovascular disease, cardiovascular disease mortality, and all-cause mortality in a general population of middle-aged adults. J Am Heart Association. 2019;8(16):e012865.
26. Aykan NF. Red meat and colorectal cancer. Oncol Reviews. 2015;9(1).
27. Schwingshackl L, Schwedhelm C, Hoffmann G, Knüppel S, Laure Preterre A, Iqbal K, Bechthold A, De Henauw S, Michels N, Devleesschauwer B. Food groups and risk of colorectal cancer. Int J Cancer. 2018;142(9):1748–58.
28. Chan DS, Lau R, Aune D, Vieira R, Greenwood DC, Kampman E, Norat T. Red and processed meat and colorectal cancer incidence: meta-analysis of prospective studies. PLoS ONE. 2011;6(6):e20456.
29. Vogtmann E, Xiang Y-B, Li H-L, Levitan EB, Yang G, Waterbor JW, Gao J, Cai H, Xie L, Wu Q-J. Fruit and vegetable intake and the risk of colorectal cancer: results from the Shanghai men's health study. Cancer Causes Control. 2013;24(11):1935–45.
30. Michels KB, Giovannucci E, Chan AT, Singhania R, Fuchs CS, Willett WC. Fruit and vegetable consumption and colorectal adenomas in the nurses' health study. Cancer Res. 2006;66(7):3942–53.

31. Voorrips LE, Goldbohm RA, Verhoeven DT, van Poppel GA, Sturmans F, Hermus RJ, van den Brandt PA. Vegetable and fruit consumption and lung cancer risk in the Netherlands cohort study on diet and cancer. Cancer Causes Control. 2000;11(2):101–15.
32. Voreades N, Kozil A, Weir TL. Diet and the development of the human intestinal microbiome. Front Microbiol. 2014;5:494.
33. Borges-Canha M, Portela-Cidade JP, Dinis-Ribeiro M, Leite-Moreira AF, Pimentel-Nunes P. Role of colonic microbiota in colorectal carcinogenesis: a systematic review. Revista Española De Enfermedades Digestivas. 2015;107(11):659–71.
34. Bhawana D, Neetu S. Availability of prebiotic and probiotic foods at household and commercial level: constraints ahead for health.
35. Edwards C, Havlik J, Cong W, Mullen W, Preston T, Morrison D, Combet E. Polyphenols and health: interactions between fibre, plant polyphenols and the gut microbiota. In.: Wiley Online Library; 2017.
36. Ozdal T, Sela DA, Xiao J, Boyacioglu D, Chen F, Capanoglu E. The reciprocal interactions between polyphenols and gut microbiota and effects on bioaccessibility. Nutrients. 2016;8(2):78.
37. Wu B, Zhou R-L, Ou Q-J, Chen Y-M, Fang Y-J, Zhang C-X. Association of plant-based dietary patterns with the risk of colorectal cancer: a large-scale case–control study. Food Funct. 2022;13(20):10790–801.
38. Kim H, Lee K, Rebholz CM, Kim J. Association between unhealthy plant-based diets and the metabolic syndrome in adult men and women: a population-based study in South Korea. Br J Nutr. 2021;125(5):577–90.
39. Arts IC, PC H. Polyphenols and disease risk in epidemiologic studies. Am J Clin Nutr. 2005;81(1):S317–25.
40. Voorrips LE, Goldbohm RA, Verhoeven DTH, van Poppel GAFC, Sturmans F, Hermus RJJ. ea. Vegetable and fruit consumption and lung cancer risk in the Netherlands cohort study on diet and cancer. Cancer Causes Control. 2000;11(2):101–15.
41. Godos J, Bella F, Sciacca S, Galvano F, Grosso G. Vegetarianism and breast, colorectal and prostate cancer risk: an overview and meta-analysis of cohort studies. J Hum Nutr Dietetics. 2017;30(3):349–59.
42. Tavasoli S, Taheri M, Taheri F, Basiri A. FB. A: Evaluating the associations between urinary excretion of magnesium and that of other components in calcium stone-forming patients. Int Urol Nephrol 2018:1–6.
43. SN. Y: In vitro digestion/Caco-2 cell model for assessing dietary folate bioavailability. 2009.
44. Fava M. Folate in depression: efficacy, safety, differences in formulations, and clinical issues. J Clin Psychiatry. 2009;70(5):12–7.

Publisher's Note