



The Association between Breast Cancer and Alcohol Consumption: Review Articles

By Abdulraouf Lamoshi

Tripoli Medical Center

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The Association between Breast Cancer and Alcohol Consumption: Review Articles

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I. INTRODUCTION

About 10% of women will be diagnosed with breast cancer during their lifetime; however in majority of cases the underlying cause is unknown. Across the globe, breast cancer is the second most common type of cancer and the second leading cause of cancer death in women; the risk factors for breast cancer include older maternal age at birth of first child, earlier onset of menses, later age at menopause, increased mammographic density and the presence of specific genetic alterations (Beasley et al, 2010). Both alcohol and tobacco have significant causal roles in numbers of cancers including breast cancer (Kristan, 2003). A prospective follow-up clinical study that tracked 1.3 million women over 7.3 years demonstrated that among women who reported recent alcohol consumption, a 12% elevation in breast cancer risk was observed for each additional drink (Beasley et al, 2010). Notwithstanding studies such as those cited above the impact of smaller amounts of drinking is not documented well. Information on drinking styles, such as regular drinking and heavy episodic drinking, aka binge drinking, is also deficient. Also, it is important to assess the role of alcohol intake at different times in a woman's life (Chen et al, 2011). Consumption of alcohol could be a modifiable risk factor which could reduce the cancer burden among women in the Western world. (Tjønneland et al, 2007).

When alcohol consumption is initiated during earlier years of life, the cumulative risk can be more serious; in a case-control study of pre- and postmenopausal women, breast cancer was related with alcohol use of < 13 g/day solely for those who consumed alcohol before the ages of 30 years and regardless of recent use, where as no significant increase in risk was associated to recent consumption of a same amount among women with low-to-moderate intake of alcohol before age 30 y (Tjønneland, 2004). There are many examples showing that exposure to some dietary or environmental changes could enhance the development of different cancer types.

Asian and African women are potential victims to such modification because of some changes in their lifestyles. The incidence of breast cancer in the United States was about 6 times higher than in Asian

populations this rate gradually has become approximately 3 times higher in US white women than in Asian women; the migration of Asian women to the United States led to increase of breast cancer rates and continue to rise in next generations to the level of rates in white women living in the United States (Brown et al, 2010). According to Adebamowo and Adekunle (1999), in the United States and Canada, the lifetime risk of breast cancer is 10 % for white women and 7.3% for African-American women; some 3.5% will die from breast cancer. The incidence of breast cancer in Nigeria in 1976 was 15.3 / 100 000 but this number jumped to 33.6 / 100 000 in 1992; moreover, from 1960 to 1980, the cancer record of one Nigerian hospital registered 17 496 cases of cancer; by that time breast cancer was the fourth commonest tumor in Nigeria (6%) and the second most common among women, dramatically, from 1980 to 1989 this tumor became the most common malignant cancer in the country (Adebamowo and Adekunle, 1999).

II. METHODS

A MEDLINE search was conducted to identify epidemiological studies on the relationship between alcohol consumption and breast cancer incidence among different ethnic backgrounds from 1980 to 2011. Fifteen papers written in English were reviewed. The objectives, findings, population samples, strengths and weaknesses, and conclusions have been reviewed. Key words: Alcohol consumption, breast cancer

III. MAIN FEATURES AND COMMENTS

Fifteen studies to evaluate the association of breast cancer with alcohol consumption were identified including eight cohort and seven case control studies. The analyzed components of the studies including age range, study period, numbers of women enrolled, the risk of breast cancer due to alcohol drinking and covariates used in adjustment. Studies that presented separate estimates of risk were assessed in terms of: frequency of alcohol drinking, amount of consumed alcohol, type of alcohol, or/and menopausal status, genotype status of the participants, age at consumption, folate as protective factor, dietary intake, smoking, postmenopausal hormones treatment, and the mechanism of causality. The studied populations had some shared and unique characteristics. The first study

Author: MBBCh, MPH, ABPS, MS CTS, MS, Tripoli Medical Center, Tripoli, Libya. e-mail: raofdr@yahoo.com

started in 1983 4 and the last one was completed by 2007 9. The youngest participants in these studies was 20 years old 13 whereas two studies analyzed postmenopausal women without defining an upper age limit, however the majority of studies did not go beyond 79 years of age 5. The sample sizes in these studies ranged from 57 12 to 1.3 million women 11.

The participants have different ethnic backgrounds; the majority is Western women, in addition to Asian Americans, Mexicans, Japanese, Chinese, Filipino, and Nigerian 9, 13, 15. The average response rate is about 90%, and the samples had been selected from different resources. All studies consider drinking alcohol as an independent variable in addition to some other variables such as smoking, coffee, folate, vitamin B12, postmenopausal hormonal therapy, antioxidant nutrients, and other dietary and environmental factors 1, 2, 4, 13. Breast cancer is the dependent variable but some studies looked with more details at its different types and the age of diagnosis 6. Alcohol use was studied in terms of the amount of consumption on daily and weekly bases, type of alcohol (beer and/or cider, wine, liquor, spirits, or fortified wine), the duration of use, and the age of consumption 2, 4, 10. To measure the variables most of the studies collected the data about the alcohol use, other dietary and environmental factors, and demographic information through conducting questionnaires either by mail or during face to face interviews 3, 13. The diagnosis of the cancer was carried out in the majority of cases through checking the medical records of the participants; however, there are two studies dependent on the follow up questionnaire to gather that information 2, 11. In one study the patients had been subjected to blood drawing samples to determine gene phenotype 7.

The main findings of these studies show that there is an increased risk of breast cancer observed in women with a higher absolute and dose dependent intake of alcohol 1, 3, 4, 6, 8. Thirteen out of the fifteen studies demonstrated this correlation regardless of the amount or the age of drinking commencement with different levels of measured certainty 1,2,5,7. Only one study showed that low alcohol intake is not related to an increased breast cancer risk in Asian-American women 13. The final study did not support an association between alcohol intake and alcohol metabolism with breast cancer risk 7. One study pointed out that decreasing recent alcohol consumption, independent of early lifetime exposure to alcohol, may reduce the risk of breast cancer in postmenopausal women 14. Another study that showed positive correlation specified that women who drank more heavily than their average lifetime rate for a period of 6 months or more were at higher risk for breast cancer 4. An important implication of these studies' findings is that even small amounts of

alcohol (5 g/day, 3 glasses of wine per week) can increase the risk of breast cancer 1, 5, 9, 11.

Results of many studies did not vary by type of alcohol ingested, and their observations did not show significant change in risk related to any beverage type 1, 6, 11. The increased risk of breast cancer is associated with recent but not lifetime or early total alcohol intake 6. One study pointed out that there is no association between alcohol intake, alcohol metabolism enzymes (Aldehyde dehydrogenases genotype (ADH1C, and ADH1B)) and breast cancer risk among sisters discordant for breast cancer 7. One study connected increased risk for breast cancer with drinking alcohol, taking postmenopausal hormones, and, especially, both together 8. More than one study emphasized that low levels of alcohol intake also can increase the risk for breast cancer among both pre- and postmenopausal women 1, 5, 9. Only one study explored that alcohol use may be more strongly associated with risk of hormone-sensitive breast cancers than hormone-insensitive subtypes, suggesting distinct etiologic pathways for these two breast cancer subtypes 10. One study suggested that moderate alcohol consumption increases some biomarkers of oxidative stress in postmenopausal women which could lead to development of breast cancer 12. Conversely, one article shows that low alcohol intake is not related to increased breast cancer risk in Asian-American women, and neither alcohol nor cigarette use contributed to the elevated risks in Asian-American women associated with migration patterns and westernization 13. Tjønneland's et al study suggests that baseline intake of alcohol is a more important determinant of postmenopausal breast cancer risk than earlier lifetime exposure 14.

A Nigerian study insisted that, acquisition of 'western' lifestyle, and the changing socioeconomic patterns of the country contributes to development of breast cancer 15. There are proved significant factors that could contribute to dietary prevention strategies to reduce breast cancer incidence such as alcohol ingestion, which remains one of the few risk factors for breast cancer that can be prevented 3. According to Duffy et al (2009), however the increased risk of breast cancer with alcohol use is relatively small (13% for 1 drink/day), the results emphasize the necessity to include breast cancer risk among the list of consequences for even the low levels of alcohol drinking, which is considered "safe" according to the National Institute on Alcohol Abuse and Alcoholism (NIAAA) guidelines 5. Chronic alcohol consumption of moderate amounts of alcohol by healthy postmenopausal women may lead to important changes in biomarkers associated with oxidative stress where high levels of reactive oxygen species can enhance lipid peroxidation, damage cells, and participate in chronic diseases, including breast cancer 12. Berstad's et al study shows that recent collective alcohol ingestion of

two or more drinks per day may be associated with a high risk of breast cancer before age 50 years 6.

Concerning the strength of the studies, most of the (ten) studies have thousands of participants 1, 2, 4, 5, 6, 8, 9, 10, 11, 14 and high response rate 1, 3, 10, 12. Some studies focused on specific populations 9, 15 whereas others try to explore that association among the Western women in general 1, 2, 3, 10. One study uniquely studied the association of both frequency of alcohol consumption and binge drinking and breast cancer 1. One study was a multi-center study by inclusion of subjects living in countries from all over Europe 2. Only incident cases that had undergone genetic testing for the six most common BRCA gene mutations among French-Canadians were studied in one remarkable research 3. Trained interviewers carried out well designed interviews to decrease the risk of information bias, and the RR of breast cancer did not depend on ever drinking alcohol 4, 6. Duffy's et al, (2009) study did not confirm the protective effect of folate on breast cancer risk for postmenopausal women who are moderate alcohol consumers 5. A study examined full sisters discordant by breast cancer status to see if alcohol, and its potential impact by genotype, could participate in differences in breast cancer risk within families; this approach removes any potential confounding by race/ethnicity due to population stratification 7. The greatest power to examine an interaction effect, with longer follow-up of 20 years was provided by Chen et al, 2002 8. Beasley et al, 2010 used, uniquely, US Department of Agriculture food composition tables for estimating nutrient intake in a Mexican population to control the other breast cancer dietary factors 9. One research had a large size sample, which allows examination of the association of alcohol intake on individual cancer sites 11. Hatman et al, 2005, focused on mechanism of the development of breast cancer because of alcohol use 12. A wide range of lifestyles and acculturation in Asian-American women, including the role of smoking and alcohol consumption, particularly low levels of intake was the core of Brown's et al, 2010 study 13. The timing of the initiation of alcohol consumption was considered both in terms of chronological age and relative to first birth in one research 14. Another study focused on the epidemiological risk factors, including alcohol use, of breast cancer in Nigerian women 15.

In terms of disadvantages and bias of the reviewed studies, eight of them are observational, so alcohol use was not randomly assigned to women 1, 2, 3, 5, 8, 10, 11, 14. Some studies relied on self-reported alcohol use, which may have resulted in recall bias; consequently, women with breast cancer might be more likely to overestimate consumption of certain foods they believe to be related to their disease 1, 3, 8, 9, 15, and, compared with some studies done in Europe, the study does not have as many women with higher levels of

alcohol consumption 1. Lash's and Aschengrau's study did not address an age-specific history of alcohol ingestion rates and the proxy respondents may have participated in non-differential misclassification of alcohol consumption rates, which bias the expected results toward the null; the crude assessment of alcohol ingestion may have obscured an underlying dose-response association 4. Alternatively, it may be that the low doses of alcohol consumed by most women in this study are not associated with breast cancer risk, and solely high doses could associate with breast cancer 4. Two studies considered the use of only one baseline measurement of alcohol and folate and underestimated dietary folate intake because of changes in the fortification of cereals and grains which began in the early 1990s and was completed by the end of 1997 as part of a federal policy 5, 10. Short length of follow-up (3-6 years) was one disadvantage of some studies in contrast to other previous cohort studies (10-16 years) 2, 5, 11. In Berstad et al study, the number of control subjects was much smaller than the number of cases; this gave the study limited power to distinguish differences between cases and controls, and its response rate was relatively low (62%) 6, and it could not exclude the possibility of selection bias in this study 6. The participants in two studies were not able to differentiate between red and white wine, and there is some indication that white wine may increase the density of mammary tissue, whereas red wine may reduce the density; they were not able to assess the effect of binge drinking, and they did not obtain data on other dietary intakes 6,9.

One of a study's problems is non differential measurement error of self-reported alcohol consumption and/or genotype, and a low statistical power because of high concordance of genotype and alcohol use 7. Some studies were not able to assess the cancer risk for never drinkers and former drinkers separately because the used questionnaire did not differentiate between lifelong nondrinkers and those who had stopped drinking (not exclude the possibility of non differential misclassification) 11, 13, 14; the increased risk seen in women who were currently nondrinkers compared with small amount drinkers, for many cancer sites, shows that many nondrinkers could be former drinkers who have stopped drinking because of medical problems, and this may have caused a non-genuine high relative risk in this group 11. In the experimental study, the measurement of selected antioxidant nutrients and one marker of oxidative stress in blood may or may not represent what is occurring at the tissue level; these changes were observed over a relatively short time frame 12. Limitation on estimating the influence of moderate to heavy intake of alcohol in this Asian population is the small percentage of subjects who drank 5 or more grams of alcohol per day 13. Adebamowo's and Adekunle's study was a case-

controlled study but it was not a blind one, so the patients tend to be more interested about any possible risk factor than the controls 15.

Concerning the generalizability, most of the studies, especially, those have large numbers of western women^{1, 2, 4, 5, 6, 8}, can be generalized. Two studies were too specific and have relatively small numbers 13, 15, thus cannot be safely applied to the rest of the women.

IV. CONCLUSION

A majority of epidemiologic studies provide evidence for a positive association between breast cancer risk and alcohol consumption but that causality relationship is not proved in case of Asian-American women. Evidence from human biomarkers assay support plausible biological mechanisms where chronic alcohol consumption of moderate amounts of alcohol by healthy postmenopausal women may lead to breast cancer. Significant changes in biomarkers associated with oxidative stress where high levels of reactive oxygen species can promote lipid peroxidation, damage cells, and contribute to chronic diseases, including breast cancer.

Findings of this analytic study suggest that breast cancer is strongly associated with alcohol consumption. These findings may have broad implications for the prevention and reduction of breast cancer. Since the prevalence alcohol drinking is very high, and there is a causal relationship linking breast cancer with alcohol, that has serious public health influences in terms of the number of breast cancer cases due to drinking alcohol. The different incidence of breast cancer across the globe shows that environmental impacts are significant in the etiology. Although the high risk associated with alcohol consumption is relatively small compared with the major risk factors for breast cancer, but it is a modifiable risk factor. Determination of these factors may improve the ability to prevent this type of cancers by providing more focused health education and other prophylactic ways.

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