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Association between processed and ultra-processed food intake and the risk of breast cancer: a case-control study

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Abstract

Background Results from studies investigating the association between ultra-processed foods (UPFs) and breast cancer are scarce and, in some cases, contradictory. Therefore, we aimed to evaluate the association between the intake of processed foods (PFs) and UPFs with the risk of breast cancer in Iranian women.

Methods The present case ($n=133$) - control ($n=266$) study was carried out at two general hospitals in Tehran, Iran. A 168-item semi-quantitative food frequency questionnaire was used to assess the participants' dietary intake. Also, the NOVA classification was used to identify PFs and UPFs. The association between PFs and UPFs with the odds of breast cancer was analyzed using logistic regression models.

Results According to Model 1 of conditional logistic regression, the odds of breast cancer were higher in the last tertile of UPFs than in the first tertile (odds ratio (OR) = 1.930; 95% confidence interval (CI): 1.080–3.449). In Model 2, no significant association was observed between the second and last tertiles of PFs and UPFs with the odds of breast cancer compared to the reference tertile. Also based on menopause status, the odds of breast cancer increased in the last tertile only among premenopausal women in Model 2 (OR = 3.656; 95% CI: 1.326–10.079).

Conclusions This study demonstrated that higher consumption of UPFs is associated with higher odds of breast cancer in premenopausal women.

Keywords Food, Processed, Breast neoplasms, Iran

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Introduction

Breast cancer was the most commonly diagnosed cancer, with 2.26 million new cases in 2020 [1]. This cancer is the most common cancer among Iranian women with an age-standardized incidence rate of 35.8 per 100,000 people [2]. Genetic and lifestyle/environmental factors are involved in the development of breast cancer [3]. It is estimated that 90–95% of cancer cases are related to environmental and lifestyle factors [4]. Diet modification and lifestyle changes are suggested to prevent one-third of breast cancer-related morbidity and mortality [5]. Diet-related factors are believed to contribute to approximately 30% of cancer cases in developed countries [6], and healthy/prudent dietary patterns can reduce the risk of breast cancer by 11% [7].

Food processing has advanced significantly due to the industrialization and globalization of food systems [8]. Considering the degree of food processing, the NOVA classification categorizes foods into four groups: minimally processed, processed culinary ingredients, processed foods (PFs), and ultra-processed foods (UPFs) [9]. UPFs are affordable, easy to access, palatable, and microbiologically safe [10] and contribute to 25–50% of people's energy intake in high- and middle-income countries [11]. However, these foods are usually energy-dense, with high sugar, salt, and saturated fatty acids, and low micronutrients and fiber, so they are considered foods with poor nutritional values [9, 12, 13]. In addition, these foods can contain additives, including sodium nitrites and titanium dioxide, newly formed substances, including heterocyclic amines, aromatic polycyclic hydrocarbons, and acrylamides, and substances from packaging such as bisphenol A [14–17].

Results from studies investigating the association between UPFs and breast cancer are scarce and, in some cases, contradictory (15–18). The French NutriNet-Santé prospective cohort study and a multicentric population-based case-control study (MCC) demonstrated that a higher intake of UPFs is associated with an increased risk of breast cancer [18, 19]. Many studies indicate that the increased consumption of UPFs is a primary contributor to the obesity epidemic [18–20]. Obesity has a complicated relationship with both breast cancer risk and the clinical behavior of the established disease [21]. On the other hand, studies conducted among women from South Africa and Spain did not show any significant association between UPFs and the risk of breast cancer [20, 21]. To address the discrepancies between the studies, we aimed to evaluate the association between the intake of PFs and UPFs with the risk of breast cancer in Iranian women.

Methods

Study participants

The present study was conducted at two general hospitals in Tehran, Iran and randomly selected by convenient sampling method. The sample size was calculated by the study of Ching et al. (odds ratio (OR) = 0.47, α error = 0.05, and β error = 20%) [22]. In the current research, 136 women aged 30 to 65 years, whose breast cancer was recently confirmed by histology, were selected. Also, 272 females in the control group were admitted to the same hospitals for a broad spectrum of non-neoplastic diseases unrelated to alcohol abuse, smoking, and long-term dietary modifications (1 case −2 controls). The conditions of the participants from the control group included acute surgical conditions (such as appendicitis, inguinal hernia, and kidney stones), trauma and orthopedic conditions, disc disorders, and eye, nose, ear, or skin disorders. For the matching process, the control group participants were age-matched to the cases within a five-year range. Seven participants (5 controls and 2 cases) were excluded from the analysis because their energy intake was outside the range of ± 3 standard deviations (SDs) from the mean energy intake separately in each case and control group, and 2 participants were excluded due to missing data (1 control and 1 case). All protocols and procedures of the current study were approved by the medical research and ethics committee of Shiraz University of Medical Sciences. Also, written informed consent was obtained from all patients. Some details of the present study were published previously [23, 24].

Dietary assessment

A 168-item semi-quantitative food frequency questionnaire (FFQ) was used to assess the participants' dietary intake. The questionnaires included participants' dietary intake one year before the interview for the control group and one year before the cancer diagnosis for the case group. The questionnaire used in this study was based on the common foods consumed by Iranians and had high reliability and reproducibility in this population [25, 26]. A validated food album [27] was provided to patients along with a set of household measuring items (e.g., cups, tablespoons, teaspoons, bowls, plates, spatulas, and glasses) to facilitate the estimation of food type and portion size. The portion size of each food item was converted into grams, and then the consumption of each food was determined by the portion size multiplied by the frequency of daily intake. The composition table of Iranian food nutrients [28] and the data of food compositions from the United States

Department of Agriculture (USDA) were used to calculate foods' energy and nutrient content.

The NOVA classification was used to identify PFs and UPFs [29, 30]. Foods and beverages that were identified as PFs and UPFs included [31] baguette bread, toast bread, crackers, cookies, Yazdi cake, homemade cakes, other cakes, biscuits, pastries, cream sweets, gaz, sohan, noghl, chocolate, donuts, caramel cream, candies, pizza, meat products, kielbasa, sausage, hamburger, French fries, puff, chips, industrial beverages, soft drinks, cola, industrial jams, packaged salty snacks, milk sweetened with sugar, cacao milk, yogurt cream, cream cheese, traditional ice cream, non-traditional ice cream, gravies, margarine, sauces, ketchup, mayonnaise, etc. To determine the contribution of each subgroup of UPFs in the total consumption of UPFs, the mean daily consumption was divided by the total daily UPF intake and then multiplied by 100.

Other measurements

All measurements and data collection were carried out by trained nutritionists. Participants were weighed to the nearest 0.1 kg using a digital scale (Seca, Germany) while wearing lightweight clothing and without shoes. In addition, height was measured using a non-elastic measuring tape installed on the wall with an accuracy of 0.5 cm. Body mass index (BMI) was calculated by dividing weight (kilograms) by the square of height (meters).

The socio-demographic, lifestyle, and clinical information of the participants was collected through a checklist. This information included age (years), age at the first pregnancy (years), abortion history (yes, no), breastfeeding history (months), menopausal status (premenopausal, postmenopausal), history of taking oral contraceptive pills (yes, no), family history of breast cancer (yes, no), wearing a bra during the day (yes, no) and at night (yes, no), family history of cancer (yes, no), smoking (yes, no), and history of supplement use (yes, no). Also, physical activity was evaluated using a valid and reliable questionnaire [32], and questions changed to metabolic equivalents of tasks (METs)-hours per day.

Statistical analysis

In this study, all analyses were performed using SPSS software (version 26.0, SPSS Inc. Chicago IL, USA) and STATA (version 17). The Kolmogorov-Smirnov test was used to evaluate the normality of the data. At first, the intake of PFs and UPFs was calculated based on energy percent and then converted to tertile. For the basic characteristics of the subjects (continuous and categorical variables), independent samples T-test or Mann-Whitney test and chi-square test were used, respectively. The association between the intake of PFs and UPFs and breast cancer risk was analyzed using conditional logistic regression models. The role of potential confounding variables (BMI (kg/m^2), marriage age (years), age at the first pregnancy (years), breastfeeding time (months), fiber intake (g/day), abortion history (no/yes), family history of cancer (no/yes), family history of breast cancer (no/yes), wearing a bra during the day (less than 12 h/more than 12 h), wearing a bra at night (no/yes), vitamin D supplement (no/yes), omega-3 supplement (no/yes), and herbal drugs (no/yes)) was adjusted (adjusted for variables with p-value < 0.25 based on Table 3, and energy was not added in the adjusted model, because the intake of PFs and UPFs was calculated based on energy percent). The OR and their 95% confidence intervals (CIs) were calculated. P-values less than 0.05 were considered significant.

Results

Baseline characteristics of the study based on case and control groups are shown in Table 1. According to the tables, age ($P=0.028$), menopausal status ($P=0.033$), wearing a bra during the day ($P=0.012$), family history of cancer ($P=0.046$), abortion history ($P=0.046$), and taking vitamin D supplements ($P=0.038$) were significantly different between the groups of cases and controls.

The dietary intake of the study participants based on case and control groups is reported in Table 2. The median intake of PFs ($P=0.012$), monounsaturated fatty acids (MUFAs) ($P=0.006$), and polyunsaturated fatty acids (PUFAs) ($P=0.012$) were significantly different between the two groups.

The association between some baseline variables and the risk of breast cancer is shown in Table 3. In the univariate analysis, higher odds of breast cancer were found with each unit change in age at the first pregnancy (OR = 1.041, 95% CI: 1.003–1.079). Also, in categorical variables, higher odds of breast cancer were observed in postmenopausal women (OR = 1.589, 95% CI: 1.051–2.430), those with a positive abortion history (OR = 1.576, 95% CI: 1.017–2.441), those with a positive family history of cancer (OR = 1.642, 95% CI: 1.021–2.640), and those wearing a bra during the day for more than 12 h (OR = 2.287, 95% CI: 1.171–4.467), compared to the reference group. However, lower odds of breast cancer were seen in those taking vitamin D supplements (OR = 0.556, 95% CI: 0.320–0.966), compared to the reference group.

Table 4 represents the association between PF and UPF intake and the risk of breast cancer. According to the crude model of conditional logistic regression, the chance of breast cancer was higher in the last tertile of UPFs than in the first tertile (OR = 1.930; 95% CI: 1.080–3.449). After adjusting for confounders, no significant associations were seen between the second

Table 1 Basic characteristics of the study based on case and control groups

Variables	Cases ($n=133$)	Controls ($n=266$)	*P*-value
BMI (kg/m^2)[a]	29.64 (25.96–33.32)	28.52 (25.39–31.64)	0.119
Age (years)[b]	49.51 ± 10.71	47.11 ± 10.09	**0.028**
Marriage age (years)[a]	19.00 (16.00–22.00)	18.00 (16.00–20.00)	0.077
Age at the first pregnancy (years)[a]	20.00 (17.00–25.00)	20.00 (17.00–22.00)	0.055
Breastfeeding time (months)[a]	39.00 (20.00–60.00)	48.00 (24.00–70.00)	0.162
Physical activity (MET-h/day)[a]	32.10 (29.10–35.50)	31.42 (29.10-34.98)	0.677
Menopausal status, %[c]			**0.033**
Pre-menopause	45.90	57.50	
Post-menopause	54.10	42.50	
Wearing a bra during the day, %[c]			**0.012**
Less than 12 h	9.00	18.50	
More than 12 h	91.0	81.50	
Wearing a bra at night, %[c]			0.116
Yes	78.90	71.30	
No	21.10	28.70	
Family history of cancer, %[c]			**0.046**
Yes	30.10	20.80	
No	69.90	79.20	
Family history of breast cancer, %[c]			0.171
Yes	8.30	4.50	
No	91.70	95.50	
Abortion history, %[c]			**0.046**
Yes	40.10	28.90	
No	59.90	71.10	
Smoking, yes, %[c]	3.00	3.40	1.000
OCP use, no, %[c]	49.60	44.20	0.338
Multivitamin-mineral supplements, no, %[c]	94.00	93.20	0.833
Vitamin D supplement, no, %[c]	85.00	75.80	**0.038**
Omega-3 supplement, no, %[c]	94.00	88.30	0.076
Herbal drugs, no, %[c]	81.20	72.80	0.083

Values are percentage for categorical variables and median (25^{th} -75^{th}) or mean ± SD for continuous

BMI Body mass index, *kg* kilogram, *m* meter, *MET* Metabolic equivalent of task, *OCP* Oral contraceptive pill

[a] Using Mann-Whitney for abnormal continuous variables

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

[c] Using chi-square test for categorical variables

and last tertiles of PFs and UPFs with the odds of breast cancer compared to the reference tertile.

The association between the intake of PFs and UPFs and the risk of breast cancer by menopausal status is presented in Table 5. In the crude model, no significant associations were seen between PFs and UPFs with the odds of breast cancer. After adjusting for potential confounders, the odds of breast cancer increased in the last tertile only among premenopausal women (OR = 3.656; 95% CI: 1.326–10.079).

Discussion

In the present case-control study conducted on Iranian women, results demonstrated that higher consumption of PFs and UPFs was not associated with breast cancer. However, subgroup analysis of this association, considering pre-and post-menopausal women, showed a significant association between UPFs and breast cancer risk in premenopausal women.

Our findings are in line with some previous studies. A study conducted in Canada did not show any

Table 2 Dietary intake of the study participants based on case and control groups

Variables	Cases ($n=133$)	Controls ($n=266$)	*P*-value
Energy (kcal/day)[a]	2482.3 (2079.7-2979.6)	2546.2 (2150.2-3220.6)	0.079
PFs (% energy/day)[a]	21.52 (15.29–29.25)	18.18 (12.63–26.43)	**0.012**
UPFs (% energy/day)[a]	11.29 (6.97–18.11)	9.70 (6.42–15.60)	0.088
Protein (% energy/day)[b]	12.68 ± 2.06	13.03 ± 2.13	0.117
Carbohydrate (% energy/day)[b]	53.79 ± 6.68	54.23 ± 7.05	0.553
Fiber (g/day)[a]	34.86 (27.43–45.03)	38.20 (27.01–50.08)	0.195
Fat (% energy/day)[a]	32.76 (29.30–38.10)	32.60 (28.11–38.38)	0.343
SFAs (% energy/day)[a]	10.90 (9.97–11.89)	10.38 (8.97–11.70)	0.127
MUFAs (% energy/day)[a]	12.49 (10.75–14.39)	11.73 (10.04–14.24)	**0.006**
PUFAs (% energy/day)[a]	7.97 (6.66–10.65)	7.64 (5.80–9.93)	**0.012**

Values are percentages for categorical variables and median (25^{th} -75^{th}) or mean ± SD for continuous variables

Kcal kilocalorie, *PFs* Processed foods, *UPFs* Ultra-processed foods, *g* gram, *SFAs* Saturated fatty acids, *MUFAs* Monounsaturated fatty acids, *PUFAs* Polyunsaturated fatty acids

[a] Using Mann-Whitney for abnormal continuous variables

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

association between the intake of UPFs and cancer [33]. Also, a study conducted on South African women failed to show any significant association between the intake of UPFs and the risk of breast cancer. In this study, they observed that a higher intake of minimally PFs was inversely associated with the risk of breast cancer [33]. In a MCC study, non-adjusted models showed a significant association between UPFs and a higher risk of breast cancer. They lost their significance after adjusting for energy and alcohol intake. This might suggest, that in this population, energy and alcohol intake, as recognized risk factors [34, 35] of breast cancer, mediated the observed association. In addition, a MCC study showed that the association between UPFs and breast cancer in former and current smokers was significant. Smoking is a risk factor for breast cancer [36] and also might have some synergistic effects with UPFs [37], which need more investigation. However, due to cultural stigmas about smoking and alcohol consumption in Iran, we could not evaluate these factors. Therefore, our findings need to be interpreted with caution. Additionally, a MCC study conducted by Romaguera et al. showed that UPF consumption did not affect the odds of developing breast cancer [19]. However, results from the NutriNet-Santé study on 105,000 individuals in France showed that a 10% higher intake of UPFs was associated with a significantly increased risk of overall cancer (hazard ratio (HR) = 1.12; 95% CI: 1.06–1.18) and breast cancer (HR = 1.11; 95% CI: 1.02–1.22) [18]. Also, a case-control study conducted by Queiroz et al. in Brazil revealed that regular consumption of UPFs more than five times a week increases the risk of breast cancer by 2.35 times [38]. Discrepancies between the findings might be due to different study designs and/or study populations [19].

The results of the present study showed a significant relationship between the consumption of UPFs and the risk of breast cancer in premenopausal women. There is evidence showing that the association between UPF intake and the risk of breast cancer is stronger in younger women [34]. This observation is in line with our findings, showing that the association between UPFs and the risk of breast cancer is significant only in premenopausal women. The association observed in the NutriNet-Santé study was significant in the overall cancer and postmenopausal subgroup but not in the premenopausal subgroup. This discrepancy might be due to the differences in French and Iranian populations, such as smoking habits, alcohol consumption, and lower UPF consumption in Iran (8.5%) [35] (in the present study in the case group: 11.3% and in the control group: 9.6% energy from UPFs) compared with the total consumption of UPFs in France (18.7%) [18]. On the other hand, studies showed that the mean age of patients with breast cancer in Iran is 10–15 years lower than in developed countries [36, 37], and 23% of diagnosed cases are younger than 40 years [39]. Additionally, in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort [34], low-fat and high-fiber intake was associated with a reduction in breast cancer risk in premenopausal women, suggesting that lower fat intake reduces sex hormone concentrations and bioavailability and contributes to a lower risk of breast cancer [40, 41].

Several mechanisms may explain the association between UPFs and breast cancer risk. UPFs have poor nutritional values, such as high energy, sugar, sodium,

Table 3 Association between some baseline variables and the risk of breast cancer

Variables	OR	95% CI	*P*-value
Marriage age (years)	1.033	0.996–1.071	0.079
Age at the first pregnancy (years)	**1.041**	**1.003–1.079**	**0.034**
BMI (kg/m^2)	1.035	0.997–1.075	0.069
Breastfeeding time (months)	0.996	0.991–1.002	0.158
Physical activity (MET-h/day)	1.007	0.968–1.047	0.728
Fiber intake (g/day)	0.988	0.975–1.001	0.070
Menopausal status			
Pre-menopausal	Ref.	Ref.	Ref.
Post-menopausal	**1.589**	**1.051–2.430**	**0.028**
Abortion history			
No	Ref.	Ref.	Ref.
Yes	**1.576**	**1.017–2.441**	**0.042**
Family history of cancer			
No	Ref.	Ref.	Ref.
Yes	**1.642**	**1.021–2.640**	**0.041**
Family history of breast cancer			
No	Ref.	Ref.	Ref.
Yes	1.901	0.816–4.431	0.137
Smoking			
No	Ref.	Ref.	Ref.
Yes	0.889	0.269–2.942	0.847
Wearing a bra during the day			
Less than 12 h	Ref.	Ref.	Ref.
More than 12 h	**2.287**	**1.171–4.467**	**0.015**
Wearing a bra at night			
No	Ref.	Ref.	Ref.
Yes	1.508	0.920–2.473	0.104
OCP use			
No	Ref.	Ref.	Ref.
Yes	0.803	0.529–1.218	0.302
Multivitamin-mineral supplements			
No	Ref.	Ref.	Ref.
Yes	0.878	0.372–2.076	0.767
Vitamin D supplement			
No	Ref.	Ref.	Ref.
Yes	**0.556**	**0.320–0.966**	**0.037**
Omega-3 supplement			
No	Ref.	Ref.	Ref.
Yes	0.483	0.216–1.083	0.077
Herbal drugs			
No	Ref.	Ref.	Ref.
Yes	0.620	0.372–1.036	0.068

Obtained from logistic regression

These values are odds ratios (95% CIs)

Significant values are shown in bold

OR Odds ratio, *CI* Confidence interval, *BMI* Body mass index, *kg* kilogram, *m* meter, *MET* Metabolic equivalent of task, *g* gram, *Ref* Reference, *OCP* Oral contraceptive pill

saturated and trans-fatty acid content, and low micronutrient, protein, and fiber [33]. Higher intake of carbohydrates, glycemic index, and glycemic load has been shown to be associated with a higher risk of breast cancer [42]. Industrial bread, fruit juices, and packaged sweet snacks, as categories of UPFs, have a high glycemic index and glycemic load, which might explain their association with breast cancer [21, 43]. The EPIC study has previously shown that trans-fatty acid blood concentrations are associated with the risk of estrogen receptor (ER)-negative breast cancer [44]. Trans-fatty acids are present in ready-to-eat/fast foods and are part of UPFs [33].

It is documented that UPFs are associated with reduced gut-brain satiety signaling [45]. Additionally, the physical and chemical characteristics of UPFs and their high availability, convenience, and palatability result in their overconsumption [46–49]. Some studies [18], have shown that even after adjustments for nutritional factors, including energy intake, the association between UPFs and adverse health outcomes remains significant. These observations suggest that factors other than the energy, carbohydrate, and fat content of UPFs might affect the association between UPFs and undesirable health outcomes. For instance, additives such as sodium nitrite in processed meat products might produce new compounds, such as nitrosamines, with carcinogenic effects during industrial processes [50, 51]. Additionally, the accumulated effects of food additives are still unknown. Various carcinogenic compounds, such as acrylamides, might be produced during heat treatment [52]. Various compounds, including phthalates, titanium dioxide (TiO_2), and bisphenol A, that have been associated with endocrine disruption, might migrate from packages to packaged foods [53, 54]. Some components of UPFs might induce inflammatory responses that change gut microbiota and intestinal permeability [55–57]. These aspects of UPFs need to be studied more. Also, genes that play a role in deoxyribonucleic acid (DNA) repair, cell-cycle regulation, and apoptosis are crucial in the progression of cancer [58]. The consumption of UPFs is associated with more DNA damage, which can contribute to the occurrence of cancer [59]. Additionally, UPFs are high in fat and sugar, which can contribute to obesity, a potential risk factor for breast cancer [60]. However, in the present study, no significant differences were observed between the two groups regarding BMI.

Strengths and limitations

Our study has some strengths and limitations. With the rapid rise of PF and UPF consumption, investigating the association between this type of food and breast cancer seems relevant. Considering the menopausal status of the patients, which is a critical aspect when studying breast

Table 4 Association between processed and ultra-processed foods intake and the risk of breast cancer

Tertiles of Indices	Case / Control	Crude model			Adjusted model		
		OR	95% CI	*P*-value	OR	95% CI	*P*-value
Processed foods							
T_1 (≤ 15.82)	37/96	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
T_2 (15.83–23.56)	43/90	1.130	0.640–1.997	0.673	1.319	0.676–2.573	0.415
T_3 (≥ 23.57)	53/80	1.633	0.937–2.847	0.083	1.234	0.650–2.342	0.520
Ultra-processed foods							
T_1 (≤ 7.49)	34/95	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
T_2 (7.50-13.92)	44/89	1.309	0.730–2.348	0.365	1.337	0.688–2.596	0.390
T_3 (≥ 13.93)	55/82	**1.930**	**1.080–3.449**	**0.026**	1.800	0.923–3.513	0.084

Obtained from conditional logistic regression

These values are odds ratios (95% CIs)

Significant values are shown in bold

Adjusted for variables with *p*-value < 0.25 based on Table 3

Adjusted model: adjusted for BMI (kg/m^2), marriage age (years), age at the first pregnancy (years), breastfeeding time (months), fiber intake (g/day), menopausal status (premenopausal/postmenopausal), abortion history (no/yes), family history of cancer (no/yes), family history of breast cancer (no/yes), wearing a bra during the day (less than 12 h/more than 12 h), wearing a bra at night (no/yes), vitamin D supplement (no/yes), omega-3 supplement (no/yes), and herbal drugs (no/yes)

T Tertile, *OR* Odds ratio, *CI* Confidence interval

Table 5 Association between the intake of processed and ultra-processed foods and the risk of breast cancer by menopausal status

Tertiles of Indices	Case / Control	Crude model			Adjusted model		
		OR	95% CI	*P*-value	OR	95% CI	*P*-value
Pre-menopausal							
Processed foods							
T_1 (≤ 15.82)	15/55	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
T_2 (15.83–23.56)	22/53	1.557	0.717–3.382	0.263	2.483	0.905–6.812	0.077
T_3 (≥ 23.57)	24/45	1.663	0.474–3.703	0.213	2.000	0.759–5.285	0.161
Ultra-processed foods							
T_1 (≤ 7.49)	12/50	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
T_2 (7.50-13.92)	18/54	1.166	0.505–2.690	0.718	2.008	0.731–5.515	0.176
T_3 (≥ 13.93)	31/49	2.260	0.992–5.150	0.052	**3.656**	**1.326–10.079**	**0.012**
Post-menopausal							
Processed foods							
T_1 (≤ 15.82)	22/41	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
T_2 (15.83–23.56)	21/37	0.758	0.322–1.785	0.527	0.982	0.311–3.098	0.976
T_3 (≥ 23.57)	29/35	1.422	0.644–3.137	0.383	1.225	0.422–3.555	0.708
Ultra-processed foods							
T_1 (≤ 7.49)	24/45	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
T_2 (7.50-13.92)	26/35	1.418	0.621–3.241	0.407	1.163	0.381–3.551	0.790
T_3 (≥ 13.93)	24/33	1.403	0.586–3.357	0.447	1.583	0.505–4.955	0.430

Obtained from conditional logistic regression

These values are odds ratios (95% CIs)

Significant values are shown in bold

Adjusted for variables with *p*-value < 0.25 based on Table 3

Adjusted model: adjusted for BMI (kg/m^2), marriage age (years), age at the first pregnancy (years), breastfeeding time (months), fiber intake (g/day), abortion history (no/yes), family history of cancer (no/yes), family history of breast cancer (no/yes), wearing a bra during the day (less than 12 h/more than 12 h), wearing a bra at night (no/yes), vitamin D supplement (no/yes), omega-3 supplement (no/yes), and herbal drugs (no/yes)

T Tertile, *OR* Odds ratio, *CI* Confidence interval

cancer, was one of the strengths of this study. In addition, the classification of the foods and drinks from the validated FFQ was done by a panel of nutritionists based on the NOVA system. Intrinsic limitations of case-control retrospective design and self-reporting of dietary intake can result in selection and recall bias. To minimize these limitations, patients and controls were matched based on age, and we tried to use a validated questionnaire with high validity and reproducibility in the Iranian population, and trained nutritionists to gather the data. The FFQ used in this study was not designed to evaluate the consumption of UPFs, which might lead to an underestimation of the association between the consumption of UPFs and breast cancer [61]. This questionnaire only captures the dietary intake one year before the cancer diagnosis. Therefore, there might be a reverse causation, and the results from this study need to be interpreted with caution. Additionally, as it takes decades for cancer to develop and progress [62], long-term prospective cohort studies are needed to confirm the observed association. Lastly, although several confounding factors were considered in this study, the effects of the remaining confounding factors could not be entirely excluded due to the study's observational design.

Conclusions

In conclusion, this study demonstrated that higher consumption of UPFs is associated with a higher odds of breast cancer in premenopausal women. More studies are warranted to discover the underlying mechanisms of this observed association.

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Authors' contributions
M.N., F.M., F.J, M.R.Z., and Z.S.; Contributed to writing the first draft and revision. S.J and Z.H; Contributed to data collection. M.N., F.M., and B.R.; Contributed to all data and statistical analysis and interpretation of data. M.N. and B.R.; Contributed to the research concept, supervised the work, and revised the manuscript. 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

Ethics approval and consent to participate
This study was conducted in accordance with the ethical standards of the Declaration of Helsinki and was approved by the Research Institute of Nutrition and Food Sciences of Shahid Beheshti University of Medical Sciences. All participants read and signed the informed consent form.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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