Dietary Habits and Physical Activity are Associated With the Risk of Breast Cancer Among Young Iranian Women: A Case-control Study on 1010 Premenopausal Women

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Abstract

This case-control study was conducted on 1010 women to examine the association of several dietary and behavioral factors with the risk of breast cancer. It was reviled that physical activity and dietary pattern are important factors in the incidence of breast cancer. This helps in providing more pragmatic approaches in cancer prevention.

Background: Several studies conducted in developed countries introduced diet and physical inactivity as major risk factors for several types of cancers. However, the impact of diet and physical inactivity on the risk of breast cancer (BC) is understudied, and the limited findings are controversial. In addition, no or limited knowledge is available from the developing world. **Patients and Methods:** This case-control study was performed from November 2014 to March 2016 on 1010 young women aged 20 to 50 years who were newly diagnosed with BC. Data was obtained via a validated questionnaire and the global physical activity questionnaire (GPAQ2). Also, patients' medical and histopathology reports were reviewed. **Results:** The results of multiple logistic regression suggested that, except for the common risk factors for BC (older marital age, family history of BC, smoking, and being a passive smoker), eating red meat (adjusted odds ratio [aOR] >8 portions/week [p/w] vs. 0-2 p/w, 1.15; 95% confidence interval [CI], 1.04-1.28); eating fish (aOR >8 p/w vs. 0-2 p/w, 1.55; 95% CI, 1.12-2.76), fruit consumption (aOR 0-4 p/w vs. >8 p/w, 1.96; 95% CI, 1.07-3.82), pickle consumption (aOR >8 p/w vs. 7-8 p/w, 1.46; 95% CI, 1.31-1.70), and intensity of physical activity (aOR light vs. vigorous, 1.68; 95% CI, 1.47-1.98) were directly associated with a higher risk of BC in young women. **Conclusion:** Our study supported the hypothesis that unhealthy dietary habits and physical inactivity are risk factors for BC. We found that a healthy diet containing low fat and high fruits and vegetables with regular exercise are effective ways to reduce the risk of BC among young women.

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Introduction

Unhealthy dietary pattern and physical inactivity have been introduced as important risk factors for hypertension, diabetes, cardiovascular diseases, lipid disorder, and even depression.[1,2] It has also been shown that diet and physical activity are effective factors for the occurrence of several types of cancers.[1] Although several studies have also shown significant associations between unhealthy diet and physical inactivity and the risk of breast cancer (BC),[3-5] the results are not conclusive and, in several studies, are controversial. However, these studies are predominantly conducted in populations from developed

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countries, which are completely different than those in the developing world with respect to genetics, lifestyle, and environment. It has been suggested that the Iranian population is different from those in the developed world with respect to genetics, lifestyle, diet, and environment. For example, it seems that some factors associated with BC, including lifestyle, are considerably different among Iranian women when compared with women from Western countries.[6] In other words, the rapid demographic change, urbanization, and social development are causing several important health-related changes, including nutritional transition and sedentary lifestyle, among the Iranian population.[7]

The change in diet or the Westernization of the diet includes a higher intake of red meat, processed food, fatty food, refined grains, sugar, butter, fries, and carbonated drinks.[8] It has been suggested that the Westernized diet not only increases the risk of BC but also reduces the survival of the patients.[9]

A small number of studies in Iran have studied the influence of diet on BC mostly among postmenopausal women and did not consider the effects of reproductive and dietary factors at the same time.[10,11] Definitions of the role of diet and physical activity in BC would help in preventing BC, the most common type of cancer in women. In this case-control study, we aimed to measure the association of physical activity and diet with risk of BC in Iranian women.

Ascertainment of the role of diet and physical activity would also help in planning preventive strategies for BC by the Iranian health policy makers.

Materials and Methods

Setting

This is the second phase of a case-control study which was conducted from November 2014 to March 2016 in Namazi Hospital, Shiraz, Iran.[12] This study was conducted to investigate the association of dietary habits and physical activity with the risk of BC in Iranian women of premenopausal age. The study's sample of participants consisted of 505 patients with BC and 505 female controls.

Ethical Approval

Written consent was obtained from all study participants, and verbal consent was obtained from illiterate participants. Ethical approval was obtained from Shiraz University of Medical Sciences (no: 1396-01-04-14732).

Criteria for Subject Recruitment

A post hoc power analysis suggested that with alpha value and power set at 0.05 (2-sided) and 80%, respectively, a sample of 453 for each group would be enough to detect an increase as small as 1.5 times in the risk of BC among those consuming no or very little fruits compared with those consuming a large amounts of fruits on a daily basis.

Patients with BC were selected among females aged 20 to 50 years, newly diagnosed with BC, and having positive histopathology report at Namazi Hospital. Control participants were randomly selected among patients with no cancer who were also admitted to the same hospital during the same period. Cases were interviewed when they were visiting surgery/radiotherapy departments. Controls were interviewed at almost the same date during their stay in the hospital. Controls and cases were matched for age (± 5 years).

The case participants were excluded if they had relapsed or recurrent cancer after treatment. Also, patients who experienced a recent significant change in their weight or size from the last 6 months were not included.[13] The latter was done to eliminate the possibility of reverse causation of the association between weight or diet and BC.[13]

Data Collection

The required data was collected via an interview administered questionnaire (which was designed and used before) and the patient's medical file. Briefly, based on the results from a pilot study, using test-retest analysis, the questioner's reliability was estimated as good (Cronbach alpha = 0.72). The procedures of designing and evaluation of the questionnaire and interview has been discussed previously.[12] All participants were interviewed in a private and quiet place. The main questionnaire included questions regarding a wide range of information (eg, marital status, age, education, body mass index [BMI], occupation, age at first marriage, history of breast benign disease, family history of BC, oral contraceptive pill [OCP] use, smoking and intensity of physical activity). A second questionnaire was also designed and evaluated similar to the first one to collect data on consumption of several predominant nutrients in Iranian diet as portion per week (p/w) among the participants. In that regard, usual consumption of red meat of any kind (p/w), chicken meat (p/w), fish of any kind (p/w), pickles (p/w), intake of white sugar (p/w), type of oil consumed (saturated or unsaturated), vegetables (p/w), fruits (p/w), and dairy products (p/w) were defined.

Dietary Habits Assessment

The participants were asked to report the frequency of consumption for each of the above food items in terms of portion per week. The number of portions per week was categorized into 0 to 2 p/w, 3 to 4 p/w, 5 to 6 p/w, 7 to 8 p/w, and >8 p/w.[14]

Anthropometric and Physical Activity Assessment

During the interview at the clinic, weight was measured with minimal clothing and without shoes. To calculate the BMI, the weight was divided by the square of height (kg/m^2).

The Global Physical Activity Questionnaire (GPAQ2) was used to estimate the physical activity of the study participants. This validated questionnaire is comprised of 16 questions. It divides the participants into 3 domains of physical activity and sedentary behavior. The 3 domains of physical activity include: activity at work, travel to and from places, and recreational activities. Definitions of these 3 domains are given by the World Health Organization (WHO) (2016).[15] The metabolic equivalent (MET) was used to calculate the intensity of physical activity, which is classified into 3 categories: light intensity (< 600 MET-minutes per week), moderate intensity (600-3000 MET-minutes per week), and vigorous intensity (3000 MET-minutes per week).[15,16]

Statistical Analysis

Unadjusted and adjusted associations of independent variables and risk of breast cancer were measured using univariate (χ^2, independent sample t test) and multivariable (multiple logistic regression) analysis. Backward logistic regression (LR) variable selection strategy was used to include variables in the regression model. In addition to dietary factors (eating red meat, eating fish, eating chocolate, eating pickles, and eating fruits, vegetables, and dairy) and physical activity, several other study variables were

included in the final model. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using the multivariable logistic regression. All *P*-values were 2-sided, and statistical analysis was conducted assuming a 2-sided 5% level of significance. All analyses were conducted using Stata version 12.0 (Stata Corporation, College Station, TX).

Results

Of 550 participants with breast cancer, 45 (8%) were excluded owing to missing or incomplete diagnosis reports. As a result, a final sample of 505 cases and 505 age-matched controls were included in the analysis. The participants in case and control groups had an average age of 41.78 years (± 10.65 years), and 42.24 years (± 10.62 years), respectively ($P = .42$). Overall, 184 (36.4%) patients and 183 (36.2%) controls were illiterate or had primary education. In addition, both cases (92.1%) and controls (94.3%) were predominantly married.

Results of Univariate Analysis

Table 1 illustrates the unadjusted associations between sociodemographic and dietary variables and BC. In that regard, significant unadjusted associations were observed between the risk of BC and the participant's education, occupation, age at first marriage, history of breast problem, history of breast cancer in relatives, intensity of physical activity, and smoking. There were also direct associations between BC and consumption of red meat, fish of any kind, dairy products, sugar, and pickles ($P < .05$ for all). On the other hand, an inverse association was observed between fruit consumption and risk of BC.

Multivariable Analysis

Table 2 illustrates the adjusted associations of demographic, reproductive, dietary variables, and physical activity with BC.

Demographic Variables. Accordingly, the risk of BC was higher among participants with no or primary education compared with those with a college degree (OR primary or no education vs. college degree, 2.22; 95% CI, 1.31-3.78), those who were employed (OR employed vs. housewife, 2.03; 95% CI, 1.34-3.08), those who had previous history of breast diseases (OR yes vs. no, 4.71; 95% CI, 2.67-8.34), those with BC among first-degree relatives (OR yes vs. no, 3.41; 95% CI, 1.93-6.01), those who used OCPs (OR yes vs. no, 1.77; 95% CI,1.32-2.38), and smokers (OR yes vs. no, 2.48; 95% CI, 1.56-3.96). The results also suggested an increase in the risk of BC among passive smokers (OR yes vs. no, 1.71; 95% CI, 1.28-2.27).

Reproductive Variables. Among reproductive variables, marriage at a younger age (under 18 years vs. > 30 years) decreases the risk of BC (OR, 0.35; 95% CI, .018-0.65).

Dietary Variables. The results suggested that eating red meat increases the risk of BC (OR >8 p/w vs. 0-2 p/w, 1.15; 95% CI, 1.04-1.28). In addition, eating fish was associated with a higher risk of BC (OR >8 p/w vs. 0-2 p/w, 1.55; 95% CI, 1.12-2.76). Also consuming no or less fruits (OR 0-4 p/w vs. >8 p/w, 1.96; 95% CI,

Table 1 The Unadjusted Association of Sociodemographic Variables, Dietary Factors, and Physical Activity With Breast Cancer Development

Variables[a]	New Cases N = 505, n (%)	Controls N = 505, N (%)	*P* Value[b]
Age, y			.303
< 40	115 (22.8)	137 (27.1)	
40-45	171 (33.9)	169 (33.5)	
46-50	219 (43.4)	214 (42.4)	
Education			.018
Primary or illiterate	184 (36.4)	183 (36.2)	
Secondary	76 (15.1)	110 (21.8)	
High school	160 (31.7)	127 (25.2)	
College	85 (16.8)	85 (16.8)	
BMI,[c] kg/m^2			.062[d]
Underweight (<18.5)	11 (2.2)	10 (2.0)	
Normal (18.5-24.9)	149 (29.5)	151 (29.9)	
Overweight (25-29.9)	222 (43.9)	254 (50.3)	
Obese (≥30)	123 (24.4)	90 (17.8)	
Occupation			.002
Housewife	375 (74.3)	415 (82.2)	
Employed	130 (25.7)	90 (17.8)	
Age at first marriage, y			< .001[d]
< 18	194 (38.4)	246 (48.7)	
18-24	166 (32.9)	171 (33.9)	
25-30	73 (14.5)	44 (8.7)	
> 30	31 (6.1)	15 (3.0)	
Not married	41 (8.1)	29 (5.7)	
History of breast disease			< .001[d]
Ever	84 (16.6)	18 (3.5)	
Never	421 (83.4)	487 (96.5)	
Family history of breast cancer			< .001[d]
No	406 (80.4)	456 (90.3)	
First-degree relative	41 (8.1)	28 (5.5)	
Second-degree relative	58 (11.5)	21 (4.2)	
Oral contraceptive usage			.113
Ever	237 (46.9)	212 (42.0)	
Never	268 (53.1)	293 (58.0)	
Intensity of physical activity			.009
Light (<600 MET-minutes per week) and moderate (600-3000 MET-minutes per week) intensity	423 (83.8)	390 (77.2)	
Vigorous intensity (3000 MET-minutes per week)	82 (16.2)	115 (22.8)	
Smoking			< .001
Non-smoker	430 (85.1)	466 (92.3)	
Smoker	75 (14.9)	39 (7.7)	
Passive smoker			< .001
No	205 (40.6)	283 (56.0)	
Yes	300 (59.4)	222 (44.0)	

Table 1 Continued

Variables[a]	New Cases N = 505, n (%)	Controls N = 505, N (%)	*P* Value[b]
High carbohydrate/sugar, p/w			.004[d]
0-2	54 (10.7)	71 (14.1)	
3-4	226 (44.8)	231 (45.7)	
5-6	114 (22.5)	129 (25.5)	
7-8	67 (13.3)	56 (11.1)	
>8	44 (8.7)	18 (3.6)	
Pickles use, p/w			.004[d]
0-2	18 (3.6)	21 (4.2)	
3-4	93 (18.4)	90 (17.8)	
5-6	136 (27.0)	133 (26.3)	
7-8	131 (25.9)	176 (34.9)	
>8	127 (25.1)	85 (16.8)	
Fruit use, p/w			.015
0-4	27 (5.4)	21 (4.2)	
5-6	64 (12.7)	56 (11.0)	
7-8	182 (36.0)	145 (28.8)	
>8	232 (45.9)	283 (56.0)	
Vegetable use, p/w			.716
0-4	43 (8.5)	44 (8.7)	
5-6	69 (13.7)	79 (15.6)	
7-8	186 (36.8)	171 (33.9)	
>8	207 (41.0)	211 (41.8)	
Type of oil			.494
Saturated	388 (76.8)	128 (23.4)	
Unsaturated	117 (23.2)	419 (76.6)	
Dairy use, p/w			.044[d]
0-2	5 (1.0)	13 (2.5)	
3-4	54 (10.7)	37 (7.3)	
5-6	81 (16.0)	76 (15.0)	
7-8	167 (33.1)	198 (39.0)	
>8	198 (39.2)	183 (36.2)	
Dairy kind			.011
Low fat	255 (50.5)	295 (58.4)	
Medium fat	100 (19.8)	100 (19.8)	
High fat	150 (29.7)	110 (21.8)	
Red meat use, p/w			.021[d]
0-2	15 (2.97)	12 (2.38)	
3-4	58 (11.49)	48 (9.50)	
5-6	76 (15.05)	65 (12.87)	
7-8	167 (33.07)	186 (36.83)	
>8	189 (37.43)	194 (38.42)	
Fish use, p/w			.001[d]
0-2	13 (2.57)	23 (4.55)	
3-4	94 (18.61)	49 (9.70)	
5-6	130 (25.74)	156 (30.89)	
7-8	148 (29.31)	182 (36.04)	
>8	120 (23.76)	95 (18.81)	
Chicken use, p/w			.342
0-2	57 (11.29)	49 (9.70)	
3-4	75 (14.85)	87 (17.23)	
5-6	186 (36.83)	157 (31.09)	
7-8	107 (21.19)	165 (32.67)	
>8	80 (15.84)	47 (9.31)	

Abbreviations: BMI = body mass index; MET = metabolic equivalent; p/w = portion per week.
[a]Measures reflect the participant's status during her normal life (ie, in case of participants, before the first symptom of breast cancer being noticed).
[b]χ^2 test.
[c]Based on the World Health Organization classification for BMI.
[d]Fisher exact test.

1.07-3.82) and eating pickles increase the risk of BC (OR>8 p/w vs. 6-8 p/w, 1.46; 95% CI, 1.31-1.70).

Physical Activity. According to the results of multivariable analysis, vigorous physical activity (ie, 3000 MET minutes per weeks) was associated with a lower risk of BC (OR light and moderate intensity vs. vigorous intensity, 0.68; 95% CI, 0.47-0.98).

Discussion

After adjusting for potential confounders, the results suggested that employment, history of breast disease, history of BC in first-degree relatives, smoking, and passive smoking increase the risk of BC among young women. Among reproductive variables, OCP use and marriage at a younger age (under 18 years) decreases the risk of developing BC for about 65%. With regard to dietary habits, significant associations were observed between eating red meat and fish. However, consuming no or less fruits and eating pickles with all meals decrease BC. With regard to physical activity, vigorous physical activity decreases the risk of BC among young women.

Employment is a demographic factor that is associated with increased risk of BC. In the current study, employed women had a higher risk of BC than homemakers. These findings are in accordance with the results of previous studies where employed women had a higher risk of BC.[17] Work-related stress and /or exposure to carcinogens may be the possible cause of increased risk of BC. Higher socioeconomic status, which includes higher education and more family income, may also contribute to the higher risk of BC in employed women.[18] However, we previously reported no positive association between being employed and risk of BC. These contradictory results may have occurred because older women were selected for study in the previous study.[12]

Two other important factors related to the risk of BC were the history of breast benign diseases and family history of breast cancer. In our study, the presence of breast benign diseases was associated with a higher risk of BC for young women. This finding is in accordance to the findings of previous studies, which suggested that having history of breast cancer among relatives could increase the

Table 2 Adjusted Association Between The Study Variables And Breast Cancer Risk Among Young Women Using Multiple Regression

Variables	OR	95% CI		*P* Value
		Lower Limit	Upper Limit	
Education				
College	1	—	—	—
Primary or illiterate	2.22	1.31	3.78	.003
Secondary	1.51	0.86	2.67	.146
High school	2.19	1.34	3.57	.002
Occupation				
Housewife	1	—	—	—
Employed	2.03	1.34	3.08	.001
History of breast disease				
Never	1	—	—	—
Ever	4.71	2.67	8.34	.001
Age at first marriage, y				
> 30	1	—	—	—
< 18	0.35	0.18	0.65	.001
18-24	0.49	0.26	0.88	.021
25-30	0.91	0.46	1.80	.799
Not married	1.07	0.44	2.55	.881
Family history of breast cancer				
No	1	-	-	-
Second relative	1.52	0.88	2.64	.132
Close relative	3.41	1.93	6.01	< .001
Oral contraceptive usage				
Never	1	—	—	—
Ever	1.77	1.32	2.38	< .001
Smoking				
No	1	—	—	—
Yes	2.48	1.56	3.96	< .001
Passive smoker				
No	1	—	—	—
Yes	1.71	1.28	2.27	< .001
Intensity of physical activity[a]				
Light intensity	1	—	—	—
Vigorous intensity	0.68	0.47	0.98	.036
Pickle use, p/w				
>8	1	—	—	—
0-2	0.65	0.30	1.40	.274
3-4	0.59	0.37	0.96	.032
5-6	0.64	0.42	0.98	.044
7-8	0.46	0.31	0.70	< .001
Fruit use, p/w				
>8	1	—	—	—
0-4	1.96	1.07	3.82	.001
5-6	2.26	1.41	3.62	.048
7-8	1.84	1.32	2.57	.001
Red meat use, p/w				
0-2	1	—	—	—
3-4	1.02	0.08	1.06	.061
5-6	1.08	1.00	1.18	.058
7-8	1.18	1.09	1.23	.063
>8	1.15	1.04	1.28	.004
Fish use,[b] p/w				
0-2	1	—	—	—
3-4	1.04	0.59	1.71	.365
5-6	0.69	0.09	1.28	.084
7-8	1.40	1.03	2.10	.068
>8	1.55	1.12	2.76	.003

All study variables were included in the final model including: age, education, body mass index, occupation, age at first marriage, history of breast disease, family history of breast cancer, oral contraceptive usage, intensity of physical activity, smoking, passive smoker, and dietary habit factors (high carbohydrate/sugar use, pickle use, fruit use, vegetable use, dairy use, and meat, fish, and chicken per week and dairy kind).
Abbreviations: CI = confidence interval; MET = metabolic equivalent; OR = odds ratio; p/w = portions per week.
[a]Light: < 600 MET-minutes per week; Vigorous intensity: 3000 MET-minutes per week; moderate intensity: 600-3000 MET-minutes per week.
[b]Any kind of fish.

risk of breast cancer.[19,20] A study reported that family history of BC among first relatives is not associated with the risk of BC, but in the current study, it was reported as a predictor variable.[12] These controversial findings support the hypothesis of a previous study that family history of BC is more highly related to the risk of BC among young women than postmenopausal women.

Results of the multivariable analysis suggested a significant association between OCP usage and risk of BC. The results of previously published studies suggested an association between OCP usage and BC,[21] but another study on a high proportion of postmenopausal women reported no statistically significant association.[16] This association is also reported by several Iranian studies.[18,22] Compared with a previously published paper,[12] this association is event stronger (OR, 1.77 vs. 1.46), which indicated that OCP usage can have negative effects on the risk of BC, especially for young women. Among other reproductive variables, marriage at a younger age was associated with a lower risk of BC; women who married at an older age were at greater risk of BC. This finding is in line with Ghiasvand et al, who suggested that getting married at a younger age has a protective role on the risk of BC.[18] This finding is in line with the result of the first phase of our study in which we found a direct association between age of marriage and risk of BC.[12]

Different aspects of the association of BC and smoking, such as being a current or former smoker, passive smoking, duration of smoking, and type of cigarette have been investigated by others[23-26] and with some uncertainties; the results supported the presence of a causal association. A meta-analysis showed that the rate of smoking

among Iranian women varies between 0.6% and 9.8%, depending on ethnicity and region of residency. It is also estimated that 38.5% of the Iranian population are passive smokers.[27] Despite a large number of epidemiologic studies that examined the relationship between cigarette smoking and risk of BC, there is still no scientific consensus owing to some concerns over the effect of confounders, especially alcohol, on the association.[28] However, the results of the present study are unlikely to be confounded by alcohol as consumption of alcohol is illegal in Iran, and none of the participants in case and control groups reported regular alcohol consumption. Similar results were found in the previously published article between smoking (OR, 2.02 vs. 2.48) and passive smoking (OR, 1.57 vs. 1.71) and the risk of BC.[12]

We found that vigorous physical activity lowers the risk of BC. This is consistent with a study that suggested vigorous physical activity is associated with a lower risk of BC.[29] The association between physical activity and a decreased risk of BC observed in our study is also in line with the conclusion of a recently published meta-analysis of 139 prospective and retrospective studies.[30] Indeed, physical activity is associated with prevention of several other diseases. According to the World Health Organization, physical inactivity increases all-cause mortality, increases the risk of obesity, diabetes, high blood pressure, lipid disorder, osteoporosis, depression, anxiety, and colon cancer.[31] According to the American Cancer Society, the risk of breast cancer is 20% to 30% lower in physically active women than physically inactive women. Possible explanations include the fact that physical activity increases basal metabolism, improves tissue oxygenation, and decreases weight. Weight control reduces body fats and insulin resistance and hence insulin levels. Physical inactivity causes chronic inflammation and increase the levels of growth promoting hormones.[1] All these changes are associated with cancer.

The globally accepted definition of an unhealthy dietary pattern includes: high content of refined grains, potatoes, sweets, high-fat food, coffee, black tea, soft drinks, dressing, sauce, mayonnaise, red meat, and/or processed foods.[8] This study revealed that the risk of BC was 1.15 times higher in women who consumed more portions of red meat than those consumed less. Red meat is known for causing many types of cancer, including colorectal, endometrial, bladder, gastric, and kidney cancers.[1] Previous studies on BC also supported these findings. For example, a recently published meta-analysis on premenopausal women revealed a significant positive relationship between red meat consumption and the risk of BC in young women.[32] The results of this meta-analysis suggested that the women who consumed more red meat had a 1.27-times greater risk of breast cancer compared with those who consumed less. However, a recent meta-analysis on 3 cohort, 3 nested case-control, and 2 clinical trial studies has demonstrated that processed meat is associated with a higher risk of BC but not red meat.[33]

Heterocyclic aromatic amines, hem iron, and exogenous hormones in red meat may work as potential carcinogens. Cooking meat at high temperature can generate heterocyclic aromatic amines, which act on DNA and cause point mutations, deletion, and insertion.[34] Hem iron damages DNA and cause lipid peroxidation because of its pro-oxidant properties.[35,36] Exogenous hormones are steroid hormones, which are given to cattle to promote their growth and muscle mass. These hormones can cause BC by increasing cell proliferation and angiogenesis and suppressing apoptosis.[36]

In our study, fish intake was also associated with the risk of BC. Another study supports our findings.[37] The hypotheses for the mechanism of this finding includes that fish might be contaminated with water-absorbed heavy metals and pesticides, which have estrogenic effects. These metals and compounds activate estrogen receptors in the absence of estrogens and increase the risk of BC. Also, cooking fish at high temperature can produce heterocyclic aromatic amines like red meat and can cause BC.[38] Fish is among the prudent/healthy diet ingredients according to the globally accepted definition of healthy dietary patterns. An increased risk of BC with fish intake can raise concerns of fish remaining as a health food.[8] Certainly, more studies with a focus on the type of fish and carcinogenic environmental factors are needed.

The results of the unadjusted model demonstrated that consuming foods rich in carbohydrates are associated with an increased risk of BC. However, the association was not statisticaly significant in the multivariable analysis. Another study found similar results, as positive correlations were introduced between consumption of carbohydrate-rich foods, especially sweets and chocolates, with an increased risk of BC.[39] Foods with high glycemic index (the glycemic index represents the digestibility of carbohydrates and their absorption in blood stream as glucose), such as refined sugar, cause insulin resistance and increased insulin-related growth factor, which is accused of being carcinogenic to the breast. Moreover, s higher intake of sucrose raises glycemic load and obesity, which will in turn increase the endogenous estrogen levels.[39] Furthermore, insulin also stimulates and increases the concentration of estrogens and androgens, all associated with the risk of BC.[40]

Vegetables and fruits are potentially categorized as prudent or healthy foods for prevention of not only cardiovascular and inflammatory diseases but also for cancer. The World Cancer Research Foundation recommends the intake of fruits and vegetables for cancer prevention. Many studies showed the protective role of vegetables and fruits against BC.[41,42] Our study supports those studies. We found that patients with BC consumed less fruits and vegetables than the control group. Baglietto et al concluded that intake of fruits and salads had greater impact on decreasing BC risk than vegetables.[43] We also found that fruits were more protective than vegetables. The possible reason for this difference is the effect of cooking and high temperature on vegetables. Cooking destroys antioxidants such as carotenoids and vitamins, which decreases the anti-carcinogenic properties of vegetables.

Polyphenolic compounds, flavonoids, isoflavones, epigallocatechin-3-gallate, lycopene, daily trisulfide, isothiocyanates, resveratrol, selenium, beta carotenoids, vitamins E, D, C, A, B12, and B6, and folic acid are some of the anti-carcinogenic components of vegetables and fruits. These compounds inhibit oncogenic cell proliferation, promote apoptosis, inhibit angiogenesis, enhance pathways that detoxify carcinogens, and generally inhibit pathways to breast cancer.[1] Although vegetables provide protection against breast cancer, pickled vegetables do not. We found a high consumption of pickled vegetables in patients with BC. Previous studies support our finding, as they also found positive association between consumption of pickled vegetables and the risk of BC.[44] Nitrates, nitrites, and extra salt in pickled vegetables are suggested to be potential carcinogens.[45]

In our study, according to the univariable analysis, intake of dairy products, especially high-fat dairy products, was associated with a higher risk of BC (but the association was not statisticaly significant in the multivariable analysis). Several studies support these findings, but some others contradicted them. For example, a meta-analysis showed that dairy consumption is inversely associated with BC development. However, they found an inverse correlation between low-fat dairy and BC.[46] Another study found that high-fat dairy products increased the mortality of BC.[47] But, in line with the our results, one study suggested no overall association between dairy consumption and BC.[48] The possible explanations include that high fat content is estrogenic and dairy products contain carcinogenic contaminants (such as pesticides) and growth factors such as insulin-like growth factor I (IGF-I). Animal studies have supported the role of high-fat dairy products in cancer, but human studies have not.[49]

Strengths and Limitations of Our Study

The strengths of our study include a larger sample size than many other Iranian studies and the fact that the interviews with the case and control participants were conducted by trained nurses in the same setting with a very high participation rate. The study measured self-reported habits of consuming the main groups of foods, which could be helpful in measuring habits long before onset of the disease. However, asking the participants to refer to months before the interview will put the findings at the risk of recall bias, a common pitfall for case-control studies. However, the method of selecting controls (hospital controls) should have reduced the risk of recall bias in the reporting of study variables. Also, we found that fish consumption can play a significant role in the risk factor of BC. However, there was no additional information on type of fish that our participants used, and this requires further research to detect the possible impacts of different kinds of fish consumption on the risk of BC.

Conclusions

Our study revealed that an unhealthy/Westernized dietary pattern and physical inactivity are risk factors for the development of BC in young Iranian women. Fish consumption was also found as a risk factor of BC. This contradicts the global view on healthy foods. Eating vegetables and fruits and vigorous physical activity were protective factors for BC.

Guidelines have placed red meat consumption for BC risk in category B (ie, no clear harm or benefit). The results of our study indicate a need for revision of the guidelines.

We suggest women should restrict calories and eat more vegetables and fruits. Vegetables should be prepared uncooked to avoid damage to nutrients, which helps in prevention of BC. Low-fat dairy products should also be recommended as a healthy ingredient in our diet.

Clinical Practice Points

- The basics of the association of diet and physical activity with BC were studied.
- This study provided applicable evidence about the preventive effects of diet and physical activity on BC.
- Based on the results of our study, preventive measures, including raising public awareness about lifestyle and diet, are to be focused on more pragmatic and effective interventions in cancer prevention.
- Eating vegetables and fruits and vigorous physical activity were protective factors for BC.

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Disclosure

The authors have stated that they have no conflicts of interest.

References

1. Ruiz RB, Hernández PS. Diet and cancer: risk factors and epidemiological evidence. *Maturitas* 2014; 77:202-8.
2. Khosravi M, Sotoudeh G, Majdzadeh R, et al. Healthy and unhealthy dietary patterns are related to depression: a case-control study. *Psychiatry Investig* 2015; 12: 434-42.
3. Cottet V, Touvier M, Fournier A, et al. Postmenopausal breast cancer risk and dietary patterns in the E3N-EPIC prospective cohort study. *Am J Epidemiol* 2009; 170:1257-67.
4. Chlebowski RT. Nutrition and physical activity influence on breast cancer incidence and outcome. *Breast* 2013; 22:S30-7.
5. Deschasaux M, Julia C, Kesse-Guyot E, et al. Are self-reported unhealthy food choices associated with an increased risk of breast cancer? Prospective cohort study using the British Food Standards Agency nutrient profiling system. *BMJ Open* 2017; 7:e013718.
6. Naderimagham S, Alipour S, Djalalinia S, et al. National and sub-national burden of breast cancer in Iran; 1990-2013. *Arch Iran Med* 2014; 17:794-9.
7. Ghassemi H, Harrison G, Mohammad K. An accelerated nutrition transition in Iran. *Public Health Nutr* 2002; 5:149-55.
8. Nanri A, Mizoue T, Shimazu T, et al, Japan Public Health Center-Based Prospective Study Group. Dietary patterns and all-cause, cancer, and cardiovascular disease mortality in Japanese men and women: the Japan public health center-based prospective study. *PLoS One* 2017; 12:e0174848.
9. Abdi F, Atarodi Z, Mirmiran P, Esteki T. A review of nutritional status in Iranian population. *Focus on Sciences* 2016; 2:1-10.
10. Ataollahi M, Sedighi S, Masoumi SZ. Nutritional and unhealthy behaviors in women with and without breast cancer. *Iran Red Crescent Med J* 2014; 16:e19684.
11. Karimi Z, Jessri M, Houshiar-Rad A, Mirzaei H-R, Rashidkhani B. Dietary patterns and breast cancer risk among women. *Public Health Nutr* 2014; 17:1098-106.
12. Dianatinasab M, Fararouei M, Mohammadianpanah M, Zare-Bandamiri M, Rezaianzadeh A. Hair coloring, stress, and smoking increase the risk of breast cancer: a case-control study. *Clin Breast Cancer* 2017; 17:650-9.
13. Vagenas D, DiSipio T, Battistutta D, et al. Weight and weight change following breast cancer: evidence from a prospective, population-based, breast cancer cohort study. *BMC Cancer* 2015; 15:28.
14. Tayyem RF, Bawadi HA, Shehadah I, et al. Fast foods, sweets and beverage consumption and risk of colorectal cancer: a case-control study in Jordan. *Asian Pac J Cancer Prev* 2018; 19:261-9.
15. World Health Organization. Global Physical Activity Questionnaire (GPAQ), Available at: http://www.who.int/chp/steps/GPAQ/en/. Accessed: February 25, 2018.
16. Khalis M, Charbotel B, Chajès V, et al. Menstrual and reproductive factors and risk of breast cancer: a case-control study in the Fez region, Morocco. *PLoS One* 2018; 13:e0191333.
17. Ozmen V, Ozcinar B, Karanlik H, et al. Breast cancer risk factors in Turkish women—a University Hospital based nested case control study. *World J Surg Oncol* 2009; 7:37.
18. Ghiasvand R, Maram ES, Tahmasebi S, Tabatabaee SHR. Risk factors for breast cancer among young women in southern Iran. *Int J Cancer* 2011; 129: 1443-9.
19. Kotsopoulos J, Chen WY, Gates MA, Tworoger SS, Hankinson SE, Rosner BA. Risk factors for ductal and lobular breast cancer: results from the nurses' health study. *Breast Cancer Res* 2010; 12:R106.
20. Phipps AI, Li CI, Kerlikowske K, Barlow WE, Buist DS. Risk factors for ductal, lobular, and mixed ductal-lobular breast cancer in a screening population. *Cancer Epidemiol Biomarkers Prev* 2010; 19:1643-54.
21. Rosenberg L, Zhang Y, Coogan PF, Strom BL, Palmer JR. A case-control study of oral contraceptive use and incident breast cancer. *Am J Epidemiol* 2008; 169: 473-9.
22. Sepandi M, Akrami M, Tabatabaee H, et al. Breast cancer risk factors in women participating in a breast screening program: a study on 11,850 Iranian females. *Asian Pac J Cancer Prev* 2014; 15:8499-502.
23. Land SR, Liu Q, Wickerham DL, Costantino JP, Ganz PA. Cigarette smoking, physical activity, and alcohol consumption as predictors of cancer incidence among women at high risk of breast cancer in the NSABP P-1 trial. *Cancer Epidemiol Biomarkers Prev* 2014; 23:823-32.

24. Rosenberg LU, Magnusson C, Lindstrom E, Wedren S, Hall P, Dickman PW. Menopausal hormone therapy and other breast cancer risk factors in relation to the risk of different histological subtypes of breast cancer: a case-control study. *Breast Cancer Res* 2006; 8:R11.
25. Xue F, Willett WC, Rosner BA, Hankinson SE, Michels KB. Cigarette smoking and the incidence of breast cancer. *Arch Int Med* 2011; 171:125-33.
26. Hosseinzadeh M, Eivazi Ziaei J, Mahdavi N, et al. Risk factors for breast cancer in Iranian women: a hospital-based case-control study in Tabriz, Iran. *J Breast Cancer* 2014; 17:236-43.
27. Moosazadeh M, Ziaaddini H, Mirzazadeh A, Ashrafi-Asgarabad A, Haghdoost AA. Meta-analysis of smoking prevalence in Iran. *Addict Health* 2013; 5:140-53.
28. Gaudet MM, Gapstur SM, Sun J, Diver WR, Hannan LM, Thun MJ. Active smoking and breast cancer risk: original cohort data and meta-analysis. *J Natl Cancer Inst* 2013; 105:515-25.
29. Hildebrand JS, Gapstur SM, Campbell PT, Gaudet MM, Patel AV. Recreational physical activity and leisure-time sitting in relation to postmenopausal breast cancer risk. *Cancer Epidemiol Biomarkers Prev* 2013; 22:1906-12.
30. Hardefeldt PJ, Penninkilampi R, Edirimanne S, Eslick GD. Physical activity and weight loss reduce the risk of breast cancer: a meta-analysis of 139 prospective and retrospective studies. *Clin Breast Cancer* 2018; 18:e601-12.
31. Physical inactivity a leading cause of disease and disability, warns WHO. *J Adv Nurs* 2002; 39:518.
32. Rezaianzadeh A, Ghorbani M, Rezaeian S, Kassani A. Red meat consumption and breast cancer risk in premenopausal women: a systematic review and meta-analysis. *Middle East J Cancer* 2018; 9:5-12.
33. Farvid MS, Stern MC, Norat T, et al. Consumption of red and processed meat and breast cancer incidence: a systematic review and meta-analysis of prospective studies. *Int J Cancer* 2018; 143:2787-99.
34. Sutandyo N. Nutritional carcinogenesis. *Acta Med Indones* 2010; 42:36-42.
35. Kotepui M. Diet and risk of breast cancer. *Contemp Oncol* 2016; 20:13-9.
36. Huang X. Iron overload and its association with cancer risk in humans: evidence for iron as a carcinogenic metal. *Mutat Res* 2003; 533:153-71.
37. Dai Q, Shu XO, Jin F, Gao YT, Ruan ZX, Zheng W. Consumption of animal foods, cooking methods, and risk of breast cancer. *Cancer Epidemiol Biomarkers Prev* 2002; 11:801-8.
38. Stripp C, Overvad K, Christensen J, et al. Fish intake is positively associated with breast cancer incidence rate. *J Nutr* 2003; 133:3664-9.
39. Patel A, Pathak Y, Patel J, Sutariya V. Role of nutritional factors in pathogenesis of cancer. *Food Qual Safe* 2018; 2:27-36.
40. Tavani A, Giordano L, Gallus S, et al. Consumption of sweet foods and breast cancer risk in Italy. *Ann Oncol* 2005; 17:341-5.
41. Donaldson MS. Nutrition and cancer: a review of the evidence for an anti-cancer diet. *Nutr J* 2004; 3:19.
42. Zhang CX, Ho SC, Chen YM, Fu JH, Cheng SZ, Lin FY. Greater vegetable and fruit intake is associated with a lower risk of breast cancer among Chinese women. *Int J Cancer* 2009; 125:181-8.
43. Baglietto L, Krishnan K, Severi G, et al. Dietary patterns and risk of breast cancer. *Br J Cancer* 2011; 104:524-31.
44. Yu H, Hwang JY, Ro J, Kim J, Chang N. Vegetables, but not pickled vegetables, are negatively associated with the risk of breast cancer. *Nutr Cancer* 2010; 62:443-53.
45. Ren JS, Kamangar F, Forman D, Islami F. Pickled food and risk of gastric cancer–a systematic review and meta-analysis of English and Chinese literature. *Cancer Epidemiol Biomarkers Prev* 2012; 21:905-15.
46. Zang J, Shen M, Du S, Chen T, Zou S. The association between dairy intake and breast cancer in western and Asian populations: a systematic review and meta-analysis. *J Breast Cancer* 2015; 18:313-22.
47. Kroenke CH, Kwan ML, Sweeney C, Castillo A, Caan BJ. High-and low-fat dairy intake, recurrence, and mortality after breast cancer diagnosis. *J Natl Cancer Inst* 2013; 105:616-23.
48. Farvid MS, Eliassen AH, Cho E, Chen WY, Willett WC. Dairy consumption in adolescence and early adulthood and risk of breast cancer. *Cancer Epidemiol Biomarkers Prev* 2018; 27:575-84.
49. Moorman PG, Terry PD. Consumption of dairy products and the risk of breast cancer: a review of the literature. *Am J Clin Nutr* 2004; 80:5-14.