

**ADDIS ABABA UNIVERSITY
COLLEGE OF HEALTH SCIENCES
SCHOOL OF PUBLIC HEALTH**



**Association of Non breast feeding and breast cancer among patients
on chemotherapy and radiotherapy at Tikur Anbessa Specialized
Hospital: A case-control study**

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the requirements for the degree of masters' in public health**

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DECLARATION

I, the undersigned, declare that this MPH thesis is my original work, has not been presented for a degree in any other University and that all sources of materials used for the thesis have been duly acknowledged.

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LIST OF ABBREVIATIONS AND ACRONYMS

AAU	Addis Ababa University
MOH	Ministry Of Health
NIH	National Institute of Health
OR	Odds Ratio
SPSS	Statistical Package for Social Science
TASH	TikurAnbessa Specialized Hospital
UK	United Kingdom
USA	United States of America
WHO	World Health Organization
YNHH	Yew New Haven Hospital

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ABSTRACT

Background: Breast cancer is a major life-threatening public health problem of great concern, with more than one million cases occurring worldwide annually. In Ethiopia breast cancer is the second most often occurring cancer among women. Even though there were studies that were done on risk factors of breast cancer worldwide there are very few studies in developing country especially in Ethiopia. Clarifying the role of non-breastfeeding in developing breast cancer may be helpful to establish preventive and control program to reduce the occurrence of the disease and serve as a baseline for further studies.

Objectives: To assess the association between non breastfeeding practices and breast cancer development among patients who are on chemotherapy or radiotherapy at TikurAnbessa Specialized Hospital.

Methods: This is unmatched case-control study design that tried to assess the association between non breast feeding practice and breast cancer. The study was done at TikurAnbessa Specialized Hospital radiotherapy center which is located in Addis Ababa, Ethiopia. Eligible cases were female breast cancer positive patient (pathology proven) and the controls were female breast cancer negative patient who were diagnosed for other non-reproductive system cancer, both cases and controls were either on chemotherapy or radiotherapy treatment service at TikurAnbessa Specialized Hospital. Theratio was 1:1 with 217 female breast cancer patients and 217 females without breast cancers. The analyses were performed with Statistical Package for Social Sciences (SPSS) version 20. Odds ratio and 95% confidence interval done to quantify association between an exposure and disease.

Result: , the odds of cases to report positive family history for breast cancer is about 2.6 times higher than the odds of controls to report the same. [AOR = 2.7(95%CI, 1.53, 4.93)]. The odds of cases to report menopausal status for breast cancer is about 2.4 times higher than the odds of controls to menopausal status to breast cancer. [AOR=2.4 (95% CI(1.2,4.7)]. The odds of cases that breastfed for breast cancer is about 50% lower than the odds of controls to report the same. [AOR = 0.05(95%CI, 0.34, 0.87)]

Conclusion: The study document show that family history of breast cancer, women who never breast fed, and women in menopausal status were associated with Breast cancer risk. An inverse association between breastfeeding and breast cancer was found in this study among women on chemotherapy and radiotherapy in TikurAnbessa Hospital.

1. INTRODUCTION

1.1 Background: Breast cancer, one of the non-communicable diseases, is the most common cancer in women worldwide. An American woman born today has about a 1 in 8 chance of being diagnosed with breast cancer at some time during her life [1]. It accounts for over one million of the estimated 10 million neoplasms' diagnosed worldwide each year [2]. It affects the perception of sexuality and self-image to a degree far greater than any other cancer [3].

Incidence rates vary greatly worldwide from 19.3 per 100,000 women in Eastern Africa to 89.7 per 100,000 women in Western Europe .In most of the developing regions the incidence rates are below 40 per 100,000. Even though it is generally increasing, the lowest incidence rates are found in most African countries [4]. This is because data for developing countries are limited and also researchers believed that this is because socio-economic and lifestyle changes (for example, later childbearing and dietary changes) and associated changes in menstrual patterns and increases in life expectancy will cause the burden of breast cancer. [2]

Breast cancer is an increasingly visible disease, and a rapidly growing cause of mortality, in developing countries [5]. In Africa, where breast cancer may often present at an earlier age and can progress more aggressively [6, 7], little is known about pathways and triggers for women to take action (e.g., seek medical advice) based on their recognition of symptoms.

Hospital records show that in Ethiopia there are more than 200,000 cancer cases per year where cervical & breast cancers are the top two cancer types having a lion's share for the high maternal deaths in the country [8]. In Ethiopia, breast cancer is typically a fatal disease with high mortality [9, 10], unlike the experience of the western world where breast cancer is frequently treatable and with lower mortality [11].Breast cancer is becoming the number one killer in females. Therefore, it has become an increasingly important problem of research all over the world.

Breast cancer survival rate is much lower in developing country especially in Ethiopia also the treatments are very expensive so we have to focus on prevention, one of the strategies of prevention is identifying the risk factors. Breastfeeding is one of the few known risk factors for breast cancer that is modifiable, but research has given somewhat inconsistent results regarding whether lactation is associated with a decreased risk of breast cancer.

1.2 Statement of the problem and Significance

Breast cancer is the primary cause of cancer death among women globally. Long-term increases in the incidence of the disease are being observed in both industrialized and developing world. Breast cancer impacts on women's health and development across the lifecycle, causing morbidity and mortality. Deaths of women from breast cancer during their most productive years could result in tragedy for families, food insecurity, children withdrawal from school, increased work burden on children and loss of assets.

Evidence in favor of an association of breast feeding with a breast cancer risk reduction remains limited and inconsistent, especially in Ethiopia, there is no study regarding risk factor of breast cancer.

The finding of the study could help us to show the modifiable risk factors of breast cancer, this may help to increase knowledge about risk factors associated to breast cancer. The result may contribute the health management at higher levels to develop strategies to alleviate this problem

The expected outcome of appreciating relevant risk factors for breast cancer in the population is central to any preventive and control program aimed at reducing the burden of the disease. Furthermore, the output of this study can serve as a base line for further studies in assessing the risk factor of breast cancer.

2. LITERATURE REVIEW

2.1. Prevalence of breast cancer

In 2012, breast cancer accounted for 25% of newly diagnosed cancers among women around the world with the highest incidences in high-income countries[1]. According to world cancer report, the prevalence of breast cancer could go up by 50% by 2020, from the current prevalence of 1.2 million worldwide to 1.5 million [9].

African-Americans have the lowest incidence rates among the American groups but are diagnosed with the disease at a younger age [12]. African women are diagnosed with the disease in between the ages 35 to 45 years, which is 10 to 15 years earlier than women in the North America and Europe [12]. African women also die from the disease around the ages of 40 years [12].

More African-American women have the hormone receptor-negative disease thus accounting for mortality rates higher than the general prevalence rates [13].

In general, the prevalence of breast cancer in African women in Africa is lower than in Europe and the USA. Although there are low prevalence rates, women from Nigeria, Senegal and of African origin are likely to have a more aggressive form of breast cancer than women from the European origin because breast cancers in African women produce a different pattern of gene expression [14].

In Sub-Saharan Africa mortality rates are high when compared to the prevalence rates following the same pattern as among African-American women in the USA [12].

In Ethiopia the oncology unit at TASH currently has approximately 6,000 cancer patients and there are more than 200,000 new cancer cases added per year. Out of these 21% are with breast cancer [8].Cervical& breast cancers are the top two cancer types having a lion's share for the high maternal deaths in the country [8].

2.2. Risk factors for Breast cancer

Risk factor is anything that increases the risk of developing breast cancer. Many of the most important risk factors for breast cancer are beyond control (non-preventable), such as age, family

history, and medical history. However, there are some risk factors that are preventable, such as weight, physical activity, alcohol consumption, cigar rate smoking and breast feeding [15].

2.2.1. Age

The incidence of breast cancer increases with age[16]. Although one possible definition of aging is “the accumulation of cell mutations and tissue damage that leads to disease”, aging does not itself induce all such changes, but is rather thought to reflect of the occurrence different life-events. Thus, the risk of breast cancer may be influenced by genetic changes, exposures during prenatal and early life, reproductive factors and late-life exposures such as those associated with hormone replacement therapy and menopause [16].

2.2.2. Life style

Alcohol: -Numerous early researches revealed a relation of alcohol drinking to an increased risk of breast cancer. Women who had alcohol consuming history got the risk of breast cancer almost 1.2 times greater than women who never drank alcohol with (95% Confidence Interval 0.7-1.8) [17]. Compared with women who reported drinking no alcohol, the Relative Risk of breast cancer was 1.32 (1.19-1.45, $p < 0.00001$) for an intake of 35-44g per day alcohol, and 1.46(1.33-1.61, $p < 0.00001$) for ≥ 45 g per day alcohol [18].

Tobacco: -According to Young et al. (2009), some evidence linked between usage of tobacco and breast cancer. It stated that mammary tissue might have increased possibility to carcinogenic exposures during the puberty and first full term pregnancy. Moreover, a comparison also had done among women who were nonsmoker, active smoker and passive smoker. The result was so obvious that active or passive smoker got more possibility to increase the risk of getting breast cancer. Women who began smoking before 26 years old or had more than five years of smoking history had more risks of breast cancer [19].

Physical inactivity: -Physical inactivity commonly was regarded as one of the risk factors for breast cancer. Several studies revealed that enough physical activity cause the reduction in the risk of breast cancer. It stated that physical activity could improve the hormone balance, strengthened the immune system by raising the T cells and decrease the body fat. As a result, total estrogen levels could decrease to prevent the breast cancer [20].

Stress: -Women with major life events stress of daily activity or depression had 3.7 times higher risk compared to those which did not experience such stress. Those who reported having stress in her work had 16% higher risk for breast cancer than those who had no stress [21].

Obesity: Body mass index is a static measurement. It is always used to justify obesity. Increased Body Mass Index more than 25 (kg/m²) has association with increased breast cancer risk. It could be a clear indicator to show the metabolic role of obesity in altering the glucose metabolism, ovarian hormone and growth factor which could stimulate the mammary carcinogenesis. [22]

2.2.3. Family history

Approximately from 15% to 20% of women who developed breast cancer had a family history of the disease. [23] A fivefold breast cancer risk existed when two first degree relatives (sister, mother or daughter) were diagnosed with the disease [24]. More specifically, the meta-analysis by Pharoah and colleagues find that the relative risk of developing breast cancer was 1.9 if any first-degree relative had breast cancer, 1.8 in the case of daughters, 2.0 for mother and 2.3 for sisters, and highest among women with both a sister and mother with breast cancer [25].

2.2.4. Pregnancy

The later age at first full-term childbirth (older than 30 year-old) and null parity are common factors for breast cancer. The collaborative team from Britain (2002) reported that a woman's risk of developing breast cancer decreased by 7.0% for each birth and decreased by an additional 4.3% for every 12 months of breastfeeding. The protective effects of early age at first full-term pregnancy, parity and lactation are important factors which can contribute to reducing breast cancer risk [26].

2.2.5. Breast feeding

A study done in 2009 to find the risks of not breastfeeding for mothers and infants suggest that for mothers, failure to breastfeed is associated with an increased incidence of premenopausal breast cancer [27].

For women who do have children, breastfeeding may slightly lower their breastcancer risk especially if they continue breastfeeding for one and half to two years. Women who give birth and breastfeed by the age of 20 may have even greater protection[15].

3. Association of Breast feeding and Breast cancer

Study on Breast feeding and risk of breast cancer in young women in UK in 1993. It is a case control study group. Cases are women before age of 36. 755 case control pairs interviewed and the result suggests that breast feeding protects against the development of breast cancer in young women and the risk decreases with increasing duration of breast feeding, with breast feeding each baby for three months or longer giving greatest protection. And also risk of breast cancer was not linked to number of birth. [28]

British Journal of cancer in 1996 published a case control study done in Greece, Athens by the title lactation and cancer of breast. A hospital based 820 cases and 1548 controls. The study suggested that breast feeding of prolonged duration may reduce the risk of breast cancer among premenopausal women but not among postmenopausal women. [29]

British Journal of cancer in 2001 published a case control study in USA by the title lactation and breast cancer risk. 608 incident breast cancer cases and 609 age matched controls in Tolland country in Connecticut hospital and New Haven country in Yale-New Haven Hospital (YNHH). The result from this study suggests that an inverse association between breast feeding and breast cancer risk. The relationship, however, seems more consistent among premenopausal women and stronger among those who breastfed more than three children and whose duration of breast feeding was longer, particularly with regard to breast feeding their first child. [30]

East Africa Medical Journal in 2005 published that in Nigeria by the title risk factor for breast cancer a case control study with 51 cases and 51 controls. The study has shown that high parity and long duration of breast feeding are associated with reduced risk while high birth order and late age at first term pregnancy are associated with increased risk of breast cancer. [31]

Even if most of the study support the inverse relation of breast feeding and breast cancer some studies show no association of the two.

A Study in southern Brazil published in 2003 a case control study on breast feeding and breast cancer. 250 cases and 1020 hospital and community control with a control case ratio of 4:1. data taken from March 1995 - July 1998. According to this study breast feeding does not have a protective effect against breast cancer. [32]

A prospective cohort study published in biomedical center research in 2014. The study was done in Sweden Malmö Diet and Cancer study, including 14092 women, were followed during a mean of 10.2 years and a total of 424 incident breast cancers were diagnosed. The aim of this present study was to examine duration of breastfeeding in relation to the risk of different subgroups of breast cancer. The result was Breastfeeding duration was not associated with breast cancer risk and no strong results were seen with regard to breast cancer subgroups. [33]

Although many studies have been done globally, to find an association between breastfeeding and breast cancer, no study in Ethiopia document such a benefit. So the following study was done to find out the association between breastfeeding and breast cancer.

3. OBJECTIVES

3.1. General Objective:

To assess the association between non breastfeeding practices and breast cancer development among patients who are on chemotherapy or radiotherapy at TikurAnbessa Specialized Hospital

3.2. Specific Objectives:

- To determine the proportion of breast feeding practices among breast cancer patients who are on radiotherapy or chemotherapy
- To determine the proportion of breast feeding practices among non-breast cancer patients who are on radiotherapy or chemotherapy
- To determine the association between non-breastfeeding and breast cancer development

4. METHODS

4.1. Study design- A Hospital based unmatched case-control study was conducted among patients on chemotherapy or radiotherapy at Tikur Anbessa Specialized Hospital to determine the association between of breast cancer and non-breast feeding practices.

4.2. Study area- TikurAnbessa Hospital is located in Addis Ababa, Ethiopia. The opening of TikurAnbessa Specialized Hospital (TASH) was in 1972, it is the largest general public hospital in the country. In 1998 TikurAnbessa Specialized Hospital, which is also the largest referral hospital in the country was given to Addis Ababa University (AAU) by the Ministry of Health (MOH) for the faculty as a main teaching hospital. The faculty is the oldest and the largest among the health training institution in the country, staffed with the most senior specialists.

Volunteer health care corps a project of the twinning center in 2011 stated that the Hospital provides a tertiary level referral treatment and is open 24 hours for emergency service. This Hospital offers diagnosis and treatment for approximately 370,000-400,000 patients a year.

Currently cancer treatment is given in Ethiopia at TikurAnbessa Specialized Hospital, the only government cancer treatment center in the country.

4.3. Study population- the study population was a hospital based population who were being treated at TikurAnbessa Specialized Hospital. Cases were female breast cancer confirmed patients (Pathology proven) who were on chemotherapy or radiotherapy treatment in TikurAnbessa Specialized Hospital during the study period. Controls were selected from female patients on chemotherapy or radiotherapy treatmentdiagnosed for other non-reproductive system cancer (proven to be free from any reproductive system cancers including breast cancer)

4.4. Sample size - A total of 217 female breast cancer patients were included in the study for the case and 217 female non breast cancer patients for control. The case-to-control ratio is 1:1

4.5. Sampling procedure:The sample size was determined using Epi-info version 7 software using the following parameter: the exposure proportion of breastfeeding is 79.7% among controls 67.4% among cases, 5% significance level, power of 80%, a case to control ratio of 1:1 and by using the following formula

$$n = \left(\frac{r+1}{r}\right) \frac{(\bar{p})(1-\bar{p})(Z_{\beta} + Z_{\alpha/2})^2}{(p_1 - p_2)^2}$$

$$\bar{p} = \frac{P_1 + rP_2}{1+r}$$

$$r = n_2/n_1$$

$$n_1 : n_2 = 1:1$$

P_1 = proportion of exposure in cases

P_2 = proportion of exposure in controls

α = type=1 error (0.05)

$Z_{\alpha/2}$ = Critical value at 95% level of confidence (1.96)

Z_{β} = Standard normal distribution value corresponding to power (0.84)

Sample size was calculated for breast feeding exposure status in developing breast cancer. Due to financial and time constraint I took the proportion of exposure from a research done at southern Brazil in 2003 which is a case control study in breast feeding and breast cancer [33], with exposure proportion of breastfeeding 79.7 %among controls and 67.4 %among cases. The calculated Sample size was 434 samples with 217 controls and 217 cases.

4.6. Data collection procedures – the study relies on primary data that was collected through interview from the target group. A face to face interview using a pre tested structured questionnaire adopted and modified from previously done similar studies [31, 33, 34] was done. The data collectors were four nurses having experience in data collection. The principal investigator was also the supervisor.

Though the interviewers were experienced, there was a one day intensive training about the study and the contents of the questionnaire included.

The following inclusion criteria were defined for participation.

The entire respondent must be female and aged above 15 years old.

For the cases

- Breast cancer positive

For the controls

- Breast cancer negative

Study subjects were interviewed face to face and the information were recorded in the questioner format. Written consent was taken from all the study subjects.

4.7. Operational definitions

CASES: - Female breast cancer positive patient (pathology proven) who were on either chemotherapy or radiotherapy treatment service at TikurAnbessa Specialized Hospital.

CONTROLS: - Female breast cancer negative patient who were diagnosed for other non-reproductive system cancer (proven to be free from any reproductive system cancers including breast cancer) and who were either on chemotherapy or radiotherapy treatment service at TikurAnbessa Specialized Hospital.

PRE MENOPAUSE: - The respondent is still menstruating.

MENOPAUSE: - The respondent is not menstruating. `

4.8. Data Analysis procedures- Data were initially entered into SPSS version 20 then cleaned through an analysis of the range and distribution of study variables and their mutual consistency. Descriptive statistics were computed for all variables according to their type. Frequency, mean and standard deviation were obtained for continuous variables while the categorical variables were assessed by computing frequency and percentages. Significance was determined using crude and adjusted odds ratios with 95% confidence interval. To assess the association between the different predictor variables with the dependent variable, first bivariate relationships between each independent and outcome variable was analyzed using a binary logistic regression model. Those independent models found to be significant with p-value less than 0.05 further analyzed using multivariate logistic regression model. All the analyses were performed with Statistical Package for Social Sciences (SPSS) version 20

4.9. Data quality management: - The principal investigator who is the study facilitator taken the responsibility to pre-test the questionnaire, editing/coding and entry of the data to the

computer. Computer data cleaning will be also taken place to check for the consistency of data and identify errors that will be occurred during data collection or coding process. In the actual data collection process, the principal investigator was strictly ensure that the data collected fulfills the expected procedures and keep every question responded properly by the respondent, through spot checking. When data collectors face/encounter problem during interview, the principal investigator was actively supporting them.

Initially the questionnaire and the informed consent was developed in English language for ease of understanding and then translated into Amharic to ensure consistency of understanding among data collectors and respondents.

4.10. Ethical consideration- To maintain the broadly agreed upon norms of ethical research, the following issues were carefully considered:

Approval was requested and obtained from the management of TikurAnbessaSpecialized Hospital Radiotherapy center to access the necessary data. Participation in the research was voluntary, that they had the freedom to withdraw from the study at any time without any consequences. The purpose of the research was clearly communicated to the participants and the stations on who is conducting the study, for what purpose, what outcomes are expected, and who will benefit from the results. The process of administrating the questionnaire will ensure anonymity. All information obtained in the process of the research was maintained confidentially. The data was solely used for research purposes and final report was made available to the organization for perusal.

4.11. Dissemination of results- The thesis will be submitted to department of community health, AAU as partial fulfillment of master's in public health. After the presentation at school of public health, necessary comments will be offered. Then, study will be disseminated to the policy makers in Ministry of Health (MOH), Ethiopia cancer Association , Addis Ababa University school of public health library. It will be also present on professional seminars. Pertinent findings will also be published in scientific journals.

5. RESULT

5.1 Socio economic and demographic Variables of the Study Participants

A total of 434 hospital based population who were treated at Tikur Anbessa Hospital were interviewed. Cases were 217 female breast cancer confirmed patients who are on chemotherapy or radiotherapy treatment in Tikur Anbessa Hospital during the study period and controls were 217 female patients on chemotherapy or radiotherapy treatment for any other types of cancer other than breast cancer included in the study yielding 100% response rate.

The ages of all the respondents ranged from 16-75 years (23-75 years from cases and 16-71 years from controls) with the mean age of 44.9 while it was 42 and 47.7 for cases and controls, respectively. The standard deviation is 11.4 (9.7 for cases and 12.3 for controls). The majority 263(60.6%) of the respondents 114(52.5%) for the cases and 149(68.7%)for the controls were in the age group of ≥ 41 years followed by age group 31-40 years, with 111(25.6%)from the cases 68(31.3%)and 43(19.8%)are from the controls.

Regarding marital status majority of the respondents 344 (79.3%) were married with 167(77.0%) and 177(81.6%) for the cases and controls, respectively.

Regarding educational level of respondents the majority 174(40.1%) were illiterate, 105(48.4%) of them were from the controls while 69 (31.8%) from the cases followed by 160(36.9%)were secondary and above 100(46.1%)from cases and 60(27.6%)from controls.

Majority of the respondents, 360 (82.9%), had monthly income of <2500 ETB (183(84.3%) of the cases and 177(81.6%) of the controls). About five percent, 21(4.8%) of the respondents (11(5.1%) cases and 10(4.6%) controls) reported a monthly household income of ≥ 5000 ETB. (Table 1)

Table 1 – Distribution of socio economic and socio demographic variables of cases and controls at Tikur Anbessa Hospital, Addis Ababa, 2015 (n=434)

	Case(n=217)	Control (n=217)	Total (n=434)
	No (%)	No (%)	No (%)
Age			
≤30	35(16.1)	25(11.5)	60(13.8)
31-40	68(31.3)	43(19.8)	111(25.6)
≥41	114(52.5)	149(68.7)	263(60.6)
Marital status			
Not married	50(23.0)	40(18.4)	90(20.7)
Married	167(77.0)	177(81.6)	344(79.3)
Education			
Illiterate	69(31.8)	105(48.4)	174(40.1)
Primary	48(22.1)	52(24.0)	100(23.0)
Secondary and above	100(46.1)	60(27.6)	160(36.9)
Monthly House Hold income in ETB			
<2500	183(84.3)	177(81.6)	360(82.9)
2500-4999	23(10.6)	30(13.8)	53(12.2)
≥5000	11(5.1)	10(4.6)	21(4.8)

5.2 Family, personal and reproductive history of the study participants

Of the total of study participants 90(20.7%) [65(30.0%) cases and 25(11.5%) controls] reported to have had family history of breast cancer. Majority of the respondents 297(68.4%) [127(58.5%) cases and 170(78.3%) controls] reported to drink alcohol sometimes in their life while 129 (29.7%) respondents never drank alcohol in their life.

There were no respondent who ever smoked cigarette both from cases and control groups. Majority, 95.4% of respondents attained menarche after 12 years of life [205(94.5%) cases and 209(96.3%) controls]

Women who had three or more live births were 262(60.4%)[112(51.6%) from cases and 150(69.1%)] while nulliparous women were 70 (16.1%) [41(18.9%) cases and 29(13.4%) controls]. 351(80.9%) of study participants delivered their first child at the age of 30 years or less with 168(77.4%) cases and 183(84.3%) controls. The mean age at first birth was 17.7 with 16.7 for cases and 17.5 for controls.

Majority of the study participants 299(68.9%) did not have abortion [151(69.6%) for cases and 148(68.2%) for controls]. 54(12.4%) had abortion greater than or equal to two times [28(12.9%) from cases and 26(12.0%) from controls].

From the total of study subjects majority 273(62.9%) [114 cases (52.5%) and 159 controls (73.3%)] had attained menopause. (Table 2)

Table 2: Distribution of family, personal and reproductive history of cases and controls in Tikur Anbessa Hospital, Addis Ababa, 2015 (n=434)

	Case(n=217) No(%)	Control (n=217) No (%)	Total (n=434) No (%)
Do you have a Family breast cancer history?			
Yes	65(30.0)	25(11.5)	90(20.7)
No	152(70.0)	192(88.5)	344(79.3)
Is this a biopsy proven diagnosis? (Pathology result seen)			
Yes	217(100.0)	0(0.0)	217(50.0)
No	0(0.0)	217(100.0)	217(50.0)
Alcohol			
Never	87(40.1)	42(19.4)	129(29.7)
Sometimes	127(58.5)	170(78.3)	297(68.4)
Usually	3(1.4)	5(2.3)	8(1.8)
Smoking			
No	217(100.0)	217(100.0)	217(100.0)
Menarche age			
<12	12(5.5)	8(3.7)	20(4.6)
≥ 12	205(94.5)	209(96.3)	414(95.4)
No of live birth			
0	41(18.9)	29(13.4)	70(16.1)
1-2	64(29.5)	38(17.5)	102(23.5)
≥3	112(51.6)	150(69.1)	262(60.4)
Age at first child			
≤ 30	168(77.4)	183(84.3)	351(80.9)
>30	8(3.7)	5(2.3)	13(3.0)
No child	41(18.9)	29(13.4)	70(16.1)
No of abortion			
0	151(69.6)	148(68.2)	299(68.9)
1	38(17.5)	43(19.8)	81(18.7)
≥ 2	28(12.9)	26(12.0)	54(12.4)
Are you still menstruating?			
Yes	103(47.5)	58(26.7)	161(37.1)
No	114(52.5)	159(73.3)	273(62.9)

5.3 Breast feeding history of the study participants

The proportion of women who had breastfed were 326(75.1%) [143(65.9%) cases and 183(84.3%) controls]. From the total study subject's 215(49.5%) breastfed greater than or equal to three babies while 73(33.6%) from cases and 142(65.4%) from controls 210(48.4%) breastfed greater than or equal to three babies more than three months, among these 73(33.6%) were cases and 137(63.1%) were controls. Concerning total duration of breast feeding in months 229(52.8%) breastfed their babies for more than 22 months [89(41.0%) of cases and 140(64.5%) of controls]. (Table 3)

Table 3: Distribution of breast feeding history among cases and controls in TikurAnbessa Hospital, Addis Ababa, 2015 (n=434)

	Case(n=217) No (%)	Control (n=217) No (%)	Total (n=434) No (%)
Ever breastfed			
Yes	143(65.9)	183(84.3)	326(75.1)
No	74(34.1)	34(15.7)	108(24.9)
No of babies breastfed			
0	74(34.1)	34(15.7)	108(24.9)
1-2	70(32.3)	41(18.9)	111(25.6)
≥ 3	73(33.6)	142(65.4)	215(49.5)
No of babies breastfed for >3 months			
0	77(35.5)	44(20.3)	121(27.9)
1-2	67(30.9)	36(16.6)	103(23.7)
≥ 3	73(33.6)	137(63.1)	210(48.4)
Total duration of breast feeding in months			
0	74(34.1)	34(15.7)	108(24.9)
1-9	17(7.8)	15(6.9)	32(7.4)
10-21	37(17.1)	28(12.9)	65(15.0)
≥ 22	89(41.0)	140(64.5)	229(52.8)

5.4.1 Logistic regression analyses (bivariate)

A crude analysis was done using binary logistic regression to assess the association between all variables and breast cancer. According to this analysis age, education, family history of breast cancer, number of live births, menopausal status, breastfeeding exposure, number of babies breastfed, number of babies breastfed for more than three months and total duration of breastfeeding history in months showed significant association with breast cancer at a p-value of <0.05 . However Marital status, monthly household income, alcohol consumption, age at menarche, age at first child birth and number of abortions in the past not found to be significantly associated with breast cancer. Table 4a,4b shows the crude analysis results.

Table 4a. Association of breast cancer with socio demographic variables of cases and controls in Tikur Anbessa Hospital, Addis Ababa, 2015

	Breast Cancer		COR(95%CI)	P-value
	Cases	Controls		
Age				
≤30	35(16.1)	25(11.5)	1	
31-40	68(31.3)	43(19.8)	1.13(0.60,2.14)	0.71
≥41	114(52.5)	149(68.7)	0.55(0.31,0.97)	0.04*
Marital status				
Not married	50(23.0)	40(18.4)	1.34(0.83,2.11)	0.24
Married	167(77.0)	177(81.6)	1	
Education				
Illiterate	69(31.8)	105(48.4)	1	
Primary	48(22.1)	52(24.0)	1.41(0.86,2.31)	0.18
Secondary and above	100(46.1)	60(27.6)	2.54(1.63,3.94)	0.00*
Monthly House Hold income in ETB				
<2500	183(84.3)	177(81.6)	1	
2500-4999	23(10.6)	30(13.8)	0.74(0.42,1.32)	0.31
≥5000	11(5.1)	10(4.6)	1.06(0.44,2.57)	0.89
Family history of breast cancer				
Yes	65(30.0)	25(11.5)	3.28(1.98,5.46)	0.00*
No	152(70.0)	192(88.5)	1	
Alcohol				
Never	87(40.1)	42(19.4)	3.45(0.79,15.1)	0.10
Sometimes	127(58.5)	170(78.3)	1.25(0.29,5.31)	0.78
Usually	3(1.4)	5(2.3)	1	

* = p < 0.05 - Significant, COR –Crude Odds Ratio; CI – 95% Confidence interval

Table 4b. Association of breast cancer with reproductive health related variables among cases and controls in Tikur Anbessa Hospital, Addis Ababa, 2015

	Breast Cancer		COR(95%CI)	P-value
	Cases	Controls		
Age at menarche				
<12 years	12(5.5)	8(3.7)	1.53(0.61,3.82)	0.36
≥12 years	205(94.5)	209(96.3)	1	
Number of live birth				
None	41(18.9)	29(13.4)	1.89(1.11, 3.23)	0.02*
1-2	64(29.5)	38(17.5)	2.26(1.41,3.61)	0.00*
≥3	112(51.6)	150(69.1)	1	
Age at first birth (n=364)				
≤30 years	168(95.5)	183(97.3)	1	
>30 years	8(4.5)	5(2.7)	1.74(0.56,5.43)	0.34
No of abortion				
0	151(69.6)	148(68.2)	1	
1	38(17.5)	43(19.8)	0.87(0.53,1.42)	0.57
≥2	28(12.9)	26(12.0)	1.06(0.59,1.89)	0.86
Are you still menstruating?				
Yes	103(47.5)	58(26.7)	1	
No	114(52.5)	159(73.3)	0.40(0.27,0.60)	0.00*
Ever breastfed				
Yes	143(65.9)	183(84.3)	0.36(0.23,0.57)	0.00*
No	74(34.1)	34(15.7)	1	
No of babies breastfed				
1-2	70(49.0)	41(22.4)	3.32(2.06,5.36)	0.00*
≥3	73(51.0)	142(77.6)	1	
No of babies breastfed for >3 months				
1-2	67(30.9)	36(16.6)	3.49(2.13,5.73)	0.00*
≥3	73(33.6)	137(63.1)	1	
Total duration of breast feeding in months				
1-9	17(11.9)	15(8.2)	1.78(0.85,3.75)	0.127
10-21	37(28.9)	28(15.3)	2.08(1.19,3.63)	0.01*
≥22	89(62.2)	140(76.5)	1	

5.4.2 Multivariable Logistic regression analyses

For those variables which were significantly associated with breast cancer in a bivariate logistic regression we run a multivariable logistic regression model to determine independent variable that is associated with breast cancer. The following variables showed significant association at a p-value of <0.05.

Accordingly, the odds of cases to report positive family history for breast cancer is about 2.6 times higher than the odds of controls to report the same. [AOR = 2.7(95%CI, 1.53, 4.93)]

The odds of cases to report menopausal status for breast cancer is about 2.4 times higher than the odds of controls to menopausal status to breast cancer. [AOR=2.4 (95% CI (1.2,4.7))]

The odds of cases that breastfed for breast cancer is about 50% lower than the odds of controls to report the same. [AOR = 0.05(95%CI, 0.34, 0.87)]

Table 5. Multivariate Logistic Regression Analyses of selected variables to see their independent association with breast cancer among cases and control in Tikur Anbessa Hospital, Addis Ababa, 2015

Variables	Breast Cancer		COR (95%CI)	AOR (95%CI)	P-Value
	Cases	Controls			
Age in years					
<30	35	25	1.00	1.00	
31-40	68	43	1.13(0.60, 2.14)	1.75 (0.86,3.56)	0.13
>40	114	149	0.55 (0.31, 0.97)	2.0(0.82,4.8)	0.13
Education					
Illiterate	69	105	1.00	1.00	
Primary	48	52	1.41 (0.86, 2.31)	1.12(0.65,1.93)	0.67
Secondary or above	100	60	2.54 (1.63, 3.94)	1.68(0.99,2.85)	0.05
Family History of BC					
Yes	65	25	3.28 (1.98, 5.46)	2.57(1.5,4.4)	0.01*
No	152	192	1.00	1.00	
Menstrual status					
Menstruating	159	58	1.00	1.00	
Menopause	114	103	2.48 (1.63, 3.78)	2.4(1.2,4.7)	0.01*
Ever breast fed baby					
Yes	143	183	0.36 (0.23, 0.57)	0.05 (0.34, 0.87)	0.01*
No	74	34	1.00	1.00	

* = p < 0.05 - Significant, COR –Crude Odds Ratio; AOR – Adjusted Odds Ratio; CI – 95% Confidence interval

6. DISCUSSION

This study has tried to assess the association of non-breast feeding practice and breast cancer. The result shows the odds of cases that breastfed for breast cancer is about 50% lower than the odds of controls to report the same. This is consistent with those of several other studies on risk of breast cancer.

In several epidemiological investigations breastfeeding has been identified as a protective factor against breast cancer. According to researchers possible mechanisms by which breastfeeding protects against breast cancer include: Reduced systemic estrogen and progesterone levels during lactation, increased prolactin due to breastfeeding, excretion of estrogens and carcinogens out of the breast ducts, terminal differentiation of breast epithelial cells caused by breastfeeding and delay in return of ovulation, which decreases estrogen and progesterone levels[34,35].

In this study statistically significant association was found in those women having a family history of breast cancer and the risk of acquiring breast cancer. The results of our study that showed the odds of cases to report positive family history for breast cancer is about 2.6 times higher than the odds of controls to report the same. This study is consistent with the findings of previous studies [36, 37].

Other studies show a family history of certain types of cancer can increase risk of breast cancer. This increased risk may be due to genetic factors (known and unknown), shared lifestyle factors or other family traits. Families with a strong family history of breast cancer often carry gene mutations. Inherited gene mutations account for only five to 10 percent of all breast cancers diagnosed in women in the U.S. [38].

A family history of female breast cancer is associated with an increased risk of breast cancer in first-degree female relatives by approximately two-fold, however, the magnitude of risk depends on a number of factors such as age at diagnosis [39].

The study also revealed that the odds of cases to report in menopausal status for breast cancer is about 2.4 times higher than the odds of controls to menopausal status to breast cancer. This is also consistent with other studies.

Many breast cancer risk factors are associated with higher levels of sex hormones, and it is thought to be by this mechanism that they are linked with breast cancer risk [40]. Sex hormones (also known as sex steroids) include oestrogen, progesterone and testosterone. In post-menopausal women, breast cancer risk is around twice as high in those with the highest sex hormone levels (including oestradiol, oestriol, androstenedione and testosterone) compared with the lowest, showed [41].

7. Strength and Limitation of the study

7.1 Strength of the study

- Even if it is difficult to get large number of control group I tried to exclude patients with reproductive system cancer like cervical cancers because some literatures suggest that cervical cancer has association with breast feeding practice.

7.2 Limitation of the study

- The study being a case control, the question of bias always arises. Recall bias remained a challenge particularly when remembering the past events like age at menarche, age at first birth which might have influenced the outcome of these study variables.
- The ratio of case: control of this study is 1:1; to have a good output the ratio of should be 1:2 or more. The reason for this is due to small number of patients for controls.
- Since there has not been any study conducted in Ethiopia regarding the prevalence of the known risk factors of breast cancer and no well documented cancer registry it was so difficult to get literatures.
- Majority of respondents had low income level and had to travel long distances because the only government center for cancer treatment in our country is TikurAnbessa Hospital, they have to wait more than a year to get the treatment, most to the respondents are very weak patients so they have the difficulty to answer the questioner because of their illness.

8. Conclusion and recommendation

8.1 conclusions

In conclusion, the study document show that family history of breast cancer, women who never breast fed, and women in menopausal status were associated with breast cancer risk among women on chemotherapy and radiotherapy in TikurAnbessa Hospital.

Since there has not been any study conducted in Ethiopia regarding the prevalence of the known risk factors this study has provided a ground work from which other studies can be conducted. The study provides valuable information that will be useful for policy makers in the fields of health.

8.2 Recommendation

Breastfeeding reduces breast cancer, so information, education, and communication activities for the promotion of breastfeeding and to create awareness of this fatal disease should be done.

It is recommended that family breast cancer history and being in menopausal status have risk for breast cancer, women in early age and women who had family breast cancer history should have examination for early detection like mammography and other physical examinations.

It is recommended that, since the majority of these patients had low income level and had to travel long distances and the only government center for cancer treatment in the country is TikurAnbessa Hospital, the government should facilitate to start the service to other regional hospitals.

The Ministry of Health ought to train health workers to promote health education enclosing breast cancer to increase the women's awareness about breast cancer and the associated risk factors because some of the risk factors are potentially modifiable like breast feeding

Cancer statistics from the developing countries are inadequate due to lack of cancer registries. It is recommended that cancer registries be established in various countries within the region to facilitate the formulation of appropriate policies for improved cancer care and prevention.

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Annexes

Addis Ababa University, School of public Health

Association of non breast feeding practice and breast cancer among patients on chemotherapy and radiotherapy at TikurAnbessaSpecialized Hospital: A case-control study

Annex I. Information sheet

Dear respondent,

You are invited to participate in a research study to be conducted by MSc student at Addis Ababa University, School of Public Health. Please read the following statement and ask any unclear questions before you agree to participate.

1. Topic: Association of non breast feeding practice and breast cancer among patients on chemotherapy and radiotherapy at TikurAnbessa Hospital: A case-control study
2. Objective of the study; to investigate the relationship between non breastfeeding practice and breast cancer in patients on chemotherapy and radiotherapy in TikurAnbessa Hospital. The information you provide will help us better understand risk factors to breast cancer. We would greatly appreciate your help in responding to this question. The results of the study would hopefully serve as an important input to any preventive and control program aimed at reducing the burden of the disease.
3. Participation procedure and guide line
 - a. The information you provide will be kept completely anonymous. That is, your name will not be on any of the forms.
 - b. It will take about 15 minutes to complete the survey.
 - c. The questions are written in Amharic and English, and it is to be filled by interviewer .
4. Participation benefits and risks
 - a. Your participation in this study does not involve risks. Any information you give me will be maintained confidentially.
 - b. No incentive will be given for participating in this study.
5. Right to refuse or withdraw: your participation is volunteer and there is no penalty for you not wanting to participate.
6. Right as a participant: you have a right to have any questions about this research project answered. Please direct any question to the interviewer.

7. Agree to participate

Yes _____ No _____

Signature _____ Date _____

*I thank you in advance for taking your time to respond to my questions!

Annex II. Consent form

I, the undersigned have been informed that the purpose of this particular research project is to investigate the relationship between non breastfeeding practice and breast cancer in patients on chemotherapy and radiotherapy in TikurAnbessa Hospital. I have been informed that the information I give will be used only for the purpose of this study; my identity, the information I give will be kept confidentially. I have also been informed that I can refuse to participate in the study.

Based on the above information I agree to participate in the research voluntarily with the hope of contributing (on behalf of one) to the effort of knowing risk factors for breast cancer.

Signature: _____ Date: _____

Address of investigator

Name: - Hanna Mengesha (Addis Ababa University School of Public Health student)

Cell phone: - +251-911-615423

E-mail:- hmengesha2001@gmail.com

Annex IV. Amharic version information sheet

በአዲስ አበባ ዩኒቨርሲቲ የህብረተሰብ ጤና ሳይንስ ትምህርት ክፍል የመረጃ ወረቀት

የተከበሩ መላሽ

በአዲስ አበባ ዩኒቨርሲቲ የህብረተሰብ ጤና ሳይንስ ትምህርት ክፍል የማስትሬት ዲግሪ ተማሪ በምትሰራበት ጥናት ላይ ለመሳተፍ ተጋብዛችኋል። ከዚህ በታች የተጻፉትን አረፍተ ነገሮች በማንበብ ግልጽ ያልሆነ ነገር ካለ በመጀመሪያ ይጠይቁ።

፩. የጥናቱርዕ :- በጥቁር አንበሳ ሆስፒታል ውስጥ ኬሞቴራፒ እናራዲዮቴራፒ ህክምና በሚወስዱ ታካሚዎች ላይ ጡት አለማጥባት ከጡት ካንሰር ጋር ያለውን ግንኙነት ለማየት የሚሰራ ጥናት

፪. ዓላማ:- ጡት አለማጥባት ከጡት ካንሰር ጋር ያለውን ግንኙነት ማየት ሲሆን ይህ እርሶ የሚሰጡት ምላሽ የጡት ካንሰርን በመቀነስ ረገድ በሀገር አቀፍ ፕሮግራሞች ላይ ጠቃሚ ሚና ሊኖረው ይችላል ።

፫. የተሳትፎ ሂደትና መመሪያ

ሀ. ስምዎትን መጻፍ አይጠበቅዎትም፡ እንዲሁም የሚሰጡኝ መረጃ በሚስጥር ይያዛል

ለ. ጥናቱን ሞልተው ለመጨረስ አስራ አምስት ደቂቃ ሊወስድብዎ ይችላል

ሐ. ጥያቄው በአማርኛና በእንግሊዘኛ የተጻፈ። ጥያቄው በጠያቂዋ አማካኝነት ይሞላል።

፬. መሳተፍ ያለው ጥቅምና ጉዳት

ሀ. በዚህ ጥናት መሳተፍ ጉዳት አያደርስም። ማንኛውም የሚሰጡኝ መረጃ በጥብቅ የተያዘ ይሆናል።

ለ. በዚህ ጥናት ተሳታፊ ስለሆኑ ምንም አይነት ክፍያ አይከፈልዎትም።

፭. የአለመሳተፍ መብት

ተሳትፎው በፈቃደኝነት ላይ ተመሰረተ ስለሆነ አለመሳተፍ ቢፈልጉ ምንም አይነት ቅጣት የለውም።

፮. የተሳታፊው መብት

ምንም አይነት ጥያቄ ካለዎት በማንኛውም ጊዜ ጥናት አስከጃን መጠየቅ ይችላሉ።

፯. ለመሳተፍ ፈቃደኝነዎት

አዎ ----- አይደለሁም -----

ፊርማ ----- ቀን-----

ስለተሳትፎዎ አመሰግናለሁ ።

Annex V. Amharic version consent form

የስምምነት ቅጽ

በጥቁር አንበሳ ሆስፒታል ውስጥ ኬሞቴራፒ እና ራዲዮቴራፒ ህክምና በሚደረግባቸው ታካሚዎች ላይ ጡት አለማጥባት ከጡት ካንሰር ጋር ያለውን ግንኙነት ለማየት የሚሰራ ጥናት

እኔ ከዚህ በታች የፈረምኩት የዚህ ጥናት ዋና አላማው ጡት አለማጥባት ከጡት ካንሰር ጋር ያለውን ግንኙነት ለማየት የሚሰራ ጥናት እንደሆነ ተገልጿል። ለእነዚህም ጥያቄዎች የምሰጠው መረጃ ለጥናቱ ብቻ አንደሚውል ተነግሮኛል። በተጨማሪም የኔ ማንነትና የምሰጠው መረጃ ሚስጥራዊነቱ እንደሚጠበቅ ተነግሮኛል። በተጨማሪም ፈቃደኛ ካልሆንኩ አለመሳተፍ እንደምችል ተነግሮኛል።

ከላይ በተጠቀሰው ስምምነት ላይ በመመስረት ጡት አለማጥባት ከጡት ካንሰር ጋር ያለውን ግንኙነት ለማየት በሚረገው ጥናት የራሴን አስተዋጽኦ በማድረግ በጥናቱ ላይ ለመሳተፍ ፈቃደኛ መሆኔን እገልጻለሁ።

ፊርማ ----- ቀን-----

የአጥኝው አድራሻ

ስም ሃና መንገሻ -(በአዲስ አበባ ዩኒቨርሲቲ የህብረተሰብ ጤና ሳይንስ የማስተርስ ዲግሪ ተማሪ)

ስልክቁጥር +251-911-615423

ኢሜል hmengesha2001gmail.com

Annex VI. Amharic version questionnaire

የመጠይቅ ጥያቄዎች

በጥቁር አንበሳ ሆስፒታል ውስጥ ኬሞቴራፒ እናራ ዲዮቴራፒ ህክምና በሚደረግ ታካሚዎች ላይ ጡት አለማጥባት ከጡት ካንሰር ጋር ያለውን ግንኙነት ለማየት የሚሰራ ጥናት

ቀን-----ፊርማ -----የሚሰጥር ቁጥር-----

ትክክለኛውን መልስ አክብቡ።

ሀ. ማህበራዊ እና የግል መረጃዎች

1. የመላሹ እድሜ _____

2. የጋብቻ ሁኔታ 1. ያላገባ 2. በትዳር ውስጥ ያሉ 3. ከትዳር ውጭ ያሉ

3. የትምህርት ደረጃ 1. ያልተማረ 2. ማንበብና መጻፍ የሚችል 3. አንደኛ ደረጃ

4. ሁለተኛ ደረጃ 5. ከፍተኛ ትምህርት

4. የቤተሰብ ወርሃዊ ገቢ በብር 1. <2500 2. 2500-4999 3. >5000

ለ.1 የቤተሰብ ሁኔታ

5. ከቤተሰብዎ ውስጥ በጡት ካንሰር የተያዘ አለ? 1. አለ 2. የለም

ለ.2 የግል ሁኔታ

6. በጡት ካንሰር መያዝዎ በናሙና ተረጋግጧል? (ከቻርት)

1. አዎ 2. አልተያዘኩም

7. አልኮል ይደብዳሉ? 1. በጭራሽ 2. አልፎ አልፎ 3. በአብዛኛው

8. ሲጋራ አጭሰው ያውቃሉ? 1. አውቃለሁ 2. አላውቅም

ለ.3 የተዋልዶ ሁኔታ

9. የወር አበባ ማየት የጀመሩበት እድሜ 1. <12 አመት 2. ≥12 አመት

10. የልጆች ቁጥር/በህይወት የተዎለዱ 1. የለኝም 2. 1 3. 2 4. 3

5. ≥4 (ከ ለ-ሠ ከመረጡ ወደ ቁጥር 11 ይሂዱ ሀ ን ከመረጡ ወደ ቁጥር 12 ይሂዱ)

11. የመጀመሪያ ልጅ ሲዎልዱ አድሜዎ ስንት ነበር? _____

12. ምን ያህል ወርጃ ነበርዎት? _____

13. የወር አበባ እያዩ ነው? 1. አዎ አልቀረም 2. ቀርቷል

ሐ. ጡት ሰለ ማጥባት

14. ጡት አጥብተው ያውቃሉ? 1. አውቃለሁ 2. አላውቅም

15. ምን ያህል ልጆችን ጡት አጥብተዋል? 1. 0 2. 1 3. 2 4. ≥3

16. ከሶስት ወር በላይ ጡት የጠቡ ልጆች ቁጥር	1. 0	2.1	3.2	4. <u>3</u>
17. አጠቃላይ ጡት ያጠቡበት ጊዜ (በወራት)	1. 0	2.1-9	3.10-21	
4. <u>22</u>				

ስለ ተሳትፎዎ አመሰግናለሁ