Dietary patterns and risk of breast cancer: a case-control study in the Northeast of Brazil

Padrões dietéticos e risco de câncer de mama: um estudo caso-controle no Nordeste do Brasil

ABSTRACT

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The objective of this study was to investigate dietary patterns and breast cancer etiology. This work concerns a hospital-based case-control study in the Northeast region of Brazil (João Pessoa, Paraíba). Cases were 89 women age-matched to 94 controls. Socio-demographic, reproductive factors, physical activity, weight and height characteristics were investigated. Dietary data were collected using a food frequency questionnaire developed and validated for the study. The risk associated with the intake of food groups defined a posteriori*, through factor analysis, was assessed. Two factors were identified: the first one was characterized by the intake of meat, both red and poultry, and fat-dense foods, but also by vegetables and fruits. The second factor was represented by rice, beans, sweets, milk and a negative correlation with red meat. After categorization of factor scores into tertiles,* odds ratios *and 95% confidence intervals were calculated using unconditional multiple logistic regression. After adjustment for age, region of residence, oral contraceptive use, age of menopause, BMI and energy, the first factor showed a positive association with breast cancer (OR=7.3; 95% CI: 2.1-25.7); whereas the second factor was inversely associated with the outcome (OR=0.2; 95% CI: 0.07-0.61). The study results suggest that the traditional Brazilian diet, consisting of rice and beans, may provide protection against breast cancer.*

Keywords: Breast Cancer. Diet. Factor analysis statistical. Diet Surveys. Dietary Patterns.

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RESUMEN

El objetivo del trabajo fue investigar los patrones de dieta como agente etiológico del cáncer de mama. El estudio, del tipo caso-control, realizado en la región Noreste de Brasil (João Pessoa, Paraíba), con 98 mujeres, pareadas por edad con 94 controles. Se investigaron características demográficas, factores reproductivos, práctica de actividad física, peso y altura. Los datos de ingesta dietética se recolectaron por medio de un cuestionario de frecuencia alimentar desarrollado y validado para el estudio. Se verificó el riesgo asociado con la ingestión de grupos de alimentos definidos, a posteriori *por análisis factorial. Fueron identificados dos factores, el primero caracterizado por la ingestión de carne, tanto roja como blanca, pero también por vegetales y frutas. El segundo factor, fue representado por arroz, frijoles, dulces, leche y por una correlación negativa con carne roja. Después de la categorización de los escores originados del análisis factorial, en terciles, fue calculada una razón ODD con intervalo de confianza de 95% por regresión logística no condicional. Después del ajuste por edad, región de residencia, uso de anticonceptivo oral, edad de la menopausia, IMC y energía, el primer factor mostró una asociación positiva con el cáncer de mama (OR= OR=7.3; IC95%: 2.1-25.7), mientras que el segundo mostró una relación inversa (OR=0.2; IC95% I: 0.07-0.61). Los resultados sugieren que la dieta tradicional del brasileño, que consiste en arroz y frijoles, puede conferir protección contra el cáncer de mama.*

Palabras clave: Cáncer de mama. Dieta. Análisis factorial. Encuesta alimentar. Patrones de dieta.

RESUMO

O trabalho teve por objetivo investigar padrões da dieta e etiologia de câncer de mama. Foi realizado um estudo caso-controle na região Nordeste do Brasil (João Pessoa, Paraíba). A amostra foi composta por 98 mulheres, pareadas por idade com 94 controles. Investigaram-se as características demográficas, os fatores reprodutivos, a prática de atividade física, o peso e a altura. Os dados dietéticos foram coletados por meio de um questionário de freqüência alimentar desenvolvido e validado para o estudo. Verificou-se o risco associado com a ingestão de grupos de alimentos definidos a posteriori, *por análise fatorial. Dois fatores foram identificados: o primeiro caracterizou-se pela ingestão de carne, tanto vermelha quanto branca, mas também por vegetais e frutas. O segundo fator foi representado por arroz, feijão, doces, leite e por uma correlação negativa com carne vermelha. Após a categorização dos escores, derivados a partir da análise fatorial, em tercis, foi calculada a* odds ratios *e o intervalo de confiança de 95% por regressão logística não condicional. Após o ajuste por idade, região de moradia, uso de contraceptivo oral, idade da menopausa, IMC e energia, o primeiro padrão mostrou uma associação positiva com câncer de mama (OR= OR=7.3; IC95%: 2.1-25.7), enquanto o segundo padrão associou-se inversamente com o desfecho (OR=0.2; IC95%I: 0.07-0.61). Os resultados sugerem que a dieta tradicional do brasileiro, que consiste em arroz e feijão, pode conferir proteção contra o câncer de mama.*

Palavras-chave: Câncer de mama. Dieta. Análise fatorial. Inquéritos dietéticos. Padrões da dieta.

INTRODUCTION

Breast cancer ranks first among women throughout the world, and its impact is not restricted to industrialized societies (STEWART; KLEIHUES, 2003). In Brazil, breast cancer is the most common cause of death in women aged 40 to 69 years, and approximately 50,000 new cases of breast cancer are diagnosed annually (MINISTÉRIO DA SAÚDE, 2007).

Much of the observed international variation in incidence and mortality rates is due to differences in established reproductive risk factors, but diet might also contribute and provide a potentially modifiable target for prevention. Nevertheless, despite considerable research, the issue of diet and breast and other female hormone-related cancers is still open to discussion. Several studies have examined the role of selected micronutrients, macronutrients, foods, energy and alcohol intakes (CHO et al., 2006; GANDINI et al., 2000; LAJOUS et al., 2005; LAJOUS et al., 2006; WILLETT, 2005). Apart from a consistent direct association between alcohol intake and breast cancer (FERRARONI et al., 1998; SMITH-WARNER et al., 1998) most of the other relations remain controversial.

Although most recent debate on the relationship between diet and breast cancer risk has been concentrated on specific nutrients and/or food, overall dietary patterns may be of greatest importance for primary prevention recommendations. People eat meals consisting of a variety of foods with complex combinations of nutrients, so that broad dietary patterns reflect many simultaneous dietary exposures. Factor analysis is a statistical tool that has been increasingly employed to determine such patterns. It derives dimensions that, when interpreted and understood, describe the data as a much smaller set of items than that yielded by the analysis of individual variables (HAIR et al., 1995).

Dietary patterns in different regions of Brazil have specific characteristics. This study reports the relationship between patterns of food intake and risk of breast cancer among women in Northeast Brazil.

MATERIAL AND METHODS

A hospital-based case-control study was performed in the municipality of João Pessoa, State of Paraíba (Northeast Brazil), from August 2002 to November 2003. There were 89 cases and 94 controls participating in the study, aged 30 to 80 years, who had been sent to the two referral hospitals in the state. Eligible cases included women who were newly diagnosed with primary breast cancer. Cases were interviewed after diagnosis and before the onset of treatment. Patients with recurrent breast cancer, adjuvant therapy (radiotherapy or chemotherapy) prior to the surgery or some past history of cancer were excluded from the study. Briefly, for each case, a control was

selected, matched by age (± 5 years), from the various outpatient clinics in one of the referral hospitals selected. Controls were selected randomly from the cardiology, rheumatology, internal medicine, psychology, gastroenterology, gynecology, ophthalmology and ear, nose and throat outpatient clinics. Patients with a history or suspicion of breast cancer at that time of interview, or who had any disease that was positively or negatively associated with the exposure of interest, were excluded from the study.

The questionnaire was applied in a face-to-face interview. Questions relating to socio-demographic, reproductive and anthropometric data and family history of cancer were asked.

The dietary information was collected using a Quantitative Food Frequency Questionnaire (QFFQ) developed and validated for the present study. Development of this questionnaire has already been published (LIMA; FISBERG; SLATER, 2003). Cases and controls were asked how often they consumed 68 food items per unit of time (day, week, month or year), and also the portion size of each food consumed over the 1-year period preceding the confirmation of the disease (or over the year preceding the interview date, for the controls). All participants signed an informed consent. The study protocol was approved by the ethical committee of the School of Public Health, University of São Paulo.

The 68 items were grouped according to their similarities concerning nutritive value, namely: “cereals, roots and tubers”, “breads and biscuits”, “dairy foods”, “vegetables”, “fruits and juices”, “fats and sauces”, “sugars and sweets”, “red meat”, “sausage and sandwich meat”, “white meat”, “cooked meat”, “fried meat”, “eggs” and “beans”. All the estimates for food groups were calculated by means of Dietsys 4.0 nutritional analysis software (BLOCK et al., 1994). This software contains information on food compositions provided by the United States Department of Agriculture (USDA). For additional Brazilian regional food, tables of food composition were utilized as references. The intake frequencies for some fruits were adjusted for seasonality, multiplying the frequency of intake by a factor (f=0.15). The FFQ was satisfactorily reproducible and valid: Pearson de-attenuated correlation coefficients ranged from 0.36 for vitamin C to 0.67 for carbohydrates; 0.64 for energy and 0.68 for vitamin A (LIMA et al., 2008; PHILIPPI, 2002; PINHEIRO; LACERDA; BENZECRY, 2001).

STATISTICAL ANALYSIS

Factor analysis was used to identify dietary factors or combinations of foods consumed by the studied sample. Factor analysis is a generic name given to multivariate statistical analysis that is applied to the identification of factors in a group of performed measurements. Such factors would correspond to indicators, as a process to provide

data reduction. In this method, all variables are considered simultaneously, each one in relation to the other (HAIR et al., 1995; KIM; MUELLER, 1978).

Principal component analysis was used for the extraction of the factors. This method studies the spatial distribution of the objects so as to identify clusters of variables and the relationships between them. The first factor to be extracted accounts for the maximum possible variance in the data set. The second component, independent from the first, explains as much of the remaining variance as possible, and so on, without any correlation between the components (HAIR et al., 1995; KIM; MUELLER, 1978).

When determining the number of factors to retain, it is a common practice to consider all factors with eigenvalues greater than 1, which indicates that the factor at hand describes more of the variability in the data than does an original variable for the factor individually (HAIR et al., 1995). However, in the present study only factors lying above the inflection point on the curve were selected, since these ones correspond to the factors with greater joint variance. Thus only factors with eigenvalues of more than 1.25 were retained. This limited the number of factors, thus retaining only those with greater interpretability and significance, in accordance to the procedure adopted by Slattery et al., 1998 and Schulze et al., 2001.

Separate models for each factor were fitted, allowing for potential confounding variables. The same confounding variables included in all the models were: age, region of residence, oral contraceptive use, age of menopause, BMI and total energy intake (Figure 1).

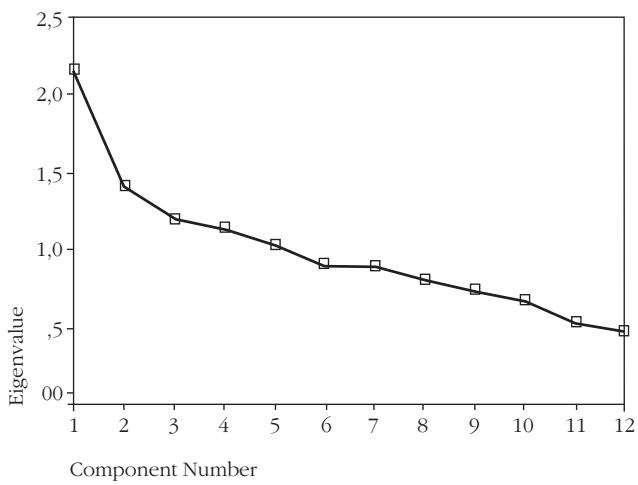

Figure 1 - Scree plot – Dispersion graph for the eigenvalues of retained factors, Paraíba, João Pessoa, 2002-2003

Factor loadings – measures of correlation between derived factors and the original measures – were analyzed after orthogonal rotation using the varimax method (HAIR et al., 1995; KIM; MUELLER, 1978), that is, each factor is independent from the others, maintaining axes at 90°. This operation allows for a simpler structure by distributing the explained variance among the individual components, achieving more interpretable and meaningful factors. Factor loadings higher than 0.25 were considered as significantly contributing to the factor. Within a factor, negative loadings indicate that the food group is inversely associated with the factor, while positive loadings indicate direct association. The higher the factor loading of a food group, the greater the contribution of that group to the factor, since the square of the factor loading corresponds to the percentage variance of the food group that is explained by the factor. Labels were assigned to each factor on the basis of an approximate description of the food items most highly represented. Factor scores for each component retained were calculated for cases and controls (HAIR et al., 1995). Subjects were assigned scores to indicate the degree to which their diet adhered to each factor retained. Factor scores were categorized into tertiles.

STATISTICAL MODELING

To determine the associations between dietary factors and breast cancer, the odds ratio and a 95%-confidence interval were calculated using an age-specific unconditional and energy-adjusted uncondicional logistic regression models. Previously known risk factors and potential confounders were included in statistical modeling. Statistical analyses were performed using the SPSS for Windows program (version 10.0.1, 1999, SPSS Inc., Chicago, IL).

RESULTS

Table 1 shows the distribution of cases and controls according to non-dietary variables. The mean age was 56±11.86 years, and the subjects had a mean of 6.6 ± 4.8 years of schooling. For both cases and controls, the age of menarche was predominantly between 12 and 15 years. Both groups also had similar numbers of children. Most of the women were less than 25 years old when their first child was born (71.9% of the cases and 66.0% of the controls) and had not used oral contraceptives. The age of menopause was statistically different between groups ($p < 0.01$), with a greater number of cases (43.8% versus 31.9% of the controls) reaching menopause age before 50 years. Cases and controls did not differ regarding previous history of cancer among the first-degree relatives ($p=0.572$). A sedentary lifestyle was predominant and the Body Mass Index (BMI) was 24.86 kg/m^2. Around 52% of the cases and 48% of controls presented a normal nutritional status at the time of the interview.

Table 1 - General characteristics of the study population, Paraíba, João Pessoa, 2002-2003

Variables	Cases (n=89)		Controls (n=94)		p
	n	%	n	%	
Age of menarche *					
Under 12 years	21	23.6	15	16.0	
12-15 years	55	61.8	68	72.3	0.486
15 years or over	9	10.1	8	8.5	
Parity					
Nulliparous	14	15.7	14	14.9	0.917
1-3 children	37	41.6	37	39.4	
4 children or over	43	42.7	43	45.7	
Age at first birth					
No children	14	15.7	14	16.0	0.544
< 25 years	64	71.9	62	66.0	
> 25 years	11	12.4	18	18.0	
Oral contraceptives					
Yes	31	34.8	22	23.4	0.123
No	58	65.2	72	76.6	
Age of menopause **					
Under 50 years	39	43.8	30	31.9	**0.006**
50 years or over	16	18.0	35	37.2	
Family history of cancer					
Yes	47	52.8	54	58.1	0.572
No	42	47.2	39	41.9	
Physical activity					
Yes	32	36.0	30	31.9	0.544
No	57	64.0	64	68.1	
Body mass index(kg/m²)**					
Normal nutritional status	33	51.6	32	47.8	0.083
Overweight	17	26.6	28	41.8	
Obese	14	21.9	7	10.4	

* information not available for 4 cases and 3 controls;
** 34 cases and 43 controls were premenopausal;
*** information not available for 23 cases and 27 controls.

Two factors were retained (Table 2) after principal component analysis. These chosen factors accounted for 30% of total variance, or, in other words, these factors together explained 30% of the variation in the original measurements. The factor loadings obtained for each dietary variable in each factor are presented in table 2. Values of more than 0.25 or less than -0.25 have been shaded in grey, and are considered as having significantly contributed to the factor.

Table 2 - Matrix of factor loadings for cases and controls participating in the study. Paraíba, João Pessoa, 2002-2003

Variables	1	2
Vegetables	**0,77**	- 0,13
Fruits and juices	**0,66**	0,13
Fats and sauces	**0,60**	**0,69**
Dairy foods	**0,51**	**0,49**
White meat	**0,37**	0,17
Red meat	**0,35**	**-0,28**
Eggs	0,08	-0,10
Breads and biscuits	0,05	0,00
Sugars and sweets	**0,23**	**0,61**
Beans	**-0,31**	**0,54**
Sausage and sandwich meat	-0,06	**0,49**
Cereals, roots and tubers	0,12	**0,46**
% explained variance	18,1	11,9
% cumulative variance	18,1	29,9

The first factor was characterized by the intake of meat, both red and poultry, fat-dense foods, but also by vegetables and fruits. The second factor was represented by rice, beans, sweets, milk and a negative correlation with red meat.

Table 3 gives the ORs and corresponding CIs for and breast cancers by tertiles of factor scores for both dietary patterns.

Table 3 - *Odds ratios* and 95% confidence intervals for breast cancer, obtained using multiple non-conditional logistic regression, in approximate tertiles for food groups defined *a posteriori* by factor analysis. Paraíba, João Pessoa, 2002-2003

Factors	Tertiles of scores	OR (95% CI)[1]
1	1st	1.00
	2nd	0,51 (0,17 – 1,56)
	3rd	7,28 (2,06 -25,66)
2	1st	1.00
	2nd	0,41 (0,15-1,19)
	3rd	0,20 (0,06-0,61)

[1]Adjusted for age, region of residence, oral contraceptive use, age of menopause, BMI and total energy intake.

The high consumption of the first factor was associated with increased risk of breast cancer (OR=7.3; 95% CI: 2.1-25.7). On the other hand, consumption of the second pattern in the highest tertile was shown to be protective concerning breast cancer (OR=0.2; 95% CI: 0.07-0.61).

DISCUSSION

In the present study, the dietary patterns of participating subjects were identified using principal component analysis, and these patterns were used for estimating the risk of breast cancer. Two major dietary patterns that explained about 30% of the total variance in food intake were identified.

Despite the convincing evidence supporting a reduction in the risk of developing breast cancer in association with the consumption of fruit and green vegetables, such an effect was not observed in the present study for a higher consumption of the first pattern, which is characterized by the presence of not only such food groups, but also meat (red and white), dairy products and sweets. Fruits and vegetables are expensive items, and their consumption is strongly associated with income. People that have access to fruits and vegetables usually can buy processed food, which is rich in fat, salt and sugar. The second pattern extracted was inversely associated with breast cancer, in an independent manner. This pattern featured the consumption of traditional Brazilian food, mainly beans and rice, but also included processed meats, which have high sodium and saturated fat contents, and sweets, which contain high levels of carbohydrates. Pulses, also known as legumes, have aroused special interest as potentially protective against cancer, and the World Research Cancer Fund (1997) recommends that studies be carried out to elucidate this potential effect. The mean intake of dairy foods and fat and sauces were similar in both cases and control groups (data not shown), and as they had high loadings in both factors extracted, which is possible in a factor solution, they are not considered to contribute to the interpretation of the factors extracted.

Other *a posteriori* studies have been published on breast cancer, all of them using food groups to identify dietary patterns (ADEBAMOWO et al., 2005; FUNG et al., 2005; MANNISTO et al., 2005; NKONDJOCK; GHADIRIAN, 2005; RONCO et al., 2006; SIERI et al., 2004; TERRY et al., 2001; VELIE et al., 2005).

A previous analysis of these data, focused on food items, has shown that "cereals, roots and tubers" and "breads and biscuits" were the primary food groups consumed by the subjects, followed by fruits and juices, vegetables and coffee and soft drinks among cases; and fruits, meats and vegetables among controls, and a strong association of beans with reduced risk of breast cancer was observed (LIMA et al., 2008). In a survey on family budgets presented recently in Brazil, it could be seen that, although the overall consumption of beans and other leguminous vegetables had decreased, the State of Paraíba is the biggest consumer of this group in the country, with a relative share in total energy of 11.96% for this group (INSTITUTO BRASILEIRO DE GEOGRAFIA E ESTATÍSTICA, 2004). Beans are a staple food, or in other words, they form part of the very heterogeneous dietary habits of

the Brazilian people, as demonstrated in a multicenter study carried out by Galeazzi, Domene and Sichieri (1997). In the study by Marchioni et al. (2007), performed in the southeastern region of this country, it was observed that the traditional dietary pattern, consisting of rice, beans and meat, was associated with reduced oral cancer. A population-based Household Budget survey conducted recently in Brazil (POF 2002-2003) demonstrated a pattern where people purchased both food rich in fat and sugar and healthy food, and this pattern was positively associated with years of schooling and income (MARCHIONI et al., 2007).

This study presents all the pros and cons of a hospital-based case-control investigation. Selection bias should be limited, on account of the high participation rate and of the comparable catchment areas of cases and controls. The comparability of the recall between cases and controls was improved by interviewing all the subjects in a hospital setting (D'AVANZO et al., 1997).

Factor analysis has emerged as a method able to estimate cancer risk more comprehensively than other methods based on single foods or nutrients. Intake of different foods or nutrients may interact to increase or decrease cancer risks, and this interaction may make it difficult to differentiate associations between individual foods and cancers. However, there are many subjective decisions that must be taken: the choice of the solution method, of the number of common factors to be extracted and of the type of rotation.

CONCLUSIONS

There are well known non-genetic risk factors for breast cancer, such as advanced age, long-term exposure to estrogen due to early menarche and/or late menopause, and no child-bearing history. These factors are difficult to control. Nevertheless, certain lifestyle-related risk factors are potentially modifiable. They include dietary habits, physical activity, smoking and alcohol intake. This is the first study to date in Brazil that has examined the exposure to dietary patterns that may be related to risk of breast cancer occurrence. The present investigation used data from a hospital-based case-control study in one of the poorest regions of Brazil, the Northeast. It emerged that two dietary patterns were associated with the risk of breast cancer, one directly and the other one inversely. The findings of this study have shown that food patterns considered healthy are combined with unhealthy, and they are consumed together. This finding reinforces the need for looking at diet through a global approach.

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