RESEARCH ARTICLE

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Alcohol Consumption as a Risk Factor for Breast Cancer Development: A Case-Control Study in Brazil

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Abstract

Background: Alcohol consumption is a well-established risk factor for breast cancer, but the evidence is mostly from developed countries. Brazil is going through a rapid demographic expansion, and studies of this relationship are also needed in such unexplored settings. **Methods:** We assessed the relationship between alcohol consumption and breast cancer risk among 1,506 Brazilian women (406 cases and 1,100 controls). Regression models were used to calculate odds ratios (OR) and 95% confidence intervals (CI). All statistical tests were two-tailed. **Results:** The mean age of the 1,506 women was 42.0 (standard deviation, ±15.0) years. There was a significant association between breast cancer and age, body mass index, age at menarche, menstrual flow and menstrual cycle. Multivariate analysis showed an increased risk of invasive breast cancer in regular alcohol consumers (<50 years old: OR 4.7; 95% CI 1.4–16.2; ≥50 years old: OR 3.9; 95% CI 1.2–13.4) compared with abstainers or occasional drinkers. Women with a regular alcohol intake for 10 years or more who were less than 50 years old had a threefold higher risk of developing breast cancer (OR 3.0; 95% CI 1.2–7.6). **Conclusion:** Regular alcohol consumption increases the risk of breast cancer mainly among women less than 50 years old.

Keywords: Breast cancer- alcohol consumption- risk- Brazilian women

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Introduction

Alcohol consumption is a well-established risk factor for breast cancer. This association has been confirmed by many epidemiologic studies and is accepted by the International Agency for Research on Cancer (IARC - World Health Organization) (Baan et al., 2007; IARC, 2010; Stewart and Wild, 2015). There is a dose-dependent increase in the risk of breast cancer with alcohol consumption (Bagnardi et al., 2001). However, the precise role of alcohol in breast cancer development remains unclear. Seitz et al., (2012) showed that alcohol may increase the levels of estrogen, and that estrogen may exert its carcinogenic effect on breast tissue directly or via the estrogen receptor. Other mechanisms for ethanol-induced breast cancer cited by these authors are acetaldehyde exposure, oxidative stress, epigenetic changes and decreased retinoic acid concentration.

Even if numerous epidemiological surveys have explored the relationship between alcohol drinking and the risk of breast cancer, this information is typically derived from investigations performed in developed countries. As exposure to risk factors for breast cancer can differ between countries, further studies are needed in unexplored settings. While Brazil is a country that is going through a rapid demographic expansion involving different ethnic and multi-racial groups that include a larger population of African descent than from either the US or Europe, such associations may yield different conclusions from those reported in the literature (Telles, 1995; Joseph, 2015). As part of the BRICS (Brazil, Russia, India, China and South Africa), an association of five major emerging national economies, the rapid economic growth and demographics of Brazil are expected to give rise to a large middle-class population whose consumption of alcohol may affect the pattern of chronic diseases, such as breast cancer (Ozturk, 2015).

The World Health Organization's Global Status Report on Alcohol showed that Brazil's consumption of pure alcohol is between 7.5 and 9.99L per capita, per annum, which is considered medium to high (WHO, 2011). In the First Brazilian National Alcohol and Drugs Survey, in 2001, 1,7% of females aged 12 to 65 years old reported regular alcohol consumption (having consumed at least three or four days per week) (Laranjeira, 2013). However, recently, the percentage of women who had at least one alcoholic drink in the past year reached 38% (INCA, 2016). The reasons for the large amounts of alcohol consumed

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are the economy growing and the increase in thefamily salary (Laranjeira, 2013).

According to the Brazilian National Cancer Institute (INCA), the incidence rate of breast cancer for the year 2016 adjusted for the world population is estimated to be 56.2 per 100,000 with a mortality rate of 12.7 per 100,000 (Lenz et al., 2002). Taking these factors into account, we initiated this study to investigate the association between alcohol consumption and breast malignancy in a developing country.

Material and Methods

This case-control study was performed at the Fernandes Figueira Institute / Oswaldo Cruz Foundation (IFF/FIOCRUZ) in Rio de Janeiro. Data collection was performed on 1,506 woman (406 cases and 1,100 controls) using face-to-face interviews by trained staff using a questionnaire about their medical history and lifestyle, including potential risk factors for breast cancer. The study sample size was determined by the following parameters: statistical significance level was set at 5% (one-tailed), the power of the study at 80% with an expected odds ratio of 2.3 (Carlini et al., 2001), and assuming a frequency of alcohol abuse of 2.2% in the female population (Laranjeira, 2013). The minimum sample size required to achieve the planned power was 354 cases and 1,062 controls. The Ethics and Research Commission of IFF/FIOCRUZ approved this study according to the standardized institutional review board procedures and protocols.

The case group (n= 406) was selected from female patients who were diagnosed with breast cancer that was confirmed via histopathological analysis, between 20 and 70 years old, and residents of the metropolitan area of Rio de Janeiro. The control group (n= 1,100) was selected from patients in whom the clinical and histological investigations had dismissed the presence of breast cancer and were between 20 and 70 years old in the same period of time in which the cases were recruited. All consecutive women suspected to have breast cancer admitted to the IFF/FIOCRUZ Mastology Service were selected for the study. Women with breast cancer history and with physical or emotional health condition that made the face-to-face interview difficult were excluded. All cases and controls were interviewed between 2000 and 2008.

The following variables were considered: age group (<50, ≥50 years old); ethnic group (classified according to the Brazilian Geography and Statistics Institute (IBGE) into white, black, Asian Brazilians, mulatto and indigenous, with the latter categorized into white and non-white); body mass index (BMI; <25 (under weight and acceptable weight), ≥25 (over weight and obese)); age at menarche (≤14, >14 years); duration of menstrual flow (2–7 days (normal), <2 or >7 days (abnormal)); menstrual cycle interval (21–35 days (normal), <21 or >35 days (abnormal)); parity (nulliparous, ≥1 parous); age at first pregnancy (<30, ≥30 years); breastfeeding (<12, ≥12 months); age at menopause (<45, ≥45 years); level of alcohol consumption (abstainers, occasional consumers, regular drinkers – 3 to 4 times a week); and duration of alcohol consumption (<10, ≥10 years).

The collected data were analyzedusing SPSS software version 21 (SPSS Inc., Chicago, USA). Descriptive analyses were performed by comparing the distribution of the variables between cases and controls. Univariate and multivariate analyses using logistic regression to identify risk factors for breast cancer were used to estimate the crude and adjusted odds ratios (ORs) and the corresponding 95% confidence intervals (CI). Each fitted regression equation was adjusted by the following variables: age, age at menarche, ethnic group, menstrual flow, and BMI (variables associated with the risk of developing breast cancer in the univariate analysis). A p-value <0.05 was considered statistically significant in all analyses.

Results

The distribution of cases and controls according to their socio-demographic characteristics is compared in Table 1. The mean age of cases was 50.7 years (±14.5) and of controls 38.8 (±13.9). Considering general risk factors, there was a significant association of breast cancer with age, BMI, age at menarche, menstrual flow and menstrual cycle. Additionally, cases were more likely to be current alcohol consumers than controls.

Table 2 shows the results of the multivariate analyses, which show an increased risk of invasive breast cancer in alcohol consumers (<50 years old: OR 4.7; 95% CI 1.4–16.2; ≥50 years old: OR 3.9; 95% CI 1.2–13.4), compared with abstainers or occasional drinkers. Women with alcohol intake for 10 years or more of<50 years of age had a threefold higher risk of developing breast cancer (OR 3.0; 95% CI 1.2–7.6). In those women ≥50 years old, there was no statistically significant association (OR 0.8; 95% CI 0.2–3.3).

Discussion

In this single-institution study with a large number of cases and controls, we documented the association between alcohol intake and the risk of breast cancer. This association occurred regardless of age group (<50, ≥50 years old). However, the analysis of the duration of alcohol consumption (<10 vs. ≥10 years) showed that this association remained statistically significant only for women women less than 50 years old. We are not familiar with any published study that has analyzed the association between alcohol intake and breast cancer risk in other populations living in South America.

The frequency of alcohol consumption among the controls was very low (0.9%) if we compare it with the First Brazilian National Alcohol and Drugs Survey (Laranjeira, 2013) that shows a frequency of 2.2% in the same period. Also, another study with a similar population in the city of Rio de Janeiro showed an alcohol consumption of 1.7% (de Almeida and da SF Coutinho, 1993). These figures for the control group may suggest misclassification bias once a person may underestimate the question - giving inaccurate answers, by not assuming the need for giving correct answer to the

Table 1. Characteristics of Cases and Controls (Univariate Analysis)

	Case Group No. (%)*	Control Group No. (%)*	P - Value**
Age (years)			< 0.001
< 50	218 (53.7)	907 (82.5)	
≥ 50	188 (46,3)	193 (17.5)	
Ethnic Group			0.066
White	186 (45.8)	519 (47.2)	
Others	214 (52.7)	480 (43.6)	
Body Mass Index			< 0.001
< 25	48 (11.8)	415 (37.7)	
≥ 25	142 (35)	379 (34.5)	
Age at menarche (years)			< 0.001
≤ 14	256 (63.1)	630 (57.3)	
> 14	40 (9.9)	184 (17.7)	
DurationMenstrual flow (days)			< 0.001
2 - 7	226 (55.7)	783 (71.2)	
< 2 or > 7	56 (13.8)	68 (6.2)	
Menstrual cycle interval (days)			< 0.001
21 - 35	234 (57.6)	855 (77.7)	
< 21 or >35	74 (18.2)	73 (6.6)	
Parity			0.714
Nulliparous	54 (13.3)	251 (22.8)	
≥ 1	346 (85.2)	845 (76.8)	
Abortion			0.898
No	230 (56.7)	668 (60.7)	
Yes	176 (43.3)	430 (39.1)	
Age at first pregnancy (years)			0.953
< 30	230 (56.7)	653 (59.4)	
≥ 30	38 (9.4)	76 (6.9)	
Breastfeeding (months)			0.145
< 12	144 (35.5)	275 (25)	
≥ 12	142 (35)	377 (34.3)	
Age at Menopause (years)			0.312
< 45	48 (11.8)	79 (7.2)	
≥ 45	124 (30.5)	132 (12)	
Alcohol consumption			< 0.001
Absteiners / occasional	384 (94.6)	1075 (97.7)	
Regular drinkers	22 (5.4)	10 (0.9)	
Duration of alcohol consumption (years)		0.009	
< 10	252 (62.1)	531 (48.3)	
≥ 10	20 (4.9)	15 (1.4)	
Total	406	1100	

*, Differences are due to missing data; **, In bold statistically significant p-values

question (Moradzadeh et al, 2015) - or a non-response bias - since the non-anonymity of the interview could have reduced the likelihood of truthful responses due to socially desirable responding (de Almeida and da SF tinho, 1993; Laranjeira, 2013; Garcia and Freitas, 2015).

A few studies have reported that alcohol consumption has no relationship with breast cancer, particularly in premenopausal women, in contrast to our results (Nagata, 2007; Bessaoud, 2008; Kabat, 2010), supporting the value of conducting this study in our country.

In this study, the risk of developing breast cancer was 3.9 greater among regular drinkers. Other authors have shown lower risks, varying from 1.08 to 1.32 (Zhang et al., 2007; Allen, 2009; Li et al., 2010). A study in Brazil involving 203,506 cancer patients analyzed the association between alcohol consumption and the risk of different kinds of cancer. Of those, 39,472 were patients with breast cancer, and there was a 60%

Table 2. Relative Risks and 95% Confidence Intervals for Breast Cancer According to Alcohol Consumption

Age group	Unadjusted OR	95%CI	p-value	Adjusted OR*	95%CI	p-value
Daily alcohol consumption						
No consumption	1			1		
Consumption all ages	6.2	(2.9-13.1)	<0.001	3.9	(1.7-9.3)	0.002
Consumption < 50 years	5.6	(1.9-16.4)	0.002	4.7	(1.4-16.2)	0.013
Consumption ≥ 50 years	3.8	(1.2-11.7)	0.021	3.9	(1.2-13.4)	0.028
Alcohol consumption ≥ 10 years						
No consumption	1			1		
Consumption all ages	2.8	(1.4-5.6)	0.003	2.1	(0.9-4.5)	0.071
Consumption < 50 years	4.3	(1.9-9.7)	<0.001	3.0	(1.2-7.6)	0.022
Consumption ≥ 50 years	1.2	(0.3-4.4)	0.785	0.8	(0.2-3.3)	0.746

*Adjusted OR by: age, age at menarche, ethnic group, menstrual flow and BMI (multivariate analysis); OR, odds ratio; CI, confidence interval

(OR, 1.6; 95% CI, 1.4–1.7) increase in the risk of developing cancer in alcohol consumers (de Menezes, 2015). In contrast, a recent study showed that the odds ratio of breast cancer was 3.13 (95% CI: 1.81–5.43) in women who consumed >5 drinks/week compared with non-drinkers for ≥10 years, which is similar to our results (Strumylaite, 2015).

Four large cohort studies – the Swedish Mammography Cohort (Suzuki et al., 2005), the Iowa Women's Health Study (Gapstur et al., 1992), the Nurses' Health Study (Colditz and Stampfer, 1990) and the Boston Women's Health Study (Zhang et al., 2007) – showed a stronger association between alcohol consumption among women using estrogen replacement therapy than in those who did not. In the present study, 74.7% of the women were under 50 years old, 67% had a normal menstrual flow and 72.3% had a normal menstrual cycle. We might speculate that approximately 70% of the women had a regular hormonal cycle at the moment of the interview. These data underscore the role of alcohol in premenopausal women, suggesting that the alcohol–breast cancer association may be at least partially mediated by the estrogen pathway (Li et al., 2010).

Evidence from other epidemiological studies also found that the alcohol intake increased the relative risk of breast cancer among premenopausal women (Petri et al., 2004; Scoccianti et al.,2014; Colditz and Bohlke, 2014). According to Liu et al., (2012, 2013) alcohol intake during adolescence and the intake from menarche to the first birth are unequivocally related to an increased risk of both proliferative benign lesions and invasive breast cancer in premenopausal women.

The total alcohol content in beer, wine and liquor varies from one country to another and, consequently, from one study to another. Studies like The Boston Women's Health Study (Zhang et al., 2007) and The Million Women Study (Allen et al., 2009) from the United Kingdom collected amount of alcohol intake by the type of beverage. Nonetheless, limitations should be considered in these studies, even with the adjustment of the intake using a regression dilution approach.

In the present study, limited information was collected on alcohol consumption: the exposition to alcohol was categorized as being regular drinkers versus abstainers/occasional drinkers. Another limitation that should be considered is recall bias as is a concern with all case-control studies. Most of the data were obtained from self-reports from the cases and controls, so recall bias is likely. Another limitation is that the result of this study cannot be generalized to the whole country, as it was conducted in one of the largest cities in Brazil, located in the more developed region of the country. In addition, the sampling was limited to only women attending one public hospital.

In conclusion, regular consumption of alcohol by women with normal menstrual cycle increases the risk of breast cancer, in contrast to those women that have already entered menopause. Compared with many of the studies that have reported an increased risk of breast cancer, the general mean age of patients and controls in the present study was 42 years old, a 13-year difference in the general mean age reported by other authors (Zhang et al., 2007; Allen et al., 2009), showing that this gap may be the key to finally understand the role of alcohol as a risk factor for breast cancer. Our results provide valuable information about the local situation in Brazil, and might be convenient for planning lifestyle changes for future interventions countrywide.

Ethics statement

The study protocol was approved by the independent ethical committee and institutional review board of IFF/FIOCRUZ. Written informed consent was obtained from each participant. All patient data were anonymous and de-identified prior to analysis.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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