SOCIODEMOGRAPHIC CORRELATES AND MANAGEMENT OF BREAST CANCER IN RADIOTherapy DEPARTMENT, LAGOS UNIVERSITY TEACHING HOSPITAL

A TEN YEAR REVIEW BETWEEN JANUARY 2004 AND DECEMBER 2013

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BY

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DECLARATION

This dissertation has not been previously submitted to any college for consideration

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This is to certify that this research project "SOCIODEMOGRAPHIC CORRELATES AND MANAGEMENT OF BREAST CANCER IN RADIOThERAPY DEPARTMENT, LAGOS UNIVERSITY TEACHING HOSPITAL (LUTH): A TEN YEAR REVIEW BETWEEN JANUARY 2004 AND DECEMBER 2013" was conducted in the department of radiotherapy, LUTH, Idi Araba, Lagos and supervised by:

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ABSTRACT

Introduction: Worldwide, breast cancer is the most frequently diagnosed life threatening cancer in women and the leading cause of cancer death in women. Late presentation is still a dilemma in developing countries. Identifying the modifiable socio-demographic factors associated with breast cancer is important in reducing the incidence.

Aim: To determine the socio-demographic correlates and management of Breast Cancer in Department of Radiotherapy, Lagos University Teaching Hospital (LUTH) between January 2004 and December 2013.

Method: Data was retrieved from breast cancer patients’ case notes and analysed using Statistical Package for Social Sciences (SPSS)

Results: A total of 1,141 cases were analysed with a mean age was 46.84±12.36 years which ranged between 17 and 84 years and modal age group was 40 – 49 years. There were 1132(99.2%) female and 9(0.8%) male, 920(81.3%) were premenopausal while 212(18.7%) were post-menopausal. The mean number of children born was 3.75±1.76 and age at first pregnancy revealed a mean of 24.26±4.73 years. Out of the 1141 patients analysed, 514(45.0%) of female patients were found to have breastfed their children for a mean duration of 13.75±5.66 months which ranged between 6 - 24months. Highest incidence of breast cancer was recorded as 164(14.37%) in year 2010. Invasive ductal carcinoma 956(82.8%) was the commonest histological type seen. Only 998(87.5%) of cases had stage of disease recorded in which the commonest
stage at presentation was stage IV 425(42.6%). A total of 139(12.18%) had Immunohistochemistry recorded, molecular subtype seen mostly was Lumina A. 135(63.2%) had biopsied lymph nodes were positive for malignancy out of 214(18.8%) cases recorded. 153(13.4%) had a positive family history of breast cancers, 125(11.1%) had history of oral contraceptive use. 28.55±6.39kg/m², 387(33.9%) were of normal weight, while 258(22.6%) and 202(17.7%) were obese and morbid obese respectively. The commonest comorbidity out of the 176 patients recorded was found to be hypertension 136(77.3%). Treatment combination surgery-chemotherapy-radiotherapy 213(30.9%) was the commonest form of management given with mastectomy 289(59.4%) as the major form of surgery received, FEC chemotherapy regimen was mostly administered 216(40.6%) and radiotherapy intention mostly given was radical 294(71.6%). 48.1% of the patients were lost to follow-up. In addition, 447(39.3%) were dead, while 145(12.7%) were on follow-up treatment. Out of these patients on follow-up, 42.2% had complete response while 24.1% had disease progression.

**Conclusion and Recommendation:** There is need to encourage early detection, through screening, advocacy and health education (breast self-examination BSE). Multidisciplinary approach in the management of breast cancer is recommended

**INTRODUCTION**
Worldwide, breast cancer is the most frequently diagnosed life threatening malignant disease in women and the leading cause of cancer death in women with a male: female ratio of 1:1001,2. In the United State, breast cancer accounts for 29% of all cancers in women and is second to lung cancer as a cause of cancer death in women3. UK breast cancer are estimated to be the 6th highest in Europe, where 29% of female cases and 13% of the total in Europe4,5.

Jedy et al in their report from population based registry in 2012 found that breast cancer is now the commonest malignancy affecting women in Nigeria with age standardized incidence rates of 52 per 100,000 and 64.6 per 100,000 at Ibadan and Abuja population based registry respectively6.

In Nigeria, the number of women at risk of breast cancer increased steadily from approximately 24.5million in 1990 to approximately 40million in 2010 and is projected to rise over 50million in 20207. Presentation in Nigeria has been reported to be in advanced stages8.

Breast cancers are mostly invasive or non-invasive, with invasive ductal carcinoma accounting for the largest proportion. Other variants of breast cancer histology are sarcoma, medullary, tubular, papillary and mucinous9. Many early breast carcinomas are asymptomatic and are often first detected as an abnormality on a mammogram before it is felt by the patient or healthcare provider.
Aetiological factors such as oral contraceptives, alcohol, obesity which are modifiable have been identified with breast cancer, though there are non-modifiable risk factors, such as gender, age and genetic mutation.

Surgery and radiation therapy along with adjuvant hormonal and chemotherapy are now considered the primary treatment for breast cancer. In many patients with low risk early stage breast cancer, surgery with local radiation may be curative\textsuperscript{10}.

In advanced disease, depending on the model of risk reduction, adjuvant therapy has been estimated to be responsible for 35\% - 72\% of the decrease in mortality\textsuperscript{11}.

It is important to apply a multidisciplinary team approach in the management of breast cancer owing to the associated burden.
JUSTIFICATION

Breast cancer is arguably the commonest cancer type that affects women in Nigeria\textsuperscript{12,13}. It is also one of the leading causes of cancer deaths, despite advanced improvement in screening and improved treatment opportunities. The lifetime risk of dying from breast cancer is about 3.4\%\textsuperscript{14,2} and this reduces the life expectancy of the population at risk. Human capital is most often affected and as such, weakens the economy of the nation. The survival rate of advanced stage breast cancer is relatively low, and patients in Nigeria mostly present at this stage. Socio-demographic correlates associated with breast cancer risk includes: age, marital status, parity, family history, comorbidity, body mass index. Determining the socio-demographic correlates of breast cancer cases will help in patients counselling. It will define what lifestyle could be changed or modified to reduce the risk of cancer and to achieve early presentation by screening and also help forecast the possible outcome of treatment. The need for proper management of these patients is important in order to optimize utilization of limited resources, avoid under treatment or overtreatment and improve the quality of life of patients.

The burden associated with breast cancer is envisaged to increase as large numbers of Nigerians present late. This burden will be borne by the patients, their relations and health care delivery system. It is therefore important to study the challenges encountered in the management of these patients and determine the most appropriate treatment.
AIM AND OBJECTIVES

Aim:

The aim of this study was to determine the socio-demographic correlates and management of breast cancer in Radiotherapy department of Lagos University Teaching Hospital (LUTH) during a ten year period between January 2004 and December 2013

Specific Objectives:

1. To determine the prevalence of breast cancer in Radiotherapy department, LUTH

2. To determine the risk factors associated with breast cancer in Radiotherapy department, LUTH

3. To determine the pattern of presentation and management of breast cancer in Radiotherapy department, LUTH

4. To determine the outcome of treatment among patients with breast cancer in the Radiotherapy department, LUTH.
LITERATURE REVIEW

Anatomy

The normal breast of a woman covers a fairly large area on the pectoralis major muscles lying over the chest, it extends from the clavicle to the armpit and overlies the 2\textsuperscript{nd} to the 6\textsuperscript{th} ribs from the sternum to the axilla\textsuperscript{16}.

It is made up of the mammary gland, fatty tissues which are guided by the connecting tissues to give the shape the woman’s breast possesses. A breastfeeding woman has milk being transported from the acini which forms 15 - 20 lobules of the gland through the ducts. The peripheral ducts converge into the lactiferous ducts which communicate radially on the summit of the nipple that is surrounded by the areola \textsuperscript{16}.

Blood supply into the breast is mainly from the internal mammary artery, while the lymphatics is to the axillary lymph nodes mainly, these are described in levels according to their relative location with the pectoral muscles. The superolateral quadrant of the breast is the quadrant that is mostly affected by cancer\textsuperscript{17}.

Epidemiology

Worldwide, it is estimated that more than one million women are diagnosed with breast cancer annually\textsuperscript{18}. More than 410,000 will die from the disease, which represent 14\% of female cancer deaths\textsuperscript{18}, about 1 in 8 in U.S. women, 1 in 12 Caucasian women in UK\textsuperscript{19}. 
In Nigeria, it is the most prevalent cancer in women, resulting in highest cancer deaths. A study in Abuja population based registry reported breast cancer age standardized incidence rate as 64.6 per 100,000 and Ibadan population based registry as 52 per 100,000\textsuperscript{6}.

Breast cancer incidence has been increasing yearly, however, this varied from location to location, within the developed countries, incidence has increased by 5\% annual incidence rate and developing countries such as China has recorded increase in incidence rate between 20\% and 30\%\textsuperscript{20,21} this rise can be attributed to improved healthcare system and awareness of breast cancer, mortality rate has declined also with disparities in the western world and the developing nations.

It is generally believed to affect more women in their premenopausal period, the peak incidence in Nigeria occurs in the 3\textsuperscript{rd} to 4\textsuperscript{th} decade of when compared to their Caucasian counterpart which is a decade ahead\textsuperscript{22}. Adenipekun et al reported a mean age of 49.4 years in Ibadan\textsuperscript{23}.

Presentation of breast cancer varies all over the world, patients in high income countries present earlier than low and mid income countries due to the presence of infrastructure and resources for routine screening, this contributes to the increased rate of incidence and abated mortality rate\textsuperscript{24,25}. In Nigeria, presentation of breast cancer has been reported to be mainly in the advanced stage\textsuperscript{26}. 
Aetiology

The risk associated with cancer is never exhaustive, however, with thorough research done so far, some factors have been identified as either non-modifiable or modifiable factors. The following risk factors have been seen to be associated with breast cancer development.

Non-modifiable risk factors:

These are factors that are not controlled by the decisions made by the individual at risk, they simply predispose such individuals to the disease without recourse, and they include:

1. **Gender**: This is the main risk factor associated with breast cancer. Women are 100 times more commonly affected than men. This could be as a result of men having less oestrogen and progesterone hormones that promote breast growth\textsuperscript{27,2}.

2. **Age**: The risk of having breast cancer increases with age. The incidence rate increases rapidly in the 5\textsuperscript{th} decade (4\textsuperscript{th} decade in Africans) and slows down after the 8\textsuperscript{th} decade\textsuperscript{28}.

3. **Genes**: About 5-10\% of breast cancer cases had been linked to mutated genes inherited from parents. BRCA1 and BRCA2 are the most common genes associated with breast cancer. These genes help prevent cancer by making protein that keep the cells from growing abnormally in normal cells, a mutated copy of this gene make one highly vulnerable to the breast cancer disease\textsuperscript{29}. BRCA1 possess more risk as high as 80\% and
averagely 55-65% when compared to the BRCA2 which is 45%\textsuperscript{30}. Other mutated genes with less risk of breast cancer are ataxiataleangiectasia (ATM), TP53, CHEK2, PTEN, CDHI, STKII, PALB2\textsuperscript{26}.

4. **Family history**: The mutated genes that has been mostly linked with breast cancer is being inherited with 5-10% of breast cancer cases. Having one first degree relative with breast cancer will have a double fold risk for such a woman, while the presence of 2 first degree relatives will increase her risk to 3 folds\textsuperscript{31}.

5. **Personal history of breast cancer**: Women with previous history of breast cancer have about 3 to 4 folds increased risk than those without a history of breast cancer\textsuperscript{11}.

6. **Estrogen window**: this is the duration between the onset of menstruation at puberty to the stoppage of menstruation at menopause. Women who experience menarche early (before age 12) and/or late menopause (after age 55) are at higher risk. This may be due to a longer lifetime exposure to the estrogen and progesterone hormones\textsuperscript{32}.

7. **Benign breast conditions**: some of these conditions are more closely linked to breast cancer than the others, there are three general groups namely; non-proliferative lesions, proliferative lesions without atypia, and proliferative lesions with atypia. Women with history of hyperplasia or atypical hyperplasia have a higher risk\textsuperscript{33}.
Modifiable factors

1. **Childbearing**: Women who have their first child above the age of 30 years are more at risk of breast cancer. Each live birth reduces the probability by 7%, as such nulliparous women are at higher risk than the multiparous women. This can be linked to breastfeeding by reducing the lifetime of menstrual cycles.\(^{34}\).

2. **Oral contraceptives (OCS)**: Women who use OCS are found to be at higher risk compared to those who never use them. The risk becomes insignificant 10 years or more after stopping use.\(^ {27,35}\).

3. **Breastfeeding**: This has been found to reduce the menstrual cycles of women consequently reducing the exposure to oestrogens and abating the risk of breast cancers in women who engage in such for continued 1.5 – 2 years.\(^ {35}\).

4. **Alcohol intake**: This factor has been clearly linked with breast cancer and other type of cancers, consumption has been associated with higher levels of sex hormones. 10 grams per day of alcohol consumed will lead to an increase of 7-10% risk.\(^ {35,36}\).

5. **Overweight and obesity**: Menopausal women who are overweight are at increased risk, ovaries produce most of the oestrogen and fat tissue produces fewer amount prior to menopause, beyond this, fat tissue produces most of the oestrogen, as more fat tissue increases with cancer risk. Insulin level also is found to be higher in the blood of obese people.
and higher insulin levels have been associated with breast cancer\textsuperscript{36}. Waist-Hip-Ratio (WHR) a measure of central adiposity has been found by Adebamowo et al to have statistically significant association with breast cancer in premenopausal women\textsuperscript{34}.

There are other unconfirmed aetiological factors such as height, density of breast, diet, ionising radiation, occupational exposure, induced abortion, breast implants, wearing of bra, antiperspirant\textsuperscript{14,37,38,39,40}.

**Pathology**

80\% of the breast cancer are carcinoma, this histological type of cancer arise from the epithelial component of the breast. The epithelial component consists of the cells that line the lobules and terminal ducts of the breast. While cancer can be grouped into in situ or invasive based on locality of the cancer, most of the carcinomas are invasive ductal carcinoma followed by invasive lobular carcinoma\textsuperscript{41}. These two common cancer types have distinct pathologic features despite their terminal duct origin. The lobular carcinoma type grows as single cells, arranged individually in single file or sheets and have different molecular and genetic aberrations that distinguish them from ductal carcinoma\textsuperscript{41}.

Li et al reported the proportion of the histology as follows: Infiltrating ductal 76\%, mixed ductal and lobular 7\%, mucinous (colloid) 2.4\%, tubular 1.5\%, medullary 1.2\%, papillary 1\%\textsuperscript{9}. 
Sarcoma is another major type of histopathology found in breast cancer, though rarer, they arise from the stroma, the connective tissue consisting of myofibroblasts and blood vessel cells. Angiosarcoma and phyllodes tumours are the subtypes of this cancer type.

Other types of cancer that are less common are medullary carcinoma, tubular/cribriform carcinoma, mucinous/colloid carcinoma, papillary carcinoma and primary lymphoma of the breast (NHL).

The grading of cancer is based on the degree of mitosis the cells undergo and how closely the cancer cells are to the normal breast cells, Greenhough\textsuperscript{42} described a system of grading mammary carcinoma based on some histological characteristics of the tumour cells such as the degree of tubule formation, the size, shape and chromatism of the nucleus and frequency of mitosis. Nottingham grading system also known as Elston-Ellis modification of Scarfbloom-Richardson (SBR) grading system is a system that grades breast tumours based on the following features\textsuperscript{43}:

- **Tubule formation**: how much of the tumour tissue has normal breast (milk) duct structures
- **Nuclear grade**: an evaluation of the size and shape of the nucleus in the tumour cells
- **Mitotic rate**: how many dividing cells are present, which is a measure of how fast the tumour cells are growing and dividing.
Each of the categories gets a score between 1 and 3; a score of “1” means the cells and tumour tissue look the most like normal cells and tissue, and a score of “3” means the cells and tissue look the most abnormal. The scores for the three categories are then added, yielding a total score of 3 to 9. Three grades are possible:

• Total score = 3–5: G1 (Low grade or well differentiated)
• Total score = 6–7: G2 (Intermediate grade or moderately differentiated)
• Total score = 8–9: G3 (High grade or poorly differentiated)

**MOLECULAR SUBTYPES**

Molecular subtypes of breast cancer may be useful in planning treatment and developing new therapies. Most studies divide breast cancer into four major molecular subtypes:

1. Luminal A
2. Luminal B
3. Triple negative/basal-like
4. HER2 type

These same subtypes also appear in ductal carcinoma in situ\(^{42,43}\). Other less common molecular subtypes have also been described including normal breast-like, apocrine molecular type and claudin-low type, and others are listed as unclassified. The complex profile of each subtype is determined using molecular and genetic information from tumour cells. However, some characteristics (including hormone receptor status and proliferation rate) can be
used to roughly define the four major subtypes. The table below gives more details -

<table>
<thead>
<tr>
<th>Subtypes</th>
<th>These tumours tend to be*</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luminal A</td>
<td>ER+ and/or PR+, HER2- , low Ki67</td>
<td>40%</td>
</tr>
<tr>
<td>Luminal B</td>
<td>ER+ and/or PR+, HER2+ (or HER2- with high Ki67)</td>
<td>20%</td>
</tr>
<tr>
<td>Triple negative/basal-like</td>
<td>ER-, PR-, HER2-</td>
<td>15-20%</td>
</tr>
<tr>
<td>HER2 type</td>
<td>ER-, PR-, HER+</td>
<td>10-15%</td>
</tr>
</tbody>
</table>

*these are the most common profiles for each subtype. However, not all tumours within each subtype will have all these features.

**LUMINAL A**

Most breast cancers are luminal tumours, luminal tumour cells look the most like the cells of breast cancers that start in the inner (luminal) cells lining the mammary ducts. Luminal A tumours tend to be:

- Estrogen receptor-positive+(ER+) and/or progesterone receptor-positive (PR+)
- HER2/neu-negative (HER2-)
Tumour grade 1 or 2

Fewer than 15% of luminal A tumours have p53 mutations, a factor linked with a poorer prognosis\textsuperscript{47,48}. Luminal A tumours tend to have the best prognosis out of the four subtypes, with fairly high survival rates and fairly low recurrence rates, because luminal A tumours are estrogen receptor positive, treatment for these tumours often includes hormone therapy\textsuperscript{46-47,49-51}.

**LUMINAL B**

Luminal tumours have cells that look like those of breast cancers that start in the inner (luminal) cells lining the mammary ducts. Luminal B tends to be:

- ER+ and/or PR+
- Highly positive for Ki67 (have a high number of cancer cells actively dividing) and/or HER2/neu-positive (HER2+)

Women with luminal B tumours are often diagnosed at a younger age than those with luminal A tumours. And, compared to luminal A tumours, they tend to have factors that lead to a poorer prognosis including: poorer tumour grade, larger tumour size, lymph node-positive, $p53$ gene mutations (about 30 percent)\textsuperscript{46-53}.

In some studies, women with luminal B tumours have fairly high survival rates, although not as high as those with luminal A tumours\textsuperscript{47,49-50}. 
TRIPLE NEGATIVE/BASAL-LIKE

Triple negative breast cancers are:

- ER- negative
- PR- negative
- HER2- negative

There are several subsets of triple negative breast cancer. One subset is referred to as basal-like because the tumours have cells with features similar to those of the outer (basal) cells surrounding the mammary ducts. Most basal-like tumours contain p53 mutations\(^{47,48,54}\).

Most triple negative tumours are basal-like and most basal-like tumours are triple negative. However, not all triple negative tumours are basal-like and not all basal-like tumours are triple negative\(^ {55}\).

About 15 to 20 percent of breast cancers are triple negative or basal-like\(^ {47,48,54}\). These tumours tend to occur more often in younger women and African American women\(^ {47,49,52,56-60}\). And, most BRCA1 breast cancers are both triple negative and basal-like\(^ {49,57,61-62}\).

Triple negative/basal-like tumours are often aggressive and have a poorer prognosis (at least within the first five years after diagnosis) compared to the estrogen receptor-positive subtypes (luminal A and luminal B tumours)\(^ {47,54,49,50-}\).
Triple negative/basal-like tumours are usually treated with some combination of surgery, radiation therapy and chemotherapy.

The genes linked to basal-like tumours are not well understood at this time and thus, targeted therapies do not yet exist. However, potential targets for future therapies include the EGF receptor, a B-crystallin and cyclin E.

**HER2 type**

The molecular subtype HER2 type is not the same as HER2+ and is not used to guide treatment. Although most HER2 type tumours are HER2+ (and named for this reason), about 30 percent are HER2-. HER2 type tumours tend to be: ER-, PR-, Lymph node-positive with poorer tumour grade

About 10 to 15 percent of breast cancers have this molecular profile. About 75 percent of HER2 type tumours contain p53 mutations.

HER2 type tumours have a fairly poor prognosis and are prone to early and frequent recurrence and metastases. Women with HER2 type tumours appear to be diagnosed at a younger age than those with luminal A and luminal B tumours. HER2/neu-positive tumours can be treated with the drug trastuzumab (Herceptin).
**Normal-like**

About 6 to 10 percent of all breast cancers are classified as normal-like. Although called “normal-like,” these tumours are not more common than others. These tumours are usually small and tend to have a good prognosis.

At this time, it is unclear whether normal-like tumours are a distinct molecular subtype. It may be that some tumours are unable to be classified into another subtype because the tissue sample tested did not contain enough cancer cells.

**Presentation**

The pattern of presentation is largely dependent on the stage of the disease, common symptoms include breast lump which is the commonest presenting complain, the lump is typically hard, irregular, non-tender, solitary. Nipple discharge is the second most common, seen both in breast cancer and benign diseases. Left breast is seen to be affected mostly though few do present with bilateral affectation. It also occurs in the opposite breast after six months of primary disease (metachronous), diagnosed simultaneously or within an interval of about six months or less (synchronous). The upper outer quadrant of the breast is mostly affected.

Metastatic cases present with features that are peculiar to the site of spread, spread can be by direct, lymphatic or blood borne. Direct spread is to the surrounding breast tissue, underlying muscle and chest wall, infiltration of the lactiferous ducts causes nipple retraction. Lymphatic spread is mainly to the
axillary nodes and internal mammary nodes, the infraclavicular, supraclavicular, cervical and mediastinal nodes and rarely to the lymphatics of the opposite breast may also occur. Malignant spread of the axillary nodes may cause lymphedema of the breast and/or upper limb. Dermal lymphatics may be infiltrated and blocked leading to peau d’ orange and if extensive gives rise to skin nodules or carcinoma en cuirasse. Blood borne metastasis is to several sites such as lymph nodes, lungs, bones, liver adrenals, brain and meninges, even though the primary site is small or impalpable, most breast cancer have distant metastasis when first detected.

Skeletal metastasis present with pain at the site involved, erythema, fracture or non-functional affected limb. Spinal metastasis present with severe pain, paraesthesia, paresis or paraplegia depending on the affected site while pulmonary metastasis present with cough, breathing difficulty and chest pain. Liver metastasis present with jaundice, abdominal pain/swelling or features of liver decompensation. Brain metastasis is accompanied with personality changes, vomiting and persistent headache, vertigo, and/ increased intracranial pressure.

Globally, metastasis occurs mostly to the bone. Patanaphan et al in 1988 found distant metastasis in bone 51%, followed by lungs 17%, brain 6% and liver 6%. Ketiku in Lagos showed a regional lymph nodes metastasis of 52%, 44% recurrent chest wall, 33% to the bones, 27% to the liver, 17% to the lungs and 3% to the brain, a decade later Ketitku et al using X-ray and radioisotope bone
scan reported that 26% of 38 patients with stage III breast cancer have detectable bony metastasis\textsuperscript{70}. A study in Ile-if\-e in 2006 by Adesunkanmi et al reported metastasis of 84% of regional nodes, 20% to the lungs, 19% to the liver, 11% to the bones and 2% to the brain\textsuperscript{64}. An autopsy study of breast cancer patients revealed metastasis of 26% of them to regional nodes, 27% to the liver, 20% to the bones, 10% to the heart and pericardium 6% to the brain and meninges, 5% to the adrenal gland, 4% to the stomach, 2% to the kidney and 1% each to the pancreas, spleen and ovaries\textsuperscript{72}.

**Investigation**

Management of breast cancer begins with a good history taking, here the physician obtains details such as the duration of disease, complications, treatment received hitherto. The breast is then examined thoroughly through palpation or clinically for the presence of cancer. Physically, the breast is inspected for colour change, nipple retraction. Examination such as palpating the supraclavicular region, neck and axilla for lymph nodes as well as breast for mass or lump and the abdomen for any organomegally. The eye is examined for jaundice due to spread of the disease to liver.

A definite diagnosis of breast cancer is obtained through tissue biopsy which can be done through fine needle aspiration, core needle biopsy technique, incisional or excisional biopsy.
Fine needle aspiration biopsy technique (FNAB) is the easiest type of biopsy where very thin and hollow needle is used to withdraw (aspirate) a small amount of tissue from the suspected area, and this tissue is viewed under the microscope to determine if it is cancerous, a clear fluid suggests a benign cyst while a bloody or cloudy fluid can be benign cyst or cancer, this technique though can sometimes miss a cancer if the needle is not placed among cancer cells and even when the cancer cells are found, it is not usually possible to determine if the cancer is invasive.

Core needle biopsy technique uses a larger needle and as such, the likelihood of diagnosing cancer is more than in the fine needle aspiration biopsy. This technique can also be done with vacuum assisted to ensure this technique is more viable.

- Incisional biopsy technique which involves the removing of small part of the surrounding area of the lesion while excisional biopsy removes even more area in question, for cosmetic reasons, biopsy is preferred for large lesions, otherwise excisional biopsy is considered.

- Mammogram, Breast Ultrasound, Magnetic Resonance Imaging (MRI) of the breast, X-ray, CT scan, PET CT scan of the chest and abdomen are some of the investigative measures used to detect the presence of breast cancer.
Laboratory assessment such as full blood count, serum creatinine, serum electrolytes, urea, liver function test and retroviral screening are important for pre-treatment assessment.

**Immunohistochemistry**

Estrogen receptors (ER), progesterone receptors (PR) and Human epidermal growth receptor 2 (HER2) are proteins which are used to classify and prognosticate breast cancer based on their presence in the breast cancer. Hormone receptor-positive contains either estrogen or progesterone receptors, hormone receptor negative have neither of estrogen or progesterone receptor, HER2 positive are cancers that have overexpression HER2 protein or extra copies of the HER2 while HER2 negative do not have excess HER2, triple-negative if the cancer does not have either of estrogen or progesterone receptors and less HER2, and triple-positive are cancers that have ER positive, PR positive and have overexpression HER2. Immunohistochemistry is mandatory before commencement of treatment of breast cancer in order to give the best line of management.

**Staging**

Staging can be achieved clinically by physical examination, palpation of the skin, mammary gland, lymph nodes, imaging and pathological examination of the breast tissue. Pathologically, staging of breast cancer includes all the data above in clinical staging and data from surgical exploration and resection. The
widely used breast cancer staging in Nigeria are the Tumour-Node-Metastasis (TNM) staging by American Joint Committee Classification (AJCC)\textsuperscript{43} and Manchester/clinical classification (Appendix 1).

Management

There are varied factors in the treatment of breast cancers. These options include factors such as age, clinical and pathological characteristics of cancer, menopausal status, biological prognostic factors and personal preference of the patient are being considered before treatment is being administered. Treatment should be combination therapy or individual administration of surgery, chemotherapy, radiotherapy, hormone therapy, targeted therapy and bone directed therapy. The management of breast cancer is multidisciplinary, involving a wide array of professionals such as the surgeons, oncologists, radiographers, radiologists, pathologists, nurses, psychologist and physiotherapist.

Surgery

Surgery is vital treatment modality in the management of breast cancer. Most breast cancer patients need surgery, this depends on the stage of the disease. Breast conserving surgery (lumpectomy or quadrantectomy) and mastectomy are options to consider. Breast conserving surgery involves the removal of cancer cells and some surrounding normal tissue. Mastectomy is the removal of the entire breast, it can be simple mastectomy where the entire breast including
the nipple are removed but the underarm lymph nodes or muscles tissue beneath the breast are left, or skin-sparing mastectomy where most of the skin over the breast is left behind a procedure mostly used for immediate breast reconstruction. Another variant of surgery is modified radical mastectomy which involves the removal of axillary (underarm) lymph nodes and the entire breast. The choice between breast conserving surgery (BCS) options and mastectomy largely depend on the preference of the patients, moderate dose radiation therapy is used to accompany BCS while reconstruction of the breast follows mastectomy. For clinical stages I and II, breast conserving surgery with radiotherapy and possibly chemotherapy may be indicated if one or two sentinel lymph nodes are found to have cancer which is not extensive, however, mastectomy may be a better option for women with more complications from breast cancer such as inflammation, pregnancy and size of cancer.

Radiotherapy

A treatment with high energy rays or particles that destroy cancer cells is a form of radiation therapy used, this can be given externally (external beam radiation) or internally (brachytherapy). It involves the use of high energy radiation which is beamed from a machine outside of the body to the affected area using a linear accelerator or Cobalt 60 machine Brachytherapy involves the placing of radioactive seed or pellet in the breast tissue where cancer affects. MammoSite Radiation Therapy System (RTS) is a simpler, less invasive method of
delivering breast brachytherapy which involves the placement of radioactive seeds (\(^{192}\)Ir or HDR \(^{60}\)Co) (using just a single catheter) directly to the area where a breast tumour has been surgically removed via lumpectomy.

**Radiotherapy treatment for early stage breast cancer**

Breast-conserving surgery followed by radiation therapy to the intact breast is now clearly established as the most acceptable standard of care for majority of women with early-stage invasive breast cancer. In 1992, the Journal of the National Cancer Institute published a monograph stating that breast-conservation treatment is an appropriate method of primary therapy for most women with stage I and II breast cancer and is preferable because it provides survival equivalent to that of total mastectomy and axillary dissection while preserving the breast\(^7\).

**Radiotherapy treatment for locally advanced breast cancer**

Neoadjuvant chemotherapy has now become a standard initial therapy for most patients with locally advanced breast cancer, which is followed by surgery and thereafter postmastectomy radiotherapy. The administration of radiation therapy is predominantly on the basis of the pathologic extent of disease. Neoadjuvant chemotherapy changes the extent of pathologic disease in 80% to 90% of cases. The correlations between pathologic extent of disease and locoregional recurrence after mastectomy are different for patients treated with chemotherapy first compared with those treated with surgery first. A study
found that the local-regional recurrence rate associated with pathologic extent of disease after surgery was less among patients treated with chemotherapy first than among patients treated with surgery first\textsuperscript{74}.

**Postmastectomy radiation techniques**

This includes the treatment to the chest wall and lymphatics in the undissected axillary apex supraclavicular fossa. The chest wall is the most common site for disease recurrences, while stage III patients have a clinically relevant risk of recurrence in the axillary apex supraclavicular fossa. Patients should be immobilized with their ipsilateral arm abducted (90 – 120 degrees) and externally rotated, it is important to have the soft tissues of the arm cranial to the junction of the tangent and supraclavicular fossa field. Skin folds within the supraclavicular fossa should be avoided if possible. Patients are placed on a 10 – 15 degree angle board to flatten the slope of the chest wall in the region of the sternum. Radiopaque wires are placed on the mastectomy scar and the patient undergoes a treatment-planning non-contrast CT scan. The border between the chest wall and the supraclavicular fields is typically placed at the bottom of the clavicular head. Appropriate iso-centres and set up points are determined and marked. Targeted areas of interest are then contoured on the CT slices\textsuperscript{73}. Simulation of radiotherapy treatment also known as planning varies per patient and involves finding the exact area to be treated using the highest dose of radiation of 50Gy in 25 fractions given in 5 weeks, while causing the fewest
possible side-effects, using a TeleCobalt 60 machine with energy of 1.25MeV or Linear Accelerator with energy 5 – 15 MeV.

**Chemotherapy**

This is the use of cytotoxic drugs either as neo-adjuvant chemotherapy or adjuvant chemotherapy. This is usually given intravenously for breast cancer treatment. These drugs are usually given in combinations for effective outcome. Common chemotherapy drugs given in cycles are Paclitaxel, Docetaxel, Cyclophosphamide, Epirubicin. Patients are exposed to side effects of chemotherapy drugs such as vomiting and nausea, hair loss and nail changes, mouth sores, loss or increase in appetite, low blood cell counts and so on.

**Targeted therapy**

Trastuzumab (Herceptin) or pertuzumab or lapatinib is included for cancers that are HER2 positive.

Everolimus mammalian target of rapamycin inhibitor (mTOR) is used in patient with hormone receptor positive advanced breast cancer who had recurrence of progression while receiving previous therapy with a non-steroidal aromatase inhibitor in the adjuvant settings or to treat advanced disease (or both)

T-DM1 or ado-trastuzumab emtaseine (Kadcyla) is included for HER2 positive cancers that progressed on trastuzumab.
**Hormonal therapy**

This is a form of systemic therapy, mostly used as an adjuvant therapy to reduce the risk of recurrence of cancer after surgery. This therapy involves the use of drug that lowers or stops estrogen that promotes the growth of cancers that are hormone receptors-positive in breast. Selective estrogen receptors modulator (SERM) eg Tamoxifen is a type of drug that acts either as anti-Estrogen in some tissues. Aromatase inhibitors (AIs) have now replaced tamoxifen as the standard of care for adjuvant endocrine therapy in the treatment of Postmenopausal Women with hormone-sensitive breast cancer.75.

Invasive breast cancer can be divided clinically into three groups, for each group, namely, early, locally and metastatic and management of the each group differs, clinical groups and their corresponding management options are as follows:

**Management of early stage breast cancer**

Early stage cancer under the Manchester staging ranges from I to II, multidisciplinary approach includes surgery (conservative or radical mastectomy), adjuvant hormonal or chemotherapy and radiotherapy. At this stage breast conservative surgery followed by radiotherapy (radical dose – 45.50Gy in 25# given over 5weeks) to the whole breast and boost to the tumour bed and scar – 10-15Gy in 5 to 7# over 7-9 days) and chemotherapy are feasible treatment options. The goal here is to remove all the cancer from the breast, to
achieve a clean, clear margin (distance between the outer edge of the tumour and the outer edge of the normal tissue surrounding it) which dictate how much breast tissue is ultimately removed. Postoperative radiation following BCS is beneficial as it increases the survival rate by decreasing the reoccurrence of the cancer in the breast. Adjuvant systemic therapy can also be recommended which includes chemotherapy and hormonal therapy for hormone receptor positive breast cancer patients. Biological/targeted therapy are also indicated for patients who may require them.

**Locally advanced breast cancer**

This includes stage III breast cancer which involves cancer that has not spread to distant sites. The tumours are larger than 5cm, ulceration of the skin overlying the breast, inflammatory breast cancer are included and tumours with supraclavicular metastases. Neo-adjuvant chemotherapy, surgery, post operation radiotherapy and hormonal therapy if included, all play vital role in management of locally advanced breast cancer. Most often, the treatment is neo-adjuvant chemotherapy to shrink the tumour and thereafter mastectomy is considered. Adjuvant endocrine therapy can also be given to patients with hormone receptor positive, often, radiotherapy is needed after surgery.
Metastatic breast cancer

This is stage IV cancer normally called advanced or metastatic cancer that has progressed to other sites of the body. The most common sites are the bones, lungs, liver, brain. The metastasis could be classified as low risk metastasis which are those developing after a long disease free interval, with less visceral organs involvement or as high risk metastasis with rapidly progressive disease or extensive visceral involvement\(^76\). At this stage, treatment aim is palliative, to control the tempo of the disease, improve symptoms and maintain of good quality of life. Systemic therapy is the main form of treatment, this may consist of hormone therapy, chemotherapy, targeted therapies or combination of these treatments. Assessment of the tumour biology, hormonal status, age, menopausal status, location of metastases (visceral or non-visceral) are important determinants guiding the choice of treatment.

Radiotherapy is a well-tolerated method of treating bone metastasis, in addition to analgesics, immobilization and mechanical stabilization by the orthopaedic surgeon.

Liver metastasis can be treated with surgical resection of the univocal lesion with or without radiotherapy and systemic therapy\(^77\), other forms of treatment includes laser induced interstitial therapy and intra-arterial chemotherapy.

Lung metastasis characterized by pleural effusion is managed by closed thoracotomy tube drainage (CTTD) and pleuridesis, tetracycline, talc and bleomycin have been effective in this respect\(^78\). Multiple lung parenchymal
metastasis is managed symptomatically using diuretic, morphine, bronchodilators, steroids, anxiolytics, mucolytic, chest physiotherapy and supplementary oxygen. Radiotherapy can be given afterwards as a palliative measure to the lungs as well as adjuvant chemotherapy and hormonal therapy to control the tempo of the tumour.

Brain metastasis is initially treated with high dose corticosteroids which shrink the edema, followed by palliative radiotherapy to the brain. However, multiple cerebral masses are usually treated with whole brain irradiation.

Eye metastasis is best treated using $^{125}$I plaque therapy, which is more tolerable than the external beam radiotherapy. Surgical resection and systemic therapy may be the appropriate treatment option for larger metastatic lesion.

**Prognostic factors**

Anatomic features such as tumour size and lymph node status are important prognostic features. Biologic features of the tumour are equally important or possibly even more important than anatomic features.

1. Number of positive axillary lymph nodes: this is an important prognostic indicator, prognosis is worse with increasing number of lymph nodes.
2. Tumour size: in general, tumour smaller than 1cm have a good prognosis in patients without lymph node involvement
3. Histologic or nuclear grade: patients with poorly differentiated histology and high nuclear grade have worse prognosis than others
4. **ER/PR status**: ER and/or PR positive tumours have better prognosis and these patients are eligible to receive endocrine therapy.

5. **Histologic tumour type**: prognosis of infiltrating ductal and lobular carcinoma are similar. Mucinous (colloid) and tubular histologies have good prognosis. Inflammatory breast cancer is one of the most aggressive forms of breast cancer.

6. **HER2/neu expression**: this is a poor prognostic marker and patients with HER2/neu overexpression are candidates for HER2-targeted therapies. HER2/neu testing can be done with immunohistochemistry (IHC) or fluorescence in situ hybridization (FISH).

7. **Gene expression profiles**: oncotype DX is a diagnostic genomic assay based on paraffin-embedded tissue. This assay was initially developed to quantify the likelihood of cancer recurrence in women with newly diagnosed stage I or II, node-negative, ER-positive breast cancer. Patients are divided into low-risk, intermediate-risk and high-risk groups on the basis of the expression of a panel of 21 genes. The recurrence score determined by this assay is found to be a better predictor of outcome than standard measures such as age, tumour size and tumour grade.\(^{83}\)
METHODOLOGY

STUDY SETTING
The study was carried out at the Radiotherapy and Oncology department, Lagos University Teaching Hospital, Idi-araba. It is situated within the metropolitan city of Lagos, South Western part of Nigeria. The Hospital is one of the 2 tertiary hospitals in the state. It is a referral hospital for general and private hospitals in Lagos State as well as adjoining states.

STUDY DESIGN
This is a cross sectional retrospective study

STUDY POPULATION
All case notes of histologically confirmed breast cancer patients between January 1<sup>st</sup> 2004 and December 31<sup>st</sup> 2013 were retrieved from the Radiotherapy departmental records office.

DATA COLLECTION TOOLS AND TECHNIQUE
Relevant data on the socio-demographic characteristics and management of patients were extracted using the data extraction form (Appendix 2) which included the following details:

- Age of patient
- Gender of patient
- Hospital Number of patient
• Address of patient at diagnosis
• Presenting complaints of the patient
• Histological Diagnosis
• Molecular subtype
• Clinical stage at presentation
• Treatment of patient
• Patient’s treatment outcome. (Partial, Complete or No Response)
  ➢ Complete Response (CR): this is defined as total disappearance of all clinical disease
  ➢ Partial response (PR): this is defined as 50% reduction in the size of some or all lesions without concomitant increase of other lesions of the appearance of new lesions
  ➢ No Response (NR): this is defined as a reduction in size of less than 50% of some or all lesions or progressing disease.
• Side effects of treatment
  o Early effects and late effects of chemotherapy
  o Early and late effects of radiotherapy

Inclusion criteria
1. All Breast cancer patients that presented between 2004 and 2013.
2. Histo-pathologically confirmed cases of breast cancer.
3. All case notes with adequate clinical data on management of patient.
Exclusion criteria

1. Breast cancer cases without histological diagnosis.

2. Cases notes with incomplete data.

DATA ANALYSIS

Data extracted was coded and analysed using Statistical Package for Social Sciences (SPSS) version 20. Result presentation will be done using Frequency tables, bar charts and pie charts.

ETHICAL APPROVAL

Before the commencement of the study, ethical approval was obtained from the Joint Ethical Review Committee of the Lagos University Teaching Hospital, Idi -Araba, Lagos.
RESULTS

Table 1 shows the obstetric history of the patients, majority of the subjects were female 1132(99.2%) and male 9 (0.8%), with a male to female ratio of 1:126. The obstetric characteristics of these females revealed that the mean age at menarche was 14.67±2.16 years with a range between 9 and 20 years, 920(81.3%) were pre-menopause, 212(18.7%) of the female were post-menopause with age range between 40-62 years and mean age of 48.86±5.56 years.

The mean age of female patients at first pregnancy was 24.26±4.73, with a range between 13 – 37 years. Assessment of patients parity revealed that 778(68.7%) were parous with an average number of children of 3.75±1.76 between the range 1 – 10, number of recorded patients who breastfed their babies were 509(45.0%) for a mean duration of 13.73±5.66 months, with a maximum and minimum duration of 2 years and 6 months respectively (Table 1).
Table 1: Obstetric characteristics of breast cancer patients

<table>
<thead>
<tr>
<th>Obstetric history</th>
<th>Frequency (N)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at menarche (Years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>14.67 ± 2.16</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>9 – 20</td>
<td></td>
</tr>
<tr>
<td>Menopausal status*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>920</td>
<td>81.3</td>
</tr>
<tr>
<td>Post</td>
<td>212</td>
<td>18.7</td>
</tr>
<tr>
<td>Age at menopause (Years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>48.86 ± 5.56</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>40 – 62</td>
<td></td>
</tr>
<tr>
<td>Parity*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parous</td>
<td>778</td>
<td>68.7</td>
</tr>
<tr>
<td>Nulliparous</td>
<td>354</td>
<td>31.3</td>
</tr>
<tr>
<td>Number of Children</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>3.75 ± 1.76</td>
<td></td>
</tr>
<tr>
<td>range</td>
<td>1 – 10</td>
<td></td>
</tr>
<tr>
<td>Age at first pregnancy (Years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>24.26 ± 4.73</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>13 – 37</td>
<td></td>
</tr>
<tr>
<td>Breast feeding history*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>509</td>
<td>45.0</td>
</tr>
<tr>
<td>No</td>
<td>623</td>
<td>55.0</td>
</tr>
<tr>
<td>Breastfeeding duration (Months)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>13.73 ± 5.66</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>6 – 24</td>
<td></td>
</tr>
</tbody>
</table>

* - female patients only (1132)
A total of one thousand one hundred forty one cases were seen between the 10-year periods. Patients were referred to the Radiotherapy department for treatment from locations across the country.

Presentation of breast cancer at the centre peaked in 2010 with 164 (14.37%), followed by 157(13.76%) and 133(11.66%) in 2009 and 2011 respectively. The lowest occurrence was in 2013 with 67 (5.87%) cases (Figure 1.1).

![Figure 1.1](image.png)

**Figure 1.1:** Incidence of breast cancer between 2004 and 2013
The mean age of patients that presented at the clinic within this period was 46.84±12.36 years, with a range between 17 – 84 years. The peak decade was the 5th decade (40 – 49 years) with 374 (32.8%) patients followed by 262 (22.96%) and 241 (21.12%) in 6th decade (50 – 59 years) and 4th decade (30 – 39 years) respectively. The lowest occurrence was in the 2nd decade (10 – 19 years) with a proportion of 9 (0.8%) cases (Figure 1.2).

![Figure 1.2: Age group distribution of patients](image.png)
The marital status of patients that presented within this period showed a preponderance in the married category 961 (84.2%), single patients seen were 108 (9.46%) and widow were 66 (5.78%) the disease least occurred in those patients that were separated or divorced 6 (0.4%). (Figure 1.3)

Figure 1.3: Marital status of patients
Majority of the histologically confirmed cancer cases were located in the left breast 553 (48.5%), 79 (6.9%) presented with bilateral breast cancer, while 501 (43.9%) had cancer on the right breast (Figure 1.5).

Figure 1.5: Breast cancer laterality of patient
Histopathology of the recorded cases during this period was mostly Invasive Ductal Carcinoma 986 (86.4%). Other histology types recorded with low percentage of occurrence were mucinous 36(3.2%), invasive lobular carcinoma 47(4.1%), medullary 38(3.3%), phylloides 15(1.3%) and papillary 19(1.7%). (Figure 2.1)

**Figure 2.1: Histopathology of patients**
998 (87.47%) of the total number of patients who presented within this period had their stage of disease recorded. The prevalent stage of disease was stage IV 425 (52.59%), followed by stage III 396 (39.68%), stage II 145 (14.53%) and the least stage I 32 (3.21%).

Figure 2.2: Stage of disease
Immunohistochemistry test was done for 139 out of the 1141 subjects recorded, ER positive was the most prevalent with 58(35.6%) cases, 43(26.4%) had PR positive and 38(23.3%) were HER2+. (Figure 2.3)

Figure 2.3: Immunohistochemistry of breast cancer patients
Hormone receptor positive and HER2 negative – Lumina A seen in 87(53.2%) was the commonest molecular subtype found, followed by ER negative in combinations with PR negative and HER2 negative – Basal like/Triple negative molecular subtype 39(23.8%) and HER2 type 24(14.63%), the least molecular subtype seen was Lumina B (combinations of ER/PR positive and HER2 positive) 14(8.54%). (Figure 2.4)

**Figure 2.4: Molecular subtypes of patients**
Figure 2.5 shows that 214 (18.8%) out of the 1141 had lymph node status recorded out of which 135 (63.2%) of the patients had lymph node metastasis.

Figure 2.5: Lymph node status of breast cancer patients
153(13.4%) of the entire patients in record had positive family history of breast cancer. 79(6.9%) drank alcohol who were social drinkers, lesser proportion 9(0.8%) was recorded as those who smoke. Oral contraceptives use was recorded amongst 11.1% of the female patients (Table 2).

Table 2: Risk factors of breast cancer patients

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Frequency (N)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family history of breast cancer</td>
<td>153</td>
<td>13.4</td>
</tr>
<tr>
<td>Alcohol</td>
<td>79</td>
<td>6.9</td>
</tr>
<tr>
<td>Smoking</td>
<td>9</td>
<td>0.8</td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td>125</td>
<td>11.1</td>
</tr>
</tbody>
</table>
The mean body mass index of patients was 28.55±6.39kg/m^2, 457(40.05%) were obese (where 253(22.17%) were class I; 146(12.8%) were class II; 58(5.08%) were class III), 264(23.14%) were overweight and 390(34.18%) were of normal weight. The least stratum of BMI recorded was underweight patients 30(2.63%) (Figure 3.1).

Figure 3.1: Body Mass Index of Breast Cancer patients
The major co-morbidity out the 176(15.4%) patients with record of co-morbidity was hypertension 136(77.3%), while diabetes was present in 13(7.4%) of those that presented, 27(15.3%) had both hypertension and diabetes. (Table 3).

Table 3: Co-morbidity of breast cancer patients

<table>
<thead>
<tr>
<th>Co morbidity</th>
<th>Frequency (N)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>136</td>
<td>77.3</td>
</tr>
<tr>
<td>Diabetes</td>
<td>13</td>
<td>7.4</td>
</tr>
<tr>
<td>Hypertension + Diabetes</td>
<td>27</td>
<td>15.3</td>
</tr>
<tr>
<td>Total</td>
<td>176</td>
<td>100</td>
</tr>
</tbody>
</table>
The most common mode of treatment administered was chemotherapy 123(17.7%), while the most common combination therapy given was surgery, chemotherapy and radiotherapy 230(30.9%). The most frequent mode of surgery performed for both lone and combination therapy was mastectomy 299(59.4%). Radical (71.6%) was the most common form of radiotherapy intention given to the patients (Table 4).

Table 4: Treatment modalities of breast cancer patients

<table>
<thead>
<tr>
<th>Treatment modalities</th>
<th>Frequency</th>
<th>Percentage(%) in combination therapy N = 693</th>
<th>Percentage (%) in total N = 1141</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Combination Therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>19</td>
<td>2.7</td>
<td>1.7</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>123</td>
<td>17.7</td>
<td>10.8</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>27</td>
<td>3.9</td>
<td>2.4</td>
</tr>
<tr>
<td>Chemotherapy + Surgery</td>
<td>141</td>
<td>20.4</td>
<td>12.4</td>
</tr>
<tr>
<td>Chemotherapy + Radiotherapy</td>
<td>56</td>
<td>8.1</td>
<td>4.9</td>
</tr>
<tr>
<td>Radiotherapy + Surgery</td>
<td>114</td>
<td>16.3</td>
<td>10.0</td>
</tr>
<tr>
<td>Surgery + Chemotherapy + Radiotherapy</td>
<td>213</td>
<td>30.9</td>
<td>18.7</td>
</tr>
<tr>
<td>Total</td>
<td>693</td>
<td>100.0</td>
<td>60.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B Surgery</th>
<th>Frequency</th>
<th>Percentage(%) in surgery N = 487</th>
<th>Percentage(%) in total N = 1141</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumpectomy</td>
<td>198</td>
<td>40.6</td>
<td>17.4</td>
</tr>
<tr>
<td>Mastectomy</td>
<td>289</td>
<td>59.4</td>
<td>25.3</td>
</tr>
<tr>
<td>Total</td>
<td>487</td>
<td>100.0</td>
<td>42.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>C Radiotherapy intention</th>
<th>Frequency (N)</th>
<th>Percentage(%) in radiotherapy N = 410</th>
<th>Percentage(%) in total N = 1141</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palliative</td>
<td>116</td>
<td>28.4</td>
<td>10.2</td>
</tr>
<tr>
<td>Radical</td>
<td>294</td>
<td>71.6</td>
<td>25.8</td>
</tr>
<tr>
<td>Total</td>
<td>410</td>
<td>100.0</td>
<td>35.9</td>
</tr>
<tr>
<td>Mean(SD)</td>
<td>40.48(8.69)</td>
<td></td>
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</tr>
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</table>
Chemotherapy treatment being the most administered therapy had 5FU, Epirubicin and Cyclophosphamide FEC (43.4%) as the most given regime, other 3- drug combination were Cyclophosphamide, Adriamycin and 5FU CAF 84(15.7%) and Cyclophosphamide, methotrexate and 5FU CMF 37(6.9%). For 2 – drug combination therapy, the commonest was Adriamycin and Cyclophosphamide AC 71(13.4%) followed by Epirubicin and cyclophosphamide EC 28(5.2%). Taxane based drugs which included docetaxel and paclitaxel in combinations with AC, EC, CMF and FEC was seen in 76(14.2%). Other types of drugs administered 21(4.0%) were vinorelbine, gemcitabine, carboplatin, cisplatin and zeloda (Table 5).

Table 5: Chemotherapy regime administered to patients

<table>
<thead>
<tr>
<th>Chemotherapy regime</th>
<th>Frequency (N)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>3 – Drug combination</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEC</td>
<td>216</td>
<td>40.6</td>
</tr>
<tr>
<td>CAF</td>
<td>84</td>
<td>15.7</td>
</tr>
<tr>
<td>CMF</td>
<td>37</td>
<td>6.9</td>
</tr>
<tr>
<td><strong>2 – Drug combination</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EC</td>
<td>28</td>
<td>5.2</td>
</tr>
<tr>
<td>AC</td>
<td>71</td>
<td>13.4</td>
</tr>
<tr>
<td>Taxane based drugs</td>
<td>76</td>
<td>14.2</td>
</tr>
<tr>
<td>Others</td>
<td>21</td>
<td>4.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>533</td>
<td>100</td>
</tr>
</tbody>
</table>
Outcome of treatment of patients after second year of follow-up showed that majority (48.1%) of patients that presented were lost to follow-up, closely followed by dead outcome (39.2%). Only 12.7% were on follow-up (Table 6).

**Table 6: Outcome of treatment of breast cancer patients**

<table>
<thead>
<tr>
<th>Outcome after 2nd year of follow up</th>
<th>Frequency (N)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>On follow up</td>
<td>145</td>
<td>12.7</td>
</tr>
<tr>
<td>Lost to follow up</td>
<td>549</td>
<td>48.1</td>
</tr>
<tr>
<td>Dead</td>
<td>447</td>
<td>39.2</td>
</tr>
<tr>
<td>Total</td>
<td>1141</td>
<td></td>
</tr>
</tbody>
</table>
Out of those who were on follow-up 145 (12.7%), majority had complete response (42.2%) followed by those who whose disease progressed (24.1%). Partial response was seen in 23.5% while 10.2% experienced no response in their cancer management (Table 7).

**Table 7: Treatment response of patients on follow up after second year**

<table>
<thead>
<tr>
<th>Treatment response of patients on follow up</th>
<th>Frequency</th>
<th>Percentage</th>
<th>Percentage (%) in Total N=1141</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Response</td>
<td>15</td>
<td>10.2</td>
<td>1.31</td>
</tr>
<tr>
<td>Partial Response</td>
<td>34</td>
<td>23.5</td>
<td>2.98</td>
</tr>
<tr>
<td>Complete Response</td>
<td>61</td>
<td>42.2</td>
<td>5.35</td>
</tr>
<tr>
<td>Disease Progression</td>
<td>35</td>
<td>24.1</td>
<td>3.07</td>
</tr>
<tr>
<td>Total</td>
<td>145</td>
<td>100</td>
<td>12.7</td>
</tr>
</tbody>
</table>
DISCUSSION

The ten year retrospective review revealed 1141 cases of breast cancer between 1\textsuperscript{st} of January 2004 and 31\textsuperscript{st} of December 2013. Presentation was low between 2012 and 2013 due to the protracted industrial action by medical practitioners. In a study of breast cancer incidence in Nigeria, breast cancer was seen as the most prevalent cancer type across 5 cities\textsuperscript{84}. Prevalence in this study is low when compared with other studies in Nigeria these may be due to the one-study location (Radiotherapy department) considered.

Several studies done in Nigeria showed an annual incidence which vary with location. 156 cases were seen in Maiduguri\textsuperscript{8}, 116 cases in Ibadan\textsuperscript{85}, 57 cases in Ilorin\textsuperscript{86} and 16 cases in Calabar\textsuperscript{87}. The varying prevalence of breast cancer in different cities across Nigeria also showed the significance of awareness on breast cancer. Prevalence was seen to be high in urban centres than in sub-urban centres, while patients who presented at these sub-urban areas were of higher socio-economic status\textsuperscript{87}.

Breast cancer is known to be a disease that is prevalent in middle-aged women. The mean age of patients in this study was 46.84±12.36 years with a peak age group of 30 – 59 years accounting for majority of the entire study population. The peak decade was 5\textsuperscript{th} decade (40 – 49 years) which is in consonance with several studies internationally and locally. Popoola et al in Lagos\textsuperscript{88} and Godwin et al in Calabar\textsuperscript{85} found the peak decade as the 4\textsuperscript{th} decade, while Afolayan in Ilorin\textsuperscript{86}, Parkin in Kenya and South Africa and Clegg in Ghana\textsuperscript{89} found the peak
decade as 5th decade. Eniojukan and Adepoju in Ibadan\textsuperscript{85} also found the peak age group to be 31-50 years, which further buttressed the prevalence in young adult women. However, some other studies done amongst African and African American women have reported a high prevalence of breast cancer among younger women\textsuperscript{90,91}. The reason for this disparity is yet to be fully investigated.

The male to female ratio of 1:126 found was in consonance with several studies, 99.2\% of the entire population in this study were female, 98.3\% was found in Ibadan, 96.8\% was found in Ilorin, 97.5\% in Maiduguri, while a study in Calabar found 100\%, Ramasamy and Russell in their study found that women are 100 times more commonly affected than men. This could be as a result of men having less oestrogen and progesterone hormones that promote breast growth\textsuperscript{2,27}

Majority(87.6\%) were Yoruba and residents of the south western part of Nigeria (93.5\%) with Lagos residents accounting for 79.2\% of the entire study population which is understandable due to the location of the institute. The occupation of these patients from this location was found to be majorly trading/business (52.7\%) and civil servants (26.0\%), a similar result from Calabar which supports findings of Eniojukan that those presenting with breast cancer are those who are economically capable to foot its management\textsuperscript{85}.

The laterality of the diseases was left-sided bias (48.5\%), while those found in right and bilateral breast were 43.9\% and 6.9\% respectively. This is similar to Ekanem et al findings in Benin where left was 53.3\%, right 45.7\% and bilateral
0.8%\textsuperscript{92}, however this was in disparity with findings in Gombe by Dauda et al where left 71.1% and right 28.3% and 0.6% bilateral\textsuperscript{93}. In Tanzania, Ashley found 45.77% left, 48.04% right and 6.19% bilateral\textsuperscript{94}. Full reasons had not yet been established, however, left breast is larger than the right breast consequently, which lends credence to the logic that presence of more breast tissue is a risk for cancer development\textsuperscript{95}. Tulinuis et al stated that excess risk of developing cancer remains for the left breast also for women who have lost one breast because of cancer\textsuperscript{96}.

Invasive ductal carcinoma (NOS) was the commonest histological diagnosis seen (82.8%), this is comparable with other studies locally and internationally\textsuperscript{97-105}.

A common clinical finding that characterizes Nigerian breast cancer patients is late presentation, about eighty percent of those with recorded cancer stage presented late (stage III & IV) in this study. Popoola in his findings, revealed that late stage breast cancer have distant metastatic involvement to sites such as lungs, spine, lymph node and anterior chest wall\textsuperscript{88}. Low awareness about early signs and symptoms of cancer, dearth of cancer specialists and diagnosticians, poor economic status, inadequate policies and poor access to equipment to curtail the breast cancer menace are factors that contribute to the late presentation of patients, while complaints that characterize these presentations include lump, bleeding, lymph node positive status, increasing lump size, and so on at the clinic which were symptoms of late stage and metastatic breast cancer.
In a pathological analysis of the proliferative activity in tumours of 300 Nigerian women, it was noted that mitotic indices were notably higher than the range of values typically reported from the western world, there is possibility of inherently more aggressive tumour biology among African women\textsuperscript{106}. While the goal of breast cancer screening is to detect cancer before symptoms commence, a study in Lagos revealed that self-breast examination which drives this objective home more is majorly practised by educated persons\textsuperscript{107}.

Immunohistochemistry started in 2008 in our centre which gained popularity as the year progressed, out of the 139 cases that recorded immunochemistry findings, the commonest was ER positive (35.6%), PR positive and HER2 positive were 26.4% and 23.3% respectively, this is in consonance with a study done in Ibadan by Adebamowo et al ER positive was the commonest (65.1%) and the least HER+ (20.3%)\textsuperscript{108} also a study in Ghana by Bernard showed similar order as ER, PR and HER2 receptor positivity was 32.1%, 25.6% and 25.5% respectively\textsuperscript{109}. This was used in reclassifying the disease into molecular subtypes, the commonest molecular subtypes was Lumina A (53.2%) followed by Basal Like/triple negative (23.8%). This is consistent with Adebamowo’s study but in contrast to other studies by Bernard (basal like 49.4%)\textsuperscript{109} and Huo in Nigeria and Senegal where majority were basal like (27%)\textsuperscript{110}. Huiyan et al in their study, found ER and PR positive to be significantly higher in Caucasian than in blacks\textsuperscript{111}. Recent research through genomic has considered breast cancer to be heterogeneous, Lumina A subtype has the best survival in the first
five year, while HER2 had the worst\textsuperscript{96}. Breast cancer is regarded as a collection of separate diseases and subtyping is regarded as essential to better identify new molecular prognostic, predictive and/or therapeutic targets, an important step toward tailoring the treatment.

Positivity of lymph nodes (63\%) was seen to be higher than negative nodes involvement (37\%) in this study which is similar to what Popoola found to be have lymph node involvement (87.6\%). Clinical and experimental data suggest that migration of tumour cells into the lymph node is greatly facilitated by lymphangiogenesis. This process is dynamic during embryogenesis but is relatively rare in adulthood. Enhanced lymph node lymphangiogenesis and lymph flow in tumour-draining lymphatic vessels have also been reported to contribute to metastatic spread (Ran et al., 2010)

The mean age at menarche of patients in this study was 14.67±2.16 years, which is similar to mean age (15.06±2.17 years) found by Eniojukan in Ibadan and Anyanwu in Eastern Nigeria found 13.67 years Vorobiof et al found 14.7years in rural black, 13.9years in urban black and 12.6 years in white women in South Africa\textsuperscript{112}. Majority (52\%) of patients in this study attained menarche between 14 and 16 years, which is also similar to a study in India (14 -14.5years)\textsuperscript{113}. Attaining menarche at an early age in life exposes female patients to estrogen hormones, consequently exposes the patients to breast cancer.

The preponderance of menopausal status in this study was seen in the pre-menopausal female patients (81.3\%) which is consistent with Eniojukan in
Ibadan (62.5%)\textsuperscript{85}, Ganiy in his study found that black women both within and outside Africa have a higher incidence of premenopausal breast cancer than Caucasians. For the menopausal patient, the average age of attaining menopause was 55 years\textsuperscript{32}, however, 20\% were menopausal at about average age of 48.86 years which is similar to other studies\textsuperscript{85,114,115}. Late menopausal age increases the chances of developing breast cancer in female patients due to the prolonged estrogen exposure from age at menarche. As a result, longer estrogen window exposes female to higher risk of breast cancer.

Majority of the patient were multiparous this signifies that a large percentage have had either pregnancy or child bearing history\textsuperscript{85}. Godwin in Calabar found 86.1\% of patients in his study to be parous women, this is replicated in this study where about 70\% of the patients were parous with an average age at first pregnancy of 24.26 years who had an average number of children of 3.75 ≈ 4 which range between 1 – 10 who were breastfed for an average of 13.73±5.66 months. These reproductive characteristics are not peculiar to this study as Godwin\textsuperscript{87} also found same characteristics at a different study location in Calabar. Indian women were also seen to bear an average of 3.63 children\textsuperscript{113}. Okobia et al., in another study reported that women who were para 4 and above had a decreased risk for breast cancer. Child bearing and the high number of full term pregnancies have been found to reduce the risk of breast cancer with risk reducing by 30\% for each full term pregnancy compared to nulliparous
women. Studies in Nigeria have also associated high parity or multiparity with decreased risk for breast cancer.

The duration of breast feeding in this study ranged between six months and 2 years with a mean duration of 13.73±5.66 months. Breast feeding for a long duration has been associated with breast cancer risk reductions as great as 40-60%.

Only 7% of the population in this study took alcohol occasionally and less than one percent of the patients smoke, this is valid as smoking is not rampant in Nigerian females, this is similar to a study done by Anyanwu in Eastern Nigeria where non-smokers were the entirety of the population and 15% were social drinkers. Alcohol appears to increase circulating levels of estradiol, Marsha reported that two drinks of ethanol a day elevate serum estrogens and exposure to estrogen increases the risk of breast cancer.

Only 125(11.1%) admitted to have used oral contraceptives, long term use of oral contraceptives is associated with increased risk of premenopausal women however, duration of usage was not captured in this study.

Majority of the patients were obese (40%). Obesity as an associated aetiological factor of breast cancer is being, further bolstered here with similar findings in Ibadan. Obesity had been found to increase risks of breast cancer in postmenopausal women
Hypertension was seen to be the commonest comorbidity (77.3%) followed by the combination of hypertension and diabetes (15.3%) which was similar in Zaria, stroke alongside diabetes was also found by Stariano\textsuperscript{123}.

Out of the 693(60.7%) patients with record of treatment modality, chemotherapy was the commonest lone treatment given (17.7%), followed by surgery (2.7%). Almost three quarter received combination therapy (i.e. more than one form of chemotherapy), where majority 213(30.9%) received a combination of chemotherapy, surgery and radiotherapy followed by chemotherapy and surgery alone (20.4%). 533(76.9%) out of those with treatment modality (693) of the patients received chemotherapy as a form of treatment either as neoadjuvant or adjuvant treatment, three-drug regimen received include FEC (43.4%), CAF (15.7%), CMF (6.9%), the most common two-drug regimen given was AC (Adriamycin and cyclophosphamide). 14.2% had taxane-based drugs, which is administered to patients that presented late or with triple negative or recurrence diseases. Six courses were the commonest which majority completed over five to six months duration. Mastectomy was also the most form of surgery performed which is due to the advanced stage in which the disease is presented, this better explains the reason adjuvant therapy (chemotherapy and radiotherapy) were received more than neoadjuvant therapy.

Adjuvant radiotherapy was the commonest radiotherapy approach following neoadjuvant chemotherapy given to shrink advanced staged tumours.
Spinal cord metastasis, bleeding, pain, fungating breast lesions characterised cases that were treated with palliative radiation majorly in this specifications; 25-30Gy in 10 fractions for a duration of 2 weeks. The mean and standard deviation dosage of radiation given was 40.48 ± 8.69. The type of machine used for treatment at the centre is Linear Accelerator Machine (LINAC) with energy of 6MeV and the technique used was Tangential Fields (medial and lateral) Following our treatment with surgery, chemotherapy and radiotherapy for 693(60.7%) patients, 145(12.7%) were on follow up. Out of this 145 patients on follow up, complete response was 42.2%, partial response 23.5%, disease progression 24.1% and no response 10.2%.

Late presentation that is characterized by the patients in this study warranted the form of management administered. The role of chemotherapy has been found to be significant in the management of breast cancer. Chemotherapy can either be neoadjuvant or adjuvant, in this study, majority of patients were treated with neoadjuvant chemotherapy to downstage the tumour prior to surgery, this correlated well as majority of the patient presented at stage III and IV.
LIMITATIONS

Being a retrospective study, some case notes were incomplete, information were therefore not fully available in all the case notes.

The effect of the prolonged duration of the oral contraceptive usage could not be ascertain in this study as the length of use of this pill could not be captured from the case notes.

Survival rate was difficult to arrive at since most patient were lost to follow up due to their late presentation at the clinic or there default from the clinic.
CONCLUSION

Advocacy should be made for lifestyle pattern that prevents or reduces the risk of breast cancer. Obesity was clearly seen to be a modifiable factor that is associated with the breast cancer patients in this study. Adjusting diets and consistent exercising to contain the body mass index within the normal weight category should be encouraged, adjoining sedentary lifestyle with physical activities and maintaining a work-life balance are opportunities where prevention of obesity can be prevented.

Late presentation at the clinic undoubtedly has enormous impact on breast cancer management and outlook. Therefore patients should be encouraged to present early through public education and screening clinician is left with no other choice than to administer treatment to cushion the adverse effects of the advanced cancer.

Breast cancer being the most prevalent malignancy and cause of death globally and in Nigeria, calls for systematic and political approach. Thorough accurate data gathering and data management across the country will give a broad view of necessary ways of combating this menace with the establishment of Cancer Registries. Treatment facilities should be adequately provided with training of personnel.
RECOMMENDATION

1. Sensitisation of the public on the modifiable factors (preventive strategy) that could be adjusted to reduce the risk of breast cancer which includes maintenance of healthy lifestyle, dietary and weight management as most patients seen in this study were obese.

2. Aim to reduce incidence of late presentation through
   - Health literacy and improved government policy and infrastructure which should be polished to sensitize and drive the reduction of morbidity rate and incidence rate of breast cancer in Nigeria as seen in the developed world.
   - Cancer screening such as
     - Self-breast examination
     - Mammographic screening especially for subjects at high risk to develop breast cancer,
     - Genetic profile especially for subjects with family history of breast cancer
     - Extend the coverage of cancer care in the National Health Insurance Scheme

3. Improve management of breast cancer to reduce morbidity and mortality
   - Increase diagnostic facilities such as immunohistochemistry
   - Training of more oncology experts
   - Increase the number of effective cancer chemotherapy, radiotherapy and surgical oncology facilities
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WHO histological classification of tumours of the breast

<table>
<thead>
<tr>
<th>WHO Classification of Breast Tumours</th>
</tr>
</thead>
</table>

### Epithelial tumours

- Intraductal carcinoma, not otherwise specified
- Mucinous carcinoma
- Tubular carcinoma
- Lobular carcinoma
- Medullary carcinoma
- Mucinous (colloid) carcinoma
- Invasive micropapillary carcinoma
- Mucinous (mucoid) carcinoma
- Infiltrating ductal carcinoma
- Phyllodes tumours

### Adenocarcinoma

- Adenocarcinoma
- Infiltrating ductal carcinoma
- Tubular carcinoma
- Medullary carcinoma
- Mucinous (colloid) carcinoma
- Invasive micropapillary carcinoma
- Mucinous (mucoid) carcinoma
- Infiltrating ductal carcinoma

### Mixed tumours

- Solid tumours with prominent myoepithelial component
- Pleomorphic adenoma
- Myoepithelial adenoma
- Myoepithelial carcinoma
- Myoepithelial carcinoma

### Neuroendocrine tumours

- Solid tumours with prominent neuroendocrine component
- Neuroendocrine carcinoma
- Small cell carcinoma
- Large cell carcinoma

### Inflammatory carcinoma

- Inflammatory carcinoma
- Infiltrating ductal carcinoma
- Medullary carcinoma
- Adenoid cystic carcinoma
- Intraductal papillomatosis
- Invasive papillomatosis

### Other tumours

- leiomyosarcoma
- Angiosarcoma
- Ewing sarcoma
- Rhabdomyosarcoma
- Lymphoma
- Leukaemia

### Staging and grading

- T staging
- N staging
- M staging
- TNM classification

### Metastatic tumours

- Metastatic carcinoma
- Metastatic sarcoma
- Metastatic melanoma

### Intraepithelial lesions

- Intraepithelial neoplasia
- Intraepithelial carcinoma
- Intraductal papillomatosis

### References


[3] for metastatic tumours, and/or for benign or uncertain behaviour.
APPENDIX B

AJCC TNM STAGING CLASSIFICATION OF BREAST CANCER

There are five tumour classification values (Tis, Ti, T2, T3 or T4) which depend on the presence or absence of invasive cancer, the dimensions of the invasive cancer and the presence of invasion outside of the breast (e.g. to the skin of the breast, to the muscle or to the rib cage underneath)

T- Primary Tumour

TX - Primary tumour cannot be assessed.

T0 - No evidence of primary tumour found.

Tis Carcinoma in situ: intraductal carcinoma, or lobular carcinoma in situ, or Paget disease of the nipple with no tumour (Note: Paget disease associated with a tumour is classified according to the size of the tumour.)

T1 Tumour < 2 cm in greatest dimension

T1a < 0.5 cm in greatest dimension

T1b 0.5 cm but < 1 cm in greatest dimension

T1c > 1 cm but not > 2 cm in greatest dimension

T2 Tumour > 2 cm but not > 5 cm in greatest dimension

T3 Tumour > 5 cm in greatest dimension

T4 Tumour of any size with direct extension to chest wall or skin

T4a Extension to chest wall

T4b Edema (including peau d'orange), or ulceration of the skin of the breast, or satellite skin nodules confined to the same breast
T4c Findings of both 4a and 4b

T4d Inflammatory carcinoma

N Lymph node

NX Regional lymph nodes cannot be assessed.

N0 No regional lymph node metastasis

N1 Metastasis to movable ipsilateral axillary node(s)

N2 Metastasis to ipsilateral axillary node(s) fixed to one another or to other structures

N3 Metastasis to ipsilateral internal mammary lymph node(s)

MX Presence of distant metastasis cannot be assessed.

M0 No distant metastases are found.

M1 Distant metastases are present.
APPENDIX C

MANCHESTER STAGING/CLASSIFICATION

Stage I  Tumour confined to the breast and it is not attached to the underlying muscle, skin attachment or ulceration if present must be in continuity with the tumour and not beyond it. There is no axillary node involvement.

Stage II  As in stage I, but axillary lymph nodes are involved but mobile.

Stage III  i. Skin involvement is beyond the periphery of the tumour or
           ii. Tumour is attached to underlying muscle, or
           iii. Axillary lymph nodes are mobile or fixed. There are no distant metastasis.

Stage IV  i. Lymphatic spread beyond the ipsilateral axilla or
           ii. Distant blood borne metastasis are present.
APPENDIX D (Data Extraction Form)

S/No.................. Hospital No......................

SECTION A: SOCIO-DEMOGRAPHIC DATA

Name (Initials only) .........................

Age(at presentation) ..............

Sex 1. Male....... 2. Female......

4.Others......


Address ........................................................................

Section B: OBSTERIC HISTORY

1. Age at menarche:.........................
2. Menopausal status:.........................
3. Age at menopause: ....................... 
4. Parity:.........................
5. Age at first pregnancy:..............
6. Family history of breast cancer: A. Yes B. No
7. Site of disease: A. Left B. Right C. Bilateral
8. Alcohol intake. A. Yes B. No
9. Smoking: A. Yes B. No
10. Use of Oral contraceptives: A. Yes B. No
11. Any History of benign tumour: A. Yes B. No

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12. Obesity:  A. Yes  B. No

13. Any other co-morbid factors or diseases:  A. Yes  B. No  If yes specify……………..

14. Recurrence of breast cancer after treatment:  A. Yes  B. No

If yes what is the duration from treatment to recurrence (Months):………..

SECTION B:  DISEASE CHARACTERISTICS

1. Histological Diagnosis…………………………………………

2. Molecular subtype:

……………………………………………………………………

3. Investigation done:

……………………………………………………………………

4. Presenting Complaints:

……………………………………………………………..

……………………………………………………………………

5. Constitutional Symptoms:  …………………

6. Stage of disease:  I  II  III  IV

SECTION C:  TREATMENT OFFERED

1. Surgery (Yes/No)  If yes please specify:  …………………

A. Conservative  B. Radical surgery

2. Chemotherapy (Yes/No)  if yes A. Neoadjuvant  B. Adjuvant

a. Regimen used………………………………...
b. Number of cycles had………………

3. Radiotherapy (Yes/No) If yes state: 1. Neoadjuvant …… 2. Adjuvant ……
   1. Dose of Radiation………

2. Number of Fractions… ……………

3. Duration of Treatment ………………..

b. Intent of Radiotherapy 1. Radical……………2. Palliative……………………

SECTION D: TREATMENT OUTCOME AND FOLLOW-UP

Patient is I. Lost to follow up II. Dead III. On follow-up

If on follow up, state outcome: a. Complete response………b. Partial response……

c. No response………………… d. Disease recurrence…………………

SECTION E: TREATMENT COMPLICATIONS

1. Type/name of complication: ………………………………………

2. Time of onset of complication: a. during treatment b. <6 weeks after completion of treatment c. >6weeks after completion of treatment