Scientia Medica

e-ISSN: 1980-6108 | ISSN-L: 1806-5562

10.15448/1980-6108.2018.2.28723

ORIGINAL ARTICLE

Open Access

Nutritional and environmental risk factors for breast cancer: a case-control study

Fatores de risco nutricionais e ambientais para câncer de mama: estudo de casos e controles

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How to cite this article:

Queiroz SA, Sousa IM, Silva FRM, Lyra CO, Fayh APT. Nutritional and environmental risk factors for breast cancer: a case-control study. Sci Med. 2018;28(2):ID28723. http://doi.org/10.15448/1980-6108.2018.2.28723

ABSTRACT

AIMS: To investigate the associations between breast cancer diagnosis and nutritional and environmental factors in women from Northeast Brazil.

METHODS: A case-control study included women evaluated in two hospitals specialized in cancer treatment. The case group was composed by women with breast cancer whose data were obtained during the hospitalization period for surgical treatment of the disease. The control group was selected in the same hospitals excluding the oncology ward. The following risk factors were investigated: household environmental sanitation, breastfeeding history, social class, smoking exposition, alcohol consumption and family history of cancer. A food frequency questionnaire was completed by the subjects and an evaluation of anthropometric nutritional status was made. Comparison for quantitative variables was performed using independent t-test or Mann-Whitney test. Chi-square or Fisher's exact test were used to compare categorical variables. The estimated risk associated with consumption of nutrients and food groups was assessed by OR, with a 95% confidence interval. In order to assess the effect of possible confounding factors such as excess weight or excessive caloric intake, a multivariate analysis was performed with the variables with $p<0.15$ in the food consumption analysis. The significance level for all analyses was set at $p<0.05$.

RESULTS: The total sample consisted of 118 women, 59 in each group. Of all environmental risk factors investigated, poor sanitation (OR [odds ratio]=3.2, 95%CI 1.43-7.11) and family history for cancer (OR=3.11, 95%CI 1.42-6.78) were significantly associated with the diagnosis of breast cancer. Regarding anthropometric assessments, overweight or obesity and waist circumference ≥88cm were more prevalent in the case group (OR=2.70, 95%CI 1.28-5.70 and OR=3.10, 95%CI 1.46-6.56, respectively). Regular consumption of ultra-processed foods was identified as a risk factor for breast cancer (adjusted OR=2.35, 95%CI 1.08-5.12).

CONCLUSIONS: Higher consumption of ultra-processed food, presence of overweight or obesity, waist circumference ≥88 cm, poor sanitation, and family history of cancer were risk factors for breast cancer in this sample of women living in Rio Grande do Norte state, Brazil.

KEYWORDS: breast neoplasms; risk factors; diet; obesity; case-control studies.

RESUMO

OBJETIVOS: Investigar associações entre o diagnóstico de câncer de mama e fatores nutricionais e ambientais em mulheres do Nordeste do Brasil.

MÉTODOS: Um estudo caso-controle incluiu mulheres avaliadas em dois hospitais especializados em câncer. O grupo de casos foi composto por mulheres com câncer de mama cujos dados foram obtidos durante o período de internação para tratamento cirúrgico da doença. O grupo controle foi selecionado nos mesmos hospitais, excluindo as unidades de oncologia. Os seguintes fatores de risco foram investigados: saneamento básico nas moradias, história de amamentação, classe social, exposição ao tabagismo, consumo de álcool e história familiar de câncer. Um questionário de frequência alimentar foi completado pelas participantes e foi feita uma avaliação do estado nutricional antropométrico. Foram usados o teste t independente ou o teste de Mann-Whitney para comparação entre variáveis quantitativas, e o qui-quadrado ou o teste exato de Fisher para variáveis categóricas. O risco estimado associado ao consumo de nutrientes e grupos de alimentos foi avaliado por OR, com intervalo de confiança de 95%. Para avaliar o efeito de possíveis fatores de confusão, como excesso de peso ou ingestão calórica excessiva, foi realizada uma análise multivariada com as variáveis com $p<0,15$ na análise do consumo de alimentos. O nível de significância para todas as análises foi definido em $p<0,05$.

RESULTADOS: A amostra total consistiu de 118 mulheres, 59 em cada grupo. De todos os fatores de risco ambientais investigados, um saneamento deficiente (OR [*odds ratio*]=3,2, IC95% 1,43-7,11) e história familiar de câncer (OR=3,11, IC95% 1,42-6,78) foram significativamente associados ao diagnóstico de câncer de mama. Em relação às avaliações antropométricas, excesso de peso ou obesidade e circunferência da cintura >88 cm foram mais prevalentes no grupo de casos (OR=2,70, IC95% 1,28-5,70 e OR=3,10, IC95% 1,46-6,56, respectivamente). O consumo regular de alimentos ultraprocessados foi identificado como um fator de risco para câncer de mama (OR ajustada=2,35, IC95% 1,08-5,12).

CONCLUSÕES: Maior consumo de alimentos ultraprocessados, presença de excesso de peso ou obesidade, circunferência da cintura ≥88 cm, saneamento básico deficiente e história familiar de câncer foram fatores de risco para o câncer de mama nesta amostra de mulheres que vivem no estado do Rio Grande do Norte.

DESCRITORES: neoplasias da mama; fatores de risco; dieta; obesidade; estudos de casos e controles.

Received: *2017/10/03*
Accepted: *2017/12/03*
Published: *2018/01/07*

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Abbreviations: BMI, body mass index; FFQ, Food Frequency Questionnaire.

INTRODUCTION

Cancer is an important public health issue, and its incidence is increasing in developing countries. According to data from the World Health Organization, malignant neoplasms caused over six million deaths globally in 2002, and this figure increased to 8.2 million in 2012 [1]. In Brazil, the trend is similar, with estimations for the biennium 2016-2017 indicating an occurrence of around 600 thousand new cases of cancer. Excluding non-melanoma skin cancer (approximately 180 thousand new cases), about 420 thousand new cases of cancer will occur [2].

In women, breast cancer is the most frequent and accounts for 22% of new cases of cancer [1-3], representing the leading cause of death from cancer among Brazilian women since 1980. The etiology of breast cancer is still poorly understood and the known risk factors only explain a small proportion of cases. It is known that cancer is the result of an interaction between endogenous and environmental factors, and dietary habits are among them [4, 5]. Among the factors documented for the increase in breast cancer incidence, hereditary factors (genetic and family history) and some environmental factors standout, such as poor eating habits (for example, low consumption of fruit and high consumption of ultra-processed foods), physical inactivity, exposure to smoking and alcohol intake [6, 7].

Food intake has an important role in the initial stages, promotion and propagation of cancer, standing out from the other risk factors [6, 8]. However, it is not clear at present whether the different results of various studies can be explained by the amount of nutrients or by the differences between the demographic characteristics of subjects, measurement error in prospective studies or selection and recall biases in case-control studies. In recent years, some systematic reviews and meta-analyses have been made in order to investigate associations between dietary factors and breast cancer in different populations [9-12], but there is still no agreement among experts. In general, it seems that diets rich in fruits, vegetables and legumes offer protection against breast cancer [13], and increased consumption of fat and ultra-processed foods increases the risk [10]. These eating habits are also associated with increased risk of obesity and changes in body fat, which in turn increase the risk of breast cancer [14].

Given the conflicting findings in studies of risk factors for breast cancer, more research towards a better understanding of the issue is needed, especially when evaluating the factors related to food intake. Thus, the present study aims to investigate the association between nutritional and environmental risk factors and the development of breast cancer in women living in Rio Grande do Norte state, Brazil.

METHODS

Study design, sample and ethical considerations

This was a case-control study conducted in May to December 2015, with adult women living in Northeast Brazil. The case group consisted of women diagnosed with breast cancer and treated at two referral hospitals for cancer treatment and who were evaluated during the hospitalization period for surgical treatment of the disease. Controls were identified and selected from the various female wards of the hospitals, excluding the oncology ward. The inclusion criteria for the control group consisted of women living in the same city, without cancer. They were matched for age (two years more or less than their counterpart in the case group), ethnicity and housing location. The study protocol was approved by the Human Research Ethics Committee at the Federal University of Rio Grande do Norte (UFRN) (protocol No. 284.435, CAAE 13032813.7.0000.5568).

Measurements

The subjects completed a questionnaire with socio-demographic data, and also provided information regarding the following variables of interest: exposure to smoking, alcohol consumption, time or absence of breastfeeding, body weight and economical status. Each variable had a cut-off point defined and/or parameter set for being considered as a risk factor: Being a smoker or former smoker; consumption of alcohol more than once per day; less than 180 days of breastfeeding; being classified as vulnerable or being in poverty or extreme poverty according to the classification of the Brazilian Association for Population Studies (ABEP) [15].

All participants had their body weight and height measured without shoes and wearing minimal clothing. Body mass index (BMI) was calculated to determine nutritional status according to the cut-off points described by the World Health Organization [16]. The following cut-off points were used to classify cardiovascular risk by waist circumference: <80 cm,

low risk; ≥80 and <88 cm, moderate risk; ≥88 cm, high risk [17].

A semi-quantitative food frequency questionnaire (FFQ) was used to assess food consumption. The FFQ was adapted from an instrument validated in Brazil in the same geographical region to assess the consumption of fat in women with breast cancer [18]. This FFQ had 98 food items referent to consumption in the past 12 months. A pilot study was conducted to test the validity of this FFQ adapted against four 24-hour dietary recalls among one hundred adult residents in the same city. Based on the original questionnaire, the following adjustments were made: inclusion of some foods and replacement of the portion sizes pre-established by an additional space to each food, so that the interviewee described the size of the portion usually consumed. For assistance and more reliable data on food intake, the respondents observed an illustrated guide for assessment of food intake, in which there were images displayed showing household items of various sizes (plates, glasses, cups, silverware and others) and also different portions of food for better identification of portions consumed. The data collectors were previously trained to avoid potential errors during data collection and discrepancies between results.

The FFQ was then qualitatively and quantitatively analyzed. The frequency of consumption reported by each participant was considered for qualitative analysis, with "frequent consumption" being considered when the intake was equal to or more than five times a week [19]. Consumption of ultra-processed food was evaluated according to the classification proposed by Monteiro et al. [20]. In this classification, ultra-processed food products are considered as being from a food processing mix in order to create pre-prepared food products or ready for consumption and which are durable, affordable, convenient and palatable. Processes used in the production usually characterize these foods as salted, cured, sugared, roasted, fried, smoked or pickled, and can insert cosmetic preservatives or additives, vitamins and synthetic minerals and use sophisticated types of storage.

An electronic chart was organized for quantitative analysis containing the chemical composition for 100 g of each food present in the FFQ. Columns were then created in this chart to enter codes relating to the frequency of consumption. The analysis was performed using the following formula: *frequency of consumption* × *portion size* × *nutritional food composition.* When respondents reported that food was *never* consumed, the code used was zero (0). Among the answer choices on consumption were *never* and from *one to 10 times a day, week, month or year*. The codes related to frequency were calculated as a daily rate: *one time daily* (1), *once a week* (0.14), *once a month* (0.04) *once a year* (0.003), and so on. The portions were expressed in household measures or in the way of common presentation for consumption. Due to the large variety, *small, large and extra-large* portions were considered, corresponding to 75%, 125% and 200% of the middle portion of reference described in the FFQ, respectively.

Statistical Analysis

The sample size was calculated based on a case-control study conducted in the city of João Pessoa (Rio Grande do Norte, Brazil), finding an odds ratio (OR) of 4.3 between the consumption of red meat with fat and breast cancer diagnosis [18]. Using a power of 80% for the study and a significance level of 5%, the required number of patients in each study group would be 58 women.

Statistical analyses were performed with IBM SPSS Statistics version 19 for Windows. The normality of the data was checked using the Shapiro-Wilk test. Quantitative data are presented using mean and standard deviation for parametric variables or median and interquartile range for non-parametric variables. Categorical data are expressed as absolute and relative frequencies. Comparison of quantitative variables between the case and control groups was performed using the independent t-test or Mann-Whitney test for non-parametric and parametric variables, respectively. Chi-square or Fisher's exact test were used to compare categorical variables. The estimated risk associated with consumption of nutrients and food groups was assessed by OR, with a 95% confidence interval. In order to assess the effect of possible confounding factors such as excess weight or excessive caloric intake, a multivariate analysis was performed with the variables with $p<0.15$ in the food consumption analysis. The significance level for all analyses was set at $p<0.05$.

RESULTS

Sixty-five women diagnosed with breast cancer were evaluated, and six were excluded from the sample due to missing data or for making an error in filling-in some data, so the final case group comprised 59 patients. After obtaining the data from the case group, each control was selected in accordance with the established criteria, totaling 59 women in each group and a total of 118 volunteers for this study. The mean age of both groups was 53.1±13.8 years.

Table 1 shows the demographic characteristics of the sample. As can be seen in the table, the sample was fairly homogenous, except for sanitation and family history of cancer. The case group had a higher prevalence of poor sanitation in their environment as well as of family history of cancer.

Anthropometric characteristics and cardiovascular risk of the volunteers are described in **Table 2**. The case group had a higher prevalence of overweight and abdominal obesity compared to the control group; characteristics that confer also a higher cardiovascular risk.

Table 3 shows the quantitative analysis of food consumption. There were no statistically significant differences in these quantitative dietary patterns in women with or without a diagnosis of breast cancer.

Table 1. Association between environmental factors and breast cancer in women living in the Northeast Region of Brazil.

Variables	Case group (n=59)	Control group (n=59)	Odds ratio (95%CI)
	n (%)	n (%)	
Poor environmental sanitation	28 (47.5)	13 (22.0)	**3.20 (1.43-7.11)**
History of breastfeeding	7 (11.9)	11 (18.6)	0.58 (0.21-1.63)
Vulnerable social class or extreme poverty	15 (25.4)	11 (18.6)	1.49 (0.63-3.53)
Married	49 (83.1)	41 (69.5)	2.15 (0.90-5.13)
Smoking exposure	26 (44.1)	19 (32.2)	1.66 (0.89-3.10)
Alcohol consumption	19 (32.2)	14 (23.7)	1.53 (0.68-3.41)
Family history of cancer	45 (76.3)	30 (50.8)	**3.11 (1.42-6.78)**

CI, confidence interval.

Table 2. Association between anthropometric status and breast cancer in women living in the Northeast Region of Brazil.

Variables	Case group (n=59)	Control group (n=59)	p-value* or Odds Ratio (95%CI)†
	Mean±SD or n (%)	Mean±SD or n (%)	
Body mass index	28.1±4.7	26.2±3.3	**0.02**
Waist circumference	93.1±12.6	88.4±12.0	**0.04**
Overweight or obesity ‡	41 (69.5)	27 (45.7)	2.70 (1.28-5.70)
High cardiovascular risk §	41 (69.5)	25 (42.4)	**3.10 (1.46-6.56)**

SD, standard deviation; CI, confidence interval.
* Independent t-test; † Chi square test; ‡ BMI ≥25kg/m²; § Classified by waist circumference ≥88 cm.

Table 3. Quantitative analysis of diet from the Food Frequency Questionnaire, in women with and without breast cancer, living in the Northeast Region of Brazil.

Variables	Case group (n=59)	Control group (n=59)	p*
	Mean±SD or Median (IQR)	Mean±SD or Median (IQR)	
Energy intake (kcal)	2823.3±876.6	2800.2±780.2	0.59
Carbohydrates (g)	389.7±140.2	393.4±117.6	0.27
Carbohydrates (%)	55.2±19.9	56.2±16.8	0.73
Protein (g)	93.0 (74.3-116.3)	86.7 (69.4-112.4)	0.95
Protein (%)	13.2 (10.5-16.5)	12.4 (9.9-16.1)	0.52
Fat (g)	101.1±33.0	97.5±33.9	0.91
Fat (%)	32.2±10.5	31.3 ± 10.9	0.43
Saturated fat (g)	13.9 (10.8-19.1)	14.4 (10.9-20.4)	0.28
Fibers (g)	30.0±11.0	30.2±9.1	0.24
Vitamin A (μg)	1089.7 (603.0-1577.5)	1273.7 (938.1-2096.8)	0.71
Vitamin C (mg)	228.7 (154.3-349.2)	268.7 (160.9-355.2)	0.24
Vitamin E (mg)	18.5 (13.6-22.4)	19.1 (13,9-22.7)	0.75

SD, standard deviation; IQR, interquartile range.
* Independent t-test for parametric variables or Mann-Whitney test for non-parametric variables.

Table 4. Regular consumption (more than or equal to five days in the week) of food groups (qualitative analysis) between groups of women with and without breast cancer, living in the Northeast Region of Brazil.

Type of food	Case group (n=59)	Control group (n=59)	ORb (CI95%)	ORadj (CI95%)
Fruit	20 (33.9)	22 (37.3)	0.86 (0.41-1.83)	–
Red/processed meat	25 (42.4)	34 (57.6)	0.54 (0.26-1.12)	0.51 (0.24-1.10)
Fish	3 (5.1)	3 (5.1)	1.00 (0.19-5.17)	–
Beans	43 (72.9)	36 (61.0)	1.72 (0.79-3.73)	–
Vegetables	16 (27.1)	25 (42.4)	0.51 (0.23-1.10)	–
Whole milk	29 (49.2)	29 (49.2)	1.00 (0.49-2.06)	–
Ultra-processed food	30 (50.8)	17 (28.8)	**2.56 (1.20-5.47)**	**2.35 (1.08-5.12)**

ORb, odds ratio brute; ORadj, odds ratio adjusted by excess of weight and excessive caloric intake; CI, confidence interval.

Table 4 presents the results of food consumption frequency obtained on the FFQ. Categories *red/processed meat* and *ultra-processed foods* had a $p<0.15$ on the Chi-Square test, and binary regression analysis adjusted by excess weight and excessive caloric intake was performed. Women with cancer had a higher intake of ultra-processed foods compared to the control group, even after the statistical adjustment for excess weight and caloric intake.

DISCUSSION

These results show that ultra-processed food consumption and overweight were associated with breast cancer in this sample of Brazilian women, which is partially consistent with published studies [5, 7, 21, 22]. Additionally, poor environmental sanitation and family history of cancer were identified as risk factors for breast cancer in these women.

There was no difference between the two groups in terms of socio-demographic characteristics, except for sanitation in the place of residence. Inadequate sanitation conditions can be related to a lack of access to healthcare, not only posing as a risk factor for infectious diseases, but also for other disorders such as cancer [23]. In a Danish cohort study of 1,229 post-menopausal women diagnosed with breast cancer, association between low socioeconomic status and risk of mortality was observed, probably due to increased use of tobacco and alcohol [24]. Socio-economic factors such as income and educational level had variable effects on breast cancer risk and also affected women's knowledge about risk factors and early detection [25]. In the present study, the case group presented higher odds ratio for smoking exposition and alcohol consumption, both recognized environmental risk factors for breast cancer, but no statistical significance occurred. It is also possible that the chosen tool to characterize socio-economic conditions in this study (income) was not sensitive enough to verify differences between the groups, or the sample size was small to detect some differences.

Evidence about the protective role of breastfeeding on the risk of breast cancer is still controversial. In this study, the statistical analysis did not support the hypothesis that breastfeeding confers such protection. This result is similar to the findings of another study conducted in Brazil, which evaluated 439 women with breast cancer [26]. However, a recent cohort study of 1,636 women in the United States observed significant evidence supporting the association between breastfeeding for six months or more and decreased risk of recurrence and death from breast cancer [27]. Two recent meta-analyses also indicate a protective effect of breastfeeding on breast cancer, but there is still a lack of consensus on the amount of time of breastfeeding and the number of breastfed children required to observe this protective effect [28, 29].

Another classic risk factor for the diagnosis of breast cancer is overweight (including obesity) [30, 31], and the present data corroborates this assertion. A study among survivors also observed a high prevalence of overweight status in 154 patients from a reference center in Brazil [32]. In addition, it is recognized that the distribution of body fat, especially abdominal fat, has more influence on metabolic risk factors than total body fat [33]. In the present study we found an association between waist circumference and breast cancer, which is similar to other studies conducted in Brazil [34-36] or in other countries [37, 38]. Harvie et al. [39] suggest that central obesity may be associated with a risk of breast cancer in premenopausal women, and other studies show association between abdominal obesity and risk of breast cancer in postmenopausal women [40, 41].

The analysis of the FFQ shows that women with breast cancer reported a lower daily consumption of red meat, although the difference was not statistically significant. This finding is not consistent with other studies in the literature which found high consumption of red meat as associated with a higher risk of breast cancer, possibly due to the high content of saturated fat in this food [9,42,43]. In Brazil, other case-control studies have found a significant association between high consumption of red meat and breast cancer [44,45]. This discrepancy may be due to the fact that in the present study the case group consisted of patients who were already hospitalized for breast surgery, so they might have reduced the consumption of red meat as a prevention measure or treatment for breast cancer.

In the literature, currently the emphasis is not only on the nutrients, but also on the overall dietary patterns and the different types of food. Our results showed a higher intake of ultra-processed food in the case group, without other statistical differences in the reported dietary intake. A case-control study conducted in Iran, investigating the association between diet and breast cancer (100 cases and 178 controls), showed that healthy eating habits (regular consumption of fruit and vegetables, fish, vegetable oils and low consumption of saturated fat) was a protective factor for breast cancer [46]. McKenzie et al. [47], in a cohort study of 242,918 women followed for a mean time of 10.9 years, recorded 7,756 breast cancer diagnosis, usually in women with a combination of unhealthy behaviors, including dietary habits. Current eating habits, especially in Western populations, are characterized by a low intake of plant foods, fiber and fruit, and high consumption of processed foods rich in fats and sodium. A recent meta-analysis showed that reduced dietary fat consumption in the post-diagnosis period can increase the survival rate of women with breast cancer [12]. These results should both prompt and guide health professionals to design educational initiatives regarding dietary habits for these women.

This study has some limitations. The menopausal status of patients was not taken into account, which is a critical point when evaluating the relationship between breast cancer, obesity and nutritional habits. For future studies, we suggest case and control groups paired according to menopausal status and BMI. The patients were not paired according to anthropometric nutritional status (BMI, waist circumference), which can bias the evaluation of the main central point of food intake. In our study, most of the data was obtained from the women's self-reports, so recall bias was more probable, although medical records were checked to confirm the participants' history. Studies of food intake analysis have intrinsic limitations in the collection method and data analysis, as validated questionnaires are not easily available in the literature and had to be adapted to the population of interest. Furthermore, the dependence on individual account, the subjectivity of individuals, and especially their memory, can cause significant biases in the study design.

Notwithstanding such limitations, this study found that higher consumption of ultra-processed food, presence of overweight or obesity, waist circumference ≥88 cm, poor environmental sanitation, and family history of cancer were risk factors for breast cancer in this sample of women living in Rio Grande do Norte, Brazil.

NOTES

Acknowledgments

The authors thank to *Liga Norteriograndense Contra o Câncer*, especially to Jeane Dantas de Azevedo, for the cooperation.

Funding

This study did not receive financial support from outside sources.

Conflicts of interest disclosure

The authors declare no competing interests relevant to the content of this study.

Authors' contributions

All the authors declare to have made substantial contributions to the conception, or design, or acquisition, or analysis, or interpretation of data; and drafting the work or revising it critically for important intellectual content; and to approve the version to be published.

Availability of data

The authors declare to have had access to all available data and assume full responsibility for the integrity of these results.

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