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Breast Cancer and Its Treatments: A Comprehensive Review

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Abstract

Breast cancer is the most common type of cancer in women worldwide. Prediction models can aid in the development of screening recommendations based on the presence of identified and quantifiable hormonal, environmental, family, or genetic risk factors. This condition has an effect on a woman's physical, mental, and social well-being, among other things. During an illness, however, things such as social and family support can help to reduce its effects. While the (exact) cause of breast cancer remains unknown, the disease's risk factors have been established. Age, a family history of breast cancer, specific changes in the breast(s), gene changes, a history of productivity and menopause, a lack of physical activity, alcohol consumption, obesity, diet, race, and chest radiation therapy are all factors that contribute to breast cancer.

Keywords: Breast cancer, Cancer, Gene, Women

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INTRODUCTION

Background

The American society defines cancer as a "Group of disease characterized by uncontrollable growth and spread of abnormal cells. If the spread is not controlled, it can result in death." Cancer is a broad term that encompasses a variety of diseases. Rather, it is made up of over 100 different diseases. Cancer, neoplasia, tumor, neoplasm, and development are among the cancer-related terminology added. Medical practitioners sometimes use the term neoplasia, which is a synonym for cancer. Tumor is a synonym for neoplasm, which means "new growth." There are many other words that refer to abnormal cell development.

The distinctions between normal and cancer cells are defined by cancer cell biology. Normal, healthy cells perform unique roles for the body, and their growth is regulated by a complex biochemical mechanism. Cancer cells develop uncontrollably and are unable to identify their own natural limits due to faulty gene mutations. Despite the fact that scientists have yet to pinpoint an exact cause for cancer, many factors are believed to play a role in the development of cancer in the body. "Cancer risk factors" include things such as smoking, diet, genetics, occupation, environment, and infectious agents.[1]

Breast Cancer

Breast cancer is a cancer that starts in the breast and spreads to other parts of the body. As cells proliferate uncontrollably, cancer grows. A tumor, which can be seen on X-rays or felt as a lump, is formed by breast cancer cells. Breast cancer is almost exclusively a female disease, but it may also strike men.[2]

Epidemiology of Breast Cancer

For decades, cervical cancer was the most common cancer in Indian women, and it was responsible for more deaths in women than any other cancer.[3] Breast cancer, on the other hand, has been gradually rising over the last decade or so, and in 2012, it overtook cervical cancer as the most common cancer in Indian women for the 1st time.[4] This is due in part to a decrease in the number of cases of cervical cancer. Breast cancer incidence, on the other hand, has been gradually increasing, with 50% rise between 1965 and 1985, owing mainly to a drastic increase in the number of cases.[5] The annual percentage change in breast cancer incidence ranged from 0.46 to 2.56. In India, 155,000 new cases of breast cancer are expected to be diagnosed in 2015, with 76,000 people expected to die as a result of the disease. Breast cancer tends to be more common in India's younger age groups, with 52% of all breast cancer patients in Mumbai being between the ages of 40 and 49. The majority of the patients are under the age of 30.[6] According to population-based registries, the prevalence of breast cancer differs greatly between rural and urban areas. Hospital-based registries, on the other hand, may be skewed due to different comparative patterns/socioeconomic and other variables.

Breast cancer is the most commonly diagnosed cancer in women and the leading cause of cancer-related deaths. In 2018, breast cancer claimed the lives of 2.08 million people out of 18.08 million new cancer cases (11.6% incidence rate) and 626,679 people out of 9.55 million cancer-related deaths (6.6% of all cancer-related deaths).[7]

Types of Breast Cancer

In terms of clinical course, gross and microscopic pathology, and imaging characteristics, breast cancer is a complex disease. There are several histological classifications, which is as shown as Figure 1.

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Non-invasive Carcinoma

Breast cancers that are not invasive stay in the milk ducts or lobules. They do not infiltrate or extend into normal breast tissues. Non-invasive cancers are referred to as carcinomas *in situ* ("in the same place") or pre-cancers.[8] Breast cancer is usually divided into two types: Non-invasive (*in situ*) and invasive. *In situ* carcinoma is characterized by growth within the ducts without penetration of the basement membrane and thus without the ducts involving the stroma. There are two types of *in situ* carcinoma: Ductal carcinoma *in situ* (DCIS) and lobular carcinoma *in situ* (LCIS).[9]

DCIS

DCIS is frequently classified as comedo or non-comedo based on the presence or absence of comedogenesis, growth pattern (e.g., solid, papillary, and cribriform), and nuclear grade. The comedo type is distinguished by a growth pattern in which the cells in the involved ducts' centers are necrotic and the surrounding viable cells have a high nuclear grade. Dystrophic calcification is common in the central area of necrosis. Endocrine DCIS is a type of DCIS with a cell arrangement that suggests an endocrine structure. This is a descriptive term with no clinical or prognostic meaning.[9]

LCIS

LCIS is characterized by a population of uniform, discohesive cells with no nuclear pleomorphism, nucleoli, or mitotic activity that distends lobular ducts. The presence of one complete lobule in a biopsy is sufficient for diagnosis, though some experts believe that the presence of most of the lobular ducts is sufficient. Since the lesion is neither palpable nor visible on mammography, its diagnosis is generally based on its proximity to a clinically or mammographically observable lesion. LCIS is typically multicentric and bilateral in nature. It should be regarded as a sign of a patient's increased relative risk of developing invasive carcinoma.[9]

Invasive Carcinoma

Neoplastic penetration of a duct's basement membrane and extension of neoplastic cell aggregates into the mammary stroma is known as invasive carcinoma.[10]

Breast cancer that has spread into the surrounding tissue is known as invasive breast cancer. Invasive breast cancer accounts for the majority of cases, although there are different forms of invasive breast cancer. The most common forms are invasive ductal carcinoma (IDC) and invasive lobular carcinoma.[11]

IDC

IDC, also known as infiltrating ductal carcinoma, is the most common type of breast cancer. The majority of breast cancers are IDCs, which account for around 80% of all cases. Cancer that has "invaded" or spread to the underlying breast tissues is referred to as "invasive." The "pipes" that carry milk from the milk producing lobules to the nipple are known as the milk ducts, and cancer in them is known as ductal cancer. Carcinoma is a cancer that begins in the skin or other tissues that surround internal organs, such as breast tissue. IDC is a form of cancer that has penetrated through the milk duct wall and spread to the breast tissues. IDC is a form of cancer that has penetrated through the milk duct wall and spread to the breast tissues. Overtime, IDC can spread to the lymph nodes and other parts of the body.

According to the American Cancer Society, more than 180,000 people in the United States are diagnosed with invasive breast cancer each year. IDC affects the majority of them.

IDC can strike women at any age, but it becomes more frequent as they get older.[12]

Neoplastic cells developing in single cell cords (so-called Indian files) and surrounding ducts in a concentric targetoid structure characterize the growth pattern of invasive lobular carcinoma. Cellular cytoplasmic vacuolation may be caused by intracellular mucin. The neoplasm may be difficult to detect clinically or mammographically due to the often weak desmoplastic response and the lack of associated microcalcifications. This growth pattern can be linked to either lobular or DCIS, and it can also be mixed in with ductal forms of invasive carcinoma.[10]

Medullary Carcinoma

Medullary carcinoma of the breast is a rare subtype of IDC (cancer that starts in the milk duct and spreads beyond it), accounting for just about 3% of all cases of breast cancer. Since it is a soft, fleshy mass that resembles the medulla, a part of the brain, the tumor is referred to as "medullary" carcinoma.

Medullary carcinoma can affect women of any age, but it is most prevalent in their late forties and early fifties. Medullary carcinoma is more common in women who carry the BRCA1 gene mutation. According to research, the incidence of medullary carcinoma is higher in Japan than in the United States.

The presence of medullary carcinoma cells is normally high grade, but their behavior is low grade. To put it another way, they resemble vicious, highly abnormal cancer cells but do not behave like them. Medullary carcinoma grows slowly and seldom spreads to the lymph nodes outside of the breast. As a result, it is usually less difficult to treat than other forms of breast cancer.[13]

Papillary Carcinoma

Papillary breast cancer is a very rare form of invasive ductal breast cancer that affects less than 1% of all women. Papules, or finger-like projections, can be seen when cells are examined under a microscope, hence the term.

The vast majority of papillary tumors are non-cancerous. Papillomas are the medical term for them. Even if a biopsy shows that the tumor is cancer free, the pathologist must still inspect the entire tumor under a microscope to be confident of the diagnosis. This is why despite the fact that a papilloma is benign, surgery to remove it is usually recommended.[14]

Tubular Carcinoma

Invasive ductal breast cancer, also known as tubular breast cancer, accounts for <2% of all breast cancers. Tubular breast cancer, like other forms of invasive ductal cancer, starts in the milk duct of the breast before spreading to the tissues surrounding the duct. When cells in a tubular breast tumor are studied under a microscope, they appear to be tubes, hence the term.

Tubular breast cancer cells are less aggressive than the more common types of invasive ductal cancers. The tumors are normally tiny and low grade, which means they do not divide rapidly and resemble normal cells. Tubular invasive ductal cancer is often

caused by DCIS, or ductal carcinoma *in situ*, which are abnormally dividing cells that have not yet spread beyond the duct.

The estrogen and/or progesterone receptors (ER/PR+) are normally positive in tubular breast cancers, whereas the HER2 receptor is usually negative (HER2–). Tubular breast cancer is less likely to spread to the lymph nodes, is more treatable, and has a better prognosis than other forms of invasive ductal cancer. DCIS, or ductal carcinoma *in situ*, is a form of tubular invasive ductal cancer caused by abnormally dividing cells that have not yet spread beyond the duct.

Adenoid Cystic

Mucin-containing cylinders surrounded by epithelial and myoepithelial cells form a low-grade invasive carcinoma. Myoepithelial involvement is normal only in this form of invasive carcinoma.[10]

Carcinoma with Metaplasia

Despite the fact that metaplastic shift foci are common in IDC, some tumors are almost entirely made up of this growth pattern. The most of these neoplasms occur in postmenopausal women and are circumscribed. Squamous cells, spindle cells, chondroid, osteoid, and even skeletal muscle growth patterns are all examples of metaplasia. In certain cases, only a few foci of detectable DCIS or IDC are evident, making it difficult to distinguish from a primary mammary sarcoma. Immunohistochemistry for high-molecular-weight cytokeratin may be helpful in resolving the situation described above.[10]

Paget's Disease

Paget's disease of the nipple, also known as Paget's disease of the breast, is a rare breast cancer-related disorder. The skin of the nipple and the layer of darker skin around the nipple develop eczema-like changes (areola). In the tissue below the nipple, it is typically a symptom of breast cancer. Paget's disease of the nipple affects 1–4% of women with breast cancer. Men may be affected as well, although this is highly uncommon. Paget's disease of the nipple is used to differentiate the disorder from Paget's disease of the bone (in which the bones become fragile and deformed).[15]

Breast Cancer Stages

Breast cancer is classified into stages depending on the size of the tumor or tumors and how far they have spread. Cancers that are wide and/or have spread to surrounding tissues or organs are in a more advanced stage than those that are small and/or only confined in the breast. Doctors need to know the following information to stage breast cancer:

- Whether the cancer is invasive or noninvasive
- The size of the tumor
- The presence of lymph nodes
- If the cancer has spread to other tissues or organs in the area. Stages 0–5 are the five primary stages of breast cancer.

Breast Cancer in Stage 0

- DCIS is Stage 0 of the disease (DCIS). DCIS cancer cells are limited to the breast ducts and have not spread to surrounding tissue.

Breast Cancer in the First Stage

- Stage 1A: The primary tumor is <2 cm in diameter and lymph nodes are unaffected
- Stage 1B: Cancer has been detected in surrounding lymph nodes, but there is no tumor in the breast or it is <2 cm in size.

Breast Cancer in Stage 2

- Stage 2A: The tumor is <2 cm in diameter and has spread to 1–3 adjacent lymph nodes, or it is between 2 and 5 cm in diameter and has not spread to any lymph nodes
- Stage 2B: The tumor is between 2 and 5 cm in diameter and has spread to 1–3 axillary (armpit) lymph nodes, or it is >5 cm in diameter but has not spread to any lymph nodes.

Breast Cancer in the Third Stage

- Stage 3A: The cancer has spread to 4–9 axillary lymph nodes or swollen the internal mammary lymph nodes, and the primary tumor is any size.
- The cancer has spread to 1–3 axillary lymph nodes or any breastbone nodes and the tumors are larger than 5 cm.
- Stage 3B: A tumor has penetrated the chest wall or skin, with or without invasion of up to 9 lymph nodes.
- Stage 3C: Ten or more axillary lymph nodes, lymph nodes near the collarbone, or internal mammary nodes have cancer.

Breast Cancer in Stage 4

- The tumor size in Stage 4 breast cancer can be any size, and the cancer cells have spread to nearby and distant lymph nodes, as well as distant organs. Your doctor's tests will assess the stage of your breast cancer, which will influence your treatment options.[16]

Risk Factors

The following factors have been linked to an increased risk of breast cancer:

- **Being a woman.** Breast cancer is much more common in women than it is in men
- **Getting older.** As you get older, the chances of developing breast cancer increase
- **A personal experience with breast cancer.** If you've had breast cancer in one of your breasts, you're more likely to get cancer in the other
- **Breast cancer runs in the family.** Your risk of breast cancer is increased if your mother, sister, or daughter were diagnosed with breast cancer at a young age. Despite this, the vast majority of breast cancer patients have no family history of the disease
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- **Inherited genes that increase cancer risk.** Certain breast cancer-causing gene mutations may be passed on from parents to children. BRCA1 and BRCA2 are two of the most well-known gene mutations. These genes will significantly increase the risk of breast cancer and other cancers, but they do not guarantee that you will develop cancer

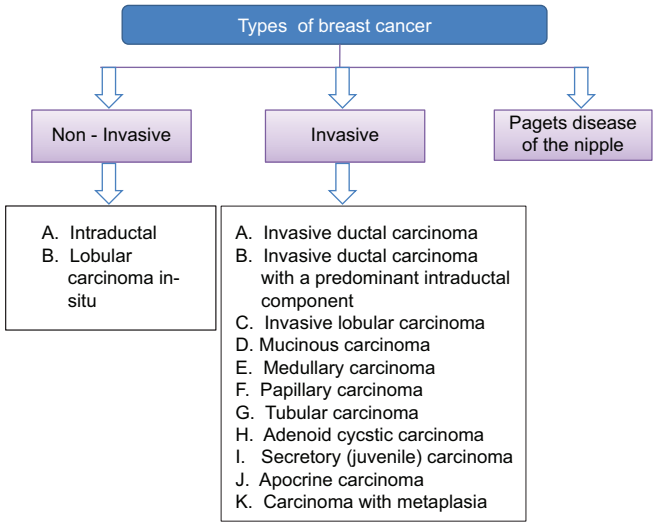

Figure 1: Types of breast cancer

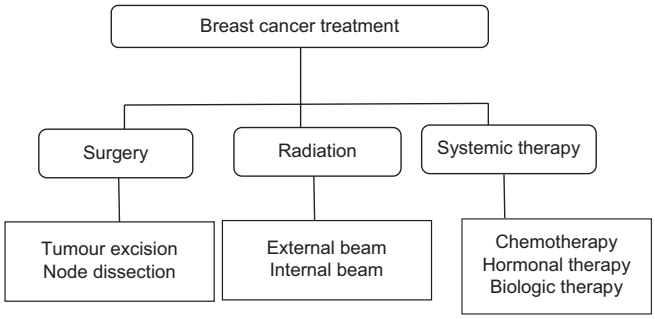

Figure 2: Flowchart of breast cancer treatment

- **Radiation exposure.** Your chance of breast cancer is higher if you had radiation treatments to your chest as a child or young adult
- **Obesity.** Being obese increases your risk of breast cancer
- **Beginning your period at a younger age.** Beginning your period before age 12 increases your risk of breast cancer
- **Beginning menopause at an older age.** If you began menopause at an older age, you're more likely to develop breast cancer
- **Having your first child at an older age.** Women who give birth to their first child after age 30 may have an increased risk of breast cancer
- **Having never been pregnant.** Breast cancer is more common in women who have never been pregnant than in women who have had one or more pregnancies
- **Postmenopausal hormone therapy.** Breast cancer is more likely in women who take hormone therapy drugs that combine estrogen and progesterone to relieve the signs and symptoms of menopause. When women avoid taking these drugs, their risk of breast cancer decreases
- **Drinking alcohol.** Drinking alcohol increases the risk of breast cancer.[17]

Etiology

Scientists are making significant strides in their understanding of how such genetic variations can cause normal breast cells to become cancerous. DNA is a molecule that contains the instructions for almost all of our cells' functions. Since our DNA comes from our ancestors, we normally look like them. However, DNA has an effect on more than just our appearance. Some genes (DNA segments) provide instructions for how our cells divide, expand, and die. Oncogenes are genes that facilitate the division of cells. Tumor suppressor genes are those that delay cell division or trigger cells to die at the appropriate time. DNA mutations (changes) that "turn on" oncogenes and "turn off" tumor suppressor genes are known to cause cancer. Certain inherited DNA variations put people at a higher risk of developing cancer, and they're what's behind the cancers that run in some families.[18]

Although the precise causes of breast cancer are unclear, years of medical studies have identified many risk factors. It is also uncertain why some women with no risk factors develop breast cancer and those with high risk never do. It's best to be on the lookout for warning signs, risk factors, and preventive measures. Genetics and heredity, sedentary lifestyle, late or no pregnancy, use of oral contraception, early start to menstruation, late menopause, excessive drinking, smoking, rising obesity among young people, stress, and low dietary intake are all risk factors for breast cancer. These factors have been linked to an increase in the incidences of breast cancer among young Indian women.

Unfortunately, there is still no way to fully remove breast cancer risk. We have little influence over risk factors such as hereditary variations in some genes (BRCA1 and BRCA2), family history, and so on. If your mother or sister has a family history of breast cancer, get a cancer tumor marker performed on a regular basis or as directed by your doctor. However, we can lessen its effect by detecting it as soon as possible. The best protection against breast cancer is early detection.[19]

Diagnosis

- Changes in the breasts, such as the appearance of a lump, changes to the nipple, discharge from the nipple, or changes in the skin of the breast, are the most common signs of breast cancer.
- A physical examination, mammography, and ultrasound scan are the first steps in diagnosing breast cancer. Breast magnetic resonance imaging may be used in some cases. If a tumor is discovered, a biopsy will be performed to determine the extent of the cancer before any therapy is considered.[20]

Treatment

Breast cancer treatments are getting better all the time, and people have many more options today than ever. With so many choices, it's a good idea to learn as much as you can about the ones that can help you the most. All breast cancer treatments have two main goals:

- To rid your body of as much of the cancer as possible
- To keep the disease from coming back In Figure 2, several types of breast cancer treatment are listed.
- Treatment for breast cancer is determined by how far the cancer has progressed (Stage 0 IV) and the type of cancer present
- Breast cancer is treated with surgery, radiotherapy, chemotherapy, and systemic therapy
- According to the TNM scheme (T – tumor, N – nodes, and M – metastases), breast cancer is "staged" based on tumor size,

lymph node involvement, and if it has spread beyond the breast and lymph nodes to other sections of the body. These data are used to help determine the appropriate care option.

Conclusion

In the past decade, breast cancer has become one of the most common and increasing malignant diseases among Indian women. Breast cancer is a disease that affects the patient, their families, and their culture, as well as wasting a lot of money and spiritual energy. This cancer develops in the tissues of the breast, including the ducts (tiny tubes that hold milk) and lobules (milk producing glands). Breast cancer is not gender specific, but it affects men infrequently. While there is no definitive cause for breast cancer, specific risk factors have been reported. There are various risk factors for different forms of cancer. Any of these risk factors, such as cigarette smoking, alcohol consumption, and diet, are modifiable and dependent on one's lifestyle. Other variables, such as age, race, gender, and family background, are, on the other hand, fixed and unchangeable. It is not necessary to have one or more of these risk factors to be infected. Today, there are a variety of options for treating breast cancer, including surgery, radiation therapy, chemotherapy, and hormone therapy.

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