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# Systemic Therapies Used To Treat Breast Cancer Including Chemotheraphy, Hormone Theraphy, and Targeted Therapy: A Review

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**ABSTRACT**:Breast cancer is a major global health concern. For women, breast cancer is the second most common cause of cancer. A metastasized breast cancer is one that has spread to other areas of the body. There are five stages of Breast cancer from stage 0 to stage 4. The most common therapies for breast cancer include chemotherapy, surgery, endocrine (hormone) therapy (ET), radiation therapy (RT), and targeted therapy. Despite developments in cancer treatment tactics over the last few decades, chemotherapy is still regarded as the primary method of cancer treatment. Risk factors are age, blood group, personal history, Breast pathology,Genetic predisposition. Breast cancer examination (BCE), Clinical breast examination (CBE) and mammography are the three screening methods. When comparing the incidences of states with lesser incidences to those in Arunachal Pradesh, Mizoram, Meghalaya, Tripura, and Manipur have 18%, 26%, 57%, and 233% more cases, respectively.

**KEYWORDS:** Breast Cancer, Breast cancer examination, Chemotherapy, Mammography, Non-invasive and invasive breast cancer.

## I. INTRODUCTION:

Worldwide, breast cancer is a serious health issue [(1)]. Breast cancer is the second major cause of cancer among women. Where the breast cancer spreads to other parts of the body it is said as a metastasized. Experiments using animal and cell models have demonstrated the potential of probiotics as a functional food to prevent breast cancer. By modifying the gastrointestinal flora and the systemic immune system, probiotics may be helpful in the prevention or treatment of breast cancer [(2)].

Cancer treatment in its early stages is less expensive and more effective, with far better outcomes. Thus, early detection can result in an increase in survival chances [(3)]. Screening is looking for signs of disease before person had symptoms. Screening is looking for signs of disease before person had symptoms. Knowledge, attitude and practice on screening methods required to aid in the early detection of breast cancer. Treatment outcomes for late-stage breast cancer are low because lack public knowledge. The probability of surviving breast cancer detected by stage 1 and represents 85% however in the late diagnosis it is just 10%. Thus, the stage 4 is complete is complete regular checkups and early warning indicators breast can aid in early diagnosis management illness [(1)].

Breast cancer examination (BCE), Clinical breast examination (CBE) and mammography are the three screening methods. Breast cancer screening means that the examing a women's breast for cancer before symptoms appear. Breast cancer cannot be avoided with screening, when breast is easier to treat, it can help discover it faster. BCE is done at home by women on their own. It is non-invasive and only takes 5mins.The two fundamental components of breast self-examination are visual examination when standing and tactile examination while either lying down or standing. those who are menstruating should have this examination done often, ideally five days after each cycle, and those who have gone through menopause should also have it done on a designated day once a month [(4)].

CBE is done by doctors to identify the irregularity. In mammography low energy X rays are used. It is commonly recognized that mammograms an be utilized as screening tools, but for this is ton successful women must right information and mindset.Mammography is widely regarded as the most effective and dependable screening procedure for detecting breast lesions in their early stages [(1,22)]. Recent years are seen an increase of breast cancer and the availability of more information about it, which has led to higher number of women seeking medical attention relatively early, even with mild symptoms.All age groups of females are affected by breast cancer, with the exception of children. While the majority of occurrences occur in the fifth and sixth decades of life, the incidence rate typically rises with age [(5)].

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Breast cancer risk is factor to be influenced by a number of factors which age, family historyand reproductive factors are the strongest factor and the most major risk factor is not physically active, being overweight, drinking alcohol. The two most important elements influencing women's motivation to prevent, identify & treat breast cancer early and their awareness of disease risk factors [4,10]. However, it has also been found that one significant factor that may discourage women from taking part in breast cancer screening is a lack of awareness about the disease and its factors. When used with other screening methods mammography can reduce the death rate from breast cancer by approximately 20-30% in women aged 50-60 & slightly less in those aged 40-49. This decrease in mortality is probably caused by a number of factors, including earlier diagnosis, which has been made possible in great part by mammography screening, and the availability of new and better therapies. [4,6]

Men are capable for breast cancer but 100 times more of the women frequently. Guidelines for low-income countries and the WHO stressed that the national program to prevent breast cancer should support early detection of disease, particularly for women between ages 40-69 who are visiting primary care facilities or hospitals for other reasons. This can be achieved by providing clinical breast exams to individuals who are self conscious about their breast and raising community awareness Due to the more severe outcomes that young women and adolescents face, early diagnosis and awareness-based BC prevention are essential. [7]

It is a highly fatal disease especially when diagnosed early detection of disease is associated with better prognosis. In Egypt majority of the cases will be detected in last stage about 60% of cases detected by 3rd stage of disease limited treatment options and high fatal rate. Due to high incidence of Egyptian women's KAP about BSE which has been shown to diagnose breast cancer early and improve prognosis [8]. Around 60% of the middle-class people survived with BC compared to less than 40% of people in low-income countries. When we looked at comparing various Indian states found that up had almost 125% more incidence case of Tamil Nadu. In comparison to Tamil Nadu, Maharashtra, West Bengal, and Bihar were found to have increases of approximately 55%, 15%, and 5%, respectively. When comparing the incidences of states with lesser incidences to those in Arunachal Pradesh, Mizoram, Meghalaya, Tripura, and Manipur have 18%, 26%, 57%, and 233% more cases, respectively [9].

However, when comparing the mean age of menarche in these states to Uttar Pradesh, increases were noted in the same study, with mean ages increasing by almost 8% in Himachal Pradesh, 2.2% in Maharashtra, 1% in Haryana, and 0.64% in Delhi. When compared to the mean age at menarche in Arunachal Pradesh, enhancements of 0.83 percent were found in Assam, 7.5% in Andhra Pradesh, and 8.3 percent in Jammu & Kashmir and Manipur [9].

Breast cancer risk rises with age. The illness affects older women more than younger women, who are less likely to get it. More than 80% of breast cancer cases occur in women over the age of 50, and 40% of breast cancer patients are over the age of 70[10]. Although early identification is critical, many women may not have proper health-related attitudes toward this condition and do not participate in screening programs, particularly in poor countries. Many studies have indicated that cancer awareness is an essential risk factor for early identification of breast cancer [11].

Growing aging populations and the introduction of lifestyle factors linked to an increased risk of breast cancer such as obesity, excessive eating of junk food or unhealthy meals, and use of dangerous substances have resulted in an increase in the prevalence of breast cancer in emerging countries[12].Several factors have been identified as influencing the likelihood of developing breast cancer are not physically active, being overweight, some forms of hormone replacement therapy taken during menopause, drinking alcohol. The strongest risk variables are age, family history, and reproductive factors. Lifestyle and hormonal risk factors have also been identified [13].Breast cancer is linked to reproductive characteristics such as early menarche, late menopause, and late age at first childbirth [14].

Breast cancer prevalence is increasing in developing countries as the population of senior individuals grows [15].It is the most frequent cancer in women in Delhi, Mumbai, Ahmedabad, Kolkata, and Trivandrum, according to National Cancer Registries and Regional Cancer Centers [16].Breast cancer mortality has decreased in developed nations due to the widespread use of screening mammography as a standard of therapy. While breastfeeding, physical activity, and maintaining a healthy body weight all help to reduce the risk [17].However, in developing countries such as Bangladesh, particularly in rural regions where access to CBE and mammography is limited, BSE appears to be a viable technique to detecting breast cancer early enough for mass treatment. Patients with breast cancer in Bangladesh and other underdeveloped nations typically present late and at

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an advanced stage, resulting in a dismal prognosis [18].

Around 20-30% of women wait 12 weeks or longer following self-discovery of a breast symptom before seeking treatment from a health-care provider, and such delays may result in poor survival [19].Breast cancer survival rates vary greatly over the world, with estimates ranging from 80% in high-income countries to less than 40% in low-income ones. Clinicians are increasingly interpreting preoperative therapy response to modify surgical options and the requirement for post-operative care. New targeted medicines are being developed for physiologically defined cancer subgroups [20].

Early-stage breast cancer is a heterogeneous illness, and optimum treatment is dependent on morphological and molecular characterization of the tumor subgroup to define tumors as estrogen receptor (ER) positive or negative, HER2-positive or negative, or, by default, triple negative.Following breast conserving surgery, total breast irradiation remains the usual therapy prescription for best results. Following breast conservation, the Panel advised hypofractionated radiation treatment schedules for the majority of patients [21].A tiny fraction (4.3%) of all diagnosed tumors were stage 0 (in situ) and fewer than one-third (27.8%) of breast cancer cases were stage 1 (localized).Women in developing nations have a higher mortality rate due to a lack of education and late-stage diagnosis [22].

The epidemiology of breast cancer in several Population Based Cancer Registries (PBCRs) in India reveals growing trends in incidence and mortality, owing mostly to fast urbanization, industrialization, population expansion, and increasing age.Every woman should be aware of how her breasts naturally appear, according to the American Cancer Society's recommendations for Early Detection of Breast Cancer. They should be aware of their shape, size, and look so that she can detect any changes that may be an early symptom of breast cancer [23].

A study of young undergraduate ladies from 23 nations discovered that they had less knowledge of breast cancer risk factors than older women.This demands the study's focus on young girls (15-35 years), as this age group is both at the highest risk of mortality from aggressive breast disease and has the greatest potential of benefiting from early detection therapies such as breast self-examination [24].Every year, around 700,000 cases are recorded worldwide, with poor nations accounting for 57% of these instances.Breast cancer awareness is not widely documented in poor nations, and what is known is not encouraging [25].

## TYPES OF BREAST CANCER:

### According to site:

- **Non-invasive breast cancer:** Cells that are restricted to the ducts and do not penetrate the breast's fatty and connective tissues. DCIS is the most frequent type of non-invasive breast cancer (90%). Lobular carcinoma in situ (LCIS) is less common and is regarded as a risk factor for breast cancer.
- **Invasive breast cancer:** Cells that infect the surrounding fatty and connective tissues of the breast after breaking through the duct and lobular walls. Cancer can be invasive without metastasis to lymph nodes or other organs.

### Frequently occurring breast cancer:

Lobular carcinoma in situ: LCIS is characterized by a significant increase in the number of cells within the milk glands (lobules) of the breast. **Ductal carcinoma in situ:** DCIS, the most frequent type of non-invasive breast cancer, is restricted to the breast ducts [26].

## RISK FACTORS OF BREAST CANCER:

### Age:

Age is the second most important known risk factor for breast cancer after gender. Breast cancer incidence rates grow considerably with age, peaking at menopause and then gradually decreasing or remaining constant.31 In a case-control study, age more than 50 years was linked to an increased risk of breast cancer [27].

### Blood group:

Because women with blood group A and Rhesus positive have a higher risk of having breast cancer, whereas women with blood group AB and Rhesus negative have a lower risk of developing breast cancer [27].

### Personal history:

Personal breast cancer history is also a substantial risk factor for developing a second ipsilateral or contralateral breast cancer. In fact, metachronous contralateral breast cancer is the most prevalent cancer among breast cancer survivors. An initial diagnosis of DCIS, stage IIB, hormone receptor negative tumours, and young age are all related with an increased chance of developing a second breast cancer [20,28].

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**Breast pathology:**

Personal breast cancer history is also a substantial risk factor for developing a second ipsilateral or contralateral breast cancer. Breast cancer risk is higher in those with proliferative breast disease. Proliferative breast lesions without atypia, such as typical ductal hyperplasia, intraductal papilloma, sclerosing adenosis, and fibroadenomas, confer only a minor increase in the chance of developing breast cancer, about 1.5-2 times that of the general population [20,28].

**Genetic predisposition:**

Although 20%-25% of breast cancer patients have a favourable family history, only 5%-10% of breast cancer cases show autosomal dominant inheritance.Half of the breast cancer risk syndromes are linked to BRCA1 and BRCA2 mutations. Women who have detrimental BRCA1 or BRCA2 mutations are at a greatly increased risk of getting breast cancer. For BRCA1 mutant carriers, the lifetime risk of breast cancer ranges from 65% to 81%, while for BRCA2 mutation carriers, the risk ranges from 45% to 85% [20].


Figure:1 Protective factors of breast cancer [28]

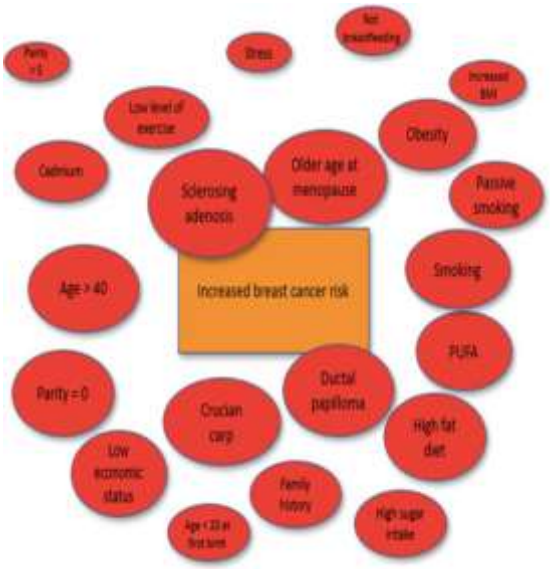


Figure:2 Risk Factors for Breast Cancer [28]

**STAGES OF BREAST CANCER:**

Breast cancer treatment is determined by the size and type of tumour, as well as how deeply the malignant cells have infiltrated the breast tissues. Stage 0 tumours are non-invasive, whereas stage 4 tumours are invasive.

**Stage 0:**

This is a non-invasive stage of tumour that indicates that both cancerous and non-cancerous cells are within the boundaries of the part of the breast where the tumour begins to grow and there is no evidence of their invasion in the surrounding tissues of that part; ductal cell carcinoma in situ (DCIS) is an example of this tumour stage.

**Stage 1:**

It is divided into two stages: 1A and 1B. Stage 1A refers to a tumour that is up to 2 cm in size and does not involve any lymph nodes, whereas stage 1B refers to a small group of cancer cells larger than 0.2 mm that are identified in lymph nodes.

**Stage 2:**

Stage 2 also has two categories: 2A and 2B. Stage 2A represents a tumour identified in axillary or sentinel lymph nodes but not in the breast. The tumour can be less or larger than 2 cm, but not more than 5 cm. Stage 2B indicates that the tumour is larger than 5 cm but cannot reach the axillary lymph nodes.

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**Stage 3:**

It has been classified into three subcategories: 3A, 3B, and 3C. Stage 3A describes that no tumour is found in the breast but it can be observed in 4-9 axillary lymph nodes or in sentinel lymph nodes, whereas stage 3B indicates that the tumour can be of any size but has caused swelling or ulcer on the skin of the breast and can have spread up to 9 axillary lymph nodes or to sentinel lymph nodes. Stage 3B is an indication of inflammatory breast cancer because it includes red, warm, and swollen skin. Stage 3C describes tumour progression to 10 or more axillary lymph nodes, as well as lymph nodes above and below the collarbone.

**Stage 4:**

This is the advanced and metastatic stage of cancer, and it explains the spread of cancer to other organs of the body such as the lungs, bones, liver, brain, and so on. [29]

**TREATMENT OF BREAST CANCER:**

The most common therapies for breast cancer include chemotherapy, surgery, endocrine (hormone) therapy (ET), radiation therapy (RT), and targeted therapy. Despite developments in cancer treatment tactics over the last few decades, chemotherapy is still regarded as the primary method of cancer treatment. [30]

Natural products are a valuable source of inspiration for the creation of innovative anti-tumor medications. Currently, botanical sources provide more than half of the current anticancer medicines. A variety of commonly used anticancer therapies are derived from natural sources, including irinotecan, vincristine, etoposide, and paclitaxel from plants, actinomycin D and mitomycin C from bacteria, and marine-derived bleomycin. Some of these chemicals are still used in cancer therapy and will continue to play an important role for the foreseeable future. Among these, camptothecin and Taxol are likely the two most effective examples, both of which were uncovered between 1950 and 1960 in a program undertaken by the National Cancer Institute (NCI) to identify therapeutic properties of natural chemicals. [31]

**Radiation therapy:**

Radiation therapy for breast cancer patients is a complex and ever-changing treatment [32]. Radiation treatment uses high-energy X-rays or gamma rays to target a tumour or post-surgical tumour location. These radiations are extremely efficient in eliminating cancer cells that may linger after surgery or return where the tumour was excised. In addition to this treatment, implanted radioactive catheters (brachytherapy), similar to those used to treat prostate cancer, can be employed. However, electron beam radiation to the breast scar has overtaken this therapeutic strategy. Radiation treatment for breast cancer is often administered following surgery and is an essential component of breast-conserving therapy. The radiation dose must be high enough to eliminate cancer cells completely. Treatments are normally administered for five to seven weeks, five days a week. Each therapy lasts roughly 15 minutes [26,32].

**Chemotherapy:**

Chemotherapy is a conventional approach used to treat several forms of cancer. Many breast cancer patients are discovered in the middle or late stages, limiting their ability to have surgery [33]. Chemotherapy uses anti-cancer medications to treat malignant cells. Specific therapy for breast cancer will be determined by factors such as overall health, medical history, age (whether or not menstruation occurs), kind and stage of the disease, tolerance for specific drugs and treatments, and so on. Chemotherapy treatments are sometimes administered in cycles, with one treatment followed by a period of recuperation before the next. Chemotherapy can be used before surgery to decrease the tumour and, in some cases, allow for breast saving surgery instead of a mastectomy. It is frequently administered following surgery and may be given every three or two weeks in a "dose dense" method [26,33]. Exercise training may be a useful non-pharmacological technique for reducing cognitive difficulties following (breast) cancer therapy. Whereas many therapies, such as cognitive rehabilitation techniques, address the symptoms of cognitive decline, exercise training may influence the underlying processes [34].

**Surgery:**

Depending on the stage and kind of tumour, a lumpectomy (removal of only the lump) or a mastectomy (surgical removal of the entire breast) is done. Standard practice requires the surgeon to ensure that the tissue taken during the surgery has cancer-free margins, suggesting that the malignancy has been thoroughly excised. Additional procedures to remove additional tissue can be required if the excised tissue lacks distinct borders. The pectoralis major, the primary muscle of the anterior chest wall, may occasionally need to be partially removed in order to accomplish this. Sentinel lymph node (SLN) dissection is a

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procedure that has gained popularity recently since it involves the removal of considerably fewer lymph nodes, resulting in less adverse effects. Over the last ten years, advances in sentinel lymph node mapping have improved the accuracy of sentinel lymph node detection from 80% when using blue dye alone to 92%–98% when employing mixed modalities. With the goal of providing the greatest oncologic care and enhancing women's quality of life, axillary surgery has developed over time. Sentinel lymph-node biopsy (SLNB) has taken the role of axillary lymph-node dissection (ALND) in women with early-stage clinically node-negative breast cancer. SLNB offers sufficient axillary nodal staging information with little morbidity and is quickly becoming the gold standard in breast cancer care [26,35].

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