

A Comprehensive Review on Breast Cancer

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ABSTRACT

On occasion, a routine radiological test, laboratory test, or for some other cause, cancer may be discovered "incidentally." Generally speaking, cancer cannot be identified until it is 1 cm in size or has 1 million cells. It can now be called a "mass," "growth," "tumor," "nodule," "lump," or "lesion." There are few exceptions to this general pattern, such as blood and bone marrow cancers (leukemias and lymphomas), which often do not generate a "mass" but will show up on lab testing. The transformation of a normal cell into a malignant cell is unlikely to be a significant event in the genesis of cancer; rather, it is the incapacity of the body's immune cells to identify and destroy newly generated cancer cells when they are in small numbers. However, both undergraduate and postgraduate breast cancer education are insufficient (Starmer, 2019). In the United Kingdom, there is limited focused exposure for general surgical students subspecialising in breast surgery. The clinical breast examination is extremely difficult to teach and conduct correctly. This review gives junior practitioners a thorough understanding of breast cancer, including epidemiology, pathology, clinical breast examination method, diagnostic criteria, referral pathways, and treatment choices.

KEYWORDS-

Breast cancer, epidemiology, diagnostic, bone marrow.

I. INTRODUCTION

Unusual cell development is what causes cancer. Cancers are made up of small cells that have lost the ability to stop growing and can originate from any organ or body structure. On occasion, a routine radiological test, laboratory test, or for some other cause, cancer may be discovered "incidentally." Generally speaking, cancer cannot be identified until it is 1 cm in size or has 1 million cells. It can now be called a "mass," "growth," "tumor," "nodule," "lump," or "lesion." There are few exceptions to this general pattern, such as blood and bone marrow cancers (leukemias and lymphomas), which often do not generate a "mass"

but will show up on lab testing. The transformation of a normal cell into a malignant cell is unlikely to be a significant event in the genesis of cancer; rather, it is the incapacity of the body's immune cells to identify and destroy newly generated cancer cells when they are in small numbers. The risk of cancer increases in those whose immune systems are reduced by any reason, including chronic stress, old age, chronic debilitating disease, past chemotherapy usage, and drug addiction such as analgesics, antibiotics, and corticosteroids. [1]

TYPES OF CANCER

Types of cancer include:

Carcinoma: Cancer that arises from epithelial cells. This category comprises many of the most common malignancies that affect elderly persons. Carcinomas account for almost all malignancies that originate in the breast, prostate, lung, pancreas, and colon.

Sarcoma: Sarcomas are cancers of connective tissue (bone, cartilage, fat, nerve) that arise from mesenchymal cells outside of the bone marrow.

Lymphoma and leukemia: These two types of cancer are caused by immature cells that develop in the bone marrow and are meant to fully differentiate and grow into normal immune system and blood components. Acute lymphoblastic leukemia is the most frequent malignancy in children, accounting for roughly 30% of cases. However, adult lymphoma and leukemia are significantly more common than childhood lymph.

Germ cell tumors: Germ cell tumors are cancers that develop from pluripotent cells and most commonly appear in the testicular or ovary.

Blastoma: Cancers that arise from immature "precursor" cells or embryonic tissue. Blastomas are more common in youngsters (e.g., neuroblastoma, retinoblastoma, nephroblastoma, hepatoblastoma, medulloblastoma) than in older individuals. [2]

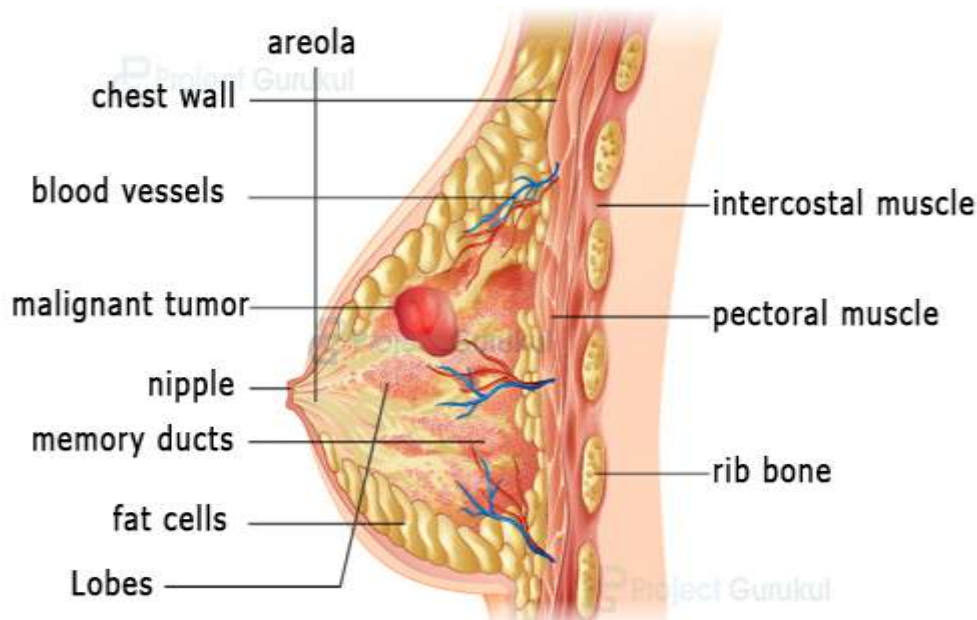
BREAST CANCER

Breast cancer is a group of malignancies that arise in the mammary glands and is the most

common cancer in the United Kingdom and around the world (World Health Organization, 2021). Clinicians must be skilled and confident in recognizing, assessing, and recommending patients with probable breast cancer. However, both undergraduate and postgraduate breast cancer education are insufficient (Starmer, 2019). In the United Kingdom, there is limited focused exposure

for general surgical students subspecialising in breast surgery. The clinical breast examination is extremely difficult to teach and conduct correctly (Veitch et al, 2019). This review gives junior practitioners a thorough understanding of breast cancer, including epidemiology, pathology, clinical breast examination method, diagnostic criteria, referral pathways, and treatment choices.^[3]

Breast Cancer



SIGNS AND SYMPTOMS

- A variation in the size, shape, or contour of your breast cancer.
- A tumor or lump that can feel as little as a pea.
- A lump or thickening in or around your breast or underarm that remains throughout your menstrual cycle.
- A change in the appearance or texture of the skin on your breast or nipple. Your skin may appear dimpled, puckered, scaly, or irritated. It may appear red, purple, or darker than other areas of your breast.
- A marble-like firm region beneath your skin.
- A bloody or clear fluid discharge from your nipple.^[4]

ETIOLOGY

Currently, one in twelve females in Britain between age of 1 and 85 years gets breast cancer. With one million new cases of cancers reported in the World, breast cancer is common in females and comprises 18% of all women cancer. Incidence of breast cancer is predicted to increase to 85 per 100,000 women by 2021^[5]. In 2012, 1.67 million new cases of breast cancer were diagnosed that is 25% of all cancers among women. Ferlay et al. stated that 883,000 cases are in less developed countries and 794,000 in most developed countries. According to the data, [145.2 women in Belgium and 66.3 in Poland between 100,000 suffer from breast cancer^[6]. Incidence of breast cancer in the United States is one out of eight women and In Asia one woman suffers from breast cancer out of 35. In Iran, there are 10 cases in 100,000 populations and 7000 new cases have been reported

annually [7]. Prevalence of breast cancer is increasing in Pakistan. Breast cancer is found mostly in highly populated areas of South Asian developing countries [8]. Breast cancers in males have been detected in Northern areas of Pakistan. Yang et al [9] stated that new cases of breast cancer in China were 168,013 in 2005 and 121,269 in 2000.

PATHOLOGY

The majority of breast cancers are adenocarcinomas, with 85% of adenocarcinoma cases arising from the breast ducts and 15% from the lobular epithelium. The ductal pathology ranges from ductal carcinoma in situ, to invasive carcinomas which have spread beyond the basement membrane into adjacent breast parenchyma. Other forms of breast cancer include Paget's disease of the breast, inflammatory breast cancers and papillary carcinomas. Sarcomas, such as malignant phyllodes and angiosarcomas, are rare. Tumorigenesis occurs as a result of dysregulation of the pathways controlling cell proliferation and apoptosis. The presence or absence of oestrogen receptors, progesterone receptors and human epidermal growth factor 2 receptors on breast cancer cells are important in determining treatment option. [10]

Most breast cancers are sporadic (90%-95%), with just 5% to 10% of patients having a known genetic mutation. [21] BRCA 1 and 2 are the most often related genetic disorders. Invasive ductal carcinoma and invasive lobular carcinoma are the most frequent pathologic types of invasive breast cancer. Carcinogenesis results from a complex interaction of genetic and environmental risk factors, hormonal impacts, and patient-related factors. The pathogenesis, therapy, and prognosis of breast cancer are intimately related to the following molecular subtypes:

Luminal A: Hormone receptor-positive, HER-2 negative.

Luminal B is hormone receptor-positive and HER-2 positive.

Basal-like: Hormone receptor and HER-2 negative.

HER-enriched: HER-2 positive, hormone receptor negative. Hormone receptor-positive cancers (such as luminal A and B) are less aggressive and have higher survival rates. [22] HER-2-enriched tumors are more aggressive and have a poor prognosis in the absence of targeted therapy. The paradigm has evolved with the introduction of tailored anti-HER therapy (for example, trastuzumab). [23] Basal-like cancers test negative for molecular markers and have a dismal prognosis with low survival rates. [24]

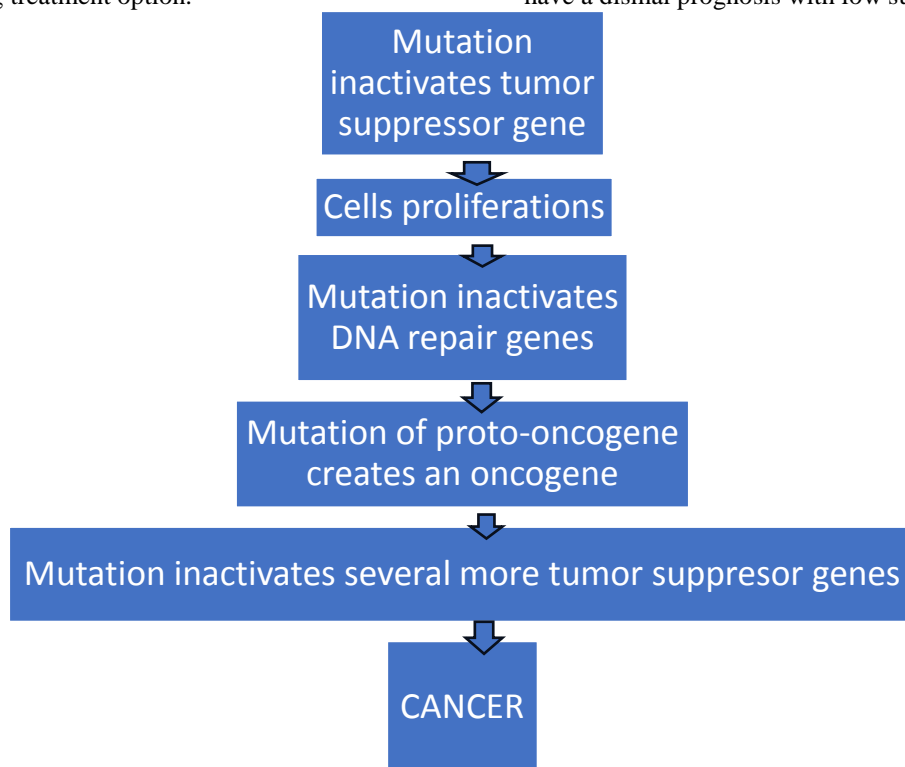


Figure1: Pathophysiology of breast cancer

TYPES OF BREAST CANCER

According to site, it is divided into invasive and non-invasive breast cancers

Non-invasive breast cancer

It is cancer that has not spread beyond the lobule or ducts in which it is located^[11]. Ductal carcinoma in situ is one example of a non-invasive breast cancer. Ductal carcinoma in situ occurs when abnormal cells develop within the milk ducts but do not spread to adjacent tissue or the outside. The word "in situ" refers to "in place." Even if the abnormal cells have not spread beyond the lobules or ducts, they can continue and develop into invasive breast cancer. Every scientific unit's typical background is demonstrated, and a biological interpretation of the available knowledge is offered. Lobular carcinoma in situ is viewed as only a dangerous sign rather than a precursor for the subsequent growth of invasive cancer, so that once the decision is taken, extra operating participation is avoided, and only sequential follow-up is recommended. The management of ductal carcinoma in situ should keep in mind that breast-preserving treatment is now regarded as the best therapy for breast cancer, which we are striving to eradicate^[12]. The drawbacks of suggested treatments based on retrospective data have been considered, and the need for clinical research to define the best potential beneficial treatment for non-invasive breast cancer has been confirmed^[13]

Invasive breast cancer

It occurs when aberrant cells from the lobules or milk ducts divide into close proximity with breast tissue^[14]. Cancer cells can spread from the breast to other regions of the body via the immune system or systemic circulation. They may move early in the formation when the tumour is a minute, or later when the tumour is big. Invasive breast cancer is the most common type of general carcinoma in females. The rich populations of Australia and Europe are at high risk, with 6% of females developing aggressive breast cancer before the age of 75. The frequency of breast cancer rises rapidly with age^[15]. Invasive breast cancer that spreads to other parts of the body is also identified.

STAGES OF BREAST CANCER

According to the report by breast cancer organisation. The stages of breast cancer are

determined by the size and kind of tumor, as well as the extent to which malignant cells have invaded the breast tissue.

STAGE 0

This is the non-invasive stage of tumor, which indicates that both cancerous and non-cancerous cells are within the boundaries of that part of the breast in which the tumor begins to grow, and there is no evidence of their invasion in the surrounding tissues of that part. The example of this tumor stage is ductal cell carcinoma in situ (DCIS)^[16]

STAGE 1

This stage is described as invasive breast cancer, with microscopic penetration probable. It is divided into two categories: 1A and 1B stages. Category 1A represents a tumor that reaches up to 2 cm and does not involve any lymph nodes, whereas stage 1B describes a tiny group of cancer cells larger than 0.2 mm detected in a lymph node.^[17]

STAGE 2

Stage 2 contains two categories: 2A and 2B. Stage 2A indicates that the tumor is identified in the axillary or sentinel lymph nodes but not in the breast. The tumor can be less or larger than 2 cm, but no bigger than 5 cm. However, stage 2B depicts a tumor that may be larger than 5 cm but cannot reach the axillary lymph nodes^[18]

STAGE 3

It has been classified into three subcategories: 3A, 3B, and 3C. Stage 3A describes that no tumor is found in the breast but it can be found in 4-9 axillary lymph nodes or in sentinel lymph nodes, whereas stage 3B describes that the tumor can be of any size but have 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 breast cancer is classified as inflammatory, with red, heated, and swollen breast skin. However, stage 3C defines the spread of the tumor up to ten or more axillary lymph nodes, as well as the lymph nodes^[19]

STAGE 4

This is the advanced and metastatic stage of cancer and this stage describes the spread to other organs of the body that is lungs, bones, liver brain etc^[20].

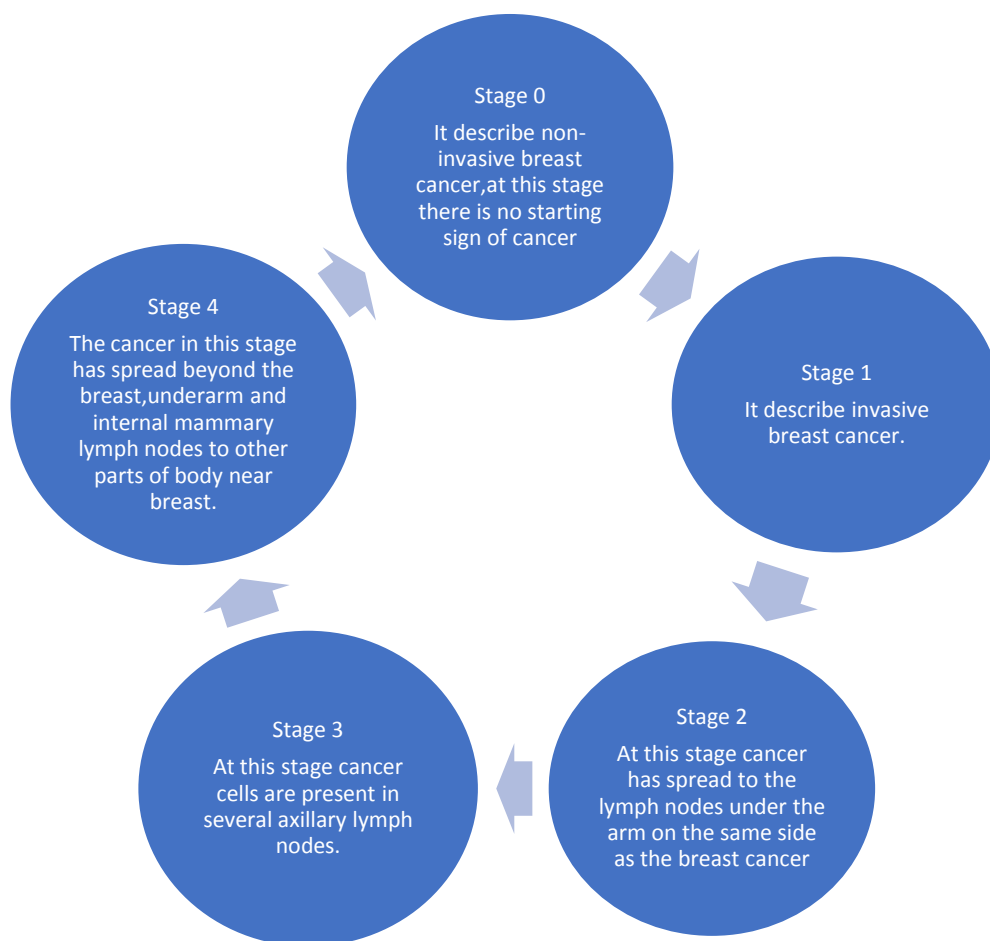


Figure 2: Stages of cancer

TREATMENT OF BREAST CANCER

The goal of breast cancer treatment is to maintain quality of life while also increasing life expectancy. Breast cancer management options vary based on the stage of the disease—its size, location, whether it has spread to other organs of the body, and the individual's physical state. Current breast cancer treatment options include targeted therapies, hormone treatment, radiation therapy, and surgery.

SURGERY

This is the foremost management strategy for individuals whose breast cancer has not extended to further areas of the body and is also a choice for further complex stages of the illness [25]. The kinds of breast cancer surgery vary in the quantity of tissue that is excised with the cancer; this depends on the cancer's characteristics, whether it has extended, and the patient's special feelings. A few of the most familiar kinds of surgery include:

1.1 LUMPECTOMY (BREAST CONSERVING SURGERY)

Some patients diagnosed with breast cancer undergo some type of surgery. According to American cancer society, lumpectomy or partial mastectomy is the procedure of removing the part of the breast that contains malignant tumor along with some healthy tissues and surrounding lymph nodes leaving the major part of the breast intact as possible [26]. This practice generally experienced in women that are in their initial phase of cancer, however the patient also requires another type of treatment such as radiation therapy, chemotherapy or hormone replacement therapy along with this procedure. Most surgeons and patients prefer lumpectomy initially rather than having the complete breast removal, especially if the patient is more concerned about losing her breast [27]. However, adverse effects of lumpectomy are tenderness, temporary inflammation, sclerosis and changed appearance of breast, etc.

1.2 MASTECTOMY

Mastectomy reduces the risk of developing breast cancer. Bilateral preventive mastectomy reduces the risk of developing breast cancer, although it does not remove it altogether [28]. Aromatase and tamoxifen reduce the incidence of contralateral breast cancer and are thought to be more effective than contralateral preventive mastectomy [29]. Mastectomy is regarded the most effective approach of treating an already advanced case of breast cancer for which a lumpectomy was insufficient. Nonetheless, for most women, breast loss causes feelings of asexuality, loss of self-image, and sadness.

1.3 RECONSTRUCTIVE SURGERY

Females who have had a mastectomy may benefit from breast reconstruction, either immediately or later. It is performed to improve the appearance of the breast after tumor surgery. All ladies undergoing mastectomy must be given the choice of reconstructive surgical treatment. Mastectomy is a relatively easy surgical procedure that normally requires a stay in the hospital for 1-2 days. Breast mass deficiency alters the patient's appearance and makes it difficult to wear certain types of apparel. The use of an external prosthesis to address these issues can be uncomfortable and scratchy, especially for women with large breasts. However, the most major issue of mastectomy is the emotional impact of the physical and cosmetic deformation, which can include nervousness, sadness, and negative impact on body figure.

OVARIAN ABLATION AS ADJUVANT THERAPY FOR BREAST CANCER

Ovarian ablation has been used to treat breast cancer. There are several ways for ovarian ablation, including radiation-induced ablation, surgical removal of ovaries, and long-term use of luteinizing hormone-releasing hormone (LHRH) analogs. Furthermore, there are a few hypotheses that cytotoxic chemotherapy may work by promoting ovarian ablation in premenopausal women with breast cancer. Many of the previous case series and clinical trials on ovarian ablation were plagued by methodological difficulties [30]. A meta-analysis of randomized clinical studies shows that females who underwent ovarian ablation as adjuvant treatment had significantly higher overall survival and disease-free survival than females who did not. A literature review indicates that ovarian ablation may be used as an alternative therapy for breast cancer.

ANTI-ESTROGEN THERAPY

It can be employed in hormone-dependent malignancies where the tumor contains hormone receptors such as estrogen receptors. The most prevalent category of medications used in breast cancer is anti-estrogen, which includes compounds such as tamoxifen, raloxifene, and toremifene. Tamoxifen blocks the hormone oestrogen from entering breast cancer cells. This technique prevents breast cancer cells from growing. Tamoxifen can be used to treat females of any age. Tamoxifen, on the other hand, is regarded as the preferred treatment for women with positive estrogen receptor breast cancer. Tamoxifen is a selective estrogen receptor modulator (SERMS) that operates like estrogen in different regions of the body, including uterus [31]. Females on tamoxifen have reported a number of side effects, including venous thrombosis, cataracts, endometrial cancer, menstrual irregularities, and hot flushes. A study demonstrated that the risk-reducing activity of tamoxifen grows beyond the vigorous management phase of 5 years and persists for at least 10 years, whereas the majority of adverse effects do not carry over after the 5-year treatment duration.

RADIATION THERAPY

It is useful in minimizing the need for mastectomies. In the early stages of breast cancer, a lumpectomy combined with radiation therapy is frequently employed instead of a mastectomy. A study was done in India. The study included 135 women, the majority of whom had undergone mastectomy. At the time of study, there was no local recurrence following hypofractionated radiation therapy, and only four patients had metastatic disease [32]. The radiation therapy is helpful in patients with early breast cancer. This study included 143 women who received either regular or intraoperative radiation therapy following breast conservation surgery. At 54 months of follow-up, the tumor had been significantly controlled locally.

BRACHYTHERAPY

This is a type of radiation. It may be characterized as rapid partial breast irradiation. It only sends radiation to the area near where the cancer existed [33]. This may replace the need to give radiation to the entire breast. It also reduces the frequency of management sessions.

CHEMOTHERAPY

Chemotherapy refers to the procedure of destroying cancer cells with certain drugs. It can be

given either before or after surgery, depending on the patient's health. According to the American Cancer Society, chemotherapy drugs include Docetaxel, Paclitaxel, Platinum agents (cisplatin, carboplatin), Vinorelbine (Navelbine), Capecitabine (Xeloda), Liposomal doxorubicin (Doxil), Cyclophosphamide (Cytoxan), Carboplatin (Paraplatin), and others. However, there are several adverse effects^[34]. Metastatic or secondary breast cancer is difficult to treat, but it can be managed for several years. Chemotherapy can be used to manage metastatic breast cancer and slow its progression. It can also be used to reduce some symptoms. Other therapeutic options can be initiated prior or simultaneously.

MEDICINAL PLANTS

The National Cancer Institute in the United States began screening plant extracts for anticancer activity in 1961, and by 1981 (20 years later), approximately 1,14,045 plants had been screened, with only 3.4% (representing approximately 3400 different species) found to be active in one or more biological systems.

Ganoderma lucidum (Polyporaceae)

It includes ganoderic acid, ganoderic acid G, ergosta, ergosterol peroxide, methyl ganoderate A, B, and ganoderic acid C2. It is an anti-cancer agent. Jiang et al. found that *Ganoderma lucidum* inhibits the development of breast cancer cells via inhibiting Akt/NF-kappa B signaling. It's used to cure cancerous cells. It suppresses the transcription factor NF-kappa B, as well as breast cancer cells' invasive aggressiveness^[35]. The specific method that inhibits cancer cells is unknown. The study found that breast cancer MDA-MB-231 cell proliferation is decreased, as is Akt/NF-kappa B signaling. This plant suppresses Akt phosphorylation at Ser473, as well as Akt expression, which reduces NF-kappa B activity.

Momordica charantia (Cucurbitaceae)

Fruits, leaves, and seeds are utilized as ingredients. It contains glucosides, albuminoids, fatty acids, non-polar lipids, linolenic acid, palmitic acid, myrtenol, hexenol, benzyl alcohol, acylglycosylsterols, and glycoproteins. It has hepatoprotective, tonic, stimulant, emetic, laxative, stomachic, and anticancer properties. It is prescribed to treat gout and rheumatism. Ray et al. discovered that *Momordica charantia* extract suppresses breast cancer by influencing cell cycle regulatory genes^[36]. This investigation was conducted using in vitro models. This plant extract

was tested on human breast cancer cells (MCF-7 and MDA-MB-231), as well as primary human mammary epithelial cells. This extract inhibited cell growth and promoted apoptosis. This extract suppressed the expression of survivin and claspin.

Viscum album (viscaceae)

The leaves and stem are utilized as parts. It includes sinapylflavanon, glucopyranoside, flavanone, hydroxy flavanone, and viscin. It has antioxidant, heart tonic, and anticancer properties^[37]. It treats palpitations, vascular spasms, asthma, dizziness, vertigo, and migraines. Gunver et al. investigated the usefulness of this plant in breast cancer.

Calendula officinalis (Asteraceae)

The parts used are leaves. It contains triterpenes, calendula glycosides, butyl esters, flavonol glycosides, and carotenoids. It has anti-inflammatory and anticancer properties. It is utilized in cases of vaginal and cervix cancer. Pommier et al.^[38] observed that *Calendula officinalis* was effective in preventing acute dermatitis after breast cancer irradiation.

Citrullus cococynthis (Cucurbitaceae)

The components used include seeds and fruit. It has phytosterol, flavones, C-glycosides, saponins, aspartic acid, arginine, colocynthin, colocynthinin, and cucurbitacin glycosides. It treats constipation and breast cancers. It has emmenagogue, ecboic, cathartic, hydrating, and antioxidant properties^[39]. This plant exhibits growth-inhibitory action. Cucurbitacin glucosides have been extracted from this plant. These glycosides inhibit human breast cancer cells.

II. CONCLUSION

It was concluded that breast cancer is a complex and diverse diseases that varies in its causes, progression and response to treatment. Early detection through regular screenings, such as mammograms, and being aware of personal risk factors can significantly improve outcomes. Advances in research has led to more targeted therapies and personalized treatment plans, increasing survival rates. However, continued awareness, education and support are crucial in the fight against breast cancer. The importance of life style choices, genetic factors and medical advancements with main central to both prevention and treatment and strategies. Conclusion

highlighting the importance of early detection, advancements in treatment, and the need for continued research. It could emphasize that while breast cancer remains a significant health concern worldwide, progress in medical science and awareness has significantly improved outcomes for many individuals. The articles would likely encourage individuals to stay informed, get regular screenings and support initiatives that aim to reduce the impact of breast cancer globally.

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