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ORIGINAL ARTICLE

Association between dietary phytochemical index and breast cancer: a case–control study

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Abstract

Background Dietary intake of isoflavones has been positively associated with risk of breast cancer (BC) in some earlier studies. In addition, most studies on diet–disease associations came from western countries and limited data are available in the Middle-East.

Methods This case–control study was performed on 350 women with BC aged over 30 years who were recruited from hospitals or private clinics in Isfahan, Iran. All patients were diagnosed with BC during the maximum of the last 6 months using physical examination and mammography findings. Using cluster method sampling, 700 apparently healthy age- and socioeconomic status-matched controls were randomly selected from healthy women who had no relationship with BC patients and had no familial history of BC. Data on dietary intakes were collected using a validated food-frequency questionnaire. The DPI was calculated based on dietary energy derived from foods rich in phytochemicals (kcal) divided by total daily energy intake (kcal) of each participant.

Results Mean ± SD age and BMI in the study participants were 62.4 ± 10.8 years and 24.3 ± 5.2 kg/m^2, respectively. In the crude model, participants in the highest quartile of DPI had 63% lower odds of breast cancer compared to those in the lowest quartile (95% CI 0.26, 0.54; *P*-trend < 0.001). After adjustment for potential confounders, this inverse association became strengthened (95% CI 0.22, 0.49; *P*-trend < 0.001). Further adjustment for BMI did not change the association (OR for the highest quartile vs. the lowest quartile = 0.40, 95% CI 0.26, 0.60; *P*-trend < 0.001).

Conclusion In conclusion, a protective association was observed between DPI and BC in this case–control study. Therefore, high consumption of foods rich in phytochemicals such as fruits, vegetables, and whole grains might help reducing the odds of BC among women.

Keywords Phytochemicals · Antioxidants · Breast cancer · Diet · Case–control

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Introduction

Breast cancer (BC) is one of the most common types of cancer in the world. It is the leading cause of cancer deaths among women in both developing and developed countries [1–4]. In most western countries, mortality rate from BC has risen rapidly to about 40% in the past 30 years [5]. In 2019, 30% of new cancer cases in the US were patients with breast cancer [5]. In Iran, breast cancer is the most prevalent cancer among women [1].

In addition to well-known risk factors for BC including age, family history, early menstruation [1], smoking [6], high adiposity [7], hormone replacement therapy and not breast feeding [8], dietary intakes play an important role [1]. Our group has previously reported some important associations between some foods and dietary patterns with BC [9–12]. In terms of dietary intakes, fruit and vegetables consumption has been inversely linked with the risk [13–16]. The protective association of these food groups with BC might be mediated through their high content of phytochemicals, which are a wide part of dietary components linked to reduced risk of several chronic disease including cardiovascular disease [17], diabetes [18], inflammatory bowel disease [19] and Alzheimer's disease [20]. These components are non-nutritive bioactive compounds including polyphenols (phenolic acids, flavonoids, isoflavones, lignans, stillbenes, curcuminoids, and calcones), Terpenoids, Organosulfurs, and phytosterols [21]. Diets containing a variety of fresh fruits and vegetables, whole grains, nuts, legumes are rich in phytochemicals. As quantification of phytochemicals in food sources is expensive and impractical for large epidemiological studies, McCarty et al. developed a simple and practical tool, named dietary phytochemical index (DPI), for representing the phytochemical content of a whole diet [21]. This index is defined as the percentage of energy intake derived from phytochemical-rich foods [21–23]. Although, the association between DPI and a variety of cancers such as skin cancer [24] and gastrointestinal cancer [25] have been previously examined, limited studies are available linking DPI to the risk of BC [13, 15, 26–28]. In a case–control study, individuals with higher DPI had a decreased risk for BC than those with the lower DPI [26]. On the other hand, dietary intake of isoflavones has been positively associated with the risk of BC in Asian women [27]. Given these controversies, it seems that additional data are required to further investigate the association between DPI and risk of breast cancer, in particular in women residing in the Middle East, where dietary intakes are different from other parts of the world. Most studies on diet–disease association came from western countries and limited data are available in Middle-East. Nutritional transition in this region has been resulted in a decreased intake of nutrient-dense foods, which are originally high in phytochemicals. Such differences might result in a different overall pattern of phytochemicals in the diet than those in western nations [29]. Therefore, we aimed to investigate the association between DPI and risk of BC among Iranian adult women.

Methods

Study population

In this population-based case–control study, women aged older than 30 years were recruited from hospitals or private clinics from July 2013 to July 2015 in Isfahan, Iran. All patients were diagnosed with BC during the maximum of the last 6 months using physical examination and mammography findings. They all had primary tumors with invasive behaviors in the breast. Patients were enrolled from those who underwent BC surgery, chemotherapy, radiotherapy, or any of these. Individuals with any history of neoplastic lesions or cysts (except of current BC) or any type of hormone replacement therapy were not included in our study. Using cluster method sampling, age and socioeconomic status-adjusted controls were randomly selected from healthy women who had no relationship with BC patients and had no familial history of BC. Our inclusion criteria for control group were: being woman, having Iranian ethnicity and not having any history of malignancy, cysts and medical disorders and hormone replacement therapy and not following a special diet. The required sample size was calculated by considering the type I error of 5% and the type II error of 20%. Using a common ratio of 25% and ratio of controls to cases as 2, and assuming a 1.5-fold increase in the risk of BC following an unhealthy diet, we eventually reached 350 BC patients and 700 individuals in the control group. A written consent form was completed by all individuals. The whole project was ethically approved by the ethics committee of Isfahan University of Medical Sciences.

Assessment of dietary intakes

Using a 106-item food-based semi-quantitative Willett-format food-frequency questionnaire, dietary data were collected from all participants. Details about the design and validity of the FFQ have been reported elsewhere [30]. The questionnaire included five categories of foods: (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, 9 items); (4) fruit and vegetables (22 items); and (5) miscellaneous food items and beverages (including sweets, fast foods, nuts, desserts, and beverages, 36 items). People in the study were asked to report their food intake based on nine options ranging from "never or less than once a month" to "12 times or more per day." We calculated the daily consumption for different foods and reported them as grams per day. Consumption of nutrients is calculated using the Nutritionist IV software, which was modified for Iranian food. The amount of nutrients consumed is obtained by adding the amount of nutrients in different foods. Our previous study showed that the validity and reliability of this FFQ to obtain the average long-term dietary intake was reasonable [30].

Calculation of phytochemical index

Dietary PI was calculated using the method developed by McCarthy [23] as follows:

$$\text{DPI} = \left(\text{Dietary energy derived from foods rich in phytochemicals (kcal)}/\text{total daily energy intake (kcal)}\right) \times 100.$$

The following food items were considered as phytochemical-rich foods in the present analysis: whole grains (toast, oat, bulgur and traditional Iranian breads including Sangak and Barbari), fruits (yellow,red and orange fruits), vegetables (red/orange vegetables, starchy vegetables, dark green vegetables and other vegetables), natural fruit and vegetable juices (orange juice, lemon juice, cantaloupe juice, apple juice, grapefruit juice), tomato sauces, soy products (soy bean), nuts (almond, walnut, peanut, pistachio and hazelnut), legumes (split bean, lentil, chickpea, beans, mung bean and vicia faba), seeds, olive, and olive oil. Except for potatoes, which are low in phytochemicals, other vegetables are considered foods rich in phytochemicals.

Assessment of breast cancer

All female patients were Iranian with a recent diagnosis of stage I–IV BC, for whom in-situ or invasive status of BC was confirmed by physical examination and mammography.

Assessment of other variables

The face-to-face interview questionnaire was used to collect data on age, region (urban/rural), education (educated/non-educated), family history of breast cancer (yes/no), alcohol consumption (yes/no), smoking (non-smoker/smoker), marital status (single/ married), menopausal status (premenopausal/postmenopausal), and disease history (yes/no). Weight was measured using a digital scale without shoes and with the least possible clothing. Height was measured with an accuracy of 0.5 cm, when the person was standing without shoes in a normal position. Body mass index was obtained by dividing weight in kilograms by the square of height in meters. To evaluate the level of physical activity of participants, we used the short form of the International Physical Activity Questionnaire (IPAQ). Earlier studies have shown that the information from this questionnaire is accurate and valid [31–33]. Participants were classified based on <1 h per week (physically inactive) and ≥ 1 h per week (physically active).

Statistical analysis

To examine the association between dietary phytochemical index and odds of breast cancer, first, we classified participants based on the quartiles of DPI. Then, ANOVA and Chi-square tests were used to evaluate the differences between continuous and categorical variables across different quartiles of DPI. To determine the odds ratios (ORs) and 95% confidence intervals (95% CI) for BC among different quartiles of DPI, a regression logistic was applied in different models, in which we controlled for age (continuous), residence place (urban/rural), marital status (non/married/not married), SES (poor/middle/high class), education (educated/non-educated), family history of BC (yes/no), menopausal status (post-menopause/pre-menopause), breast feeding (yes/no), history of disease (yes/no), supplement use (yes/no), smoking (yes/no), and alcohol (yes/no) consumption in the first model. BMI was additionally adjusted for in the second model to identify obesity-independent association. *P* value <0.05 was considered as statistically significant. All analyses were done using SPSS software (version 26).

Results

Mean ± SD of BMI and age in this study participants were 24.3 ± 5.2 kg/m^2 and 62.4 ± 10.8 years, respectively. The mean ± SD of the DPI in our study was 54.76 ± 12.96. General characteristics of study participants across quartiles of DPI are presented in Table 1. Compared to people in the bottom quartile, those in the top quartile of DPI had higher weight and BMI and were more likely to use supplements, be post-menopause, married and educated. They were also less likely to reside in urban areas, have family history of BC, use alcohol, and to be smoker, physically active, breast fed the child and were of poor socioeconomic status compared to individuals in the first quartile of DPI. No other significant association was seen across quartiles of DPI.

Table 2 indicates dietary intakes of study participants across quartiles of DPI. Compared to the bottom quartile, individuals in the top quartile of DPI had higher intakes

Table 1 General characteristics of study participants across quartiles of dietary phytochemical index

Variables	Quartiles of dietary phytochemical index					P^{a}
	Total	Q1 <46.30	Q2 46.30–54.45	Q3 54.45–63.31	Q4 >63.31	
Age (year)	62.4 ± 10.8	62 ± 11.6	63.1 ± 10.2	61.2 ± 11.4	63.4 ± 9.8	0.077
Weight (kg)	63.6 ± 14.4	60.6 ± 14.2	62.9 ± 14.5	64.7 ± 14.8	66.3 ± 13.6	< 0.001
BMI (kg/m^2)[b]	24.3 ± 5.2	23.4 ± 5.5	24.2 ± 5.4	24.4 ± 5.3	25.1 ± 4.7	0.044
Physical activity (MET-h/week)	35 ± 6.6	35.3 ± 6.5	34.6 ± 6.8	34.9 ± 6.5	35.2 ± 6.6	0.601
Urban residency (%)	36.1	40.1	34.2	31.9	38.2	0.199
Married (%)	83.7	83.6	81.4	88.2	81.7	0.036
Educated (%)	25	24.4	21.7	31.2	22.9	0.056
Family history of BC (%)[c]	5.4	6.1	6.1	4.9	4.6	0.815
Smoker (%)	14.5	15.3	14.1	14.4	14.1	0.978
Alcohol use (%)[d]	6.5	8	3.8	6.8	7.3	0.217
Post-menopause (%)	81	76.7	86.3	76	85.1	0.002
Breast feeding (%)	33.8	35.5	36.5	37.6	30.5	0.165
Poor social economic status (%)	30.5	32.1	28.1	34.2	27.5	0.232
History of disease (%)	9.2	12.6	4.9	6.5	13	0.001
Supplement use (%)	9.9	9.5	9.1	14.1	6.9	0.045

Continuous variable are expressed as means ± SD and categorical variables are expressed as percentages

[a]Obtained from ANOVA or Chi-square test, where appropriate

[b]Body mass index

[c]Breast cancer

[d]History of alcohol use in the past 6 months

Table 2 Dietary intakes of participants by quartiles of dietary phytochemical index

Variables	Quartiles of dietary phytochemical index				*P* value
	Q1 <46.30	Q2 46.30–54.45	Q3 54.45–63.31	Q4 >63.31	
Total energy (kcal/day)	2412 ± 42	2342 ± 42	2277 ± 42	2106 ± 42	< 0.001
Nutrients					
Carbohydrates (g/day)	282 ± 2.8	312 ± 2.8	326 ± 2.8	348 ± 2.8	< 0.001
Proteins (g/day)	75.5 ± 1.2	76.5 ± 1.2	79.6 ± 1.2	78.4 ± 1.2	0.084
Fats (g/day)	100.4 ± 1.1	86.8 ± 1.1	79.9 ± 1.1	71.2 ± 1.1	< 0.001
Total fiber (g/day)	17.7 ± 0.2	21.5 ± 0.2	23.7 ± 0.2	26.5 ± 0.2	< 0.001
Vitamin E (IU/day)	6.7 ± 0.1	6.3 ± 0.1	6.4 ± 0.1	6.3 ± 0.1	0.425
Folate (mcg/day)	262 ± 3.9	274 ± 3.96	285 ± 3.96	297 ± 4.00	< 0.001
Calcium (mg/day)	737 ± 13.7	772 ± 13.7	768 ± 13.7	781 ± 13.8	0.122
Zinc (mg/day)	9.3 ± 0.1	9.9 ± 0.1	10.5 ± 0.1	10.8 ± 0.1	< 0.001
Foods					
Meats (g/day)	110 ± 116	85 ± 57	79 ± 51	59 ± 48	< 0.001
Egg (g/day)	11.5 ± 0.8	13.4 ± 0.8	11 ± 0.8	8.6 ± 0.9	0.002
Trans fatty acids (g/day)	0.5 ± 0.01	0.4 ± 0.01	0.3 ± 0.01	0.3 ± 0.01	< 0.001
Fruit (g/day)	175 ± 8.6	171 ± 8.5	146 ± 8.6	166 ± 8.6	0.086
Vegetables (g/day)	71.8 ± 4.3	77.4 ± 4.2	81.7 ± 4.2	92.8 ± 4.3	0.006
Grains (g/day)	311 ± 79	408 ± 72	471 ± 68	534 ± 98	< 0.001
Dairy (g/day)	275 ± 8.7	246 ± 8.6	218 ± 8.6	186 ± 8.7	< 0.001
Legumes (g/day)	14.2 ± 0.9	13.9 ± 0.9	15.5 ± 0.9	15.3 ± 0.9	0.529

Data are presented as mean ± SE

All values were adjusted for age and energy, except for dietary energy intake, which was only adjusted for age using ANCOVA of protein, total fiber, folate, calcium, zinc, vegetables, grains, legumes and lower intakes of energy, carbohydrates, fats, vitamin E, meat, egg, trans FA, and dairy. No other significant differences were seen in terms of dietary intakes across quartiles of DPI.

Multivariable-adjusted ORs and 95% CI for breast cancer across quartiles of DPI are presented in Fig. 1. In the crude model, participants in the highest quartile of DPI had 63% lower odds of breast cancer compared to those in the lowest quartile (95% CI 0.26, 0.54; P-trend < 0.001). After adjustment for potential confounders, this inverse association became strengthened (95% CI 0.22, 0.49; P-trend < 0.001). Further adjustment for BMI did not change the association (OR for the highest quartile vs. the lowest quartile = 0.40, 95% CI 0.26, 0.60; P-trend < 0.001).

Table 3 indicates multivariable-adjusted ORs and 95% CI for breast cancer across quartile of DPI, stratified by menopausal status. In pre-menopause participants, no significant relationship was seen between DPI and BC. Although, among post-menopause participants, in the crude model, participants in the highest quartile of DPI had 70% lower odds of breast cancer compared to those in the lowest

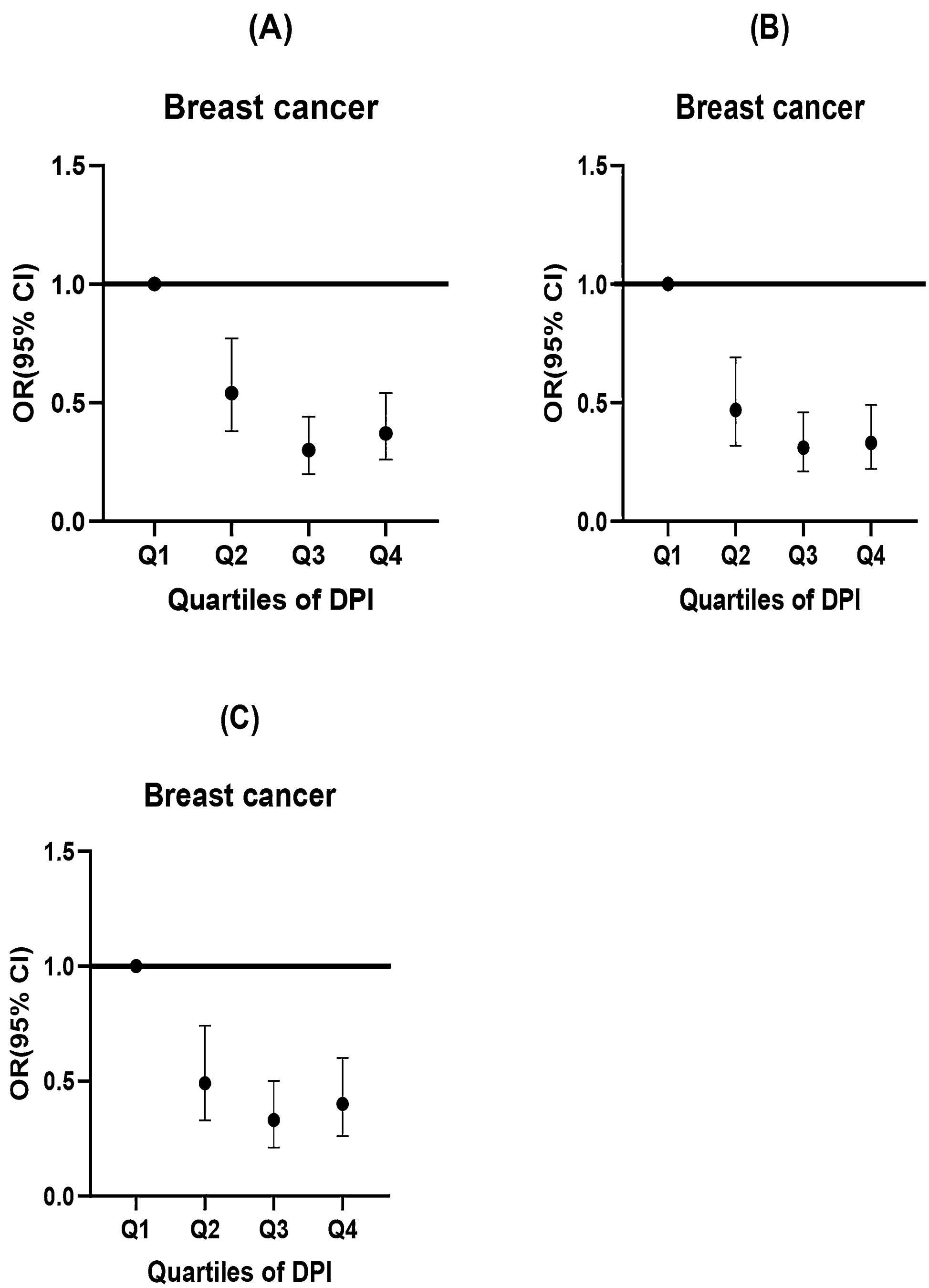

Fig. 1 Multivariable-adjusted odds ratios and 95% CIs for breast cancer across quartiles of dietary phytochemical index. **A** Crude model; **B** Adjusted for age, residence, marital status, SES, education, family history of BC, breast feeding, menopausal status, history of disease, supplement use, smoking, and alcohol; **C** Further controlled for BMI

Table 3 Multivariable-adjusted odds ratios (95% CIs) for breast cancer across quartile categories of DPI, stratified by menopausal status

Variables	Quartiles of dietary phytochemical index				*P*-trend
	Q1	Q2	Q3	Q4	
Premenopausal					
n	61	33	69	36	
Cut points for quartiles	< 46.49	46.49–55.25	55.25–61.68	> 61.68	
Crude	1.00	0.08 (0.01–0.69)	0.91 (0.41–2.02)	0.67 (0.24–1.85)	0.814
Model 1[a]	1.00	0.09 (0.11–0.74)	0.83 (0.35–1.98)	0.70 (0.24–2.06)	0.798
Model 2 [b]	1.00	0.11 (0.01–1.05)	0.89 (0.33–2.44)	0.88 (0.25–3.04)	0.982
Postmenopausal					
n	158	289	151	253	
Cut points for quartiles	< 44.26	44.26–54.29	54.29–63.88	> 63.88	
Crude	1.00	0.55 (0.37–0.82)	0.21 (0.13–0.35)	0.30 (0.20–0.46)	< 0.001
Model 1[a]	1.00	0.55 (0.36–0.83)	0.22(0.13–0.37)	0.30 (0.19–0.46)	< 0.001
Model 2[b]	1.00	0.59 (0.38–0.91)	0.22 (0.13–0.39)	0.38 (0.24–0.60)	< 0.001

[a]Adjusted for age, residence, marital status, SES, education, family history of BC, menopausal status, history of disease, breast feeding, supplement use, smoking, and alcohol

[b]Further controlled for BMI

quartile (95% CI 0.20, 0.46; *P*-trend < 0.001). This relationship was significant after adjusting the confounders (95% CI 0.19, 0.46; *P*-trend < 0.001). Further adjustment for BMI did not change the association (OR for the highest vs. the lowest quartile = 0.38, 95% CI 0.24, 0.60; *P*-trend < 0.001).

The contribution of each confounding variable to odds BC is shown in Table 4. There was a significant association between age, BMI, marital status, education, family history of breast cancer and menopausal status, and BC. However, the relationship between residence place, socioeconomic status, history of disease, breast feeding, supplement use, smoking and alcohol, and BC was not significant. Given the small contribution of each of these variables to the risk, we preferred to retain them in the model to reach an independent association between out independent variable (DPI) and BC.

Discussion

In this case–control study, high intake of dietary phytochemicals was inversely associated with the odds of BC. This association remained significant after adjustment for several confounding variables. To the best of our knowledge, this study was among the first investigations on the association between DPI and odds of BC in the world.

Table 4 Odds ratios and 95% confidence intervals (CIs) for the association between confounder variables and breast cancer

Variable	Breast cancer Odds ratio (95% CI)	*P* value
Age (continuous)	1.03 (1.02–1.05)	< 0.001
BMI (continuous)	0.84 (0.82–0.87)	< 0.001
Residence place (urban*/rural)	1.00 (0.77–1.31)	0.964
Marital status (non*/married/not married)	0.37 (0.27–0.53)	< 0.001
Social economic status (poor*/middle/high class)	0.90 (0.73–1.09)	0.493
Education (non-educated*/educated)	0.52 (0.37–0.71)	< 0.001
Family history of BC[a] (no*/yes)	2.93 (1.70–5.04)	< 0.001
Menopausal status (pre-menopause*/post-menopause)	2.19 (1.51–3.18)	< 0.001
History of disease (no*/yes)	1.20 (0.77–1.85)	0.408
Breast feeding (no*/yes)	1.01 (0.77–1.32)	0.926
Supplement use (no*/yes)	0.92 (0.59–1.42)	0.715
Smoking (no*/yes)	1.41 (0.99–2.01)	0.055
Alcohol use (no*/yes)	0.59 (0.33–1.06)	0.079

[a]BC breast cancer

*References

Dietary intakes vary greatly with age, family structure, occupation, and time period [34–36]. The usual staple foods in Iranian diets are bread and rice [37]. Iranians get more than 60% of their energy from carbohydrates, in particular from refined sources [38]. The amount of fat consumption among Iranians does not seem to be high; however, the quality of dietary fat intake in this population is not appropriate [39]. For instance, they get almost 4.2% of their energy from trans fats [40]. Nutrition transition is happening rapidly across developing nations [41, 42]. Iran is not an exception in this regard [43]; following a rapid change in fertility and mortality patterns as well as urbanization in Iran [43]. Secular trend in dietary patterns in Iranian population was seen toward the willingness to healthy dietary pattern, a reduction of the Western dietary pattern, and an enhancement in the Mixed dietary pattern [44]. Such changes in dietary intakes might result in changes in the pattern of chronic diseases.

Breast cancer is the leading cause of cancer deaths among women in both developing and developed countries [45]. In the present study, we found that people in the top quartile of DPI were 67% less likely to have breast cancer compared to those in the bottom quartile. The association between DPI and some chronic diseases including cardiovascular disease [17], diabetes [18], psychological distress [46], Alzheimer's [20], and inflammatory bowel disease [19] have been previously investigated. However, we are aware of very limited and controversial data on the linkage between dietary phytochemicals content and risk of BC. Despite an inverse association between DPI and breast cancer in some studies [47], others failed to find any significant relationship between DPI and odds of breast cancer [28]. In agreement with our findings, another case–control study reported that women in the highest quartile of dietary phytochemical index (DPI) had 92% decreased odds of BC compared to women in the lowest quartile [26]. Postmenopausal women with higher intake of leafy vegetables, any fruits and fruit juices, had approximately 30% lower risk of BC compared to those with a lowest intake in another investigation [13]. However, in a large prospective cohort study, dietary intake of whole grain products was not associated with risk of breast cancer in postmenopausal women [28]. On the other hand, consumption of some phytochemical-rich food groups was even associated with a greater odds of BC in some other studies [48]. Moreover, some ingredients of phytochemical-rich foods were also associated with greater odds of BC in some other studies [47]. Due to the differences in the studies, such as study design, sample size, characteristics of the subjects, and inclusion and exclusion criteria, there are inconsistency in the results of the studies. Therefore, more investigation is needed to explore the association between DPI and BC in the feature.

There are several mechanisms which might explain the linkage between DPI and BC. Bioactive compounds in phytochemical-rich foods including soluble and insoluble fiber, sterols and stanols, lignans, chlorophyll, flavonoids, indoles, isothiocyanates, phytoestrogens, polyphenolic compounds, protease inhibitors, sulfides, and other biologically active metabolites might reduce the risk of various cancers through different cellular pathway including: inhibiting phase I enzymes, inducing phase II enzymes, scavenging DNA-reactive agents [49], interruption of cell proliferation, inhibiting angiogenesis, and stimulating apoptosis [50, 51]. In addition, a diet with a high phytochemical content contains high amount of antioxidants, vitamins E and C, carotenoids, and various fibers [23]. These components have been shown to have positive effects on the prevention of various cancers [14, 16, 52].

Our study had several strengths. This study was among the first investigations that examined the association between DPI and odds of BC in a Middle-East country. A validated FFQ was used to obtain data on usual dietary intakes of participants. In addition, several confounders were adjusted for in the final analysis to reach an independent association between DPI and BC. Moreover, this study has applied the holistic approach of investigating total dietary phytochemicals rather than focusing on a single dietary component. However, our study had some limitations. First, the design of our case–control study is subject to selection and bias. Therefore, one might assume that this study design is not appropriate for identification of risk factors such as dietary habits which are difficult to recalling the past in detail. Designing prospective cohort studies would be necessary to further investigate the associations we found. Measurement errors may lead to misclassification of individuals based on their consumption of phytochemical-rich foods. Second, DPI may include different components in different regions and our findings may not be generalizable to all regions. Third, the status of the hormone receptor is very important in the study of BC-related factors, but there was no information about it in the current study.

Conclusion

In conclusion, a protective association was observed between DPI and BC in this case–control study. Therefore, high consumption of foods rich in phytochemicals such as fruits, vegetables, and whole grains might help reducing the odds of BC among women. Therefore, the efforts of the authorities to create comprehensive nutrition policies and facilitate access to foods rich in phytochemicals, to encourage people in the community to consume these substances are very important. Further studies with prospective design are needed to confirm this finding.

Author contributions SMG, AA, and AE contributed to study concept, search, data analysis, and drafting of the manuscript. SBK and LA contributed to data processing, data analysis, and drafting of the manuscript. AE supervised the research. All authors read and approved the final manuscript.

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Availability of data and materials The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors declare that they have no conflict of interests.

Ethics approval and consent to participate The research project was approved by Isfahan University of Medical Sciences, Isfahan, Iran Ethics Committee. The purpose of the study was fully explained.

Consent for publication Participants were provided a study overview and verbal consent was attained.

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