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"Western" and "prudent" dietary patterns are associated with breast cancer among Mexican pre- and postmenopausal women

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ABSTRACT

Breast cancer (BC) is the leading cancer worldwide among women. "Prudent" dietary patterns have been consistently and negatively associated with the risk of BC. However, prospective studies have shown a positive association between "Western" dietary patterns and the risk of BC, but only among postmenopausal women. In this regard, evidence from Latin America is scarce. Our aim was to assess the hypothesis that 2 dietary patterns (Western or prudent) were contrastingly associated with BC in pre- and postmenopausal women from Northern Mexico. We recruited 1045 BC incident cases and 1030 age matched (±5 years) population controls. Sociodemographic, reproductive, and dietary characteristics were obtained by direct interviews. We used a semiquantitative food frequency questionnaire to obtain information about diet 1 year before diagnosis for cases and 1 year before the interview for controls. Dietary patterns were identified through factor analysis. A Western-like pattern, which was mainly determined by positive loads in red and processed meats and foods rich in fats and sugars, was positively associated with BC both in pre- (odds ratio [OR] =23.47; 95% CI, 14.01-36.96) and in postmenopausal women (OR = 18.85; 95% CI, 13.74-25.87). In contrast, a prudent-like pattern, which was characterized by positive loads of vegetables, legumes, and corn, was negatively associated with pre- (OR = 0.35; 95% CI, 0.26-0.49) and postmenopausal BC (OR = 0.25; 95% CI, 0.19-0.32). Our results show the importance of dietary patterns in BC development regardless of menopausal status.

1. Introduction

Breast cancer (BC) is the leading cancer worldwide among women [1]. Exposure to endogenous estrogens, mainly 17β-estradiol, has been consistently associated with BC. Estrogen synthesis differs by menopausal status. In premenopausal women, the main sources of production are ovaries, whereas in postmenopausal women, estrogens are formed from the aromatization of androstenedione in adipocytes [2,3]. Some nutrients in the diet, such as fats, intervene in the synthesis of estrogens in postmenopausal women; others, such as phy-

Abbreviations: BC, breast cancer; BMI, body mass index; FFQ, food frequency questionnaire; OR, odds ratio; USDA, US Department of Agriculture.

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toestrogens, modulate the estrogenic response. As a result, diet may alter the risk of BC according to menopausal status [4,5]. Foods are not consumed in isolation; thus, the study of dietary patterns has recently gained attention because they consider interactions and correlations among foods [6].

According to the results from prospective cohort studies, both pre- and postmenopausal women have lower BC risk by consuming foods that are consistent with a "prudent" dietary pattern (characterized by fruits, vegetables, fish, whole grains, and low-fat dairy). In contrast, a positive relationship has been suggested between BC and consumption of foods in "Western" and inflammatory dietary patterns (i.e., red and processed meats, sugary drinks, high-fat products, and refined grains); however, this remains inconclusive among pre- and postmenopausal women [3,7]. Although the 2 dietary patterns share some foods in common, the Western pattern was significantly associated with a higher risk of BC only in postmenopausal women in a meta-analysis of cohort studies [3], whereas an inflammatory pattern showed a significant higher risk of BC only in premenopausal women in the Nurses' Health Study II [7]. These discrepancies may be due to the mediation of diet on the estrogen-BC relationship by menopausal status [3], different inflammatory pathways in the development of mammary tumors in pre- and postmenopausal women [8], and/or variations in the quantity and type of foods included in the patterns among studies [9].

So far, the evidence that associates the Western and the inflammatory patterns with BC by menopausal status comes mainly from North American [7,10–14], European [15,16], Asian countries [17–23], and 2 studies from South America [24,25]. In Mexico, at least 3 dietary patterns have been identified. Two of them have similarities with the patterns found in other countries but include additional foods such as corn tortillas in the Western [26–28] and legumes in the prudent pattern [27–29]. Additionally, another pattern characterized by high-fat and animal protein has been described, which contains red meat, saturated fat, and some typical Mexican dishes that mainly have corn, tomato, onion, and chili [26,27,30,31]. The Western pattern has been associated with higher serum estradiol concentrations [32]; however, no information regarding BC and dietary patterns is available by menopausal status.

Our research group previously identified 2 dietary patterns in women residing in Northern Mexico. One of them shares several foods with the pattern known as Western and was positively associated with BC whereas, the other pattern that was like the prudent diet, was negatively associated [33]. Our objective was to test the hypothesis that Western and prudent dietary patterns are not associated in the same way between pre- and postmenopausal Mexican women.

2. Methods and Materials

A population-based case-control study was carried out between 2007 and 2011 in the Northern states of Mexico (Coahuila, Chihuahua, Durango, Nuevo León, and Sonora). Its aim was to evaluate the association between BC and environmental and genetic factors. The methodology of this study has been extensively described elsewhere [34].

Briefly, a total of 1045 incident cases of BC were identified. These cases were histopathologically confirmed in the main public and university tertiary hospitals in the study area, the inclusion criteria were at least 18 years old, without history of any other type of cancer, and at least 1 year of residence in the study area.

Controls consisted of 1030 healthy women that were matched by age (±5 years) with cases. Inclusion criteria were minimal age of 18 years, without any cancer history and at least 1 year of residency in the study area. They were identified through the Master Sample Framework used for the Mexican National Health and Nutrition Survey, which consists of a housing list for urban and rural areas that are grouped into primary sampling units. A sample of those units was chosen at random and selected homes were visited systematically until an eligible woman was identified. In households where no eligible woman was found, or she declined participation, another home was systematically located. The participation rates were above 90% in both cases and controls.

Women were interviewed face to face to obtain information about sociodemographic, lifestyle, diet, and reproductive characteristics. Anthropometric measures (weight and height) were obtained to calculate body mass index (BMI). Patients were interviewed after their diagnosis and before any kind of treatment (average time from diagnosis to treatment: 2 months).

The Research, Ethics, and Biosecurity Committees at the Mexican National Institute of Public Health evaluated and accepted the study protocol and informed consent forms (approval number CI:507). Written informed consent forms were obtained from each participant.

2.1. *Food consumption*

Among cases, information about food consumption over the year before diagnosis was collected; controls provided the same information for the 1 year before the interview. A validated semiquantitative food frequency questionnaire (FFQ) was used to evaluate the frequency of consumption of 119 foods and 14 dishes [35]. Predetermined frequencies and portions of each food item included 10 options ranging from "never" to "6 or more times a day" as follows: a glass (i.e., milk and wine), a cup (i.e., yogurt, some fruits and vegetables, tea, juices, alcoholic and nonalcoholic beverages), a spoon (i.e., oils, sour cream, sauces, and nuts), a slice (i.e., cheeses, some fruits and meats), a plate (i.e., legumes and local dishes), and a piece (i.e., some fruits and breads).

Our group has previously reviewed the consistency of foods included in the FFQ with those in the reference tables of the United Sates Department of Agriculture (USDA), from which energy of each food item was obtained [36]. Two local food items were not found in the USDA tables (quince and tejocote), and their energy values were gathered from the reference tables of the National Institute of Medical Sciences and Nutrition in Mexico "Salvador Zubiran" [37]. The consumption frequency of fruits and vegetables was adjusted according to their availability throughout the year [38]. For example, only half the consumption of plums was accounted for because they are only available during 6 months of the year. We estimated total daily energy intake for each participant based on food portion size and frequency of consumption.

2.1.1. Dietary patterns

We previously identified two dietary patterns in this population. The methodology for obtaining the dietary patterns has been described in greater detail elsewhere [33], briefly: individual foods and beverages contained in our FFQ were categorized into 27 food groups. Energy consumption from each food group was converted to a percentage of the total daily energy intake that was later standardized using Z score. The resulting values were used to obtain the dietary patterns and factor loadings through factor analysis among the entire study population. Factors with an eigenvalue greater than 1.5 were maintained to facilitate interpretability. Each factor was defined by a subset of at least 4 food groups with an absolute load factor equal to or greater than –0.20 or 0.20. The Kaiser-Meyer-Olkin index was computed to assess the adequacy of the data in relation to the factor analysis, observing a value of 0.5. In addition, the Bartlett sphericity test was performed to evaluate the correlations among the variables, and we observed a P value of 1.0.

2.2. Estrogenic index

Estimation of the years of exposure to endogenous estrogens through an estrogenic index has been explained previously [39]. For postmenopausal women, we obtained the difference in years between the age of menopause minus the age of menarche; likewise, for premenopausal women, we used the age difference at the time of the study minus the age at menarche; from these respective results, number of pregnancies and the duration of breastfeeding in years were subtracted. In our study sample, this index ranged from 0 years (multiparous women, with long breastfeeding periods and hysterectomized at an early age) to 49 years (women with only 1 pregnancy who did not breastfeed and with late menopause).

2.3. Statistical analyses

Breast cancer risk factors were compared between cases and controls according to preestablished categories, except for the estrogenic index, in which the median in the control group was used as the cutoff point. After adjusting for age, we performed nonconditional logistic regression models to test each individual covariate already known to be associated with BC.

In addition to age, the variables that changed the crude estimators of the dietary patterns and BC by more than 10% (total energy and estrogen index) were maintained in the multivariate models as covariates along with the other pattern. Adjusted odds ratios between BC and each dietary factor were estimated using non-conditional logistic regression. We further included interaction terms between menopausal status and dietary patterns. A P value $< .05$ was considered statistically significant. All analyses were performed with the Stata 14.0 statistical package.

3. Results

By design, the mean age between cases and controls was similar. In this sample, the known BC factors associated with a risk reduction (older age at menarche, higher number of pregnancies, lactation, and BMI in premenopause) and with a higher risk (higher educational level, older age at first pregnancy, late age of menopause, alcohol consumption, and higher estrogen index) were confirmed (Table 1).

For all the participants, the food groups that were consumed more frequently were: corn tortilla, refined cereals, vegetable oils, and legumes; these groups contributed more than 50% of total daily energy intake (Table 2). Two dietary patterns were identified. Pattern 1 (Western) loadings comprised: fruits (0.69), red meat (0.60), fish and other seafoods (0.58), high fat and sugar cereals (0.52), and nonstarchy vegetables (0.51), among others; negative loads were observed for corn tortilla (–0.77). In contrast, pattern 2 (prudent) showed positive loads for corn (0.59), cruciferous vegetables (0.57), starchy vegetables (0.47), allium vegetables (0.33), and legumes (0.28), and negative loads for high fat and sugar cereals (–0.43), saturated fats (–0.32), and red meat (–0.28), among others (Fig. 1).

After adjusting by age, total energy, the estrogenic index and the other pattern, a lower BC risk was observed with the consumption of prudent, in both premenopausal (odds ratio [OR], 0.35; 95% CI, 0.26-0.49) and postmenopausal women (OR, 0.25; 95% CI, 0.19-0.32), with a nonsignificant interaction. In contrast, a positive association between the Western pattern and BC was observed among postmenopausal (OR, 18.85; 95% CI, 13.85-25.87) and premenopausal women (OR, 23.47; 95% CI, 14.01-36.96) with a nonsignificant interaction (Table 3).

4. Discussion

Our results show that in both pre- and postmenopausal women, the Western pattern was positively associated with BC, whereas the prudent pattern was negatively associated. Therefore, our hypothesis that Western and prudent dietary patterns are associated differently between pre- and postmenopausal women was not supported by the results of the present study. Most case-control studies [3,16] have found a positive association between the Western pattern and BC in pre- and postmenopausal women, which was confirmed by our results. Because in a meta-analysis of cohort studies [3], the association between the Western pattern and BC is only observed in postmenopausal women, it has been suggested that the results of the association between the Western pattern and premenopausal BC in retrospective studies may be explained by recall bias [3] and/or by an increase in BMI among postmenopausal women that along with the production of estrogens through adiposity increases the risk of BC [40]. However, other authors have pointed out that it could be possible that premenopausal women had a higher risk of BC because they could have had less healthy lifestyles than postmenopausal women [9,15] and/or possibly have been earlier exposed to other BC risk factors (i.e., alcohol) [41] that may interact synergistically with diet on BC risk. In any case, if the menopausal status really modified the association between the Western pattern and BC, significant interaction tests would be obtained, which has only been observed in one prospective study [11] from many others [14,16,20,22]. In this context, although our results suggest that the positive association between the Western pattern could be significantly higher

Table 1 – Age-adjusted odds ratios for known breast cancer risk factors in a study sample of Mexican women

Factors	Cases/controls[a]	OR[b]	95% CI	P trend
Age at menarche (years)				
<12	443/389	1.00		.108
≥12	601/641	0.83	0.69-0.99	
Education (years)				
≤6	529/717	1.00		<.001
>6	515/313	2.53	2.07-3.08	
Number of pregnancies				
0	80/29	1.00		
1-3	454/342	0.49	0.31-0.77	<.001
≥4	510/659	0.27	0.17-0.42	
Age at first pregnancy (years)				
<19	225/414	1.00		
≥19-29	620/542	2.10	1.72-2.57	<.001
≥30	105/42	4.60	3.11-6.82	
Breastfeeding (months)				
0	217/111	1.00		
≤24	447/314	0.74	0.57-0.97	<.001
>24	381/605	0.30	0.23-0.40	
Age at menopause (years)				
<50	429/505	1.00		<.001
≥50	237/192	1.48	1.17-1.87	
Body mass index (kg/m^2)				
Premenopause				
<25	111/70	1.00		
25-29.9	146/105	0.81	0.54-1.20	<.001
≥30	136/171	0.44	0.30-0.65	
Postmenopause				
<25	103/107	1.00		
25-29.9	222/234	0.99	0.71-1.37	.268
≥30	313/342	0.95	0.70-1.30	
Alcohol intake (g/week)				
No	803/914	1.00		<.001
Yes	242/116	2.40	1.88-3.07	
Smoking (cigarettes/day)				
0	754/735	1.00		
<4	121/143	0.82	0.63-1.07	.004
≥4	166/151	1.08	0.85-1.38	
Estrogenic index (years)				
≤22.75	279/516	1.00		<.001
>22.75	756/511	2.75	2.29-3.30	

[a] Numbers that add to less than the total number of cases or controls are due to missing values.
[b] Adjusted by age.

among premenopausal women, these should be considered with caution while future studies clarify the underlying mechanisms.

On the other hand, retrospective studies have shown contradictory results regarding the association between the prudent pattern and BC, which may also be due to recall bias [3]. A recent meta-analysis suggests that there is no significant association according to menopausal status. In contrast, cohort studies showed a statistically significant lower BC risk with consumption of foods in the prudent pattern, in pre- and postmenopausal women [3], which is consistent with our results.

Exogenous hormones ingested through red meat, processed meat, and poultry activate hormone receptors in breast tissue and stimulate tumor proliferation and growth as well as metastatic activity [42–44]. Foods with a high glycemic index or glycemic load, such as cereals rich in fat and sugar, dairy products with fat and sugar, sweets, and sugary drinks, have also been reported to raise estrogen levels [45,46]. In addition, high glycemic index foods, such as cereals, promote tumor cell growth, proliferation, and survival through an increase in insulin growth factor-1 [47]. Likewise, there are several mechanisms by which foods in the prudent pattern might cause a negative association with BC, among them: inhibition of cell proliferation and tumor growth (allium [48] and cruciferous vegetables [49], legumes [50], and carrots [51]); antioxidant activity (carrots [52], allium [48], and cruciferous vegetables [49]); inhibition of adducts formation (allium vegetables [48]); higher estrogen excretion (foods rich in fiber [53]); and induced apoptosis (carrots [51], cruciferous vegetables [49]). In contrast, foods in the Western pattern may increase BC risk though DNA alkylation because of the N-nitroso compounds and heterocyclic amines that are present in red and processed meats [54]. In addition, the saturated fats in cheese, milk, and red meat modulate the expression of genes that reg-

Table 2 – Foods grouping and their daily percentage energy contribution used in the dietary patterns analysis in a study sample of Mexican women

Food groups	Food items	% Energy/day Mean	(SD)
Soda	Cola, flavored soft drink	4.12	(4.94)
Diet soda	Diet cola, diet flavored soda	0.02	(0.09)
Saturated fats	Butter, lard, pork rinds, cream, mayonnaise	0.97	(1.19)
Fat dairy	Chihuahua cheese, asadero cheese, Mennonite cheese, fresh cheese, milk	4.88	(4.60)
Fat and sugary dairy	Yogurt and ice cream	1.50	(2.53)
Red meat	Pork, beef, barbecue, carnitas, salted meat, goat, machaca[a], liver	3.95	(3.85)
Processed meat	Sausage, ham, chorizo, bacon	1.77	(2.00)
Refined cereals	White bread, rice, bolillo, pasta, cereal, flour tortilla	13.28	(9.83)
Starchy vegetables	Potato, beet, carrot	2.11	(1.54)
Alcoholic drinks	Red wine, white wine, beer, spirits	0.09	(0.53)
Fish and other seafoods	Tuna, sardine, fish, shellfish	0.86	(1.11)
Cruciferous vegetables	Broccoli, cauliflower	0.41	(0.49)
Allium vegetables	Garlic, onion	0.26	(0.20)
Fruits	Banana, orange, juice, mamey, cactus fruit, quince, plum, peach, apple, blackberry, strawberries, pear, figs, watermelon, melon, pineapple, mango, zapote[b], papaya, guava, hawthorn, grapes	5.09	(4.56)
Nonstarchy vegetables	Purslane, spinach, chayote, raw tomato, stewed tomato, chili, nopal[c], squash flower, zucchini, lettuce	3.75	(2.83)
Legumes	Beans, peas, lentils, dry beans, green beans	8.69	(6.29)
Corn	Corn	1.11	(1.22)
Vitamin E-rich foods	Avocado, walnuts, pistachios	1.27	(1.73)
Eggs	Egg	4.57	(4.49)
Poultry	Chicken	1.10	(0.94)
Tea and coffee	Coffee, black tea, herbal tea	2.35	(2.48)
Corn tortilla	Corn tortilla	25.50	(17.42)
High fat and sugar cereals	Sweet bread, cupcake, cereal bar, cookies, popcorn, potato chips, cake, coyota[d]	2.33	(3.32)
Sweets	Jam, cajeta[e], quince	0.14	(0.49)
Vegetable oil	Vegetable oil, corn oil, olive oil, canola oil, margarine, liquid margarine, low-fat margarine	9.09	(5.28)
Corn-based drinks	Atole[f], corn chocolate[f]	0.79	(1.65)
Root beer	Root beer	0.00	(0.04)

[a] Local dried beef meat.
[b] Local fruit.
[c] Local cactus leaf.
[d] Local wheat-based sweet bread.
[e] Milk-based sweet.
[f] Local corn-based drink.

Table 3 – Association and interaction between dietary patterns and breast cancer by menopausal status in a study sample of Mexican women

Pattern/ menopausal status	Cases/ controls	OR[a]	95% CI	P interaction[a] Pattern × menopausal status	OR[b]	95% CI	P interaction[b] Pattern × menopausal status	OR	95% CI	P interaction Pattern × menopausal status
Western like										
Premenopausal	(401/346)	21.45	13.87-33.16	.011	21.52	13.91-33.30	.012	23.47[c]	14.91-36.96	.163[c]
Postmenopausal	(644/684)	11.95	9.22-15.48		11.99	9.22-15.58		18.85[c]	13.74-25.87	
Prudent like										
Premenopausal	(401/346)	0.54	0.44-0.65	.671	0.54	0.44-0.66	.979	0.35[d]	0.26-0.49	.071[d]
Postmenopausal	(644/684)	0.55	0.47-0.63		0.54	0.47-0.63		0.25[d]	0.19-0.32	

[a] Adjusted by age and total energy.
[b] Adjusted by age, total energy, and estrogenic index.
[c] Model B + prudent pattern.
[d] Model B + Western pattern.

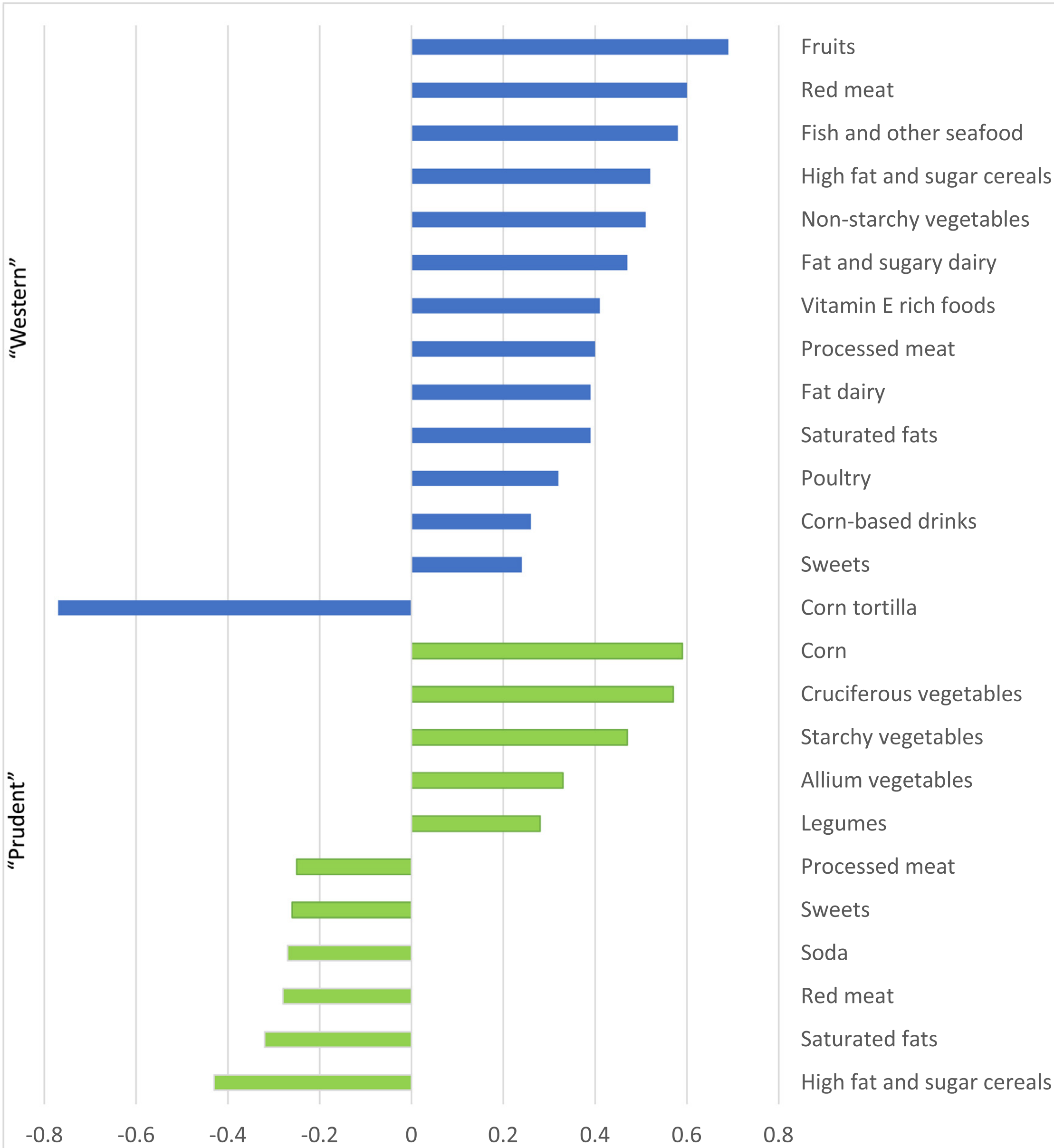

Figure 1 – Foods factor loadings ≥−0.20 or ≥0.20 in dietary patterns identified in a study sample of Mexican women.

ulate breast carcinogenesis, as well as promote the formation of mutagenic compounds and free radicals [55].

To interpret our results, the possibility that BC patients overreported some foods that correspond to the Western pattern should not be ruled out; this would produce an artificially high OR. However, all the reproductive factors associated with BC reported by these women resulted in the expected direction and magnitude of risk, as may have happened with the diet report. The high magnitude of OR between the Western pattern and BC may also be a real increase in risk because of the way foods are cooked. In this report, such information was not considered, but it is known that in the study area, it is common to roast meat [56]. In this process, heterocyclic amines, polycyclic aromatic hydrocarbons, and N-nitroso compounds, which are carcinogenic compounds, are formed [17]. Therefore, we cannot rule out that the way certain foods included in the Western pattern are cooked affects this relationship. Furthermore, another limitation of our study is the lack of detailed information on hormone receptor positivity, so it was not possible to perform a sensitivity analysis to determine if our results remained in estrogen receptor-positive disease. In contrast, the presence of nondifferential measurement error inherent in the use of dietary questionnaires is a methodological limitation that may have attenuated all the ORs reported in this work, as well as the possibility of social desirability bias [57]. In addition, a particular characteristic of this study population is its low alcohol consumption (83% nonalcohol drinkers), so our results are not altered by this BC risk factor; moreover, we adjusted by other possible confounders of the diet-BC relationship. Furthermore, we consider that our results could be extrapolated to the Northern region of Mexico because, according to the total energy intake, the studied controls might represent the target population: median total energy intake of our sample (1938 kcal/day) vs Mexican National Health and Nutrition Survey (ENSANUT 2006) (1743 kcal/day) in the Northern region of Mexico [58].

CRediT authorship contribution statement

M. Karen Flores-García: Formal analysis, Writing – original draft, Visualization. **Ángel Mérida-Ortega:** Writing – review & editing, Formal analysis, Visualization. **Edgar Denova-Gutiérrez:** Writing – review & editing, Formal analysis. **Stephen J. Rothenberg:** Writing – review & editing, Formal analysis. **Lizbeth López-Carrillo:** Conceptualization, Supervision.

Author declarations

None of the authors reported any conflicts of interest related to this study.

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