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Original

Breast cancer in southern Brazil: association with past dietary intake

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Abstract

Objective: To determine possible associations between the risk of breast cancer in Brazilian women and demographic, social and economical variables, and past dietary intake.

Methods: A case-control study was conducted in Joinville, Santa Catarina, Brazil, between june and november 2003 involving a group of 33 women recently diagnosed with breast cancer and a control group of 33 healthy women volunteers. Personal details, health history and past dietary intake were obtained via questionnaires and interviews. Data between groups were compared using χ^2, Fisher, and Student's t test, whilst associations were evaluated using a non-conditional logistic regression method and odds ratio (OR).

Results: Statistically significant differences between the two groups were revealed with respect to age distribution ($P = 0.007$), family income level ($P = 0.02$), educational level ($P < 0.0001$) and attainment of menopause ($P < 0.0001$). After adjustment, with regard to family income level, of the data concerning past dietary intake, the consumption of pig lard (OR = 6.32) and fatty red meat (OR = 3.48) were found to be associated with an increase in the risk of breast cancer. The regular ingestion of apples (OR = 0.30), watermelons (OR = 0.31), tomatoes (OR = 0.16), plain cakes (OR = 0.30) and desserts (OR = 0.20) afforded some degree of protection against the development of the disease.

Conclusions: Age (> 45 years), low family income (< $520/month), poor educational level (primary school level or lower) and past regular consumption of pork fat and fatty meat may be factors associated with an increased risk of breast cancer.

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Key words: *Breast cancer. Case-control study. Past dietary intake. Protection factors. Risk factors.*

CÁNCER DE MAMA EN EL SUR DE BRASIL: ASOCIACIÓN CON LA INGESTIÓN PASADA

Resumen

Objetivo: Determinar las posibles asociaciones entre el riesgo de cáncer de mama en mujeres brasileñas y las variables demográficas, sociales y económicas, y la ingestión pasada.

Métodos: Se realizó un estudio de casos-control en Joinville, Santa Catarina, Brasil, entre junio y noviembre de 2003, implicando a un grupo de 33 mujeres con un diagnóstico reciente de cáncer de mama y un grupo control de 33 mujeres sanas, voluntarias. Se obtuvieron detalles personales, antecedentes de salud e ingestión alimentaria pasada mediante cuestionarios y entrevistas. Los datos entre los grupos se compararon usando las pruebas de χ^2, Fisher y t de Student, mientras que las asociaciones se evaluaron utilizando el método de regresión logística no condicional y la razón de probabilidades (odds ratio; OR).

Resultados: Se observaron diferencias estadísticamente significativas entre ambos grupos en relación con la distribución por edades (P = 0,007), el nivel de ingresos familiares (P = 0,02), el nivel educativo (P < 0,0001) y el estado menopáusico (P < 0,0001). Tras el ajuste, y respecto al nivel de ingresos familiares y los datos relativos a los hábitos dietéticos pasados, se halló que el consumo de grasa de cerdo (OR = 6,32) y carne roja grasa (OR = 3,48) se relacionaba con un riesgo aumentado de cáncer de mama. La ingestión habitual de manzanas (OR = 0,30), sandías (OR = 0,31), tomates (OR = 0,16), bizcochos (OR = 0,30) y postres (OR = 0,20) produjo cierto grado de protección frente al desarrollo de la enfermedad.

Conclusiones: La edad (> 45 años), los ingresos familiares bajos (< 520$/mes), el nivel educativo bajo (escolaridad primaria o inferior) y el consumo pasado habitual de grase de cerdo y carne grasa podrían ser factores de riesgo asociados con un aumento del riesgo de padecer cáncer de mama.

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Palabras clave: *Cáncer de mama. Estudio de casos-control. Ingestión pasada. Factores de protección. Factores de riesgo.*

Introduction

Worldwide, breast cancer is the second most frequent form of carcinoma and the most common type amongst women. According to estimates of the Brazilian Ministry of Health, some 48,930 new cases of breast cancer are expected to be diagnosed in the country in 2006, and of these 1,610 will be in the State of Santa Catarina (SC), southern Brazil.[1] In Joinville, a major city in SC comprised (in 2003) of 461,576 inhabitants of which 95,099 were women in the age range of 30 to 70 years,[2] figures from the Municipal Secretary of Health[3] indicate that a total of 150 mastectomies were performed during 2002 as a result of breast cancer.

A large number of risk factors for breast cancer have been identified including, amongst others, sex, genetic predisposition, age, early menarche, late menopause, age of first pregnancy, not having breast fed, benign breast lesions, hormonal replacement therapy, race, social and economic conditions, education, civil status, high body fat, alcoholism, smoking and diet.[4]

Since the incidence of breast cancer varies worldwide, and alterations in frequency may be observed between migrant populations, it has been postulated that diet could represent a significant risk factor for the development of the disease.[5,6] In 1982, the National Academy of Science recommended the reduction of total fat consumption on the basis of evidence pointing to an association between diet and cancer.[7] Since that time, the nature of the relationship between fat intake and cancer has received considerable attention and it is now acknowledged that total fat ingestion is not the only factor responsible for the development of the disease.[8] Thus obesity, and a high intake of meat, fat, dairy products and alcohol all increase the risk of breast cancer, whilst the increased consumption of fibre, fruits, vegetables, and sources of antioxidant compounds and phytoestrogens can reduce the risk.[4]

Although potential associations between diet and breast cancer have been studied extensively, few consistent associations exist with many studies providing conflicting results.[9-17] Unfortunately, data concerning the risk of breast cancer in Brazilian women in relation to demographic, social and economical variables and to past dietary intake are rather limited. The aim of the present case-control study was, therefore, to investigate such possible associations by evaluating a group of women suffering from breast cancer who were being treated in a public hospital located in Joinville, SC, Brazil.

Materials and methods

Details of the study were presented to, and approved by, the Ethical Committee of the Universidade Federal de Santa Catarina (Florianópolis, SC, Brazil). Appropriate informed consent in writing was obtained from each participant prior to the commencement of the study.

Population studied

The study was conducted from june to november 2003 in Joinville, the population of which is predominantly of Germanic origin, and involved a group of women who had recently been diagnosed with breast cancer and treated in the municipal mastology clinic of a public health centre in Joinville. The control group consisted of an equivalent number of healthy women recruited at the gynecology clinic of a public hospital, Joinville. The exclusion criteria were: i) history of breast cancer; ii) previous surgery, chemotherapy or radiotherapy in the treatment of cancer; iii) hysterectomy and iv) pregnancy. A total of 66 subjects (33 in each group) were selected and re-directed to the nutritional clinics of either the public health centre or of the Hospital Municipal São José, as appropriate, for anthropometric, nutritional and dietetic evaluation. Each subject was asked to record their personal particulars, information about their educational background, social and economic status, clinical condition, age of menarche, previous pregnancies, intake of alcohol, smoking habits and physical activity by completing a detailed questionnaire. This questionnaire had been previously optimised in a pilot study that had involved 15 healthy women of different professions and socio-economic classes, and had included psychologists, physiotherapists, occupational therapists, social assistants, cleaners, waitresses and house wives.

Anthropometric measurements

Body weight and stature were determined with the participants barefoot and wearing only their underwear. The body mass index (BMI) was calculated by dividing body weight (kg) by the square of the height (m^2). In order to classify subjects according to their BMI values, the cut-off point proposed by the World Health Organization (WHO) was employed.[18]

Food frequency questionnaire

A food frequency questionnaire (FFQ) was developed based on information provided by the Municipal Health Service concerning local dietary intake during the period 2000 to 2002. The data were collected by nutritionists as part of the regular assistance provided to the local population. The FFQ was tested during the pilot study and was modified in order to contain culture-specific foods that were not included in the original questionnaire. The final version of the FFQ contained 91 food items classified into 10 groups, namely: meat and derivatives; milk and dairy products; fats; snacks; fruits; vegetables; pasta and bread or cakes, cereals and sweets; fatty foods, alcoholic beverages; and others foods. The frequency of dietary intake was assessed as being weekly (i.e. 1 to 7 times a week) and rarely or never, and aimed qualitatively to evaluate dietary inta-

	Case group		Control group		Total		p-value[a]
	n	%	n	%	n	%	
Table I *Descriptive characteristics of the population studied*							

	Case group		Control group		Total		p-value[a]
	n	%	n	%	n	%	
Age							0.007
Up to 44 years	11	33.3	22	66.7	33	50.0	
≥ 45 years	22	66.7	11	33.3	33	50.0	
Family income							0.020
> 4 minimum wage[b]	7	21.2	16	48.5	23	34.8	
> 4 minimum wage[b]	26	78.8	17	51.5	43	65.2	
Education							< 0.0001
≥ 4 years	10	30.3	29	87.9	39	59.1	
< 4 years	23	69.7	4	12.1	27	40.9	
Family history of cancer in general							0.620
No	17	51.5	19	57.6	36	54.6	
Yes	16	48.5	14	42.4	30	45.4	
Family history of breast cancer							0.250
No	23	69.7	27	81.8	50	75.8	
Yes	10	30.3	6	18.2	16	24.2	
Problem with alcohol abuse							0.200
No	32	97.0	28	84.8	60	90.9	
Yes	1	3.0	5	15.2	6	9.1	
Use of nutritional supplements							1.000
No	32	97.0	32	97.0	64	97.0	
Yes	1	23.0	1	3.0	2	3.0	
Attained menopause							< 0.0001
No	14	42.4	29	87.9	43	65.2	
Yes	19	57.6	4	12.1	23	34.8	
Use of oral contraceptives or hormone replacement drugs							0.720
No	26	78.8	24	75.0	50	76.9	
Yes	7	21.2	8	25.0	15	23.1	
Regular gynecological examinations							0.140
No	10	30.3	5	15.2	15	22.7	
Yes	23	69.7	28	84.8	51	77.3	
Regular mammographic examinations							0.060
No	6	18.2	13	39.4	19	28.8	
Yes	27	81.8	20	60.6	47	71.2	
Breast fed a child							0.510
No	4	12.1	7	21.2	11	16.7	
Yes	29	87.9	26	78.8	55	83.3	
Duration of breast feeding							0.770
0-6 months	26	78.8	25	75.8	51	77.3	
> 6 months	7	21.2	8	24.2	15	22.7	
Smoking habit							0.280
Never smoked	21	63.6	25	75.8	46	69.7	
Smoker or former-smoker	12	36.4	8	24.2	20	30.3	
BMI (kg/m^2)							1.000
Up to 24.99	11	33.3	11	33.3	22	33.3	
≥ 25	22	66.7	22	66.7	44	66.7	

[a] are statistically significant with *p*-values < 0,05.
[b] 1 minimum wage = US$ 130.00/month (september 2005 - exchange rate 1 US$ = R$ 2.3).

ke over the previous four years. In order to help subjects in remembering their retrospective food intake, participants were asked to associate their dietary intake with significant personal experiences such as leaving the parental home, divorce, change of address, relationships with family members and involvement in activities promoted by health support groups.[19]

Concomitant with the application of the FFQ, subjects were interviewed by a nutritionist. Participants were questioned about the weekly frequency of intake of each type of food that they had consumed and how that particular food had been prepared (i.e. fried, boiled, grilled, roasted, battered with eggs and flour, etc). Thus meat (and fish) that had been fried or battered were considered to be in the fatty category, whilst grilled or boiled meat (or fish) without fat and skin were considered to be in the lean category. Foods of a similar nature were grouped under the same headings: thus sweets, jam, cream, condensed milk and biscuits were all considered to be in the same group, whilst tinned fruit, puddings, jellies and mousses were considered to be desserts.

Statistical analysis

All statistical analyses were performed using Stata 6.0 software.[20] The distributions between the groups of variables in categories were compared using χ^2 and Fisher tests, whilst the mean values of weight, height, BMI, age, age of menarche and number of children were compared between groups using Student's t test.[21] For the statistical analysis of the data, a confidence interval of 95% was established.

The demographic, social and economical variables were age and age range, family income, level of education, family history of cancer in general and/or breast cancer, alcoholism, use of nutritional supplements, attainment of menopause, use of oral contraceptives or hormone replacement drugs, submission to regular gynaecological and mammographic examinations, occurrence and duration of breast feeding, smoking habits, and BMI category. The variables concerning the historical frequency of intake of particular foodstuffs were recorded as either "rarely or never" or "weekly" (i.e. 1 to 7 times a week).

In order to evaluate the association of breast cancer with respect to past dietary intake, and to demographic, social and economical variables, a non-conditional logistic regression method was applied.[22] The results obtained from the univariate logistic regression were analysed by odds ratio (OR; with a power of 80% to detect OR of 5) and those variables presenting OR values of $P < 0.25$ were selected.

Results

Table I shows the distribution of investigated characteristics between the group of women suffering from breast cancer and the group of healthy women. Statistically significant differences between the groups were observed with respect to age distribution ($P = 0.007$), family income ($P = 0.02$), educational level ($P < 0.0001$) and attainment of menopause ($P < 0.0001$). The ages of women within the control group varied between 31 and 63 years, whilst those in the group suffering from breast cancer ranged between 33 and 65 years. Comparatively, the average age of women with breast cancer (48.9 ± 8.3 years) was significantly higher ($P = 0.0002$) than that of healthy women (41.4 ± 7.1 years) (data not shown).

The age of attainment of menopause in the healthy group varied from 43 to 53 years, but the mean value (47.25 ± 4.34 years; $n = 4$) was not significantly different from that (48.37 ± 4.0 years; $n = 19$; range 42-57 years) recorded for women suffering from breast cancer. There were no significant differences between the groups regarding weight, height, BMI, number of children or age of menarche (data not shown).

Univariate logistic regression demonstrated that the risk of breast cancer was higher in the groups of women characterised by ages of 45 years or more (OR = 4.00; $CI_{95\%}$ = 1.44-11.13), a family income up to an equivalent of four minimum wage (OR = 3.50; $CI_{95\%}$ = 1.19-10.28), an educational level corresponding to primary school or inferior (OR = 16.7; $IC_{95\%}$ = 4.63-60.10) and attainment of menopause (OR = 9.84; $IC_{95\%}$ = 2.81-34.44). Following adjustment according to the age group, the variables corresponding to law family income (OR = 4.51; $IC_{95\%}$ = 1.32-15.45) and low education level (OR = 11.02; $IC_{95\%}$ = 2.87-42.26) remained as possible risk factors of breast cancer. However, the attainment of menopause could no longer be included as a risk factor (OR = 4.75; $IC_{95\%}$ = 0.90-25.0), a result that can be explained by the fact that only two menopausal women were younger than 45 years and both had breast cancer. Since the number of menopausal women younger than 45 years was low in both groups, the analysis of the individual, social and economical characteristics were adjusted according to age.

The results obtained from the study of past dietary intake were adjusted according to family income in order to remove the confusing factors associated with this variable. Table II shows both the unadjusted and adjusted OR values for the association between dietary intake and risk of breast cancer. Univariate logistic regression indicated that the dietary intake of pig lard (OR = 6.32; $IC_{95\%}$ = 1.52-26.28) and fatty red meat (OR = 3.48; $IC_{95\%}$ = 1.21-10.06) was significantly associated with the risk of breast cancer, whilst the consumption of apples (OR = 0.30; $IC_{95\%}$ = 0.09-0.94), watermelons (OR = 0.31; $IC_{95\%}$ = 0.10-0.93), tomatoes (OR = 0.16; $IC_{95\%}$ = 0.03-0.78), cakes (OR = 0.30; $IC_{95\%}$ = 0.09-0.97) and desserts (OR = 0.20; $IC_{95\%}$ = 0.06-0.65) could be considered as protective elements against breast cancer. The results also indicated a small positive association, which was not statistically significant, between the consumption of chicken with

Dietay intake	Case group n	Control group n	Unadjusted[a] (CI[b] = 95%)	Adjusted OR[c] (CI = 95%)
Lard from pigs				
Never/rarely	20	30	1.00	1.00
Weekly	13	3	6.50 (1.64-25.76)	6.32 (1.52-26.28)
Fatty beef				
Never/rarely	10	20	1.00	1.00
Weekly	23	13	3.54 (1.28-9.80)	3.48 (1.21-10.06)
Lean beef				
Never/rarely	20	14	1.00	1.00
Weekly	13	19	0.48 (0.17-1.28)	0.48 (0.17-1.34)
Chicken with skin				
Never/rarely	11	18	1.00	1.00
Weekly	22	15	2.40 (0.88-6.50)	2.64 (0.92-7.55)
Skinless chicken				
Never/rarely	22	15	1.00	1.00
Weekly	11	18	0.42 (0.15-1.13)	0.38 (0.13-1.09)
Apples				
Never/rarely	15	6	1.00	1.00
Weekly	18	27	0.27 (0.09-0.82)	0.30 (0.09-0.94)
Watermelons				
Never/rarely	17	8	1.00	1.00
Weekly	16	25	0.30 (0.10-0.86)	0.31 (0.10-0.93)
Tomatoes				
Never/rarely	9	3	1.00	1.00
Weekly	24	30	0.27 (0.06-1.10)	0.16 (0.03-0.78)
Cake				
Never/rarely	15	9	1.00	1.00
Weekly	18	24	0.45 (0.16-1.26)	0.30 (0.09-0.97)
Dessert				
Never/rarely	17	7	1.00	1.00
Weekly	16	26	0.25 (0.09-0.74)	0.20 (0.06-0.65)
Corn flour				
Never/rarely	19	14	1.00	1.00
Weekly	14	19	0.54 (0.20-1.44)	0.35 (0.11-1.07)

[a] Unadjusted odds ratio.
[b] CI = confidence interval.
[c] Adjusted odds ratio in non-conditional logistic regression model of according to family income.

skin and the risk of breast cancer (OR = 2.64; $IC_{95\%}$ = 0.92-7.55), whilst the consumption of skinless chicken (OR = 0.38; $IC_{95\%}$ = 0.13-1.09) and corn flour (OR = 0.35; $IC_{95\%}$ = 0.11-1.07) was weakly associated with a protective action against cancer (table II).

Discussion

Although some associations between dietary intake and risk of breast cancer could be detected in this study, the methods employed in the evaluation presented various distinct limitations. Salvo & Gimeno[23] state that the FFQ technique leads to the underestimation of food consumption by both men and women alike. The particular disadvantages mentioned by these authors are the excessive long list of items on the questionnaire that can cause confusion to the participants, and the loss of relevant information about some types of food not included in the FFQ. One of the major limitations of the FFQ technique is that it depends on information provided by the participants of the study and upon the ability of the interviewer not to induce a possibly inaccurate answer.[24] Despite these difficulties, FFQ is one

of the tools most commonly used in epidemiological studies in order to assess long-term nutritional exposure,[25] since it represents a low cost and facile technique by which to classify individuals according to their dietary habits.[26]

This case-control study was conducted in two public health services with the objective of minimizing the possibility of occurrence of selection bias, considering that the women who are assisted in these services present similar socioeconomic situation. Both groups of women presented similar characteristics regarding family history of all kinds of cancer and breast cancer, in particular, parity, breast feeding, anthropometrical measurements, smoking habits, use of nutritional supplements and hormone therapy, regularity of mammografic and gynecological examinations. However, the control group was composed by younger women and presented higher family income and educational level when compared to the breast cancer cases-group. The occurrence of selection bias might have affected the estimates for the disease exposition, although, age ranges in both, control (31-63 y) and case groups (33-65 y) were within the age range that presented risk for breast cancer.[27] Other limitation of the study constitutes the size of sample that difficult the removal of the potential confounders.

After adjusting the OR according to the age of the subjects, the present study indicated that the risk of breast cancer was higher amongst women of low economic status (family income up to four minimum wage) and poor educational level (incomplete primary school or less) compared with more affluent and better educated women. This finding may be a reflection of a more stressful life style, an inadequate diet, and an inequality in terms of access to health services and to information concerning cancer prevention. Campbell[28] reported that educated women are well informed about disease-prevention methods and this fact may very well influence the likelihood of developing breast cancer.

In contrast to the results from the present study, research carried out in Belo Horizonte, MG, Brazil,[29] from 1978 to 1987 involving 300 women with breast cancer and 600 healthy women in the age range 25 to 75 years, showed a positive association between family income and risk of breast cancer (OR = 1.69; IC$_{95\%}$ = 1.18-2.42). Similarly, a study conducted in the United States from 1988 to 1995 involving a total of 14,667 women showed that those who lived in wealthier communities were exposed to a higher risk of acquiring breast cancer than those living in poorer areas.[30] The divergence between our results and the Brazilian study mentioned above may be due to regional differences with respect to life style, food customs, and social and economical habits.

With respect to the association between age and risk of breast cancer, the present study confirms previous findings, i.e. according to records for the period 1996 to 2000 maintained in various cities in Brazil (Goiânia, São Paulo and Manaus), 60 to 70% of women suffering from breast cancer were 40 to 69 years old.[31-33]

A positive association between the frequency of breast cancer and the consumption of fatty red meat and/or pig lard was found in the present investigation. These types of food are all rich in saturated fatty acids that are believed to be factors leading to an increased risk of breast cancer.[34] Although the mechanism of action is not clear, it is known that saturated fatty acids stimulate the production of endogenous estrogens that induce cell proliferation in the epithelium of the alveolar sacs and lactiferous ducts of the breasts. Furthermore, the ingestion of saturated fat and cholesterol is associated with an increase in breast density, which itself increases the risk of cancer in this glandular tissue.[35] Additionally, red meat contains potent carcinogens, such as heterocyclic amines, polyaromatic hydrocarbons and other nitrogen containing compounds,[36, 37] that are also believed to increase the risk of cancer.

However, the results of more than 20 different studies have revealed contradictory indications regarding a relationship between the consumption of meat and cancer.[9] Both cohort and case-control studies[10, 11, 17] have established a positive association between the consumption of fatty red meat and an increased risk of breast cancer. In contrast, other case-control studies, have found no significant associations between either total meat consumption or the ingestion of red or white meat, and the risk of breast cancer.[9, 12] Regarding the consumption of fats, Hebert et al.[13] demonstrated that the ingestion of butter, margarine, lard, red meat, liver and streaky bacon was associated with an increased risk in the recurrence of breast cancer.

In the present study, the weekly consumption of cakes and desserts was associated with protective traits against breast cancer. These findings must be interpreted with due care, however, since they may be indirectly reflecting the attendant healthy dietary habits, which themselves are associated with less risk of breast cancer. The results also conflict with those of the case-control study conducted in the USA, that established a positive association between the weekly ingestion of sweets (especially soft-drinks and desserts) and breast cancer.[14] On the other hand, Holmes et al.[15] investigated a cohort of 88,678 women, between 1980 and 1998, from which 4,092 women were diagnosed with breast cancer, and found no association between carbohydrate consumption and increased risk of this form of cancer.

The consumption of apples, watermelons and tomatoes were also apparently associated with a protective action against breast cancer according to the results of the present study. In a case-control study conducted in Heidelberg,[16] Germany, between 1998 and 2000, were observed that total vegetable consumption as well as the level of ingestion of raw vegetables and of integral cereals, were inversely associated with the risk of breast cancer. There was, however, no statistically significant association between the ingestion of fruits and cooked vegetables and the risk of breast cancer. In other study, Suárez-Varela et al.[17] observed that high

intake of tomatoes exerted a significant protection against development of this form of neoplasm.

A number of other case-control studies[38, 39] have claimed that the consumption of fruits and vegetables confers some level of protection against cancer, whilst a cohort study produced no such evidence.[40] In the last few years, a weaker association between the protective effects of fruits and vegetables and cancer has been observed from cohort studies compared to observations obtained from case-control studies.[16, 38] In contrast to case-control studies,[40-42] the analysis of data derived from cohort studies has not revealed any association between the consumption of fruits and vegetables and the reduction of risk of breast cancer.[39] Recent research has focused on the identification those substances present in fruits and vegetables that are responsible for the protective effects against breast cancer, such as antioxidant compounds and fibres.[43-44]

In the present investigation, we have demonstrated that the historic weekly consumption of some types of foods and the attendant risk of breast cancer could be correlated with OR values in the range of 0.25 to 0.35, whilst the risk for those who did not consume these types of foods varied from 2.97 to 3.95. In a sample population consisting of 66 women (33 in each group), the statistical tests applied showed modest power in identifying differences between the groups when the OR was inferior to 5. With such a small number of women, the power of the test to detect OR values equal to 3 would have been only 50%, ie. an error of 50%. From the described analyses, the risk factors directly associated with breast cancer in the studied population were age, family income, level of education, attainment of menopause and weekly consumption of pig lard and fatty red meat. The regular consumption of apples, watermelons, tomatoes, cakes and desserts were inversely associated with the occurrence of the disease. It is clear that further studies are required in order to determine the effective relationship between dietary intake and risk of breast cancer, and the consequent establishment of intervention strategies aimed at reducing the incidence of this pathology.

Acknowledgements

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