A Review: Breast Cancer, a Global Threat to Women

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Abstract: Breast cancer is the most usual female cancer, the second most common cause of cancer death in women. Over a million new cases of breast cancer are diagnosed every year. Both mortality and burden are high. It has become a major health issue in the world over the past 50 years, and its incidence has increased in recent years. Early detection is an efficacious way to diagnose and manage breast cancer. Investigators have analyzed numerous diagnostic approaches for breast cancer, including mammography, magnetic resonance imaging, ultrasound and biopsy. However, these techniques have some drawback such as being expensive, time consuming and not suitable for young women. Family record is an important risk factor for breast cancer occurrence. Presently, people have various drug choices for the chemoprevention of breast cancer, while biological prevention has been recently developed to enhance patients’ quality of life. In this review, we will summarize epidemiology, pathogenesis, risk factors, diagnosis, treatment and preventative methods on breast cancer.

Keywords: Breast Cancer, Mammography, Breast Cancer Surgery, Breast Cancer Chemotherapy, Oncology.

1. INTRODUCTION
Cancer is a group of diseases causing uncontrolled growth and proliferation of cells[1, 4, 27]. There are over 200 different types of cancer that affect mankind [4]. Most of all types of cancer cells eventually form a lump or mass called as tumor [1, 27]. Tumors originate from normal cells due to accumulated genetic and epigenetic alterations, but the identity of the tumor-initiating cells is unknown. Stem cells are the attractive targets since they share many characteristics with cancer cells, including the capacity to self-renew, produce heterogeneous progeny, migrate and invade into surrounding tissues [5]. The tumor growths often invade surrounding tissues and can metastasize to distant sites of the body [4, 27, 34]. Breast cancer begins within the breast tissue that contains glands for milk production, called as lobules, and they also have ducts that connect the lobules to the nipple [1, 27]. Breast cancer is the second leading cause of cancer-related death in women across worldwide, after lung cancer [9, 29]. The breast cancer is the most frequently diagnosed cancer type in females in the world [2, 11, 14, 28]. Breast cancer typically is detected either during a screening process, before symptoms have developed, or after symptoms have developed, when a woman feels a lump [1]. Breast cancer can also progress into a metastatic disease, where axillary nodes are the most common sites, but distant metastases can also occur, where major locations include bone and bone marrow [2]. The breast cancer is not a single disease but is highly heterogeneous at molecular, clinical and genetical level [6, 17, 35, 38]. Male breast cancer (MBC) is very rare type of breast cancer with the peak age of onset at 71 years [3]. The most common type of breast cancer is a carcinoma that originates in epithelial cells. Noncarcinomatous breast cancers are rare and originate in the connective tissues of the breast [1]. Male breast cancer is a relatively rare disease in the western world accounting for less than 1% of all breast cancers [3, 25].

2. EPIDEMIOLOGY

Fig 1: Labelled diagram of female mammary gland with tumor cells
Breast cancer is one of the more complicated type of cancer due to being multifactorial in an epidemiologic view. There was about 14.9 million cases across the world in 2012. It is predicted that it will reach up to 22 million new cases in next two decades. One of the most common carcinoma is breast cancer and it has very high incidence rate in all countries. It includes 1.7 million new cases per year and 25% of all types of cancers[9]. It is the leading cause of cancer deaths among females in India [11]. It was estimated that there was around 1, 671,149 new cases of breast cancer in the world in 2012[9, 11]. Among the breast cancer cases, 882.9(per 100,000) were attributed to developing underdeveloped countries, while 793.7(per 100,000) of them were attributed to developed countries. It was estimated that 521,907 cases of deaths was mainly due to breast cancer in the world in 2012 [9]. Breast carcinoma has ranked as the leading cancer among Indian women with the rate of 25.8 per100,000 women and mortality 12.7 per 100,000 women. Earlier cervical cancer was considered most common cancer in Indian woman but now the incidence of breast cancer has surpassed cervical cancer, although cervical cancer still remains as the most common cancer in rural India[11]. Out of the 150 patients with breast cancer (cases), and 100 apparently healthy individuals (controls); 38 (25.3%) and 38(38%) were identified as having a previous history of oral contraceptives usage, respectively [7]. Out of the 150 cases and 100 controls, 22 (14.7%) and 14(14%) were found with a family history of breast cancer (First degree mother side), as well as, 20 (13.3%) were found to have a previous history of breast cancer, respectively[7]. In India women incidence rate of breast carcinoma was 41 per 100,000 women for Delhi, followed by Chennai (37.9), Bangalore (34.4) and Thiruvananthapuram District (33.7)[11]. The incidence of breast cancer is lower among Africanwomen than their European counterparts [12]. Breast canceris responsible for over one million of the estimated 10 million neoplasms diagnosed worldwide each year in both sexes[10]. Having a mother affected withbreastcarcinoma is found to increase the risk of male breastcarcinoma to 2.33-fold, and having an affected sister is foundto increase the risk of breast carcinoma in males to 2.23-fold. In 15–20% of overall male breast carcinoma cases there is a positive familyhistory. [3, 14]The risk of breast cancer increase with the decreased number of children or with nulliparity[7, 8, 9]. Increasing urbanization and westernization associated with changing lifestyle and food habits has lead breast cancer to attain top position in all major urban regions [11].

3. ETIOLOGY
The etiology of human breast carcinoma is essentially unknown [6, 18]. Family history is one of the strongest determinants of breast cancer, implying hereditary factors [6, 28].

3.1. Family history: Women (as well as men) having a family history of breastcancer, especially in a first-degree relative (mother, sister, daughter), are at high risk of developing breast cancer; this risk is higher if more than one first-degree relative developed breast cancer[1, 3, 7, 13, 14, 17, 22, 29].

3.2. Genetics: Women with mutations in either BRCA1 or BRCA2 genes (breast cancer gene) are at significantly elevated lifetime risk (55–85%) compared with 12% for the general population) for developing breast cancer [1, 18, 28, 29, 34]. The tumor suppressor gene p53 is recognized as the most commonly mutated gene in human cancers[18, 28]. The HER-2/neu(c-erbB-2) proto-oncogene (human epidermal growth factor receptor-2/neu (erythroblastic oncogene B)) is a member of the epidermal growth factor receptor family and overexpression of this gene has been detected in 10–40% of human breast tumors [18, 34]. More rarely, men are found to have BRCA1 and BRCA2 mutations, usually the latter. A male BRCA2 carrier has a 6% lifetime risk of developing the disease, compared with 0.1% in the normal population [3].

3.3. Age and Gender: Breast cancer is most common in females compared to males [29, 21, 3]. Onset of this disease in females is at age greater than 50 years [29]. Men with breast cancer have an average age of diagnosis at 71 years, approximately ten years older than in women [3].

3.4. Hormones: Postmenopausal women with high levels of endogenous hormones like estrogen produced naturally in the body, have about twice the risk of developing breast cancer compared to women with the lowest levels[1, 10, 21, 22, 28]. Use of oral contraceptives may increase the risk of breastcancer [1, 7, 8, 10, 29].

3.5. Menstrual cycle: Women who have had more menstrual cycles because they startedmenstruating before the age of 12 and/or went through menopause after age 55 have a slightly higher risk of developing breast cancer[1, 7, 8, 10, 11, 19, 22, 29]. Early menarche was more consistently associated with ER-positive/PR-positive than ER-negative/PR-negative tumors (ER-estrogen receptor and PR-progesterone receptor) [20].

3.6. Reproductive factors and Nursing: Women who have never had children or who start their families late also have a higher lifetime exposure to estrogens [7, 1, 28, 29, 8, 10, 13]. The risk of breast cancer increase with the decreased number of children[7, 29]. An increase in the gestation time period was associated with the risk of breast cancer [15]. The possibility that long-term nursing provides a protective effect against carcinomaof breast has long been considered [13, 1, 10].

3.7. Diet and Lifestyle factor: a high-fat diet during adolescence was associated with a moderate increase in premenopausal breast cancer risk [1, 16, 18, 10, 13, 28, 29]. Obesity increases the risk of postmenopausal breast cancer[1, 8, 16, 10, 28, 29]. Women who get regular physical activityhave lower risk of breast cancer compared to women who are inactive, for postmenopausal than premenopausal women [1]. Alcohol consumption increases the risk of breast cancer in women[1, 10, 18, 28, 29]. Tobacco smoking causes breast cancer in women[1, 18, 28]. Breast cancer increases in women with higher socioeconomic lifestyle[10, 29].

4. CLINICAL MANIFESTATION
Breast lump is the first and most common presenting symptom among women with breast cancer [1, 23, 24, 25, 27, 28, 30, 34]. Classification was made based on presentation of individual symptoms into three main symptom categories: (a) breast lump, (b) non-lump breast like symptoms (involves breast pain, abnormal breast skin or shape and nipple abnormalities), and (c) non-breast like symptoms (involves fatigue, breathing difficulty, axillary symptoms, neck lump, and back pain)[23]. The most commonly reporting symptoms after breast lump were nipple abnormalities, breast pain, and breast skin abnormalities. The classic symptom for carcinoma of breast is a lump that is found in the breast or armpit [1, 25, 27, 28]. Pain of breast was found to be significantly related to the woman’s accommodation to stress, total mood disturbance score, use of analgesics, and beliefs about the meaning of
the pain [26]. The signs of breast cancer includes change in the size, contour, texture, or temperature of the breast. A reddish, pitted surface like an orange-coloured skin could be a sign of an advanced breast cancer. A change in the nipple, such as a nipple retraction, dimpling, itching, a burning sensation, or ulceration was also encountered[27, 1, 25]. Inflammatory breast cancer is a type of breast cancer that usually presents with itching, pain, swelling, nipple inversion, warmth and redness throughout the breast, as well as an orange-peel texture to the skin that is referred to as peau d’orange[1, 28]. Paget’s disease of the breast is another type of breast cancer that usually presents with redness, discoloration, or mild flaking of the nipple skin. Then there will be appearance of tingling, itching, increased sensitivity, burning pain and discharge from the nipple[1, 28]. Common sites of metastasis of breast cancer include bone, liver, lung and brain. Symptoms that mainly depends on the site of metastasis and include unexplained weight loss, fever, chills, pain in the bones, jaundice or neurological symptoms[1,28]. Most of the women with breast cancer presents a painless lump that is typically solitary, unilateral, soft, hard, irregular, and nonmobile[39, 29, 34]. Other most common symptoms of breast cancer include:

- Swelling of all or part of a breast
- Skin irritation or dimpling
- Breast or nipple pain
- Nipple retraction (turning inward)
- Redness, scale formation, or thickening of the nipple or breast skin
- Nipple discharge (discharge other than breast milk)[1, 30, 34, 27, 28].

5. RISK FACTORS

Well known breast cancer risk factors such as sex, age, family history, early menarche, and late menopause, are fixed, that is they cannot be changed. However, other factors related with increased breast cancer risk, including postmenopausal obesity, use of combined estrogen and progesterin menopausal hormones, cigarette smoking, and alcohol consumption are modifiable. Many risk factors affect lifetime exposure of breast tissue to hormones (early menarche, late menopause, obesity, and hormone use). Treatment with tamoxifen or raloxifene can also reduce the risk of breast cancer among women at high risk[1].

Some identified risk factors for breast cancer include[43]:

5.1. Family history: Family history is the most important breast cancer risk factor[1,40,41,42,43,44]. 5% to 10% of breast cancer cases result from inherited mutations, including those in the breast cancer susceptibility genes BRCA1 and BRCA2 [42,46,47,50]. Women, whose mother or sister has a breast cancer, are prone to this disease [47]. A woman’s risk of breast cancer is two or more times greater if she has a first degree relative (mother, sister, or daughter) who developed the disease before the age of 50, and the younger the relative when she developed breast cancer the greater the risk [1,46,47,50].

5.2. Age: Apart from sex, age is one of the chief risk factors of breast cancer. Since the incidence of breast cancer is highly related to the increasing age[46,47,42,50]. Some of the excess risk of subsequent breast cancers, particularly among women diagnosed at a young age[1]. Women who had more menstrual cycles because they started menstruating before the age of 12 and/or went through menopause after age 55 have a slightly higher risk of developing breast cancer. [1,46]Nulliparity and late age at first birth both increase the lifetime incidence of breast cancer[46]. The risk is higher if the diagnosis was at a younger age. Women diagnosed with early onset breast cancer (age <40) have almost a 4.5-fold increased risk of subsequent breast cancer[1].

5.3. Diet: Premenopausal women who are overweight actually have a lower risk of developing breast cancer.[50] Too much dietary fat intake can increase the risk of breast cancer,[47]high-fat diet during adolescence was associated with a moderate increase in premenopausal breast cancer risk.[1,47]. Obesity is associated with a twofold increase in the risk of breast cancer in postmenopausal women whereas among premenopausal women it is associated with a reduced incidence[46]. Modern western diet contains too much fat and excess intake of fat, especially the saturated fat, is associated with mortality[47].

5.4. Alcohol and cigarette smoking: The risk of breast cancer is also elevated in women who both smoke and drink[47]. Tobacco smoking appears to increase the risk of breast cancer[28]. Risk may be greater for women who begin smoking before first childbirth[1,50]. Over 80 different cancer-causing substances (carcinogenic agents) are present in tobacco.[43]Smoking is thus an important risk factor for breast, lungs and other kinds of cancer[43]. smoking, particularly at young ages, with breast carcinogenesis, which include the induction of mammary cancers[45,47]. Alcohol can increase the risk of breast cancer[42,43,45]. including mouth, throat, pharyngeal cancer, laryngeal, cancer of the foodpipe, liver, and bowel cancer (in men) [43]. Even moderate alcohol intake increases the risk of cancer[43,45]. Risk increases about 7% for each alcoholic drink consumed. This increased risk may be related to alcohol’s effect on estrogen; estrogen levels are higher in women who consume alcohol[50].

5.5. Oral contraceptives: The risk of oral contraceptive usage appeared to be clearly establishedshowing a small increased risk of breast cancer with long-term usage of oral contraceptives,especially at a young age[42]. Women who begin use before the age of 20 appear to have a higher relative risk than women who begin oral contraceptive use at an older age. [46]oral contraceptives do not increase the risk of breast cancer in women who stop to use them for more than 10 years[1,47]. Recent use of oral contraceptives may increase the risk of breast cancer by about 10% to 30%. [1]

5.6. Radiation: The link between radiation exposure and breast cancer has been demonstrated in studies of atomic bomb survivors and women who have received high-dose radiation therapy to the chest, particularly for those who were first exposed at younger ages [1]. A doubling of risk of breast cancer was observed among teenage girls exposed to radiation during the Second World War. Ionising radiation also increases risk later in life,particularly when exposure is during rapid breast formation[46].

6. CLASSIFICATION
Most of the breast cancers are derived from the epithelial lining of the ducts or lobules of the breast tissue, and these carcinomas are classified as ductal or lobular carcinoma[28]. However, breast cancer can be broadly categorized into in situ carcinoma and invasive (infiltrating) carcinoma[35].

6.1. Ductal carcinoma in situ:
Ductal carcinoma in situ (DCIS) is also known as intraductal carcinoma. It is considered noninvasive or pre-invasive type of breast cancer [34]. DCIS means that cells that lined the ducts have changed to look like cancer cells [1, 34]. DCIS is defined as a proliferation of malignant epithelial within the breast parenchymal structures with no evidence of invasion across the basement membrane[36].

6.2. Lobular carcinoma in situ:
This is not a true cancer or pre-cancer[1, 34]. A risk factor is anything that affects your chance of getting a disease, such as cancer [34]. Carcinoma in situ is growth of precancerous cells within a particular part of the breast without invasion of the surrounding tissue[28].

6.3. Invasive (or infiltrating) ductal carcinoma:
This is the most common kind of breast carcinoma. Invasive (or infiltrating) ductal carcinoma (IDC) originates in a milk duct of the breast tissue, then breaks through[34].

6.4. Invasive (or infiltrating) lobular carcinoma:
Invasive lobular carcinoma (ILC) starts in the milk-producing glands (lobules) of the breast. Like IDC, it has ability to spread (metastasize) to other parts of the body [34].

Less common types of breast cancer includes:

6.5. Inflammatory carcinoma: It is a very aggressive type of breast cancer with different clinical and pathological criteria. Clinical symptoms include rapid breast enlargement, and skin changes (redness, edema, peau d’ orange) involving more than a third of the breast [33].

6.6. Triple-negative breast cancer: This is a type of breast cancers (usually invasive ductal carcinomas) in which, cells lack estrogen receptors and progesterone receptors, and do not have an excess of the HER2 protein on their surfaces [34].

6.7. Paget disease of the nipple: This type of breast cancer starts in the breast ducts and spreads to the skin of the breast and then gradually to the areola, the dark circle around the nipple [34].

Molecular subtypes of breast cancer includes following:

6.8. Luminal A: About 40% of breast cancers are luminal A, making it the most common breast cancer subtype[1]. These type of tumors tend to be ER+ and/or PR+ and HER2-, slow-growing, and less aggressive than other subtypes of breast cancer[1, 37].

6.9. Luminal B: About 10% to 20% of breast carcinomas are luminal B. Like luminal A tumors, most of the luminal B tumors are ER+ and/or PR+, but they are distinguished by either expression of HER2 or by increased proliferation rates (more numbers of cancer cells are actively dividing)[1].

6.10. Basal-like: About 10% to 20% of breast cancers are basal-like, and the majority of basal-like carcinoma of breast are referred to as “triple negative” because they are ER-, PR-, andHER2[1, 37].

6.11. HER2 enriched: About 10% of breast cancers produce excess HER2 (a growth promoting protein) and do not express hormone receptors[1]. Breast cancer cases that were ER-negative, PR-negative, and HER2-positive were classified as HER2 type [37].

The tumor-node-metastasis (TNM) system was first developed by Pierre Denoix in 1942[31, 32]. It represents an attempt to classify cancer based on the major morphological attributes of malignant tumors that were thought to influence disease prognosis: size of the primary tumors (T), the presence and extent of regional lymph node involvement (N), and the presence of distant metastases of tumors (M)[31, 32, 39].

TNM stages of breast cancer:
- Early Breast Cancer
- Locally Advanced Breast Cancer
- Advanced or Metastatic Breast Cancer

Stage 0: Carcinoma in situ or disease that has not invaded the basement membrane of the breast tissue.
Stage I: The small primary tumors without lymph node involvement.
Stage II: Involvement of the regional lymph nodes.
Stage III: Usually a large tumor with extensive nodal involvement in which node or tumor is found fixed to the chest wall; also includes inflammatory breast carcinoma, which is rapidly progressive in nature.
Stage IV: Metastases in organs distant from the primary tumor[39].

7. PATHOPHYSIOLOGY
Breast cancer, Compareable cancers, happens as of an interaction linking an environmental factor and a genetically susceptible host [1,28]. Human carcinomas most likely arise from undifferentiated epithelial stem cells as a sequence of a series of two or more errors in normal cell division[22]. Breast cancer frequently move from an E2-dependent (E2-estriadiol), nonmetastatic, anti-estrogen-sensitive phenotype to an E2-independent, anti-estrogen-resistant, highly invasive and metastatic phenotype [48]. In isolation from the ERE-dependent pathway, ERs also have the capability of transcription regulation without the involvement of EREs (ERE-estrogen receptor element). In ER-mediated transcription regulatory process, numerous co-activators and co-repressors, as well as BRCA183 play important roles. BRCA1 acts as a tumor suppressor partially by inhibiting ERα signaling [49]. Human
Epidermal growth factor receptors (EGFRs, or HERs) are capable of affecting many cellular functions through various pathways. These signaling pathways are steadily correlated with breast tumorigenesis. HER2 signaling amplification arise in HER2 protein repression which is associated with tumor cell proliferation and cancer progression. [49] Normal cells will carryout cell suicide (apoptosis) when they are no longer needed. Meanwhile, they are protected from cell suicide by several protein clusters and pathways [1]. One of the protective pathways is the PI3K/AKT pathway; another is the RAS/MEK/ERK pathway [1,28]. Abnormal growth factor signaling in the interaction linking stromal cells and epithelial cells can facilitate malignant cell growth [1,28]. In breast adipose tissue, over expression of leptin leads to increased cell proliferation and cancer [1]. A few mutations are related with cancer, such as p53, BRCA1 and BRCA2, occur in mechanisms to correct errors in DNA [1,28]. These mutations are either inherited or acquired after birth. This implicates environmental and other causes as triggers for breast cancers [1]. The inherited mutation in BRCA1 or BRCA2 genes can disrupt with renovation of DNA cross links and DNA double strand breaks [1, 28]. These carcinogens cause DNA damage such as DNA cross links and double strand breaks that often require repairs by pathways containing BRCA1 and BRCA2. Mutations in BRCA genes account for only 2 to 3 percent of all breast cancers [1]. GATA-3 directly controls the expression of Estrogen Receptor (ER) and other genes held by epithelial differentiation, and the dropping of GATA-3 leads to loss of differentiation and poor prognosis due to cancer cell invasion and metastasis [1,28].

8. DIAGONOSIS
Breast cancer sometimes start after symptoms appear, yet many women with early breast cancer possess no symptoms. This is why getting the recommended screening tests before any symptoms develop is so important [34]. Diagnosis of breast cancer is carried out by triple assessment which includes clinical evaluation, breast imaging and diagnosis of tissue (cytological or histological assessment) [3, 53]. Breast cancer is generally diagnosed through either screening or a symptom (e.g., pain or a palpable mass) that prompts a diagnostic exam [56]. Investigators have studied many diagnostic methods for diagnosing early-stage breast cancer, including Mammography, Magnetic resonance imaging, Ultrasonography and biopsy [28, 52].

8.1. Breast examination: During the breast examination, the doctor will carefully sense the lump and the tissue around it. Breast cancer normally feels different (in size, texture and movement) than benign lumps [28, 34].

8.2. Mammography: Mammographic screening is suitable for asymptomatic women [29]. A mammogram is an X-ray picture of the breast [51, 54, 34]. American Cancer Society (ACS) and the National Cancer Institute recommend screening mammograms every year for asymptomatic women 40 years and older [29, 56, 55, 52]. The sensitivity of mammography is related to the age, ethnicity, personal history, radiologist’s experience, and technique quality [52]. The wrong-positive and wrong-negative rates of mammography are comparatively high, especially for patients with dense breasts (such as subjects under 40 years old) [52, 54]. Currently, there are two types of mammography:

8.2.1. Film mammography: In film mammography, the image is created directly on film [51].

8.2.2. Digital mammography: Electronic image of the breast is taken by digital mammography and stored directly in a computer [51, 29]. Although both types of mammography have their advantages and dis-advantages, digital mammography has some potential advantages over film mammography [51].

8.3. Ultrasonography: Ultrasonographic screening is useful to distinguish between solid and cystic breast masses when a palpable mass is not well seen on a mammogram [34, 29]. Ultrasonography of breast has been recommended as a supplement to mammography in concern with high breast cancer risk, pregnant women and those who cannot to have mammography [52].

8.4. Magnetic Resonance Imaging [MRI]: MRI is a powerful imaging tool that produces high-resolution images. [54] MRI is less specific but more sensitive to detect small tumors in subjects with high breast cancer risk when compared to mammography and ultrasound [52].

8.5. Biopsy: The only decisive method for diagnosing breast cancer is with a breast biopsy. There are various different types of breast biopsies [54],

- Fine Needle Aspiration (FNA) [55, 54, 50, 29].
- Core Needle Biopsy (CNB) [28, 29, 54, 50, 55].
- Stereotactic Core Needle Biopsy.
- Vacuum-Assisted Core Biopsy.
- Surgical (Open) Biopsy [50].

9. TREATMENT
The kind of treatment recommended will depend on the dimensions and site of the tumor within the breast, the results of lab tests done on the cancer cells, and the stage or extent of the disease. Breast cancer treatments are local or systemic. Local treatments are used to remove, eliminate or control the cancer cells in a specific area. Surgery and radiation treatment are local treatments. In most cases, surgery is the first course of action, with additional treatment decisions made based on surgical findings, including extent of disease. Systemic treatments are used to demolish or manage cancer cells everywhere in the body. Chemotherapy and hormone therapy are systemic treatments. A patient may have just one form of treatment or a combination, depending on their needs [34].

The leading types of treatment for breast cancer are:

9.1. Local Treatment
9.1.1. Surgery: The primary means of local and regional breast cancer treatment remains surgical intervention [56]. Surgery is often needed to remove a breast tumor [34].
Breast Conserving Surgery (Lumpectomy): Tumor is removed as well as a small amount of normal tissue around it[50, 43, 34, 56, 28].

Mastectomy: Surgical removal of the entire breast is called mastectomy[28, 50, 56, 34, 43]. Surgery in addition is used to check the lymph nodes under the arm for cancer spread. Alternatives for this include a sentinel lymph node biopsy and an axillary (armpit) lymph node dissection[57, 34, 28].

9.1.2. Radiation Therapy: Radiation therapy involves high-energy rays or particles that destroy cancer cells[28, 34]. Radiation to the breast is often given after breast-conserving surgery to help lower the chance that the cancer will come back in the breast cancer or nearby lymph nodes[34, 3, 57, 28]. Radiation is commonly used to treat painful bone metastases or other localized sites of disease including brain and spinal cord lesions[39, 34]. Postmastectomy radiotherapy reduces the incidence of local and regional recurrences by 50 to 75 percent, but in most randomized trials, and according to a meta-analysis, this reduction was not accompanied by increased survival[55].

9.2. Systemic Therapy
Systemic therapy is treatment that moves throughout the bloodstream and affects all parts of the body, not just the cancer. These cancer drugs are given intravenously or orally. Systemic therapy comprise of chemotherapy, hormone therapy, and targeted therapy, all of which work through unlike mechanisms [1, 28, 39,55].

9.2.1. Chemotherapy: Chemotherapy is usually administered after surgery in women with operable breast cancer. But, for women with large operable tumors, preoperative chemotherapy may have some benefits[55, 28]. The most common chemo drugs used for early breast cancer include the anthracyclines (such as doxorubicin/Adriamycin and epirubicin/Elleance) and the taxanes (such as paclitaxel/Taxol and docetaxel/taxotere)[34]. Chemotherapy is most effective when the full dose and cycle of drugs are completed in a timely manner[1].

9.2.2. Hormonal Therapy: Hormone, a hormone produced by the ovaries, promotes the growth of many breast cancers. Tamoxifen and toremifene (Fareston) are drugs that prevent estrogen from binding to breast cancer cells and are effective in both postmenopausal and premenopausal women[1,50].

Selective Estrogen Receptor Modulators (SERMs): Selectively inhibit or stimulate estrogen receptors on different targets[50]. Toremifene has similar efficacy and tolerability as tamoxifen and is an alternative to tamoxifen in postmenopausal patients[34, 39,50].

Aromatase Inhibitors (AI’s): AI’s take a different approach to hormone therapy; they prevent postmenopausal women from producing estrogen rather than blocking its activity. AIs hinder the enzyme aromatase, which catalyzes the last step in the synthesis of estrogen from its steroid precursors [50, 1].

9.2.3. Targeted Therapy: Targeted therapies target mutations unique to neoplastic cells, killing only the malignant cells and causing little or no damage to normal tissue, thus, less toxicity results. Targeted agents used frequently in breast cancer are the particular agents that block the overexpression of HER2[50]. Approximately 15% to 20% of breast cancers overproduce the growth-promoting protein HER2. Tumors overproducing HER2 are more likely to recur compared to those that do not overproduce the protein[1]. Trastuzumab (Herceptin), a monoclonal antibody that directly targets the HER2 protein and has been considered a gene based approach to minimizing the effects of HER2[1, 34, 50].

9.2.4. Immunotherapy: The immune system can fight many types of tumors including breast cancer. A new clinical trial is designed to use oncofetal antigen (OFA) to enrol the patient’s own immune system to target and attack the cancer cells to improve patient survival and standard of life [28].

10. CONCLUSION
In the past years, there has been marked increase in understanding the Breast Cancer. Early detection of breast cancer can play a significant role in reducing its incidence and burden. Breast cancer mortality can be reduced if cases were detected and treated early. Constant mammograms and breast examinations nevertheless do not prevent cancer, but these screening tests enables it’s early detection; when treatment is most likely to be effective. Both frequent and high consumption of alcohol should be stopped or significantly reduced. Increased consumption of fatty foods and red-meat should be replaced with increase intake of fruits, vegetables and fish. We can control our exposures to ionizing radiation from work place and gadgets such as phones and laptops. Treatment regimen should consist of combination therapy to achieve high cure rate and reduce the risk of recurrence.

REFERENCES


[34] https://www.cancer.org/cancer/breast.html


