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AN OVERVIEW OF BREAST CANCER

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ABSTRACT

The second most frequent cancer and the most common cause of cancer mortality is breast cancer. In 2002, it accounted for more than 1 million new cases and was the most prevalent cancer globally. Breast cancer is a complicated condition, and treatment guidelines are always evolving. Regarding the prognosis' impact on therapy and survival as a whole, there is a great deal of worry and concern. Breast cancer is a complicated condition, and treatment guidelines are always evolving.. This review cover the , treatments, and diagnostics. screening, which over the past few years has progressively decreased the death rate from breast cancer. This article's objective is to emphasise the prevalence, stages, therapies, and diagnosis , preventative measures, survivorship, and treatments include surgery, hormonal therapy, and chemotherapy

KEY WORDS : Epidemiology of breast cancer , imaging techniques for screening breast cancer, types of breast cancer, treatments, diagnosis.

INTRODUCTION

Cancer is one of the leading causes of death globally. Breast cancer is the most frequent malignancy in women and one of the leading causes of mortality in this population. Breast cancer is a complex disease that is caused by a variety of causes. Although the illness occurs globally, the incidence, mortality, and survival rates vary significantly around the worldwide, which might be attributable to a

variety of variables such as population structure, lifestyle, genetic factors, and environment[1] Despite the emergence of targeted medicines that have improved significantly mortality, effective breast cancer assessment remains difficult owing to the disease's complexity.. Cancer develops when normal cells become crowded by out-of-control body cell growth and abnormal cell division. Additionally, cancer cells have the capacity to outgrow their original tumour and may even separate from it, allowing the disease to spread though the specific organ invasion, lymphatic system spread, and/or circulatory system spread (Merkle & Loescher, 2005). Metastasis is the term for this process, which can happen at the diagnosis stage or after a patient has been disease-free follow therapy. Breast cancer is a carcinogenic tumour that develops from breast tissue cells and predominantly affects women, however it can also affect men. However, some women experience the development of benign or noncancerous breast lumps, which are abnormal benign tumors that do not extend beyond the breast and are not life-threatening but raise a person's risk for breast cancer. [2]

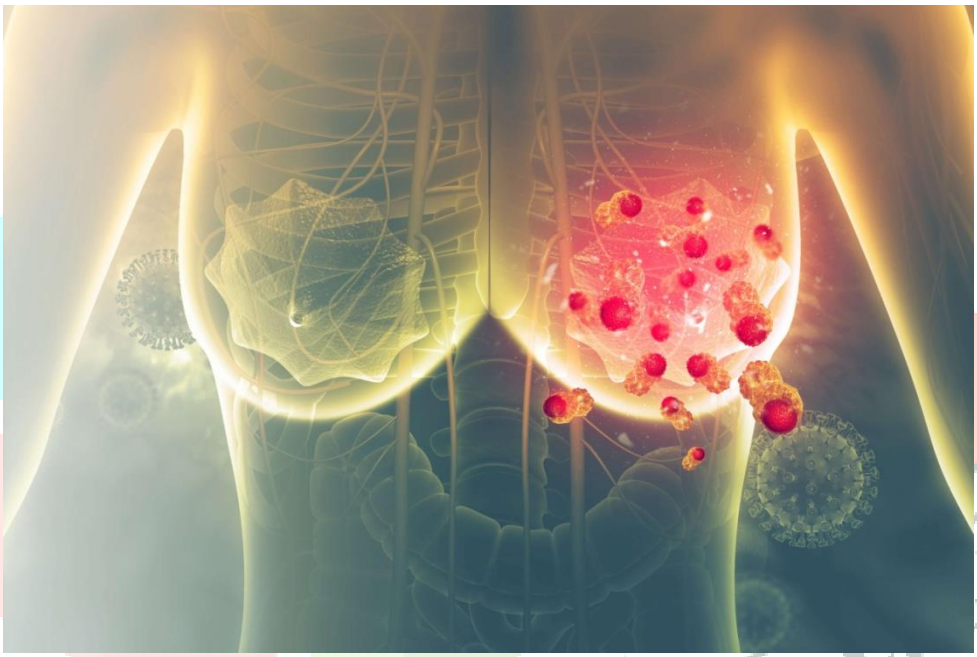

FIG 1 : BREAST CANCER

STAGES OF BREAST CANCER

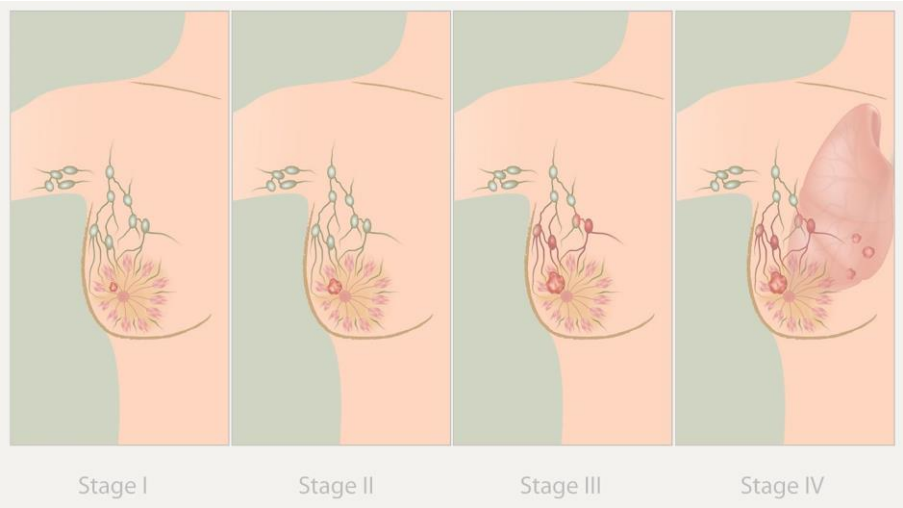

FIG 2 : STAGES OF BREAST CANCER

STAGE : The cancer cells have spread to the nearby breast tissue

STAGE II The tumour is either less than 2 centimetres in diameter and has migrated to the underarm lymph nodes, or it is more than 5 centimetres in diameter but has not spread to the underarm lymph nodes. Tumors at this stage can range in size from 2 to 5 cm in diameter and might or might not influence the surrounding lymph nodes.

STAGE III The cancer has already spread past its origin site at this time. It could have expanded to neighbouring lymph nodes and tissue, but it hasn't reached distant organs. Breast cancer at stage III is typically referred to as locally progressed[3].

STAGE IV The malignancy has spread to various parts of your body, including your bones, liver, lungs, and brain. Breast cancer at stage IV is also characterized as metastatic breast cancer.[4]

TYPES OF BREAST CANCER

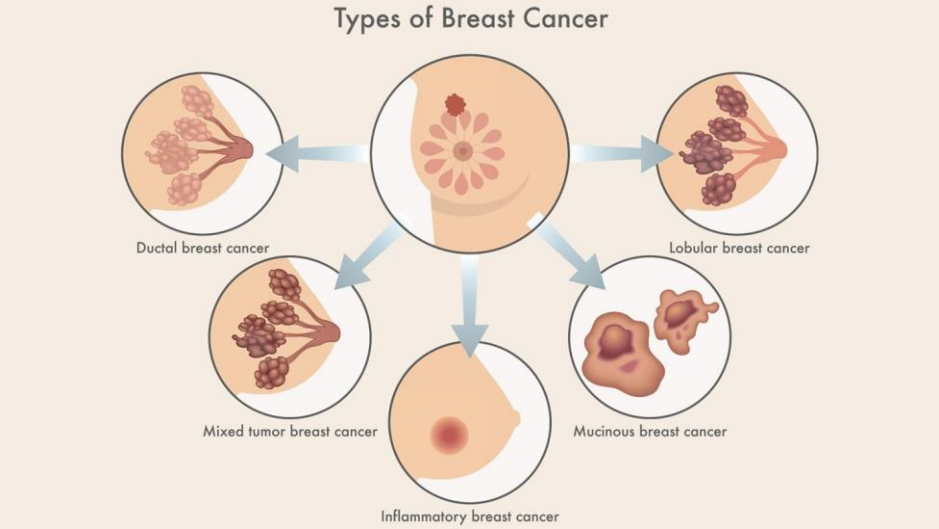

FIG 3 : TYPES OF BREAST CANCER

DUCTAL BREAST CANCER

DCIS [Ductal carcinoma in situis] a growth of malignant cells that do not penetrate the basement membrane of the breast ducts. DCIS is a risk factor for infiltrating ductal carcinoma of the breast (IDC). A significant majority of people with IDC have DCIS as well. According to the research, the percentage of DCIS cases related with invasive cancer ranged from 21.3% to 76.9%.[5] The prevalent hypothesis of mammary carcinogenesis is a series of pathologically defined phases beginning with atypical ductal hyperplasia (ADH) and advancing to pre - malignant ductal carcinoma in situ (DCIS), a non-obligate precursor of the final stage, invasive breast cancer (IBC) near to 70% of women with pure DCIS (pDCIS) are treated with lumpectomy in conjunction with radiation and antihormonal therapy, and that only a minority (15–30%) of pDCIS patients to develop a subsequent breast tumour within the first decade after lumpectomy alone, it is likely that many pDCIS patients are receiving overtreatment.[6] The impact of diagnosing and treating DCIS, particularly for any specific woman, is unclear because it is unknown what percentage of untreated DCIS may develop into invasive breast cancer. In these circumstances, treating certain DCIS lesions would be viewed as beneficial since it would likely halt the spread of the disease and, as a result, would lower the death rate for breast cancer. However, certain lesions may be indolent and not respond to treatment, leaving only side effects from the treatment (representing overdiagnosis and overtreatment)[7]

MIXED TUMOR BREAST CANCER

According to data from the Global Cancer Survey, China has the sixth-highest mortality rate for female malignant tumours and breast cancer has the greatest incidence of malignant tumours among women globally, accounting for 15% of all malignant tumour fatalities[8] Breast cancers are not just collections of rapidly developing cells. Instead, they coexist with a variety of naturally occurring and artificially introduced non-cancerous cells, including immunological, fibroblastic, and endothelial cells. The extracellular matrix

proteins that are insoluble and the soluble substances that these cells release together make up the tumour microenvironment (TME)[9] DCIS is a pre-invasive lesion of tumor cancer cells within the breast duct which are separated from either the surrounding stroma by a near-continuous layer of myoepithelium and basement membrane proteins. This histologic trait is the fundamental feature that separates DCIS from invasive breast cancer (IBC), in which this barrier is missing and tumour cells are in direct contact with stroma.[10]

INFLAMTORY BREAST CANCER

An aggressive and lethal subtype of breast cancer is inflammatory breast cancer[11] IBC accounts for 2-5% of all invasive breast cancers and has a poorer prognosis when compared to non-IBC. The standard treatment method for patients who have newly diagnosed nonmetastatic disease is trimodality therapy, which consists of neoadjuvant systemic therapy followed by total mastectomy and radiotherapy, followed by endocrine therapy when indicated.[12] 90% of local breast cancer relapses happen in the original tumor's quadrant, suggesting that the tumor's own cancer cells and/or dormant cancer stem cells (CSCs) could be to responsible for the tumor's recurrence.[13] IBC is a diverse illness with molecular manifestations, according to histomorphology. Additionally, molecular subtypes seen in IBC include luminal, basal, and HER2-positive types (Bertucci et al., 2010). Despite the fact that all of the molecular subtypes, including the triple-negative breast cancer (TNBC), HER2-positive, and hormone receptor (HR)-positive subtypes, are present in both non-IBC and IBC, the ratios of these subtypes varies.[14]

MUCINOUS BREAST CANCER

A significant amount of extracellular mucins are the main symptom of the uncommon and rare breast cancer known as mucinous breast cancer (MBC). Of all initial breast cancers, it accounts for 1%–6%. MBC is more common and more likely to survive in postmenopausal women. Human epidermal growth factor receptor 2 expression was shown to be lower in MBC than in healthy controls, according to earlier studies. Due to its uncommon occurrence, MBC differs from common breast cancers in general in terms of its clinical, histopathological, and biological characteristics. Additionally, there aren't many reports of large sample studies on MBC, which puts patients at risk for receiving either insufficient or excessive treatment. Multiple factors all work together to affect the prognosis of MBC.[15] Mucinous cancers are of luminal A molecular subtype, according to transcriptomic studies. The gene expression patterns of mucinous Breast tumours are comparable to those of neuroendocrine carcinomas, while the transcriptome characteristics of mucinous A tumours are unique from those of mucinous B tumours.[16] The two main subtypes of mucinous breast carcinoma, the pure type and the mixed type, are distinguished by the presence of a significant quantity of extracellular mucin . The measurement of cellularity serves as the basis for the differentiation between these kinds. A tumor's mucoid component can make up 30% to 90% of the tumour.[17]

LOBULAR BREAST CANCER

Approximately 15% of cancers diagnosed are breast carcinomas (BC). They have an infiltrative development pattern, which makes them challenging to identify both clinically and radiologically. With dissemination to the serosal surfaces, retroperitoneum, GI/GU tracts, and a greater incidence of leptomeningeal spread than IDC, the pattern of metastasis of LC is uncommon.[18] The CDH-1 gene on chromosome 16q22, which codes for E-cadherin, is assumed to be the main mediator for the lobular breast cancer(LBC). E-cadherin is a

calcium-dependent transmembrane protein that promotes cell-to-cell adhesion, preserves tissue integrity, and inhibits tissue invasion. The E-cadherin gene serves as a tumour suppressor gene as a result of these actions, which hinder tumour invasion[19] ILC is characterised by the concentric expansion of tumour cells around pre-existing breast structures, often known as the "targetoid pattern," or the infiltrative proliferation of dyscohesive cells in a single file (WHO classification of Tumours 5th edition, breast tumours 2019)[20]

EPIDEMIOLOGY OF BREAST CANCER

Breast cancer is one of the most prevalent malignant tumours in the world, accounting for 10.4% of all cancer cases and the main cause of mortality for females between the ages of 20 and 50, yet there are still regional variations across other nations. When compared to the United States and other European nations, Asian nations like China and Japan have lower breast cancer death rates. Further evidence that environmental variables and lifestyle choices may be crucial in the aetiology of breast cancer comes from the fact that persons from low mortality regions experience an increase in breast cancer incidence and death when they move to nations with higher rates.[21] Some occurrences of breast cancer have been linked to genetic variations and mutations in genes that code for proteins involved in DNA repair pathways and the homologous recombination of DNA double strand breaks (APEX1, BRCA1, BRCA2, XRCC2, XRCC3, ATM, CHEK2, PALB2, RAD51, XPD).[22] Numerous epidemiological studies have been conducted on the risk factors for breast cancer, but it is challenging to compile a comprehensive analysis because the identified risk factors interact and differ depending on whether the cancers develop before or after menopause and depending on their histological, biological (receptors), or molecular characteristics. Additionally, their frequency changes over time and between different regions[23] The three main types of important risk factors for breast cancer are reproductive (hormone exposure), genetic, and environmental. Since very few risk variables may be easily changed, epidemiology is crucial in identifying high-risk patient populations and designing efficient screening procedures.[24]

TREATMENT OF BREAST CANCER

I]SURGERY

During an operation, the tumour and some surrounding healthy tissue are removed. Surgery is frequently performed to evaluate the axillary lymph nodes, which are located beneath the arm. A surgeon oncologist is a specialist who specialises in the surgical treatment of cancer. Discover more about the fundamentals of cancer surgery. The type of surgery you choose has no bearing on whether you will require medication-based therapy such as chemotherapy, hormone therapy, and/or targeted therapy (see below). Drug therapy are prescribed depending on the features of the tumour rather than the sort of surgery you have had.[25]

II]NEOADJUVANT CHEMOTHERAPY

NAC was first used to make locally advanced, incurable breast cancer operable. NAC has lately been utilised to downstage illness in the breast and axilla in operable tumours with the goal of aiding breast conservation and, in some cases, preventing ALND. Numerous randomised trials have examined NAC's oncologic safety and comparable survival results. 78–80 No changes in survival or LRR have been seen between patients treated with NAC vs surgery followed by chemotherapy, and the number of mastectomy procedures performed in NAC patients has decreased by 17%. 81percent is a low estimate since many of the women who participated in these trials were BCT candidates at presentation and so were not eligible for NAC[26].

Chemotheray is commonly given to people with operable breast cancer after surgery. Preoperative chemotherapy may offer some advantages for women with big operable tumours. Several studies53,58 have found that almost 90% of primary operable tumours shrink by more than 50% following chemotherapy, making lumpectomy a viable option for many women who would otherwise require a mastectomy.[27]

III]HARMONAL THERAPY

Beatson discovered breast cancer regression following oophorectomy in 1896, which was the first indication of cancer cell reliance on endogenous signalling pathways. 7 Continued surgical study into adrenalectomy and hypophysectomy revealed tumour shrinkage, although with significant morbidity. As a result, the early use of endocrine treatment (now known to be the template for targeted therapy in breast cancer) was hampered by the absence of a recognised target. The identification of the estradiol/estrogen receptor (ER) and progesterone receptor (PR) signalling pathways resulted in the creation of medicinal therapies used to treat both advanced and localised breast cancer.[28]

IV]NOVEL THERAPIES

Through genetic changes in the ER and/or activation of other signalling pathways, metastatic HR+ BC may become resistant to conventional hormone treatments. As a result, new drugs are being created with the goal of breaking hormone therapy resistance.[29]

V]RADIATION THERAPY

In the context of breast-conserving therapy, postoperative radiation therapy increases disease-free and overall survival for patients with early breast cancer and lymph node involvement, either by eradicating recurrent tumour cells158,159 or by inducing an abscopal effect160. With a dose-effect relationship for local control161, the proportionate decrease of locoregional recurrences with radiation treatment after surgery is, in most cases, 75%. The advantages of any recurrences, including distant metastases, however, demonstrate a complicated interplay with the risk factors of the underlying tumour and the efficiency of the adjuvant systemic therapy162. Endocrine therapy, chemotherapy, and targeted therapies are examples of primary or adjuvant systemic treatments that may be recommended based on risk factors for the emergence of distant metastases.[30]

IMAGING TECHNIQUES FOR SCREENING BREAST CANVER

Imaging methods are mostly used for breast cancer screening, including mammography, ultrasound (US), and magnetic resonance imaging (MRI). The table below provides a summary of these imaging methods' characteristics, benefits, drawbacks, and performance.[31]

Technique	Current recommendations	Advantages	Disadvantages	Sensitivity (%)	Specificity (%)	Recall rate (%)	PPV (%)	Cancer detection rate (per 1000)
Mammography	Recommended for women who have reached the initial age for breast cancer screening	Convenient; economical; sensitive to microcalcification	Insensitive to high density breasts and deep lesions	69.0–86.0	57.0–96.6	3.5–4.0	13.0–22.9	3.2–7.1
DBT	Recommended, particularly for women with dense breasts, replacing DM	3D imaging, reducing tissue overlay	Greater radiation dose, examination time and cost	82.6–89.0	72.0–97.6	3.1–3.9	20.7–21.4	4.6–9.4
CEM	Recommended for women at high risk	Vascular functional imaging	Use of contrast agents; greater radiation dose	87.5–92.7	67.9–93.7	–	11.9–20.9	13.1–15.5
Ultrasound	Recommended, particularly for women with dense breasts, and pregnant and lactating women	Noninvasive; real-time; no radiation; elastography; identification of cystic and solid masses	Dependent on technologist experience; insensitive to lesions without clear mass	80.0–90.6	81.0–94.5	4.1–6.9	3.0–6.6	4.4

ABUS	Recommended, particularly for women with dense breasts, and pregnant and lactating women	Less dependent on technologist skill; reproducible	Unable to assess the axillary lymph node status	67.6–99.8	74.6–91.6	1.5–13.5	4.1–5.4	1.8–15.1
MRI	Recommended for women at high risk	Most precise identification of soft tissue; reflects both the anatomical structure and lesions; displays small lesions, multifocal lesions, and lesions located deep in the tissue	Insensitive to calcification; expensive; long examination time; use of contrast agents	95.2–97.5	83.8–92.0	9.5	8.0–17.4	11.8–16.5

PREVENTION OF BREAST CANCER

According to research, even among high-risk women, changing one's lifestyle can lower the chance of developing breast cancer. Reduce your risk by:

1] LIMIT ALCOHOL:

Similar to dietary fat intake, alcohol use has generated debate in the field of breast cancer research. Several factors can contribute to ethanol's potential to raise the risk of breast cancer. It may accelerate the hepatic metabolism of carcinogens like acetaldehyde, raise levels of circulating oestrogen, stimulate pituitary production of prolactin, enhance the transfer of carcinogens into breast tissue, and modify cell membrane integrity with an influence on carcinogenesis[32]. The more alcohol you consume, the more likely you are to get breast cancer. Based on research on the influence of alcohol on breast cancer risk, the general guideline is to limit oneself to no more than one drink per day, as even tiny quantities raise risk[33]

2]MAINTAIN A HEALTHY WEIGHT

Work to keep up your current weight if it's healthy. Consult the doctor for advice on effective weight-loss methods if you want to reduce your weight. Reduce the quantity of calories you consume daily and gradually increase your workout.[34]

3] BE PHYSICALLY ACTIVE

People may avoid breast cancer by eating a nutritious diet and exercising regularly. The majority of healthy individuals should aim for 75 minutes per week of strenuous aerobic activity or at least 150 minutes per week of moderate aerobic activity, plus at least twice per week of strength training.[35]

4] Limit postmenopausal hormone therapy.

Breast cancer risk might be raised with combined hormone treatment. The advantages and disadvantages of hormone treatment should be discussed with your doctor. Nonhormonal therapy and drugs may help you control your symptoms. Use the lowest dose that works for you and continue to have your doctor assess the duration of your hormone use if you determine that the advantages of short-term hormone treatment outweigh the hazards[36]

CONCLUSION

The most typical breast cancer-related mortality factor in females. Screening and early detection are essential. Self-examination of the breasts is crucial, although screening tests should still be performed. maintain a healthy weight, include exercise into our lifestyle, consume less alcohol, and quit smoking. Despite several modern treatment options and the invasiveness of some kinds of breast cancer, this disease continues to be the number one cause of cancer-related death in women.

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