

Original Article



The Lack of Association between Plant-Based Dietary Pattern and Breast Cancer: a Hospital-Based Case-Control Study

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ABSTRACT

Our purpose was to assess the association between plant-based dietary patterns and breast cancer (BrCa) among Iranian women. This hospital-based case-control study included 150 newly diagnosed BrCa cases and 150 age-matched controls from the Cancer Research Center, Imam Khomeini hospital, Iran. Three indices of a plant-based diet were first calculated: plant-based diet index (PDI), the healthy PDI (hPDI), and the unhealthy PDI (uPDI). In the overall PDI, all plant foods scored positively. In hPDI and uPDI, healthy and less healthy plant foods scored positive, respectively. The adjusted odds ratio (OR) in the highest adherence of PDI was 1.00 (95% confidence interval [CI], 0.55–1.83). In hPDI, 0.89 (95% CI, 0.49–1.62); in uPDI, 1.80 (95% CI, 0.95–3.42). The adjusted OR after subgroup analysis for body mass index (BMI) was as follow, BMI > 25: 0.77(95% CI, 0.37–1.61) comparing highest with the lowest tertile of PDI, 0.91(95% CI, 0.44–1.89) comparing highest with the lowest tertile of hPDI and this value for uPDI was 2.04 (95% CI, 0.91–4.56). BMI < 25: OR for top tertile of PDI was 1.82 (95% CI, 0.48–6.93), top tertile of hPDI was 1.47 (95% CI, 0.35–6.22) and top tertile of uPDI was 2.29 (95% CI, 0.54–9.70). Our results revealed no significant association between none of the PDIs and the chance of BrCa in Iranian women. Continued and expanded research, evaluated by different methods and BrCa is urgently needed to build the foundation for future progress in evidence-based public health efforts.

Keywords: Diet; Breast cancer; Cancer

INTRODUCTION

The general term cancer refers to many diseases in which the body's cells proliferate uncontrollably, invade nearby tissues, and spread throughout the body through the circulatory and lymphatic systems [1]. The world health organization has identified cancer as the second leading cause of death worldwide and it's predicted that there are 16 million new cancer cases and 10 million cancer deaths annually in 2020 [2]. The risk of breast cancer

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Conflict of Interest

The authors declare that they have no competing interests.

(BrCa) increases with some immutable factors such as age, genetic and familial diseases, menstruation at a younger age and menopause at an older age [3]. Factors that may be modifiable include late pregnancy, avoidance of breastfeeding, radiation exposure [4], and the use of hormone replacement therapy (HRT) [5,6]. Some of the factors contributing to BrCa can be completely changed, including body mass index (BMI) [7], lifestyle [8], eating habits [9] and, diet [6].

In addition, the results of studies showed that eating habits play an important role in preventing various types of cancer, especially BrCa [10-12]. A study by Jung et al., [7] showed that the amount and composition of dietary fat in the adult's dietary plan might be important in preventing BrCa. The findings of a study by Farvid et al. [5] also supported the hypothesis that higher fiber intake reduced the risk of BrCa. According to the previous studies to date, the relationship between consumption of different dietary patterns and its effect on diseases such as Alzheimer's [13], BrCa [10], cardiovascular disease [14], and cardiometabolic risk factors [15] has been seen. A plant-based diet is one of the dietary patterns that has been considered by researchers [16]. Plant-based dietary patterns are those that emphasize plant-based foods that contain less or no animal products. It seems that the plant-based dietary pattern has the potential to control and prevent chronic diseases, including type 2 diabetes and gestational diabetes mellitus [12,16,17], cardiovascular disease [18,19], and cancer [20]. Plant-based dietary patterns were introduced as 3 indices, including the general plant-based diet index (PDI), the healthy PDI (hPDI), and the unhealthy PDI (uPDI) [11]. PDI is a high-quality diet rich in whole grains, fruits, and, vegetables, as well as nuts. This index does not include juices, refined grains and, sweets, but these are part of the hPDI and uPDI [18,21]. In 2016, Pennicook-Sawyers et al. [22] noted in their cohort study that individuals who adhere to vegetarian dietary patterns did not experience a lower odd of BrCa in contrast with non-vegetarians. One possible mechanism for reducing the risk of BrCa by following a plant-based diet is that in this type of diet, people consume higher amounts of fruits and vegetables as well as soy, and a lower BMI is a characteristic of people who follow a vegetarian diet [22]. On the other hand, consumption of fruits and vegetables can prepare an antioxidant environment to maintain cell membranes, reduce and clear nitrite and free radicals [23]. As some studies have suggested vegan diets contain non-essential amino acids that can regulate the insulin-glucagon axis and also, they can improve insulin sensitivity of issues, which in turn reduces liver production and serum level of insulin-like growth factor (IGF)-1 and IGF-1 is known to promote cancer development by inhibiting apoptosis and stimulating cell proliferation [23].

Therefore, we hypothesized that adherence to plant-based dietary patterns might be associated with the risk of BrCa. Therefore, the present study investigates the relationship between plant-based dietary patterns and BrCa in women referred to the Iran Cancer Research Center located in Imam Khomeini Hospital in Tehran, the capital city of Iran.

MATERIALS AND METHODS

Study design and sample

In this case-control study, participants were recruited across the cancer research center affiliated with Imam Khomeini Hospital. Also, we selected 150 women recently diagnosed with BrCa as well as 150 seemingly healthy women. Posters for research collaboration were attached in different wards to gather age-matched and healthy women without having a family relationship with our cases, including dermatology, urology, orthopedics, etc. In this

study, the patient cases were among women with a 3-month history of a BrCa diagnosis. The reason for this choice was to reduce errors in their food reporting.

Eligibility criteria

All cases with a history of other cancers were excluded from the study, and even the control group selected in this study had no history of BrCa. Women who had a previous history of breast or other cancers or diagnosis of BrCa more than 3 months were not eligible for this study. In addition, those who were on a special diet were not included in the study. On the other hand, age-matched controls were selected from healthy women, who have no relationship with BrCa patients or had no family history of BrCa. In addition to age, we did our best to match controls in terms of socioeconomic status with the cases. Controls with the following inclusion criteria: female, no history of any malignancy, cysts and, medical disorder, having no special diet, were selected. Controls were randomly selected through poster installation, from visitors, relatives and friends of non-cancer patients in other wards of Imam Khomeini Hospital, such as dermatology, urology, orthopedic, etc., which had no family relationship with cases. Eligible subjects culminated in 150 cases and 150 controls.

Demographics

The variables of this study include age (year), weight (kg), height (cm), BMI (kg/m²), marital status (single, married, divorced, widowed), physical activity (PA) level (low activity, moderate, high), smoking status (never smoked), alcohol consumption (never used), and also menarche age (year), weight at 18-year-old (kg), first pregnancy age (year), menopause age (year), length of breastfeeding (year), dietary supplement and medication use (never used), history of HRT (percentage), comorbidities (percentage), family history of BrCa (yes or no) were assessed. To retrieve information from the participants, 2 trained interviewers were used. The face-to-face interview lasted 45 minutes. All items such as smoking and PA, income and, drug history was collected using a valid questionnaire.

Assessment of dietary intake

To evaluate dietary intakes of subjects using a valid and reliable semi-quantitative food frequency questionnaire (FFQ), this FFQ had 147 food items [24]. Trained researchers via face-to-face did interviews, asking subjects to report their frequency of intake of each food item during the past year daily, weekly, or monthly. These reports were converted to daily intakes. The nutrient content of each food item was calculated based on the protocol using Nutritionist IV software designed for Iranian foods.

Identification of PDI

We used this dietary data to generate 3 versions of a plant-based diet [21]. We made 18 food groups based on nutrient and culinary similarities within the larger categories of healthy plant foods (whole grains, fruits, vegetables, nuts, legumes, vegetable oils, tea/coffee), less healthy plant foods (fruit juices, refined grains, potatoes, sugar-sweetened beverages, sweets/desserts), and animal foods (animal fat, dairy, eggs, fish/seafood, meat, miscellaneous animal-based foods) (**Supplementary Table 1**). We ranked food groups into tertiles and given positive or reverse scores. With positive scores, participants above the highest tertile of a food group received a score of 3, and those below the lowest tertile received a score of 1. With reverse scores, this pattern of scoring was inverted. For making PDI, plant food groups were given positive scores, while animal food groups were given reverse scores. For creating hPDI, positive scores were allocated to healthy plant food groups, and reverse scores to less healthy plant food groups and animal food groups. Finally, for uPDI, positive scores were allocated

to less healthy plant food groups, and reverse scores to healthy plant food groups and animal food groups. The 18 food group scores were summed to established the indices.

Assessment of anthropometric measures

Afterward, the weight was recorded to the nearest 100 g while the subjects were minimally clothed and barefoot and stood on a digital scale (Seca, Hamburg, Germany). Using a stadiometer, the height of participants was measured and recorded to the nearest 0.5 cm when they stood upright without shoes while their shoulders were in a normal position. BMI was obtained by dividing the weight of subjects by the square of their height (m^2). If the subjects had BMI in the range of 25–30 kg/m^2 and $\geq 30 kg/m^2$, they were considered overweight and obese, respectively [25]. Using an outstretched tape measure, waist circumference was measured at umbilical fossa without applying pressure on body surfaces, recorded to the nearest 0.1 cm.

PA

PA was evaluated through the short weekly original International Physical Activity Questionnaire (IPAQ) form [26], which is used to assess habitual PA during the past seven days. For each type of activity, IPAQ data were converted to metabolic equivalent scores (MET-minutes/week) by multiplying the minutes devoted to each activity class by the specific MET score of that activity [27].

Statistical method

The SPSS version 22.0 for Windows (IBM Corp., Armonk, NY, USA) was used to perform the statistical analysis. Individuals were categorized according to the tertiles of PDI, hPDI, and uPDI. Characteristic and dietary intakes of participants according to the tertile of PDI, hPDI, and uPDI were tested by 1-way analysis of variance. The χ^2 tests also were performed for comparing qualitative variables. Moreover, binary logistic was used to analyze the association between tertiles of PDI, hPDI, and uPDI and the risk of BrCa after confounders adjustment. The results were adjusted for BMI, PA (MET-minutes/week), energy intake, education, marital status (married or single/divorced/widowed), physical activity level, menopause status, alcohol use, smoking status, dietary supplements and medication use, comorbidities, history of HRT and oral contraceptive use, age at menarche, time since menopause, weight at age 18 years old, first pregnancy age, length of breastfeeding and family history of BrCa. To assess potential interaction effects of BMI, we used binary logistic after subgroup analysis for BMI. The level of significance was set at 0.05.

RESULTS

Sociodemographic, anthropometric, and lifestyle variables for both BrCa cases and controls are shown in **Table 1**. The mean age of participants was 46.6 years. Women in the control group have higher mean age at first pregnancy (20.1 years), breastfeeding length (4.24 years), and history of BrCa (51.9%) than cases. The cases and controls were similar for all other variables.

Dietary intakes of participants across tertiles of PDI, hPDI, and uPDI are presented in **Tables 2 and 3**. According to **Table 2**, vitamin D, vitamin B12 intake increased significantly across tertiles of PDI and hPDI. Moreover, participants with great adherence to PDI had a higher intake of vitamin A, vitamin C, vitamin B9 and also the Participants in the top tertile of hPDI, had a lower intake of fat, vitamin B12, D compared to the first tertile of hPDI. Top tertile of

Table 1. General characteristics of breast cancer cases and controls

Characteristics	Control (n = 150)	Case (n = 150)	p value*
Age (yr)	46.6 ± 10.7	46.6 ± 10.7	0.43
Weight (kg)	72.0 ± 13.4	72.5 ± 12.3	0.37
Height (cm)	159 ± 6.40	160 ± 5.37	0.26
First menstruation age (yr)	14.4 ± 9.72	13.4 ± 1.65	0.14
BMI (kg/m ²)	28.0 ± 5.21	28.1 ± 4.66	0.26
Weight at 18-year-old (kg)	51.4 ± 9.18	52.0 ± 8.92	0.71
First pregnancy age (yr)	20.1 ± 4.66	19.1 ± 6.90	0.01
Menopause age (yr)	45.9 ± 5.22	48.3 ± 4.60	0.09
Length of breastfeeding (yr)	4.24 ± 3.50	3.55 ± 2.74	0.01
Marital status			0.06
Married	136 (51.3)	129 (48.7)	
Single	11 (57.9)	8 (42.1)	
Divorced	2 (28.6)	5 (71.4)	
Widowed	1 (11.1)	8 (88.9)	
Smoking			0.36
Never smoked	147 (50.5)	144 (49.5)	
Alcohol			0.60
Never used	149 (50.2)	148 (49.8)	
Dietary supplement use	70 (51.5)	66 (48.5)	0.09
Medication use	86 (49.4)	88 (50.6)	0.44
HRT	138 (49.3)	142 (50.7)	0.35
Comorbidities	69 (43.9)	88 (56.1)	0.14
Activity level			0.10
Low	7 (25.0)	21 (75.0)	
Moderate	31 (53.6)	27 (46.3)	
High	15 (51.7)	14 (48.3)	
Family history of BrCa	120 (51.9)	111 (48.1)	0.01

Values are shown as mean ± standard deviation or number (%).

The χ^2 test for categorical variables and t-test for continuous variables have been used.

BMI, body mass index; HRT, hormone replacement therapy; BrCa, breast cancer.

*The p value less than 0.05 was considered significant.

uPDI was associated with greater intake of vitamin D and vitamin B12. In contrast, there was a lower intake of vitamin A, C, B9 in participants with higher adherence to uPDI. The cases had significantly lower animal fat, vitamin D than controls (**Table 2**).

Dairy and red and processed meat consumption decreased and, legumes intake increased significantly across tertiles of PDI and hPDI. In comparison to the first, participants in the top tertile of hPDI and uPDI had a lower intake of refined grains and sweets, and desserts. Moreover, participants in the top tertile of PDI had a higher intake of fruits, vegetables, legumes, vegetable oil, tea and coffee, refined grains, sugar and sweetened beverages, sweets, and desserts. Participants in the top tertile of hPDI, had a lower intake of nuts, fruit juice, potatoes, dairy, egg, fish and seafood, and red or processed meat compared to the first tertile. A higher uPDI is associated with a greater intake of dairy and red or processed meat intake. Lower intake of fruits, vegetables, legumes, vegetable oil, tea and coffee, and sugar and sweetened beverages was found in participants with higher adherence to uPDI. Cases had significantly lower sugar and sweetened beverages, and red or processed meat than controls (**Table 3**).

Odds ratio (OR) and 95% confidence intervals (CIs) for cases and controls across tertiles of PDI, hPDI, and uPDI are reported in **Table 4**. The results showed that there was no association between PDI, hPDI, uPDI and BrCa risk after adjustment for potential confounders (comparing highest tertile with the lowest, for PDI (OR, 1.00; 95% CI, 0.55–1.83), for hPDI (OR, 0.89; 95% CI, 0.49–1.62), for uPDI (OR, 1.80; 95% CI, 0.95–3.42). In **Table 5**, the association of PDI, hPDI, uPDI score using subgroup analysis (by BMI) and risk

Table 2. Dietary intakes of the study participants (macronutrients, vitamins, and minerals) across the tertiles of PDI, hPDI, and uPDI

Variables	PDI score			hPDI score			uPDI score					
	T1 (n = 105)	T2 (n = 101)	T3 (n = 94)	p value*	T1 (n = 103)	T2 (n = 94)	T3 (n = 103)	p value*	T1 (n = 93)	T2 (n = 111)	T3 (n = 96)	p value*
Energy (kcal/day)	2,568 ± 1,071	2,712 ± 710	3,876 ± 7,374	0.06	3,233 ± 1,348	2,625 ± 710	3,187 ± 7,052	0.53	3,089 ± 1,030	3,504 ± 6,818	2,414 ± 754	0.17
Macronutrient												
Carbohydrate (g/day)	366 ± 126	409 ± 97.9	631 ± 1,381	0.04	472 ± 196	395 ± 103	519 ± 1,322	0.54	454 ± 172	548 ± 1,274	376 ± 111	0.28
Protein (g/day)	91.0 ± 33.9	94.3 ± 29.4	133 ± 290	0.14	109 ± 44.9	91.8 ± 28.8	113 ± 277	0.62	112 ± 40.7	123 ± 266	77.8 ± 23.6	0.12
Total fat (g/day)	90.4 ± 60.0	86.7 ± 32.9	107 ± 129	0.18	110 ± 61.8	83.7 ± 33.5	88.1 ± 122	0.04	103 ± 36.5	104 ± 127	74.0 ± 33.7	0.01
Dietary fiber (g/day)	52.9 ± 25.4	60.6 ± 22.4	92.6 ± 207	0.04	68.1 ± 33.0	58.2 ± 26.7	76.6 ± 198	0.55	66.0 ± 29.8	81.1 ± 191	54.5 ± 25.9	0.27
Vitamins, minerals												
Thiamin (mg/day)	2.23 ± 0.92	2.46 ± 0.74	4.12 ± 12.0	0.10	2.85 ± 1.41	2.43 ± 0.79	3.39 ± 11.4	0.61	2.72 ± 1.34	3.61 ± 11.0	2.26 ± 0.79	0.34
Riboflavin (mg/day)	2.34 ± 0.92	2.35 ± 0.78	3.22 ± 5.98	0.12	2.76 ± 1.09	2.36 ± 0.79	2.72 ± 5.72	0.66	2.76 ± 0.93	3.06 ± 5.50	1.99 ± 0.73	0.07
Niacin (mg/day)	26.5 ± 12.1	27.9 ± 9.53	42.9 ± 114	0.14	32.6 ± 16.1	27.2 ± 9.01	36.0 ± 109	0.63	32.6 ± 14.9	38.6 ± 105	24.1 ± 7.95	0.27
Vitamin B6 (mg/day)	2.27 ± 0.96	2.38 ± 0.60	3.32 ± 6.00	0.06	2.71 ± 1.15	2.31 ± 0.71	2.86 ± 5.72	0.51	2.81 ± 0.86	3.00 ± 5.55	2.05 ± 0.60	0.12
Folate (µg/day)	621 ± 192	704 ± 161	991 ± 1,502	< 0.001	787 ± 279	681 ± 187	820 ± 1,440	0.50	772 ± 240	868 ± 1,389	639 ± 187	0.16
Vitamin D (µg/day)	2.08 ± 1.66	1.49 ± 1.16	1.34 ± 1.20	< 0.001	2.03 ± 1.69	1.55 ± 1.32	1.37 ± 1.04	< 0.001	1.97 ± 1.20	1.75 ± 1.54	1.23 ± 1.31	0.01
Vitamin E (mg/day)	15.4 ± 10.8	14.4 ± 4.38	18.8 ± 27.3	0.16	171 ± 10.7	14.5 ± 5.23	16.8 ± 26.1	0.50	16.8 ± 5.83	17.9 ± 26.5	13.5 ± 5.48	0.16
Vitamin A (µg/day)	668 ± 291	691 ± 272	810 ± 383	< 0.001	769 ± 353	678 ± 276	710 ± 324	0.12	846 ± 318	749 ± 333	565 ± 243	< 0.001
Vitamin C (mg/day)	204 ± 112	237 ± 74.4	286 ± 109	< 0.001	239 ± 103	223 ± 89.7	260 ± 117	0.04	275 ± 97.8	236 ± 92.0	214 ± 117	< 0.001
Vitamin B12 (µg/day)	4.20 ± 2.17	3.64 ± 1.60	3.53 ± 1.58	0.01	4.53 ± 1.85	3.80 ± 2.07	3.08 ± 1.20	< 0.001	4.46 ± 1.74	4.00 ± 1.97	2.93 ± 1.37	< 0.001
Zn (mg/day)	13.2 ± 5.20	13.9 ± 4.74	22.0 ± 57.0	0.10	16.0 ± 7.41	13.8 ± 4.97	18.5 ± 54.5	0.60	16.5 ± 6.70	19.7 ± 52.4	11.8 ± 4.07	0.20
Ca (mg/day)	1,442 ± 512	1,454 ± 476	1,851 ± 2,199	0.04	1,681 ± 644	1,448 ± 495	1,582 ± 2,082	0.45	1,702 ± 530	1,762 ± 2,015	1,233 ± 470	< 0.001
Fe (mg/day)	36.7 ± 19.4	39.6 ± 16.0	60.8 ± 103	< 0.001	46.5 ± 30.2	37.9 ± 14.3	50.5 ± 97.4	0.33	48.1 ± 22.9	52.5 ± 94.7	33.9 ± 18.9	0.07

Values are shown as mean ± standard deviation or number (%).

One-way analysis of variance has been used.

PDI, plant-based diet index; hPDI, healthy plant-based diet index; uPDI, unhealthy plant-based diet index.

*The p value less than 0.05 was considered significant.

Table 3. Dietary intakes of the study participants (18 food groups) across the tertiles of PDI, hPDI, and uPDI

Food groups	PDI score			hPDI score			uPDI score					
	T1 (n = 105)	T2 (n = 101)	T3 (n = 94)	p value*	T1 (n = 103)	T2 (n = 94)	T3 (n = 103)	p value*	T1 (n = 93)	T2 (n = 111)	T3 (n = 96)	p value*
Whole grain (g/day)	140 ± 179	163 ± 153	516 ± 3,026	0.22	177 ± 315	156 ± 147	453 ± 2,883	0.38	230 ± 306	427 ± 2,780	112 ± 135	0.40
Fruits (g/day)	517 ± 296	652 ± 244	709 ± 303	< 0.001	570 ± 258	586 ± 269	708 ± 327	< 0.001	726 ± 296	605 ± 273	542 ± 284	< 0.001
Vegetables (g/day)	186 ± 99	209 ± 97	240 ± 116	< 0.001	211 ± 112	200 ± 97.8	221 ± 107	0.38	260 ± 106	213 ± 102	160 ± 86.4	< 0.001
Nuts (g/day)	6.71 ± 18.0	8.45 ± 29.6	12.3 ± 19.3	0.21	8.89 ± 19.1	9.69 ± 31.6	8.66 ± 16.3	0.94	11.7 ± 18.6	9.06 ± 28.9	6.50 ± 18.5	0.29
Legumes (g/day)	42.9 ± 31.5	56.1 ± 32.0	64.9 ± 43.6	< 0.001	51.8 ± 32.6	45.6 ± 26.0	64.5 ± 46.1	< 0.001	63.8 ± 45.6	59.5 ± 34.5	38.9 ± 23.0	< 0.001
Vegetables oil (g/day)	11.7 ± 2.41	1.89 ± 2.89	2.69 ± 3.89	< 0.001	0.87 ± 1.96	1.81 ± 3.01	2.98 ± 3.83	< 0.001	3.23 ± 3.88	1.59 ± 3.04	0.93 ± 1.76	< 0.001
Tea and coffee (g/day)	641 ± 457	790 ± 520	1,019 ± 748	< 0.001	839 ± 620	810 ± 609	780 ± 578	0.78	960 ± 609	768 ± 621	712 ± 546	0.01
Fruits juice (g/day)	40.0 ± 103	30.3 ± 55.2	89.7 ± 170	< 0.001	64.6 ± 117	50.6 ± 122	41.6 ± 120	0.38	42.7 ± 101	60.4 ± 138	52.2 ± 114	0.58
Refined grains (g/day)	316 ± 131	355 ± 157	418 ± 241	< 0.001	429 ± 222	357 ± 145	298 ± 151	< 0.001	313 ± 144	374 ± 219	394 ± 167	< 0.001
Potatoes (g/day)	12.6 ± 75.1	8.51 ± 7.02	13.3 ± 29.3	0.43	18.4 ± 76.4	8.24 ± 24.3	4.51 ± 11.6	0.09	6.99 ± 13.6	14.0 ± 73.8	9.75 ± 24.4	0.56
Sugar & sweetened beverages (g/day)	11.2 ± 36.5	8.81 ± 13.6	28.9 ± 73.1	< 0.001	32.6 ± 74.4	10.5 ± 23.9	4.26 ± 11.5	< 0.001	7.32 ± 21.9	12.6 ± 25.9	28.2 ± 75.1	< 0.001
Sweets & desserts (g/day)	23.5 ± 20.1	24.5 ± 14.6	37.0 ± 30.0	< 0.001	39.5 ± 26.9	26.4 ± 19.8	18.3 ± 15.3	< 0.001	24.3 ± 17.6	28.9 ± 23.7	30.8 ± 26.2	0.13
Animal fat (g/day)	31.9 ± 30.8	27.3 ± 23.1	26.6 ± 24.7	0.30	37.2 ± 30.5	25.1 ± 22.5	23.4 ± 23.6	< 0.001	34.1 ± 26.9	28.9 ± 28.1	23.2 ± 23.4	0.02
Dairy (g/day)	407 ± 221	364 ± 210	370 ± 211	0.05	433 ± 222	370 ± 219	307 ± 171	< 0.001	428 ± 196	393 ± 210	288 ± 203	< 0.001
Fish & sea foods (g/day)	12.6 ± 16.5	9.85 ± 9.55	10.1 ± 10.2	0.22	14.6 ± 17.1	9.57 ± 7.84	8.38 ± 9.91	< 0.001	13.3 ± 11.4	12.0 ± 16.1	7.18 ± 7.50	< 0.001
Egg (g/day)	19.7 ± 16.4	18.5 ± 14.1	19.3 ± 18.1	0.80	23.7 ± 19.5	18.3 ± 12.0	15.1 ± 14.8	< 0.001	22.1 ± 17.0	19.6 ± 18.5	15.5 ± 11.3	0.01
Red or processed meats (g/day)	57.7 ± 49.1	52.5 ± 46.1	38.8 ± 24.9	< 0.001	61.8 ± 43.2	49.9 ± 43.4	38.5 ± 37.9	< 0.001	66.6 ± 60.2	47.3 ± 29.5	37.2 ± 26.9	< 0.001
Animal-based food (g/day)	11.5 ± 17.7	10.6 ± 15.5	16.2 ± 51.9	0.42	16.9 ± 24.6	9.86 ± 18.9	11.1 ± 45.4	0.25	15.6 ± 20.7	14.1 ± 44.2	8.28 ± 23.3	0.24

Values are shown as mean ± standard deviation or number (%).

One-way analysis of variance has been used.

PDI, plant-based diet index; hPDI, healthy plant-based diet index; uPDI, unhealthy plant-based diet index.

*The p value less than 0.05 was considered significant.

Table 4. ORs and 95% CI for breast cancer according to tertiles of PDI, hPDI, and uPDI scores

Breast cancer	PDI score				hPDI score				uPDI score			
	T1 (n = 105)	T2 (n = 101)	T3 (n = 94)	p value	T1 (n = 103)	T2 (n = 94)	T3 (n = 103)	p value	T1 (n = 93)	T2 (n = 111)	T3 (n = 96)	p value
	OR	OR (95% CI)	OR (95% CI)		OR	OR (95% CI)	OR (95% CI)		OR	OR (95% CI)	OR (95% CI)	
Crude	1	1.04 (0.60–1.79)	1.01 (0.58–1.77)	0.99	1	0.94 (0.53–1.65)	0.89 (0.51–1.53)	0.91	1	1.39 (0.80–2.43)	1.63 (0.91–2.90)	0.23
Model 1*	1	1.03 (0.60–1.79)	1.00 (0.57–1.77)	0.99	1	0.94 (0.53–1.67)	0.88 (0.50–1.55)	0.91	1	1.39 (0.79–2.43)	1.65 (0.92–2.95)	0.22
Model 2†	1	1.08 (0.60–1.95)	1.00 (0.55–1.83)	0.95	1	0.96 (0.53–1.77)	0.89 (0.49–1.62)	0.93	1	1.49 (0.81–2.74)	1.80 (0.95–3.42)	0.18

Binary logistic regression models were used to obtain ORs and 95% CI. The overall trend of ORs across increasing tertiles was examined by considering the median score in each category as a continuous variable.

OR, odds ratio; CI, confidence interval; PDI, plant-based diet index; hPDI, healthy plant-based diet index; uPDI, unhealthy plant-based diet index.

*Model 1: adjusted for age (continuous) and energy intake (kJ/day or kcal/day) and body mass index; †Model 2: this model was additionally adjusted for physical activity, family history of cancer, socioeconomic status, smoking, alcohol consumption, menopause status, first menstruation age, weight at 18 years old, length of breastfeeding, hormone replacement therapy, dietary supplement use, medication use, comorbidities.

Table 5. ORs and 95% CI for breast cancer according to tertiles of PDI, hPDI, and uPDI scores

Breast cancer	PDI score				hPDI score				uPDI score			
	T1 (n = 105)	T2 (n = 101)	T3 (n = 94)	p value	T1 (n = 103)	T2 (n = 94)	T3 (n = 103)	p value	T1 (n = 93)	T2 (n = 111)	T3 (n = 96)	p value
	OR	OR (95% CI)	OR (95% CI)		OR	OR (95% CI)	OR (95% CI)		OR	OR (95% CI)	OR (95% CI)	
Crude (all cases)	1	1.04 (0.60–1.79)	1.01 (0.58–1.77)	0.99	1	0.94 (0.53–1.65)	0.89 (0.51–1.53)	0.91	1	1.39 (0.80–2.43)	1.63 (0.91–2.90)	0.23
Model 1* (BMI > 25)	1	1.23 (0.64–2.39)	0.81 (0.42–1.55)	0.46	1	0.99 (0.50–1.96)	0.79 (0.42–1.51)	0.73	1	1.51 (0.79–2.86)	1.81 (0.92–3.56)	0.19
Model 2† (BMI > 25)	1	1.36 (0.64–2.87)	0.77 (0.37–1.61)	0.34	1	1.01 (0.47–2.19)	0.91 (0.44–1.89)	0.95	1	1.63 (0.77–3.46)	2.04 (0.91–4.56)	0.20
Model 1* (BMI < 25)	1	0.70 (0.24–2.02)	1.87 (0.54–6.48)	0.27	1	1.08 (0.35–3.33)	1.40 (0.42–4.62)	0.83	1	1.39 (0.41–4.76)	1.78 (0.50–6.33)	0.67
Model 2† (BMI < 25)	1	0.68 (0.20–2.32)	1.82 (0.48–6.93)	0.37	1	1.27 (0.33–4.82)	1.47 (0.35–6.22)	0.86	1	1.86 (0.47–7.29)	2.29 (0.54–9.70)	0.51

Binary logistic regression models were used to obtain ORs and 95% CI. The overall trend of ORs across increasing tertiles was examined by considering the median score in each category as a continuous variable.

OR, odds ratio; CI, confidence interval; BMI, body mass index; PDI, plant-based diet index; hPDI, healthy plant-based diet index; uPDI, unhealthy plant-based diet index.

*Model 1: adjusted for age (continuous) and energy intake (kJ/day or kcal/day); †Model 2: this model was additionally adjusted for physical activity, family history of cancer, socioeconomic status, smoking, alcohol consumption, menopause status, first menstruation age, weight at 18 years old, length of breastfeeding, hormone replacement therapy, dietary supplement use, medication use, comorbidities.

of BrCa was not statistically significant. Within > 25 BMI, PDI score was not associated with BrCa risk (OR, 1.82; 95% CI, 0.48–6.93). The score of hPDI also was not associated with BrCa risk (OR, 1.47; 95% CI, 0.35–6.22). The uPDI score was similar for BrCa cases and controls independent of the BrCa risk (OR, 2.29; 95% CI, 0.54–9.7). There was no other significant association observed between each score and risk of BrCa in women who had < 25 BMI.

DISCUSSION

In this case-control study, we did not find a significant association between plant-based dietary patterns and the risk of BrCa. As mentioned earlier, BMI is one of the most important factors in the development of BrCa [7]. However, after the subgroup analysis for BMI, no significant relationship was seen based on BMI above 25 and below 25.

This is the first study assessing the relationship between plant-based dietary patterns and the risk of BrCa in Iranian women to the best of our knowledge. Some studies were conducted on the effect of vegetarian diets and dietary patterns on a lower risk of BrCa [28–31]. In a study performed by Chang et al [28], vegetarians with higher daily consumption of soy isoflavones than non-vegetarians, as well as higher serum albumin levels were inversely associated with BrCa risk. On the other hand, plant-based diets have a protective role against the risk of BrCa,

in contrast to meat and processed meat in an unhealthy dietary pattern that is associated with a higher risk of BrCa [28]. Also, a limited number of previous studies indicated that higher soy and fiber consumption [32-35] have an inverse association with odds of BrCa, whereas red meat has been suggested to increase the risk of BrCa only in premenopausal women [36-39]. The results of Kim et al. [40] prospective cohort study indicated that the odds of BrCa increased by 1.3 times in all postmenopausal women by grilled meat consumption. It is also showed that high cholesterol diets and eating irregular meals increase BrCa risk in all groups of women [40]. Concerning the general, hPDI and uPDI and the risk of cancer, very limited studies have been performed on different populations [39,41]. In this regard, the results of a case-control study by Liu et al. [39] showed that a high intake of fiber, nuts, vegetable fats, and vegetable protein could significantly reduce the risk of BrCa in women. A clinical trial in the United States of 14 patients with prostate cancer showed that an average increase in whole grain consumption was associated with a significant decrease in prostate-specific antigen levels. They also reported that plant-based diets play an important and immediate role in the progression of prostate cancer. It also has a potential role in the management of recurrent types of the disease [41]. In contrast, a study by Godos et al. [30] showed no association between plant diets with complete deprivation of protein sources from the diet with greater benefits for human health. There is no significant relation between a vegetarian diet and a lower risk of some cancers, including BrCa, colorectal and prostate cancer, compared to a non-vegetarian diet [30]. The results of a dose-response meta-analysis by Benisi-Kohansal et al. [42] also suggested that high consumption of whole grains was generally associated with a lower risk of death from cancer and cardiovascular disease. However, the same amount of whole grain consumption has no significant relationship with mortality from certain cancers [42]. As mentioned, the study results of the relationship between plant-based dietary patterns and the risk of cancers, including BrCa, are contradictory. To explain the controversies, we can compare the average consumption of fruits and vegetables in Iran with other parts of the world. According to the World Health Organization and the Food and Agriculture Organization recommendations, the average daily consumption of fruits and vegetables should be at least 400 grams [43]. The consumption of fruits and vegetables in Iran is lower than in other countries and less than the World Health Organization and the Food and Agriculture Organization [43-45]. In this regard, Esmailzadeh et al., [45] in their study, stated that the average consumption of fruits and vegetables in Iran is in the range of 228-186 g per day. Also, in the study by Esteghamati et al., [44] the average intake of fruits was 1.26 units and the average intake of vegetables was about 1.32 units. Another possible cause for conflicting results is considering a wide range of healthy and unhealthy plant foods with possible interactions in the form of general, healthy and unhealthy plant-based dietary patterns. Evidence also suggests the undeniable impact of genetics, hormonal status, tumor receptor type, and environmental conditions such as lifestyle and eating habits of adolescents in relation to BrCa risk [46-48]. Studies have shown that genetics can be responsible for 30% of BrCas, and women with a family history of BrCa are twice as likely to develop BrCa [46].

The possible mechanism of the beneficial effect of vegetarian diets on cancer was described by the study of Gerber [49]. They suggested that dietary fiber might decrease levels of plasma estrogen through inhibiting colonic β -D-glucuronidase activity. Finally, it reduces deconjugation and estrogen reabsorption and increases fecal excretion [49-51]. Dietary fiber can reduce the risk of BrCa by increasing insulin sensitivity and decreasing IGFs [52,53].

Some limitations should be addressed. The main issue when considering results from the present study is that: 1) this study included only a small number of BrCa cases (n = 150), 2)

this was a case-control study and the cause-and-effect relationship is not completely clear, 3) due to the dependence of the FFQ on memory, we may encounter a measurement error in the field of food intake. We tried to reduce these problems by getting help from experts and increasing the reviews, and D) lack of information about the type of BrCa receptor. Our study has several strengths; 1) this is the first study to examine the association between plant-based diets and the risk of BrCa, which is particularly prevalent in the female population, 2) Since age is the most important factor of BrCa [54], we matched the case and control groups in terms of age, and 3) Also, in this study, the effect of a wide range of confounders were adjusted to estimate the relationship between a plant-based diet and BrCa risk.

CONCLUSION

In conclusion, we did not observe any evidence for the protective association of plant-based dietary pattern and BrCa in women with BMI > 25. Women with BMI < 25 referred to the Iran Cancer Research Center located in Imam Khomeini Hospital in Tehran. Due to the limitations of the present study, it is suggested that future studies examine the relationship between plant-based diets and BrCa in prospective studies. It is also suggested that information about the type of BrCa receptor be considered to examine this relationship more accurately.

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SUPPLEMENTARY MATERIAL

Supplementary Table 1

Examples of food items constituting the 18 food groups

[Click here to view](#)

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