ASSESSMENT OF BREAST CANCER TREATMENT OUTCOME AT TIKUR ANBESSA SPECIALIZED HOSPITAL ADULT ONCOLOGY UNIT, ADDIS ABABA, ETHIOPIA

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This is to certify that the thesis prepared by Selamawit Dagne, entitled *Assessment of breast cancer treatment outcome in adult oncology unit of TikurAnbessa Specialized Hospital, Addis Ababa,Ethiopia.* Submitted in partial fulfillment of the requirements for the degree of Master of Pharmacy in Pharmacy Practice complies with the regulations of the University and meets the accepted standards with respect to originality and quality.

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Abstract

Assessment of breast cancer treatment outcome in adult oncology unit of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

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Breast cancer is a leading cause of death worldwide, and ranks as the fifth cause of death from all cancers, and the most common cause of cancer death in women in both developing and developed countries. However, information regarding treatment outcome of breast cancer is scarce in Ethiopia. The aim of this study was therefore to assess treatment outcome among breast cancer patients at Tikur Anbessa Specialized Hospital adult oncology unit. To this effect a hospital, based retrospective cross-sectional study was conducted. Data were collected by reviewing the medical records and by phone interview. A total of 303 patients were included in the study, more than one fourth (31.02%) of the patients were in the age range of 30-39 years, with a mean age of 42.10 years. More than half (54.10%) of the patients were diagnosed to have breast cancer with clinical tumor, nodal status and metastasis stage III. The frequently used combination chemotherapy was FAC (5-fluorouracil, Doxorubicin, and Cyclophosphamide) in (66.9%) patients. At the end of three years treatment follow up, (46.53%) of patients were dead, while 34.32% were alive. The result of logistic regression analysis showed that age (AOR= 0.32, 95% CI: 0.12, 0.95, P=0.040), chemotherapy cycle (AOR= 7.36, 95% CI: 2.28, 23.79, P=0.001), stage of the disease (AOR= 0.11, 95% CI: 0.05, 0.29, P=0.000), endocrine therapy (AOR= 0.09, 95% CI: 0.04, 0.22, P=0.000) were significantly associated with the outcome of death. Treatment outcome of breast cancer is poor

and requires health education and sensitization on preventive approach through screening to prevent the late stage presentation at health facilities.

Key words: Breast cancer, treatment outcomes, treatment options, stage of cancer

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List of Abbreviations and Acronyms

AC	Adriamycin (doxorubicin) and Cyclophosphamide
CMF	Cyclophosphamide, Methotrexate, and 5-fluorouracil
ER	Estrogen Receptor
FAC	5-fluorouracil, Doxorubicin, and Cyclophosphamide
HER2	Human Epidermal Growth Factor Receptor 2
NCCN	National Comprehensive Cancer Network
PR	Progesterone Receptor
TASH	Tikur Anbessa Specialized Hospital
TNM	Tumor Size, Nodal Involvement and Metastasis
WHO	World Health Organization

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1. Introduction

1.1 Background

Breast cancer is a leading cause of death worldwide, and ranks as the fifth cause of death from all cancers, and the most common cause of cancer death in women in both developing and developed countries [WHO, 2015]. Prevalence of breast cancer alone accounts for 25% of all cancer cases and 15% of all cancer deaths among females [Torre *et al*., 2015]

Breast cancer is the most frequent cause of cancer death in women in less developed regions (324,000 deaths, 14.3% of total). It is now the second cause of cancer death in more developed regions (198,000 deaths, 15.4%) after lung cancer [WHO, 2012] .The mortality rate of breast cancer ranges from six per 100,000 in Eastern Asia to 20 per 100,000 in Western Africa [WHO 2012].Estimates of age-standardized incidence rates (per 100,000 women) are 30.4 in eastern Africa, 26.8 in central Africa, 38.6 in western Africa, and 38.9 in southern Africa [Brinton *et al*.2014]. Breast cancer was found to be the second prevalent cancer next to gynecological malignancy according to a study done in Tikur Anbessa specialized hospital (TASH) [Tigeneh *et al*., 2015].

Many lifestyle and environmental risk factors influence the course of the disease including age at menarche, age at menopause, parity, age of first and subsequent pregnancies, breastfeeding, exogenous estrogen use, body mass index (BMI) and alcohol consumption[Barnett *et al* .,2008]. Additional risk factors for breast cancer is ethnicity. White women are slightly more likely to develop breast cancer than are African American women, but African-American women are more likely to die of this cancer [American Cancer Society, 2015].

Initial workup for a woman presenting with a lesion or symptoms suggestive of breast cancer should include a careful history, physical examination of the breast, 3-D mammography, and

possibly other breast imaging techniques such as ultrasonography or magnetic resonance imaging [Dipiro *et al*., 2011].

Breast cancer is classified by whether the cancer started in the ducts or lobules, whether it grows or spread through the duct or lobule and how the cancer cells look under a microscope [NCCN, 2010]. It is broadly grouped in to those that are still in the breast lobules or ducts called noninvasive or carcinoma in situ and those that have started to grow and spread beyond the walls of the ducts or lobules called invasive carcinoma [NCCN, 2010].Breast cancer stage is defined on the basis of the primary tumor extent and size (T1–4), presence and extent of lymph node involvement (N1–3), and presence or absence of distant metastases (M0–1) [Dipiro*et al* ., 2008].

Treatment of breast cancer is dependent on disease stage, histologic and molecular subtypes and menopausal status [Di Leo *et al*., 2015] .Treatment of breast cancer includes surgery, radiation therapy, or both, and systemic treatment with chemotherapy, endocrine therapy, biologic therapy or combinations of these. The selection of various local or systemic therapies are based on several prognostic and predictive factors including tumor histology, clinical and pathologic characteristics of the primary tumor, axillary lymph node status, tumor hormone receptor (estrogen receptor (ER)/ progesterone receptor (PR)) content, tumor human epidermal receptor (HER2) status, presence or absence of detectable metastatic disease, patient comorbid conditions, patient age, and menopausal status [NCCN ,2015].

The development of metastasis and local recurrence also vary for different treatments, and for different population groups [Youlden *et al*, 2012]. Diverse factors are responsible for such variations, including demographics, ethnicity, disease stage of diagnosis, and co-morbidities. Although studies on predictors of breast cancer treatment outcome have been undertaken in developed countries, there is paucity of data on predictive indicators of breast cancer treatment

outcomes in Africa including Ethiopia [Sant *et al*, 2004]. This study was therefore initiated to assess the treatment outcomes of breast cancer in patients attending adult oncology unit of TikurAnbessa specialized hospital (TASH).

1.2. Statement of the problem

Breast cancer is the predominant cancer in women both in the developed and in the developing world [WHO, 2015]. Many developed countries have reduced the incidence of the cancer and hence treatment burden through screening programs. Several studies have reported that factors implicated in poorer breast cancer outcome among black and white women, many and varied include demographic factors ,clinical characteristics, biologic aspects of the disease, socioeconomic status, and related health care factors may contribute to poorer outcomes for African-American women [Dignam,2000].

Breast cancer mortality rate among women is correlated to the stage of the breast cancer. When breast cancer is diagnosed in its early stage and treated, the women have a greater chance of survival. Breast cancer screening can detect cancer at an early stage when it is done correctly. Unfortunately, Ethiopia does not have a routine screening scheme like many developing countries in the world. Consequently, patients present at late stage, which results a significantly high morbidity and mortality related to breast cancer. The late presentation mostly requires costly and advanced treatment methods presenting a challenge to the inadequately resourced health institutions. In addition, there are no concrete data on the exact burden of the disease in the country, and the treatment outcome of breast cancer in Ethiopia. Hence, the result of this study would help to provide information regarding treatment outcome of breast cancer and associated factors. This would in return help to improve the service provided to breast cancer patients.

1.3. Literature review

1.3.1. Epidemiology of breast cancer

Breast cancer is the most common type of malignancy in the world and one of the major reasons of mortality among women worldwide [Jemal *et al*., 2010]. Cancer is increasingly recognized as a critical public health problem in Africa in which breast cancer in women has now become the most commonly diagnosed cancers in some parts of Africa [WHO, 2011].

Worldwide, more than 12 million individuals are newly diagnosed with cancer annually [Torpy *et al*., 2010]. Among 8.2 million cancer deaths in 2012, 65% occurred in less developed regions. The most prevalent cancers were lung (13.0%), breast (11.9%) and colorectal (9.7%) [IARC, 2012].

For all racial and ethnic groups, most breast cancers are diagnosed at an early stage, when tumours are small and localized. However, a higher proportion of disease is diagnosed at more advanced stages in African American and other minority women than in white women. The death rate is also higher among African American women than white women despite the lower incidence rate. Breast cancer is the leading cause of cancer deaths for females between the ages of 20 and 59 years [Dipiro *et al*., 2008].

1.3.2. Risk factors of breast cancer

Different studies reported many risk factors for breast cancer. A systematic review reported that risk factors for breast cancer include reproductive factors; such as early age at menarche, late age at first birth, null parity, and late age at menopause; family history of breast cancer , alcohol intake, exposure to ionizing radiation, use of combined estrogen plus progestin postmenopausal hormone therapy, recent use of oral contraceptives, physical inactivity,

leanness in early life and obesity in later life[Howell *et al*., 2014;Colditz*et al*.,2015]. Marked adult weight gain in premenopausal women is associated with a doubling of risk of postmenopausal breast cancer compared with no or little weight gain [Eccles *et al,* 2013]. Moreover, extremely dense breasts on mammography was associated with greater than two-fold increase in breast cancer. Prior breast biopsy and heterogeneously dense breasts were associated with 1.5–2 fold increased risk of breast cancer while current oral contraceptive use was associated with 1.0–1.5 increased risk [Nelson *et al.,* 2013].

A research by Kakarala *et al.* (2010) indicated that Asian women particularly those under 40years of age were more likely to be affected with ER/PR negative invasive ductal and inflammatory cancer than Caucasians. Although biological, genetic and physiological factors play significant roles in breast cancer development, how it is treated,and who survives from it; social, political, economic, and psychological variables also substantially contribute to breast cancer racial/ethnic disparities in treatment outcomes [Penner *et al*.,2012]

A family history of breast cancer in first-degree relatives, especially if the breast cancer was bilateral or diagnosed at an early age, strongly increases the risk of developing the disease [Hopper, 1996]. A study from UK showed women with a history of breast cancer in a first-relative are approximately two-fold higher risk than women without a family history [Mavaddat *et al*., 2015]. Moreover, women with two or more relatives with breast cancer diagnosed at <50 years had even higher risks [Nelson *et al*.,2013].

From reproductive factors, the influential risk factors for breast cancer are a woman's menstrual life and her childbirth history [Ursin *et al*., 1999]. A study from Australia reported thatwomen who had their first menstrual period at age 12 or later have a slightly lower risk of breast cancer (10–25%) than women who had their first menstrual period earlier [National Breast and Ovarian Cancer Centre, 2009]. With regard to childbirth history a study by Nelson

et al.,(2013) showed that null parity and age ≥30 years at first birth were associated with 1.0–1.5 increased risk of breast cancer.

1.3.3. Factors associated with treatment outcome of breast cancer

Disparities in breast cancer outcomes result from not only racially specific tumor differences, but also modifiable social and health system determinants of individual behavior and decision-making as well as characteristics of the patient-health system interaction and the health system itself [Wheeler,2013].

The most important demographic risk factor for breast cancer is age [AIH, 1998].A retrospective, population-based cohort study from San Francisco-Oakland, showed thatyounger women were more likely to die compared with older women if diagnosed with stage I or stage II disease and less likely to die if diagnosed with stage IV disease [Gnerlich *etal*.,2008]. Similar result was obtained from a cohort study done inSweden in which women under 40 years of age had a poor prognosis [Brandt *et al*., 2015]. Moreover, a systematic review reported that in USA young women with early stage disease who were not treated with cytotoxic therapy had an increased risk of dying compared to older age groups. [Gabriel *et al.*, 2010]. Additionally, a study conducted inEgypt showed that younger women presentedwith more hormone non-responsive tumors than older ones and recurrence rates were significantly higher among young women compared to older women [Alieldin *et al*., 2014].

Additional factor associated with breast cancer outcome is stage of the disease at initiation of treatment. Women who were at stage II of breast cancer at the time of initiation of treatment were less likely to develop metastasis compared to those who were in cancer stage III, the probability of survival also decreased with increasing stage of breast cancer[Chung *et al*., 2011; Wata *et al*.,2013]

Breast cancer mortality has been found to be decreasing gradually since 1990s, after improvement of breast cancer screening techniques and the advancement of treatment approaches [Tabar *et al*., 2003]. Better treatments include targeted chemotherapy, endocrine therapy, radiotherapy and surgery, inhibitors of certain proteins and more recently immune therapy (monoclonal antibodies) [Treatment of Breast Cancer New Approaches, 2012].A study from American Academy of Family Physicians reported that chemotherapy is the standard of care for women with node-positive cancer or with a tumor larger than 1 cm addingusing a taxane to an anthracycline-based regimen improved disease-free survival and overall survival [Karen.*et al*.,2010].On the other hand, a study in France as for younger patients, poly chemotherapies are more efficient than monotherapy that standard adjuvant chemotherapy with CMF or doxorubicin plus cyclophosphamide was superior to capecitabine alone [Le Saux *etal*., 2015].

Another study from the American Academy of Family Physiciansreported that hormone receptor–negative disease derives more benefit from chemotherapy than hormone receptor–positive disease[Karen *et al.*, 2010]. Endocrine therapy is not effective against cancers that are lacking hormone receptors so five years of treatment with tamoxifen reduces the breast cancer death rate. Moreover, the Brazilian National Cancer Institute retrospective study showed that adjuvant endocrine therapy was associated with lower rates of disease recurrence and metastasis and, thus, improved mortality rates and disease-free survival [Brito *et al*., 2014]. A case–control study conducted in California showed that tamoxifen reduces the risk of subsequent contralateral breast cancer as well as breast cancer recurrences and mortality [Bernstein *et al*., 1999].

Socioeconomic status of the patient is another factor found to have association with breast cancer treatment outcome according to a study from Australia which reported women living in

the lowest socioeconomic status areas had highest percent of advanced stages (III, IV) and ≥ 4 lymph nodes positive and much worse survival [Yu,2009].

2. Objectives

2.1.General objective

To assess treatment outcome among breast cancer patients at Tikur Anbessa Specialized Hospital adult oncology unit.

2.2. Specific objectives

- To describe the clinical characteristics of breast cancer patients
- To describe treatment modalities of breast cancer
- To determine the proportion of breast cancer patients death at the end of three years treatment.
- To identify factors associated with treatment outcome of patients with breast cancer

3. Methods

3.1. Study setting and period

The study was conducted at adult oncology unit of TASH. TASH is a large referral teaching hospital, under the administration of Addis Ababa University, located in Addis Ababa, Ethiopia. TASH has divisions such as internal medicine, surgery, gynecology and obstetrics, pediatrics, radiotherapy, adult oncology, pediatric oncology /hematology, nuclear medicine, psychiatry, laboratory, orthopedics and pharmacy. The hospital has more than 800 beds, give diagnostic, and treatment service for about 370,000-400,000 patients per year. The oncology unit of TASH is the only oncology unit for the country and has an outpatient department, which gives service to new and follow-up patients, and an in-patients department, which has 19 beds. Breast cancer contributed to 24.49% of all malignancies admitted at TASH from 12thSeptember, 2011 to 10thSeptember 2012. The study was conducted from 01, July to01, September 2015.

3.2.Study design

The study was a hospital based retrospective cross-sectional study.

3.3. Population

3.3.1 Source population

The source population constitutes all medical records of breast cancer patients who attended oncology unit of TASH.

3.3.2 Study population

The study population constitutes all medical records of breast cancer patients who attended the oncology unit of TASH from 12thSeptember, 2011 to 10thSeptember 2012 that fulfill the inclusion criteria of the study.

3.3.3. Inclusion and exclusion criteria

Inclusion

- Medical charts of female breast cancer patients
- Age ≥ 18 years.
- First visit to TASH from September 12, 2011 to September 10, 2012.

Exclusion

- Patients who were diagnosed with other cancer.

3.4. Sample size

All breast cancer patients who attended the oncology unit of TASH from September 12, 2011 to September 10, 2012 and fulfilled the inclusion criteria of the study were included in the study. As a result, there were 416 patients who visited the oncology unit of TASH from September 12, 2011 to September 10, 2012 and 303 patients fulfilled the inclusion criteria and hence were included in the study.

3.5. Data entry and analysis

The data was entered and analyzed using Statistical Package for the Social Sciences (SPSS) version 20.0. Descriptive statistics were used to summarize study variables. Logistic regression was used to analyze the associations between independent variables and treatment outcome by using crude odds ratio (COR) and adjusted odds ratio (AOR) at 95% confidence level. A p-value of less than 0.05 was considered statistically significant.

3.6. Study variables

3.6.1. Independent variables

- Demographic characteristics (Age, Region)
- Clinical characteristics (TNM-tumor size, nodal involvement and metastasis stage, histologic differentiation)
- Mode of treatment
- Treatment modality (number of chemotherapy cycle, type of chemotherapy combination)

3.6.2. Dependent variables

- Treatment outcome

3.7. Data collection and technique

A data abstraction format was used to record the necessary information from patients' medical record (Annex I). Data were collected by reviewing the medical records of breast cancer patients who attended the oncology unit of TASH from September 12, 2011 to September 10, 2012 and by phone interview. Information entered in the medical records for three years after

patient's first visit were reviewed and data including demographic characteristics, clinical characteristics and treatment modalities were recorded on data abstraction format. Additional information was collected by calling patients using their phone number recorded on medical record to confirm status of some missed patients from follow up.

The data were collected by two pharmacist who were given a one day training prior to data collection on how to use the data abstraction format to gather information from patients' medical records.

3.8. Data quality control

To ensure quality of the data, pre-test was done on 5% of the study population to ensure the agreement of the data abstraction format with the need of the study. Any error found during the process of pre-test was corrected and modification was made into the final version of the data abstraction format. The data collectors were trained for one day before the process of data collection. Supervision and checking was made by the principal investigator to ensure completeness and consistency of the collected data. All collected data were examined for completeness and consistency during data management, storage and analysis.

3.9.Ethical considerations

Ethical clearance was obtained from the Ethical Review committee of School of Pharmacy of Addis Ababa University. Before the start of data collection, permission was obtained from oncology unit of TASH. To ensure confidentiality, name and other identifiers of patients and health care professionals were not recorded on the data abstraction format.

4. Results

4.1. Socio-demographic characteristics

A total of 303 patients were included in the study. More than one fourth (31.02%) of the patients were in the age range of 30-39 years, with a mean age of 42.10 years and more than one-third (35.97%) were from Addis Ababa as shown in Table 1.

Table 1 :Socio-demographic characteristics of the study participants.

Characteristics		Frequency	Percent
Age	<20 years	1	0.33
	20-29 years	40	13.20
	30-39 years	94	31.02
	40-49 years	86	28.38
	50-59 years	53	17.49
	60-69 years	18	5.94
	>70 years	11	3.63
Region	Addis Ababa	109	35.97
	Amhara	50	16.50
	Benishangul	2	0.66
	Harari	3	0.99
	Oromia	99	32.67
	Somalia	2	0.66
	SNNP	26	8.58
	Tigray	12	3.96

SNNP- Southern Nations, Nationalities and Peoples

4.2. Clinical characteristics of the study subjects

The study findings show that more than half (54.10%) of the patients were diagnosed to have breast cancer with clinical TNM stage III as illustrated in Figure 1.

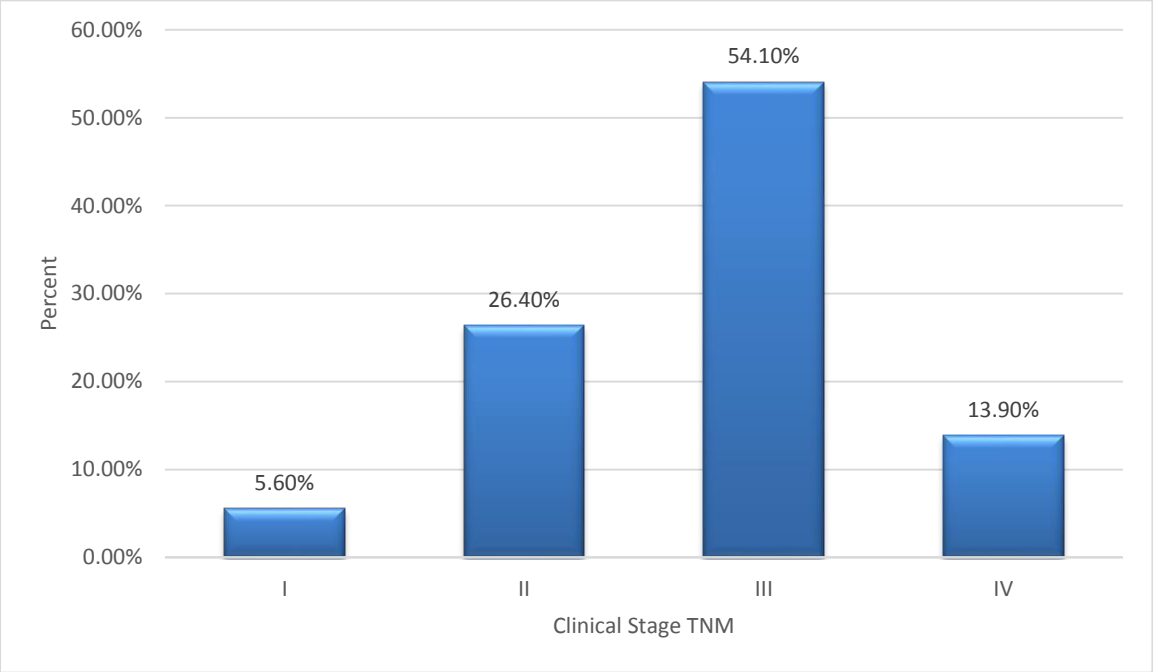

Figure 1: Breast cancer clinical stage based on tumor size, nodal involvement and metastasis**:**

TNM- tumor size, nodal involvement and metastasis

Based on histological classification almost all of the patients (98.34%) were diagnosed with invasive breast cancer among which (95.63%) were having ductal invasive breast carcinoma (Figure 2).

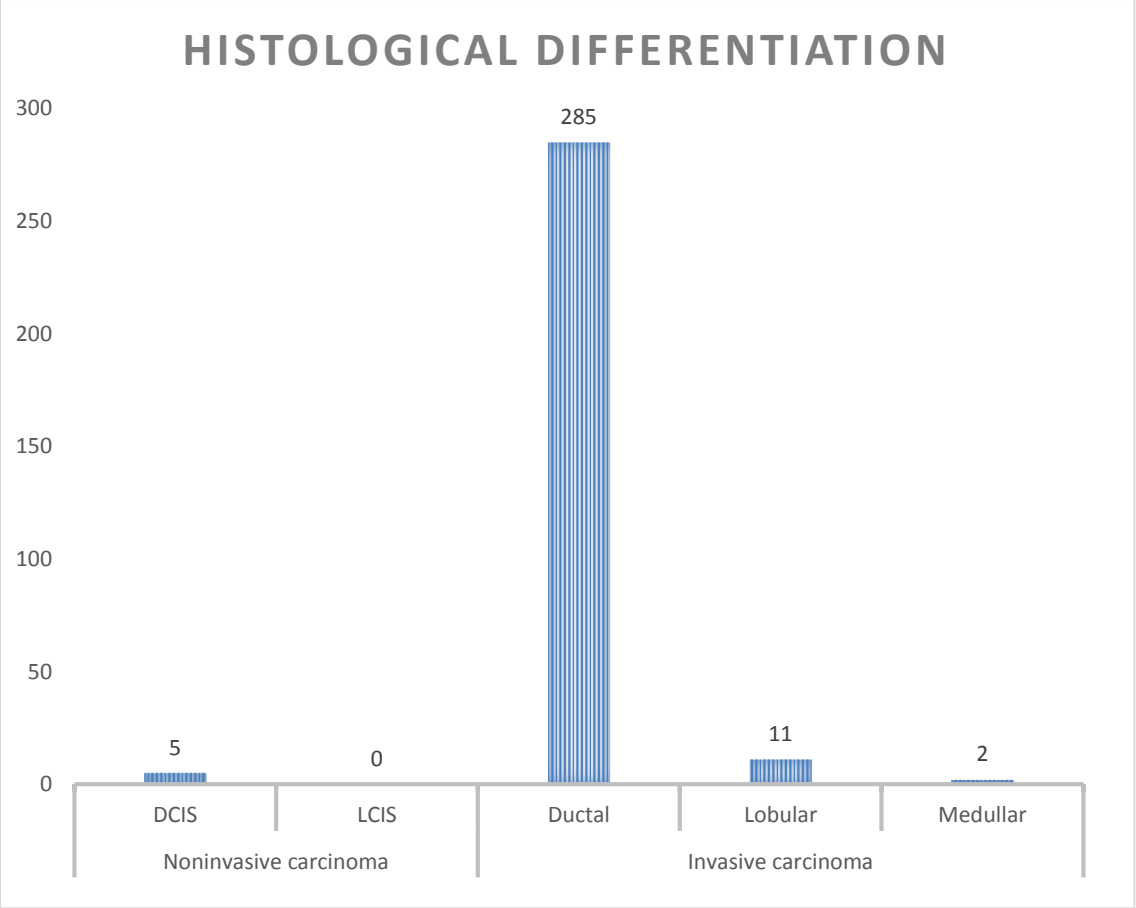

Figure 2: Histologic based classification of breast cancer in the study population: LCIS- Lobular carcinoma insitu, DCIS- Ductal carcinoma insitu

4.3. Treatment of breast cancer

4.3.1. Mode of treatment of breast cancer

Although various modes of therapy were used to treat breast cancer patents (Table 2), surgery, chemotherapy was the most common mode of treatment (55.8%) employed in the study population.

Table 2: Clinical characteristics of the study participants.

Clinical Characteristics		Frequency	Percent
	Radiotherapy	4	1.32
	Surgery, Radiotherapy & Palliative care	1	0.33
	surgery, Radiotherapy chemotherapy & Palliative care	6	2.00
Mode of Treatment	Radiotherapy, Chemotherapy Palliative care&	1	0.30
	Radiotherapy & Chemotherapy	22	7.30
	Surgery, Radiotherapy & Chemotherapy	73	24.10
	Palliative care	16	5.30
	surgery, chemotherapy	169	55.80
	Surgery	7	2.30
	chemotherapy ,Palliative Care	3	1.00
	surgery, chemotherapy, Palliative Care	1	0.30
Type of Second line Treatment	Chemotherapy	27	93.10
	Chemotherapy &Radiotherapy	2	6.90
Type of Surgery	Lumpectomy	2	0.77
	Mastictoctomy	255	99.22

4.3.2. Type of chemotherapy

The frequently used combination chemotherapy was FAC (5-fluorouracil, Doxorubicin, and Cyclophosphamide) in (66.9%) followed by AC (Doxorubicin and Cyclophosphamide) (28.37%) as shown in Figure 3.

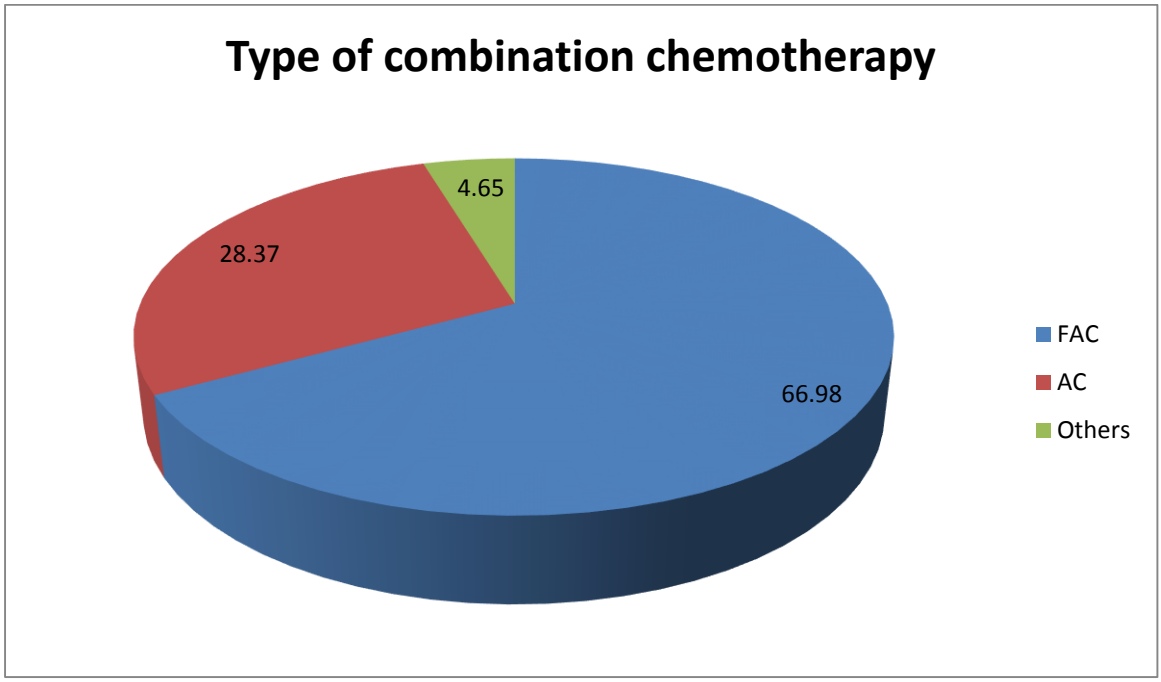

Figure 3: Types of chemotherapy given to breast cancer patients.

4.3.3. Cycle of chemotherapy

More than half (69.0%) of breast cancer patients completed the 6th cycle of chemotherapy while (4.3%) discontinued at the first cycle as shown in Figure 4.

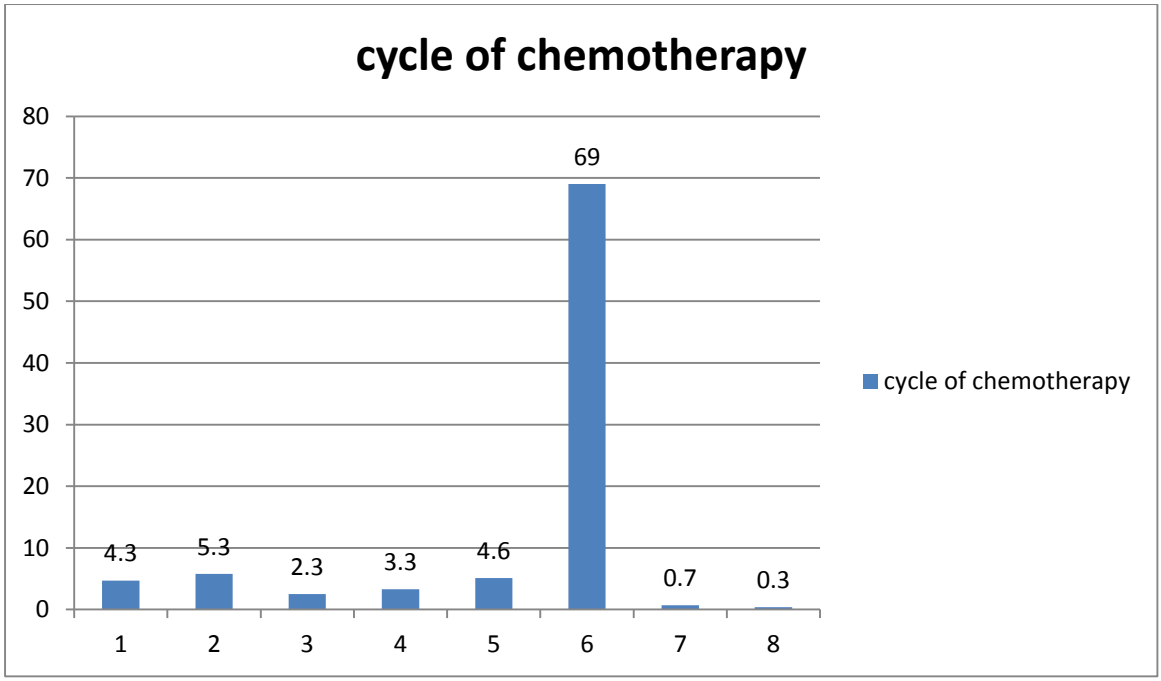

Figure 4: Patient follow-up based on treatment cycle.

4.4. Treatment outcome

At the end of three years treatment follow up (46.53%) of patients were dead while (19.14%) of patient were with unknown outcome (Table 3).

Table 3: Status of study subjects after treatment (N=303)

Status of Patient	Status	Frequency	Percentage
	Alive	104	34.32
	Dead	141	46.53
	Unknown	58	19.14

Among the death outcome (46%) were before completion of the 6th chemotherapy cycles while (40%) were after completion of the 6th chemotherapy cycles as illustrated in Figure 5.

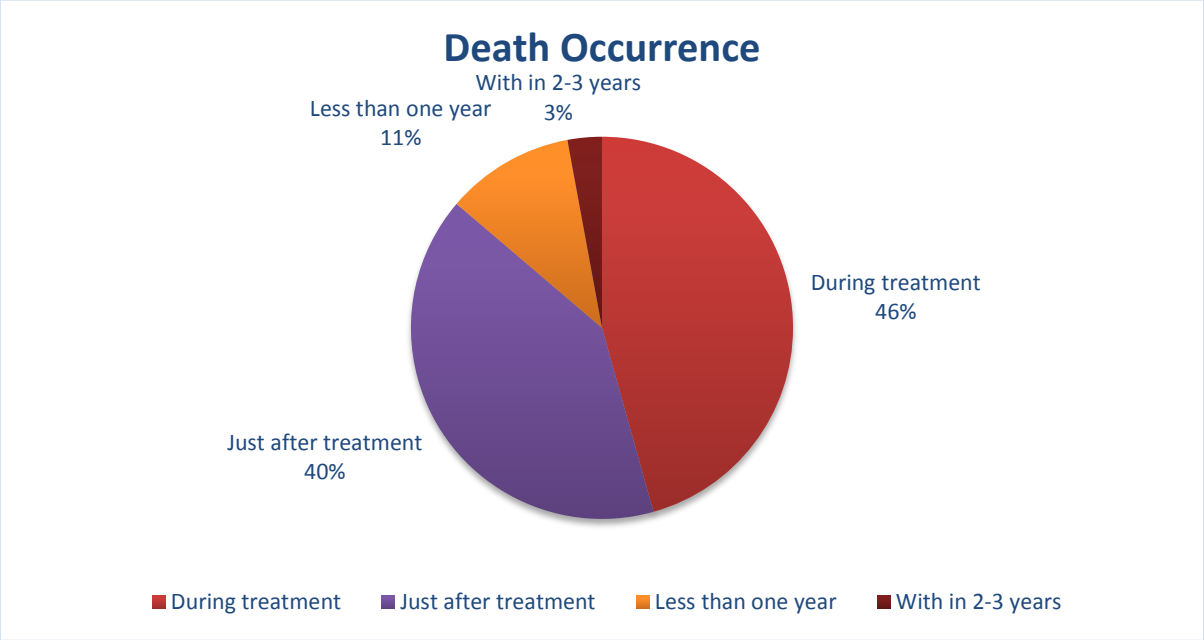

Figure 5: Patient Death occurrence event

Figure 6 shows the number of visits per year of breast cancer patients. As shown in the figure, the number of visits per year declined from the first year of treatment through the third year.

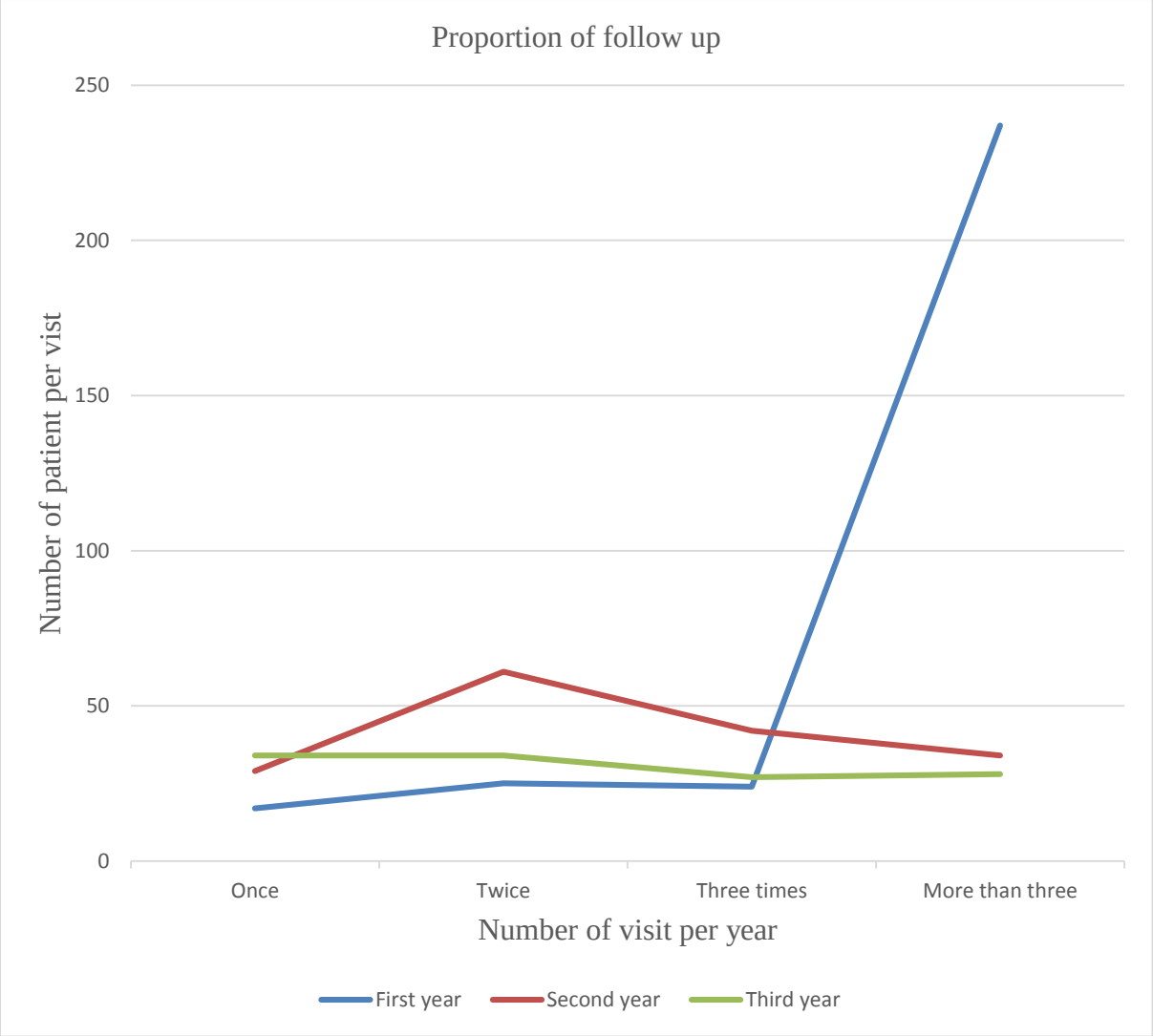

Figure 5: Proportion of women followed up for three years.

4.5.Factors associated with death of breast cancer patients

The association of independent variables with the dependent variable was investigated using both univariate and multivariate logistic regression technique (Table 4). In univariate logistic regression analysis; age, number of chemotherapy cycle, clinical stage, type of chemotherapy, mode of treatment and endocrine therapy showed association with death of breast cancer patients and were used in multivariate analysis.

In multivariate analysis, the odds of death in patients in the age group of 50-59 was reduced by 68% when compared to patients in the age group of 30-39 (AOR= 0.32, 95% CI: 0.12, 0.95, P=0.040).Number of chemotherapy cycle was found to have association with treatment outcome in that the odds of death among patients who took less than 6 chemotherapy cycle was increased by 7.36 times than those who took 6 or more chemotherapy cycles (AOR= 7.36, 95% CI: 2.28, 23.79, P=0.001). On the other hand, the odds of death was decreased by 89% among patients who were diagnosed at early stage of the disease (stage 1&2) than those patients who were diagnosed at late stage of the disease (stage 3&4) (AOR= 0.11, 95% CI: 0.05, 0.29, P=0.000).Similarly, the odds of death was reduced by 91% among patients who were on endocrine therapy than those who were not on endocrine therapy (AOR= 0.09, 95% CI: 0.04, 0.22, P=0.000).

Table 4: Clinical parameters and association with treatment outcomes

Characteristics		Total N (%)	Treatment out-come n (%)		Crude OR 95% CI	P value	Adjusted OR 95% CI	P value
			Alive	Dead				
Age	30-39	80(32.7)	35(14.3)	45(18.4)	1.00		1	
	20-29	32(13.1)	8(3.3)	24(9.8)	2.33(0.94, 5.82)	0.069	2.04(0.54, 7.69)	0.293
	40-49	67(27.3)	27(11.0)	40(16.3)	1.15(0.59, 2.26)	0.673	0.99(0.39, 2.47)	0.987
	50-59	43(17.6)	24(9.8)	19(7.8)	0.62(0.29, 1.29)	0.203	0.32(0.12, 0.95)	0.040
	60-69	16(6.5)	8(3.3)	8(3.3)	0.78(0.27, 2.28)	0.647	0.69(0.16, 3.09)	0.638
	≥70	7(2.9)	2(0.8)	5(2.0)	1.94(0.36, 10.63)	0.443	1305149170	0.999
Cycle	≥6	167(77.7)	89(41.4)	78(36.3)	1.00		1.00	
	<6	48(22.3)	6(2.8)	42(19.5)	7.99(3.22, 19.79)	0.000	7.36(2.28, 23.79)	0.001
Clinical stage	Late stage (stage 3&4)	184(75.1)	58(23.7)	126(51.4)	1.00		1	
	Early stage (stage 1&2)	61(24.9)	46(18.8)	15(6.1)	0.15(0.08, 0.29)	0.000	0.11(0.05, 0.29)	0.000
Type of chemotherapy	FAC	144(58.8)	69(28.2)	75(30.6)	1.00		1.00	
	AC	61(24.9)	24(9.8)	37(15.5)	1.42(0.77, 2.61)	0.261	1.57(0.65, 3.78)	0.319
	Other chemotherapy	10(4.1)	2(0.8)	8(3.3)	3.68(0.76, 17.93)	0.107	3.50(0.37, 33.02)	0.273
	Not taking chemotherapy	30(12.2)	9(3.7)	21(8.6)	2.15(0.92, 5.01)	0.077		
Mode of treatment	surgery & Chemo	123(50.3)	45(18.4)	78(31.8)	1.00		1.00	
	Surgery, radio & Chemo	65(26.5)	39(15.9)	26(10.6)	0.39(0.21, 0.71)	0.002	0.93(0.39, 2.23)	0.876
	radio & Chemo	21(8.6)	9(3.7)	12(4.9)	0.77(0.30, 1.97)	0.584	1.67(0.52, 5.46)	0.400
	Palliative	15(6.1)	3(1.2)	12(4.9)	2.31(0.62, 8.62)	0.213		
	Surgery	5(2.0)	2(0.8)	3(1.2)	0.87(0.14, 5.38)	0.877		
	Surgery, radio, Chemo & palliative	6(2.4)	2(0.8)	4(1.6)	1.15(0.20, 6.55)	0.872	4.75(0.62, 36.75)	0.135
	Others*	10(4.1)	4(1.6)	6(2.4)	0.87(0.23,3.23)	0.830	0.09(0.01, 1.08)	0.057
endocrine therapy	No	159(64.9)	43(17.6)	116(47.3)	1.00		1.00	
	Yes	86(35.1)	61(24.9)	25(10.2)	0.15(0.09,0.27)	0.000	0.09(0.04,0.22)	0.000

Others*Radiation; Surgery, radio, & Palliative; radio, Chemo & palliative; Chemo & palliative; Surgery& Palliative.

5. Discussion

The study assessed treatment outcome among breast cancer patients at TASH. The findings of this study showed that during the three years treatment follow up (46.53%) of breast cancer patients were dead. Most of the patients were in the age range of 30-39 years, with a mean age of 42.10 years. This might be a result of increased hormonal activity and tissue responsiveness or use of hormonal contraceptives in this age group. The study also showed that many patients were from Addis Ababa and Oromia region. This can be explained by the fact that people in Addis Ababa and nearby regions have easy access to TASH for diagnosis and treatment.

In this study, 303 histologically proven treated breast cancer patients were included. Based on histologic classification majority of the cases (95.63%) were found to have invasive ductal carcinoma. This is in line with other studies that showed majority of breast cancer cases to be of invasive type [Breast cancer treatment guideline 2006;Kakarala *et al*., 2010; Syed *et al*., 2011;Tovar *et al*.,2014;Rahal *et al*., 2015], This could probably be due to a result of spread to the axillary lymph nodes.

In multivariate logistic regression, the odds of death in patients in the age group of 50-59 was reduced by 68% when compared to patients in the age group of 30-39 (AOR= 0.32, 95% CI: 0.12, 0.95, P=0.040). Similar result was obtained in California [Bernstein *et al*.,1999], Saudi Arabians [Elkum *et al* ., 2007], Egypt [Alieldin *et al*.,2014;Ibrahim *et al*., 2014], Brazil [Tovar *et al*.,2014], Atlanta [Cancer Treatment Facts 2014-2015], France [Rahal *et al*.,2015], Sweden [Brandt *et al*., 2015], and United States [Gnerlich *et al*., 2009]. This might be a result of advanced and aggressive nature of the disease in the young age group. Additionally, younger age group are more likely to have larger tumor sizes, invasive cancers, positive lymph nodes, hormone receptor negative carcinomas, according studies done in the United States [Gnerlich *et al*., 2009], and Egypt [Alieldin *et al.*,2014].Moreover, radiographic diagnosis in this

population is challenging due to increased breast density and poorly differentiated breast cancers. Hence, all this might have increased the odds of death in the younger group.

The result of the study showed that more than half of the patients came to TASH when they were on the third stage of the disease. The odds of death was decreased by 89% among patients who were diagnosed at early stage of the disease (stage 1&2) than those patients who were diagnosed at late stage of the disease (stage 3&4) (AOR= 0.11, 95% CI: 0.05, 0.29, P=0.000). Similar results were reported in other studies done in the United States [Winchester *et al.,* 1996; Gnerlich *et al*., 2009] and Kenya [David *et al*., 2013]. This might be due to low knowledge of the basic symptoms of breast malignancy and absence of a nearby diagnostic center. Majority of cancers in Africa are diagnosed at an advanced stage of disease because of lack of screening and early detection services, as well as limited awareness of early signs and symptoms of cancer among the public and health care providers. Stigma associated with diagnosis of cancer also plays a role in late-stage presentation in most parts of Africa [Tigeneh *et al*., 2015]. Thus, one can take note of that women who are diagnosed early and put on treatment is one way of improving breast cancer treatment outcomes. However, a different result was reported from a study done in Brazil , where majority of the cases 56 (93%) had an early stage tumor [Tovar *et al*.,2014].This might be is a result of difference in education, economic, social status as well as health seeking behavior between the study population of the studies.

In the present study, chemotherapy and surgical treatment appear to be a pillar component in TASH adult oncology protocol. The most commonly used chemotherapy regimen was a combination of Cyclophosphamide 600 mg/m^2 IV, Doxorubicin 60 mg/m2 IV and Fluorouracil 600 mg/m2 IV (FAC), followed by Doxorubicin 60 mg/m2 IV and Cyclophosphamide 600 mg/m2 IV (AC). FAC took the lion share from chemotherapy options (66.9%), which is similar to studies done in Spain [Martin et al., 2003], Kenya [Wata *et al*., 2013] and USA [Anampa *et*

al., 2015]. The grater proportional use of FAC is beneficial as a randomized controlled trial done in Denver that followed breast cancer patients for a period of 55 months reported a 30% reduction in mortality with FAC regimen [Mamounas *et al*., 2005]. Additionally, another study showed that antracycline-containing regimen was superior to reducing recurrence and death compared to non-Antracycline spain [Martin *et al*., 2003], United States [Crozier et al., 2014].

According to TASH protocol, the first line chemotherapy for breast cancer is the combination of Doxorubicin 60 mg/m2 IV, day 1, Cyclophosphamide 600 mg/m2 IV, day 1 (AC); Repeat cycles every 21 days for 4 cycles or Cyclophosphamide 600 mg/m2 IV, Doxorubicin 60 mg/m2 IV, and Fluorouracil 600 mg/m2 IV (FAC) , day 1; repeat cycles every 21 days for 6 cycles. Second line chemotherapy includes, Vinblastine 6-8 mg/m^2 and Cisplatin 60-80 mg/ m^2 on day 1 every 3 weeks or paclitaxel 175 mg/m^2 Carboplatin 450 mg or Cisplatin 50 mg/m^2 on day one [TASH treatment protocol 2012].The treatment cycle and chemotherapy regimen types were similar to other countries. Research done in Seoul, Korea [Bang *et al.,* 2000] and FDA approved regimen [Breast cancer treatment regimen, 2012] also used these chemotherapy medications.

The result of the study showed that 69% of patients could attend up to to their 6^{th} cycle of treatment. Number of chemotherapy cycle was found to have association with treatment outcome in that the odds of death among patients who took less than 6 chemotherapy cycle was increased by 7.36 times than those who took 6 or more chemotherapy cycles (AOR= 7.36, 95% CI: 2.28, 23.79, P=0.001).This result is closely similar to a study from USA [Anampa *et al*.,2015] and Korea [Bang *et al.,* 2000]. This signifies the need to work on adherence of chemotherapy cycles in order to improve treatment outcome among breast cancer patients.

Surgery for breast cancer usually involves breast-conserving surgery (BCS) or mastectomy [Cancer Treatment Facts, 2014-2015]. Modified radical mastectomy has traditionally been the

standard of care for early-stage invasive breast cancers [Karen *et al*., 2010].Therefore, this general mastectomy practice for majority of them in TASH might have contributed for patient survival. Similar findings where found in Lebanon that showed mastectomy rates in Arab countries are high amounting to 79.9%–82% in Egypt, 65% in Oman, 70% among Palestinians, 88% in Syria, and 82.4% in Tunisia [Tfayli *et al*., 2010]. This might be because of mastectomies were performed due to the more advanced nature of their breast cancer, more nodal involvement, or even larger tumor size. However, different results were reported in studies from France, where most of the patients had breast-conserving surgery (73 %) [Rahal *et al*., 2015]. This might be because of histologic subtypes other than invasive ductal carcinoma or acceptable cosmetic outcome can be achieved in almost all patients undergoing breast-conserving surgery without compromising the of local tumor control.

From endocrine treatment options, tamoxifen was the only drug used to prevent recurrence. The odds of death was reduced by 91% among patients who were on endocrine therapy than those who were not on endocrine therapy (AOR= 0.09, 95% CI: 0.04, 0.22, P=0.000).Women with breast cancer that tests positive for hormone receptors are candidates for treatment with hormone therapy to reduce the likelihood of recurrence. Similar result was obtained from a study done in the UK, where tamoxifen was the most commonly used first-line agent for patients on primary endocrine therapy (69.3%) [Syed *et al*., 2011]. The response or survival benefit from one endocrine therapy was clearly superior to that achieved with other therapies so choice of a particular endocrine therapy was based primarily on toxicity and patient preference based on these criteria, tamoxifen was the preferred initial agent .

The result of the study showed that at the end of three years treatment follow up (46.53%) of patient were dead. Similar result was obtained from a study in Washington, US in which breast cancer was the cause of death for 49% [Gnerlich *et al*., 2009].This might have resulted from

advanced stage at diagnosis, low access to health care and lack of screening. However, different results were reported on a case-control study from Italy (73.8%) [Puliti *et al*., 2008] and USA (72.3%) [Jung *et al*., 2012].This difference might be a result of difference in the sample size and duration of follow up of the studies. The proportion of dead patients in the present study was higher than studies done in Virginia, US (23.3%) [Karen. *et al*., 2010] and United Kingdom (38%) [Fielder *et al*., 2004].This might have resulted from difference in access to health care, educational status, stage of diagnosis and screening.

6. Limitation of the study

The major limitation of this study was patient's unknown status. This made it difficult to draw a clear conclusion as what happened to those who did not complete their follow up schedule. Although the phone numbers were used to trace some of those who were lost to follow up, still most of these numbers were not working. Some patient charts even have no phone numbers. The documentation in patients chart was also poor and it was impossible to get sufficient information on values for progesterone receptor, estrogen receptor, HER2, HIV status, treatment complications and history of contraceptive use. Moreover, there was poor data recording regarding radiation therapy as the dose of radiation was not recorded on medical records. Additionally, since the study was done on a single center , hence generalization to other breast cancer population in the country is limited.

7. Conclusion

Breast cancer treatment outcome was poor in TASH. Majority of the patients presented at late stage of the disease with invasive ductal carcinoma. Which might contributed to a poor treatment outcome. The most commonly used treatment modality was the combination of surgery, chemotherapy. Majority of the patients were treated with FAC regimen and more than three fourth of the patients were followed for ≥6 cycles. The odds of death was decreased in the age group of 50-59, among those patients who presented at early stage of the disease and those on endocrine therapy. On the other hand, the odds of death was increased among those patients who took less than 6 chemotherapy cycle.

8. Recommendation

Based on this study finding, the following recommendations can be given:

Health education and sensitization on preventive approach through screening to prevent the late stage presentation at health facilities. Also education on the necessity of the follow up after optimal treatment.

There is a need of implementing a National cancer registry, which can help to make follow up of patients who lost in follow up.

TASH need breast cancer patient data register and general patient diagnosis information shall to be improved and functioning at all times and publication of treatment protocols for breast cancer is mandatory.

Vast and more organized prospective based similar studies are mandatory to make decision on TASH breast cancer treatment options and its outcome too.

References

Addis Ababa University, TikurAnibessa Specialized Hospital Cancer Treatment Protocol 2012.

Akarolo-Anthony SN,Ogundiran TO, Adebamowo CA(2010).Emerging breast cancer epidemic: evidence from Africa.*Breast Cancer Research***2**(4):S8.

Alieldin NH, Abo-Elazm OM, Bilal D, Salem SE, Gouda E, ElmongyM,et al (2014). Age at diagnosis in women with non-metastatic breast cancer: Is it related to prognosis.Journal of the Egyptian National Cancer Institute 26:23-30.

American Cancer Society (2014). Breast Cancer.

AnampaJ, MakowerD, SparanoJA (2015). Progress in adjuvant chemotherapy for

Breast cancer: an overview. Spotlight on breast cancer13:195.

Australian Institute of Health (AIH) and Welfare, Australasian Association of Cancer Registries, NHMRC National Breast Cancer Centre. Breast cancer survival in Australian women 1982–94. Canberra: Australian Institute of Health and Welfare, 1998.

AutierP,VecchiaCL, VattenL, BoniolM, GavinA, HeanueM, (2010).Disparities in breast cancer mortality trends between 30 European countries: retrospective trend analysis of WHO mortality database.*BioMedJornal* 10:113.

Bang SM, Heo DS, Lee KH, Byun JH, Chang HM, Noh DY,et al(2000).Adjuvant Doxorubicin and Cyclophosphamide versus Cyclophosphamide, Methotrexate, and 5 Fluorouracil Chemotherapy in Premenopausal Women with Axillary Lymph Node Positive Breast Carcinoma Results of a Randomized Controlled Trial. *Cancer* 89 (12):2521–6.

Barnett GC, Shah M, Redman K, Easton DF, J. Ponder BA, Pharoah PD (2008). Risk Factors for the Incidence of Breast Cancer: Do They Affect Survival From the Disease. *American Society of Clinical Oncology* 26:3310-3316.

Bernstein L, Deapen D, Cerhan JR, Schwartz ,LiffJ,Gann-Maloney EM, et al (1999).Tamoxifen Therapy for Breast Cancer and Endometrial Cancer Risk. *Journal of the National Cancer Institute* 91(19).

Brandt J, Garne JP, Tengrup I, ManjerJ (2015). Age at diagnosis in relation to survival following breast cancer: a cohort study. *World Journal of Surgical Oncology* 13(33): 2-11.

Breast cancer treatment guideline (2006). Available at: www.emro.int/dsaf/dsa697.pdf.

Accessed on ; 01/01/2016.

Breast cancer treatment guideline (2012) [Online] Available At: www.emro.int/dsaf/dsa697.pdf. Accessed on; 01/01/2016.

Breast cancer treatment regimen, (2012).Available at:www.saskcancer.ca/Breast%20CPGs%2005-12 . Accessed on ; 01/30/2016.

Breast cancer risk factors a review of the evidence(2009). National Breast and Ovarian Cancer Centre ISBN Online: 978-1-74127-141-6.

Brito C, Portela MC, de Vasconcellos MT (2014). Adherence to hormone therapy among women with breast cancer. *Biomed Center Cancer* 14(397):1471-2407.

Cancer Treatment and Survivorship Facts & Figures 2014-2015. Atlanta: American Cancer

Society; 2014. Available at : www.cancer.org. Accessed on :01/01/2016.

Cheng CY, Ueno NT (2012). Improvement of survival and prospect of cure in patients with metastatic breast cancer .*Breast Cancer* 19(3).

Colditz GA, Bohlke K, Berkey CS(2014). Breast cancer risk accumulation starts early – Prevention must also. *NIH Public Access* 145(3): 567–579.

Copson E, Maishman T, GertyS, Eccles B ,Stanton L, Cutress RI ,et al(2014). Ethnicity and outcome of young breast cancer patients in the United Kingdom: the POSH study. British Journal of Cancer 110: 230–241.

Crozier JA, Swaika A, Moreno-Aspitia A (2014). Adjuvant chemotherapy in breast cancer: To use or not to use, the anthracyclines. *World Journal of Clinical Oncology* **5**(3): 529-538.

Dang M (2013).Treatment Outcomes for African American Women With Breast Cancer: Does Income Matter?An Integrative Review of the Literature. *McNair Scholars Journal* (15)33.

Dignam JJ (2000). Differences in Breast Cancer Prognosis among African-American and Caucasian Women. *Cancer Journal for Clinicians* 50:50-64.

Di Leo A, Curigliano G, Di-eras V, Malorni L, Sotiriou C, Swanton C, et al(2015).New approaches for improving outcomes in breast cancer in Europe. *The Breast* 24: 332-330.

Dipiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM (2011). Pharmacotherapy: A pathophysiologic approach. 8edn. McGraw-Hill, New York.

Eccles SA, Aboagye EO, Ali S, Anderson AS, Armes JO, Berditchevski F, et al().Critical research gaps and translational priorities for the successful prevention and treatment of breast cancer. *Breast Cancer Research* 15:R92.

Elkum N, Dermime S, Ajarim D, Al-Zahrani A, Alsayed A, TulbahA,et al(2007). Being 40 or younger is an independent risk factor for relapse in operable breast cancer patients: The Saudi Arabia experience. *Bio Med CenterCancer* 7:222 1471-2407.

Fielder HM, Warwick J, Brook D, Gower-Thomas K, Cuzick J, Monypenny I, *et al(2004).*A case-control study to estimate the impact on breast cancer death of the breast screening programme in Wales. *Journal of Medical Screening*11:194–198.

Gabrie CA, Domchek SM (2010).Breast cancer in young women. *Breast Cancer Research* 12: 212.

Gnerlich JL, Deshpande AD, Jeffe DB, Sweet A, White N, Margenthaler JA(2009).Elevated Breast Cancer Mortality in Young Women (<40 Years) Compared with Older Women Is Attributed to Poorer Survival in Early Stage Disease. *NIH Public Access* 208(3): 341–347.

Gradishar WJ, Giordano SH, Pierce LG, Anderson BO, Goetz M (2015) .Breast Cancer. NCCN Clinical Practice Guidelines in Oncology 10:57:48.

Gwak G, Park K, Shin E,Han S, Kim Y,Kim H, et al(2011). Comparison of CVF (Cyclophosphamide + Vinorelbine + 5 Fluorouracil) and CMF (Cyclophosphamide+Methotrexate+5-Fluorouracil) Adjuvant Chemotherapy in Early Breast Cancer. *Journal of Breast Cancer* 14(3): 223-228.

Guire AM, Brown JL, Malone C, Laughlin RM, Kerin MJ (2015). Effects of Age on the Detection and Management of Breast Cancer. *Cancers* 7: 908-929.

Heinavaara S, Sarkeala T, Anttila A(2016).Impact of organised mammography screening on breast cancer mortality in a case–control and cohort study. *British Journal of Cancer* 114:1038–1044.

Howell A, Anderson AS, Clarke RB, Duffy SW, Evans DG, Garcia-Closas M ,et al(2014) Risk determination and prevention of breast cancer .*Breast Cancer Research* 16:446.

Hutchins LF, Green SJ, Ravdin PM, Lew D, Martino S, Abeloff M, et al (2005)Randomized, Controlled Trial of Cyclophosphamide, Methotrexate, and Fluorouracil Versus Cyclophosphamide,Doxorubicin, and Fluorouracil With and Without Tamoxifen for High-Risk, Node-Negative Breast Cancer: Treatment Results of Intergroup Protocol INT-0102. *American Society of Clinical Oncology* 23:8313-8321.

International Agency for Research on Cancer (IARC) (2012). Globocan 2012: Estimated cáncer incidence, mortality and prevalence worldwide in 2012. Available at:http:// globocan.iarc.fr /Pages/fact_sheets_canceraspx. Accessed on 06/20/2015.

Ibrahim AS, Khaled HM, Mikhail NM, Baraka H, Kame H (2014). Cancer Incidence in Egypt: Results of the National Population-Based Cancer Registry Program. *Journal of Cancer Epidemiology*10:18.

Jemal A, Siegel R, Xu J, Ward E, (2010).Cancer Statistics. *cacancerjournal.org* 60:277–300.

Jung SY, Rosenzweig M, Sereika SM, Linkov F, Brufsky A, Weissfeld JL(2012).Factors associated with mortality after breast cancer metastasis.*Cancer Causes Control*. 23(1):103-12.

Kakarala M, Rozek L, Cote M, Liyanage S , Brenner DE(2010). Breast cancer histology and receptor status characterization in Asian Indian and Pakistani women in the U.S.SEER analysis .*Bio Med Central* 10.1186/1471-2407-10-191.

Mamounas EP, Bryant J, Lembersky B, Fehrenbacher L, Sedlacek S,Fisher B, *et al* (2005).Paclitaxel after Doxorubicin Plus Cyclophosphamide As Adjuvant Chemotherapy for Node-Positive Breast Cancer: Results From NSABP B-28.*Journal of clinical oncology10:517.*

Martin M, Villar A, Sole-Calvo A, Gonzalez R, Massuti B ,Lizon J, *et al (2003).* Doxorubicin in combination with fluorouracil and cyclophosphamide (i.v. FAC regimen, day 1, 21) versus methotrexate in combination with fluorouracil and cyclophosphamide (i.v. CMF regimen, day 1, 21) as adjuvant chemotherapy for operable breast cancer: a study by the GEICAM group. *Annals of Oncology* **14**: 833–842.

Maughanm KL, Lutterbie MA, Ham PS (2010). Treatment of Breast Cancer. *American Academy of Family Physicians* **81** (11):1339-1346.

Mavaddat N, Pharoah PD, Michailidou K, Tyrer J, Brook MN, Bolla MK, *e t al*(2015). Prediction of Breast Cancer Risk Based on Profiling With Common Genetic Variants.*Oxford* 107(5): 36.

Nelson HD, Zakher B, Cantor A, Fu R, Griffin J, O'MearaES, et al (2013).Risk Factors for Breast Cancer for Women Age 40 to 49: ASystematic Review and Meta-analysis. *NIH Public* 156(9): 635–648.

Penner NA, Eggly S, Griggs JJ, Underwood W, Orom H, Albrecht TL(2012). Life-Threatening Disparities: The Treatment of Black and White Cancer Patients. *NIH Public Access* 68(2): 540-4560.

Puliti D, Miccinesi G, Collina N, Lisi VD, Federico M, Ferretti S, et al (2008).Effectiveness of service screening: a case–control study to assess breast cancer mortality reduction.*British Journal of Cancer* **99**(3): 423 – 427.

Rahal S, Bohe JM,Extra JM,Tarpin C, Charafe-Jauffret E, Lambaudie E, *etal*(2015). Immunohistochemical subtypes predict the clinical outcome in high-risk node-negative breast cancer patients treated with adjuvant FEC regimen: results of a single-center retrospective study.*Bio Med Central*15:697.

Rapiti E, Fioretta G, Verkooijen HM, Vlastos G, Schäfer P, Sappino AP, *et al*(2005).Survival of young and older breast cancer patients in Geneva from 1990 to 2001. 41(10):1446–1452.

Saux OL, Ripamonti B, Bruyas A, Bonin O, Freyer G, Bonnefoy M, et al(2015). Optimal management of breast cancer in the elderly patient: current perspectives. *Dove press Journal* 10: 157–174.

Syed BM, Khyatt WA, Johnston SJ, Wong DW, L Winter bottom L, Kennedy H, *et al* (2011) Long-term clinical outcome of oestrogen receptor-positive operable primary breast cancer in older women: a large series from a single centre. *British Journal of Cancer*. **104**(9): 1393 – 1400.

Shigematsu H, Kawaguchi H, Nakamura Y, Tanaka K, Koga C, Nishimura S, *et al*(2011). Significant survival improvement of patients with recurrent breast cancer in the periods .*BioMedCenter Cancer* 11(118):1471-2407.

Tigeneh W, Molla A, Abreha A, Assefa M (2015). Pattern of Cancer in TikurAnbessa Specialized Hospital Oncology Center in Ethiopia from 1998 to 2010. *International Journal of Cancer Research and Molecular Mechanisms*1(103).

Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A (2015) Global cancer statistics.*CA Cancer J Clin*. 65(2):87–108.

Tovar JR, Zandonade E, Costa Amorim MH (2014).Factors Associated with the Incidence of Local Recurrences of Breast Cancer in Women Who Underwent Conservative Surgery. *International Journal of Breast Cancer 10:1155.*

Sparano JA, WangM, Zhao F, Stearns V, Martino S, Ligibel JA, et al(2011). Race and Hormone Receptor–Positive Breast Cancer Outcomes in a Randomized Chemotherapy Trial. *Article JNCI* 104:5.

Sant M, AllemaniC, Berrino F, Coleman MP, Aareleid T, Chaplain G, et al (2004)Breast Carcinoma Survival in Europe and the United States. *Cancer* 100 (4).

Ursin G, Wu AH, Hoover RN, West DW, Nomura AM, Kolonel LN (1994). Breast Cancer and Oral Contraceptive Use in Asian-American Women. *Breast cancer* 19(20):241–64.

Wata ED, Osanjo GO, Oluka M, Guantai AN (2013).Predictors of Breast Cancer Treatment Outcomes in Kenyan Women. *African Journal of Pharmacology and Therapeutics* 2 (4):109-115.

Wheeler SB, Reeder-Hayes KE, Carey KA (2013). Disparities in Breast Cancer Treatment and Outcomes: Biological, Social, and Health System Determinants and Opportunities for Research. *The oncologist* 18:986 –993.

Winchester DP, Osteen RT, Menck HR (1996).The National Cancer Data Base report on breast Carcinoma characteristics and outcome in relation to age. *Cancer;* 78:1838-1843.

World Health Organization (2012).A diagonal approach to combating women's cancers in Africa Doyin Oluwole & John Kraemer for Pink Ribbon Red Ribbo. Available at: http://www.who.int/bulletin/volumes/91/9/12-109777. Accessed on: 6/21/2015.

World Health Organization (2014).Breast Cancer Facts & Figures 2013-2014. Available at: http://www.cancer.org/acs/groups/content/@research/documents/document/acspc-042725. Accessed on: 6/21/2015.

Xue Qin Yu (2009).Socioeconomic disparities in breast cancer survival: relation to stage at diagnosis, treatment and race. *Bio Med Central Cancer* 9:364.

Youlden DR, Cramb SM, M. Dunn NA, Muller JM, Pyke CM, Baade PD (2012). The descriptive epidemiology of female breast cancer.*CancerEpidemio*l (36): 237–248.

Appendix

STUDY CHECKLIST

A: Sociodemographic Data:

1. Age (years) _____

2. Marital status :

   a) Married ( )
   b) Single ( )
   c) Divorced / separated ( )
   d) Widowed ( )

3. Ethnicity (tribe)_____

4. Home residence and phone number _____

5. Religion:

   a) Catholic ( )
   b) Christian ( )
   c) Moslem ( )
   d) Protestant ( )
   e) Other specify _____

6. Occupation:

   a) Peasant
   b) Private Business
   c) Employed
   d) House wife

7. Level of Education

   a) No formal Education ( )
   b) Primary school ( )
   c) Secondary education ( )
   d) College ( )
   e) University ( )
   f) Other specify _____

REPRODUCTIVE DATA:

8. Menarche (Years) ___ ___

9. First delivery (Year) ___/____/____

10. History of contraceptives

a) Yes
b) No

11. If yes, Which method :

a) Condoms
b) Oral pills
c) Injectable
d) IUD
e) Norplant’s
f) Tubal ligation
g) Others specify_____

12. HIV status:

a) Positive
b) Negative
c) Unknown

13. Estrogen receptor:

a) Negative
b) Positive
c) Not stated

14. Progesterone receptor:

a) Negative
b) Positive
c) Not stated

15. Human epidermal growth factor receptor:

a) Negative
b) Positive
c) Not stated

16. Histological differentiation of tumor cell

a) I . Noninvasive Carcinoma
   DCIS

   LCIS

b) Invasive Carcinoma
   1. Ductal
   2. Lobular
   3. Medullar
   4. Tubular
   5. other

17. Clinical stage TNM – modified Stage at diagnosis(International Federation of Gynecology and Obstetrics **System** and the American Joint Committee ..)

a) 0
b) I
c) IIA
d) IIB
e) IIIA
f) IIIB
g) IIIC
h) IV

18. Date of commencement of treatment _____/_____/_____

19. Mode of treatment given and their duration of treatment :

a) Radiotherapy _____
b) Chemotherapy_____
c) Radiotherapy & Chemotherapy _____
d) Surgery, Radiotherapy & chemotherapy_____
e) Palliative care

20. If chemotherapy,

a. what type of it and

b. how many cycles

21. If radiotherapy total dose of irradiation _____

22. If surgery was done the type: type of surgery

a)

b)

TREATMENT, FOLLOW UP AND COMPLICATIONS

23. I. Radiation complications during radiotherapy:

a) Hematological

b) Cutaneous

c) Neurological

e) Others Specify_____

II. Surgical complications during radiotherapy

a. lymphedoma
b. neuropathy
c. other

24. Recurrence of symptoms

a) Yes

b) No

25. If yes was there second line treatment?

a) Yes
b) No

26. If yes;

a) Radiotherapy _____
b) Chemotherapy (mention drugs)_____
c) Radiotherapy & Chemotherapy _____
d) Surgery &Radiotherapy_____

27. After how long did the symptoms reappear? _____

28. Clinical, pathology or Radiological examination of the breast

a) Presence of the tumor

b) No tumor seen

29. How many follow up visits within the first year

a) Not at all

b) One

c) Two

d) Three

e) More than three

30. How many visits in the second year post treatment?

a) Not at all

b) Once

c) Twice

d) Thrice

e) More than thrice

31. How many visits made in the third year post treatment

a) Not at all

b) Once

c) Twice

d) Thrice

e) More than thrice

32. Was she on endocrine therapy?

a) yes
b) no

33.If yes please mention the drug _____starting date _____total months of use _____

35. Status of the patient?

a) Alive

b) Dead

c) Unknown

36. If dead when?

a) During treatment

b) Just after treatment

c) Less than one year

d) 2-3 years

37. What was the cause of death _____