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AN OVERVIEW OF ESSENTIAL STUDIES AND PROGNOSIS OF BREAST CANCER WITH THEIR ADVERSE EFFECTS

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ABSTRACT

Breast cancer ranks among the most recurrent cancers affecting women globally, defined by the uncontrolled proliferation of breast cancer. This review examines the epidemiology, medicine interactions between treatment and cell target, contemporary treatment approaches to breast cancer & incidence rates worldwide, with higher occurrences in developed nations. Significant causing factors include genetic mutations (notably BRCA1 and BRCA2), hormonal factors, lifestyle choices, and environmental exposures. Available treatment methods comprise surgery, radiation therapy, chemotherapy, hormone therapy, and targeted therapies, with a growing focus on personalized medicine. Despite progress in early detection and treatment, disparities in healthcare access and outcomes persist. Molecular biology advancements have revealed crucial pathways in breast cancer development, such as the roles of estrogen receptors, HER2/neu, is a gene that encodes the human epidermal growth factor receptor2, a protein involved in cell growth and differentiation, amplification of this gene can play a crucial role in the development and progression glands of certain aggressive types of breast cancer and other growth factor receptors). This review highlights the necessity for ongoing clinical research, ongoing treatment with line of medication, ongoing procedures with equipment, and innovation to enhance the prognosis and quality of life for breast cancer patients.

KEYWORDS: BRCA1-Breast Cancer Gene1, BRCA2-Breast Cancer Gene2.

INTRODUCTION

Breast cancer is a malignancy that develops in the cells of the breast, it affects both men and women, though it is far more common in women. Typically, it begins in milk ducts and can metastasize to other parts of the body if not identified and treated promptly. Besides skin cancer, breast cancer ranks as the most commonly diagnosed cancer

among women in the United States, accounting for nearly one-third of all cancer diagnoses. In 2005, it was estimated that there would be 211, 240 new invasive breast cancer causes among women in the United States along with about 1,690 cases in men.[1] Approximately 1 in 8 women in the United States will be diagnosed with breast cancer during their lifetime. In 2024 alone, it's estimated that 310,720 women and 2,800 men will receive an invasive breast cancer diagnosis. However, there is reason for optimism. If breast cancer is detected early, while still localized, the 5-year relative survival rate is an impressive 99%, because of improvements in early detection and treatment, survival rates have significantly increased, and there are currently more than 4 million breast cancer survivors in the United States.[2]

Who is at risk?

The predominant risk for breast cancer is gender, notably being women. About 99% of breast cancer cases occur in women, while only 0.5-1% occurs in men. The approach to treating breast cancer in men is similar to that for women. Nearly half of breast cancer cases arise in women who have no identifiable risk factor beyond gender and age (over 40 years).

Certain inherited gene mutations significantly increase the risk factor of breast cancer, and improper mutations in the BRCA1, BRCA2, and PALB-2 genes cause the effect of breast cancer. Women with these major gene mutations can be sorted out with the following risk reduction strategies, including prophylactic mastectomy or chemoprevention.[3]

Both men and women have breast tissues. The breast tissues are located behind the nipple in men. Compared to men, women have more breast tissue. Causing of breast cancer is uncommon in men. In 2023, over 200 men were diagnosed with breast cancer. The average age of diagnosis of breast cancer in men is 71 years. The causes of breast cancer in men are to increase in age, some testicular disorders, family history, drinking alcohol, overweight.[4]

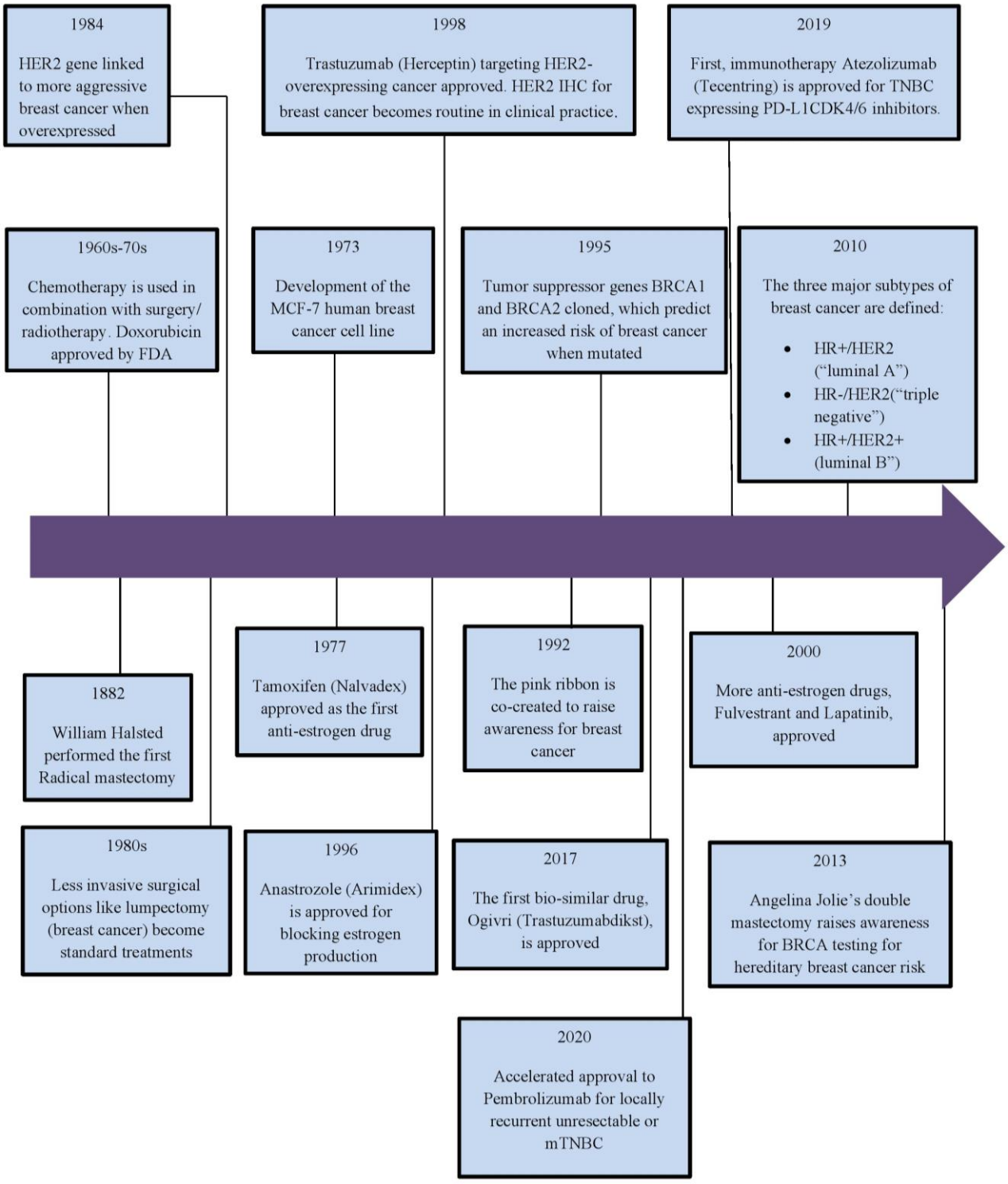
BRCA1: - BRCA1, a tumor suppressor gene, is crucial in repairing DNA damage, regulating the cell cycle, maintaining genomic stability, and overseeing other vital physiological functions.[5] and the BRCA2: -BRCA2 is a tumor suppressor gene present in all humans. It acts as a caretaker gene, with its associated protein, also known as breast cancer type 2 susceptibility protein, being essential for DNA repair.[6]

GLOBAL IMPACT

The age-adjusted breast cancer mortality rate in high-income countries declined by 40% from the 1980s to 2020. Nations that have successfully reduced breast cancer mortality rates have achieved an annual reduction of 2-4%.

Enhancing breast cancer outcomes relies on strengthening fundamental health systems to ensure the delivery of effective treatments already established. These strategies are crucial not only for breast cancer management but also for addressing other cancers and non-malignant non-communicable diseases (NCDs).[3]

Evolution of Precision Oncology in Breast Cancer from 1960s to 2020



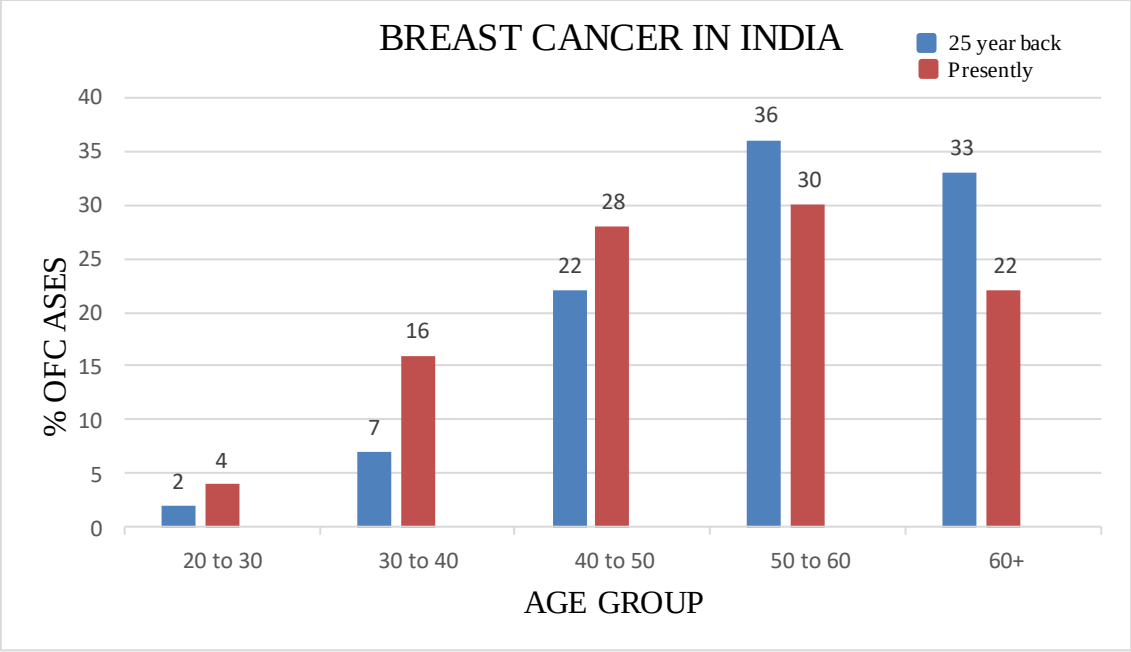
WHO responses

The objective of the WHO Global Breast Cancer Initiative (GBCI) is to decrease global breast cancer mortality by 2.5% annually, aiming to prevent 2.5 million breast cancer deaths worldwide from 2020 to 2040. Achieving this reduction in global breast cancer mortality would prevent 25% of deaths among women under 70 years old.

By offering public health education to enhance awareness among women regarding the signs and symptoms of breast cancer along with educating their families about the significance of early detection and treatment, more women would seek medical advice at the suspicion of breast cancer, even before breast cancer advances significantly. This approach remains viable even in regions where mammographic screening is currently impractical.[3]

Symptoms

- A breast lump or an area of skin that feels thicker than the surrounding tissue.
- Change in size, shape, tenderness, or appearance of a breast.
- Nipple abnormalities such as flattening or inversion.
- Changes in the skin of the breast, such as scaling or flaking.
- Unusual or bloody discharge from the nipple.[8]



Graph: Representing no. of Breast Cancer cases in India.[7]

Table 1: Representing stages of breast cancers with characterisation.

Characteristics	Stage 0	Stage 1	Stage 2	Stage 3	Stage 4
TUMOR SIZE	Very small inside glands	Less than 2cm	5-2 cm	5 cm and larger	Any size
LYMPH NODES	No cancer	No cancer	Affected by cancer	Affected by cancer and it is caused by skin and muscle	Affected by cancer.
SPREADING	-EV	-EV	Confirmed to the breast area, not outside.	Confirmed to the breast area, not outside.	Cancer has spread outside the breast area to any part of the body.
EXTRACELLULAR VESICLES	100%	100%	-EV	-EV	+++EV
5 YEAR SURVIVAL RATE			87%	67%	20%

STAGES OF CANCER

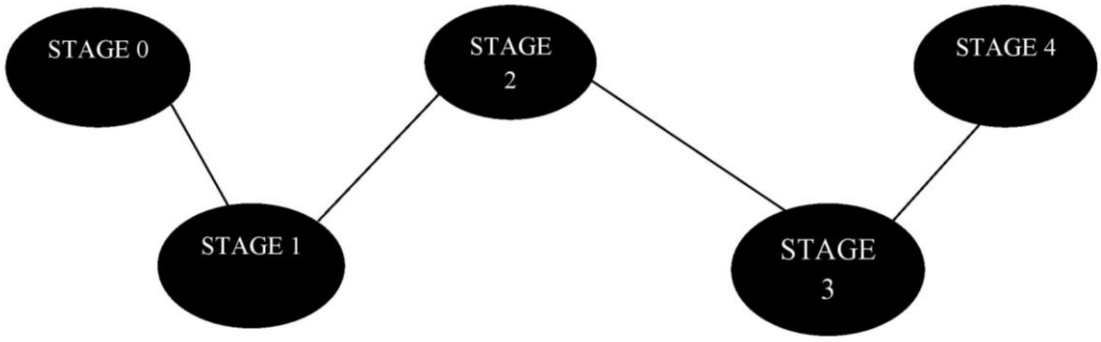


Fig: Stages of cancer.

TYPES OF BREAST CANCER

- INVASIVE CARCINOMA OF NO SPECIAL TYPE
- INFLAMMATORY BREAST CANCER
- LOBULAR CARCINOMA IN SITU
- PAGET'S DISEASE OF THE BREAST
- DUCTAL CARCINOMA IN SITU
- TRIPLE-NEGATIVE BREAST CANCER
- MALE BREAST CANCER
- ANGIOSARCOMA
- HER2-POSITIVE BREAST CANCER
- METAPLASTIC CARCINOMA
- MICROPAPILLARY CARCINOMA

INSTRUMENTS USED IN TREATMENT OF BREAST CANCER

- Positron emission tomography (PET)
- Fluorescence invivo hybridization (FISH)
- Chromogenic invivo hybridization (CISH)
- Bioinformatics (BI)
- Liquid biopsy (Lb)[9]

- **Positron emission tomography (PET) based detection**

PET (Positron Emission Tomography) is a valuable imaging technique that enables the visualization of various biological processes within the tumor microenvironment. By using molecular probes designed to target specific markers overexpressed in breast cancer, PET plays a crucial role in early detection and improved management of cancer patients. The molecular probes used in PET target a range of biological processes and molecular markers. These probes can detect metabolism, amino acid transporters, cell proliferation, hypoxia (low oxygen levels), estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), gastrin-releasing peptide receptor (GRPR), chemokine receptors, and fibroblasts. By detecting the expression of these receptors non-invasively, PET helps in identifying potential therapeutic targets and guiding treatment decisions for breast cancer patients.[10]

- **Fluorescence invivo hybridization (FISH) based detection**

FISH, or Fluorescence in situ hybridization, is a technique that can locate specific DNA sequences in cells during different stages like metaphase or interphase. Initially developed for studying mammalian chromosomes, it was first used for examining plant chromosomes by Schwarzacher and Yamamoto in 1989. FISH has been applied to identify specific DNA sequences in plant chromosomes of various species like Aegilops, Hordeum, Oryza, Arabidopsis, Brassica, soybean, and barley.[11]

- **Chromogenic invivo hybridization (CISH) based detection**

CISH (Chromogenic in situ hybridization) is a molecular cytogenetic technique frequently utilized to evaluate gene amplification, notably for assessing HER-2/neu status in breast cancer samples. HER-2/neu amplification correlates with increased mortality, recurrence rates, and poorer prognosis in breast cancer. The monoclonal antibody trastuzumab, a receptor blocker, has demonstrated clinical efficacy in treating HER-2/neu-overexpressing tumors, underscoring the importance of determining receptor status before initiating cancer therapy.[12]

CISH is also employed in the detection of chromosomal rearrangements and fusions, such as the ALK tyrosine kinase domain fusion with the promoter and 5' region of EML4 in lung cancer. ALK-positive tumors represent a clinically significant subgroup that can be effectively targeted with the ALK inhibitor crizotinib.[12] Beyond oncology, CISH has proven useful in detecting human papillomavirus infections.[12]

- **Bioinformatics (BI) based detection**

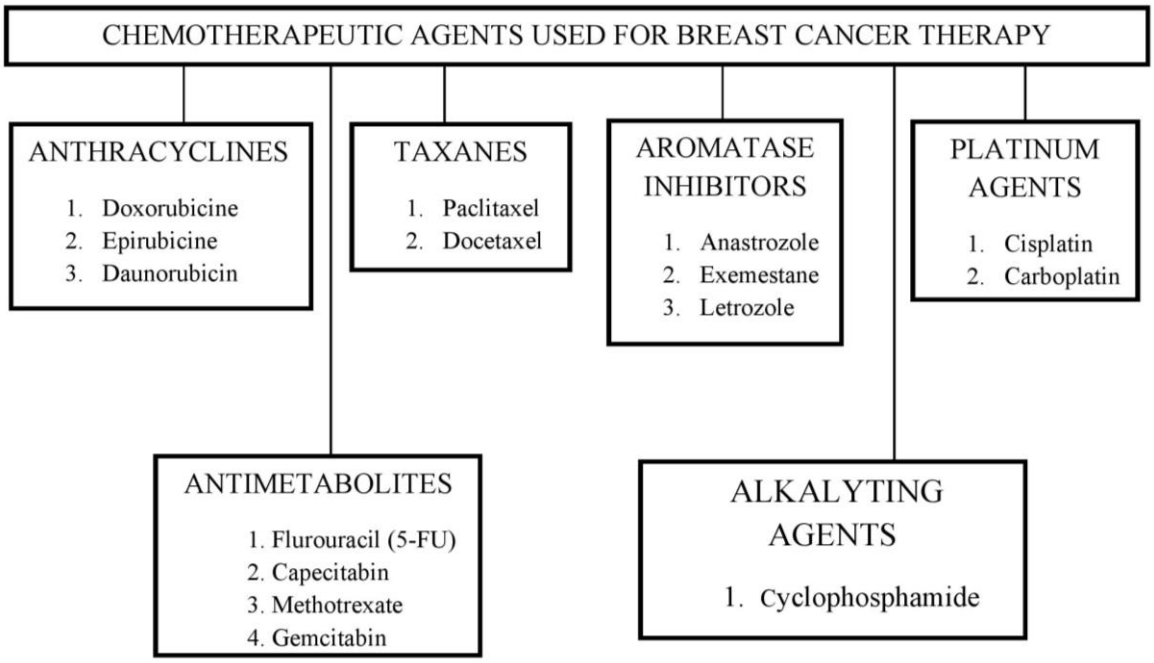
Bioinformatics is a multidisciplinary field where techniques like cluster analysis and pathway analysis help analyze large-scale gene chip data to identify important molecules and understand disease mechanisms. Gene chip and sequencing technologies are crucial in studying tumor diseases, especially with the vast genetic data available in databases today. However, effective data mining remains a challenge despite the wealth of information. Polo-like kinase 1 (PLK1) is a conserved mitotic kinase that regulates various stages of cell division by controlling processes like mitosis, spindle formation, chromosome separation, and cytokinesis. PLK1 also influences microtubule dynamics, DNA replication, chromosome behavior, p53 activity, and G2DNA damage repair. Its overexpression in many tumors is linked to increased cell proliferation.[13]

- **Liquid biopsy (Lb) based detection**

Liquid biopsy (LB) is a less invasive method that has shown great promise in diagnosing, predicting outcomes, and monitoring treatment effectiveness for various cancers by analyzing blood samples or other fluids. Unlike traditional tissue biopsies, LB can be done more frequently without causing harm to patients. Although tissue biopsy is still the gold standard for diagnosis due to its reliability and ability to assess multiple biomarkers, LB can provide real-time information on tumor status, especially in advanced cancers where identifying treatment targets is crucial. Researchers are increasingly interested in LB because it offers patient-specific information quickly and easily through serial blood samples, aiding in the early detection of changes in disease status like relapse. LB is helping to advance personalized medicine by offering valuable, non-invasive diagnostic insights.[14]

NABL-CERTIFIED DIAGNOSTIC TOOLS FOR BREAST CANCER

- Mammography machines
- Ultrasound devices
- Biopsy tools[15]



ANTHRACYCLINES

It consists of 3 drugs. They are: -

1. Daunorubicin

This is a crimson-hued medication unearthed in the early 1960s. It was extracted from a strain of Streptomyces peucetius by A. Di Marco and colleagues of Farmitalia Research Laboratories in Italy, who named it daunomycin. Around the same time, Dubsot and colleagues in France also discovered the compound and called it rubidomycin. Eventually, daunorubicin became an international name. Initially showing activity against murine tumors, it later proved effective in clinical trials against leukemia and lymphomas.[16]

Mechanism of action

Daunorubicin is indeed an anthracycline antibiotic that works by damaging DNA. It achieves this by inserting itself between the base pairs of DNA's, causing the helix to uncoil. This process ultimately hinders DNA synthesis and RNA synthesis that relies on DNA, which can help in inhibiting cancer cell growth.[17]

Adverse effects

Adverse effects associated with anthracyclines, a class of chemotherapy drugs widely used in cancer treatment, encompass a spectrum of potential complications. This includes:

- **Cardiotoxicity**

Cardiotoxicity is "heart damage caused by cancer treatments."[18] Cardiotoxicity is a significant risk associated with certain chemotherapy or targeted therapy drugs, as well as chest radiation therapy. It can lead to heart damage and is

particularly concerning because symptoms may appear years after cancer treatment, especially in those treated during childhood. Certain cancer therapies carry a heightened risk of causing cardiotoxicity.[19]

- **Myelosuppression**

Myelosuppression, or bone marrow suppression, is "decreased blood cell production in the bone marrow." [20] Myelosuppression is a common side effect of chemotherapy, occurring because these drugs target rapidly dividing cells, including both cancer cells and healthy bone marrow cells. This suppression of bone marrow can reduce the production of blood cells—such as white blood cells, red blood cells, and platelets—resulting in potential complications. Healthcare providers must monitor and address myelosuppression during chemotherapy to maintain overall health and well-being.[21]

- **Gastrointestinal toxicity**

Gastrointestinal (GI) toxicities caused by chemotherapy agents are "adverse effects on the gastrointestinal tract."[22] These effects stem from harm to rapidly dividing cells in the gastrointestinal (GI) tract, causing inflammation, ulceration, and in severe cases, perforation. Gastrointestinal toxicity is a prevalent side effect of chemotherapy, often resulting in symptoms such as diarrhoea, vomiting, weight loss, infections, and mucositis. For instance, about 40% of colorectal cancer patients treated with irinotecan experience diarrhoea. Similarly, breast cancer patients receiving docetaxel injections may encounter gastrointestinal issues such as vomiting and diarrhoea.[23]

- **Alopecia**

Alopecia, or hair loss, is a common side effect for cancer patients undergoing treatments such as taxane chemotherapy and hormonal therapy. Some patients may continue to experience hair loss even after completing treatment. However, options like topical minoxidil can promote hair regrowth in these cases. It's encouraging that the woman in the described case saw hair regrowth after using topical minoxidil following her treatment with docetaxel and hormonal therapy. This underscores the effectiveness of managing treatment-induced alopecia.[24]

- **Extravasation**

Extravasation refers to the movement of tumor cells from the vessel lumen into the surrounding organ tissue. Once considered a critical step in limiting metastasis, recent intravital microscopy studies have shown that extravasation can be highly efficient in certain contexts.[25]

- **Hepatotoxicity**

Hepatotoxicity, characterized by liver damage from chemicals such as certain breast cancer medications, is a serious yet treatable condition. Monitoring liver function throughout treatment and promptly addressing any signs of hepatotoxicity are crucial for managing this side effect effectively. Early detection allows for interventions that can mitigate liver damage and improve outcomes for patients undergoing breast cancer treatment.[26]

- **Secondary malignancies**

A secondary cancer that develops in individuals who have undergone previous cancer treatment, is characterized by the growth of new abnormal cells.[27]

- **Nephrotoxicity**

Nephrotoxicity arises when the kidneys are impaired in their ability to filter, detoxify, and expel harmful substances due to damage from anticancer drugs. Close monitoring of renal function during cancer treatment is essential to promptly detect and manage potential nephrotoxic effects. Early intervention by healthcare providers can protect kidney function and promote overall well-being in patients undergoing anticancer therapy.[28]

- **Skin and nail changes**

Some chemotherapy treatments frequently result in skin reactions like dryness, itching, redness, darkening, and peeling. These reactions, known as photosensitivity, increase susceptibility to minor rashes or sunburns. Some individuals may also notice changes in the skin pigmentation. Chemotherapy can also impact nails, resulting in darkened, cracked, and painful areas around the cuticles. If you experience these skin and nail changes during treatment, it's crucial to notify your healthcare team promptly for proper care and support.[29]

Taxane

Taxanes are a class of diterpenes. They are originally derived from plants of the Taxus genus, particularly yews, and contain a taxadiene core. Paclitaxel (Taxol) and docetaxel (Taxotere) are commonly utilized as chemotherapy agents. Cabazitaxel received FDA approval for treating hormone-resistant prostate cancer.[30]

Mechanism of action

The primary mode of action of taxane drugs involves disrupting microtubule function. Microtubules are crucial for cell division, and taxanes stabilize GDP-bound tubulin in microtubules, hindering de-polymerization and thus inhibiting cell division. Consequently, taxanes act as mitotic inhibitors. Vinca alkaloids inhibit tubulin polymerization, thereby preventing the formation of mitotic spindles. Both taxanes and vinca alkaloids are referred to as spindle poisons or mitosis poisons, but they exert their effects through distinct mechanisms. It is also theorized that taxanes may augment radiosensitivity.[31]

Adverse effects

Taxanes represent a class of chemotherapy medications frequently employed in the treatment of different cancer forms, such as breast, liver, ovarian, and prostate cancers.

Like most chemotherapy medications, taxanes can cause a range of adverse effects. Some of the common adverse effects associated with taxanes include:

- **Hematological Toxicity**

Hematological toxicity is a decrease in bone marrow and blood cells, which may lead to infection, bleeding, or anemia.[32]

- **Peripheral Neuropathy**

Neuropathy is characterized by pain or discomfort resulting from damage to the nerves that regulate movement and sensations in the arms and legs.[33]

- **Hypersensitivity Reactions**

Hypersensitivity reactions to chemotherapy drugs can vary from mild to severe and are hard to predict. Symptoms like flushing, nausea, breathing issues, back pain, low blood pressure, and fast heart rate can occur. Hypersensitivity is

becoming more common due to the increased use of chemotherapy. It's important to recognize and manage these reactions promptly for patient safety during cancer treatment. If you notice any of these symptoms, seek immediate medical help.[34]

- **Musculoskeletal Symptoms**

Breast cancer treatment like surgery, chemotherapy, radiotherapy, and endocrine therapy can raise the chances of musculoskeletal issues, particularly in the upper limb. Studies indicate that around 67% of women might experience shoulder or arm problems for up to 3 years following treatment. If you encounter any of these issues, discussing them with your healthcare team can help in managing and alleviating these musculoskeletal concerns effectively.[35]

- **Gastrointestinal effects**

Gastrointestinal (GI) metastasis is not very common and typically happens a few years after a breast cancer diagnosis. Patients often have symptoms like abdominal pain, loss of appetite, bleeding, vomiting, and other digestive issues. These symptoms can be challenging to tell apart from primary stomach cancer. If you notice any of these symptoms, it's important to consult with your healthcare provider for proper evaluation and management.[36]

- **Fluid retention**

Lymphedema after breast cancer treatment often shows up as swelling in the arm on the side where lymph nodes were removed. The degree of swelling can differ. In some cases, individuals may experience significant swelling, with the affected arm being several inches larger than the other arm. If you notice any swelling or changes in your arms after breast cancer treatment, it's essential to discuss this with your healthcare team for proper management and support. [37]

- **Mucositis**

Oral mucositis is a frequent issue with cancer chemotherapy. It typically starts 5-10 days after starting chemotherapy and can persist for 7-14 days. Chemotherapy-induced oral mucositis leads to the breakdown of the mucosal lining in the mouth, resulting in the formation of ulcers. If you experience this side effect, it's important to inform your healthcare provider for appropriate management and relief.[38]

Aromatase Inhibitors

Aromatase inhibitors (AIs) are a class of drugs primarily employed for managing breast cancer in postmenopausal women and men, addressing gynecomastia in males. They are also utilized off-label to mitigate estrogen conversion during exogenous testosterone supplementation and for chemoprevention in women at elevated breast cancer risk.

Aromatase catalyzes a crucial aromatization process in estrogen synthesis. It transforms the enone ring of androgen precursors like testosterone into a phenol, thereby finalizing estrogen synthesis. Consequently, AIs function as inhibitors of estrogen production. Since hormone-positive breast and ovarian cancers rely on estrogen for proliferation, AIs are administered to either impede estrogen production or hinder its action on receptors.[39]

Mechanism of action

Aromatase inhibitors work by inhibiting the enzyme aromatase, which is responsible for converting androgens into estrogens through the process of aromatization. Since breast tissue is stimulated by estrogens, reducing their production serves as a means to suppress the recurrence of breast tumor tissue. In premenopausal women, the primary source of estrogen is the ovaries, while in post-menopausal women; most estrogen is produced in peripheral tissues outside the

central nervous system (CNS), along with a few CNS sites within the brain. Estrogen is produced and acts locally in these tissues; however, any estrogen circulating in the bloodstream, exerting systemic estrogenic effects in both men and women, results from estrogen escaping local metabolism and spreading into the circulatory system.[39]

Adverse effects

Aromatase inhibitors (AIs) are a class of medication commonly used in the treatment of hormone receptor-positive breast cancer, as well as other conditions such as endometriosis and infertility. They first stemmed from Taxus genus flora, notably yews, and feature a taxadiene core. They can also cause a range of adverse effects. Some of the common adverse effects associated with aromatase inhibitors include:

- **Bone loss and Osteoporosis**

It's not just the disease that can lead to bone loss. Certain breast cancer treatments such as hormone therapy and chemotherapy can also contribute to weakening bones. These treatments heighten the risk of developing osteopenia, which can advance to osteoporosis and eventually increase the likelihood of fractures. It's crucial to be aware of these potential side effects and discuss bone health management strategies with your healthcare team during and after breast cancer treatment.[40]

- **Vaginal Dryness and Atrophy**

Cancers that impact hormone levels can indeed lead to fatigue. Breast and prostate cancers, for example, can alter hormone levels in the body, resulting in various side effects, including fatigue. Individuals with advanced cancer are more prone to experiencing fatigue compared to those with cancer in earlier stages. If you're dealing with fatigue due to cancer treatment, it's important to discuss this with your healthcare team for appropriate management and support. [41]

- **Fatigue**

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- **Mood Changes**

Mood swings can be a common experience for individuals facing a breast cancer diagnosis and treatment. The emotional rollercoaster that comes with the ups and downs of dealing with the diagnosis and treatment can lead to feelings of confidence, capability, sadness, distress, or anger at different times. It's essential to acknowledge and address these emotions and seek support from healthcare professionals, counselors, or support groups to help navigate through these challenging times.[43]

- **Cholesterol Changes**

Cholesterol can indeed play a role in promoting cancer cell growth by activating pathways like AKT phosphorylation. Additionally, low-density lipoprotein (LDL) has been linked to stimulating the proliferation and movement of breast cancer cells. It's crucial to maintain a healthy cholesterol level and discuss any concerns about cholesterol and its potential impact on cancer with your healthcare provider.[44]

- **Increased Risk of Vaginal Infections**

Candida albicans, a type of yeast commonly found in the vagina, show varying prevalence of estrogen levels and breast cancer subtypes. In patients with estrogen receptor (ER)-positive breast cancer, where estrogen levels are normal, Candida albicans is more frequently detected. This suggests that normal estrogen levels may support the presence of Candida albicans in these patients. Conversely, in women with ER-negative breast cancer, elevated estrogen levels might potentially encourage the growth of Candida spp. in the vaginal environment. This underscores the intricate relationship between estrogen levels, breast cancer subtypes, and the presence of Candida spp.[45]

- **Menopausal Symptoms**

Menopausal symptoms can pose significant challenges for breast cancer patients undergoing treatment. Chemotherapy can exacerbate ovarian issues, intensifying these symptoms. Discontinuing hormone therapy after diagnosis can also trigger menopausal symptoms. A survey revealed that many individuals taking tamoxifen experienced hot flashes and night sweats, which were associated with increased rates of depression and sleep disturbances.[46]

Platinum Agents

Platinum-based anti-neoplastic drugs, often referred to as platins, are chemotherapeutic agents employed in cancer treatment. The active constituents are platinum coordination complexes. These drugs are administered to nearly half of all patients undergoing chemotherapy for cancer. Frequently utilized platinum-containing medications consist of cisplatin, oxaliplatin, and carboplatin, with numerous additional options either suggested or undergoing development. The integration of platinum-based chemotherapy drugs into chemoradiation for women with early cervical cancer seems to improve survival rates and -including neurotoxicity, which manifests as peripheral neuropathy such as polyneuropathy.[47]

Mechanism of action

Platinum-based anti-neoplastic agents, primarily studied in the context of cisplatin but applicable to other members of this class, include crosslinking of DNA. This can occur as mono adducts, interstrand crosslinks, intrastrand crosslinks, or DNA-protein crosslinks. They predominately target the adjacent N-7 position of guanine, creating a 1, 2 intrastrand crosslink. This crosslinking hampers DNA repair and/or synthesis, leading to specific patterns of DNA damage that can destroy cancer cells but they elevate the risk of developing secondary tumors. These agents are sometimes referred to as "alkylating-like" due to their similar effects to alkylating anti-neoplastic agents, despite lacking of alkyl group.[48]

Adverse effects

Platinum-based chemotherapy drugs, such as cisplatin, carboplatin, and oxaliplatin, are widely used in treating various cancers, including lung, ovarian, testicular, and bladder cancers. The drugs can cause several side effects, which include:

- **Kidney Damage**

The kidneys play a critical role in maintaining electrolyte balance and filtering toxins from the blood, which are eliminated through urine. Some breast cancer treatments can affect kidney function, potentially causing damage. Monitoring kidney health throughout breast cancer treatment is essential to prevent complications.[49]

- **Hearing Loss**

Certain chemotherapy medications prescribed for breast cancer treatment may result in hearing impairments, such as hearing loss and tinnitus (a ringing sensation in the ears).[50]

- **Bone Marrow Suppression**

Blood disorders are a frequent side effect of breast cancer treatment, often resulting from bone marrow suppression, which reduces the production of blood cells. Chemotherapy, radiation therapy, and extensive surgeries can damage bone marrow tissues, impairing their normal function. Monitoring blood counts and addressing any concerns with your healthcare team is crucial during treatment.[51]

- **Allergic Reactions**

Certain types of breast cancer can cause symptoms such as skin swelling, changes in texture, or color variations. Other common causes of a breast rash include insect bites, hives, allergic reactions, or skin conditions such as eczema or dermatitis. It's crucial to seek guidance from a healthcare provider to accurately diagnose and manage any skin changes or concerns.[52]

- **Hair Loss**

It is common for individuals undergoing breast cancer treatment to suffer from hair loss. Chemotherapy, in particular, is well-known for causing this side effect. Additionally, certain other treatments for breast cancer may also result in hair loss or thinning.[53]

- **Electrolyte Imbalance**

Chemotherapy can cause electrolyte imbalances, making levels too low or too high. Side effects such as vomiting or diarrhoea, which alter the body's water content, can also contribute to these imbalances. Monitoring electrolyte levels and promptly addressing any issues during treatment is essential.[54]

Anti-metabolites

Anti-metabolites are chemicals that disrupt the function of metabolites, which are substances crucial for normal metabolic processes. These chemicals often resemble the metabolites they disrupt, such as folic acid, leading to competitive inhibition. The existence of anti-metabolites within cells can induce toxicity, halting their growth and division processes. Because of these properties, anti-metabolites are used in chemotherapy to treat cancer.[55]

Mechanism of action

Anti-metabolites encompass compounds that closely resemble precursors of purine or pyrimidine, or substances that disrupt the synthesis of these essential molecules. These agents can indirectly damage DNA by being incorrectly incorporated into the DNA, leading to irregularities in DNA synthesis timing or progression. Moreover, they have the potential to modify the activity of enzymes engaged in purine and pyrimidine synthesis.[55]

Adverse effects

Anti-metabolites are chemotherapy drugs that disrupt DNA and RNA synthesis by mimicking natural substances involved in these processes. They are effective in treating various cancers, including leukemia, breast cancer, and gastrointestinal cancers, but they can cause a range of side effects:

- **Liver Toxicity**

Liver toxicity, or hepatotoxicity, occurs when the liver becomes inflamed in response to exposure to a harmful substance. Liver damage resulting from chemicals in certain breast cancer medications is known as hepatotoxicity. The liver, located in the upper abdomen, is crucial for converting food into energy and filtering toxins from the body. Although liver damage is serious, it is treatable. Monitoring liver function during breast cancer treatment is essential to promptly address any potential issues.[56]

- **Kidney Damage**

The kidneys are essential for balancing electrolyte levels and filtering toxic wastes from the blood, which are then excreted through urine. Certain breast cancer treatments can affect the kidneys and potentially cause damage. Monitoring kidney function during treatment is crucial to identify and address any issues that may arise.[57]

- **Skin Reactions**

Certain breast cancer treatments can cause skin reactions similar to a sunburn, resulting in redness, itching, burning, soreness, peeling, blisters, or darkening of the skin. These changes may develop gradually throughout treatment and can be localized to specific areas. It is important to report any skin reactions to your healthcare provider to receive appropriate care and management.[58]

- **Lung Damage**

When breast cancer cells obstruct the lymph channels in the lungs, it can cause inflammation and scarring, a condition known as lymphangitis. This blockage hinders the proper drainage of lymph fluid, impacting blood oxygen levels. Breathlessness is a common symptom of lymphangitis. Promptly addressing this issue is vital to ensure adequate oxygenation.[59]

- **Neurological Effects**

In breast cancer, paraneoplastic syndromes can manifest as neurological complications, often caused by autoantibodies produced in response to the tumor. Symptoms may include muscle weakness, coordination issues, sensory changes, and cognitive impairments. Monitoring and addressing these neurological manifestations during treatment is crucial.[60]

- **Mouth Inflammation**

Oral mucositis is a frequent side effect of radiation therapy and chemotherapy, resulting in pain in the mucous membranes that can persist even after healing. Furthermore, surgery can damage bone, nerves, or tissue, causing pain. Effective management of these side effects is crucial to improving the overall treatment experience. [61]

- **Reproductive Harm**

Breast cancer patients receiving chemotherapy face the risk of premature ovarian failure or early-onset menopause due to the treatment's impact on the ovaries. Healthcare providers should discuss these potential side effects with patients and consider options to manage them effectively.[62]

- **Immune Suppression**

The immune-suppressed state is consistent with a chronic inflammatory profile. This immune reaction and inflammation pattern could have diverse implications for overall health and may necessitate targeted management approaches.[63]

Alkylating agents

In oncology, alkylating agents represent a class of cancer treatments that affix alkyl groups (CnH2n+1) to DNA. This alkali group commonly attaches to the guanine base of DNA at the nitrogen atom 7 of the purine ring. Because cancer cells generally proliferate more rapidly and with less error correction than healthy cells, they are more vulnerable to DNA damage, such as alkalization. While alkylating agents effectively treat various cancers, they are also cytotoxic, affecting normal cells that divide frequently, such as those in the gastrointestinal tract, bone marrow, testicles, and ovaries. This may result in adverse effects, such as diminished fertility. Additionally, many alkylating agents have carcinogenic properties.[64]

Mechanism of action

Alkylating agents function by cross-linking DNA strands, especially at the N-7 position of guanine. These agents exhibit non-specificity towards any specific cell cycle phase, making them productive across a spectrum of cell cycle stages.[64]

Adverse Effects

Alkylating agents, essential in chemotherapy, disrupt cancer cell replication by modifying DNA structure. However, they often yield a spectrum of adverse effects, including:

- **Gastrointestinal Distress**

Variations in gastrointestinal motility can result in symptoms such as cramps, diarrhoea, or constipation. Chemotherapy can also disrupt the balance of stomach bacteria, leading to problems like gas and abdominal discomfort. Effective management of these side effects is crucial for enhancing the overall treatment journey.[65]

- **Renal Impairment**

Reduced kidney function can significantly impact prognosis, particularly in individuals aged over 70 with renal complications, leading to lower breast cancer-specific survival rates. Adjusting chemotherapy doses due to renal impairment may compromise treatment effectiveness. Therefore, prioritizing renal health in elderly patients is vital to enhance treatment efficacy.[66]

- **Bladder Complications**

The urinary bladder is highly responsive to estrogen, meaning fluctuations in estrogen levels due to chemotherapy may increase the risk of urinary tract infections in breast cancer patients and survivors. Furthermore, chemotherapy medications such as Tamoxifen can cause damage to bladder cells and kidneys due to their potent chemical composition. Effective management of these potential side effects is essential during breast cancer treatment.[67]

CONCLUSION

The current challenges in breast cancer treatment include drug resistance, metastasis, access to treatment, personalized medicine, recurrence and impact on psychological treatment are the major concerns i.e., during treatment patients develop drug resistance to chemotherapy, personalized therapy and hormone treatment, spreading of tumor to other body parts.

This review explains about history of breast cancer, available therapies, and instrumentation according to NABL, including classification with their side effects, which are clearly explained above.

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