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Breast Cancer in India: Etiology, Diagnosis and Therapy

Ashok Kumar Peepliwal[1]* and Prasad Tandale[2]

[1]Clinical Trial Management Department, Lambda Therapeutic Research Ltd., Navi Mumbai-400 614, Maharashtra, India
[2]Pharmacovigilence Department, Reliance Life Sciences, Navi Mumbai-400 701, Navi Mumbai, Maharashtra, India.

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***For Correspondence**

Clinical Trial Management Department, Lambda Therapeutic Research Ltd., Navi Mumbai-400 614, Maharashtra, India

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ABSTRACT

Breast cancer accounts for more than 20% Indian women in India. The mortality is still higher than the cervix cancer even though the descriptive etiology, early diagnosis tools and best therapies are available for the breast cancer. As for as Indian women concerns, most of them are not aware about the myths and facts of hidden anatomy of breast, cause, diagnosis followed by the treatment required to cure the evil disease i.e. breast cancer. This review mainly focuses on etiology of breast cancer, types of breast cancers i.e. Ductal carcinoma in situ (DCIS), Invasive ductal carcinoma, Lobular carcinoma in situ (LCIC), Invasive lobular carcinoma, Inflammatory breast disease, various diagnostic tools used to characterize the type of diseases, various methods to detect the stages of cancers, advanced imaging techniques (Ultrasound, MRI,CT Scan, PET Scan etc.) and other biopsy tests required to assess the breast cancer followed by the better treatment to improve the morbidity. The extensive literature review done on this topic and this literature review would be helpful to the community updating about the breast cancer, how one can diagnose the evil disease on time and get the best therapy available to live life happily.

INTRODUCTION

Cancer is a class of diseases characterized by out-of-control cell growth. Cancer harms the body when damaged cells divide uncontrollably to form lumps or masses of tissue called tumors (except in the case of leukemia where cancer prohibits normal blood function by abnormal cell division in the blood stream).

Tumors can grow and interfere with the digestive, nervous, and circulatory systems and they can release hormones that alter body function. There are over 100 different types of cancer, and each is classified by the type of cell that is initially affected. Breast cancer begins in breast tissue, which is made up of glands for milk production, called lobules, and the ducts that connect the lobules to the nipple as depicted in figure 1.1. The remainder of the breast is made up of fatty, connective, and lymphatic tissue. Most masses are benign; that is, they are not cancerous, do not grow uncontrollably or spread, and are not life-threatening. Over 100,000 new breast cancer patients are estimated to be diagnosed annually in India [1,2].

Breast cancer is a tumor that starts from cells of the breast tissue, either in cells that line the ducts that carry milk to the nipples (ductal cancer) and/or in cells that line the lobules, which are glands involved in milk production. Breast tumors can be benign or malignant, the former are not life-threatening, can usually be removed, do not invade adjacent tissues or spread to other parts of the body and can include fibrocystic tissue, fibroadenomas and benign breast disease. Malignant breast tumors are cancerous and can invade surrounding tissues or metastasize to other parts of the body via the lymphatic system (lymphatic vessels and lymph nodes), such as the liver and bone. If cancer cells have spread to the surrounding lymph nodes, there is a much higher probability that the tumor has entered the bloodstream and metastasized to other parts of the body [3]. The incidence and mortality of breast cancer patients is depicted in figure-1.2. It shows 22.9% and 39.0% standardized incident cases per one lakh cases in India and Worldwide respectively while the death reported 11.1% and 12.5% respectively [4,5,6,7].

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The histological classification of breast cancer includes adenocarcinomas, cancers that originate in the glandular tissue, which include the ducts and lobules and sarcomas, cancers that originate in the connective tissue of muscle, fat or blood vessels. Carcinoma in situ (CIS) is an early stage form of cancer where the tumor is confined to the layer of the cells where the cancer began and it has not invaded deeper breast tissue or spread to other areas of the body [8]. Breast cancer includes the following types of disease [9]:

Ductal carcinoma in situ (DCIS) is the most common type of non-invasive cancer in women, where cancer cells have not spread beyond the duct walls into surrounding breast tissue. The prevalence of DCIS is strongly correlated with mammographic screening and in countries such as the US, can be as high as 18% of all newly diagnosed [10] but in countries such as India, represents a very low proportion of total disease since most cases present in late stage [11].

Invasive or infiltrating ductal carcinoma originates in the breast duct, has broken through the wall of the duct into surrounding fatty tissue of the breast and is capable of metastasizing to other organs of the body through the lymphatic system and bloodstream. This represents about 80% of breast cancers [12].

Lobular carcinoma in situ (LCIS) is not cancer but is sometimes classified as a non-invasive breast cancer and women who have this condition are more likely to develop invasive breast cancer in the future [13].

Invasive or infiltrating lobular carcinoma originates in the milk-producing glands or lobules of the breast and can spread to other parts of the body. This is less common and represents about 1 in 10 breast cancer diagnoses [14].

Other (less common) types of breast cancer: inflammatory breast cancer (1-3% of all breast cancers), triple negative breast cancers, mixed tumors, medullary carcinoma (3-5% of all breast cancers), metaplastic carcinoma, mucinous carcinoma, paget disease of the nipple, tubular carcinoma, papillary carcinoma, adenoid cystic carcinoma (adenocystic carcinoma), phyllodes tumor and angiosarcoma [13,14]. Estrogen receptor (ER) and Progesterone receptor (PR) status Confirmed carcinomas of the breast are subjected to a test to determine the estrogen receptor (ER) and progesterone receptor (PR) status. Breast cancers that contain estrogen receptors on the outside surface of their cells are ER-positive cancers while those with progesterone receptors are called PR-positive cancers. Women who are positive for either or both receptors generally have a better prognosis because they are more responsive to hormone therapy than without any of these receptors [13].

Prevalence in India

Cancer is a leading cause of death group worldwide and accounted for 7.4 million deaths (around 13% of all deaths) in 2004. The main types of cancer are:

- Lung (1.3 million deaths/year)
- Stomach (803,000 deaths)
- Colorectal (639,000 deaths)
- Liver (610,000 deaths)
- Breast (519,000 deaths)

More than 70% of all cancer deaths occurred in low- and middle-income countries. Deaths from cancer worldwide are projected to continue rising, with an estimated 11.5 million deaths in 2030.

The incidence of Breast Cancer is increasing, particularly in previously low incidence areas such as Asia. In fact in India, it is considered the leading Cancer among women in certain metros such as Mumbai, Bangalore & Thiruvananthapuram. As per the Indian Council of Medical Research-population Based Cancer Registry (ICMR-PBCR) data, breast cancer is the commonest cancer among women in urban registries of Delhi, Mumbai, Ahmedabad, Calcutta, and Trivandrum here it constitutes > 30% of all cancers in females [15]. In the rural PBCR of Barshi, breast cancer is the second commonest cancer in women after cancer of the uterine cervix. The age standardized incidence rates (AARs) range from 6.2 to 39.5 per 100,000 Indian women. The AARs vary from region, ethnicity, religion, with the highest incidence reported at 48.3 per 100,000 women in the Parsi community of Mumbai [16]. The incidence of this disease has been consistently increasing, and it is estimated it has risen by 50% between 1965 and 1985 [17].

The rise in incidence of 0.5-2% per annum has been seen across all regions of India and in all age groups but more so in the younger age groups (< 45 years) [18]. In general, breast cancer has been reported to occur a decade earlier in Indian patients compared to their western counterparts. While the majority of breast cancer patients in western countries are postmenopausal and in their 60ies and 70ies, the picture is quite different in India with premenopausal patients constituting about 50% of all patients (SGPGIMS Lucknow data) [19].

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More than 80% of Indian patients are younger than 60 years of age. The average age of patients in 6 hospital-based cancer registries ranged from 44.2 years in Dibrugarh, 46.8 years in Delhi, 47 years in Jaipur, to 49.6 years in Bangalore and Chennai. The average age of breast cancer patients has been reported to be 50-53 years in various population-based studies done in different parts of the country [20]. A significant proportion of Indian breast cancer patients are younger than 35 years of age. This proportion varies between 11% (Tata Memorial Hospital (TMH) Mumbai) [21] to 26% (SGPGIMS Lucknow) [22]. Young age has been associated with larger tumor size, higher number of metastatic lymph nodes, poorer tumor grade, low rates of hormone receptor-positive status, earlier and more frequent locoregional recurrences, and poorer overall survival [23,24].

Cause/Risk factor of breast cancer [25,46]

Studies have found the following risk factors for breast cancer:

Age: The chance of getting breast cancer increases as you get older. Most women are over 60 years old when they are diagnosed.

Personal health history: Having breast cancer in one breast increases your risk of getting cancer in your other breast. Also, having certain types of abnormal breast cells (atypical hyperplasia, lobular carcinoma in situ [LCIS], or ductal carcinoma in situ [DCIS]) increases the risk of invasive breast cancer. These conditions are found with a breast biopsy.

Family health history: Your risk of breast cancer is higher if your mother, father, sister, or daughter had breast cancer. The risk is even higher if your family member had breast cancer before age 50. Having other relatives (in either your mother's or father's family) with breast cancer or *ovarian cancer* may also increase your risk.

Certain genome changes: Changes in certain *genes*, such as *BRCA1* or *BRCA2*, substantially increase the risk of breast cancer. Tests can sometimes show the presence of these rare, specific gene changes in families with many women who ave had breast cancer, and health care providers may suggest ways to try to reduce the risk of breast cancer or to improve the detection of this disease in women who have these genetic changes. Also, researchers have found specific regions on certain *chromosomes* that are linked to the risk of breast cancer. If a woman has a genetic change in one or more of these regions, the risk of breast cancer may be slightly increased. The risk increases with the number of genetic changes that are found. Although these genetic changes are more common among women than BRCA1 or BRCA2, the risk of breast cancer is far lower.

Radiation therapy to the chest: Women who had radiation therapy to the chest (including the breasts) before age 30 are at an increased risk of breast cancer. This includes women treated with radiation for *Hodgkin lymphoma*. Studies show that the younger a woman was when she received radiation treatment, the higher her risk of breast cancer later in life.

Reproductive and menstrual history:

—The older a woman is when she has her first child, the greater her chance of breast cancer.
—Women who never had children are at an increased risk of breast cancer.
—Women who had their first *menstrual period* before age 12 are at an increased risk of breast cancer.
—Women who went through *menopause* after age 55 are at an increased risk of breast cancer.
—Women who take *menopausal hormone therapy* for many years have an increased risk of breast cancer.

Race: In the United States, breast cancer is diagnosed more often in white women than inAfrican American/black, Hispanic/Latina, Asian/Pacific Islander, or American Indian/Alaska Native women.

Breast density: Breasts appear on a *mammogram* (breast *x-ray*) as having areas of dense and fatty (not dense) tissue. Women whose mammograms show a larger area of dense tissue than the mammograms of women of the same age are at increased risk of breast cancer.

History of taking *DES*: DES was given to some pregnant women in the United States between about 1940 and 1971. (It is no longer given to pregnant women.) Women who took DES during pregnancy may have a slightly increased risk of breast cancer. The possible effects on their daughters are under study.

Being overweight or obese after menopause: The chance of getting breast cancer after menopause is higher in women who are overweight or obese.

Lack of physical activity: Women who are physically inactive throughout life may have an increased risk of breast cancer.

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Drinking alcohol: Studies suggest that the more alcohol a woman drinks, the greater her risk of breast cancer. Having a risk factor does not mean that a woman will get breast cancer. Most women who have risk factors never develop breast cancer. Many other possible risk factors have been studied. For example, researchers are studying whether women who have a diet high in fat or who are exposed to certain substances in the environment have an increased risk of breast cancer. Researchers continue to study these and other possible risk factors[25,46].

Manifestation [25,47]

Early breast cancer usually doesn't cause symptoms. But as the tumor grows, it can change how the breast looks or feels. The common changes include and depicts in Fig. 1.3:

1. A lump or thickening in or near the breast or in the underarm area
2. A change in the size or shape of the breast
3. Dimpling or puckering in the skin of the breast
4. A nipple turned inward into the breast
5. Discharge (fluid) from the nipple, especially if it's bloody
6. Scaly, red, or swollen skin on the breast, nipple, or *areola* (the dark area of skin at the center of the breast). The skin may have ridges or pitting so that it looks like the skin of an orange.

Detection and Diagnosis [25]

The detection and diagnosis of breast cancer depends upon personal and family medical history also. The physical examination like one or more imaging tests, such as a mammogram reveals the unwanted growth of cells in breast. Women who have regular *clinical breast exams* and mammograms to find breast cancer early; the treatment is more likely to work well because breast cancer is detected early. The followings are the breast cancer detection techniques.

Clinical Breast Exam

During a clinical breast examination both arms raised over head, let them hang by sides, or press hands against your hips. The difference in size or shape between breasts indicates suspicion on cancer. The skin of breasts is checked for a rash, dimpling, or other abnormal signs. Nipples may be squeezed to check for fluid. Using the pads of the fingers to feel for lumps, checking of entire breast, underarm, and collar-bone area. A lump is generally the size of a pea before anyone can feel it. The exam is done on one side and then the other. The lymph nodes near the breast to see if they are enlarged. A lump will feel its size, shape, and texture then it will also be checked to see if the lump moves easily. Benign lumps often feel different from cancerous ones. Lumps that are soft, smooth, round, and movable are likely to be benign. A hard, oddly shaped lump that feels firmly attached within the breast is more likely to be cancer, but further tests are needed to diagnose accurately.

Mammogram

A mammogram is an x-ray picture of tissues inside the breast. Mammograms can often show a breast lump show a cluster of tiny specks of calcium. These specks are called icrocalcifications. Lumps or specks can be from cancer, precancerous cells, or other conditions. Further tests are needed to find out if abnormal cells are present. Before they have symptoms, women should get regular screening mammograms to detect breast cancer early:

- Women in their 40s and older should have mammograms every 1 or 2 years.
- Women who are younger than 40 and have risk factors for breast cancer should ask their health care provider whether to have mammograms and how often to have them.

If the mammogram shows an abnormal area of the breast, clearer, more detailed images of that area can be obtained by diagnostic mammograms to know more about unusual breast changes, such as a lump, pain, thickening, nipple discharge, or change in breast size or shape. Diagnostic mammograms may focus on a specific area of the breast. They may involve special techniques and more views than screening mammograms.

Other Imaging Tests

If an abnormal area is found during a clinical breast exam or with a mammogram, the doctor may order other imaging tests:

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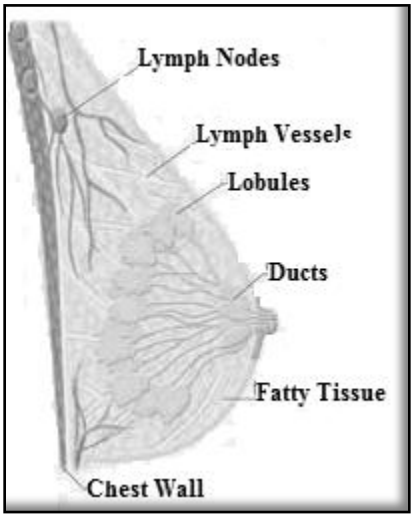

Figure 1.1: Pictorial presentation of breast with nodes, vessels, lobules, ducts

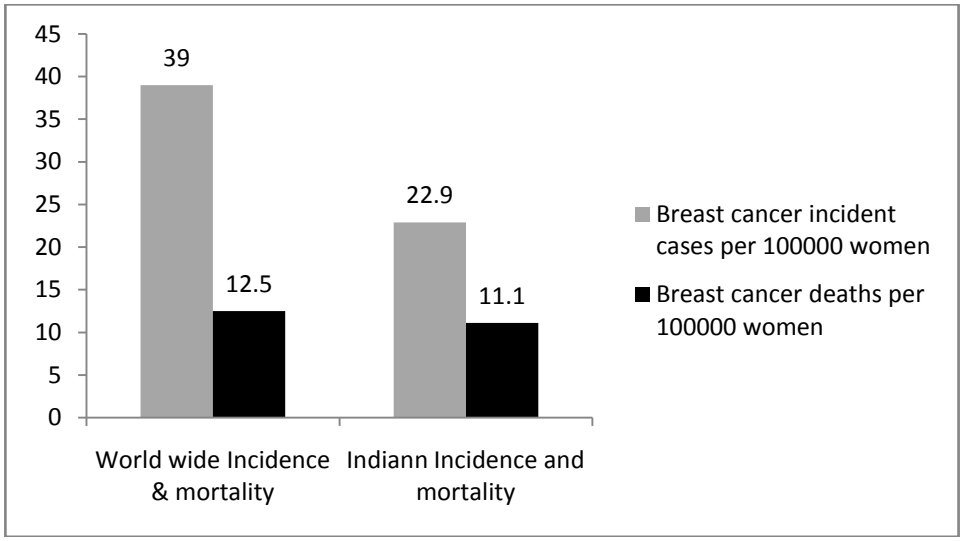

Figure 1.2: Breast Cancer Incidence and Mortality

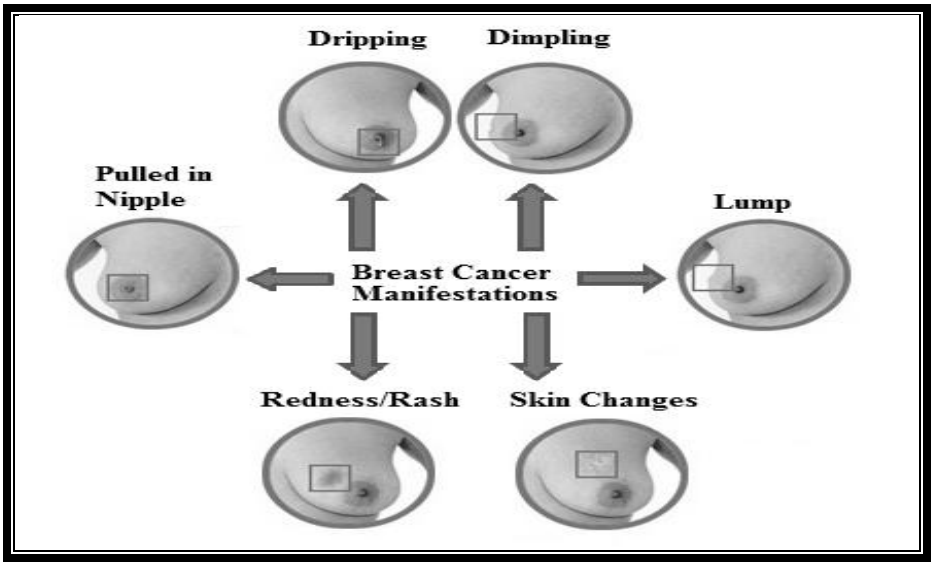

Figure 1.3: Manifestations of breast cancer

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Ultrasound: A woman with a lump or other breast change may have an ultrasound test. An ultrasound device sends out sound waves that people can't hear. The sound waves bounce off breast tissues. A computer uses the echoes to create a picture. The picture may show whether a lump is solid, filled with fluid (a *cyst*), or a mixture of both. Cysts usually are not cancer. But a solid lump may be cancer.

MRI: Magnetic Resonance Imaging (MRI) uses a powerful magnet linked to a computer. It makes detailed pictures of breast tissue. These pictures can show the difference between normal and diseased tissue.

Bone scan: In bone scan a small amount of a *radioactive* substance injected into a blood vessel. It travels through the bloodstream and collects in the bones. A machine called a scanner detects and measures the radiation. The scanner makes pictures of the bones. The pictures may show cancer that has spread to the bones.

CT scan: Computed Tomography (CT) scans used to look for breast cancer that has spread to the liver or lungs. An x-ray machine linked to a computer takes a series of detailed pictures of chest or abdomen. Patient receives *contrast material* by injection into a blood vessel in arm or hand. The contrast material makes abnormal areas easier to see.

PET Scan : PET stands for positron emission tomography and it uses radiation, or nuclear medicine imaging, to produce 3-dimensional, color images of the functional processes within the human body. The machine detects pairs of gamma rays which are emitted indirectly by a tracer (positron-emitting radionuclide) which is placed in the body on a biologically active molecule. The images are reconstructed by computer analysis. Modern machines often use a CT X-ray scan which is performed on the patient at the same time in the same machine. PET scans can be used to diagnose a health condition, as well as for finding out how an existing condition is developing. PET scans are often used to see how effective an ongoing treatment is.

Biopsy

A biopsy is the removal of tissue to look for cancer cells. A biopsy is the only way to tell for sure if cancer is present. One may need to have a biopsy if an abnormal area is found. An abnormal area may be felt during a clinical breast exam but not seen on a mammogram. Or an abnormal area could be seen on a mammogram but not be felt during a clinical breast exam. In this case, use of imaging procedures (such as a mammogram, an ultrasound, or MRI) are helpful locate the area and remove tissue. A *surgeon* or breast disease specialist required for a biopsy. There are number of ways to remove fluid or tissue from breast:

Fine-needle aspiration biopsy (FNAC): A thin needle used to remove cells or fluid from a breast lump for investigations.

Core biopsy: A wide needle used to remove a sample of breast tissue.

Skin biopsy: If there are skin changes on breast, a small sample of skin should be taken for analysis.

Surgical biopsy: It includes the removal of tissue.

—An *incisional biopsy* takes a part of the lump or abnormal area.
—An *excisional biopsy* takes the entire lump or abnormal area.

A pathologist will check the tissue or fluid removed from breast for cancer cells. If cancer cells are found, the pathologist can tell what kind of cancer it is. The most common type of breast cancer is ductal *carcinoma*. It begins in the cells that line the breast ducts. Lobular carcinoma is another type. It begins in the lobules of the breast.

If the biopsy confirms the breast cancer, its needs to examine the extent (stage) of the disease to help you choose the best treatment. The stage is based on the size of the cancer, whether the cancer has invaded nearby tissues, and whether the cancer has spread to other parts of the body. Staging may involve blood tests and other tests:

Lymph node biopsy: The stage often is not known until after *surgery* to remove the tumor in breast and one or more lymph nodes under arm. A *sentinel lymph node biopsy* used to remove the lymph node most likely to have breast cancer cells. The surgeon injects a blue dye, a radioactive substance, or both near the breast tumor. Or a radioactive substance injected under the nipple. A scanner used to find the sentinel lymph node containing the radioactive substance or looks for the lymph node stained with dye. The sentinel node is removed and checked for cancer cells. Cancer cells may appear first in the sentinel node before spreading to other lymph nodes and other places in the body.

These tests can show whether the cancer has spread and to what parts of body. When breast cancer spreads, cancer cells are often found in lymph nodes under the arm (*axillary lymph nodes*). Also, breast cancer can spread to almost any other part of the body,

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such as the bones, liver, lungs, and brain. When breast cancer spreads from its original place to another part of the body, the new tumor has the same kind of abnormal cells and the same name as the primary (original) tumor. For example, if breast cancer spreads to the bones, the cancer cells in the bones are actually breast cancer cells. The disease is *metastatic* breast cancer, not bone cancer. For that reason, it is treated as breast cancer, not bone cancer. The new tumor called as "distant" or metastatic disease.

Lab Tests with Breast Tissue and Treatment Options:

There are some special lab tests on the breast tissue (that was removed) which should be performed. On basis of these tests revelations, the cancer therapy would be suggested:

Hormone receptor tests: Some breast tumors need hormones to grow. These tumors have receptors for the hormones *estrogen*, *progesterone*, or both. If the hormone receptor tests show that the breast tumor has these receptors, then *hormone therapy* is most often recommended as a treatment option.

***HER2/neu* test**: HER2 (Human Epidermal Growth Factor Receptor 2)/neu protein is found on some types of cancer cells. This test shows whether the tissue either has too much HER2/neu protein or too many copies of its gene. If the breast tumor has too much HER2/neu, then *targeted therapy* may be a treatment option. It may take several weeks to get the results of these tests.

Lifestyle and diet factors [26]

Eating the right kinds of foods before, during, and after treatment of cancer can is helpful to keep stronger. The proper nutrition should be taken and drink enough of the foods that contain key nutrients (vitamins, minerals, protein, carbohydrates, fat, and water). The side effects of cancer and cancer treatments, however, may make it difficult to eat well. Symptoms that interfere with eating include anorexia, nausea, vomiting, diarrhea, constipation, mouth sores, trouble with swallowing, and pain. The cancer treatment may also affect appetite, taste, smell, and the ability to eat enough food or absorb the nutrients from food. As a result, patient may become malnourished from the lack of key nutrients. Malnutrition can make you feel weak, tired, and unable to resist infections or withstand cancer therapies. On the other hand, many people have mild or no side effects.

- **When cancer patient can eat, try to have meals and snacks with sufficient calories and Protein** – which will help to stay stronger, prevent body tissues from breaking down, and rebuild tissues that may harm by cancer treatment.
- **Try a liquid meal replacement for extra calories and protein.** The products that contain high levels of isolated soy isoflavone always keep the patients stronger.
- **Keep foods stocked and handy** that requires little or no preparation, such as peanut butter, pudding, applesauce, tuna fish, cheese, and eggs.
- **Try to drink plenty of fluids,** especially on days when you don't feel like eating. Water is essential to your body's proper functioning. For adults, six to eight cups of fluids per day is a good target.
- **If your symptoms persist or worsen, consult your physician immediately.**
  He or she will also be able to suggest prescription remedies that work well to control side effects.
- **Cancer and its treatments destroy the body's ability to make white blood cells.** This can weaken cancer patient's immune system and put him/her at risk for infections that you would not normally be susceptible to, including food borne illnesses.

Therapies [27]

Breast cancer treatment There are several treatment options for women diagnosed with breast cancer that include surgery, chemotherapy, radiation therapy, hormonal therapy and targeted therapies. The most appropriate treatment depends on the woman's risk profile and stage of disease, which can range from I-IV and is based on the tumor size, location, and involvement of lymph nodes and whether or not tumor has spread to surrounding tissue or distant organs.

Treatment for breast cancer depends on:

- Stage of your cancer (whether it is just in the breast or has spread to other places in the body),
- Type of breast cancer,
- Characteristics of the cancer cells,
- Menopausal status, and
- General state of your health.

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What is "staging?"

Once breast cancer has been diagnosed, more tests will be done to find out if the cancer has spread from the breast to other parts of the body. This is called staging. Your doctor needs to know the stage of your disease to plan treatment. The following stages are used for breast cancer:

Stage	Description
0	Abnormal cells in the lining of the ducts or sections of the breast Results in increased risk of developing cancer in both breasts
1	Cancer in breast tissues tumour less than 2 cm across
2	Cancer in breast tissues tumour less than 5 cm across Cancer may also spreadto axillary (armpit) lymph nodes
3	Tumor is larger than 5 cm across with extensive spread to axillary or other nearby lymph nodes Possible inflammation of breast tissue, dimpling, thickening, and change in color of the skin due to blocked lymphatic drainage
4	Spread of cancer beyond the immediate religion of the breast

Breast cancer in situ (Stage 0)

About 30 percent of breast cancers are identified very early. They are sometimes called carcinoma in situ. There are two types of breast cancer in situ. One type is ductal carcinoma in situ (also known as intraductal carcinoma). The other type is lobular carcinoma in situ. Lobular carcinoma in situ is not cancer but is a marker for patients at higher risk for future development of breast cancer. For the purpose of classifying the disease, it is also called breast cancer in situ, carcinoma in situ or stage 0 breast cancer.

Stage I

The cancer is no bigger than 2 centimeters (about 1 inch) and has not spread outside the breast, or the cancer is no bigger than 2 centimeters and there is lymph node involvement with cells measuring less than 2 millimeters (micrometastasis).

Stage II

Stage II is divided into stages IIA and IIB.

Stage IIA

- The cancer is no bigger than 2 centimeters and has spread to the lymph nodes under the arm (the axillary lymph nodes).
- The cancer is between 2 and 5 centimeters (from 1 to 2 inches) and has not spread to the lymph nodes under the arm.
- There is cancer detected in the lymph nodes under the arm with no detectable cancer in the breast (unknown primary).

Stage IIB

- The cancer is between 2 and 5 centimeters (from 1 to 2 inches) and has spread to the lymph nodes under the arm.
- The cancer is bigger than 5 centimeters (larger than 2 inches) and has not spread to the lymph nodes under the arm.

Stage III

Stage III is divided into stages IIIA, IIIB and IIIC. Stage IIIA is defined by either of the following:

Stages IIIA

- The cancer is 5 centimeters or less in size and has spread to lymph nodes under the arm that have grown into each other or into other structures, or to lymph nodes near the breastbone.
- The cancer is larger than 5 centimeters in size and has spread to the lymph nodes under the arm.

Stage IIIB

- The cancer has grown into the chest wall and/or the skin of the breast with or without evidence of spread to the lymph nodes.

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- The cancer may have spread to lymph nodes under the arm that have grown into each other or into other structures, or to lymph nodes near the breastbone.

Stage IIIC is defined by any tumor size with one of the following:

- The cancer has spread to the lymph nodes above or below the collarbone.
- There are more than 10 lymph nodes under the arm involved with cancer.
- There is involvement of the lymph nodes near the breastbone.

Stage IV

The cancer has spread to other organs of the body. The sites where breast cancer is most likely to spread are the bones, lungs, liver or brain.

Inflammatory Breast Cancer

Inflammatory breast cancer is a special class of breast cancer that is rare. The breast looks as if it is inflamed because of its swollen and red appearance. Sometimes it may feel warm. The skin may show signs of ridges and wheals (raised areas) or it may look pitted like the skin of an orange. This type of cancer tends to be more aggressive. Inflammatory breast cancer may be stage IIIB, IIIC or stage IV.

Recurrence

Recurrent disease means that the cancer has come back (recurred) after it has been previously treated. It may come back in the breast, the lymph nodes, the soft tissues of the chest (the chest wall), or in another part of the body.

How is breast cancer treated?

There are different treatments for each patient with breast cancer depending on the stage and type.

- Surgery (an operation to remove the cancer)
- Radiation therapy (using high-dose x-rays to kill cancer cells)
- Chemotherapy (using drugs to kill cancer cells)
- Hormone therapy (using hormones to stop the cells from growing)

- Targeted therapy (using drugs targeting a unique marker on the breast cancer cells)
- New types of treatment are being tested in clinical trials.
- Therapy is considered adjuvant when it is given after surgery, when no cancer cells can be seen, to prevent cancer from recurring.
- Therapy is considered neoadjuvant when it is given before surgery to shrink the tumor and make it easier to remove, or to assess the response of the tumor to a specific type of treatment options include [13,28].

Surgery includes lumpectomy (removal of a lump and the surrounding tissue), which is also called breast-conserving survey, mastectomy (removal of all the breast tissue although muscles underneath breast are no longer removed), lymph node removal (or axillary lymph node dissection) which takes place during time of lumpectomy or mastectomy if biopsy shows that breast cancer has spread. Other options include preventive surgeries such as prophylactic mastectomy for women at high-risk and prophylactic ovary removal to lower estrogen production in the body. Emerging evidence from trials suggest that the removal of axillary lymph nodes is *not* a determinant of breast cancer recurrence and survival in early-stage patients, which is contrary to prevailing practices.[56-58] In one trial of 856 early-stage patients, dissection of lymph nodes with evidence of spread did not influence breast cancer 5-year recurrence or mortality rates [29].

In another trial (the National Surgical Adjuvant Breast and Bowel Project B-32 study) of 3,986 node-negative patients, women were randomized to axillary lymph node dissection or no further surgery; the investigators found that the intervention was not associated with disease control or survival but was associated with significantly greater morbidity, including shoulder abduction deficit, arm volume, arm numbness and tingling [30].

In another study of 5,539 women undergoing breast-conserving surgery, immune system assays which are more sensitive in detecting micro-metastases in node-negative women, were not associated with improved survival [31].

Radiation therapy includes external beam and internal (implantation of radioactive seeds) radiation, and is usually given after surgery to destroy any remaining cancerous cells left behind. While the former is a well-tested, long-standing treatment option, the latter has

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recently being developed and is still being studied for its efficacy and adverse effect profile, although evidence from at least 4 trials demonstrate a consistent lower recurrence rate when radiation therapy supplements surgery [32,33,34,35].

The advantages of internal radiation include a much shorter treatment interval, a localized and focused approach of radiation to the affected area (and hence lower dose exposure) rather than the whole breast and therefore fewer adverse effects related to radiation. Disadvantages are that benefits and side effects of this newer technology are not well-understood and that it requires extra training/expertise to be correctly carried out. Two European trials have shown that 10-16 Gy boosts can reduce recurrence by 4.6% to 3.6% at 3 years ($p=0.044$) [36] and from 7.3% to 4.3% at 5 years ($p<.001$) [37].

A randomized clinical trial is underway (National Surgical Adjuvant Breast and Bowel Project (NSABP) B-39/RTOG 0413) to compare the effects of internal (partial breast) and external (whole-breast) irradiation in women with Stage 0, I and II breast cancer [38].

Chemotherapy is a systemic therapy that can be administered either before surgery (to shrink the tumor) or afterwards (to reduce the risk of recurrence). For early-stage disease, it is usually administered to help remove cancer cells from the body and to reduce the risk of recurrence. For advanced-stage disease, it is given to destroy as many cancer cells as possible. A meta-analysis of 60 trials and 28,764 women of combination chemotherapy versus no chemotherapy showed a 37% reduction in relapse and 30% reduction in death for women under the age of 50 years, and a 19% reduction in relapse and 12% reduction in death for women aged 50-69 years; the benefit on recurrence was present in all age groups and in the presence and absence of tamoxifen [39].

Hormonal therapy is a treatment option for hormone receptor-positive cancers. It can be given for early-stage disease to either reduce the amount of estrogen or block its action to reduce the risk of recurrence. It can also be given for advanced-stage or metastatic disease to shrink or slow the growth of existing tumors. Hormone therapy includes aromatase inhibitors, selective estrogen receptor modulators and estrogen receptor down regulators as well as surgical treatments such as removal of ovaries and fallopian tubes. Tamoxifen use of at least 5 years is associated with a 12% reduction in recurrence and a 9% reduction in mortality over a 15-year follow-up period, in ER-positive and ER-unknown breast tumors [40].

The benefits of tamoxifen appear to be optimized at 5 years with current recommendations to discontinue adjuvant tamoxifen after 5 years. Recent trials (Arimidex-Nolvadex study in postmenopausal women (ARNO-95) and the Intergroup Exemestane Study (IES)) have shown benefits of aromatase inhibitors over tamoxifen for disease-free survival and complications [41,42,43,44].

Targeted therapies target cancer cell properties specifically as opposed to chemotherapy which also destroys normal, healthy cells and includes treatments such as herceptin and tykerb, which both block cancer cell growth in HER2-positive breast cancers, and avastin, which blocks growth of new blood vessels depending for cancer cell growth [13,45].

CONCLUSION

This review deciphers the breast cancer and awakens the society about its cause, manifestations, possible diagnosis, therapies so that one can understand the adequate way to get appropriate therapy. It also emphasizes on life style and diet factor which can be more prominent tool to avoid and control the breast cancer by living a proper life style with adequate nutrition. Overall it can deliver the adequate information of breast cancer etiology, diagnosis and treatment primarily.

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REFERENCES

1. Agarwal G, Pradeep PV, Aggarwal V, Yip CH, Cheung PS. Spectrum of breast cancer in Asian women. World J Surg. 2007;31:1031-40.
2. Nandakumar A, Anantha N Venugopal TC, Sankaranarayanan R, Thimmasetty K, Dhar M. Survival in breast cancer: a population-based study in Bangalore, India. Int J Cancer. 1995;60:593-96.
3. Schottenfield DaF Jr, Joseph F. Cancer Epidemiology and Prevention, Second Edition. New York: Oxford University Press; 1996.
4. Ferlay J BF, Pisani P, Parkin DM. GLOBOCAN 2000: Cancer Incidence, Mortality and Prevalence Worldwide, Version 1.0. 2001. 17-45.
5. Ferlay J SH, Bray F, Forman D, Mathers C and Parkin DM. GLOBOCAN 2008 v1.2, Cancer Incidence and Mortality Worldwide: IARC Cancer Base No. 10; 2011.
6. Organization WH. The global burden of disease: 2004 update: Department of Health Statistics and Informatics; 2008. Report No.: ISBN 978b 941563710.
7. Programme NCR. Time Trends in Cancer Incidence Rates 1982-2005. Bangalore, India: Indian Council of Medical Research; 2009.

ISSN: 2319-9865

8. Armstrong D. Ovaries and fallopian tubes. In: Abeloff MD, Armitage JO, Lichter AS, Niederhuber JE, Kastan MB, McKenna WG, eds. Clinical Oncology. 4th ed. Philadelphia, PA: Elsevier; 2008.
9. Schottenfield DaF, Jr., Joseph F. Cancer Epidemiology and Prevention, Third Edition. New York: Oxford University Press; 2006.
10. Simpson PT, Gale T, Fulford LG, Reis-Filho JS, Lakhani SR. The diagnosis and management of pre-invasive breast disease: pathology of atypical lobular hyperplasia and lobular carcinoma in situ. Breast Cancer Research. 2003 5(5):258-62.
11. Moore MA, Ariyaratne Y, Badar F, et al. Cancer epidemiology in South Asia - past, present and future. Asian Pac J Cancer Prev. 2010;2:49-66.
12. Abeloff MD, Wolff AC, Weber BL, et al. Cancer of the Breast. In: Abeloff MD, Armitage JO, Lichter AS, et al, eds. Clinical Oncology. 4th ed. Philadelphia, Pa: Elsevier; 2008.
13. Avis N, Crawford S, Manuel J, et al. Quality of life among younger women with breast cancer. J Clin Oncol. 2005;23:3322-30.
14. Altekruse SF KC, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2007. Bethesda, MD: National Cancer Institute; 2009.
15. Agarwal G, Ramakant P. Breast Cancer Care in India: The Current Scenario andthe Challenges for the Future. Breast Care 2008;3:21-27.
16. National Cancer Registry Programme: Consolidated report of the population based cancer registries 1990-1996. Indian Council of Medical Research, New Delhi, 2001.
17. Saxena S, Szabo CI, Chopin S, Barjhoux L, Sinilnikova O, Lenoir G, Goldgar DE, Bhatanager: BRCA1 and BRCA2 in Indian breast cancer patients. Hum Mutat. 2002;20:473-74.
18. Murthy NS, Agarwal UK, Chaudhry K, Saxena S. A study on time trends in incidence of breast cancer -Indian scenario. Eur J Cancer Care. 2007;(16):185-86.
19. Agarwal G, Pradeep PV, Aggarwal V, Yip CH, Cheung PS: Spectrum of breast cancer in Asian women. World J Surg. 2007;31:1031-40.
20. Wingo PA, Howe HL, Thun MJ et al. A national framework for cancer surveillance in the United States. Cancer Causes Control. 2004;16:151-70.
21. Dinshaw KA, Sarin R, Budrukkar AN, Shrivastava SK, Deshpande DD, Chinoy RF, Badwe R, Hawaldar R: Safety and feasibility of breast conserving therapy in Indian women: two decades of experience at Tata Memorial Hospital. J Surg Oncol. 2006;94: 105-13.
22. McCracken M, Olsen M, Chen MS, et al. Cancer incidence, mortality, and associated risk factors among Asian Americans of Chinese, Filipino, Vietnamese, Korean, and Japanese ethnicities. CA Cancer J Clin. 2007;57:190-05.
23. Mathew A, Pandey M, Rajan B. Do younger women with non-metastatic and non-inflammatory breast carcinoma have poor prognosis? World J Surg Oncol. 2004 (2:2) DOI:10.1186/1477-7819-2-2.
24. Shavers VL, Harlan LC, Stevens JL. Racial/ethnic variation in clinical presentation, treatment, and survival among breast cancer patients < age 35. Cancer 2003;97:134-147.
25. National cancer institute, US Department of Health and Human Services, NIH Publication No.09-1556, Revised July 2009, Printed September 2009.
26. Sinha R; Anderson DE, Mac Donanald SS; Greenwald P. Cancer risk and diet in India. J. Postgrad Medicine. 2003;49:222-28.
27. Patient Education, Adapted from NCI's Breast Cancer PDQ Breast Cancer Treatment by Stage © 1995, 2011 The University of Texas MD Anderson Cancer Center, Revised 02/07/11.
28. Institute NC. PDQ Breast Cancer Treatment Breast Cancer Treatment 2011 October 7, 2011 [cited 2011 October 25, 2011]; Available from:
http://www.cancer.gov/cancertopics/pdq/treatment/breast/healthprofessional.
29. Giuliano AE, McCall L, Beitsch P, et al. Locoregional recurrence after sentinel lymph node dissection with or without axillary dissection in patients with sentinel lymph node metastases: the American College of Surgeons Oncology Group Z0011 randomized trial. Ann Surg. 2010; 252:426-32; discussion 32-33.
30. Krag DN, Anderson SJ, Julian TB, et al. Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial. Lancet Oncol. 2010;11:927-33.
31. Cote RJ, Peterson HF, Chaiwun B, et al. Role of immunohistochemical detection of lymph-node metastases in management of breast cancer. International Breast Cancer Study Group. The Lancet. 1999;354:896-900.
32. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med. 2002;347:1233-41.
33. Veronesi U, Luini A, Del Vecchio M, et al. Radiotherapy after breast-preserving surgery in women with localized cancer of the breast. N Engl J Med. 1993;328:1587-91.
34. Liljegren G, Holmberg L, Bergh J, et al. 10-Year results after sector resection with or without postoperative radiotherapy for stage I breast cancer: a randomized trial. J Clin Oncol. 1999;17:2326-33.
35. Clark RM, McCulloch PB, Levine MN, et al. Randomized clinical trial to assess the effectiveness of breast irradiation following lumpectomy and axillary dissection for node-negative breast cancer. J Natl Cancer Inst. 1992;84:683-89.
36. Romestaing P, Lehingue Y, Carrie C, et al. Role of a 10-Gy boost in the conservative treatment of early breast cancer: results of a randomized clinical trial in Lyon, France. J Clin Oncol 1997;15:963-68.

ISSN: 2319-9865

37. Bartelink H, Horiot JC, Poortmans P, et al. Recurrence rates after treatment of breast cancer with standard radiotherapy with or without additional radiation. N Engl J Med. 2001;345:1378-87.
38. NSABP B-39, RTOG 0413: A Randomized Phase III Study of conventional whole breast irradiation versus partial breast irradiation for women with stage 0, I, or II breast cancer. Clin Adv Hematol Oncol. 2006;4:719-21.
39. Ting B., Nancy ED. Adjuvant endocrine therapy for premenopausal women with early breast cancer. Breast Cancer Res. 2007; 9(6):115.
40. Cuzick J, Ambroisine L, Davidson N, Jakesz R, Kaufmann M, Regan M, Sainsbury R. Use of luteinising-hormone-releasing hormone agonists as adjuvant treatment in premenopausal patients with hormone-receptor-positive breast cancer: a meta-analysis of individual patient data from randomised adjuvant trials. The Lancet. 2007;369:1711-23.
41. Fisher B, Dignam J, Bryant J, Wolmark N. Five versus more than five years of tamoxifen for lymph node-negative breast cancer: updated findings from the National Surgical Adjuvant Breast and Bowel Project B-14 randomized trial. J Natl Cancer Inst. 2001;93: 684-90.
42. Stewart HJ, Prescott RJ, Forrest AP. Scottish adjuvant tamoxifen trial: a randomized study updated to 15 years. J Natl Cancer Inst. 2001;93:456-62.
43. Tormey DC, Gray R, Falkson HC. Postchemotherapy adjuvant tamoxifen therapy beyond five years in patients with lymph node-positive breast cancer. Eastern Cooperative Oncology Group. J Natl Cancer Inst. 1996;88:1828-833.
44. Baum M, Budzar AU, Cuzick J, et al. Anastrozole alone or in combination with tamoxifen versus tamoxifen alone for adjuvant treatment of postmenopausal women with early breast cancer: first results of the ATAC randomised trial. The Lancet. 2002;359:2131-39.
45. Lawenda BD, Mondry TE, Johnstone PA. Lymphedema: a primer on the identification and management of a chronic condition in oncologic treatment. CA: Cancer J Clin.2009; 59(1):8-24.
46. http://www.cancer.gov/cancertopics/prevention-genetics-causes/breast.
47. Elston CW. Classification and grading of invasive breast carcinoma. Verh Dtsch Ges Pathol. 2005;89:35-44.