

**Addis Ababa University**  
**College of Medicine and Health Sciences**  
**Department of Surgery**



Determinants of Breast Cancer Recurrence Among Breast Cancer Patients  
Attending Tikur Anbessa Specialized Hospital Addis Ababa, Ethiopia 2025

By: Tadesse Ejeta (Endocrine and Breast surgery fellow)

A Thesis Submitted to Department of Surgery, College of Health Sciences,  
Addis Ababa University; In Partial Fulfillment for the Requirement of Sub  
Specialty training in Endocrine and Breast Surgery.

June, 2025

Addis Ababa, Ethiopia

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**Certification sheet**

As thesis research advisor, I hereby certify that I have read and evaluated the thesis prepared under my guidance by **Tadesse Ejeta** entitled “*Determinants of Breast Cancer Recurrence Among Breast cancer Patients attending Addis Ababa University Tikur Anbessa Specialized Hospital Addis Ababa, Ethiopia 2025*”

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As mentioned of the board of examiners of the Sub specialty thesis open defense, we certified that, we have read and evaluated the thesis prepared by Tadesse Ejeta and examined the candidate. We recommend that, the thesis is accepted as fulfilling the requirement for sub specialty in **Endocrine and Breast Surgery**.

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| External Examiner | Signature | Date  |

## Declaration

I declare that this research thesis entitled “*Determinants of Breast Cancer Recurrence Among Breast cancer Patients attending Addis Ababa University Tikur Anbessa Specialized Hospital Addis Ababa, Ethiopia 2025*” is my own work that have not been addressed in the study area as far as my knowledge touched and all the sources of materials used has been indicated and acknowledged as complete reference.

Name of the student:

**Tadesse Ejeta**

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Date \_\_\_\_\_

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## **Abbreviations**

BCS: Breast Conserving Surgery

BCR: Breast Cancer Recurrence

EORTC: European Organization for Research and Treatment of Cancer

EBCTCG: Early Breast Cancer Trialists' Collaborative Group

DCIS: Ductal Carcinom In Situ

DFI: Disease free interval

IHC : Immuno histo chemistry

TASH: Tikur Anbessa Specialized Hospital

WHO: World Health Organization

## Abstract

**Background:** Breast cancer is one of the most common cancers in women and it is the leading cause of cancer related death. Multi modality treatments are provided to improve the outcome of patients with breast cancer. Patients with post treatment recurrence have poor prognosis than those with no recurrence. Factors related to the patient, tumor histopathology and treatment modalities determine the recurrence of this disease.

**Objective:** The study was aimed at identifying determinants of breast cancer recurrence among breast cancer patients attending Tikur Anbessa specialized Hospital, college of Health sciences, Addis Ababa University, Ethiopia 2025

**Methods:** Facility based, unmatched case-control study design was conducted among 237 breast cancer patients attending Addis Ababa University Tikur Anbessa Specialized hospital from November 1, 2024- December 1, 2024 GC.. The cases were recurrent breast cancer patients and controls were patients with no breast cancer recurrence. Cases were selected consecutively and following each case two controls were selected. Data were extracted from patients chart using structured questioner by trained nurses. Data were entered into Epi data version 3.1; exported and analyzed by SPSS version 25. All independent variables with p-value < 0.25 in the bi-variate logistic regression analysis were entered into multivariable binary logistic regression analysis. Model fitness was checked by Hosmel-lemshow goodness of fit. An adjusted odds ratio with a 95% CI and a p-value of <0.05 was used to identify determinants of breast cancer recurrence.

**Result:** A total of 237 patients (79 cases and 158 controls) were included in the study. The mean age of cases and controls were 46.2 (SD  $\pm$  13.3) and 48.5 (SD  $\pm$  12.9) years, respectively. No family history of breast cancer(AOR=0.17, 95% CI: 0.03, 0.08), tumor size (AOR= 0.76, 95% CI: 0.60, 0.96),High nuclear grade (AOR= 3.4, 95% CI: 1.49,7.71), Lympho vascular invasion(AOR= 2.3, 95 % CI: 1.02, 5.34) positive surgical margin(AOR= 4.4, 95% CI: 1.05, 38.6) and Estrogen receptor negative(AOR= 5.7, 95%CI: 1.51, 21.5)were found to be determinants of breast cancer recurrence.

**Conclusion and Recommendations:** Family history, tumor size, high nuclear grade tumor, positive surgical margin, lympho vascular invasion and negative estrogen receptor were determinant of breast cancer recurrence. Breast cancer with these recurrence determinants require more aggressive treatment and intensive followup.

**Key Words:** Breast cancer, recurrence, histopathology, IHC

# INTRODUCTION

## 1.1 Background

Breast cancer is one of the most frequently diagnosed malignancies worldwide, accounting for 23% of female cancer diagnoses, as well as a leading cause of cancer-related mortality in women, responsible for 14% of cancer death. [1]

According to the GLOBACON 2020, breast cancer has now surpassed lung cancer worldwide as the most diagnosed cancer in women with 2.3 million cases (11.7%) followed by lung at 11.4%. Breast cancer mortality rates are steadily decreasing in developed countries owing to better treatment facilities. However, the incidence rates of cancers have steadily risen in these countries.[2]

Breast cancer is the most prevalent type of cancer in women worldwide, despite great strides made in detection amongst patients with early stage disease; roughly 30% of patients will relapse. Approximately 80% of these loco regionally recurrent breast cancers will occur within the 5years following initial treatment. While management of recurrent breast cancer is a therapeutic challenge, in recent years, 5-year survival has steadily been increasing. [3]

The management of breast cancer (BC) has evolved over the past 50 years into a multidisciplinary approach involving local and systemic therapies. In a well-resourced centre the patient with early stage breast cancer will have breast surgery (either lumpectomy or mastectomy) with or without radiation; a sentinel lymph node biopsy is used to assess the axilla either in place of/or before axillary lymph node dissection. These local treatments are most often combined with systemic therapies including cytotoxics and those targeted to receptors in or on the nucleus of the cancer cells. [4]

These multimodal treatments have resulted in a decline in the incidence of recurrent BC. For patients undergoing surgery for early BC in the 1990s, the rate of locoregional recurrence (LRR) at 5 years was approximately 10%. By 2005, LRR at 5 years had declined to about 6% and by 2010 this had fallen to 3 to 4%. However, these good results do deteriorate with time: the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) found that women who had undergone conservative breast surgery with radiation had a 10-year risk of first recurrence of 19.3% with similar results for those having had a mastectomy. [5]

Site of recurrence of breast cancer classified as; local—any epithelial breast cancer or ductal carcinoma in situ (DCIS) in ipsilateral breast tissue, or in skin and subcutaneous tissue of the ipsilateral thoracic wall, regional—breast cancer in ipsilateral lymph nodes or contralateral lymph nodes if axillary lymph node dissection was performed, or distant—breast cancer in any other location .[6]

Some of patients develop loco regional or distance recurrence after multimodality treatment and follow up. The risk of recurrence was highest in the second year after diagnosis (3.9%), with a median Disease free interval (DFI ) of 3.3 years. A second peak was present around year 8. The risk of distant metastasis was 3%during the second year, with a median DFI of 3.2 years. The annual risk of local recurrence showed a double peaked pattern with a risk of 0.7% in year two and 0.4% in year eight [[7], [8]]

Multiple factors determine the risk of local recurrence after multimodal treatment of breast cancer. Different studies indicated that modality of treatment; histo- pathologic characteristic hormonal status and family history determine the risk of tumor recurrence.[9,13,21]

This study was aimed at identifying factors that determine recurrence of breast cancer among breast cancer patients attending Tikur Anbesse Specialized Hospital.

## **1.2. Statement of the Problem**

Breast cancer remains a leading cause of cancer-related mortality among women worldwide. The American Cancer Society estimated approximately 284,200 new cases of breast cancer diagnosed in the United States in 2023, resulting in an estimated 44,130 deaths.[9]

The European Organisation for Research and Treatment of Cancer (EORTC) published the 10-year results of a study (EORTC 10801) involving patients accrued from Europe and South Africa comparing these procedures, BCT/ALND with modified radical mastectomy (MRM). Locoregional recurrence was greater in the BCT/ ALND than in the MRM (20% versus 12%). But when the EORTC 10801 trial investigators examined the 20-year follow-up data there was no significant difference in OS, DFS and DDFS between the two groups. Distant metastases and death were independent of the choice of surgical procedure. [4]

Despite advancements in breast cancer treatment, there are still a significant proportion of patients who continue to experience recurrence even after adjuvant treatment and the survival still remains low. This is largely due to acquired resistance of cancer stem cells to chemotherapeutic and biological agents used in treatment with a high risk of metastasis to distant organs and lymph nodes. Up to 30% of patients with early breast cancer still experience distant disease relapse. The nodal status remains the most powerful predictor of metastases.[10]

Tumor characteristics are the main prognostic factors for breast cancer outcome. A tumor size larger than 2 cm, axillary nodal involvement, negative estrogen and progesterone receptors, and high grade have been shown to increase the risk of death after breast cancer diagnosis and the risk of locoregional recurrence and metastases. [11], [12]

Young age at diagnosis has also been associated with a worse clinical outcome, partly because of the overrepresentation of more aggressive subtypes in young cases compared to older cases, such as triple negative or HER2positive breast cancer, or because of delayed diagnosis and presentation at an advanced stage.[13], [14]

Clinico pathological characteristics like,: demographic data (mean age at diagnosis, menopausal status at diagnosis), histo pathological characteristics (histological subtype, Nottingham tumour grade, tumor size and staging, degree of nodal involvement and staging), immunohistochemical tumor characteristics (e.g.; estrogen (ER) and progesterone receptor (PgR) status, human epidermal growth factors receptor-2 (HER2) status, etc.), site of metastasis and therapies received (neo)adjuvant chemotherapy, adjuvant radiotherapy, endocrine therapy, and targeted monoclonal antibodies were implicated determinants of breast cancer recurrence.[15]

According to retrospective study conducted in morocco to determine factor that increase the risk loco regional breast cancer recurrence, inadequate, margin, axillary lymph node involvement, positive lymph node ratio, lymphovascular invasion and hormonal status were increased risk of loco regional recurrence.[16]

Recurrence of breast cancer increase the morbidity and mortality of patients, increase the cost of health care and financial burden. It also exposes individuals for more toxic medical treatments and its related complications. In Tikur Anbessa Specialized Hospital there is no study related to

determinants of breast cancer recurrence. So this study was aimed at determinants of breast cancer recurrence among breast cancer patients attending Tikur Anbessa Specialized Hospital in the past five years (April,2019- March,2024, GC)

### **1.3. Significance of Study**

Breast cancer is one of the most common cancers in the world, recurrence of the disease after treatment is challenging to treat. The burden is more pronounced in Ethiopia where there are limited resources and facilities.

This study is helpful to provide information on determinants of breast cancer recurrence among breast cancer patients attending Tikur Anbessa Specialized Hospital.

The result of the study will help to mitigate the determinants of breast cancer recurrence identified in study area.

The result of the study is used as a source of data for further study.

## **2. Literature Review**

### **2.1 Magnitude of Breast Cancer Recurrence**

According to the GLOBACON 2020, breast cancer has now surpassed lung cancer worldwide as the most diagnosed cancer in women with 2.3 million cases (11.7%) followed by lung at 11.4%. 2020. Breast cancer incidence has increased by more than 20%, this is largely due to frequent testing and regular screening program, while breast cancer mortality rates are steadily decreasing in developed countries owing to early diagnosis, better treatment and regular follow up.[1]

Breast cancer is one of the leading causes of cancer-related deaths in women across the world which is mainly due to its ability to metastasize and pose a high risk of recurrence after treatment. Despite tumor regression in response to multi modality therapy, residual tumor cells are still detected in most patients after treatment. These residual tumors are then seen to remain dormant for years even before resuming their growth which results in tumor recurrence with time.[2]

According to study conducted in Brazil in 2014 to determine breast cancer recurrence and survival in women at five year, 6.5% local and regional recurrences and 25.2% of distant metastasis were identified in the total population, for a period of five years. Of this total, 3.0% women presented both local/regional recurrence and metastasis in the five-year period. More than 62.6% of the cases of metastasis occurred in the first two years after diagnosis.[17]

In Ethiopia, breast cancer is the leading cause of cancer-morbidity among adult women, accounting for one- third of all cancer cases among women and one in five of all cancer cases. An estimated 16,133 new breast cancer cases and 9061 breast cancer deaths occur annually in the country. There are striking differences in mortality rates from breast cancer in developed and developing countries attributed to late presentation and lack of therapy. In most high-income countries, more than 70% of breast cancer patients are diagnosed in stages I and II. However, only 20–50% of patients in the majority of low- and middle-income countries are diagnosed at early stages. The majority of breast cancer in women in low-income countries present at an advanced clinical stage, resulting in limited and difficult therapeutic options and contributing to the poor survival rate.[1], [18], [19]

Study conducted in Tikur Anbessa specialized hospital in 2019, on the assessment of breast cancer treatment outcome, multi-modality of treatments, like surgery, chemotherapy, radiotherapy, hormonal treatments showed that during 3 years follow up 46.53% of patients were dead, whereas 19.14% of patients were with an unknown outcome. Among the death outcome, 46% were before completion of the 6th chemotherapy cycles. Age, number of chemotherapy cycle, clinical stage, type of chemotherapy, mode of treatment, and endocrine therapy showed association with the death of breast cancer patients[20]

## **2.2 Determinants of Breast Cancer Recurrence**

### **2.2.1 Socio demographic determinants**

According to study conducted in South Africa (2017) on the risk factors for breast cancer recurrence, Young age at diagnosis, obesity, black race and patients carrying high penetrance genetic mutations namely BRCA 1/2, TP53 and PTEN had high risk of local and distant recurrence. When compared to sporadic breast cancer these genetic mutations, cases have an increased risk of loco regional recurrence, contra lateral breast cancer and other malignancies[4]

Similarly, another study done in Netherland (2017) on patterns and predictors of first and subsequent recurrence in women with early breast cancer indicated that young age at diagnosis was significantly associated with breast cancer recurrence.[7]

In contrast study performed by Mohammad Esmaeil Akbari et al in Shahid Beheshti University of Medical Sciences on Effects of Patho- Biological Factors on the Survival of Recurrent Breast Cancer, age of more than 40 years had a negative effect on survival after recurrence and disease free survival are known to be a major contributor to recurrence breast cancer[14]

A recent study performed in Canada women's hospital on Prognosis after Local Recurrence in Patients with Early-Stage Breast Cancer Treated without Chemotherapy indicated that factors that were significantly associated with death after local recurrence were young age at diagnosis (<40 years) ER -negative status, and time to local recurrence less than 2 years.[12]

### **2.2.2 Histo pathologic related determinants**

Study conducted in Canada on risk of early recurrence among postmenopausal women with estrogen receptor-positive early breast cancer treated with adjuvant tamoxifen showed that significant prognostic factors of early recurrence were high tumor grade, axillary lymph node involvement, tumor necrosis, mitotic index, positive lympho vascular invasion, and pathologic tumor size[21]

Study done in Catholic university of Korea on clinicopathological factors and imaging features of primary breast cancer in predicting early recurrence after the primary treatment showed that higher stage of malignancy, multi-modality poorly differentiated tumour and lymph node involvement were significantly determine breast cancer recurrence.(26)

### **2.2.3 Treatment related determinants**

A retrospective stud conducted in Denmark on the incidence of breast cancer recurrence 10-32 years after primary diagnosis reveled that higher hazard of late breast cancer recurrence among women who underwent BCS, those who received endocrine therapy, younger women (<40years) those with high lymph node status (4 positive lymph nodes) and those with tumor size greater than 20mm. The study also showed that lower hazard of late breast cancer recurrence among patients with grade III tumors, ER-negative tumors and those who received endocrine therapy.[22]

Study conducted in Tikur Anbessa oncology department on the treatment outcome of breast cancer showed that less than 6cycles of chemotherapy, types of chemotherapy, mode of treatment and endocrine therapy were associated with poor outcome of breast cancer patients.[20]

### **2.2.4 Tumor Biologic (IHC) determinants**

Multiple studies on the factor associated with increased risk of breast cancer recurrence showed that, patients with Hormone receptor negative, HER 2 positive and triple negative were associated with increased risk of loco regional and distance recurrence in patients operated for breast cancer[15], [16]

A systematic review conducted in USA on risk of recurrence in patients with HER2+ early-stage breast cancer reported that residual cancer burden greater than zero (positive margin), non complete pathologic response to neoadjuvant therapy, and fewer tumor infiltrating lymphocytes were risk factors of recurrence. In addition HR Status remained an important risk factor for recurrence, with HER2+/HR+ disease more likely to recur and similarly larger primary tumor size, and low Ki67 Were more commonly associated with HER2+ EBC recurrence[11]

But study conducted in England on the long term recurrence of breast cancer after stopping endocrine therapy indicated that tumor nuclear grade, hormone receptor status, HER2 status and KI-67 level were not significantly associated with breast cancer recurrence.[27]

### 2.3. Conceptual Frame Work

The conceptual framework demonstrates the association between dependent and independent variables which was adapted from reviewing relevant literature. All of the arrows from the four determinants point to the outcome, indicating link to breast cancer recurrence.

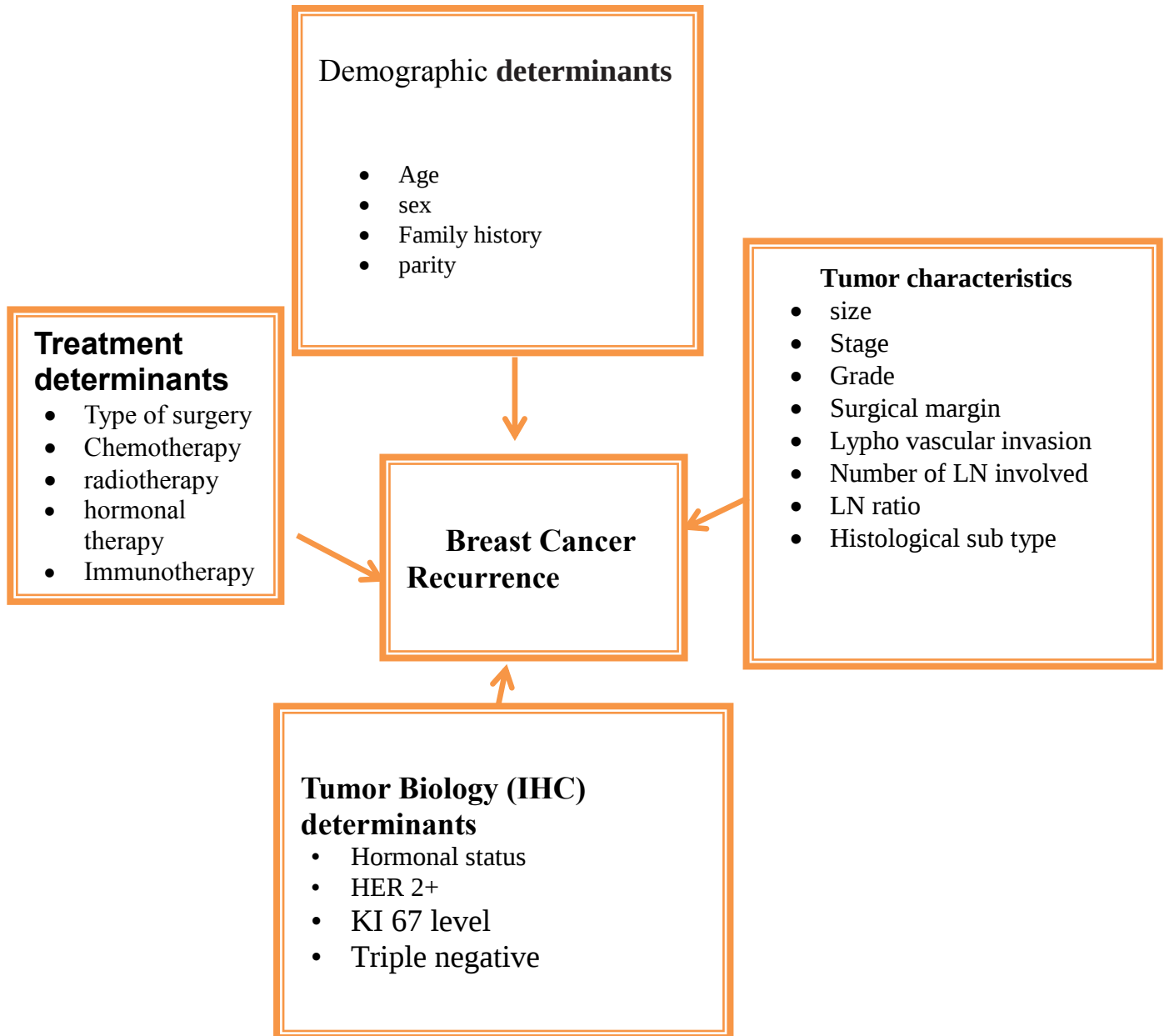


Fig. 1 conceptual frame work developed from reviewed literature on the determinant of breast cancer recurrence among breast cancer patients attending Tikur Anbessa Specialized Hospital.

### **3. Objective of the Study**

#### **3.1. General Objective**

- To assess determinants of breast cancer recurrence among breast cancer patients attending Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia 2025.

#### **3.2. Specific Objectives.**

- To assess determinants of breast cancer recurrence among breast cancer patients attending Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia 2025.

## **4. Methodology**

### **4.1. Study Area and Period**

Tikur Anbessa Specialized Hospital is found in the capital city Addis Ababa it is one of the government hospital and the highest referral center in the country. It is under college of health sciences of Addis Ababa University and serves as both teaching and clinical service center. Surgical department of the hospital has multiple units that provide sub specialized clinical and training activities. Endocrine and breast surgery unit and oncology departments are where patient with endocrine and breast cancer are treated and followed.

Patients with breast cancer are operated in both Tikur Anbessa Specialized Hospital and Churchill health center. After completion of surgical treatment patients are linked to oncology department for chemotherapy, radiotherapy, hormonal therapy or targeted therapy. Breast cancer patients operated in other hospital in the country may also be referred to this hospital for further managements. The patients are jointly followed for recurrence of breast cancer and its treatment at surgical and oncologic referral clinics. This study was conducted on breast cancer patients attending Tikur Anbessa Specialized Hospital, patients with recurrence as case and those with no recurrence as control from November 1, 2024- December 1, 2024 GC.

### **4.2. Study design**

Facility based unmatched case control study design was employed.

### **4.3. Population**

#### **4.3.1. Source Population**

All patients attending Addis Ababa University, Tikur Anbessa Specialized Hospital followed from 6 months to 5 years

#### **4.3.2. Study Population**

**Case:** All breast cancer patient with recurrence during study period

**Control:** All patients operated for breast cancer with no recurrence during follow up.

#### **4.3.3. Study Unit**

Individual with recurrent breast cancer selected as a case during the study period and individual selected by systematic random sampling from patients with no breast cancer recurrence and from which data was collected.

### **4.4. Inclusion and Exclusion Criteria**

#### **4.4.1 Inclusion Criteria**

**Case:** All recurrent breast cancer during the study period were included.

**Control:** All non recurrent breast cancer patients during study period were included

#### **4.4.2. Exclusion Criteria**

**Case:** patients with incomplete chart and perioperative distance metastasis were excluded from the study.

**Control:** patients with incomplete chart, per operative distance metastasis were excluded from the study.

### **4.5. Sample size determination and sampling procedure**

#### **4.5.1. Sample size determination**

The sample size was determined for unmatched case-control study using STATCALC program of Epi-Info version 7 statistical software based on the following assumption: confidence level =95%, power  $(1-\beta) = 80\%$ , ratio of controls to cases 2:1 and using post menopausal as determinant of breast cancer recurrence with, 66% proportion of case and 2.49 odds ratio taken from previous case-control study done on breast cancer (23 ). Considering a 10% non-response rate, the final sample size was determined to be 237 (79 cases and 158 controls) (Table 1).

**Table 2: Sample size calculated for determinants of Breast cancer recurrence among patients operated in Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, 2025**

| S/<br>N | Significant<br>determinants       | CI<br>% | Pow<br>er<br>% | Contro<br>l to<br>cases<br>ratio | AOR  | Exposure of |                  | Sample size |         | Tot<br>al |  |
|---------|-----------------------------------|---------|----------------|----------------------------------|------|-------------|------------------|-------------|---------|-----------|--|
|         |                                   |         |                |                                  |      | Case<br>%   | Contr<br>ol<br>% | Case        | Control |           |  |
| 1       | Menopausal<br>status              | 95      | 80             | 2:1                              | 2.49 | 66          | 44               | 72          | 144     | 216       |  |
| 2       | Family<br>history of<br>breast ca | 95      | 80             | 2:1                              | 2.33 | 30.6        | 69.3             | 31          | 62      | 39        |  |
| 3       | Physical<br>inactivity            | 95      | 80             | 2:1                              | 1.98 | 77          | 23               | 16          | 32      | 48        |  |

Then, the maximum sample size was taken ( $n= 216$ ) and by adding 10% non-response rate the final sample size was  $n= 237$ .

#### 4.5.2. Sampling Procedure

##### Case Selection:

From total of 96 breast cancer patient with recurrence, 79 patients with complete chart were included in the study consecutively until required sample size was reached.

##### Control Selection:

Controls were selected subsequently after cases were selected from all breast cancer patients attending Tikur Anbessa Specialized Hospital with no breast cancer recurrence after treatment by systematic random sampling method. For one case two controls were selected following selection of case. If the selected control did not meet inclusion criteria, the next patient was selected as control.

Sampling interval for control was calculated as:

Sampling interval (K) = Total number of no recurrent breast cancer

Total number of controls

$$K = N_{\text{controls}} / n_{\text{controls}}$$

$$= 849/158$$

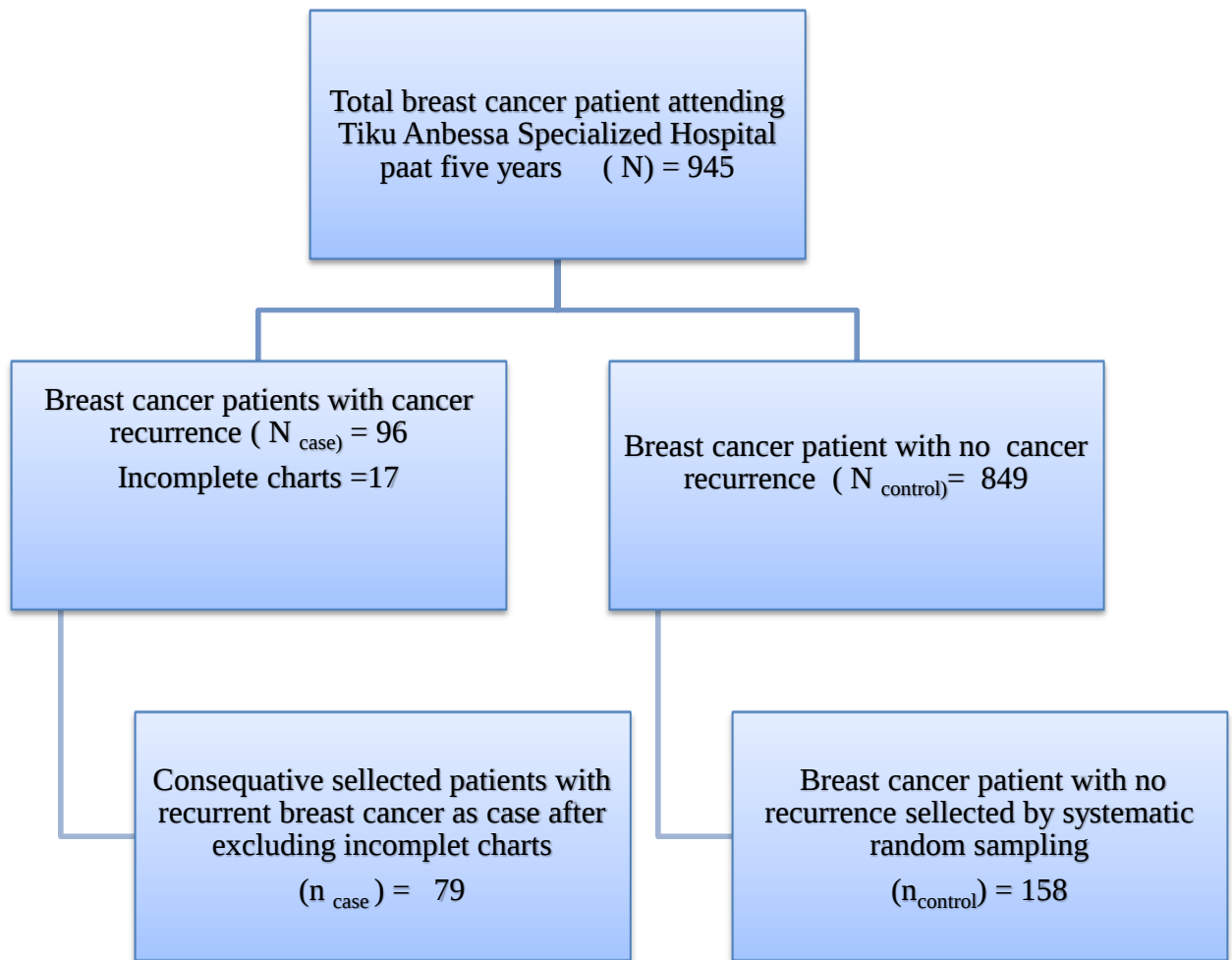
$$K = 5$$

Where:

K= sampling interval (every 5<sup>th</sup> patient is selected)

$N_{\text{control}}$  = Number of patients with no recurrent breast cancer

$n_{\text{control}}$  =total number of controls ( sample size of controls)



**Fig 2:** Flow chart for selection of case and controls among breast cancer patients attending Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, 2025.

## 4.6. Data Collection Tools and Procedures

### 4.6.1 Data Collection Tools

A questionnaire was developed after reviewing different relevant literatures (5,9, 11, 14, 15, 18 and 20) and structured questionnaire was used for data extraction from patients chart. It has four parts. Part I: socio-demographic characteristics (age, sex, Family history of breast cancer parity and co morbidity). Part II: Histo pathologic related determinants ( duration of illness, size of tumor, stage of disease, tumor nuclear grade, surgical margin, lypho vascular invasion,

number of positive lymph nodes, lymph node ratio, histological sub type and presence of carcinoma in situ) Part III: Treatment related factors (Type of surgery, Chemotherapy, Radiotherapy, hormonal therapy, and targeted therapy and duration of follow up). Part IV: immune biologic factors (Hormone receptor status, HER 2+, Triple negative and Ki67 level).

#### **4. 6. 2 Data Collection Technique**

Two trained BSc nurses were recruited to collect data and supervised by investigator. Data was collected from patients chart by using data extraction structured questionnaire to obtain information on socio-demographic characteristics, Histo pathologic related factors, treatment related factors and immune biologic factors.

### **4.7. Study variables**

#### **4.7.1. Dependent variables**

- Recurrent breast cancer ( case(1), Control (0))

#### **4.7.2. Independent variables**

- **Socio-demographic characteristics** (age, sex, Family history of breast cancer, place of residency, parity, duration of illness, Indication of surgery and co morbidities).
- **Histo pathologic related factors** (size of tumor, stage of disease, tumor grade, surgical margin, lympho- vascular invasion, Number of LN identified, number of positive lymph nodes, lymph node ratio, histological sub type and presence of carcinoma in situ)
- **Treatment related factors** (Type of surgery, Chemotherapy, Radiotherapy, hormonal therapy, immunotherapy).
- **Immune biologic factors** (Hormone receptor status, HER 2+, Triple negative and Ki67 level).

### **4.8. Operational definitions**

- **Breast cancer recurrence:** relapse of cancer after completion of treatment that is confirmed by imaging or histo pathologic study

- **Loco- regional recurrence:** breast cancer recurrence at chest wall surgical scar and/or axillary lymph nodes
- **Unknown family history of cancer** – when family history is either not documented or the patient did not know.
- **Incomplete Chart:** Charts with no Biopsy results and Immunohistochemical test

## 4.9. Data quality control

Data collection tool was prepared from different literature reviewed and modified to local context in English version. One day training was given for data collectors and supervisors on data collection tools and procedure. Supervisors monitored the data collection process daily. The collected data were reviewed and checked for consistency, clarity and completeness throughout the data collection process by investigator.

## 4.10. Data Processing and Analysis

The collected data was checked for its completeness, consistency and accuracy before analysis. Data were entered in to Epi-data version 3.1 statistical software and exported to SPSS version 25 for further analysis. Descriptive statistics like frequencies, percentages, mean, and standard division were calculated. Bi-variable and multivariable analyses were done using binary logistic regression model to examine determinants of breast cancer recurrence. Bi-variable logistic regression analysis was conducted to see the association of each independent variable to the outcome variable and variables with p-values of  $<0.25$  were entered into the multivariable logistic regression analysis. The multivariable analysis was done to examine the individual association that each explanatory variable has on breast cancer recurrence after adjusting for other variables that entered into the multivariable model. The presence of multi-co linearity between independent variables was checked using variance inflation factor (VIF)  $< 10$  assumptions of no multi-co linearity and the maximum final result was 8.42. Logistic regression assumption were checked with Analysis of Variance (ANOVA) Sum of squares= 17.025, df=27, P- value= 0.001, co linearity tolerance all  $> 0.1$ , skewness between -3 and + 3 and kurtosis between -10 and + 10 the data fulfill all the regression assumption. The Hosmer-Lemeshow goodness of fit test was used to assess the fitness of the model and the final model was fit at  $\text{Chi-X}^2 = 3.09$ , P- value = 0.929 and df= 8.

| <b>Model Summary</b> |                      |                      |                     |
|----------------------|----------------------|----------------------|---------------------|
| Step                 | -2 Log likelihood    | Cox & Snell R Square | Nagelkerke R Square |
| 1                    | 160.883 <sup>a</sup> | .381                 | .520                |

Adjusted Odd ratio with 95% Confidence Interval and p-value < 0.05 were reported to declare significant determinants of breast cancer recurrence. The results were presented by texts, and tables.

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#### **4.11 Ethical Considerations**

First the study was approved by Ethical Review Board (ERB) of Addis Ababa University College of Health Science to conduct the study. Then officials at different levels of the hospital were communicated through cooperation letter written from the post graduate coordinator. The responsible bodies at the hospital were informed about the purpose of the study. All charts of the participants were identified, kept confidential in secure place.

#### **4.12 Dissemination Plan**

The final result of the study will be presented to Addis Ababa University, College of health sciences department of surgery. The result and recommendation of the study will be submitted to Addis Ababa University in hard copy and also presented to the other concerned stakeholders. Finally, the finding of the study will be published on internationally reputable journals.

## 5. Results

### 5.1. Socio Demographic Characteristics of the Study Participants

A total of 237 (79 cases and 158 controls) participants were involved in this study with a response rate of 100%. Seventy seven (97.5%) of cases and hundred fifty (94.9%) of controls were female. The mean age of cases and controls were 46.2 (SD  $\pm$  13.3) and 48.5 (SD  $\pm$  12.9) years respectively. Forty one (51.9%) of cases and sixty six (41.8%) of control were urban dwellers. Sixteen (20.3%) of cases and seven (4.5%) of controls had identified family history of breast cancer. Twenty eight (36.4%) of cases and fifty four (36.0%) of controls female participants were nulliparous (Table 2).

**Table 2: Socio-demographic characteristics of breast cancer patients who were attending Addis Ababa University Tikur Anbessa Specialized Hospital, Addis Ababa Ethiopia, 2025**

| Variables                           | Case(n=79)    | Controls(n=158) |
|-------------------------------------|---------------|-----------------|
|                                     | Frequency (%) | Frequency (%)   |
| Sex                                 |               |                 |
| Male                                | 2(2.5)        | 8(5.1)          |
| Female                              | 77(97.5)      | 150(94.9)       |
| Place of Residency                  |               |                 |
| Urban                               | 41(51.9)      | 66(41.8)        |
| Rural                               | 38(48.1)      | 92(58.2)        |
| Any family history of breast cancer |               |                 |
| Yes                                 | 16(20.3)      | 7(4.5)          |
| No                                  | 39(49.4)      | 95(60.1)        |
| Unknown                             | 24(30.3)      | 56(35.4)        |
| Parity if Female                    |               |                 |
| Null Parous                         | 28( 36.4)     | 54(36.0)        |
| Parous                              | 49(63.6)      | 96(64.0)        |
| Co morbidity                        |               |                 |
| Yes                                 | 16(20.3)      | 36(22.8)        |

|                       |          |           |
|-----------------------|----------|-----------|
| No                    | 63(79.7) | 122(77.2) |
| Types of co morbidity |          |           |
| Diabetes mellitus     | 5(31.3)  | 9(25.0)   |
| Hypertension          | 6(37.5)  | 19(52.8)  |
| Chronic lung disease  | 2(12.5)  | 2(5.6)    |
| Others                | 3(18.8)  | 6(16.7)   |

## 5.2. Histo-pathologic Related Determinants of Breast Cancer

### Recurrence

The mean duration of illness were 7.8 (SD  $\pm$  4.3) months for case and 6.3 (SD  $\pm$  4.2) months for control respectively. Almost all of the case 74(93.7%) and controls 148 (93.7%) had invasive carcinoma type. The average size of tumor was 5.4(SD  $\pm$  1.6) cm in case and 3.9(SD  $\pm$  1.8) cm in controls. Majority of case (57.9%) had higher tumor nuclear grade but almost halve (52.5%) of controls had grade II tumor nuclear grade. Thirteen (16.5%) of case and only five (3.2%) of controls had positive surgical margin. Fifty nine (74.7%) of case and sixty one (38.6%) of controls had lympho vascular tumor invasion. Most of both case and control were with non special type of tumor histology. Majority of the case sixty three (73.4%) had stage three pathologic stage of tumor but only sixty six (41.8%) of controls had stage three tumor (table 3).

**Table 3: Histo pathologic related determinants of breast cancer recurrence among breast cancer patients attending Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, 2025**

| Variables                | Case(n=79)    | Controls(n=158) |
|--------------------------|---------------|-----------------|
|                          | Frequency (%) | Frequency (%)   |
| Type of carcinoma        |               |                 |
| Carcinoma <i>in situ</i> | 5(6.3)        | 10(6.3)         |
| Invasive carcinoma       | 74(93.7)      | 148(93.7)       |
| Tumors Nuclear grade     |               |                 |
| Grade I                  | 5(6.3)        | 49(31.0)        |

|                                              |                 |                |
|----------------------------------------------|-----------------|----------------|
| Grade II                                     | 30(37.9)        | 83(52.5)       |
| Grade III                                    | 44(55.7)        | 26(16.5)       |
| Surgical Margin Status                       |                 |                |
| Negative                                     | 66(83.5)        | 153(96.8)      |
| Positive                                     | 13(16.5)        | 5(3.2)         |
| Lympho-vascular invasion present             |                 |                |
| Yes                                          | 59(74.7)        | 61(38.6)       |
| No                                           | 20(25.3)        | 97(61.4)       |
| Axillary lymph node identified               |                 |                |
| Yes                                          | 72(91.1)        | 121(76.6)      |
| No                                           | 7(8.9)          | 37(23.4)       |
| Number of positive LN                        |                 |                |
| Mean $\pm$ SD                                | 6.3 $\pm$ 3.03  | 3.6 $\pm$ 3.6  |
| Lymph Node ratio( Positive LN/Total)         |                 |                |
| Mean $\pm$ SD                                | 0.62 $\pm$ 0.27 | 0.4 $\pm$ 0.36 |
| Histo Pathologic sub type of final pathology |                 |                |
| No Special type (NST)                        | 53( 67.1)       | 83(52.5)       |
| Lobular                                      | 18(22.8)        | 36(22.7)       |
| Medullary                                    | 5(6.3)          | 15(9.5)        |
| Mucinous                                     | 3(3.8)          | 20(12.7)       |
| Inflammatory                                 | 0(0.0)          | 2(1.3)         |
| Others                                       | 0(0.0)          | 2(1.3)         |
| Carcinoma in situ Present                    |                 |                |
| Yes                                          | 7(8.9)          | 11(7.0)        |
| No                                           | 72(91.1)        | 147(93.0)      |
| Pathological Stage of Disease                |                 |                |
| Zero                                         | 5(6.3)          | 10(6.3)        |
| Stage I                                      | 6(7.6)          | 21(13.3)       |
| Stage II                                     | 10(12.7)        | 61(38.6)       |
| Stage III                                    | 58(73.4)        | 66(41.8)       |

### 5.3. Treatment Related Determinants of Breast Cancer Recurrence

Majority of the case sixty nine (87.3%) and control hundred thirty four (84.8%) underwent modified radical mastectomy. Only few of cases six (7.6%) and controls eighteen (11.4%) have taken neo adjuvant chemotherapy. Most of cases seventy four (93.7%) and control hundred fifty one (95.6%) have taken adjuvant chemotherapy. Among the study participants twenty three (29.1%) of case and twenty eight (17.7%) of controls received radiotherapy. Sixty five (82.3%) of case and hundred forty three (90.5%) of controls have taken hormonal therapy. Both cases 31.8(SD  $\pm$  11.5) and controls 30.1(SD  $\pm$  11.2) had comparable durations of follow up post surgical intervention. (table 4).

**Table 4: Treatment related determinants of breast cancer recurrence among breast cancer patients attending Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia,2025**

| Variables                 | Case(n=79)    | Controls(n=158) |
|---------------------------|---------------|-----------------|
|                           | Frequency (%) | Frequency (%)   |
| Type of Surgery           |               |                 |
| BCS + ALND                | 2(2.5)        | 6(3.8)          |
| MRM                       | 69(87.4)      | 134(84.8)       |
| Simple Mastectomy         | 8(10.1)       | 18(11.4)        |
| Neo adjuvant chemotherapy |               |                 |
| Yes                       | 6(7.6)        | 18(11.4)        |
| No                        | 73(92.4)      | 140(88.6)       |
| Adjuvant Chemotherapy     |               |                 |
| Yes                       | 74(93.7)      | 151(95.6)       |
| No                        | 5(6.3)        | 7(4.4)          |
| Radiotherapy              |               |                 |
| Yes                       | 23(29.1)      | 28(17.7)        |
| No                        | 56(70.9)      | 130(82.3)       |
| Hormonal therapy          |               |                 |

|                  |          |           |
|------------------|----------|-----------|
| Yes              | 65(82.3) | 143(90.5) |
| No               | 14(17.7) | 15(9.5)   |
| Targeted therapy |          |           |
| Yes              | 8(10.1)  | 6(3.8)    |
| No               | 71(89.9) | 152(96.2) |

#### 5.4. Immuno Biological determinants of Breast Cancer Recurrence

Majority of the cases sixty four (81%) and controls hundred forty eight (93.7%) had estrogen receptor positive tumor. Similarly, most of the cases fifty six (70.8%) and controls hundred thirty seven (86.7%) developed progesterone positive malignancy. Fewer number of cases fourteen (17.7%) and controls twenty seven (17.1%) developed human epidermal receptor 2 (HER 2) positive breast cancer. Majority of the cases sixty three (79.7%) and controls hundred forty (88.6%) KI-67 level was not determined. Only fewer number of cases twelve (15.2%) and controls eight (5.1%) were triple negative cancer. (Table 5).

**Table 5 : Immuno biological determinants of breast cancer recurrence among breast cancer patients attending Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia,2025.**

| Variables                  | Case(n=79)    | Controls(n=158) |
|----------------------------|---------------|-----------------|
|                            | Frequency (%) | Frequency (%)   |
| Estrogen receptor positive |               |                 |
| Yes                        | 64(81.0)      | 148(93.7)       |
| No                         | 15(19.0)      | 10(6.3)         |
| Progesterone positive      |               |                 |
| Yes                        | 56(70.9)      | 137(86.7)       |
| No                         | 23(29.1)      | 21(13.3)        |
| HER 2 Positive             |               |                 |
| Yes                        | 14(17.7)      | 27(17.1)        |
| No                         | 60(75.9)      | 124(78.5)       |
| Unknown                    | 5(6.3)        | 7(4.1)          |

|                           |          |           |
|---------------------------|----------|-----------|
| KI-67 Level               |          |           |
| Less than or equal to 14% | 4(5.1)   | 4(2.5)    |
| Greater than 14%          | 12(15.2) | 14(8.9)   |
| Unknown                   | 63(79.7) | 140(88.6) |
| Triple Negative           |          |           |
| Yes                       | 12(15.2) | 8(5.1)    |
| No                        | 67(84.8) | 150(94.9) |

### **5.5. Bivariate and Multivariate Analysis of determinants of breast cancer recurrence among breast cancer patients attending Tikur Anbessa Specialized Hospital.**

Bivariate, logistic regression analysis was performed for each independent variables included in the study to identify the relationship of individual independent variable with the dependent variable.

Variables with p-value < 0.25 that were included in multivariable analysis include age of patient, place of residency, family history of breast cancer, duration of illness, type of carcinoma, size of tumor, tumor nuclear grade, surgical margin, lympho vascular invasion, number of positive axillary lymph node, lymph node ratio, pathologic stage, radiotherapy, hormonal therapy, presence of estrogen receptor, progesterone receptor and triple negative.

Those variables included in multivariate logistic regression analysis with significant p- value and adjusted odd ratio are described as follow. The odds of developing breast cancer recurrence was (AOR=0.17, 95% CI: 0.03, 0.08) 83% less likely among patients with no family history of breast cancer as compared to those patients with family history of breast cancer. The odds of developing breast cancer recurrence was (AOR= 0.76, 95% CI: 0.60, 0.96) 24% less likely as tumor size decreases by one centimeter. Those breast cancer patients with nuclear grade II tumor were 8.6 times (AOR= 8.6, 95%CI: 1.94, 38.19) more likely to develop breast cancer recurrence as compared to those with nuclear grade I tumor, as well as those with nuclear grade III were 3.4 times (AOR= 3.4, 95% CI: 1.49, 7.71) times more likely to develop recurrence as compared to those with nuclear grade I tumor. The odd of developing breast cancer recurrence

was 4.4 times (AOR= 4.4, 95% CI: 1.05, 38.6) more likely among surgical margin positive breast cancer patients, as compared to margin negative patients. The odd of breast cancer recurrence was 2.3 times (AOR= 2.3, 95 % CI: 1.02, 5.34) more likely to develop among cancer with lympho vascular invasion as compared to those with no lympho vascular invasion.

The odd of breast cancer recurrence among patients with estrogen negative tumor were 5.7 times (AOR= 5.7, 95%CI: 1.51, 21.5) more likely to develop as compared to those patients with estrogen receptor positive cancer. (Table 7)

**Table 6: Multivariate logistic regression analysis depicting the association between independent variables and breast cancer recurrence among breast cancer patients attending Tikur Anbessa Specialized Hospital (N=237), 2025.**

| Variables                        | Case (n=79)     | Control (n=158) | COR(95%CI)      | AOR(95%CI)       | P-value |
|----------------------------------|-----------------|-----------------|-----------------|------------------|---------|
| Place of residency               |                 |                 |                 |                  |         |
| Urban                            | 41(51.9)        | 66(41.8)        | 1.5(0.87,2.58)  | 0.54(0.23,1.23)  | 0.144   |
| Rural                            | 38(48.1)        | 92(58.2)        | 1               | 1                |         |
| Age                              |                 |                 |                 |                  |         |
| Mean $\pm$ SD                    | 46.2 $\pm$ 13.3 | 48.5 $\pm$ 12.9 | 1.1(0.99,1.03)  | 1.02(0.98,1.05)  | 0.284   |
| Family Hx                        |                 |                 |                 |                  |         |
| Yes                              | 16(20.3)        | 7(4.5)          | 1               | 1                |         |
| No                               | 39(49.4)        | 95(60.1)        | 0.18(0.06,0.51) | 0.17(0.03,0.80)  | 0.026*  |
| Unknown                          | 24(30.3)        | 56(35.4)        | 1.04(0.56,1.91) | 1.02(0.45,2.32)  | 0.956   |
| Duration of illness              |                 |                 |                 |                  |         |
| Mean $\pm$ SD                    | 7.8 $\pm$ 4.3   | 6.3 $\pm$ 4.2   | 0.9(0.86, 0.98) | 0.91(0.82,1.01)  | 0.087   |
| Type of carcinoma                |                 |                 |                 |                  |         |
| DCIS                             | 3(3.8)          | 14(8.9)         | 1               | 1                |         |
| Invasive carcinoma               | 76(96.2)        | 144(91.1)       | 0.4(0.11, 1.45) | 1.46(0.05,38.19) | 0.819   |
| Size of tumor                    |                 |                 |                 |                  |         |
| Mean $\pm$ SD                    | 5.4 $\pm$ 1.6   | 3.9 $\pm$ 1.8   | 0.6(0.54,0.76)  | 0.76(0.60,0.96)  | 0.022*  |
| Tumor nuclear grade              |                 |                 |                 |                  |         |
| Grade I                          | 5(6.3)          | 49(31.0)        | 1               | 1                |         |
| Grade II                         | 30(37.9)        | 83(52.5)        | 16(5.86,46.9)   | 8.6(1.94,38.16)  | 0.005*  |
| Grade III                        | 44(55.7)        | 26(16.5)        | 4.6(2.46, 8.87) | 3.4(1.49,7.71)   | 0.004*  |
| Surgical Margin                  |                 |                 |                 |                  |         |
| Negative                         | 66(83.5)        | 153(96.8)       | 1               | 1                |         |
| Positive                         | 13(16.5)        | 5(3.2)          | 6.0(2.06,17.59) | 4.4(1.05,18.6)   | 0.042*  |
| Lympho vascular invasion present |                 |                 |                 |                  |         |
| Yes                              | 59(74.7)        | 61(38.6)        | 4.6(2.57,8.54)  | 2.3(1.02,5.34)   | 0.045*  |
| No                               | 20(25.3)        | 97(61.4)        | 1               | 1                |         |

|                                |                |                |                  |                 |        |
|--------------------------------|----------------|----------------|------------------|-----------------|--------|
| Number of positive LN          |                |                |                  |                 |        |
| Mean $\pm$ SD                  | 6.3 $\pm$ 3.03 | 3.6 $\pm$ 3.6  | 0.8(0.72,0.87)   | 0.9(0.81,1.01)  | 0.07   |
| LN ratio ( positive LN/ Total) |                |                |                  |                 |        |
| Mean $\pm$ SD                  | 0.6 $\pm$ 0.27 | 0.4 $\pm$ 0.36 | 0.14(0.05,0.34)  | 0.75(0.13,4.26) | 0.751  |
| Pathologic stage               |                |                |                  |                 |        |
| Stage zero                     | 5(6.3)         | 10(6.3)        | 1.7(0.57,5.44)   | 8.3(0.49,142.4) | 0.141  |
| Stage I                        | 6(7.6)         | 21(13.3)       | 3.1(1.16,8.14)   | 9.1(0.93,89.1)  | 0.057  |
| Stage II                       | 10(12.7)       | 61(38.6)       | 5.3(2.51, 11.41) | 5.2(0.54,51.1)  | 0.151  |
| Stage III                      | 58(73.4)       | 66(41.8)       | 1                | 1               |        |
| Radiotherapy                   |                |                |                  |                 |        |
| Yes                            | 23(29.1)       | 28(17.7)       | 1.9(1.01, 3.59)  | 1.04(0.35,3.11) | 0.937  |
| No                             | 56(70.9)       | 130(82.3)      | 1                | 1               |        |
| Hormonal therapy               |                |                |                  |                 |        |
| Yes                            | 65(82.3)       | 143(90.5)      | 0.48(0.22, 1.06) | 0.42(0.39,4.57) | 0.478  |
| No                             | 14(17.7)       | 15(9.5)        | 1                |                 |        |
| Estrogen receptor              |                |                |                  |                 |        |
| Yes                            | 64(81)         | 148(93.7)      | 1                | 1               |        |
| No                             | 15(19)         | 10(6.3)        | 3.46(1.48,8.13)  | 5.7(1.51,21.5)  | 0.010* |
| Progesterone receptor          |                |                |                  |                 |        |
| Yes                            | 56(70.9)       | 137(86.7)      | 0.37(0.19,0.72)  | 1.24(0.33,4.63) | 0.744  |
| No                             | 23(29.1)       | 21(13.3)       | 1                | 1               |        |
| Triple Negative                |                |                |                  |                 |        |
| Yes                            | 12(15.2)       | 8(5.1)         | 0.29(0.11,0.76)  | 0.52(0.01,40.4) | 0.773  |
| No                             | 67(84.8)       | 150(94.9)      | 1                | 1               |        |

\* Significant at P< 0.05, COR( Crude Odd Ratio)AOR(Adjusted Odds Ratio), CI=confidence interval, 1= reference

## 6. Discussion

The aim of the study was to identify the determinants of breast cancer recurrence among breast cancer patients attending Addis Ababa University Tikur Anbessa Specialized Hospital Addis Ababa, Ethiopia. After performing multivariate analysis different determinants of breast cancer recurrence were identified.

In this study odd of developing breast cancer recurrence in patients with no family history of breast cancer were 83% less likely to develop recurrence than those with family history of breast cancer. This finding is consistent with study done in Morocco on risk factors for breast cancer recurrence and book on pathology of breast diseases (16, 24), but other study conducted on breast cancer recurrence did not reveal the significance of family history on cancer recurrence (4). Positive family history of breast cancer might be associated with germ line mutation and development of more aggressive breast cancer in younger age which pre disposes to recurrent breast cancer when compared to those with no family history of breast cancer. In addition those patients with family history of breast cancer are more likely to have hormone receptor negative cancer that affect long term hormonal treatment to prevent recurrence and the family may also have common long term environmental exposure as well socio cultural practice that may increase risk of cancer development in breast cells remnant post treatment.

The study indicated that the odd of developing breast cancer recurrence is 24% less likely to occur as the size of primary tumor decrease by one centimeter. This shows that as the size of tumor increase it is more likely to develop recurrence. This result is in line with multiple studies conducted on factors related to breast cancer recurrence in India, Netherland, Switzerland, France and Iran (2, 7, 12, 13, and 14). This could be due to the primary size of the tumor that is important predictor of stage of the disease and tumor cell burden in the body. Similarly as the size increases micro metastasis to the regional and distant site is common. In this study the mean size of tumor in patients with recurrent disease were higher than the mean size in those with no recurrent breast cancer. In addition to the above, the size of the tumor can also determine the modality of treatment that may decreases the risk of recurrence so as the size of tumor increases more aggressive treatment will be provided .

The study found that those breast cancer patients with nuclear grade II tumor were 8.6 times more likely to develop breast cancer recurrence as compared to those with nuclear grade I tumor, as well as those with nuclear grade III were 3.4 times more likely to develop recurrence as compared to those with nuclear grade I tumor. This finding is consistent with study conducted in National university of Ireland (15), Mohammed V university hospital of Morocco (16), Aarhus University Hospital of Denmark (22) and University of Bordeaux, France (25). It may be due to poorly differentiated tumor histology that lead to aggressive nature of the tumor and more resistant to treatment modalities. Additionally, higher tumor nuclear grade is associated with more hormone receptor negative cancer which affects long term hormonal treatment for prevention of breast cancer recurrence (26)

As identified in this study the odd of developing breast cancer recurrence in patients with positive surgical margin is 4.4 times more likely than those patients with negative surgical margin. The finding of this study is similar to study done in South Africa on risk factors associated with breast cancer recurrence and study performed in USA on risk of recurrence in patient with HER2+ early stage breast cancer (4, 11). This is due to the fact that in the presence of gross or microscopic positive margin the risk of recurrence is high because the remaining tumor cell will continue its proliferation and cell growth which leads to local recurrence as well as dissemination to distant organ. In addition to this in the presence of positive margin adjuvant chemotherapy, hormonal and radiotherapy are not as effective as in patient with negative surgical margin.

According to this study the likelihood of breast cancer recurrence among patients with lympho vascular invasive breast cancer is 2.3 times more likely when compared to those patients with no lympho vascular invasive tumor. This finding is in line with multiple studies conducted in different countries like, university of Bordeaux, France and Morocco university hospital (13, 16). Breast cancer with lympho vascular invasion has higher risk of recurrence. This might be due to aggressive nature of tumor with this histopathology characteristic. Additionally, these tumors have micro metastasis to loco regional organs due to their access to lymphatic or blood vessels. It is an independent prognostic factor in breast cancer recurrence irrespective of axillary node metastasis and molecular subtypes (27)

This study identified that the odd of developing breast cancer recurrence in patient with estrogen receptor negative tumor is 5.7 times more likely than those patients with estrogen receptor positive breast cancer. The finding is concordant with studies conducted on breast cancer recurrence in South Korea, France and Morocco. This could be due to aggressive nature of hormone negative cancer and inability to treat with hormone receptor antagonist as adjuvant treatment to prevent recurrence. But study performed in Aarhus University Hospital in Denmark showed that hormone receptor positivity is significantly associated with breast cancer recurrence than hormone receptor negative cancer. Similarly this study also indicated that triple negative breast cancer is more likely associated with breast cancer recurrence in bivariate logistic regression analysis but it was not found to be significant in multivariate logistic regression analysis.

## **7. Strength and Limitation of the Study**

### **7. 1. Strength of the Study**

Strength of this study is that, cases and controls were selected from same source population (controls were selected from the hospital that yielded the cases) and as a result, cases and controls were comparable. The first case control study in Tikur Anbessa Specialized Hospital on the topic.

### **7.2 Limitation of the Study**

Despite the authors' efforts to create a more representative sample by carefully identifying the study population and selecting the appropriate comparison, there may be un identified distant metastasis, detailed family member affected not known.Generalization to the country level not possible.

## **8. Conclusion and Recommendation**

### **8.1. Conclusion**

This study identified several determinants of breast cancer recurrence among breast cancer patients attending Addis Ababa University Tikur Anbessa Specialized Hospital. Family history of breast cancer, tumor size, Higher nuclear grade tumor, positive surgical margin, presences of lympho vascular invasion and estrogen receptor negative tumor were identified to be the determinants of breast cancer recurrence..

### **8.2. Recommendations**

Based on the study finding the following recommendations are made.

#### **Health Ministry**

As breast cancer is the most common cancer in female and leading cause of cancer related death as well as patients with recurrence were exposed to more toxic and costly treatment, breast cancer screening and early treatment should be established in the country.

#### **Hospital under study**

Encourage front-line health care providers to give health education on determinant of breast cancer recurrence, proved with complete surgical margin, provide radiotherapy, targeted therapy and hormonal therapy without interruption and long waiting time. The hospital should improve recording complete patient's data in patient folder (clinical, pathological, imaging and treatment information) appropriately.

#### **Researchers**

Future researches should be done on long term survival and recurrence free survival of patients with breast cancer.

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## Information sheet

**Name of Investigator:** Tadesse Ejeta ( Endocrine and Breast Surgery Fellow)

**Name of Organization:** Addis Ababa University College of Medicine and Health Sciences  
Department of surgery unit of Endocrine and Breast surgery.

**Introduction:** This information sheet is developed by principal investigator with the aim to study determinants of breast cancer recurrence among patients operated for breast cancer in Tikur Anbessa Specialized Hospital from June 1, 2019 – June 31, 2024.

**Purpose of the research project:** to assess determinants of breast cancer recurrence among patients operated for breast cancer in Tikur Anbessa Specialized Hospital from June 1, 2019 – June 31, 2024.

**Procedure:** This study will be conducted mainly on determinants of breast cancer recurrence among patients operated for breast cancer in Tikur Anbessa Specialized Hospital. Before the study is conducted ethical clearance will be obtained from Addis Ababa University College of medicine and health science IRB and permission letter from the hospital administration.

**Risk or discomfort:** By conducting this study there is no harm as the study involves only the charts of operated breast cancer patients in the past five years. The information collected will be kept confidentially throughout the study.

**Benefits:** there is no direct benefit for the patient but by identifying the determinants of breast cancer recurrence will improve treatment of the patients.

**Incentive:** there will be no incentive to be paid for the patients for using the chart of them for the study

**Confidentiality and anonymity:** the information we collect for this study will be kept confidential and the data collected will be stored without patient name.

# Appendix 1

Addis Ababa University

College of Medicine and Health Sciences

Department of Surgery units of Endocrine and Breast surgery

Determinants of breast cancer recurrence among breast cancer patients operated in Tikur Anbessa Specialized Hospital from June 2019- June 2024

## Introduction

This data extraction questionnaire is developed from different related literatures for extraction of data from charts of operated breast cancer patients in Tikur Anbessa Specialized Hospital in the past five years to assess determinants of breast cancer recurrence. The collected data will be kept confidentially and used only for the purpose of the study.

Name of data collector \_\_\_\_\_ Date of interview \_\_\_\_\_ code \_\_\_\_\_

## 1. Check list for socio demographic determinants

| Sr. No | Questionnaire                            |                                                                                                       | Remark |
|--------|------------------------------------------|-------------------------------------------------------------------------------------------------------|--------|
| 101    | Age in years _____                       |                                                                                                       |        |
| 102    | Sex                                      | 1. Male<br>2. Female                                                                                  |        |
| 103    | Place of residency                       | 1. Urban<br>2. Rural                                                                                  |        |
| 104    | Any family history of breast cancer      | 1. Yes<br>2. No<br>3. Unknown                                                                         |        |
| 105    | Parity if female                         | 1. Null parous<br>2. Parous                                                                           |        |
| 106    | Duration of illness (months)             | _____                                                                                                 |        |
| 107    | Type of carcinoma                        | 1. Ductal carcinoma insitu<br>2. Invasive carcinoma                                                   |        |
| 108    | Co morbid illness                        | 1. Yes<br>2. No                                                                                       |        |
| 109    | If yes to question 207 what co morbidity | 1. Diabetes Mellitus<br>2. Hypertension<br>3. Cardiac illness<br>4. Chronic lung disease<br>5. Others |        |

## 2. Check list on Histo pathologic Determinants

|     |                                       |                                                                                    |                         |
|-----|---------------------------------------|------------------------------------------------------------------------------------|-------------------------|
| 201 | Size of tumor in CM                   | _____                                                                              |                         |
| 202 | Clinical stage of the disease         | 1. Zero<br>2. I<br>3. II<br>4. III<br>5. IV                                        |                         |
| 203 | Tumor nuclear grade                   | 1. Grade 1<br>2. Grade 2<br>3. Grade 3                                             |                         |
| 204 | Surgical margin                       | 1. Negative<br>2. Positive<br>3. Unknown                                           |                         |
| 205 | Lymphovascular invasion               | 1. Yes<br>2. No                                                                    |                         |
| 206 | Axillary LN identified                | 1. Yes<br>2. No                                                                    | If no skip to ques .208 |
| 207 | If yes to Q206 How many LN identified | _____                                                                              |                         |
| 208 | If yes to Q206 How many positive LN   | _____                                                                              |                         |
| 209 | LN ratio ( LN+/LN total               | _____                                                                              |                         |
| 210 | Histological Sub type                 | 1. NST<br>2. Lobular<br>3. Medullar<br>4. Mucinous<br>5. Inflammatory<br>6. Others |                         |
| 211 | Carcinoma insitu                      | 1. Yes<br>2. No                                                                    |                         |
| 212 | Pathologic stage of the tumor         | 1. Zero<br>2. I<br>3. II<br>4. III                                                 |                         |

### 3. Check list for Treatment Related Factors

|     |                                                 |                                                               |  |
|-----|-------------------------------------------------|---------------------------------------------------------------|--|
| 301 | Type of surgery                                 | 1. BCS+ ALND<br>2. MRM<br>3. Simple Mastectomy<br>4. BCS only |  |
| 302 | Duration of post surgery follow up ( in months) | _____                                                         |  |
| 303 | Neo adjuvant Chemotherapy                       | 1. Yes<br>2. No                                               |  |
| 304 | Adjuvant Chemotherapy                           | 1. Yes<br>2. No                                               |  |
| 305 | Radiotherapy                                    | 1. Yes<br>2. Yes                                              |  |
| 306 | Hormonal therapy                                | 1. Yes<br>2. No                                               |  |
| 307 | Targeted therapy                                | 1. Yes<br>2. No                                               |  |

### 4. Check list for Immune Biologic related factors

|     |                                |                               |  |
|-----|--------------------------------|-------------------------------|--|
| 401 | Estrogen receptor positive     | 1. Yes<br>2. No<br>3. Unknown |  |
| 402 | Progesterone receptor positive | 1. Yes<br>2. No<br>3. Unknown |  |
| 403 | HER 2 positive                 | 1. Yes<br>2. No               |  |
| 404 | Ki-67 Level                    | 1. < 14%<br>2. <u>≥</u> 14%   |  |
| 405 | Triple negative                | 1. Yes<br>2. No               |  |