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(REVIEW ARTICLE)

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Breast cancer: A comprehensive review and it's side effect

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Abstract

People worldwide are impacted by breast cancer, which is a complex, multidimensional illness. The importance of understanding the intricate relationships between hormones and breast tissue is highlighted by the discovery that hormonal imbalance has been connected to the development of breast cancer. The many forms and phases of breast cancer have been clarified by the review. This comprehensive investigation looks at the involvement of key hormones, including progesterone and estrogen, and their receptors in tumor growth in an effort to clarify the significance of hormonal imbalance in breast cancer.

The review looks at the effects of hormonal imbalance on breast tissue, with a focus on how hormone receptor status a ffects treatment choices. The importance of hormone testing in making decisions about diagnosis and therapy, as well as the consequences of hormonal imbalance evaluation in the risk assessment of breast cancer are also covered. An important but little-known side effect of cancer is oral mucositis, which is also covered in the study. The expression "oral mucositis" describes erythematous and ulcerative lesions of the oral mucosa that occur in cancer patients' oral cavities as a result of chemotherapy or radiation therapy.

One study concluded that GI or oral mucositis developed in 303 out of 599 patients (51%) undergoing chemotherapy for solid tumors or lymphoma. This study illustrates the way a thorough knowledge of hormonal imbalance is necessary to improve breast cancer detection, treatment, and prevention strategies. The pathogenesis, clinical treatment, and risk factors of oral mucositis are also examined in this article, which will ultimately benefit those who are afflicted.

Keywords: Breast cancer; Hormonal imbalance; Progesterone; Estrogen; Oral mucositis

1. Introduction

Breast cancer is the second most common cause of cancer-related deaths worldwide and the most common malignancy in women. approximately 99% of breast cancer occurs in women & 0.5 -1% of breast cancer occurs in men. About 50% of breast cancer develop in women who do not have identifiable breast cancer risk factors other than gender (female) & age (over 40 years). Among the major causes of breast cancer, the hormonal imbalance has significantly affected breast cancer pathogenesis. The primary characteristic of breast cancer is the aberrant proliferation of cells within the breast tissue. It commonly occurs in the ductal epithelium (ductal carcinoma) and develops in the breast lobules (lobular carcinoma). The purpose of this review article is to shed light on the prevalent side effects and crucial role that hormone imbalance plays in the development of breast cancer. Hormonal imbalance concerns with the excessive production of estrogen and progesterone are extensively studied in breast cancer. Estrogen which plays a major role in the growth and development of breast tissue is predominantly produced by the ovaries.

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Similarly, progesterone the ovaries produces regulates the menstrual cycle and breast development. Disruptions in these hormones have initiated the progression of breast cancer. The antineoplastic treatments lead to various side effects one of the most common & painful of those is oral mucositis, majorly highlighted in this comprehensive review. Mucositis frequently affects about 39% of people receiving chemotherapy. It impacts the entire gastrointestinal tract, including the mouth cavity, causing discomfort, vomiting, weight loss, and local infections. It is true that female patients are more likely to get severe mucositis and require anti-neoplastic therapy [1][2].

1.1. Understanding Breast Cancer

A group of disorders collectively referred to as cancer are defined by aberrant cells that proliferate and infiltrate healthy cells throughout the body. Breast cancer begins as a collection of cancer cells that expand (metastasize) to other parts of the body or infiltrate nearby tissues.

1.2. What Causes Cancer to Develop?

Tissue is primarily composed of cells, the site for the growth of cancer cells. The breast and other body parts contain tissue. Occasionally, the body's natural process of cell growth goes awry, resulting in the formation of new cells when none are needed and the premature death of damaged or elderly cells. When this happens, an accumulation of cells frequently results in a mass of tissue known as a tumor, growth, or lump. When malignant tumors grow in the breast, it results in breast cancer. These cells can proliferate by severing from the primary tumor and penetrating blood or lymph arteries, which subsequently divide into other bodily tissues. When cancerous cells spread to different areas of the body and start causing harm to other tissues and organs, the process is called metastasis [3].

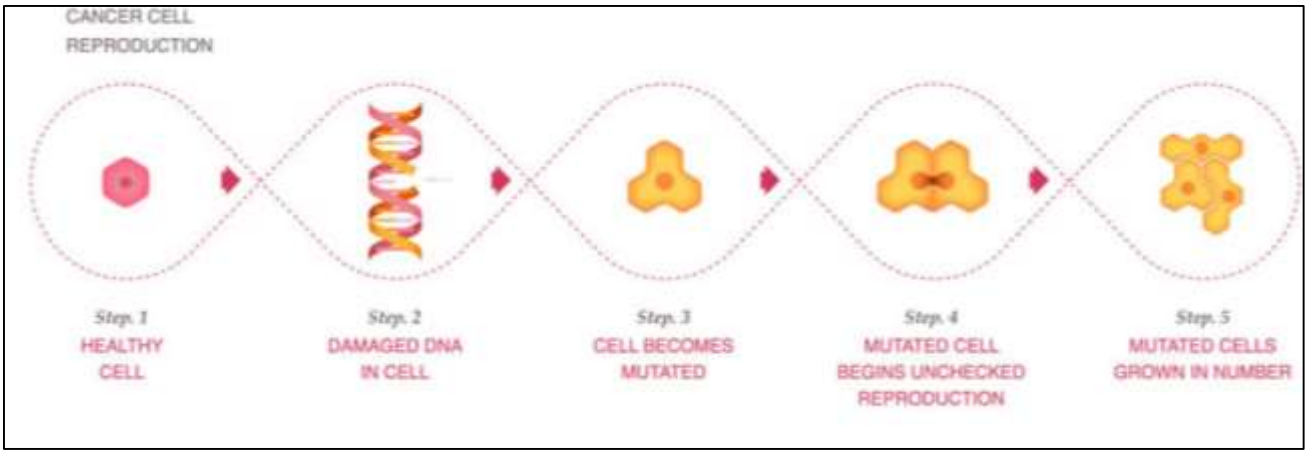

Figure 1 Cancer cell reproduction

2. Signs and symptoms

Because the majority of individuals do not show any symptoms when the disease is still in its early stages, early cancer detection is essential. Breast cancer frequently presents with a variety of symptoms, especially in its more advanced stages. Breast cancer symptoms can include:

A breast thickening or lump, frequently without any accompanying pain; changes to the breast's size, shape, or appearance; dimpling, redness, pitting, or other skin changes; changes to the look of nipple fluid that appears abnormal or bloody; the nipple or the skin encircling it (areola).

A person should seek medical assistance if they have an atypical breast lump, even if it is not painful. Not all breast lumps are cancerous. Malignant breast tumors are more likely to respond well to treatment when they are small and have not spread to nearby lymph nodes.

Breast cancers have the potential to spread to other body parts and cause additional symptoms. The lymph nodes that lie beneath the arm are often the first identifiable location of dissemination it is conceivable to have cancer-bearing lymph nodes that are not felt.

Over time, cancerous cells can spread to other organs such the liver, lungs, brain, and bones [3][4].

3. Breast Cancer Types

Breast cancer is a condition when the breast's cells multiply uncontrollably. Breast cancer comes in various forms. Breast cancer is classified based on which breast cells become cancerous. These are the most prevalent types of breast cancer:

3.1. Ductal invasive carcinoma

Cancer cells begin in the ducts and move to other parts of the breast tissue as they mature. Moreover, invasive cancer cells have the ability to metastasis, or spread, to different bodily regions. When abnormal cancer cells start growing in the milk ducts and migrate into other areas of the breast tissue, it is known as invasive ductal carcinoma (IDC). Another issue is cancer cells that spread throughout various body parts.

Lobular cancer with invasion the lobules are where cancer cells begin, and they then spread to nearby breast tissues. It is also possible for these invasive cancer cells to spread to different body areas [2][5].

3.2. Invasive lobular breast cancer (ILC)

Refers to invasive breast cancer that starts in the breast's lobules, or milk glands, and spreads to the normal tissue nearby Additionally, it can spread via the blood and lymphatic The body is impacted by various systems in multiple areas.

Invasive lobular carcinomas make up more than 10% of invasive breast cancers. Mammograms are useful and essential, but invasive lobular breast cancer is harder for them to detect than other forms of the disease. An MRI may be required in cases of invasive lobular cancer, as the disease may not always show up clearly on a mammography [5].

3.3. Ductal Carcinoma in Situ

Breast milk duct lining abnormalities are a symptom of ductal carcinoma in situ (DCIS), a noninvasive malignancy. The aberrant cells do not appear to have expanded into the surrounding breast tissue outside of the ducts.

When diagnosed in its early stages, ductal carcinoma in situ is a very curable malignancy that has the potential to expand into the surrounding breast tissue if treatment is not received [5].

3.4. Lobular Carcinoma in Situ

Lobular Carcinoma in Situ (LCIS) isn't breast cancer. It is a disorder in which the breast lobules contain aberrant cells. There is no evidence of the atypical cells penetrating the surrounding breast tissue from outside the lobules. LCIS seldom progresses to aggressive malignancy and is well-treated. However, if one breast has LCIS, the risk of developing breast cancer in both breasts increases [4].

3.5. Triple Negative Breast Cancer

When breast cancer is diagnosed as triple negative, it indicates that the cancer tumor lacks the three most prevalent receptor types—progesterone, estrogen, and the HER2/neu gene—that are known to drive the majority of breast cancer growth. This indicates that the hormone epidermal growth factor receptor 2 (HER2), estrogen receptor (ER), and progesterone receptor (PR) tests on breast cancer cells have come back negative. Common treatments including hormone therapy and medications that target HER2, progesterone, and estrogen are useless because the tumor cells do not have the required receptors. Chemotherapy is a viable treatment option for triple-negative breast cancer in fact, when caught early, triple-negative breast cancer may respond even better to chemotherapy than many other cancer forms [6].

3.6. Inflammatory Breast Cancer (IBC)

Inflammatory breast cancer (IBC) is a rare and severe kind of breast cancer, accounting for 1 to 5% of all occurrences. When cancer cells penetrate the breast's lymphatic vessels and skin, IBC results. Compared to additional kinds of breast cancer, IBC typically becomes trickier to recognize and frequently strikes younger women. In comparison to other forms of breast cancer, it also spreads more swiftly. Despite many distinct kinds of breast cancer, inflammatory breast cancer frequently fails to appear as an isolated breast tumor or palpable lump. However, when the breast's lymph vessels—tiny tubes that remove lymph from breast tissue and transport it to the lymph nodes—become clogged by breast cancer cells, symptoms begin to appear [5].

3.7. Metastatic breast cancer (MBC)

The fourth stage of breast cancer that has migrated from the breast to other areas of the body is often referred to as metastatic breast cancer (MBC). The concept of "metastatic" or "metastasis" describes the process by which cancer cells move to other bodily locations another name for metastatic breast cancer is distant or advanced. Metastatic breast cancer is the term used to describe breast cancer that spreads to other parts of the body months or years after the original diagnosis and treatment. This type of recurrence is also known as remote recurrence breast cancer that has broadened metastatically since its preliminary diagnosis is known as de novo metastasis breast cancer. This essentially signifies that the cancer has metastasized to different regions of the body after leaving the breast [4].

4. Breast Cancer Stages

Upon confirmation of breast cancer or a malignant tumor, tests are carried out to ascertain whether cancerous cells have spread throughout the breast or to investigate additional areas of the body. To figure out whether the cancer relocated outside of the breast or to other regions of the body, the staging method is used. The information gathered during the staging method has been used to assess the disease's stage. Planning a course of treatment requires knowing the stage. Planning the process of treatment requires knowing the stage. The disease's stage is determined by the outcomes of certain tests that are used to identify breast cancer.

4.1. Stage 0 breast cancer

When malignant cells are discovered in the breast milk duct lining but have not yet moved to the lymph nodes, circulation, or surrounding tissue, the condition is known as DCIS is a type of cancer that is either pre-invasive or non-invasive. DCIS is a relatively treatable, early-stage cancer that, if left untreated or not detected in time, can spread to the surrounding breast tissue [4].

4.2. Stage 1 Breast Cancer

It's breast cancer that has spread. Early-stage breast cancer, or stage 1 invasive breast cancer, is characterized by tumors that are typically tiny and discovered when the disease is still treatable.

- **Breast cancer in stage 1A:** A tumor less than 2 cm in size—smaller than a peanut—and without lymph node metastases characterize Stage 1A breast cancer.

- **Breast cancer in stage 1B**: Breast cancer typically spreads to the lymph nodes close to the breast first. Thus, lymph nodes are implied to be involved in breast cancer in stage 1B. This indicates that there is evidence of cancer in at least one lymph node because there are tiny clusters of aberrant (cancerous) cells between the size of a pinprick to the 0.2–2.0 mm width of a rice grain [4].

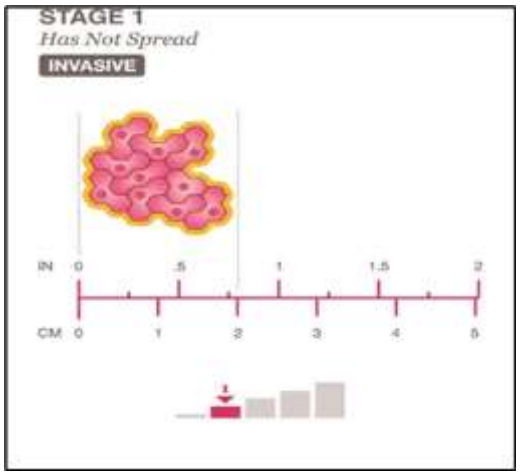

Figure 2 Stage 1 Cancer

4.3. Stage 2 Breast Cancer

- **Breast cancer in stage 2A:** There are less than four axillary lymph nodes with cancer cells, and the tumor is smaller than two millimeters.

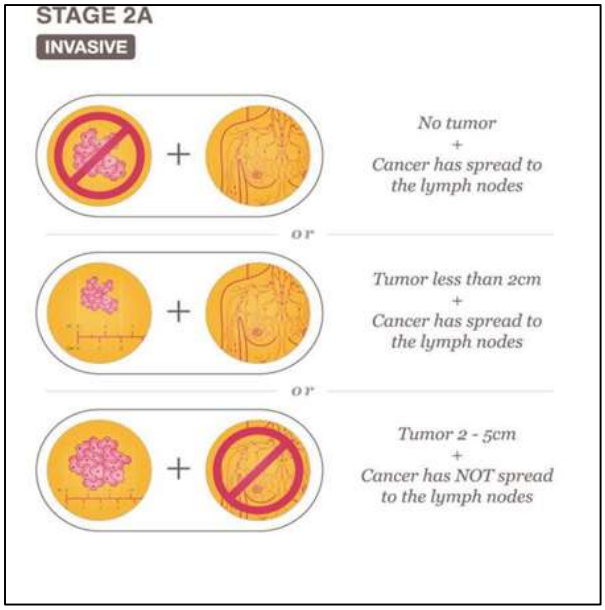

Figure 3 Stage 2A Cancer

- **Breast cancer in stage 2B:** The tumor has spread to more than four axillary lymph nodes and ranges in size from two to five cm [4].

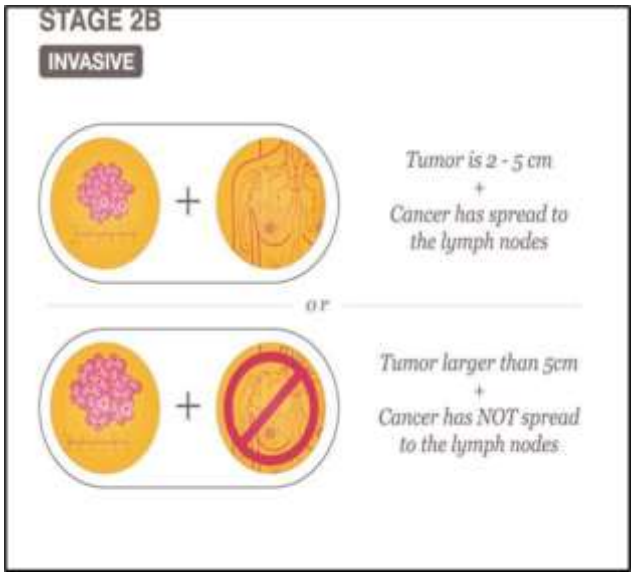

Figure 4 Stage 2B Cancer

4.4. Stage 3 Breast Cancer

In stage three breast cancer, the tumor has progressed beyond its original location and may have infected surrounding muscles and lymph nodes, but it has not yet reached distant organs such the brain, liver, lungs, or bones.

- **Breast cancer in stage 3A**: Small clusters of breast cancer cells are identified in the lymph nodes between the approximate size of a pinprick and the width of a grain of rice (approximately 0.2mm-2.0mm), and the tumor is larger than 5 cm, or about the size of a small lime.

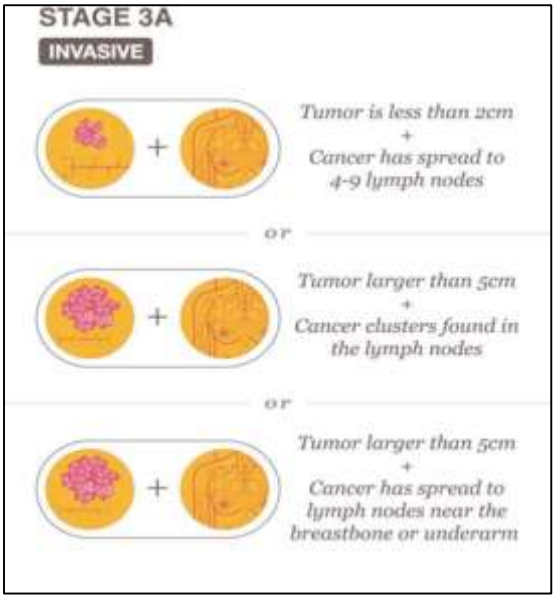

Figure 5 Stage 3A Cancer

- **Breast cancer in stage 3B:** The bones, muscles, and fat that encircle and shield the vital organs in the chest make up the chest wall, where the disease may have spread.

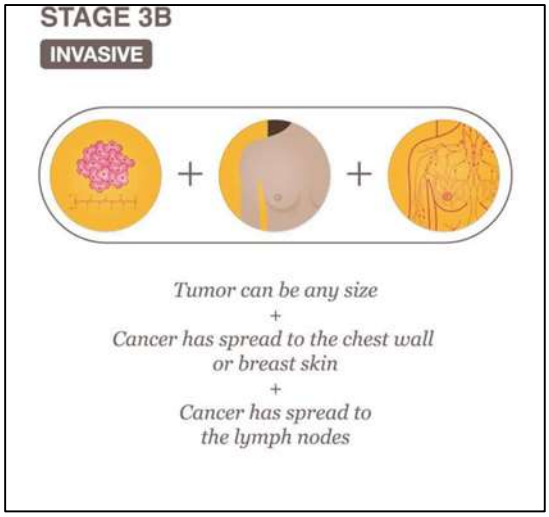

Figure 6 Stage 3B Cancer

- **Breast cancer in stage 3C:** The cancer may have progressed to ten or more neighboring lymph nodes, below the collarbone, close to the breastbone, and under the arm [4].

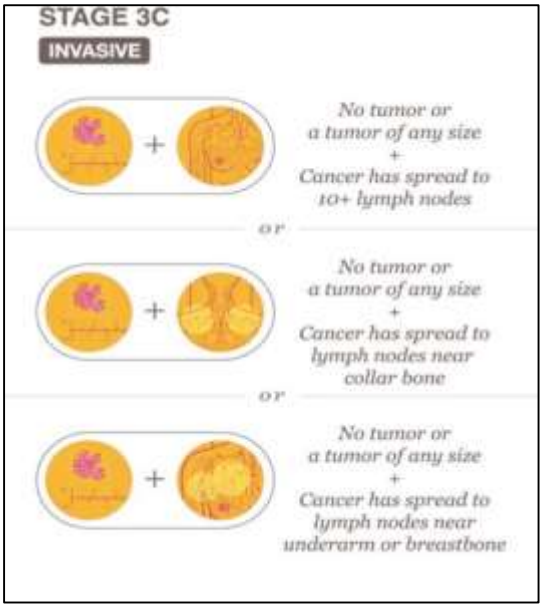

Figure 7 Stage 3C Cancer

4.5. Stage 4 Breast Cancer

An advanced stage of breast cancer is one that has progressed from its initial spot in the breast to other organs, notabl y the brain, liver, lungs, bones, or breast. Other names for stage 4 breast cancer are breast cancer recurrence and metastatic breast cancer [4].

5. Role Of Hormonal Imbalance in Breast Cancer

The etiology and progression of breast cancer have been widely linked to hormonal imbalance, specifically related to progesterone and estrogen levels. The hormone estrogen, which is mostly produced by the ovaries, is essential for the growth and development of breast tissue. It encourages cell division and controls gene expression during the course of the cell cycle and apoptosis. The vital hormone progesterone, mostly generated in the ovaries, is important for controlling a person's menstrual cycle and breast development. It's also critical to remember that, despite being less common in men, breast cancer can nonetheless strike men. It functions in conjunction with estrogen to encourage the proliferation and differentiation of mammary gland cells as well as prepare breast tissue for a possible pregnancy [7][8][9].

6. Hormonal imbalance: Mechanism & its impact on breast tissue

An irregularity or disturbance in the body's ideal hormone levels or ratios is known as a hormonal imbalance. It is crucial to remember that individual variances and the intricacy of hormonal interactions might make it difficult to define a certain numerical ratio or range of hormones as "balanced" or "normal". The activation of progesterone and estrogen receptors (ERs and PRs) in breast cells is one way that hormonal imbalances cause breast cancer. A complicated chain of intracellular signaling events is started when progesterone or estrogen attach to the ER or PR, respectively. These signaling events can help control cell growth and prevent cell death. Dysregulated pathways can lead to uncontrolled cell proliferation and tumor development in cases of excess estrogen or deficient progesterone signaling.

Moreover, the microenvironment of breast tissue might be impacted by hormone abnormalities. For instance, estrogen encourages blood vessel development and growth factor synthesis, both of which aid in tumor angiogenesis and metastasis. Additionally, it may have an effect on the immunological response within the breast, which may modify tumor immune surveillance and encourage immune system evasion of tumors [9-12].

7. Role Of Oestrogen in breast cancer

One of the primary female sex hormones, estrogen, is important for the development of breast cancer. It encourages the expansion and maturation of breast tissue and controls a number of biological functions, including as cell survival,

differentiation, and proliferation. On the other hand, chronic or excessive exposure to estrogen can upset the delicate balance between cell division and growth, which can cause breast cancer to start and spread. There are two sources of estrogen: endogenous and exogenous. Exogenous estrogen can originate from external factors like pesticides and some plastics, whereas endogenous estrogen is mostly produced in the ovaries [13][14].

8. The effects of estrogen metabolites on breast tissue

When it comes to estrogen metabolism, the body goes through various processes that include breaking down and getting rid of estrogen. The two main metabolic routes for estrogen, hydroxylation and methylation, are essential. Different metabolites of estrogen are produced by these pathways, and some of these metabolites have been related to a range of effects on breast tissue. 16α-hydroxy estrone (16α-OHE1) is a significant metabolite that is thought to possess greater estrogenic activity than the parent hormone estradiol. Elevations in 16α-OHE1 have been associated with a higher risk of breast cancer since this metabolite has been demonstrated to stimulate DNA damage and cell division.

Conversely, 2-OHE1, a weaker estrogen, is thought to have anti-carcinogenic and anti-proliferative qualities. There is a link between this metabolite and a decreased risk of breast cancer. The normal physiological effects of estrogen in breast tissue are dependent on the balance between the generation of 16α-OHE1 and 2-OHE1. The intricate relationship between estrogen metabolism and the risk of breast cancer is impacted by a number of variables, including as exposure to the environment, lifestyle decisions, and genetics. Gaining knowledge of how estrogen metabolism affects breast tissue can help identify the fundamental processes that lead to the development of estrogen-related breast cancer [14].

9. Role of Progesterone in Breast Cancer Development

Another important hormone that is progesterone, is involved in the development of breast cancer. It works in tandem with estrogen to regulate the growth and differentiation of breast tissue. In anticipation of a possible pregnancy, progesterone stimulates the growth of the mammary gland and encourages the proliferation of mammary epithelial cells.
To with of mammary epithelial cells in anticipation of a possible pregnancy. However, aberrant progesterone signaling or progesterone abnormalities may also contribute to another important hormone in the female reproductive system, progesterone, is involved in the development of breast cancer. Together with estrogen, it controls the development and differentiation of breast tissue. In anticipation of a possible pregnancy, progesterone stimulates the growth of the mammary gland and encourages the proliferation of mammary epithelial cells. However, progesterone imbalances or aberrant progesterone signaling may also contribute to the onset of breast cancer, similar to what estrogen does. Unchecked cell development and tumor formation can result from excessive progesterone exposure, particularly when paired with estrogen. Research is still being done to determine the exact mechanisms via which progesterone influences the occurrence of breast cancer. However, it is well known that progesterone plays a crucial role in the intricate hormonal network linked to the development of breast cancer [5][15-17].

10. Estrogen and Progesterone Interaction in the Development of Breast Cancer

Breast cancer is largely initiated and spread by estrogen and progesterone that are female reproductive hormones. Complex cross-talk between these hormonal pathways is made possible by the ERs and PRs found in breast cancer cells. Estrogen binding to the ER may raise PR expression, which in turn may increase susceptibility to progesterone's proliferative effects.

On the other hand, progesterone can modify ER expression and function, which in turn can affect estrogen signaling. Co-regulatory proteins that interact with the endogenous receptor (ER) and influence its transcriptional activity and consequent effects on cell growth and survival can be expressed in response to progesterone. The way that estrogen and progesterone signaling pathways interact can affect how quickly breast cancer progresses and how well a treatment works. It is crucial to comprehend the intricate relationships between these hormones in order to create focused therapy plans that target the estrogen and progesterone signaling pathways in breast cancer [18][19].

11. Importance of Hormone Testing in Breast Cancer Treatment and Diagnosis Decisions

When diagnosing and treating breast cancer, hormone testing—which includes determining the hormone receptor status—is crucial. It offers useful data for prognosis assessment and individualized treatment plans. Hormone receptor testing aids in the diagnosis process by identifying whether breast cancer is hormone receptor-positive (HR+) or negative. With their diverse biological traits and clinical behaviors, the many subtypes of breast cancer can be

distinguished with the help of this information. It helps in figuring out the best course of action and forecasting how well a given therapy will work.

In the adjuvant and neoadjuvant contexts, hormone receptor status also plays a role in treatment selection. Hormonal therapy, either by itself or in conjunction with other treatments, may be beneficial for patients with HR+ cancers. By blocking or interfering with hormone signaling pathways, these treatments seek to slow the growth of tumors and lower the chance of recurrence. Furthermore, the presence or absence of hormone receptors acts as a prognostic factor, indicating the tumor's potential aggressiveness and the chance that the illness would worsen. Because they are more likely to respond to hormonal therapy, patients with HR+ tumors often have better outcomes than those with hormone receptor-negative cancers [20-23].

12. Breast Cancer Risk Factors

12.1. Reproductive Risk Factors

- Early Menarche: Starting menstruation at a young age (typically under 12) slightly increases breast cancer risk.
- Late Menopause: Experiencing menopause at an older age (typically over 55) slightly increases breast cancer risk.
- First Full-Term Late Pregnancy**:** The risk of breast cancer is somewhat increased if you have your first child after the age of thirty**.**
- Nulliparity: Never giving birth increases breast cancer risk after age 40.
- Multiple Full-Term Pregnancies: Having multiple children decreases breast cancer risk after age 40, regardless of age at first birth [24-26].

12.2. Protective Factors

- Early Full-Term Pregnancy: Having a child at a younger age reduces breast tissue susceptibility to cancer.
- Surgical Removal of Ovaries: Removing ovaries protects against breast cancer.
- Breastfeeding: Breastfeeding may protect against breast cancer, particularly in certain populations (e.g., Chinese women) [7].

12.3. Unclear Risk Factors

- Menstrual Cycle Characteristics: Research has not clarified the role of cycle length, frequency, and other menstrual factors.
- Interval Between Births: The impact of time between pregnancies on breast cancer risk is uncertain.
- Spontaneous or Induced Abortion: The relationship between abortion and breast cancer risk remains unclear.
- Infertility: The link between infertility and breast cancer risk requires further investigation.
- Multiple Births: The effect of having twins or other multiple births on breast cancer risk is unknown.
- Hypertension During Pregnancy: Research has not established a clear connection between pregnancy-related hypertension and breast cancer risk [3].

12.4. Hormonal Influences

- Exposure to Estrogen and Progesterone**:** Breast cancer risk is increased when estrogen and progesterone are present at the same time.
- Long-term usage of combined estrogen/progesterone**:** hormone replacement therapy raises the risk of breast cancer.
- Estrogen Replacement Therapy: In postmenopausal women, it moderately raises the risk of breast cancer.
- Obesity in postmenopausal women: Exposure to estrogen raises the risk of breast cancer.

12.5. Obesity and physical inactivity

Overweight and obese are considered to have a protective effect against breast cancer in premenopausal, except aside from women with a family background of this ailment; so, body fat be a better indicator of breast cancer risk in postmenopausal women than body weight or BMI, and the distribution of body fat may also affect breast cancer risk. be a better indicator of breast cancer risk in postmenopausal women than body weight or BMI, and the distribution of body fat may also affect breast cancer risk [27].

12.6. Alcohol Consumption

Drinking alcohol frequently and excessively increases the risk of breast cancer. With increased usage, the risk increases. To reduce risk, consider limiting or avoiding alcohol altogether [26][28].

12.7. Environmental Exposure

- Ionizing Radiation: Ionizing radiation exposure can come from medical imaging procedures like CT scans and mammography
  - Radiation therapy
  - Nuclear accidents or fallout
- Chemical Exposure: Certain chemicals and pollutants, including
  - Herbicides and pesticides.
  - Industrial chemicals (e.g., benzene, formaldehyde)
  - Endocrine-disrupting chemicals (EDCs) (e.g., BPA, phthalates)
- Workplace Exposure: Certain occupations may increase breast cancer risk, including:
  - Healthcare professionals exposed to radiation or chemicals
  - Night shift workers [7][8].

13. Side- Effects: - Oral Mucositis

Figure 8 Oral mucositis

One of the most crippling side effects of cancer treatment is oral mucositis, which is also a well-known cause of anxiety for oncologists and a low quality of life for cancer patients. Produced by the early toxicity of chemotherapy and/or radiation therapy, which might limit the potential outcomes of treatment and potentially put a patient's survival in jeopardy. It's still unknown what factors will determine who and how much will be impacted.

It is primarily located in the respiratory system, GI tract, urogenital tract, and oral cavity. It is also found, to a lesser degree, in other organs like the eyes. It exhibits defensive barrier behavior, is resistant to friction and physical stimulation, and has a high cell turnover rate. Its abundant microbiota and absorptive abilities provide it special qualities related to health and wellbeing.

Oral mucositis, also referred to as mucositis, is a clinical consequence of cancer therapy that is most noticeable and feared by oncologists It is the result of chemotherapy-induced alterations in the gastrointestinal tract. Its occurrence rates vary depending on the type of cancer and the therapy used, and it has been referred to as the "hidden side" of cancer treatment [29].

The entire oral cavity, the throat, the larynx, the digestive tract, including the rectum and anus, the respiratory system, and the vagina can all be affected by mucositis. Many studies that have clarified the involvement of the oral microbiome in oral mucositis have been published as a result of the interest in the role of bacteria in the pathophysiology of oral mucositis. Antibiotics, however, are ineffective in treating mucositis, thus this does not imply that bacteria alter the course of the illness [30].

Treatment plans for cancer are made to specifically target fast-dividing malignant cells. Consequently, the cytotoxic effects of cancer therapy also expose tissues with high cell turnover, such as the oral, gastrointestinal, and vaginal mucosa, to chemotherapeutic drugs.

In patients with breast cancer undergoing targeted therapies such as the mTOR inhibitor everolimus and the TKI lapatinib, oral mucositis can occur as a side effect of both conventional chemotherapy and targeted treatment [31].

14. Pathogenesis of Mucositis

Effective treatment and prevention of mucositis depend on an understanding of its pathophysiology. According to recent research, there are several different pathways behind mucositis. The epithelium is impacted by cytotoxic treatment, just like all other mucosal tissues and cells are. Sonis et al.'s model of the pathophysiology of mucositis proposes a five-phase process that is separated into the following stages: commencement, upregulation with messenger signal production, signaling and amplification, ulceration, and healing. Whether the pathophysiology of mucositis seen in patients undergoing novel molecular targeted therapy is similar to that of mucositis brought on by radiation and traditional cancer therapies has not yet been established. Targeted therapy-induced Oral mucositis varies in appearance, course, concurrent adverse events, and toxicity, among other aspects. As a result, it might therefore be viewed as a separate entity with unique pathogenic processes from traditional Oral mucositis. Although more research is required, several writers firmly believe that immunological processes play a role in this process [32][33].

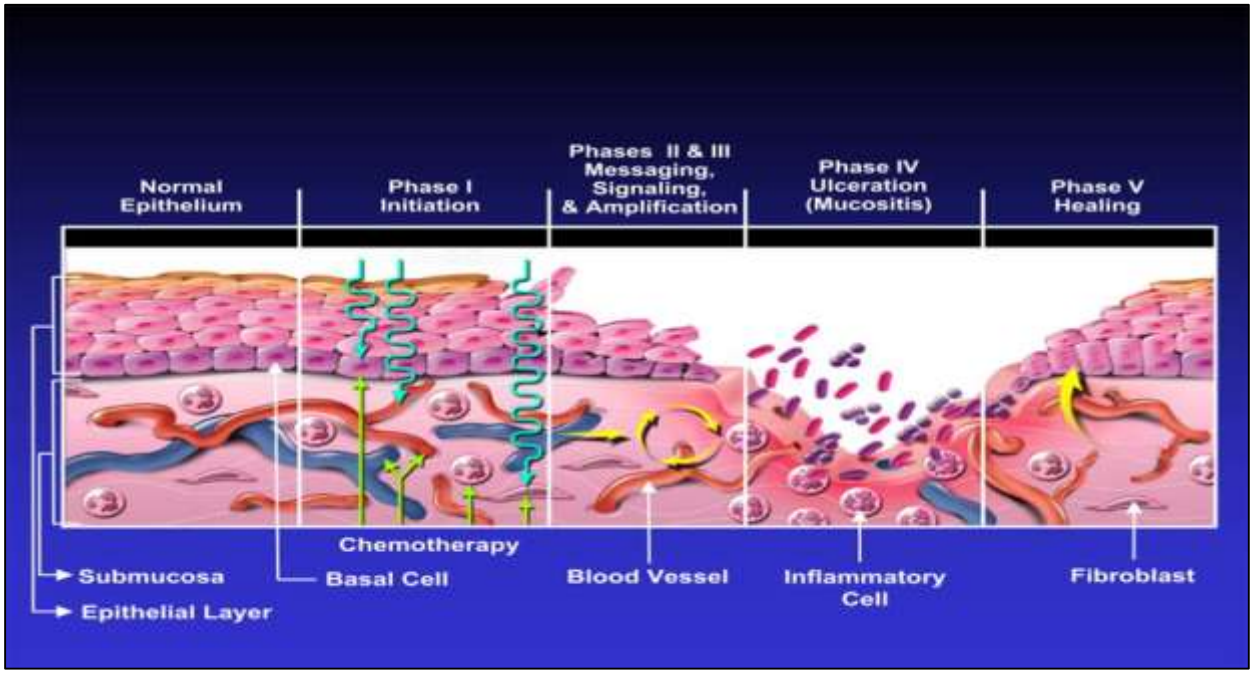

Figure 9 Pathogenies of mucositis

15. Clinical Management of Oral Mucositis

Management of oral mucositis is further discussed in the following parts: nutritional support, pain control, oral decontamination, palliation of dry mouth, and management of oral bleeding for oral mucositis.

15.1. Pain control

Pain is the main sign of oral mucositis. Pain has a major impact on dietary intake, oral hygiene, and overall quality of life. Therefore, the first step in any mucositis care plan is to address the pain associated with the condition. Saline mouthwashes, ice chips, and topical mouthwashes with anesthetics such 2% viscous lidocaine are used in several centers. Equal parts of diphenhydramine and a calming covering agent, like Kaopectate (Chattem, Inc., Chattanooga, TN) or Maalox (Novartis Consumer Health, Inc., Fremont, MI), can be combined with the lidocaine. These topical anesthetics could offer temporary comfort. Several different topical mucosal bio-adherent agents are available; these are not anesthetics, but they are thought to lessen pain by covering the ulcerated mucosa with a protective layer [34-36].

15.2. Nutritional Support

Nutritional Support The pain associated with severe oral mucositis can seriously impair nutritional intake. Furthermore, taste alterations may also result with radiation therapy and/or chemotherapy. Working with family

caregivers, a dietician or other expert must closely check nutritional intake and weight. When oral mucositis is present, a soft diet and liquid diet supplements are easier to stomach than a regular diet. A gastrostomy tube may be inserted proactively in patients who are anticipated to get severe mucositis, albeit this varies greatly between centers [36].

15.3. Oral Decontamination

For this demographic, oral decontamination may have very beneficial effects. First, it has been suggested that microbiological colonization of lesions caused by oral mucositis aggravates the condition; as a result, cleaning may aid in lessening the severity of mucositis. In fact, a number of studies have shown that maintaining proper dental hygiene helps lessen the severity of mucositis in the mouth. Patients who get hematopoietic cell transplantation and develop oral mucositis are three times more likely to have bacteremia's than those who do not, which prolongs hospital stays. Consequently, oral cleansing may lessen mucositis, which may lessen bacteremia. Moreover, oral cleaning can lessen opportunistic pathogen infection of the oral cavity [31][37][38].

15.4. Palliation of dry mouth

To ease dry mouth, perform the following steps: -

- Sip water as needed. A variety of supporting products, including artificial saliva, are available.
- Rinse alongside a solution of half a teaspoon of baking soda (or ¼ or ½ teaspoon table salt) in one cup to cleanse and lubricate oral tissues and buffer the environment. warm water many times each day.
- To increase saliva flow, chew sugarless gum.
- Use cholinergic agents as needed

15.5. Management of Bleeding

Patients who have received high-dose chemotherapy (such as those undergoing hematopoietic cell transplantation) who are thrombocytopenic may experience bleeding from oral mucositis ulcerations. Topical hemostatic treatments such as gelatin sponge 47 or fibrin glue can typically be used to control local intraoral hemorrhage. Patients with platelet counts under 20,000 need platelet transfusions because they run the risk of experiencing spontaneous internal bleeding, which can be extremely dangerous, particularly in the central nervous system [31].

16. Incidence and Risk Factors for Oral Mucositis

Tragically, it is impossible to accurately anticipate which patients will acquire Oral mucositis due to overall large variability. Many particular factors, including the underlying systemic disease, the kind of treatment, the dosage and frequency of chemotherapy drugs, and patient-related risk factors, influence the prevalence and severity of Oral mucositis in breast cancer patients. A number of common chemotherapeutic drugs, including taxanes, anthracyclines, and 5-fluorouracil (5-FU), have been linked to increased incidence of Oral mucositis. One common treatment for hormone receptor-positive, HER2-negative metastatic breast cancer (MBC) is to combine exemestane with the mTOR inhibitor everolimus. According to the National Cancer Institute Common Report, 56% of the patients acquired oral mucositis of any degree, of which 48% experienced mild to moderate grade 1-2 and 8% grade 3-5 mucositis. According to recent evaluations, the most frequent adverse event (AE) connected to everolimus treatment is oral mucositis, with an incidence of 44%. The dual TKI lapatinib reversibly inhibits the intracellular tyrosine kinase domain of the ErbB1 (EGFR) and ErbB2 (HER2) receptors. Lapatinib can be used in conjunction with capecitabine, trastuzumab, or an aromatase inhibitor to treat HER2-overexpressing MBC. Oral mucositis is a commonly documented adverse event (AE) only when administered in conjunction with capecitabine, while other TKIs including sunitinib and sorafenib, used as monotherapy to treat advanced renal cell carcinoma, for instance, can also result in Oral mucositis. Patient-related risk variables that might significantly increase the risk of Oral mucositis include age, gender, and comorbidities such poor dental health and malnutrition [39-46].

17. Conclusion

In this review, we sought to summarize current understanding regarding breast cancer, with a focus on its types, stages and the significance of hormonal imbalance in breast cancer, the value of hormone testing in breast cancer diagnosis, treatment, decisions, and risk factors. There is an urgent need to provide the most effective prevention, keeping in mind that modifiable risk factors may be vital in providing the reduction of breast cancer events, given that the morbidity and mortality rates of breast cancer have both increased dramatically over the past few decades. The review also discusses oral mucositis, a clinically significant and occasionally dose-limiting side effect of cancer treatment. The pathophysiology and clinical management of oral mucositis have been addressed in this review, with a specific focus on

palliative measures such pain control, nutritional guidance, retaining adequate oral hygiene, and risk factors for oral mucositis.

Compliance with ethical standards

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No conflict of interest is to be disclosed.

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