Original Article

# A Case-control Study on the Association of Fruit and Vegetable Consumption with Risk of Breast Cancer


## Abstract

**Background:** Limited data are available linking dietary intake of fruit and vegetables to breast cancer, in particular among the Middle Eastern population. The present study was done to investigate the association of fruit and vegetable consumption with the risk of breast cancer in Iranian adult women. **Methods:** Dietary intake of fruit and vegetables was assessed using a validated 106-item Willett-format semi-quantitative dish-based food frequency questionnaire. Logistic regression was used to determine the association between fruit and vegetable consumption and breast cancer. Women aged >30 years, residing in Isfahan, Iran from July 2013 to July 2015. Breast cancer was diagnosed during the maximum of the last 6 months by physical examination and mammography findings. **Results:** Overall, data on 350 cases and 700 controls were analyzed. After controlling for potential confounders, participants with the highest dietary intake of fruits had higher odds of breast cancer than those with the lowest intake (odds ratio [OR]: 8.23; 95% confidence interval [CI]: 4.37-15.50), while those who consumed highest amounts of vegetables were less likely to have breast cancer than their counterparts (OR: 0.12; 95% CI: 0.06-0.24). Although no significant associations were found between dietary intakes of fruits and vegetables and risk of breast cancer in premenopausal women, significant positive association between fruit consumption and breast cancer (OR: 16.80; 95% CI: 7.80, 36.21; $P < .001$) was observed in postmenopausal women. **Conclusions:** We found an inverse association between dietary intake of vegetables and breast cancer. Fruit consumption was significantly associated with greater odds of breast cancer in this study.


**Keywords:** *Breast cancer, case-control study, fruits, vegetables*


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## Introduction

Breast cancer is the most prevalent type of malignancy among women; its prevalence is continuously increasing worldwide.[1] In 2012, it was estimated that 1,671,149 new cases of breast cancer occurred.[2] International estimations showed that near 26% increase in breast cancer cases will occur by 2020, with a greater trend in developing countries.[3,4] The epidemiological model of breast cancer in Iran is similar to that of other east Mediterranean and developing countries.[4] Breast cancer is the most leading cause of cancer deaths in women, accounting for approximately 14.7% of cancer-related mortalities in women.[5] Therefore, prevention of breast cancer is a priority.

Diet is an important modifiable contributing factor to several cancers.[6,7] Greater adherence to healthy dietary patterns has been associated with a lower risk of breast cancer.[7,8] However, less attention has been paid to components of such dietary patterns. The favorable effects of healthy dietary patterns on human health have been attributed to their high content of fruits and vegetables;[8] consumption of these components has been inversely, but not consistently, associated with the risk of breast cancer.[1,9] In a meta-analysis, a weak inverse association was found between dietary intake of fruit, but not vegetables, and risk of breast cancer.[10] A meta-analysis of prospective cohort studies in 2017 revealed no significant association between the consumption of fruit and vegetables the and odds of breast cancer prognosis.[1] Overall, it seems that findings in this regard are conflicting and additional data are required to come to a definite conclusion.

Earlier studies on diet-breast cancer risk were mostly done in western countries, and limited information is available from Middle Eastern nations, where people are experiencing a nutrition transition from their


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traditional diets to food habits containing highly processed foods which means the population is undergoing changes in their dietary patterns and lifestyle behaviors, which may have negative impacts on their health.[11] Low consumption of fruits and vegetables in this area might explain the high prevalence of breast cancer among women.[12] In addition, the composition and available nutrients in fruit and vegetables are greatly different based on geographical locations.[13] In particular, raising vegetables in highly polluted areas, like that in most Middle Eastern countries, might result in taking toxic amounts of some minerals.[14] In addition, available studies frequently did not consider premenopausal and postmenopausal women as two separate groups in their analyses. Therefore, this case-control study was conducted to investigate the association of fruits and vegetables consumption with the risk of breast cancer in a group of Iranian adult women.

## Methods

### Study population

This population-based case-control study was conducted among women aged >30 years, who were currently residing in Isfahan, Iran. Breast cancer was diagnosed during the maximum of the last 6 months by physical examination and mammography findings. It was defined as primary incidence of breast tumor with invasive behavior and its histology was available from medical records. Participants were breast cancer (BC) patients who were referred to hospitals or private clinics in Isfahan, Iran from July 2013 to July 2015. The study sample size was calculated based on the type I error of 5%, with a study power of 80%. We hypothesized that unhealthy dietary patterns might increase the odds of breast cancer by 1.5 times. Considering the common ratio of 0.25 and the ratio of controls to cases as 2, we reached to almost 350 patients with breast cancer and 700 apparently healthy controls. Patients who underwent surgical resection for BC or were at chemotherapy or radiotherapy or experienced all of the treatments were selected. We did not include patients with a history of any type of neoplastic lesion or cysts (exception of current breast cancer) as well as those with a history of any hormone replacement therapy. In addition, those who were on a special diet were also not included in this study. Age-matched controls were selected from healthy women, who had no relationship with breast cancer patients or had no family history of breast cancer. In addition to age, we did our best to match controls in terms of socioeconomic status with the cases. Controls who met our inclusion criteria (female, Iranian nationally, no history of any malignancy, cysts and medical disorder, having no special diet or hormone replacement therapy) were selected from the general adult population. Finally, eligible subjects including 350 cases and 700 controls were recruited to the present study. Written informed consent was obtained from all subjects. The study was ethically approved by the Ethical Committee of Isfahan University of Medical Sciences, Isfahan, Iran.

### Dietary intake assessment

Dietary data were collected using a 106-item Willett-format semi-quantitative dish-based food frequency questionnaire which was designed and validated for Iranian adults.[15] Detailed information about design and validity of this dish-based food frequency questionnaire (FFQ) was reported elsewhere.[16,17] In this study, the questionnaires were completed through face-to-face interview by a trained nutritionist. The questionnaire contained five categories of foods and dishes: (1) mixed dishes (cooked or canned, 29 items), (2) carbohydrate-based foods (different types of bread, cakes, biscuits, and potato, 10 items), (3) dairy products (dairies, butter, and cream, nine items), (4) fruits and vegetables (22 items), and (5) miscellaneous food items and beverages (including sweets, fast foods, nuts, desserts, and beverages, 36 items). Participants were asked to report their dietary intake of foods and mixed dishes through nine multiple-choice frequency response categories varying from "never or less than once a month" to "12 or more times per day." Therefore, the frequency response for each food list varied from six to nine choices. For foods consumed infrequently, we omitted the high-frequency categories, while for common foods with high consumption, the number of multiple-choice categories increased. For instance, the frequency response for tuna consumption included six categories, as follows: never or less than once/month, 1-3 times/month, one time per week, 2-4 times/week, 5-6 times/week, and 1-2 times/day, and for tea consumption, the frequency response included nine categories, as follows: never or less than 1 cup/month, 1-3 cups/month, 1-3 cups/week, 4-6 cups/week, 1 cup/day, 2-4 cups/day, 5-7 cups/day, 8-11 cups/day, and ≥12 cups/day. Finally, we computed daily intakes of each food item and then converted them to grams per day, using household measures.[18] Daily values for each item were calculated according to food composition, average of reported frequency, and specified portion size. As for nutrient intakes, it was calculated by adding together the nutrient contents of all foods and dishes. The nutrient intake for each participant was obtained by the Nutritionist IV software, a modified version for Iranian foods. Our previous study indicated that this FFQ provided valid and reliable measures of the average long-term dietary intakes.[17,19]

**Assessment of breast cancer:** All patients with breast cancer were females with newly diagnosed stage I-IV breast cancer. They were recruited from Iranian nationality, for whom in-situ or invasive status of BC was confirmed by physical examination and mammography. Mammography is a type of X-ray imaging used for diseases diagnosis.[20] The harmful side effect of breast exposure with irradiation by mammography is very low which can be ignored.[21] This imaging method provides a black-and-white image

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of breast. For mammography, the patient was placed in a standing, horizontal, and vertical position; then breast was compressed for a few seconds between the pages and photography took place.[20]

### Assessment of other variables

Body weight was measured by a trained nutritionist, without shoes, and with light clothing, using a weighing calibrated scale (Seca, Hamburg, Germany) to the nearest 100 g. Height was measured by a mounted tape, without shoes at a standing position near the wall, using a statiometer (Seca, Hamburg, Germany) to the nearest 0.5 cm. Body mass index (BMI) was calculated through weight in kilograms divided by height in squared meters. In terms of physical activity, short form of International Physical Activity Questionnaire was used through face-to-face interviews.[22] All results of the International Physical Activity Questionnaire were expressed as Metabolic Equivalents-hours per week. A pretested questionnaire was also used to collect data on age, marital status, place of residence, education, socioeconomic status, history of disease, family history of cancer, breast feeding history, smoking, menopausal status, alcohol use, and supplement use.

### Statistical methods

Participants were categorized into quintiles based on the amounts of fruit and vegetable intake in their daily diet. General characteristics and dietary intakes of study participants across quintiles of fruit and vegetable intake were examined using one-way analysis of variance for continues variables and Chi-square for categorical variables. The association of fruit and vegetable intake with breast cancer was assessed by using logistic regression in different models. Age (continues) and energy intake (Kcal/d) were adjusted for in the first model. Additional controlling for region (urban/rural), marital status (yes/no), education (elementary/graduated/nongraduated), history of cancer (yes/no), physical activity (continues), family history of breast cancer (yes/no), menopausal status (premenopausal/postmenopausal), smoking (yes/no), alcohol consumption (yes/no), and socioeconomic status (poor/middle/high) was done in the second model. Further adjustment was done for dietary intakes of meat, soy, whole and refined grains, total dietary fat intake, and mutual effects of fruit and vegetables in the third model. Finally, we adjusted the analysis for BMI. Statistical analyses were carried out by using SPSS version 18. *P* values were considered significant at <.05.

## Results

Overall, data on 350 cases and 700 controls were analyzed. General characteristics of study participants among cases and controls are shown in Table 1. In general, cases were younger and had higher BMI than controls. The higher percentage of cases had a family history of breast cancer than controls. Moreover, they were more likely to be uneducated than controls. A lower percentage of cases were married, as compared to controls. With regards to dietary intakes, cases had more total energy intake and consumption of dietary fats than controls, while dietary intakes of carbohydrates and proteins were less among them.

**Table 1: General characteristics of study participants across cases and controls**

| | Controls (*n*=700) | Cases (*n*=350) | *P*[a] |
|---|---|---|---|
| Age (year) | 61.04±10.35 | 65.28±11.24 | <0.001 |
| BMI[#] (kg/m$^2$) | 25.55±5.05 | 21.87±4.88 | <0.001 |
| Physically activity (METs) | 34.87±6.58 | 35.43±6.73 | 0.20 |
| Married (%) | 88.3 | 74.6 | <0.001 |
| Education (%) | | | <0.001 |
| Elementary | 71.1 | 82.6 | |
| Undergraduate | 16.3 | 12.3 | |
| Graduated | 12.5 | 5.1 | |
| Current smoker (%) | 13.0 | 17.4 | 0.06 |
| Family history of cancer (%) | 3.4 | 9.4 | <0.001 |
| Supplement user (%) | 10.1 | 9.4 | 0.74 |
| Energy (Kcal/d) | 2,177.64±608.50 | 2,499.67±793.46 | <0.001 |
| Proteins (% of energy) | 80.11±18.45 | 72.26±21.29 | <0.001 |
| Fats (% of energy) | 81.87±18.26 | 90.04±25.29 | <0.001 |
| Carbohydrates (% of energy) | 320.28±45.25 | 311.20±61.64 | <0.01 |
| Soy (g/d) | 0.54±1.46 | 0.46±1.49 | 0.38 |

[a]Obtained using one-way analysis of variance for continuous variables and Chi-square test for categorical variable

General characteristics of study participants across quintiles of fruits and vegetables intake are shown in Table 2. BMI in participants in the highest quintile of fruit consumption was higher than those at the lowest quintile. They also had higher percentage of academic education than those at the lowest category. With regards to dietary intake of vegetables, those at the top category of intake were younger and had higher mean BMI than those at the bottom. Higher percentage of participants at the top category were married and had academic education than those at the lowest category, while they were less likely to be current smokers.

Energy-adjusted dietary intakes of study participants across quintiles of fruits and vegetables consumption are compared in Table 3. Participants in quintile 5 of fruit intake had higher dietary intakes of total energy, dietary fibers, refined grains, seafoods, dairy, and vegetables than those in quintile 1. In contrast, they consumed less amounts of dietary carbohydrates in comparison to participants with the lowest intake of fruits. Comparing the highest category of vegetable intake with the lowest one, participants in the former category consumed more proteins, dietary fibers, refined grains, seafoods, dairy, fruits, and soy with higher

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**Table 2: General characteristics of study participants across quintiles of fruit and vegetable intake**

| | Quintiles of fruit intake | | | | | $P^a$ |
|---|---|---|---|---|---|---|
| | $Q_1$ (*n*=210) | $Q_2$ (*n*=210) | $Q_3$ (*n*=209) | $Q_4$ (*n*=211) | $Q_5$ (*n*=210) | |
| Age (year) | 63.84±10.37 | 61.64±9.90 | 63.05±11.37 | 61.19±10.82 | 62.55±11.55 | 0.08 |
| BMI (kg/m$^2$) | 23.43±4.88 | 23.92±5.32 | 24.87±5.26 | 24.61±5.45 | 24.80±5.41 | 0.01 |
| Physically activity (METs) | 34.85±6.56 | 34.57±6.56 | 35.10±7.49 | 35.32±6.45 | 35.45±6.03 | 0.65 |
| Married (%) | 76.7 | 84.8 | 84.4 | 87.1 | 85.7 | 0.12 |
| Education (%) | | | | | | <0.001 |
| Elementary | 90.5 | 76.2 | 79.1 | 62.2 | 66.7 | |
| Undergraduate | 6.2 | 19.0 | 11.8 | 21.5 | 16.2 | |
| Graduated | 3.3 | 4.8 | 9.1 | 16.3 | 17.1 | |
| Current smoker (%) | 16.2 | 13.3 | 10.9 | 19.1 | 12.9 | 0.13 |
| Family history of cancer (%) | 4.8 | 6.2 | 4.3 | 5.7 | 6.2 | 0.86 |
| Supplement user (%) | 7.1 | 11.9 | 11.4 | 10.0 | 9.0 | 0.48 |
| | **Quintiles of vegetables intake** | | | | | $P^a$ |
| | $Q_1$ (*n*=210) | $Q_2$ (*n*=210) | $Q_3$ (*n*=210) | $Q_4$ (*n*=210) | $Q_5$ (*n*=210) | |
| Age (year) | 65.42±11.03 | 61.72±10.55 | 61.45±10.14 | 61.87±11.07 | 61.81±10.97 | <0.01 |
| BMI (kg/m$^2$) | 22.78±4.92 | 24.03±5.87 | 24.07±4.98 | 24.73±5.21 | 26.01±4.92 | <0.001 |
| Physically activity (METs) | 35.16±6.90 | 34.75±6.62 | 34.78±6.15 | 35.53±7.04 | 35.06±6.45 | 0.75 |
| Married (%) | 72.4 | 82.4 | 91.9 | 84.3 | 87.6 | <0.001 |
| Education (%) | | | | | | <0.001 |
| Elementary | 86.2 | 81.9 | 74.8 | 72.9 | 59.0 | |
| Undergraduate | 11.0 | 11.0 | 18.1 | 14.3 | 20.5 | |
| Graduated | 2.8 | 7.1 | 7.1 | 12.8 | 20.5 | |
| Current smoker (%) | 20.0 | 13.8 | 16.2 | 10.0 | 12.4 | 0.04 |
| Family history of cancer (%) | 7.1 | 5.7 | 4.8 | 5.7 | 3.8 | 0.64 |
| Supplement user (%) | 9.5 | 11.4 | 11.9 | 9.0 | 7.6 | 0.57 |

[a]Obtained by the use of ANCOVA

total energy intake than the following category adherents. However, they consumed less dietary fat than their counterparts.

Multivariable-adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for breast cancer across quintiles of dietary intake of fruits and vegetables are shown in Table 4. Participants with the highest dietary intake of fruits had higher odds of breast cancer than those with the lowest intake (OR: 3.26; 95% CI: 2.16-4.91). This association remained significant after adjustment for a wide range of confounding factors (OR: 8.23; 95% CI: 4.37-15.50). In contrast, those who consumed highest amounts of vegetables were less likely to have breast cancer, when compared to those with the lowest consumption (OR: 0.34; 95% CI: 0.23-0.52). This association also remained unchanged during controlling for the confounders, even at the full adjusted model (OR: 0.12; 95% CI: 0.06-0.24).

Multivariable-adjusted ORs and 95% CIs for breast cancer across quintiles of dietary intake of fruits and vegetables considering the menopausal status of participants are shown in Table 5. Although no significant associations were found between dietary intakes of fruits (OR: 2.56; 95% CI: 0.38, 17.17; $P$ = .08) and vegetables (OR: 0.06; 95% CI: 0.00, 0.82; $P$ = .84) with risk of breast cancer in premenopausal women, significant direct and inverse trends were found between increasing quintiles of fruits (OR: 16.80; 95% CI: 7.80, 36.21; $P$ < .001) and vegetables (OR: 0.09; 95% CI: 0.04, 0.19; $P$ < .001) intakes and risk of breast cancer in postmenopausal women, respectively.

## Discussion

We found a significant inverse association between the dietary intake of vegetables and the risk of breast cancer. In contrast, a high dietary intake of fruits was associated with an increased risk of breast cancer in the present study. Such associations were seen in postmenopausal women only.

Breast cancer is the most prevalent cancer among women worldwide.[23] We found an inverse association between vegetable intake and risk of breast cancer. This finding was in line with a recently published cohort study of women with 30 years of follow-up, in which higher intake of vegetables was associated with the reduced risk of breast cancer.[24] Consumption of vegetables was also inversely associated with the risk of estrogen receptor-negative/ progesterone receptor-negative breast cancer in another cohort study.[25] However, some studies failed to find a significant association between vegetable intake and risk of breast cancer.[26] In addition, findings from a meta-analysis of cohort studies in 2017 showed no significant association between dietary intake of vegetables and risk of breast

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**Table 3: Dietary intakes of study participants across quintiles of dietary intakes of fruits and vegetables**

| | Quintiles of fruit intake | | | | | $P^a$ |
|---|---|---|---|---|---|---|
| | $Q_1$ (*n*=210) | $Q_2$ (*n*=210) | $Q_3$ (*n*=209) | $Q_4$ (*n*=211) | $Q_5$ (*n*=210) | |
| Energy (Kcal/d#) | 1,984.36±659.01 | 2,114.66±595.83 | 2,211.96±596.30 | 2,306.60±582.44 | 2,807.78±721.68 | <0.001 |
| Proteins (% of energy) | 75.90±19.95 | 76.35±18.79 | 78.21±17.85 | 79.92±19.82 | 77.10±22.19 | 0.23 |
| Fats (% of energy) | 81.92±19.24 | 86.15±17.00 | 87.05±22.55 | 83.42±17.73 | 84.42±27.53 | 0.09 |
| Carbohydrates (% of energy) | 324.45±50.16 | 314.02±41.77 | 309.96±48.61 | 317.41±47.13 | 320.47±65.66 | 0.04 |
| Dietary Fiber (g/d) | 22.28±4.99 | 21.75±3.66 | 21.80±4.34 | 22.73±4.23 | 23.42±6.82 | <0.01 |
| Whole grains (g/d) | 334.78±180.11 | 306.66±133.83 | 300.93±146.17 | 309.69±138.35 | 332.38±168.26 | 0.07 |
| Refined grains (g/d) | 88.47±66.99 | 103.17±64.71 | 122.07±84.11 | 126.63±85.66 | 134.05±79.75 | <0.001 |
| Seafoods (g/d) | 8.98±58.69 | 4.44±10.80 | 5.30±8.74 | 8.51±13.43 | 13.67±31.88 | 0.02 |
| Dairies (g/d) | 138.51±108.62 | 225.40±180.57 | 231.91±130.34 | 240.59±127.90 | 321.44±162.61 | <0.001 |
| Fruits (g/d) | 35.72±15.26 | 78.54±11.55 | 121.68±15.09 | 184.25±22.84 | 404.41±185.04 | <0.001 |
| Vegetables (g/d) | 47.35±36.85 | 62.93±47.04 | 80.65±76.34 | 88.70±63.09 | 125.15±98.52 | <0.001 |
| Soy (g/d) | 0.54±1.60 | 0.44±1.16 | 0.58±1.83 | 0.54±1.28 | 0.48±1.39 | 0.87 |
| | **Quintiles of vegetables intake** | | | | | $P^b$ |
| | $Q_1$ (*n*=210) | $Q_2$ (*n*=210) | $Q_3$ (*n*=210) | $Q_4$ (*n*=210) | $Q_5$ (*n*=210) | |
| Energy (Kcal/d#) | 1,984.10±672.01 | 2,146.90±622.51 | 2,273.08±617.30 | 2,363.43±621.99 | 2,657.40±736.62 | <0.001 |
| Proteins (% of energy) | 79.29±24.35 | 72.53±14.55 | 76.98±18.52 | 77.06±18.33 | 81.60±20.87 | <0.001 |
| Fats (% of energy) | 84.81±18.17 | 87.29±23.27 | 80.62±1.89 | 85.71±20.13 | 84.55±25.92 | 0.02 |
| Carbohydrates (% of energy) | 314.74±48.97 | 316.05±50.96 | 326.78±44.78 | 315.02±44.40 | 313.69±64.77 | 0.05 |
| Dietary Fiber (g/d) | 20.95±4.70 | 21.10±4.82 | 22.91±3.96 | 22.35±4.23 | 24.67±5.94 | <0.001 |
| Whole grains (g/d) | 307.64±146.71 | 303.19±144.17 | 341.85±137.06 | 313.06±156.30 | 318.65±183.60 | 0.09 |
| Refined grains (g/d) | 86.06±70.28 | 103.75±69.27 | 111.67±56.59 | 125.80±76.04 | 147.10±99.96 | <0.001 |
| Seafoods (g/d) | 6.15±18.43 | 4.16±8.76 | 5.14±9.05 | 6.22±9.36 | 19.21±64.39 | <0.001 |
| Dairies (g/d) | 199.55±154.68 | 208.30±138.24 | 205.79±120.61 | 259.20±191.32 | 284.96±145.16 | <0.001 |
| Fruits (g/d) | 112.24±102.89 | 137.36±133.82 | 131.27±102.77 | 180.84±157.00 | 262.58±203.17 | <0.001 |
| Vegetables (g/d) | 15.52±8.47 | 39.76±6.93 | 65.12±7.51 | 95.84±10.85 | 188.48±90.49 | <0.001 |
| Soy (g/d) | 0.33±1.35 | 0.44±1.49 | 0.40±1.12 | 0.56±1.24 | 0.85±1.97 | <0.01 |

[a]Obtained by the use of ANCOVA

**Table 4: Multivariate-adjusted odds ratios and 95% CIs for breast cancer in relation to dietary intake of fruits and vegetables**

| | Quintiles of fruit intake | | | | | $P^a$ |
|---|---|---|---|---|---|---|
| | $Q_1$ (*n*=210) | $Q_2$ (*n*=210) | $Q_3$ (*n*=211) | $Q_4$ (*n*=209) | $Q_5$ (*n*=210) | |
| Crude | 1 | 1.20 (0.78, 1.84) | 0.83 (0.53, 1.29) | 1.29 (0.85, 1.97) | 3.26 (2.16, 4.91) | <0.001 |
| Model 1 | 1 | 1.25 (0.80, 1.94) | 0.74 (0.47, 1.17) | 1.21 (0.78, 1.89) | 2.28 (1.45, 3.59) | <0.01 |
| Model 2 | 1 | 1.39 (0.88, 2.19) | 0.84 (0.52, 1.35) | 1.55 (0.97, 2.49) | 3.03 (1.85, 4.97) | <0.001 |
| Model 3 | 1 | 1.37 (0.85, 2.22) | 0.85 (0.51, 1.42) | 1.85 (1.12, 3.07) | 4.81 (2.73, 8.47) | <0.001 |
| Model 4 | 1 | 1.49 (0.88, 2.50) | 0.98 (0.57, 1.70) | 2.35 (1.36, 4.07) | 8.23 (4.37, 15.50) | <0.001 |
| | **Quintiles of vegetable intake** | | | | | $P^a$ |
| | $Q_1$ (*n*=210) | $Q_2$ (*n*=210) | $Q_3$ (*n*=210) | $Q_4$ (*n*=210) | $Q_5$ (*n*=210) | |
| Crude | 1 | 0.43 (0.29, 0.64) | 0.22 (0.14, 0.35) | 0.47 (0.32, 0.70) | 0.34 (0.23, 0.52) | <0.001 |
| Model 1 | 1 | 0.38 (0.25, 0.58) | 0.16 (0.10, 0.26) | 0.32 (0.21, 0.50) | 0.16 (0.10, 0.26) | <0.001 |
| Model 2 | 1 | 0.38 (0.24, 0.60) | 0.17 (0.10, 0.29) | 0.32 (0.20, 0.50) | 0.15 (0.09, 0.26) | <0.001 |
| Model 3 | 1 | 0.34 (0.21, 0.54) | 0.18 (0.11, 0.30) | 0.28 (0.17, 0.46) | 0.11 (0.06, 0.20) | <0.001 |
| Model 4 | 1 | 0.32 (0.19, 0.53) | 0.17 (0.09, 0.29) | 0.31 (0.18, 0.52) | 0.12 (0.06, 0.24) | <0.001 |

Model 1: Adjusted for age and energy. Model 2: Additionally, adjusted for region, marital status, education, disease history, physical activity, family history of breast cancer, menopausal status, smoking, alcohol consumption, and socioeconomic status. Model 3: Further adjustment for intakes of fruit, vegetables, meat, soy, whole and refined grains, and total dietary fat. Model 4: Additional adjustment for BMI. [a]The *P* for trend across increasing quintiles of fruit and vegetable intake was calculated using multivariable logistic regression by considering the categories as an ordinal variable

cancer prognosis.[1] It seems that the type of consumed vegetables plays an important role in this regard. Few studies have been done on specific types of vegetables in relation to the risk of breast cancer. For instance, higher intakes of cruciferous vegetables were linked to reduced risk of breast cancer in a meta-analysis.[27]

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**Table 5: Multivariate-adjusted odds ratios and 95% CIs for breast cancer in relation to dietary intake of fruit and vegetables, stratified by the menopausal status**

| | Quintiles of fruit intake | | | | | $P^a$ |
|---|---|---|---|---|---|---|
| | $Q_1$ (*n*=210) | $Q_2$ (*n*=210) | $Q_3$ (*n*=211) | $Q_4$ (*n*=209) | $Q_5$ (*n*=210) | |
| Premenopausal women | | | | | | |
| Crude | 1 | 0.29 (0.08, 1.03) | 0.18 (0.04, 0.75) | 0.61 (0.22, 1.69) | 1.40 (0.52, 3.76) | 0.20 |
| Model 1 | 1 | 0.27 (0.07, 0.99) | 0.15 (0.03, 0.64) | 0.53 (0.18, 1.52) | 0.89 (0.30, 2.60) | 0.61 |
| Model 2 | 1 | 0.32 (0.08, 1.32) | 0.14 (0.03, 0.65) | 0.59 (0.17, 2.01) | 1.20 (0.35, 4.05) | 0.44 |
| Model 3 | 1 | 0.35 (0.07, 1.60) | 0.10 (0.01, 0.74) | 0.82 (0.21, 3.09) | 2.10 (0.50, 8.82) | 0.16 |
| Model 4 | 1 | 0.57 (0.09, 3.53) | 0.17 (0.01, 1.97) | 1.97 (0.34, 11.37) | 2.56 (0.38, 17.17) | 0.08 |
| Postmenopausal women | | | | | | |
| Crude | 1 | 1.50 (0.94, 2.37) | 1.04 (0.65, 1.68) | 1.56 (0.98, 2.49) | 3.92 (2.49, 6.17) | <0.001 |
| Model 1 | 1 | 1.58 (0.98, 2.55) | 0.91 (0.55, 1.48) | 1.38 (0.85, 2.24) | 2.63 (1.59, 4.34) | <0.01 |
| Model 2 | 1 | 1.73 (1.05, 2.85) | 1.02 (0.61, 1.70) | 1.87 (1.11, 3.14) | 3.46 (2.00, 5.98) | <0.001 |
| Model 3 | 1 | 1.78 (1.03, 3.08) | 1.23 (0.70, 2.17) | 2.94 (1.63, 5.30) | 7.75 (3.96, 15.18) | <0.001 |
| Model 4 | 1 | 2.08 (1.15, 3.75) | 1.45 (0.78, 2.68) | 4.24 (2.20, 8.17) | 16.80 (7.80, 36.21) | <0.001 |
| | Quintiles of vegetable intake | | | | | $P^a$ |
| | $Q_1$ (*n*=210) | $Q_2$ (*n*=210) | $Q_3$ (*n*=210) | $Q_4$ (*n*=210) | $Q_5$ (*n*=210) | |
| Premenopausal women | | | | | | |
| Crude | 1 | 0.19 (0.05, 0.64) | 0.24 (0.07, 0.79) | 0.40 (0.14, 1.14) | 0.39 (0.13, 1.15) | 0.45 |
| Model 1 | 1 | 0.08 (0.02, 0.34) | 0.10 (0.02, 0.39) | 0.22 (0.07, 0.71) | 0.11 (0.02, 0.40) | 0.05 |
| Model 2 | 1 | 0.07 (0.01, 0.32) | 0.09 (0.02, 0.41) | 0.22 (0.06, 0.75) | 0.11 (0.02, 0.52) | 0.12 |
| Model 3 | 1 | 0.07 (0.01, 0.38) | 0.12 (0.02, 0.63) | 0.25 (0.06, 1.03) | 0.06 (0.01, 0.38) | 0.09 |
| Model 4 | 1 | 0.02 (0.00, 0.19) | 0.05 (0.00, 0.58) | 0.42 (0.07, 2.44) | 0.06 (0.00, 0.82) | 0.84 |
| Postmenopausal women | | | | | | |
| Crude | 1 | 0.51 (0.33, 0.78) | 0.23 (0.14, 0.36) | 0.51 (0.33, 0.79) | 0.34 (0.22, 0.54) | <0.001 |
| Model 1 | 1 | 0.48 (0.30, 0.76) | 0.17 (0.10, 0.29) | 0.33 (0.20, 0.54) | 0.16 (0.09, 0.28) | <0.001 |
| Model 2 | 1 | 0.49 (0.30, 0.78) | 0.19 (0.11, 0.32) | 0.32 (0.19, 0.53) | 0.14 (0.08, 0.26) | <0.001 |
| Model 3 | 1 | 0.41 (0.24, 0.68) | 0.19 (0.11, 0.33) | 0.25 (0.14, 0.43) | 0.09 (0.04, 0.17) | <0.001 |
| Model 4 | 1 | 0.38 (0.22, 0.67) | 0.17 (0.09, 0.31) | 0.25 (0.14, 0.47) | 0.09 (0.04, 0.19) | <0.001 |

Model 1: Adjusted for age and energy. Model 2: Additionally, adjusted for region, marital status, education, disease history, physical activity, family history of breast cancer, smoking, alcohol consumption, and socioeconomic status. Model 3: Further adjustment for intakes of fruit, vegetables, meat, soy, whole and refined grains, and total dietary fat. Model 4: Additional adjustment for BMI. [a]The *P* for trend across increasing quintiles of fruit and vegetable intake was calculated using multivariable logistic regression by considering the categories as an ordinal variable

Sulforaphane is an organosulfur compound found in cruciferous vegetables like broccoli and mustard, which has shown potential in treating breast cancer. Sulforaphane has been found to effectively modulate histone deacetylases involved in chromatin remodeling, gene expression, and Nrf2 antioxidant signaling.[28] Breast cancer is a prevalent and potentially life-threatening form of cancer among women in Iran.[29]

Further studies considering different types of vegetables are recommended to shed light on this issue.

Unexpectedly, we found a positive association between dietary intake of fruits and the risk of breast cancer. This finding was against most published studies in this regard, in which a high intake of fruits has been related to reduced risk of breast cancer.[10] However, some studies failed to find such a significant inverse association.[30,31] When we examined fruit intake among those in the highest quintile, we found that the average fruit intake in this quintile was 230 g/d. This amount was not so high, compared with other studies.[24,32] Some people in this category were taking nearly 1200 gr/day of fruits. Type of fruits might help explain the association we found. For instance, the elevated risk of breast cancer among these women might be explained by the high intake of fructose-rich fruits such as apples and peaches. Earlier studies have shown that high fructose intake can in turn result in increased storage of lipids, which lead to elevated low-grade inflammation and eventually to several cancers.[33]

Menopausal status seems to affect the association between vegetable intake and breast cancer. We found the inverse association of vegetables intake with risk of breast cancer only among postmenopausal women, not in premenopausal women. Similar to our findings, a cohort study in the United States showed that greater adherence to the healthy diet was inversely linked to odds of breast cancer in postmenopausal, but not in premenopausal, women.[34] Differences in serum levels of sexual hormones, like estrogen, might provide some reason for these discrepant findings. Stage of breast cancer as well as estrogen receptors might also be involved in this story.

The exact mechanism through which dietary intake of vegetables might influence the risk of breast cancer has not

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been clearly known. However, some probable mechanisms are suggested. Vegetables are common sources of many beneficial micronutrients, including ascorbic acid.[35]

Luteolin, a flavonoid found in different fruits and vegetables has been known as an anticancer agent through inducing apoptosis and cell cycle arrest, and thorough inhibiting metastasis and angiogenesis in multiple cancer cell lines such as breast, colon, pancreatic, and lung, among others.[36]

High dietary intake of some of these micronutrients has been associated to lower risk of breast cancer incidence and mortality.[37] In addition, vegetables are rich in antioxidants, which has been protective associated with breast cancer.[38,39] For instance, plasma total carotenoid concentration has been inversely associated with breast cancer recurrence.[40] Furthermore, vegetables are also common sources of dietary fiber which was related to the reduced risk of breast cancer.[41] Phytochemical content of vegetables including monoterpenes, resveratrol, and lignans can also play a role in this regard.[42] Cyanidin-3-glucoside, an anthocyanin present in many fruits and vegetables, might block ethanol-induced activation of the ErbB2/cSrc/FAK pathway, which is necessary for cell migration and invasion.[43] Fruit and vegetable consumption were each inversely associated with the risk of breast cancer, whereas meat consumption was positively related to risk.[32] Observed no significant association of risk of BC with either total consumption of fruits and vegetables (FVs) or with their subgroups among Iranian women, except for berry fruits which were showed that greater consumption of berries resulted in lower BC risk in study population.[44] This study is among rare investigations on the association of fruit and vegetable intake with the risk of breast cancer among Middle-Eastern population. This association was independent of other confounding variables because we adjusted the analysis for a wide range of potential confounders including dietary and nondietary covariates. However, some limitations should be kept in mind. Limitations such as age at menarche, age at first live birth, number of live births, and months of breastfeeding. Because of the observational case-control design of the study, it is impossible to confer causality. Moreover, selection and recall bias should not be ignored. In addition, we used FFQ to assess dietary intake of fruits and vegetables in study participants; therefore, misclassification of study participants cannot be excluded.

## Conclusions

This study showed an inverse association between dietary intake of vegetables and a positive association between dietary intake of fruit and risk of breast cancer. These associations were observed in postmenopausal women only. Further prospective studies are required to re-examine these associations to expand the current knowledge.

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### Conflicts of interest

There are no conflicts of interest.

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