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Assessment of comorbidities and associated factors among breast cancer patients at Tikur Anbesa Hospital, Ethiopia, 2017:

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Assurance of Principal Investigator

The undersigned agrees to accept responsibility for the scientific ethical and technical conduct of the research project and for provision of required progress reports per terms and conditions of the research publications office in effect at the time of grant is forwarded as the result of this application.

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Abbreviation and Acronym

ACE---------- Adult Comorbidity Evaluation

Adj OR---------- Adjusted Odds Ratio

Ca---------- Cancer

CHF---------- Congestive Heart Failure

CI---------- Confidence Interval

COR---------- Crude Odds Ratio

DM---------- Diabetes Mellitus

Dx---------- Diagnosis

HTN---------- Hypertension

ICD-9-CM---------- International Classification Disease, 9^{th} revision, Clinical Modification

LSBC---------- Late Stage Breast Cancer

M1---------- Cancer with Metastasis

NGO---------- Non-Governmental Organization

OR---------- Odds Ratio

PUD---------- Peptic Ulcer Disease

Rx---------- Treatment

SNNPRS---------- Southern Nations Nationalities of People Regional State

SSA---------- Sub Saharan Country

T1N0M0---------- T1 tumor, no lymph Nodes with Cancer and no Metastases

UN---------- United Nations

UNICEF---------- United Nations for Child Fund

USA----------United States of America

WHO----------World Health Organization

Abstract

Back ground: Breast cancer is the most common cancer in women worldwide. Approximately 1.7 million new cases were recorded globally in 2012, accounting for 25 percent of all new cases of cancer in women. Because of an increased vulnerability to breast cancer there is increasing comorbid conditions at the time of diagnosis. Comorbidity is an illness other than the principal diagnosis that influences the outcome of treatment. The number of comorbidities per individual patient ranged from none to 13.

Objective: To assess comorbidities and associated factors among breast cancer patients who have been treated and made follow up in Tikur Anbesa Hospital, Addis Ababa, Ethiopia

Methods: A facility based cross-sectional study design was employed among a total of 404 randomly selected breast cancer patients who had follow up in Tikur Anbesa Referral Hospital. Every other patient who came for follows ups were interviewed and their charts were tracked and reviewed to assess comorbidities following their interview. The interview was done immediately following their medical checkup and the sequences of the interview was based on their medical checkup. A semi structured questionnaire prepared in English and translated to Amharic language from June to August 2017 was employed. Frequency, cross tabulation, Logistic regression applied to calculate percentage, 95% CI and Odds Ratio with SPSS version 20.0 after cleaned and edited.

Result: In this study a total of 404 female breast cancer cases were assessed of which the mean and SD, age of the study participants was 43.5$\pm$7.8 years respectively. Of all study participants 322 (79.7 %) were have comorbidities. Fatty liver 48(11.9%), Neutropenia 43 (10.6%), Gastritis/PUD 34 (8.4%), Anemia 31 (7.7%) were top listed or more prevalent comorbidities in the first and second follow up times. Participants who were not under radiation treatment were 0.37 times less odds to develop comorbidity than under those who were under radiation treatment, OR 0.37, 95% CI (0.19-0.72) and those who did not get hormone treatment were 0.26 times less chance than those who got hormone treatment, OR 0.26, 95% CI (0.16-0.74).

Conclusion and Recommendation: Large number of breast cancer patients had comorbidities. Attention should be given during patient's diagnosis not to distract breast cancer and comorbidity one with the other, develop system to identify number of comorbidities which used to use the data for action and, Neutropenia, Fatty liver, Gastritis, Anemia were with the highest prevalent comorbidities especially during the first and second follow up of the breast cancer patients so attention shall be given how to management of them.

1. Introduction

1.1. Background Information

Cancer is a group of diseases characterized by the uncontrolled growth and spread of abnormal cells. If the spread is not controlled, it can result in death (1). Comorbidity is an illness other than the principal diagnosis that influences the outcome of treatment (2). Breast cancer is the most common cancer in women worldwide. In such lower resource settings, breast cancers are commonly diagnosed at late stages, and women may receive inadequate treatment, pain relief, or palliative care (1).

Approximately 1.7 million new cases were recorded globally in 2012, accounting for 25 per cent of all new cases of cancer in women. It is the fifth most common cause of death from cancer in women (3).

It is expected that by 2020, 15 million new cases of cancer will occur every year in the world, one million of them in Africa (4). In Ethiopia, only recently has the government recognized the growing burden of cancer. The Federal Ministry of Health estimates that there could be more than 150,000 cancer cases in Ethiopia each year, but available data is limited. The Tikur Anbesa Hospital Oncology department July to September 2016 quarter report showed there were a total of 825 breast cancer cases. The hospital has been provided surgery, chemotherapy and radiation services for the patients (5). As the nation's sole cancer referral center, Tikur Anbesa Hospital is treating only about one percent of these patients. Health experts explain that many Ethiopians with cancer never seek medical treatment and, of those who do, they may not be referred to the cancer center in Addis Ababa (5).

The number of comorbidities per individual patient ranged from none to 13. The distribution of co-morbidities varied considerably by age group. Some co-morbidity characteristically occurs in middle age or earlier; others occur at older ages. Some co-morbidity may be etiologically related to the tumor, while others are age-related and chronic, but not necessarily disabling. The most prevalent condition in all age groups was hypertension. High severity heart disease affected less than 6% of patients aged 55 to 59 years, but increased to second or third in co morbidity prevalence for the 4 oldest age groups (16.4%, 22.6%, 32.5%, and 38.6% for age groups 70 to 74 years, 75 to 79 years, 80 to 84 years, and 85 years and older, respectively) (6).

1.2.Statement of the problem

Cancer caused over 8 million deaths worldwide in 2013 and has moved from the third leading cause of death in 1990 to the second leading cause behind cardiovascular disease in 2013. However, despite this progress, cancer burden is increasing owing to a growing and aging global population as well as risk factors like smoking, obesity, and dietary patterns (7).

Comorbid illness is a significant cause of death. This is particularly true for older patients with cancer, who comprise the majority of new cancers diagnosed concern in patients with cancer. For example, patients with severe underlying chronic obstructive pulmonary disease are not good candidates for resection of a lung malignancy, and therefore their chance of cure is decreased. Similarly, a diagnosis of congestive heart failure precludes some cancer treatments (8). Numerous studies have found that co morbidity's an independent predictor of survival in breast cancer patients (9).

Important questions remain the type and the magnitude of comorbidities, the patient characteristics related to the presence of comorbidities. Comorbidities do not get attention during the clinical diagnosis, treatment and follow up of the cancer patients. Those patients with comorbidities do not get special treatment. Patients with substantial comorbid disease are refusing or they are not being offered certain cancer treatments. Comorbid conditions that may be underrepresented in existing data sets because they are under-diagnosed by physicians in everyday practice or because they are not recorded in claims data, as with impaired functional status and self-reported health. There are not mechanisms or guidelines direct to assess comorbidities during cancer patient follow up. There may no effort particularly fruitful for older cancer patients, who often simultaneously have comorbid conditions, impaired functional status, and decreased social support as potential causes for poor outcomes (10).

Due to the presence of comorbidities, the complexities have influenced the cancer patient's preferences for the treatment and treatment outcomes(11). Unless comorbidity diagnosed and manage properly either they lead to miss diagnosis or limit the cancer treatment or both and vice versa ((12). In Ethiopia there is only one specialized hospital which manages all types of cancer cases and there were no reports as well as studies which show the magnitude of comorbidity, the type of comorbidity, common types of comorbidity and algorithm to diagnose and manage them in breast cancer patients. In breast cancer management center there is no guide line which helps to easily diagnose and manage comorbidity in breast cancer patients (verbal reports).

1.3. Significance of the study

The adverse consequences of comorbidity pose a major clinical challenge in the care of cancer patients. While the burden of comorbidity is clearly a major prognostic factor for long-term survival, the underlying mechanisms are not well understood. Health services research that focuses on specific comorbidities and their effects in a cancer patient's clinical trajectory (course) can produce new insights into the optimal diagnosis, treatment, and long-term surveillance of cancer patients with comorbid disease (10).

Evaluation of the comorbidity in an older person newly diagnosed with cancer and assessment of the severity of the various pre-existing conditions and their overall and individual impact on the cancer course are crucial to providing quality cancer care to individuals (13).

In Ethiopia, only recently has the government recognized the growing burden of cancer. There are few studies available which shows comorbidity for breast cancer patient but for Ethiopia comorbidity data as well as the for the overall cancer care data registration, reporting and filing yet under early stage. This study tries to show frequency of comorbidities, there relationship with different cases characteristics, comorbidity relationship with the breast tumor stage so can bring relevant information and end up with recommendations. This study result will also help as baseline for policy makers and other future study, to design appropriate intervention and also may help to develop research questions (5).

2. Literature Review

2.1.Breast Cancer

Breast cancer can occur more often than usual in some families because of their genetic make-up. This type of breast cancer is called hereditary breast cancer(14). In these cases, a mutated gene is passed from parent to child. This mutated gene increases the risk of developing breast cancer. About 5 to 10 percent of all breast cancers in the U.S. are thought to be hereditary. (15) . In the study showed that breast cancer is the leading contributor to cancer incidence among women in the United States. This tumor ranks second after lung cancer as a cause of cancer deaths among women. The brunt of this high number of breast cancer cases and deaths are borne by women in the postmenopausal period of life, defined here in as age 55 years and older(16). Two thirds of all newly diagnosed female breast cancer patients are in this age group (6) with nearly two thirds of all cancer diagnoses occurring in low and middle income countries (17).

The International Agency for Research on Cancer has estimated that the burden of breast cancer in sub-Saharan Africa in 2012 was approximately 100,000 occurrences per year and 49,000 deaths per year(18). This burden is projected to double between 2012 and 2030 due to population ageing and expansion. While breast cancer is, on average, a good-prognosis cancer in high-income countries, in SSA its prognosis is considerably lower. Excessive deaths due to breast cancer are reflected in high breast cancer mortality: incidence ratio of 0.50 in SSA in 2012, twice that of Western Europe (19).

A study done in seven areas of the world, a striking relation between age at first birth and breast cancer risk was observed. It is estimated that women having their first child when aged under 18 years have only about one-third the breast cancer risk of those whose first birth is delayed until the age of 35 years or more. The reduced risk of breast cancer in women having their first child at an early age explains the previously observed inverse relationship between total parity and breast cancer risk, since women having their first birth early tend to become ultimately of high parity (20) .

2.2.Types and prevalence of Comorbidities and its associated factors

Studies explained, Comorbidity was present in 68.7% of cancer patients, and 32.6% of these individuals had ≥2 comorbid conditions (21).

Comorbidity is an illness other than the principal diagnosis that influences the outcome of treatment. Much prior work on co-morbidity employs summary co-morbidity measures that attempt to assess the combined impact of different diseases. These summary measures can be divided into two groups: general measures intended for use in multiple disease populations, and disease-specific measures. The most commonly used general comorbidity measure is the Charlson Index (2,22).

It was developed to predict 1-year mortality in medical inpatients, and was subsequently validated in a population of breast cancer patients. Nineteen comorbid conditions are assigned weights of 1, 2, 3, or 6, based on the ratio of the mortality risk for patients with the comorbidity of interest versus the mortality risk for those without. The sum of the weights for all of the conditions is calculated to create a comorbidity index for each patient. Klabunde refined the Charlson Index by incorporating diagnostic and procedure data in physician Medicare claims, in a study predicting 2-year non-cancer mortality in cancer patients. Another example of a general comorbidity measure is the Adult Comorbidity Evaluation 27 (ACE-27), which requires the review of medical records to collect data on the presence and severity of 27 comorbid conditions in cancer patients (2).

Disease-specific comorbidity measures are developed and tested in a single disease population, and intended for use only in that disease. Several disease-specific comorbidity measures have been created for breast cancer, for example. One weakness of general measures is in the assumption that each constituent comorbidity in the measure has the same impact in different diseases and populations. One should expect that a general comorbidity measure will not explain as much variance in the outcome of interest as a disease-specific comorbidity measure could. In addition, general comorbidity measures may include conditions that actually arise as manifestations of the disease under study, rather than as independent comorbidities. For example, anemia, weight loss, pneumonia, and electrolyte disorders may all occur in the months before a diagnosis of certain cancers. This issue would normally be addressed in the design of disease-specific comorbidity measures (2).

The Charlson index, a widely-used measure of 19 comorbidities, was adapted for administrative data using ICD-9-CM (International Classification of Diseases, 9th Revision, Clinical Modification) codes. A second commonly used comorbidity measure with claims data developed by Elixhauser includes 29

medical conditions. These measures were developed and validated in hospitalized patients, and therefore may be more applicable to older, sicker populations (23).

A prospective study which done by New York University Lang one Medical Center on Comorbidities and Quality of Life among breast cancer survivors, a total of 28 comorbidities were identified through patient self-report which was verified by medical record review. Among the 134 patients, 73.8% had at least one of the comorbidities, 54.7% had 2–4, and only 7.4% had 5–8. The five most prevalent comorbidities in this patient population were as follows: hypertension (32.8%), arthritis (32.8%), thyroid problem (22.4%) hypercholesterolemia (12.7%) and diabetes (12.0%). Comorbidities assessed through self-report and verified by medical record review did not change during the 12 months after surgery. Comorbidities assessed by self-report and verified by medical record review were: Hypertension, Arthritis, Diabetes, Kidney Problems, Deep Vein Thrombosis, Vascular & Venous Problems, Heart Disease, Thyroid Problem, Hypercholesterolemia & Hyperlipidemia, GI disorders or GERD, Asthma, Depression, Anxiety, Secondary Cancers, Anemia, Multiple Sclerosis, Seizures, Hemangioma Liver, Autoimmune Lupus, Peripheral Neuropathy, Aneurysm, Myocardial Infarction, Cerebrovascular Disease, Connective Tissue Disease, Hemiplegia, Leukemia, Malignant Lymphoma, AIDS. This study also found Participants with comorbidities were older, had a trend of high BMI at 12-month after cancer surgery. More participants with comorbidities were unemployed. More African American/black participants had comorbidities (24).

A study done in Bikaner, Rajasthan, India, during the period of January to December 2012, 156 biopsies proven breast cancer patients were included in the study and female breast cancer patients enrolled were 13.94% out of total patients. The most prevalent comorbidities associated with breast cancer are hypertension (21.8%), chronic obstructive pulmonary disease (COPD) (19.9%), rheumatologic disease (18.6%), and diabetes mellitus (16.7%), all four conditions have been reported in around 75% of the cases (11) .

A study done by Laval University showed that, receiving a diagnosis of breast cancer is an experience often associated with high levels of psychological distress. Psychological and psychophysiological disturbances that have received the most attention from psycho-oncology researchers include depression, anxiety, nausea and vomiting, and pain. In contrast, insomnia has received very little attention in spite of the evidence suggesting that sleep difficulties are among the most frequent consequences of cancer. Studies conducted among heterogeneous samples of cancer patients suggest that between 31% and 54% of newly diagnosed or recently treated cancer patients (i.e., within six

months' post diagnosis) report sleep difficulties. In addition, a significant proportion of breast cancer patients (i.e. 23% and 44%) experience insomnia symptoms several years after their diagnosis (e.g., two to six years' post-diagnosis), which indirectly suggests that insomnia often becomes a chronic problem in breast cancer patients. With an estimated prevalence of about 20% in the general adult population, it would appear that insomnia complaints are more frequent in cancer patients than in the general population. This hypothesis is further supported by a comparative study in which 40% of cancer patients (mixed diagnoses) reported sleep difficulties compared to only 15% of control participants with no severe illness. Although these studies are consistent in suggesting that sleep difficulties are highly prevalent in cancer patients, all of them have not made any distinction between symptoms and syndrome of insomnia. Insomnia is frequently associated with anxiety and depression, either as a clinical feature or as a psychiatric diagnosis (25).

Cancer is one of the most frequent conditions associated with anemia of chronic disease; meantime, anemia is a common complication of cancer. The estimated prevalence of anemia varies ranging from 30% to 90% of cancer patients during the course of their diseases (26).

Fever and neutropenia in cancer patients are associated with a high medical risk, with serious medical complications reported in 21%7 and death in 4% to 30% of episodes in large series (27) .

Twenty-four percent of women reported moderate to severe levels of depressive disorder (30% of breast cancer patients and 17% of gynecologic cancer patients). Only 12% of women meeting criteria for major depression reported currently receiving medications for depression, and only 5% of women reported seeing a counselor or participating in a cancer support group. Neither cancer stage nor treatment status was correlated with depression. Primary diagnosis of breast cancer, younger age, greater functional impairment, poorer social and family well-being, anxiety, comorbid arthritis, and fears about treatment side effects were correlated with depression (32,33).

Interestingly, the distribution of conditions varied considerably by age group with the number of comorbidities per individual patient ranging from none to 13. The total number of comorbidities increased with age ($p < 0.001$). Hypertension was the most prevalent condition in all age groups and arthritis was the second most common disease. Of note, a steep increase in severe heart disease was observed from the age of seventy. In elderly women this may be partly due to the profound decrease in endogenous estrogen that independently affects high-density lipoprotein (HDL) and low-density

lipoprotein (LDL) cholesterol levels and, ultimately, increases the cardiovascular risk. Other comorbidities in which prevalence increased significantly with age were eye problems, low-severity heart disease, anemia, depression, fractures, osteoporosis, renal failure, Parkinson's disease, hearing problems and low-severity urinary tract problems (30) .

Weight management plays an important role in rehabilitation and recovery since obesity and/or weight gain may lead to poorer breast cancer prognosis, as well as prevalent co-morbid conditions (e.g. cardiovascular disease and diabetes), poorer surgical outcomes (e.g., increased operating and recovery times, higher infection rates, and poorer healing), lymphedema, fatigue, functional decline, and poorer health and overall quality of life. The meta-analysis included results from 43 studies which enrolled women diagnosed with breast cancer between 1963 and 2005, with sample sizes ranging from 100 to 424,168. Results show that obese women are at higher risk of all-cause (HR=1.33, 95% CI: 1.21, 1.47) and breast cancer specific (HR=1.33, 95% CI: 1.19, 1.50) mortality when compared to non-obese women with breast cancer (31) .

According to the study done on effects of age and comorbidity in postmenopausal breast cancer patients aged 55 years and older in the USA showed the number of comorbidities per individual patient ranged from none to 13. Seven percent of patients had no co morbidities recorded, 49% had 1 to 3, 34% had 4 to 6, and 9% had 7 to13.The total numbers of co morbidities increased with age (P.001). The percentage of patients with “high-severity” co-morbidities also increased with age (P.001) (32) . The distribution of conditions varied considerably by age group. Some comorbidity characteristically occurs in middle age or earlier; others occur at older ages. Major illnesses e.g. cancer, heart problems, and diabetes requiring insulin or conditions related to these diseases) may also be concurrent. The most prevalent condition in all age groups was hypertension. Arthritis is ranked second or third across all age groups. High severity heart disease (defined in the “Methods” section) affected less than 6% of patients aged 55 to 59 years, but increased to second or third in co morbidity prevalence for the 4 oldest age groups (16.4%, 22.6%, 32.5%, and 38.6% for age groups 70 to 74 years, 75 to 79 years, 80 to 84 years, and 85 years and older, respectively). The percentage of patients with 1 or more severe co morbidities tended to increase with each successive age group. Other co morbidities in which prevalence increased significantly with age were eye problems, low severity heart disease, anemia, depression, fractures, hearing problems, osteoporosis, Parkinson disease, renal failure, and low-severity urinary tract problems (6).

A study in USA they compared breast cancer cohort to a contemporaneous nationally-representative sample of age, race/ethnicity and education matched women without cancer ($n = 865$). Women with a hospital record of congestive heart failure significantly less often received chemotherapy or radiation following breast conserving surgery. In multivariate analysis, women who received chemotherapy alone (OR = 3.2; 95% CI: 1.5–6.8), chemotherapy plus radiation (OR = 1.9; 95% CI: 1.02–3.7) or radiation plus tamoxifen (OR = 1.9; 95% CI: 1.1–3.2) were significantly more likely to report at least one new comorbid condition following breast cancer diagnosis than women who received no chemotherapy, tamoxifen or radiation. Overall, women who received adjuvant therapy were more likely to have new comorbidities. In conclusion comorbidities were not substantially different in breast cancer patients than the non-cancer matched controls. Future research should focus on efforts to minimize comorbidities related to chemotherapy and other combination therapy (33) .

In studies of postmenopausal women describes the co-morbidity burden of postmenopausal breast cancer patients, investigates the relationship of co-morbidity to age and tumor stage, assesses the effect of co-morbidity on initial surgical treatment of breast cancer, and evaluates the impact of co-morbidity on survival in the 30 months following diagnosis(6).

Central cancer registry data (2006-2008) from three Appalachian states were linked to Medicare claims and census data. Exploratory spatial analysis preceded the statistical model based on negative binomial regression to model predictors and effect modification by geographic sub regions. Exploratory spatial analysis revealed geographically varying effects of area deprivation and screening on LSBC. The most deprived counties had a 3.31 times greater rate of LSBC compared to the least deprived. Effect of screening on LSBC was significantly stronger in northern Appalachia than elsewhere in the study region, found mostly for high-population counties. Breast cancer screening and area deprivation are strongly associated with disparity in LBSC in Appalachia. The presence of geographically varying predictors of later stage tumors in Appalachia suggests the importance of place-based health care access and risk (34) .

A Danish register based follow up study showed there is significant interaction between education and breast cancer, but it is only marginally affected by including stage and comorbidity in the regression models. Education, breast cancer stage, and comorbidity all have strong effects on later employment, and a considerable amount of the educational effect is mediated by comorbidity and pre-cancer labour market participation and income (35) .

A study on Influence of education level on breast cancer risk and survival in Sweden between 1990 and 2004 explained compared to women completing less than 9 years of education, university graduates were more likely to be diagnosed with in situ (HR = 1.44, 95% CI: 1.28-1.63) and invasive (HR = 1.28, 95% CI: 1.20-1.36) breast cancer. Compared to women completing less than 9 years of education, university graduates were associated with the highest survival following a breast cancer diagnosis (lowest fatality hazard ratio), HR = 0.68, 95% CI: 0.61-0.75 (36).

Radiation therapy can cause both early and late side effects. Acute radiation side effects are caused by damage to rapidly dividing normal cells in the area being treated. These effects include skin irritation or damage at regions exposed to the radiation beams. Examples include damage to the salivary glands or hair loss when the head or neck area is treated, or urinary problems when the lower abdomen is treated. Fatigue is a common side effect of radiation therapy regardless of which part of the body is treated. Nausea with or without vomiting is common when the abdomen is treated and occurs sometimes when the brain is treated. Late side effects of radiation therapy may or may not occur, late side effects can include: Fibrosis, Damage to the bowels, causing diarrhea and bleeding, Memory loss, Infertility (inability to have a child). Rarely, a second cancer caused by radiation exposure (8).

3. Research Questions

- What is the magnitude of comorbidities among breast cancer patients?
- What are the types of comorbidities among breast cancer patients?
- Which factors associated with comorbidity among breast cancer patients

4. Null Hypothesis

- There are no comorbid diseases among breast cancer patients
- There is no relationship among socio-demographic and other factors of breast cancer patients and presence of comorbidities in breast cancer patients.

5. Objective

5.1.General Objective

- To assess magnitude of comorbidities and associated factors among breast cancer patients registered and follow in Tikur Anbesa hospital Addis Ababa, Ethiopia

5.2. Specific objective

- To determine the magnitude of comorbidities among breast cancer patients
- To describe types of comorbidities among breast cancer patients
- Identify factors associated with comorbidity among breast cancer patients

6. Methods

6.1. Study Area

According to 2015 Addis Ababa city administration atlas the city was have 16 governments, 39 private and 3 NGO hospitals and 94 governments, 5 private and 3 NGO health centers. Tikur Anbesa Hospital, located at Lideta sub-city, is the largest specialized teaching and referral government hospital that aspires (aims) to become a center of excellence in the diagnosis, treatment and care of cancer patients. Tikur Anbesa specialized hospital is the only hospital managing patients with all types of cancer. Patients with breast cancer referred from all over Ethiopia to Tikur Anbesa Hospital for treatment like radiotherapy and chemotherapy(37).

The Federal Ministry of Health estimated that there could be more than 150,000 cancer cases in Ethiopia each year, of which breast cancer accounts about 30% (5). There were 3460 new cases of breast cancer registered at the cancer registry during the16-year period. The peak age of incidence was the 4th and 5th decade. Most of the cases were found in Addis Ababa, where the hospital is situated (17). An increase in trend of breast cancer case was observed in the hospital. As the nation's sole cancer referral center, Tikur Anbesa Hospital is treating only about one percent of these patients. The Tikur Anbesa Hospital Oncology department July to September 2016 quarter report showed there were a total of 825 breast cancer cases. The study included patients registered and under follow-up in the hospital.

6.2. Study Design.

A facility based cross-sectional study was employed to assess comorbidities of breast cancer patient.

6.3. Study period

The study was conducted from June to August 2017.

6.4. Study variables

6.4.1. Dependent Variable

- Comorbidities – presence and types of comorbidities

6.4.2. Independent variables

- Age at diagnosis, Ethnicity, Religion, Place of Residence, Marital status, education, occupation, family size, income, time since diagnosis, cancer stage, type of management (radiotherapy, mastectomy, lumpectomy, chemotherapy), other medications, hormone therapy, stages of breast cancer, Treatment status.

6.5. Source and Study population

All women with breast cancer registered and under follow-up in Tikur Anbesa Hospital and Amstegna cancer Center with follow-up history chart.

6.6. Sample size determination

Single proportional formula was used to determine the sample size. The proportion of comorbidity of insomnia among breast cancer patients found to be 23% to 44%, by considering Confidence level of 95% (CI), marginal error of 5% (d) and 10% for nonresponse rate (22). Accordingly, the following formula the final sample found to be 417.

$$n = \frac{Z^2_{1-\alpha/2} P(1-P)}{w^2} = \mathbf{379}$$

Where Zα/2 is the standard normal random variable at 95% confident level = 1.96, P=Prevalence of comorbidity (insomnia) among breast cancer patients = 0.44 (25), w is margin of error = 5% **.** Taking 10% nonresponse rate, the total sample size will be 417.

6.7. Sampling Technique

Tikur Anbesa quarterly report showed an average 250 breast cancer patients with repeat visit per month. All breast cancer patients who have follow up in Tikur Anbesa hospital and Amsetgna cancer centers were interviewed and their charts were reviewed. Every other patient who came to the hospital for follow up were interviewed until all the sample size was full filled and their charts were tracked and reviewed to assess comorbidities following their interview. The interview was done immediately following their medical checkup and the sequences of the interview was based on their medical checkup and follow that sequence.

6.8. Data collection procedure

A structured interview questionnaire was adapted from available literature, scientific plausibility, and the opinion generated. The questionnaire was developed in English version then translated to Amharic. Adapted an interviewer-administered structured questionnaire was used to capture information from breast cancer patients, who visited hospital for follow up during data collection period. Three trained nurses and one health officer were assigned to collect data. Patients chart were reviewed to extract comorbidity related information. Observed comorbidities were registered matched with number of follow up.

The supervisor reviewed the chart and tried to check filled questionnaires at the spot and doctors who were working there were consulted for any clarification or confusion over the chart. The data collection time was from June 19- August 30, 2017

6.9. Data Quality Management

Data was collected by two health professionals' (nurses& health officer) after detailed discussion with the questionnaire. Chart review was done by the principal investigator which required great commitment to go through each time of follow up. Diagnosis and treatment which were ambiguous were consulted with doctors. Extracted data was checked on daily basis and crosschecking was done by the investigator.

6.10. Data Analysis

Data were entered into SPSS version 20.0 and analyzed after cleaned and edited. Descriptive statistics were used to summary socio-demographic, awareness of respondents related to breast cancer management and its comorbidity and clinical characteristics of study subjects using proportion, measure of central tendency and variation and finding was presented using tables and figures. Factors associated with outcome variable were identified by multivariate logistic regression. Statistical significance was declared at $p< 0.05$. Variables that significant at $P<0.05$ and 95% CI level in bivariate analysis were included multivariate logistic regression. All factors which showed association during univariate analysis were loaded by binary logistic regression to identify factors associated with comorbidities. Findings were reported using Odds ratios and 95% confidence level. P-values less than 0.05 used to declare statistical significance.

6.11. Ethical consideration

Ethical approval and clearance was obtained from Addis Ababa University School of Public Health ethical committee following to final thesis proposal acceptance and submission. Then official letter was written from Addis Ababa university school of public health to the Oncology department. The people in charge of the departments were informed and their agreements were received before the onset of data collection. Permission consent was obtained from each study participants. Strict confidentiality of the data was maintained by taking only de-identified data (without any personal identification).

7. Result

7.1. Socio Demographic Characteristics of study participants

In this study a total of 404 female breast cancer cases were assessed of which the mean and SD age of the study participants were 43.5 ± 7.8 year.

Of all respondents 313 (77.5%) were urban residents and 89 (22%), 258 (63.9%), 38 (9.4%) and 19 (4.7%) were single, married, divorced and widowed respectively. In addition, 272 (67.3%), 69 (17.1%), 57 (14.1%) and 6 (1.5%) were Orthodox, Muslim, Protestant and other religions followers. (Table 1)

Table 1 Socio demographic characteristics of breast cancer patients underfollow up in Tikur Anbesa Specialized Hospital August 2017, Addis Ababa.

Variables		**Frequency**	**Percent**
Residency	Urban	313	77.5
	Rural	91	22.5
Marital Status	Married	258	63.9
	Single	89	22.0
	Divorced	38	9.4
	Widowed	19	4.7
Religion	Orthodox	272	67.3
	Muslim	69	17.1
	Protestant	57	14.1
	Others	6	1.5
Educational status	Illiterate	104	25.7
	Able to read and write	43	10.6
	Elementary	60	14.9
	Secondary	120	29.7
	College and above	77	19.1
Occupation	Housewife	217	53.7
	Civil servant	110	27.2
	Others	77	19.1

***others occupation includes farmer, merchant and private employee*

7.2. Respondents Menstrual and Birth History

The majority of respondents 298 (73.8%) were seen their first menses greater than 16 years of age while 62 (15.3%) were seen in the age of 13-15 years and 14 (3.5%) seen during less than 13 years but 30 (7.4%) did not remember it and 328 (81.8%) were exercised irregular menstruation and 76(18.2%) regular menstruation and among those stopped menstruation 210 (52%) were less than 5 years ago, 81 (20%) 5-10 years ago, and34 (8.4%) for more than 10 years ago.

Forty-five percent (183) were give their first birth in the age of 18-24 years, 71 (17.6%) gave in the age of greater than 24 years, 50 (12.4%) gave in the age of less than 18 years but 97 (24%) did not give birth. (See Table 2 for more detail)

Table 2. Menstrual and birth history for breast cancer patients underfollow up in Tikur Anbesa Specialized Hospital August 2017, Addis Ababa.

Variables	Response	Frequency	Percent
Age at first menses	Did not remember	30	7.4
	Less than 13 years	14	3.5
	13-15 years	62	15.3
	More than 16 years	298	73.8
Availability of regular menstruation	No	328	81.2
	Yes	76	18.8
Time since last menstruation	Regular and missing	79	19.6
	Less than 5 years	210	52.0
	5-10 years	81	20.0
	More than 10 years	34	8.4
Age of first pregnancy	No birth	97	24.0
	Less than 18 years of age	50	12.4
	Within 18-24 years of age	183	45.3
	Greater than 24 years of age	71	17.6
Number of live births before diagnosis of breast cancer	Less than 3 children	246	60.9
	3-5 children	129	31.9
	More than 5 children	29	7.2
History of breast feeding for the last child	No	9	2.2
	Yes	298	73.8

7.3. Comorbidity history of Respondents'

Out of total, 56(8.5%) breast cancer patients had comorbidity. Of these, 19(4.7%) were hypertension, 18(4.5%) were asthmatic, 9(2.2%) were cardiac problem, 6(1.5%) Diabetes Mellitus and 4 (1%) HIV/ AIDS (Figure 1).

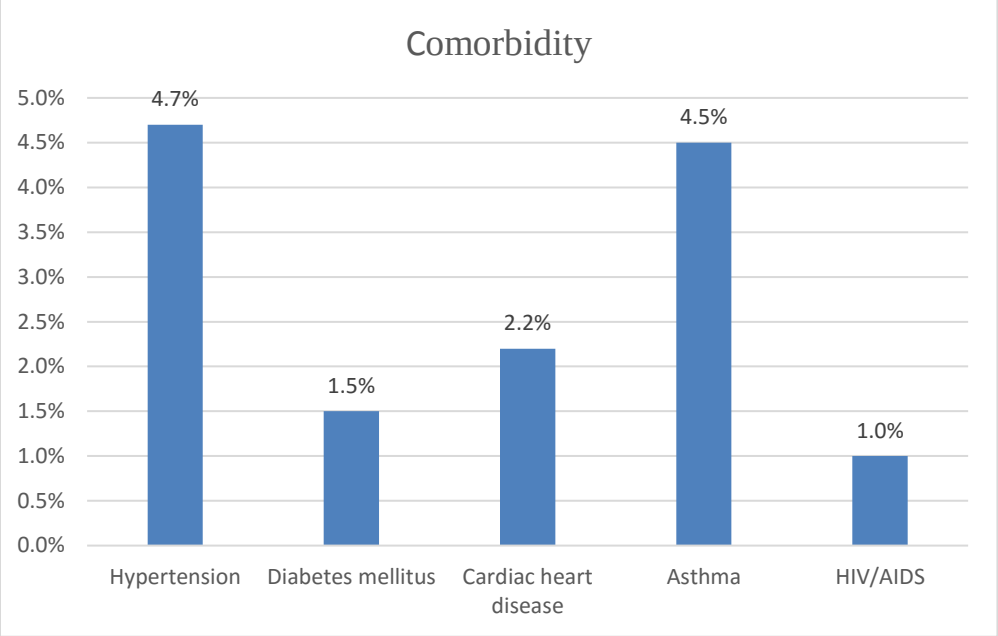

Figure 1: Comorbidity among breast cancer patient under follow up in Tikur Anbesa Hospital, August 2017, Addis Ababa

7.4. Respondents' awareness related to breast cancer treatment and comorbidities

Out of the total respondents 398 (98.5%) said cancer can be treated, 6 (1.5%) said it could not be treated and did not know. Types of cancer treatment reported by respondents were chemotherapy 395(97.8%), radiation 133 (32.9%), surgery 212 (52.5%) and traditional medicine 34 (8.4%).

Respondents said if breast cancer treatment discontinued it will cause; death 117 (29%), disseminated 94 (23.3%), problem worsened 81 (20%), relapse 66 (16.3%), did not know the outcome 34 (8.4%) and increased pain 6 (1.5%).

Of the participants 93 (23%) reported as other illness can occur together with breast cancer, 94 (23.3%) could not occur together with breast cancer and 214 (53%) said did not know. Out of respondents who reported as other illness could occur together with breast cancer 84 (90.3%) said it happened with different sign and symptom, 6 (6.5 %) said with no different sign and symptom and 3 (3.2%) did not know. Respondents mentioned different illnesses can occur together with breast cancer and some of repeatedly mentioned were hypertension 12 (3%), abdominal pain 12 (3%), Gastritis 9 (2.2%) and weakness 9 (2.2%). (See Table 3 below for more detail)

Table 3 Awareness related to breast cancer treatment and related comorbidities among breast cancer patients under follow up in Tikur Anbesa Specialized Hospital August 2017, Addis Ababa.

Variables	Response	Frequency	Percent
Does breast cancer can be treated	No	3	0.7
	Yes	398	98.5
	Didn't know	3	0.7
Respondents response for breast cancer treatment	Chemotherapy	395	97.8
	Radiotherapy	133	32.9
	Surgery	212	52.5
	Traditional	34	8.4
	Didn't Know	34	8.4
What will happen if breast cancer treatment discontinued	Disseminated	94	23.3
	Pain Increased	6	1.5
	Relapse	66	16.3
	Not cure	6	1.5
	Problem worsened	81	20.0
	Death	117	29.0
Can other illness have occurred together with breast cancer	No	94	23.3
	Yes	93	23.0
	Didn't know	217	53.7
Do comorbidities have different signs and symptoms	No	6	1.5
	Yes	84	20.8
	Did not know	3	0.7
List of comorbidities mentioned by respondents	HPN	12	3.0
	Abdominal Pain	12	3.0
	Weakness	9	2.2
	Gastritis	9	2.2
	Heart	6	1.5
	Aggravate	3	0.7
	UTI	3	0.7
	Numbness	3	0.7
	Cervical ca	3	0.7
	Lymphadenitis	3	0.7
	Neck Problem	3	0.7
	Blindness	3	0.7
	Loss of appetite	3	0.7
	Renal problem	3	0.7
	Liver dis	3	0.7
	Liver and renal	3	0.7
	H/V/AIDS	3	0.7
	Infection	3	0.7

7.5. Chart Review

7.5.1. Breast cancer stages

Stage of breast cancer during at first diagnosis were 198 (49%), 104 (25.7%), 99 (24.5%), 3 (0.7%), in stage 3, stage 4, stage 2 and stage 1 respectively and the stage during data collection or interview were 3 (0.7%), 65 (16.1%),186 (46%), 150 (37.1%), stage 1- stage 4 respectively. (Figure 2).

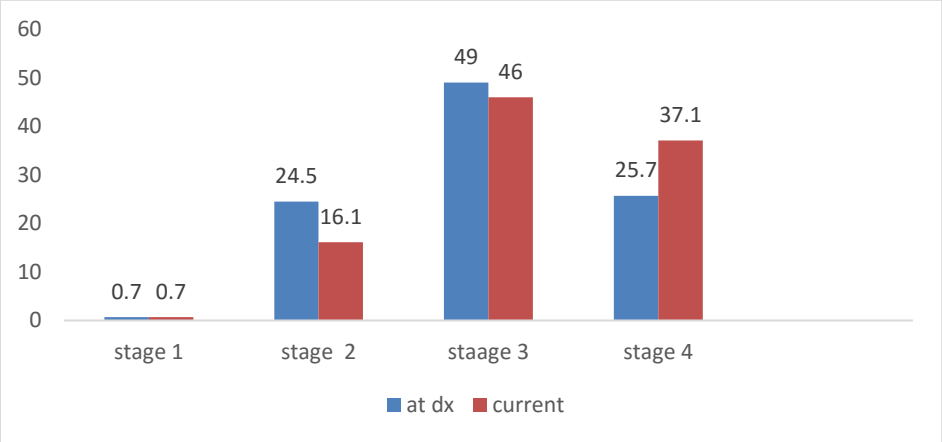

Figure 2 Breast cancer stages during diagnosis and data collection for the study participants in Tikur Anbesa Specialized Hospital, August 2017 Addis Ababa.

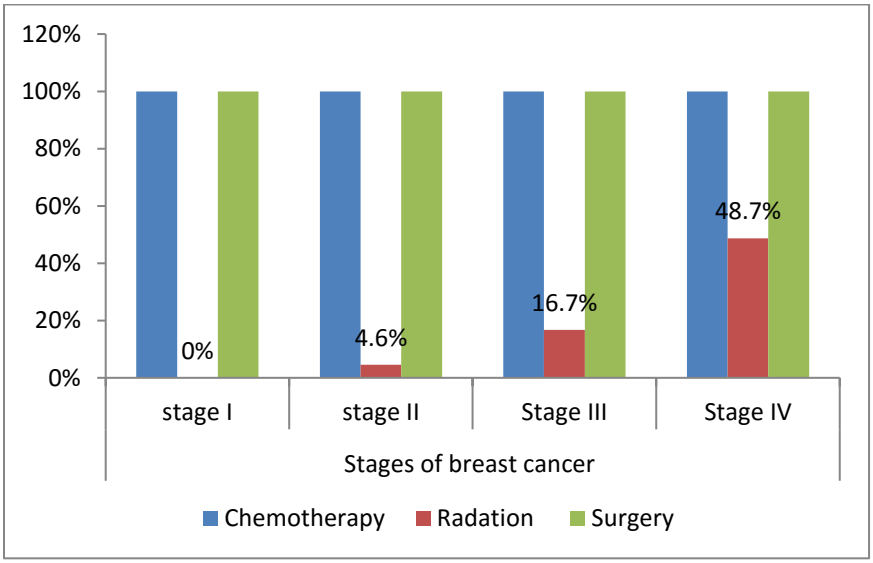

Figure 3 Types of management vs. stage of breast cancer for the study participants in Tikur Anbesa Specialized Hospital, August 2017 Addis Ababa.

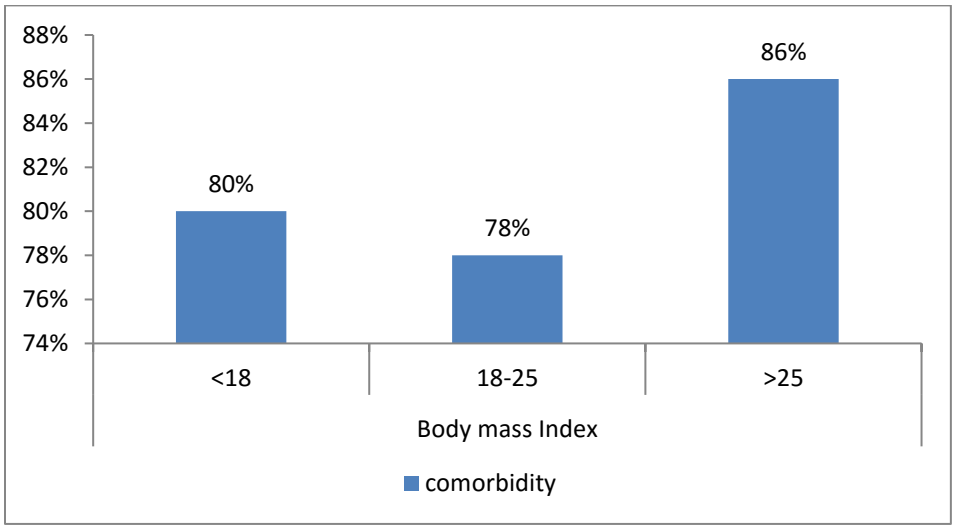

Figure 4 Comorbidity status vs. Body Mass Index of breast cancer study participants in Tikur Anbesa Specialized Hospital, August 2017 Addis Ababa.

7.5.2. **Comorbidities**

Of all study participants, 322 (79.7%) had comorbidities and the remaining 82 (20.3%) had no comorbidities (figure 5). A total of 52 different comorbidities were identified in this study (Annex 6).

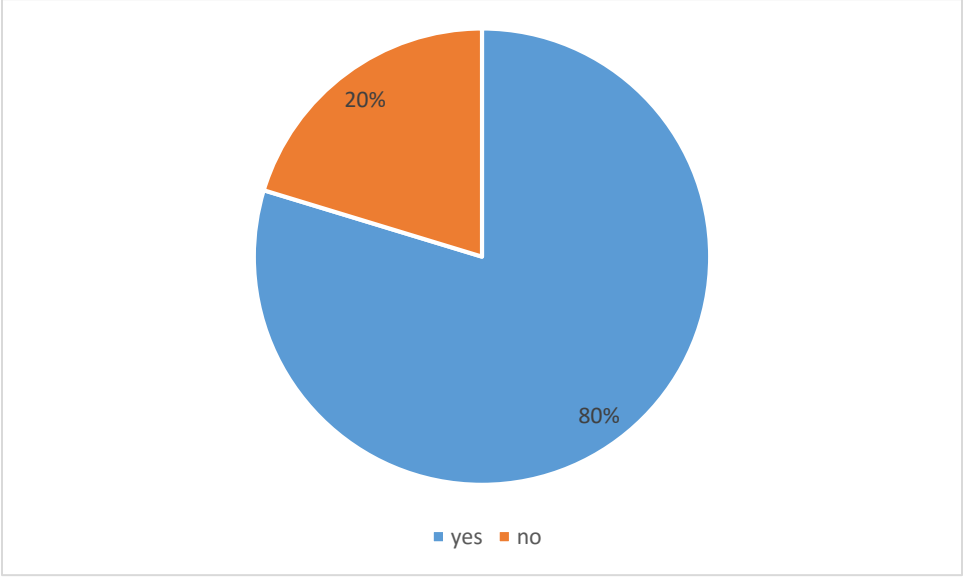

Figure 5 Overall prevalence of comorbidity among breast cancer study participants in Tikur Anbesa Specialized Hospital, August 2017

4.5.2.1 Comorbidities based on stage of breast cancer and follow up times

Of all respondents 3(100%) who were first stage, 40 (62%) second stage, 147 (79%) third stage and 132 (88%) 4th stages were have comorbidity.

Neutropenia 121 (16.3%) was the first comorbid followed by fatty liver 87 (11.7%), Gastritis/PUD 61 (8.2%) and Anemia 43 (5.8%), liver metastasis 3.9% (29), HPTN21 (2.8%), Lymph adenitis 19 (2.6%), pleural effusion 18 (2.4%), Insomnia 15 (2%), DM 15 (2%) Uterine Myoma 14 (1.9%) and Anxiety 9 (1.2%) respectively.

On the other hand, comorbidities were analyzed based on breast cancer study participants follow up. In this connection, fatty liver 48 (11.9%), Neutropenia 43 (10.6%), Gastritis/PUD 34 (8.4%), Anemia 31 (7.7%) found to be highly prevalent comorbidities in the first and second follow up times (Annex 6)

Of all comorbidities during the first follow up of participants, fatty liver was the prevalent comorbid disease with 48 (11.9%) and neutropenia was the prevalent comorbid during the second, third and fifth follow ups. While during the fourth follow up hypertension was the prevalent comorbid of all and 100% of cases were in stage three participants. Insomnia was registered as comorbidity from the first to third follow ups with 0.7%, 1.5% and 1.5% respectively. And anxiety was registered during second and third follow ups as comorbid disease with 1.5% and 0.7% respectively (Annex 7).

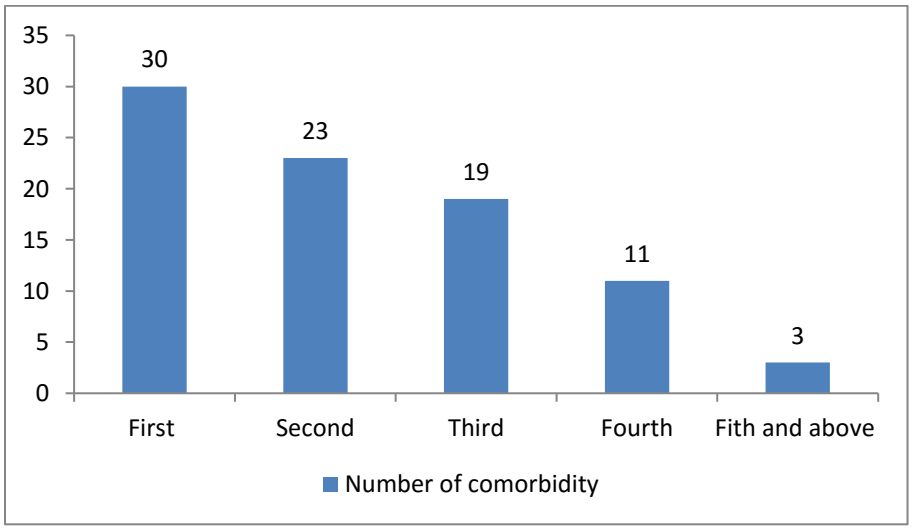

Figure 6 Total numbers of comorbidities per follow up among breast cancer study participants in Tikur Anbesa Specialized Hospital August 2017, Addis Ababa

The oncology department was not having any guideline which used to assess and treat comorbidities of breast cancer patients till the data collection time.

7.6. Associated factors

In the multivariate analysis of all selected factors **Education** (Occupation, illiterate, able to read and write and secondary school), **hormonal treatment**, and **treatment other than cancer** and **stage of cancer at diagnosis** showed significant association with comorbidity of breast cancer patients.

Housewife and civil servant respondents had 0.29 and 0.34 times less chance to develop comorbidity than respondents who had other occupation, OR 0.29, 95% CI (0.12-0.74), OR, 0.34, 95% CI (0.15-0.79) respectively.

Illiterate, able to read and write, elementary and attended secondary school participants were having 0.03, 0.04, 0.31 and 0.11 times less chance developing comorbidities than those who were have college and above educational status OR, 0.03, 95% CI (0.007-0.10), OR, 0.04, 95% CI (0.009-0.15), OR, 0.31, 95% CI (0.11-0.90) and OR, 0.11, 95% CI (0.04-0.3) respectively.

Study Participants who were not under radiation treatment were 0.37 times less odds to develop comorbidity than under those who were under radiation treatment, OR 0.37, 95% CI (0.19-0.72) and those who did not get hormone treatment were 0.03 times less chance than those who got hormone treatment, OR 0.03, 95% CI (0.01-0.11).

Respondents who did not get different treatments were have 0.04 times less chance to develop comorbidity than those who were under treatment except hormonal and antiemetic treatments, OR 0.04, 95% CI (0.01-0.21) See Table 4).

Respondents who were stage I and II during diagnosis had 0.34 times less of developing comorbidity than who were stage III and IV, OR 0.34, 95% CI (0.18-0.68).

Table 4 Associations of study variables with Comorbidity of breast cancer patients under follow up in Tikur Anbesa Specialized Hospital August 2017, Addis Ababa

Variables	Comorbidity		COR	COR (95.0% C.I)		Adj OR	Adj (95.0% C.I.)	
	No	Yes		Lower	Upper		Lower	Upper
Residency								
Urban	62	251	1.14	0.65	2.01	1.30	0.56	3.03
Rural	20	71	1.00			1.00		
Marital status								
Married	43	215	0.94	0.26	3.36	3.49	0.61	19.97
Single	22	67	0.57	0.15	2.15	2.27	0.36	14.31
Divorced	14	24	0.32	0.08	1.30	0.47	0.08	2.85
Widowed	3	16	1.00			1.00		
Religion								
Orthodox	47	225	4.79	0.94	24.46	6..29	0.93	42.48
Muslim	17	52	3.06	0.56	16.60	2.00	0.26	15.46
Protestant	15	42	2.80	0.51	15.41	2.25	0.31	16.49
Others	3	3	1.00			1.00		
Education								
Illiterate	17	87	0.71	0.39	1.27	0.03	0.007	0.10
Able read and write	7	36	0.74	0.32	1.73	0.04	0.009	0.15
Elementary	20	40	2.27	1.24	4.16	0.31	0.11	0.90
Secondary	15	105	0.46	0.25	0.85	0.11	0.04	0.3
College and above	23	54	1.94	1.10	3.39	1.00		
Occupation								
Housewife	26	191	0.32	0.18	0.57	0.29	0.12	0.74
Civil servant	33	77	0.33	0.17	0.60	0.34	0.15	0.79
Others	23	54	1.00			1.00		

Stage of cancer at Diagnosis								
Stage I and II	31	71	0.47	0.28	0.78	.34	0.18	0.68
Stage III and IV	51	251	1.00			1.00		
Types of cancer Management								
Radiation (No)	71	226	0.37	0.19	0.72	0.91	0.35	2.40
Radiation (Yes)	11	96	1.00			1.00		
Lumpectomy (No)	76	313	2.75	0.95	7.95	12.07	1.34	109.07
Lumpectomy (Yes)	6	9	1.00			1.00		
Hormone (No)	23	30	0.26	0.14	0.49	0.03	0.01	0.11
Hormone (Yes)	59	292	1.00			1.00		
Other treatment (No)	75	222	0.21	0.09	0.47	0.04	0.01	0.21
Other treatment (Yes)	7	100	1.00			1.00		

8. Discussion

In this study the mean ages of breast cancer participants during diagnosis was 43.5 years. This age is near to menopause and is older ages as compared to the country over all life span. Other results also showed the brunt of this high number of breast cancer cases and deaths are borne by women in the postmenopausal period of life, defined there as age 55 years and older. Two thirds of all newly diagnosed female breast cancer patients are in this age group (12).

The magnitude of comorbidities among breast cancer study participants was 322 (80%) and 52 comorbidities were found. Other Studies also showed similar results, for example a prospective study on comorbidities and quality of life among breast cancer survivors showed a total of 28 comorbidities were identified and 73.8% had at least one of the comorbidities (24). Another study explained, comorbidity was present in 68.7% of cancer patients (14).

Neutropenia found to be highly prevalent comorbidity during the second follow up (13.1%) third follow up (4.7%) and third listed comorbid during the fourth follow up (0.7%). This may be because of the chemo and radiation therapy and also because of older age as well as because of any other immunity lowering diseases. Other studies also showed as fever and neutropenia in cancer patients are associated with a high medical risk, with serious medical complications reported in 21% (27) .

Anemia was seen the fourth comorbid disease during first and second follow up, 7.7% and 3% respectively. This may be because of the chemotherapy since chemotherapy treatment target and kill fast-dividing cells in the body, whether they are cancer or not and chemotherapy temporarily decreases the bone marrow's ability to make new blood cells. Other studies also showed as cancer is one of the most frequent conditions associated with anemia of chronic disease; meantime, anemia is a common complication of cancer. The estimated prevalence of anemia varies ranging from 30% to 90% of cancer patients during the course of their diseases (26).

Insomnia was registered as comorbidity from the first to third follow ups with 0.7%, 1.5% and 1.5% respectively. And anxiety was registered during second and third follow ups as comorbid disease with 1.5% and 0.7% respectively. This may be because of the stress following to the disease but the result showed low prevalence as compared to other studies. For example, a study done by Laval University showed that, receiving a diagnosis of breast cancer is an experience often associated with high levels of psychological distress. Studies conducted among heterogeneous samples of cancer patients suggest that

between 31% and 54% of newly diagnosed or recently treated cancer patients (i.e., within six months' post diagnosis) report sleep difficulties. In addition, a significant proportion of breast cancer patients (i.e. 23% and 44%) experience insomnia symptoms several years after their diagnosis (e.g., two to six years' post-diagnosis), which indirectly suggests that insomnia often becomes a chronic problem in breast cancer patients. With an estimated prevalence of about 20% in the general adult population, it would appear that insomnia complaints are more frequent in cancer patients than in the general population. This hypothesis is further supported by a comparative study in which 40% of cancer patients (mixed diagnoses) reported sleep difficulties compared to only 15% of control participants with no severe illness. (25).

Fatty liver was the second most prevalent comorbid of all comorbidities. This result is in line with other case-control study of non-alcoholic fatty liver disease in breast cancer found good correlation between tamoxifen use and chemotherapy on development of non-alcoholic fatty liver disease (38).

Of all comorbidities observed in all breast cancer stages, neutropenia 121 (16.3 %) was the most prevalent comorbidity followed by fatty liver 87 (11.7%), Gastritis/PUD 61 (8.2%), Anemia 42 (5.8%), liver metastasis 3.9% (29), HTN 21 (2.8%), Lymph adenitis 19 (2.6%), pleural effusion 18(2.4%), Insomnia 15(2%), DM 15 (2%) uterine Myoma 14(1.9%) and anxiety 9 (1.2%) .This result was similar to various studies (30)(24)(11).

Participants who were illiterate, able to read- write, elementary and attended secondary school were have 0.03, 0.04, 0.3 and 0.11 times less chance of developing comorbidities than those who were have college and above educational status OR, 0.03, 95% CI (0.007-0.1), OR, 0.04, 95% CI (0.009-0.15), OR, 0.3, 95% CI (0.11-0.90) and OR, 0.11, 95% CI (0.04-0.30) respectively. This may be due to awareness difference in health seeking behavior and to be diagnosed early since those colleges and above education attendants may have better understanding about problems other than breast cancer. This result has similarity with the study done on Influence of education level on breast cancer risk and survival in Sweden between 1990 and 2004 which found compared to women completing less than 9 years of education, university graduates were more likely to be diagnosed with in situ (HR =1.44, 95% CI: 1.28-1.63) and invasive (HR=1.28, 95% CI: 1.20-1.36) breast cancer (36).

Participants who were not under radiation treatment were 0.37 times less odds to develop comorbidity than under those who were under radiation treatment, COR 0.37, 95% CI (0.19-0.72) This is because

radiation therapy can cause both early acute and late side effects. Fatigue is a common side effect of radiation therapy regardless of which part of the body is treated. Nausea with or without vomiting is common when the abdomen is treated and occurs sometimes when the brain is treated(8). Also those who did not get hormone treatment were 0.03 times less chance than those who got hormone treatment, OR 0.03, 95% CI (0.01-0.11), this is because tamoxifen (most commonly used hormonal therapy) is associated with a 2.5-fold increased risk of endometrial carcinoma and an increased risk of stroke, deep venous thrombosis (DVT), pulmonary embolus, and cataracts, serious adverse events are not common(30). This result is in line with the study done for comorbidities, therapy, and newly diagnosed conditions for women with early stage breast cancer and its multivariate analysis showed, women who received chemotherapy alone (OR = 3.2; 95% CI: 1.5–6.8), chemotherapy plus radiation (OR = 1.9; 95% CI: 1.02–3.7) or radiation plus tamoxifen (OR = 1.9; 95% CI: 1.1–3.2) were significantly more likely to report at least one new comorbid condition following breast cancer diagnosis than women who received no chemotherapy, tamoxifen or radiation. Overall, women who received adjuvant therapy were more likely to have new comorbidities (33).

Respondents who got different treatments were have 0.04 times less chance to develop comorbidity than those who were not under treatment except hormonal treatments and antiemetic, OR 0.04, 95% CI (0.01-0.21). This may be comorbidities relieved because of the treatment given for it.

Respondents who were at stage II and III during diagnosis were 0.22 and 0.51 times less odds to develop comorbidity as compared to stage IV, COR 0.22, 95% CI (0.11-0.44) and COR 0.51, 95% CI (0.28-0.94) respectively. This result has supportive and inverse relationship with other study. It is known that cancer stage at diagnosis is affected by patient comorbidity, but the evidence regarding the magnitude and even direction of this effect is highly inconsistent. This is because there are several competing mechanisms that may impact on stage at diagnosis. Increased contact with health services may result in a ‘surveillance effect’ – leading to earlier diagnosis. In contrast, comorbidity may distract both the clinician and the patient from early signs and symptoms of cancer – leading to delayed diagnosis. In some cases, the patient has such severe comorbidity that their life expectancy is so limited that diagnostic investigation does not appear warranted. Furthermore, some comorbid conditions (e.g., diabetes) may have a direct effect on cancer growth. The balance of these mechanisms is likely to vary by comorbidity and cancer type, as well as by health system factors(40,41).

The oncology department had not any guide line which used to assess and treat comorbidities of breast cancer patients till the data collection time. However, this is very important since the presence of comorbidities in patients with cancer has been negatively associated with patients' health outcomes. Poorer survival from cancer has been found overall in cancer survivors with comorbidities compared to those without. Breast cancer survivors with comorbidities are more likely to experience specific adverse outcomes such as delay and non-completion of radiation therapy, more likely to receive only breast conserving surgery without radiation therapy, and less likely to receive chemotherapy (24).

9. Strength of the study

- Chart review which was the most exhaustive work was done by the principal investigator

10. Weakness of the study

- It is a cross-sectional study
- Magnitude determined using chart reviewed which has not complete method

11. Conclusion

The study found as there was high prevalence of comorbidities with 52 different types among breast cancer patients who were have follow up in Tikur Anbesa specialized teaching hospital. Of all comorbidities observed in all breast cancer stages, neutropenia 121 (16.3 %) was the most prevalent comorbidity followed by fatty liver 78 (11.7%), Gastritis/PUD 61 (8.2%), Anemia 43(5.8%), Liver metastasis 29 (3.9%), HTN 21 (2.8%), Lymph adenitis 19 (2.6%), Pleural effusion 18 (2.4%), Insomnia 15 (2%), DM 15 (2%), Uterine Myoma 14 (1.9%) and anxiety 9 (1.2%). Comorbidities showed variation because of respondent's, education, family history, breast cancer treatment and stages of breast cancer. The oncology department has no guideline for the diagnosis and management of comorbidities

12. Recommendation

- A large number of comorbidities found in each stage of breast cancer but the cancer treatment

center has no special guideline to diagnose as well as to manage it. Therefore, the treatment center shall have guideline for it.

- Since there were many types as well as high prevalence of comorbidities together with the breast cancer patients' attention should be given during patient's diagnosis one not distract with the other.

- The center shall develop system to identify number of comorbidities in each patient in each follow up which used to use the data for action as well to consider the type of management for the patient.

- Neutropenia was the highest prevalent comorbidity of the breast cancer patients so the expert shall design preventive or early treatment mechanism for it as well as better to be conscious to establish diagnosis checkup for all other breast cancer patients.

- Neutropenia, Fatty liver, Gastritis and Anemia were with the highest prevalent comorbidities especially during the first and second follow up of the breast cancer patients so attention shall be given for the management of them.

- Neutropenia, Fatty liver, Gastritis/PUD, Anemia, Liver metastasis, HPTN, Lymph adenitis, Pleural effusion, Insomnia and DM were more prevalent comorbidities. So better medication and care shall be given for better patient outcome.

- History of breast cancer patients education, type breast cancer treatment and stages of breast cancer at diagnosis as well as throughout the treatment course shall be take in to consideration since they affected the occurrence of comorbidities.

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Annexes

Annex 1 Information sheet

I am a student at the University of Addis Ababa and Currently I am doing my thesis on Assessment of comorbidities and associated risk factor among breast cancer patients at Tikur Anbesa Hospital. As you know breast cancer and its morbidity is becoming a serious public health problem worldwide including in our country. In order to reduce the problem, the government is expanding and scaling up primary health cares and expands tertiary hospitals for regions. This study is aimed to assessing the common types of comorbidity and its risk factors among breast cancer patients in Tikur Anbesa Hospital. So it will see current status of breast cancer comorbidity and its risk factor. Participant will be asked questions related to breast cancer comorbidity and its risk factor. The interview will only last within 25 to 35 minutes. The information you provide will only be used for this study and we strictly maintain confidentiality. Data's are recorded using codes and will be kept under the controls of the investigators and will not be used for other purposes other than this study. Participants also have the right to with draw from the study at any time they want but your response will do a lot to our study. No harm will come to you nor will you get benefit as a result of participating in this study.

If you have any question and confusion regarding the questions you have the right to ask the interviewer but if goes beyond you can contact the investigator of this study on the following address.

Email address: senaitwassie@gmail.com and
Phone number: 0929093150

Annex 2 Informed consent

I have already explained to you the purpose of the study and importance of your participation to this study. Are you willing to participate in this study?

Yes I agree  No I don't Agree 

Would you show your consent with your signature?

Participant signature _____

Annex 3- English Questionnaires

Data collection tool for the assessment of comorbidities of breast cancer patients and associated factors

I. Identification

1. Name of health institution **Tikur Anbesa Hospital**
2. Questionnaire identification number _____
3. Patient card/chart number_____
4. Name of data collector _____
5. Name of supervisor _____

II. Assessment of comorbidities for breast cancer patients who were have follow up in Tikur Anbesa hospital

II. Patient socio-demographic characteristics

101. Region 1. Tigray 2. Afar 3. Amhara 4. Oromiya 5. Somali 6. B/Gumuz 7. SNNPRS 8. Gambella 9. Harare 10. Addis Ababa 11. Dire Dawa

102. Zone _____ Woreda_____

103. Age of patient at diagnosis _____Years

104. Residency 1. Urban 2. Rural

105. Marital status 1. Married 2. Single 3. Divorced 4. Widowed 5 other_____

106. Religion 1. Orthodox 2. Muslim 3. Protestant 4. Others _____

107. Ethnicity 1. Oromo 2. Amhara 3. Somali 4. Tigre 5. Sidama 6. Wolayita 7. Garage 8. Afar 99. Others(specify)_____

108. Able to read and write 1. Yes 2. No ➔ Q111

109. Attended formal education 1. Yes 2. No ➔ Q111

110. Highest grade completed (if higher education 12+1, 12+2, 12+4 or 10+ e t c) _____

111. Occupation 1. Farmer 2. Merchant 3. Housewife 4. Employee 99. Others, specify __

112. Are you happy with your work and or working area 1. Yes 2. Yes for the work but not working area 3. Yes for working area but not for the work 4. No at all

113. Usually how many hours do you work on a day_____

114. Have you owned the following items 1. Oxen 3. Farming land 4. Radio 5. Television 2. Tin sheet house 6. Car 7. Brick house 7. No all listed above

115. At what age was your first onset of menstruation_____

116. Are you still looking regular menstruation 1. Yes 2. No

117. If No, at what age do you stopped menstruation_____

118. At what age were you have the first pregnancy_____

119. How many live births do you have before you were diagnosed as breast cancer patients

1. Yes I do have _____ children 2. No, I do not have any children

120. If you have children, did you breast feed your last child 1. No 2.Yes 4. Other _____

III. Patients' attitude and practices towards possible risk factors for Breast Cancer and its comorbidities

121. Have you ever had breast biopsy, 1. Yes 2. No

122. Did any of your relative with history of breast cancer, 1. Yes 2. No

123. Were you used oral or injectable family planning methods 1. Yes 2. No

124. Have you ever smoke cigarette? 1. Never ➔ **126** 2. Yes, in the past 3. Yes, currently

125. If Ever/Yes, for how long (month/years) _____years _____months

126. Do you think cigarette smoking exposes to breast cancer 1. Yes 2. No 3. I do not Know 4. If other specify _____

127. Dietary habit of the patient 1. More of vegetables and fruits 2. More meat and fatty food 3. Anything found in the home 5. If other specify_____

128. Does the patient had any of the following chronic illness before the breast cancer diagnosed

1. Hypertension 2. Diabetes Mellitus 3. Heart diseases 3.if other specify _____

IV. Patient knowledge to wards Breast Cancer and related comorbidities

129. In your opinion what causes breast cancer (Write or list all what they said) _____

130. In your opinion, what should be done to prevent breast cancer _____

131. Does breast cancer can be treated 1. Yes 2. No➔ **Q133** 3. Do not know 4. Other specify _____

132. If Yes, can you mention some of breast cancer treatment (circle the answer when they mentioned) 1. Chemotherapy 2. Radiotherapy 3. Surgery 4. Traditional 5. If any other, specify----------

133. What will happen if a woman with breast cancer interrupt treatment (**write all what they mentioned**)_____

134. Can other illness happen together with breast cancer 1. Yes 2. No 3. Do not Know

135. If yes, do they have different signs and symptoms 1. Yes 2. No 3. Do not know

136. If yes, can you list common or possible illness that can happen _____

Card/Chart Review

1. Questionnaires Number _____ Card/ Chart Number _____

V. Patient Management Status

137. Date of first diagnosis _____/_____/___

138. Time since diagnosis_____ Years _____months

139. Stages of breast cancer at first diagnosis 1. Stage I 2. Stage II 3.Stage III 4. Stage IV

140. Current stage of breast cancer 1. Stage I 2. Stage II 3. Stage III 4. Stage IV

141. Type of management for the breast cancer 1. Radiotherapy 2. Chemotherapy 3. Mastectomy 4. Surgery 5. Lumpectomy surgery 6. Other mention_____

142. Status of breast cancer management 1. On treatment 2. Treatment was discontinued 3. Other_____

143. Other treatments 1. Antiemetic like dexamethasone 2. Hormone replacement therapy like estrogen 3. Other treatment mentioned

144. Body Mass Index of the patient 1. Less than 18.5 2. Between 18.5-25 3. It is 25 or above

VI. Comorbidities

145. Number of follow ups done for the patient_____ times

146. If the patient has confirmed comorbidities**, l**ist the types of diagnosed comorbidity, visit level, treatment given, stages of breast Cancer and date of follow up in the table below

Visit level	List the confirmed comorbidities	Stages of breast cancer	Does treatment given for the comorbidity (Yes/No)	Date of follow up
1st visit				
2nd visit				
3rd visit				
4th visit				
5th visit				

147. Does the oncology department has any guideline used to track comorbidity diagnosis- 1.Yes 2. No

148. Does the oncology department have any guideline used to treat comorbidities- 1. Yes 2. No

Date of data collection_____

ከጡት ካንሰር በሽታ ጋር ተያይዘው ስለሚከሰቱ ተጨማሪ ህመሞች ለመዳሰስ የተዘጋጀ መጠይቅ

ፈቃደኝነትን ለመጠየቅ የተዘጋጀ የጥናቱ አጠቃላይ መረጃ

በአሁኑ ሰአት በአዲስ አበባ ዩኒቨርስቲ የማህበረሰብ ጤና የማስተርስ ትምህርቴን እየተከታተልኩኝ የምገኝ ሲሆን በቀጣይ የመመረቂያ ፅሁፌን ከጡት ካንሰር በሽታ ጋር ተያይዘው ስለሚከሰቱ ተጨማሪ ህመሞች በጥቁር አነበሳ አጠቃላይ ሆስፒታል ውስጥ ከትትል በሚያደርጉ ታማሚዎች ለመስራት በዝግጅት ላይ እገኛለሁ፡፡ ስለሆነም በአሁኑ ሰአት ከጡት ካንሰር መስፋፋት ጋር ተያይዞ ከእሱ ጋር ተያይዘው የሚመጡ ተጨማሪ በሽታዎች በአለም ደረጃ እንዲሁም በአገራችን የማህበረሰብ ጤና ችግር ሆነዋል፡፡ ስለሆነም መንግስት ይህን በመረዳት የጤና መሰረት ልማት እያስፋፋ ይገኛል፡፡ የዚህ ጥናት መሰረታዊ አላማም ይህ ከጡት ካንሰር በሽታ ጋር ተያይዘው የሚከሰቱ ተጨማሪ ህመሞች በአሁኑ ሰአት በምን ደረጃ እንደሚገኝ እና በህክምና አሰጣጡ ላይ እያመጣ ያለውን ተፅኖ መዳሰስ ነው፡፡ይህ ቃለ መጠይቅ በአጠቃላይ 25-30 ደቂቃ ሊወስድ የሚችል ሲሆን ተሳታፊዎች በዚህ ጥናት ላይ የመሳተፍ ፍላጎታቸው የተጠበቀ ይሆናል፡፡በዚህ መጠይቅ ላይ የሚጠየቁ መረጃዎችን ከእርሶ ጋር በምንም አይነት ተያያዘ አገልግሎት የማይውል ሲሆን የሰጡን መረጃዎች ከምንም ጊዜ በላይ ሚስጥሩ የተጠበቀ ነው፡፡ይህንን ቃለ መጠየቅ ከጀመሩ በኃላ በማንኛውም ጊዜ ቃለ መጠይቁን ማቆም ይችላ ወይም መመለስ የማይፈልጉት ጥያቄዎች ያለመመለስ መብት አለዎት ግን ለዚህ ጥናት የሚሰጡን ምላሽ እጅግ አስፈላጊ እንደሆነ እንዲያውቁት እፈልጋለው፡፡

ከዚህ በሻገር ከጥናቱ ጋር በተያያዘ ማንኛውን ያልገባዎት ጉዳይ ካለ ቃለ መጠይቅ የሚያደርገውን ባለሞያ መጠየቅ የሚችሉ ሲሆን ከዛም ካለፈ ጥናቱን የሚያደርገውን ሰው ከዚህ በታች ባለው አድራሻ ማግኘት ይቻላል፡፡

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የስምምነት ውል

ከላይ አስቀድሜ የጥናቱን ጥቅምና አላማ ገልጨለዎታለሁ:: ስለዚህ በጥናቱ ላይ ለመሳተፍ ፈቃደኛ ነዎት?

አዎ 

አይደለሁም 

ፈቃደኛ ከሆኑ መሆነዎትን ማረጋገጫ ፊርማዎትን ያስቀምጡ_____

ከጡት ካንሰር ጋር ተያየዘው ለሚከሰቱ በሽታዎች ለሚደረግ ዳሰሳ ጥናት መረጃ መሰብሰቢያ መጠይቅ

I. መለያዎች

1. የጤና ድርጅቱ ስም ጥቁር አንበሳ ሆሲፒታል
2. መጠይቅ መለያ ቁጥር----------
3. የበሽተኛዋ ካርድ መለያ ቁጥር----------
4. የመረጃ ሰብሳቢ ስም---------- ሥ.ቁ.----------
5. የተቆጣጣሪ ሥም----------ሥ.ቁ.----------

ከጡት ካንሰር ጋር ተያየዘው ለሚከሰቱ በሽታዎች ለሚደረግ ዳሰሳ ጥናት መረጃ መሰብሰቢያ መጠይቅ			
6. የበሽተኛዋ ማህበራዊ ና ስነህዝብ ባህሪያት			
}k	**መጠይቅ**	**ምላሽ**	**ማሳሰቢያ**
101	• □**እትሜ**	----------አመት	
102	□**ክል**	1. ትግራይ 2. አፋር 3. አማራ 4. ኦሮሚያ 5. ሶማሊ 6. ቤኔሻንጉል 7. ደ/ብ/ብ/ህ/ክ 8. ጋምቤላ 9. ሃራሪ 10. አዲስ አበባ 11. ድሬዳዋ	
103	**መኖሪ□ ቦታ**	I. ከተማ 2. ገጠር	
104	**የትዳር ሁኔታ**	1. ያላገባ 2. ያገባች 3. የፈታች 4. ባሏ የሞተባት 5. ሌላ----------	

105	ሀይማኖት	1. ኦርቶደክስ 2. ሙስሊም 3. ፕሮቴስታንት 99. .ሌላ (ካለ ይገልፅ)----------	
106	**ብሄር**	1. አፋርr 2. አማራ 3. አገው 4. ትግሬ 5. ኦሮሞ 6. ሲዳማ 7. ዎላይታ 8. ጉራጌe 9. ሶማሊ 99.ሌላ (ካለ ይገልፅ)----------	
107	**ስራ**	1. አርሶ አደር 2. ነጋዴ 3. የቤት ዕመቤት 4. የመንግስት ቅጥረኛ 99. ሌላ (ካለ ይገልፅ)----------	
108	የትምህርት ደረጃ	1. ማንበብ ና መፃፍ አለመቻል 2. ማንበብ ና መፃፍ የሚችል 3. 1 – 6 ክፍል 4. 7 – 12 ክፍል 5. ስረቲፍኬት 6. ድግሪ ና ከዛ በላይ	
109	የጡት ካንሰር በሽተኛ ከሆነሽ ስንት ጊዜ ሆነሽ	----------ወር/አመት	
	7. የበሽተኛዋ አመለካከት የጡት ካንሰር ሊያጋልጡ ከሚችሉ ነገሮች ጋር ታያይዞ		

110	ሲጋራ አጭሰው ያውቃሉ	1. አዎ፣አሁንም አጨሳለው 2. አዎ፣አሁን ግን አቁሚያለው 3. የለም 4. ሌላ ----------	መልሱ የለም ከሆነ ወደ ተራ ቁጥር 112 እለፍ
111	**አወ ካሉ፣ ለስንት ጊዜ ነው/ነበር**	---------- ወር/አመት	
112	**ሲጋራ ማጨስ ለጡት ካንሰር ያጋልጣል ብለው ያምናሉ**	1. አዎ 2. የለም 3. አላውቅም 4. ሌላ ----------	
113	**ማንኛውንም አይነት አልኮል ወስደው ያውቃሉ**	1. አዎ፣አሁንም አጨሳለው 2. አዎ፣አሁን ግን አቁሚያለው 3. የለም 4. ሌላ	መልሱ የለም ከሆነ ወደ ተራ ቁጥር 115 እለፍ
114	**መልሰው አው ከሆነ፣ ለስንት ጊዜ ነው/ነበር**	---------- ወር/አመት	
115	**አልኮል ማጨስ ለጡት ካንሰር በሽተኛነት ያጋልጣል ብለው ያምናሉ**	1. አዎ 2. የለም 3. አላውቅም 4. ሌላ	
	የበሽተኛዋ እውቀት ከጡት ካንሰር ህክምና ጋር ታያይዞ		
116	**በርሰዎ አመለካከት የጡት ካንሰር በምን ምክኒያት ሊመጣ ይችላል(የተባለውን በሙሉ ዘርዝሩ)**	----------	
117	**የጡት ካንሰር ሊታከም ይችላል ብለው ያምናሉ**	1. አዎ 2. የለም 3. አላውቅም 4. ሌላ----------	መልሱ የለም ከሆነ ወደ ተራ ቁጥር 119 እለፍ
118	**መልሰዎ አዎ ከሆነ ፤የጡት ካንሰር በሽታ ህክምና ሊነግሩኝ**	1. ኬሞ ትራፒ 2. ጨረር	

	ይችላሉ	3. ቀዶ ህክምና 4. ባህላዊ 5. ሌላ ካለ ይገለፅ----------	
119	**የጡት ካንሰር በሽታ ህክምና ቢቋረጥ ምን ሊከሰት ይችላል (የተባለው በሙሉ ይፃፍ)**	----------	
	8. የጡት ካንሰር በሽታ ደረጃዎች		
120	**የጡት ካንሰር በሽታ ደረጃዎች**	**1. የጡት ካንሰር ደረጃ I** **2. የጡት ካንሰር ደረጃ II** **3. የጡት ካንሰር ደረጃ III** **4. የጡት ካንሰር ደረጃ IV**	
	9. የበሽታው የህክምና ሁኔታ		
121	**የጡት ካንሰር በሽታ ህክምና አይነቶች**	1. ኬሞ ትራፒ 2. ጨረር **3. Mastectomy surgery** **4. Lumpectomy surgery** **5.** ሌላ ካለ ይገለፅ----------	
122	**የጡት ካንሰር በሽታ ህክምና ሁናቴ**	**1. በህክምና ላይ** **2. ህክምና ያቋረጠች** **3.** ሌላ ካለ ይገለፅ----------	
123	**ሌሎች ከጡት ካንሰር በሽታ ህክምና ውጭ ያሉ ህክምናዎች**	**1. ማስመለስ ለመካለከል እንደ dexamethasone ያሉ** **2. ሆርሞን ልመተካትእንደ estrogen** **3.** ሌላ ካለ ይገለፅ----------	

Annex 4 Stages of breast cancer

- Although there are a few ways to classify stage, the most widely used is the TNM system.

  TNM stands for:

  - **T** = **T**umor size
  - **N** = Lymph **N**ode status (the number and location of lymph nodes with cancer)
  - **M** = **M**etastases (whether or not the cancer has spread to other areas of the body)

The stages of breast cancer range from 0 to IV (0 to 4).

Stage depends on the combination of tumor size (T), lymph node status (N) and metastases (M).

For example, a cancer with a T1 tumor (less than 2 cm), no lymph nodes with cancer (N0) and no metastases (M0) is classified as stage I (T1N0M0).

The highest stage (stage IV) is any cancer with metastases (M1), no matter the size of the tumor or the lymph node status.

Most often, the higher the stage of the cancer, the poorer the prognosis will be.

Table 3 below lists the TNM classifications for each stage of breast cancer.

Stages of Breast Cancer	
Ductal carcinoma in situ	
Stage 0	TisN0M0
Early breast cancer	
Stage Ia	T1N0M0
Stage Ib	T0N1miM0
	T1N1miM0
Stage IIa	T0N1M0
	T1N1M0
	T2N0M0
Locally advanced breast cancer	

Stage II b	T2N1M0
	T3N0M0
Stage III a	T0N2M0
	T1N2M0
	T2N2M0
	T3N1M0
	T3N2M0
Stage III b	T4N0M0
	T4N1M0
	T4N2M0
Stage III c	Any T, N3M0
Metastatic breast cancer	
Stage IV	Any T, any N, M1

Updated 10/19/16

Annex 5 Type and prevalence of comorbidities based on stages of breast cancer reviewed from patient card in Tikur Anbesa Specialized Hospital August 2017, Addis Ababa.

Comorbidity * Stage of breast cancer at diagnosis							
S/N	Comorbidities	Stage of breast cancer at diagnosis				Total	%
		stage I	stage II	stage III	stage IV		
1	Neutropenia	3	16	63	39	121	16.3
2	Fatty liver	0	13	48	26	87	11.7
3	Gastritis/PUD	0	15	36	10	61	8.2
4	Anemia	0	9	21	13	43	5.8
5	Liver metastasis	0	8	6	15	29	3.9
6	HPTN	0	3	12	6	21	2.8
7	Lymphadenitis	0	0	16	3	19	2.6
8	Plural effusion	0	3	6	9	18	2.4
9	Insomnia	0	3	9	3	15	2.0
10	DM	0	0	3	12	15	2.0
11	Uterine Myoma	0	8	6	0	14	1.9
12	Brain Metastasis	0	0	0	9	9	1.2
13	Pneumonia	0	0	3	6	9	1.2
14	Anxiety	0	6	3	0	9	1.2
15	CHF	0	3	3	3	9	1.2
16	Lt Ventricular stenosis	0	0	6	3	9	1.2
17	Cholelithiasis	0	0	7	0	7	0.9
18	M/head ache	0	0	3	3	6	0.8
19	Neuritis	0	3	0	3	6	0.8
20	Sepsis	0	0	3	3	6	0.8
21	Hepatoma	0	3	3	0	6	0.8
22	Lung Metastasis	0	0	3	3	6	0.8
23	Wound Infection	0	3	3	0	6	0.8
24	Splenomegaly	0	0	6	0	6	0.8
25	RVI	0	3	0	3	6	0.8
26	Toxoplasmosis	0	0	4	0	4	0.5
27	TB	0	0	4	0	4	0.5
28	Esophageal Ca	0	0	3	0	3	0.4
29	Hypovolemic shock	0	0	3	0	3	0.4
30	Bone Metastasis	0	0	0	3	3	0.4
31	Ectopic Kidney	0	0	3	0	3	0.4

32	Hypothyroidism	0	0	3	0	3	0.4
33	Bronchitis	0	0	0	3	3	0.4
34	Ductal ca	0	0	0	3	3	0.4
35	Hip joint dislocation	0	0	0	3	3	0.4
36	ovary cyst	0	0	3	0	3	0.4
37	Conjunctivitis	3	0	0	0	3	0.4
38	Neuropathy	0	3	0	0	3	0.4
39	AUB	0	0	3	0	3	0.4
40	Hydronephrosis	0	3	0	0	3	0.4
41	Osteoporosis	0	0	0	3	3	0.4
42	Abortion	0	0	3	0	3	0.4
43	Ascites	0	0	0	3	3	0.4
44	Endometrium ca	0	0	3	0	3	0.4
45	Nephrolithiasis	0	0	3	0	3	0.4
46	Small Kidney	0	0	0	3	3	0.4
47	Asthma	0	3	0	0	3	0.4
48	Dental problems	0	0	3	0	3	0.4
49	Ischemic	0	0	0	3	3	0.4
50	Secondary infertility	0	0	3	0	3	0.4
51	Super Infection	0	0	0	3	3	0.4
52	Renal Disease	0	0	0	3	3	0.4
	Total	6	151	368	216	741	100.0

Annex 6 Type and prevalence of comorbidities based on follow up time of breast cancer patients reviewed from patient card in Tikur Anbesa Specialized Hospital August 2017, Addis Ababa.

Comorbidities magnitude during 1st follow ups			Comorbidities and its magnitude during 2nd follow ups			Comorbidities and its magnitude during 3rd follow ups		
Comorbidities	**No**	**%**	**Comorbidities**	**No**	**%**	**Comorbidities**	**No**	**%**
Fatty liver	48	11.9	Neutropenia	53	13.1	Neutropenia	19	4.7
Neutropenia	43	10.6	Fatty liver	30	7.4	Gastritis/PUD	9	2.2
Gastritis/PUD	34	8.4	Gastritis/PUD	18	4.5	HPTN	6	1.5
Anemia	31	7.7	Anemia	12	3.0	Insomnia	6	1.5
Liver metastasis	17	4.2	DM	9	2.2	Chololithiasis	4	1.0
Lymphadenitis	16	4.0	Liver metastasis	6	1.5	CHF	3	0.7
Plural effusion	9	2.2	Insomnia	6	1.5	Nephrolithiasis	3	0.7
Brain Metastasis	9	2.2	Anxiety	6	1.5	Anxiety	3	0.7
RVI	6	1.5	TB	4	1.0	Ovary Cyst	3	0.7
Neuritis	6	1.5	Myoma	4	1.0	Pneumonia	3	0.7
M/head ache	6	1.5	Abortion	3	0.7	Sepsis	3	0.7
HPTN	6	1.5	AUB	3	0.7	Hepatoma	3	0.7
Uterine Myoma	6	1.5	Lymphadenitis	3	0.7	Small Kidney	3	0.7
Toxoplasmosis	4	1.0	Lung Metastasis	3	0.7	Asthma	3	0.7
Sepsis	3	0.7	Pneumonia	3	0.7	Fatty liver	3	0.7
CHF	3	0.7	Conjunctivitis	3	0.7	Liver metastasis	3	0.7
Cholelithiasis	3	0.7	Neuropathy	3	0.7	Plural effusion	3	0.7
Bronchitis	3	0.7	Wound Infection	3	0.7	Dental problems	3	0.7
Hip joint dislocation	3	0.7	Osteoporosis	3	0.7	DM	3	0.7
Pneumonia	3	0.7	CHF	3	0.7			
Hepatoma	3	0.7	Ascites	3	0.7			
Hydro nephrosis	3	0.7	Plural effusion	3	0.7			
Esophageal Ca	3	0.7	Endometrium Ca	3	0.7			
Ductal Ca	3	0.7						
Bone Metastasis	3	0.7						
Ectopic Kidney	3	0.7						
Hypovolemic Shock	3	0.7						
Hypothyroidism	3	0.7						
DM	3	0.7						

Insomnia	3	0.7							
Comorbidities and its magnitude during 4th Follow Ups			**Comorbidities and its magnitude during 5th and above Follow Ups**						
Comorbidities	**No**	**%**	**Comorbidities**	**No**	**%**				
HPN	9	2.2	Neutropenia	9	2.2				
Splenomegaly	6	1.5	Left ventricular thrombosis	3	0.7				
Ischemic HD	3	0.7	Fatty liver	3	0.7				
Liver metastasis	3	0.7							
Fatty liver	3	0.7							
Lung metastasis	3	0.7							
Neutropenia	3	0.7							
Plural effusion	3	0.7							
Renal disease	3	0.7							
Super infection	3	0.7							
Wound infection	3	0.7							

Annex 7 Conceptual Frame work

Fig 1. Model of comorbidity of breast and its associated factors.

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