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ASSOCIATION BETWEEN ALCOHOL CONSUMPTION AND BREAST CANCER DEVELOPMENT: A CASE-CONTROL STUDY

Associação entre ingesta alcoólica e desenvolvimento de câncer de mama: um estudo de caso-controle

Laís Franciele Santana Portela[1]*, César Augusto Costa Machado[2], Renata Costa Cangussú[3], Luciana Castro Garcia Landeiro[3], Susanne de Andrade Blanc Bertrand[4], Rebecca Meireles de Oliveira Pinto[5]

ABSTRACT

Objectives: To identify the association of alcohol consumption with the development of breast cancer in a patient population of Salvador, Bahia. **Methods**: Case-control study, conducted between December 2013 and May 2015, with 69 patients with breast ductal carcinoma and 71 controls. Sample calculation was made with 140 patients, with 5% presumed difference between groups and 10% acceptable difference. The x^2 test was used to evaluate the correlation between categorical variables, and Student's *t*-test was applied to compare continuous variables. **Results**: From all cases, medium alcohol intake was 3.66±8.60 g/day; among controls, the average was 3.71±7.40 g/day (p=0.890). When analyzing the association between alcohol intake and breast cancer, odds ratio was 0.99 (95% confidence interval 0.524–1.890), p=0.988. For alcohol consumption greater than 10 g/day and breast cancer, odds ratio was 1.579 (95%CI 0.624–3.995), p=0.332. **Conclusions**: Although published data suggest an association between alcohol consumption and breast cancer, in this study there was no statistical significance between the variables assessed and the onset of this pathology.

KEYWORDS: Breast neoplasms; risk factor; primary prevention; risk groups.

RESUMO

Objetivo: Identificar a associação do consumo alcoólico com o desenvolvimento de câncer de mama em uma população de pacientes de Salvador, Bahia. **Métodos**: Estudo de caso-controle realizado entre dezembro de 2013 e maio de 2015 com 69 pacientes com diagnóstico de carcinoma ductal da mama e 71 controles. Foi realizado cálculo amostral com 140 pacientes, esperando-se uma diferença presumida de 5% entre os grupos e com diferença aceitável de 10%. Realizou-se teste do x^2 para avaliação de correlação entre as variáveis categóricas e teste *t* de Student entre as variáveis contínuas. **Resultados**: Entre os casos, a ingesta alcoólica média foi de 3,66±8,60 g/dia; já entre os controles a média foi de 3,71±7,40 g/dia (p=0,890). Ao analisar-se a associação entre ingesta alcoólica e câncer de mama, obtivemos *odds ratio* de 0,99 (intervalo de confiança de 95% – IC95% 0,524–1,890), p=0,988. Em relação ao consumo de álcool maior do que 10 g/dia e câncer de mama, a *odds ratio* foi de 1,579 (IC95% 0,624–3,995), p=0,332. **Conclusão**: Apesar de dados publicados e hipóteses sugerirem associação entre ingesta alcoólica e câncer de mama, neste estudo não houve significância estatística entre as variáveis analisadas e a presença da patologia.

PALAVRAS-CHAVE: Neoplasias da mama; fator de risco; prevenção primária; grupos de risco.

Study carried out at Núcleo da Mama (NM) e no Núcleo de Oncologia da Bahia (NOB) – Salvador (BA), Brazil.
[1]Escola Bahiana de Medicina e Saúde Pública (EBMSP) – Salvador (BA), Brazil.
[2]Núcleo da Mama (NM), Hospital Português da Bahia – Salvador (BA), Brazil.
[3]Núcleo de Oncologia da Bahia (NOB) – Salvador (BA), Brazil.
[4]EBMSP – Salvador (BA), Brazil.
[5]EBMSP – Salvador (BA), Brazil.
***Corresponding author:** laisfranciele2@gmail.com
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INTRODUCTION

Breast cancer is the most common malignancy among women worldwide, with about 1 million new cases each year[1,2]. Its incidence has increased over time in association with industrialization and urbanization[3]. Although breast cancer is considered a carcinoma with relatively good prognosis if diagnosed and treated early, mortality rates remain high in Brazil, possibly because in some cases diagnosis is only made in advanced stages. Its etiology is not yet fully understood; however, some features have been proven to be related to its onset, including genetic, environmental, hormonal, and biopsychosocial factors[1,2,4].

Some studies suggest a mild association and dose/response relationship between alcoholic intake and breast cancer, pointing out the consumption of 10 g/day as a factor predisposing to its development[5,6]. These papers show that there is not a single mechanism that explains such association.

The evidence points that alcohol increases estrogen levels, a well-known risk factor for breast cancer. This hypothesis is supported by data showing the association between alcohol and breast cancer limited to women whose tumors present positive estrogen receptor (ER +)[7].

Other studies indicate that alcohol can increase the risk of breast cancer by other means, depending or not on hormones, such as the cocarcinogenic action resulting from the increased capillary permeability in cell membrane to carcinogens, inhibiting detoxification by the liver, impairing nutrient metabolism, and inducing oxidative stress[1,8].

Derivatives of alcohol metabolism such as acetaldehyde are responsible for changes in DNA that are also related to the disease development[9].

As alcohol consumption increases worldwide[5], especially in regions where female emancipation has been noticeably occurring, a better understanding of mechanisms linking this behavior to breast cancer is desirable. The present study aimed to assess alcohol consumption as a risk factor for the onset of breast cancer in patients from a mastology and an oncology clinics in Salvador, Bahia.

METHODS

Case-control study conducted from December 2013 through May 2015. Data were collected from medical records, complementary interviews, and questionnaire application at two clinics in Salvador, Bahia, which assist patients enrolled in private health insurance plans: Oncology Center of Bahia (*Núcleo de Oncologia da Bahia*), an oncology clinics, and Breast Center (*Núcleo da Mama*), a mastology clinics.

Adult women with histopathological diagnosis of breast cancer in its main variant, invasive ductal carcinoma, either by core biopsy or surgical specimen, were included in case group as systemic treatment "debuts". The control group allocated women without breast cancer in follow-up at the mastology clinics after the disease was ruled out by mammography and/or ultrasonography. Patients from both groups were paired by age, with difference of no more than five years.

Patients who had been through any oncological treatment before or started a treatment at some point before data collection were excluded from the case group. In control group, patients with BIRADS category scale 3, 4 and 5 who needed a biopsy resulting in any type of change that could increase breast cancer risk were excluded: moderate or florid ductal hyperplasia, intraductal papilloma, sclerosing adenosis, complex fibroadenoma radicular scar, complex sclerosing lesion, lobular neoplasia/atypical lobular hyperplasia, atypical columnar cell changes, atypical ductal hyperplasia, flat epithelial atypia, cystic lobular hyperplasia, clinging carcinoma, blind ductal adenosis, microcystic adenosis, and microglandular adenosis. Patients who refused to sign the Informed Consent Form were also excluded from the study.

For this study, beer was considered to have 5% alcohol in its composition; vodka, 40%; wine, 12%; and whiskey, 40%[10]. The calculation used for the amount of alcohol ingested by patients was the volume ingested multiplied by alcohol concentration in each beverage: for example, 350 mL of beer × 5% alcohol = 17.5 g of alcohol ingested.

Statistical analysis was made in the program Statistical Package for the Social Sciences (SPSS) v. 20.0. Numerical variables were expressed as mean and standard deviation. Percentage was calculated for descriptive variables. Continuous variables were compared by Student's t-test. The χ^2 test was used to assess correlation between categorical variables, including the relationship between alcohol intake and breast cancer development, and between 10 g/day alcohol consumption and breast cancer development. In order for results to be considered statistically significant, two-tailed values should have $p<0.05$.

The study was approved by the Research Ethics Committee (CEP) of Bahia Foundation for the Development of Sciences, opinion 140,996 and report in October 31, 2012.

RESULTS

A total of 140 patients were recruited, 69 having a proven diagnosis of ductal breast carcinoma and 71 being controls.

Overall characteristics of cases and controls did not show statistically significant differences (Table 1). Mean age of cases was 56.67±12.91 compared to 53.41±10.30 of controls. Regarding ethnicity, almost half of patients with breast cancer declared themselves as brown-skinned (47.8%), while 11.6% as black-skinned, and 40.6% as white-skinned. Among patients in control group, 46.5% declared themselves as brown-skinned;

18.3%, black-skinned; and 25.0% white-skinned. The mean age at menarche was 12.79±1.93 in case group and 13.07±1.78 in control group.

As to family history, 11.6% of patients in case group reported a first-degree relative (mother, sister or daughter) with breast cancer, compared to 16.9% in control group.

After subanalysis, only 29.0% of patients in case group were found to consume alcoholic beverages, while alcohol intake was positive in only 33.8% of patients in control group. Regarding type of alcoholic beverage ingested, case group had the following values: 65% beer; 20% wine; 10% whiskey; and 5% vodka. For control group, we had: 87.5% beer; 8.3% wine; and only 4.2% vodka.

When frequency of alcohol consumption was assessed, the case group had 35% of patients reporting drinking only once a week; 60% twice a week; and 5% three times or more per week. In control group, 50% reported drinking once a week and 50%, twice a week. In this group, no reference to alcohol consumption three times or more per week was made. The patterns of alcohol consumption of the sample are shown in Table 2.

Mean alcohol consumption, object of this study, was 3.66±8.60 g/day in the case group and 3.71±7.40 g/day in the control group, which configures a non-statistically significant difference (Table 3).

Table 4 shows the estimated risk of breast cancer when alcohol intake is the exposure variable. When analyzing, therefore, the association between alcohol consumption and breast cancer, odds ratio (OR) was 0.995 (95% confidence interval 0.524-1.890), p=0.988. Also, no statistical significance.

As some studies suggest a mild association between alcohol consumption greater than 10 g/day and breast cancer onset[5,6], the estimated risk for this neoplasia with 10 g/day of alcohol intake as exposure variable was calculated. OR was 1,579 (95%CI 0.624-3.995) and p=0.332, as shown in Table 5.

Table 1. Clinical profile of patients.

	Patients with breast cancer (n=69)	Controls (n=71)	P value
Age (year), mean ± standard deviation	56.67±12.91	53.41±10.30	0.101
Self-reported skin color			
White, n (%)	28 (40.6)	25 (35.2)	0.510
Brown, n (%)	33 (47.8)	33 (46.5)	
Black, n(%)	8 (11.6)	13 (18.3)	
Age at menarche (year)	12.80	13.07	0.386
Breast cancer family history			
Yes	8 (11.6)	12 (16.9)	0.365
No	61 (88.4)	59 (83.1)	

DISCUSSION

According to the World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR)[1], alcoholic beverages intake is a risk factor for the development of breast cancer in both premenopausal and postmenopausal periods.

This study did not find association between alcohol consumption and breast cancer. Our findings are believed to be the consequence of several limiting factors such as: memory bias, since patients tend to remember the most recent intake; small number of cases and controls reporting intake greater than 10 g/day; and patients mentioning champagne, prosecco and other types of alcoholic beverages.

Table 2. Patterns of alcohol consumption in the sample.

Characteristics (variables)	Cases n (%)	Controls n (%)
Alcohol intake		
Yes	20 (29)	24 (33.8)
No	49 (71)	47 (66.2)
Frequency of alcohol intake		
Once a week	7 (35)	12 (50)
Twice a week	12 (60)	12 (50)
Three times or more per week	1 (5)	0
Type of beverage		
Beer	13 (65)	21 (87.5)
Wine	4 (20)	2 (8.3)
Whiskey	2 (10)	0
Vodka	1 (5)	1 (4.2)

Table 3. Alcohol intake (in grams) per day.

Cases mean ± standard deviation g/day	Controls mean ± standard deviation g/day	P value
3.66±8.60	3.71±7.40	0.890

Table 4. *Odds ratio* for breast cancer with alcohol intake as exposure variable.

Variable	*Odds ratio*	95CI%	P Value
Alcohol intake	0.995	0.524–1.890	0.988

95%CI: 95% confidence interval.

Table 5. *Odds ratio* for breast cancer with alcohol intake >10 g/day as exposure variable.

Variable	*Odds ratio*	95CI%	P Value
Alcohol intake >10 g/day	1.579	0.624–3.995	0.332

95%CI: 95% confidence interval.

Although the present study did not show statistical significance, some studies[8,9,11-13] confirm the risk effect represented by alcoholic beverages. Setiawan et al.[11], in a cohort study involving 84,427 women, evaluated the association between alcohol consumption and breast cancer according to their hormonal receptors' status. Relative risk (RR) of 1.71 (95%CI 1.19-2.46) was found comparing alcohol intake (equal to or greater than two doses/day) and no intake of alcohol among patients with ER/PR (estrogen receptor/progesterone receptor) breast cancer. For ER/PR + type of cancer, RR was 1.40 (95%CI 1.14-1.72). These RR values were not statistically different (p=0.07), indicating that positive or negative hormone receptors did not pose change to the risk.

In a case-control study conducted in Italy, Deandrea et al.[8] stated that alcohol consumption greater than 13.8 g/day increased the risk of breast cancer compared to women who never drank alcohol, with OR 1.96 and 95%CI 1.57-2.47. However, when the analysis was performed according to the hormone receptors' status, risk effect was only found for breast tumors with positive estrogen receptors. According to these authors, the risk of breast cancer onset in the presence of alcohol consumption is more related to positive estrogen receptors. In-vitro studies have identified ethanol activity in human breast cells with positive but not negative estrogen receptors[8,12].

In a cohort conducted with 38,454 women in the United States, Zhang et al.[12] assessed the risk effect of alcohol consumption in in-situ and invasive breast cancers. When analyzing according to hormonal receptors' status and considering 10g/day alcohol intake, an increased risk for breast cancer was pointed only for ER/PR+ tumors. In addition, the consumption of 10 g/day caused a 7% increase in the risk of in-situ breast cancer (RR=1.07; 95%CI 1.01-1.14) and 9% of invasive breast cancer (RR=1.09, 95%CI 1.02-1.16). Important to point out that the increased risk was analyzed for beer, since this was the type of alcoholic beverage consumed in the sample in question.

In a cohort study with 88,530 postmenopausal women in the United States, Duffy et al.[9] identified that even low alcohol intake (5.6 g/day) may be considered a risk factor for breast cancer, with RR=1.05; 95%CI 1.01-1.09.

Berstad et al.[13] conducted a case-control study in the United States to analyze alcohol consumption according to type of beverage and time of ingestion. Significant association was found only for intake greater than or equal to two doses/day in the previous five years (OR=1.82, 95%CI 1.01-3.28). This study found no relation to consumption in other periods of life: adulthood or youth. As to the outcome of this case-control, we can consider the memory bias, since people tend to remember recent events of alcohol intake; or that the effect of alcohol on the risk for breast cancer is not accumulative over time. No significant differences were found between as to different types of beverages mentioned by women, thus indicating that ethanol relates to increased risk for such neoplasia regardless of different types ingested[12,13].

Differently from the results presented, a case-control study conducted in France by Bessaoud et al.[14] identified daily alcohol consumption of 10-15 g/day as a protection factor against breast cancer, compared to women who do not use alcohol (OR=0.21, 95%CI 0.10-0.91). The protective effect was identified for both moderate wine intake (<1 dose /day) (OR = 0.51, 95%CI 0.30-0.94) and other beverages (OR=0.63, 95%CI, 0.42-0.94). Especially relating to the protective effect of wine, the harmful effect of alcohol is suggested to be partly diminished because of antioxidant agents from the grape present in the beverage, considering moderate consumption[14].

However, although some studies suggest that alcohol acts as a risk factor and one suggests it is a protective factor, Terry et al.[15] and Brown et al.[16], after conducting case-control studies, did not identify significant associations between this variable and breast cancer onset, similarly to the results of our study.

The lack of association was partially explained by the homogeneous pattern of consumption as to type of beverage and the low alcohol intake among women in the sample. In addition to contradictory findings when studies are compared, data are not consistent with regard to the association between this neoplasm and alcohol consumption according to hormonal receptors' status, type of cancer, amount of alcohol ingested, and the period of exposure to alcohol[12,14].

Some studies have also identified the influence of skin color on breast cancer onset[17,18]. The incidence may be higher among Caucasians and African Americans, intermediate among Hispanics and Amerindians, and low among Asians[17,19]. The miscegenation in Brazil, especially in Bahia, is highly likely to influence the development of breast cancer, which justifies the need for further specific studies on this population[17,20]. Studies assessing variables and risk factors for this heterogeneous population have not yet been published, neither are there models — like Gail's[21] — that calculate the risk of breast cancer among Brazilian women.

Among the limitations of this study, its case-control design may be mentioned, as it is not ideal, although it has been adopted in view of its feasibility; the low number of patients who consumed alcohol three times or more per week (only one in case group and none in control group). Despite all that, when analyzing women who would consume alcohol above the mark of 10 g/day, the percentages in case and control groups were 18.3% and 9.8%, respectively. Would these values be statistically significant had the number of participants been larger? This and other questions posed by the present study require a response for more accurate information and orientation about breast cancer prevention for Brazilian women.

CONCLUSION

Although there is scientific evidence to prove the association between alcohol consumption and breast cancer, the present study did not found this relationship.

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