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"Global trands of Breast Cancer - Types, Causes, Stages, Risk factor, Current Treatment Strategies - An Updated Review"

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Abstract: In 2022, breast cancer remains a significant global health concern, accounting for approximately 23% of all new cancer diagnoses worldwide. Despite advancements in treatment and prevention strategies, breast cancer mortality rates have risen by 14%, underscoring the urgent need for continued research and innovative approaches.

This statistical analysis examines the epidemiology and impact of breast cancer, emphasizing its prevalence and mortality trends over time. In 2020, breast cancer was a leading cause of cancer-related deaths, highlighting the ongoing challenges in combatting this disease.The analysis explores the complex nature of breast cancer, categorizing it into non-invasive and invasive subtypes based on cellular and molecular characteristics. Molecular subtyping, such as luminal A and luminal B, underscores the diverse nature of the disease, guiding personalized treatment strategies.

Furthermore, the study investigates risk factors associated with breast cancer, including genetic predispositions, hormonal influences, lifestyle choices, and environmental exposures. Understanding these factors is crucial for implementing effective preventive measures and tailored treatment approaches.Recent therapeutic advancements, such as PARP inhibitors and DNA-targeting platinum drugs, are discussed as promising treatments for aggressive breast cancer subtypes like triple-negative breast cancer (TNBC).

Looking forward to 2032, this analysis emphasizes the importance of interdisciplinary research collaborations to refine early detection methods, address treatment resistance, and ultimately improve outcomes for breast cancer patients globally. Efforts should focus on translating research insights into practical clinical applications to meet the multifaceted challenges posed by breast cancer.

Key words: Breast cancer, Globle Health, Interdisciplinary, Statitical strategies

1. INTRODUCTION

Breast cancer is a pervasive health concern for women,itrepresent the significant part of world cancerdiagnoses,initiate 25% of new cases and affect approximately 1.7 million individuals yearly. Dreadful, itscontributes to 15% cancer related death. In ainterspersed reality. According to approximation from Word Health Organization (WHO) in 2020, cancer are first and second cause of the death before the age of 70 years in 112 of 183 countries.An estimated 685,000 women died from breast cancer in 2020.Human breast cancer health takes a conflicting course, characterized by the deep understanding of complex dynamics governing the prevention of breast cancer development.According to the examine cancer burden globally in 2022, the cancer incidence and death produce by the International Agency for Research on Cancer. The approximate provided present in do notaffectof the impact of acute respiratory syndromes. When the breast cancer has been reported in many species ahead human. The affair of breast cancer in animals register many species including mice, rats, hamster, dogs, like kangaroos and several rodents.Breast cancer arecategorized into non-invasive and invasive.Based on the expression pattern of key protein breast cancer are classified in different subtype, that included luminal A (ER+ and PR+ or, low Ki67), luminal B (ER+ and PR+,lowKi67),these type have clinical feature and treatment indication, guiding personalized therapy for patients.Breast cancer is complex and multistep disease believed arise through a series of successive steps.Despite improvement in surgical method and the uses of adjuvant therapies, it remaina many cause of mortality for many patients. Metastasis, the develop of cancer cell from the primary tumor to ceremonious organs or tissue, its primary cause of death of in breast cancer cases.This process is going advance of a cascade of normal breast epithelial cells into cancer ones. These event are involve genetic mutation, alteration in cellular pathway, and change the microenvironment surrounding the tumor.

In recent years, our conception of breast cancerboost andspread has mortally benefited from the uses of genetically altered mice models and bored transplantation methodologies.In thisarticle, we delineate the established mice models employed in studying breast cancer metastasis.

This review article surveyed some allowable studies considering different breast cancer models, on condition that insights in their strengths and limitation. Our review are study offers a through overview

the latest research on these models.

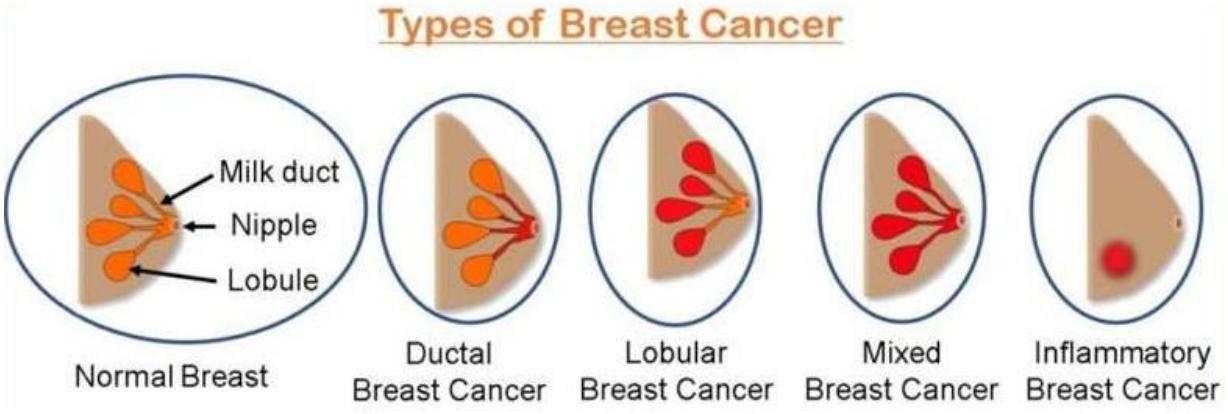

Figure 1 : Struture of breast

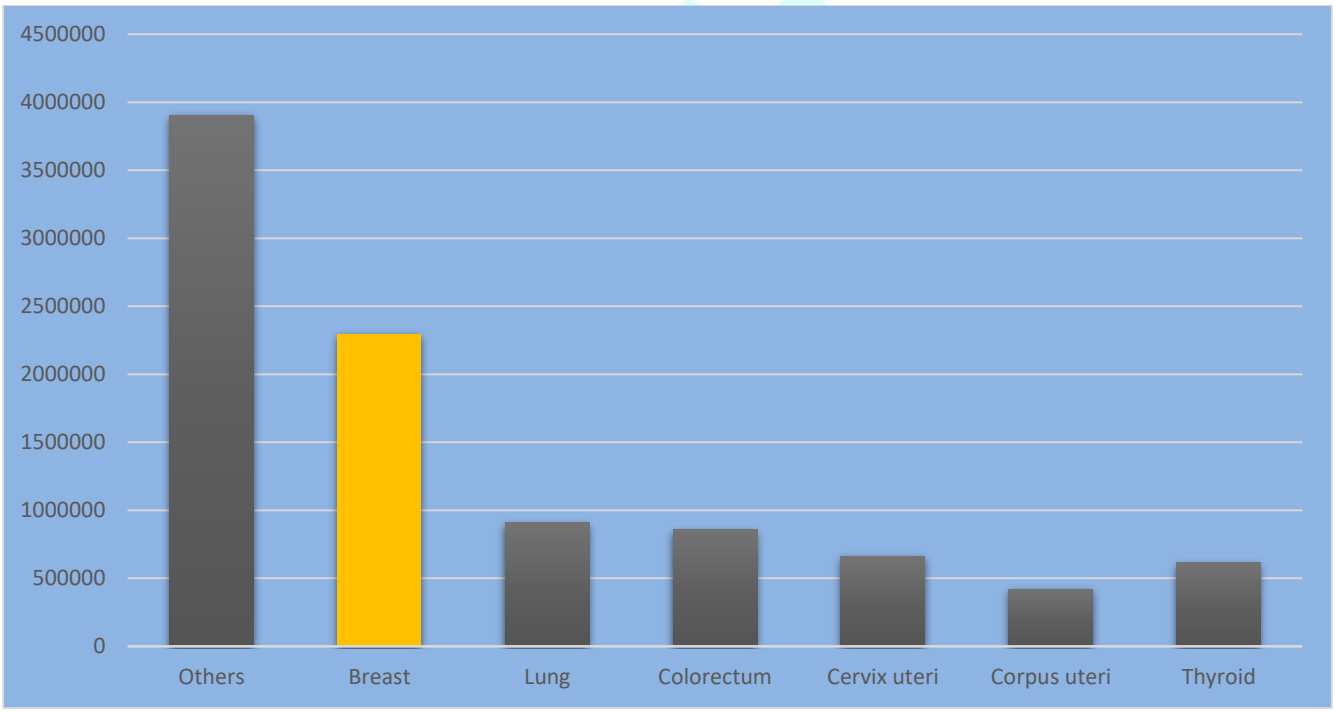

Figure 2 : Graphical analysis of breast cancer

1.2 Statistics Analysis Of Breast Cancer

Breast cancer stands out of the most prevalent form of cancer among women, with approximately 1.7 million new cases identified in 2022, comprising 23% of all cancer diagnoses globally. It holds the second position in overall cancer incidence, representing 11.9% of all cases and has experienced a concerning 14% increase in mortality. Notably, breast cancer has become the most common cancer in both developed and developing regions, ranking as the fifth leading cause of cancer-related deaths worldwide. The risk of breast cancer escalates steadily doubling with each passing decade until menopause, after which the rate of increase slows down or stabilizes, through the disease remains more prevalent post-menopause. Migration studies indicate that environmental factors play a significant role in the development of breast cancer, as evidenced by higher rares observed in areas of inceresd risk.

Data form the World Health Organizations International Agency for Research on Cancer (IARC) in 2023 revealed global breast cancer registries, demonstrating its widespread impact. Specifically, statistics from the Asian continent were outlined, highlighting the regional burden of the disease.

Furthermore,according to the Global Cancer Observatory (Globocan) reported the WHO,india reported the highest number of breast cancer-related deaths in 2022,with 70,218 fatalities, surpassing all other countries.

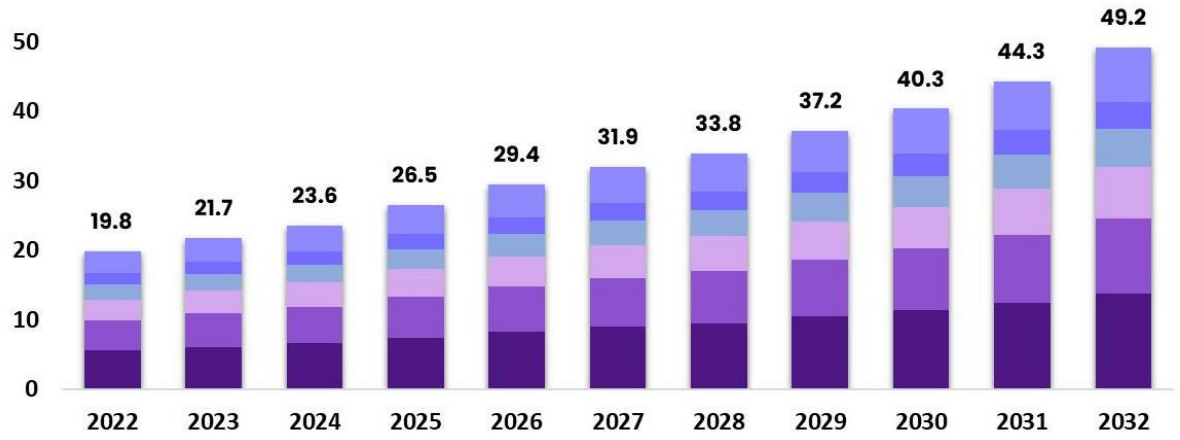

Figure 3: Statistics Analysis Of Breast Cancer

1.3 Types of Breast Cancer

According to their sites

1.3.1 Non-Invasive Breast Cancer:

refers the cancercells that have broken out from ducts or lobules the breast and have invaded surrounding fatty and connective tissues. This type of breast cancer has the potential to spread other parts of the body such as lymph nodes or distant organs.

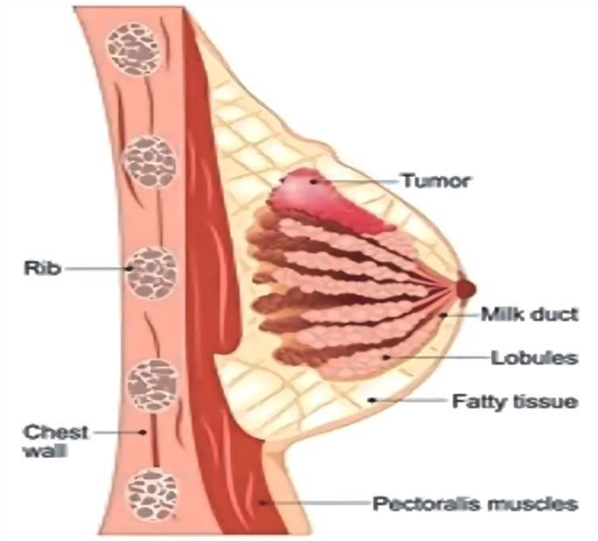

Figure 4: Non-Invasive Breast Cancer

1.3.2 Invasive Breast Cancer

invasive breast cancer cells penetrate the barriers of ducts and lobules infiltrating the adjacent adipose and connective tissue inside the breast cancer.

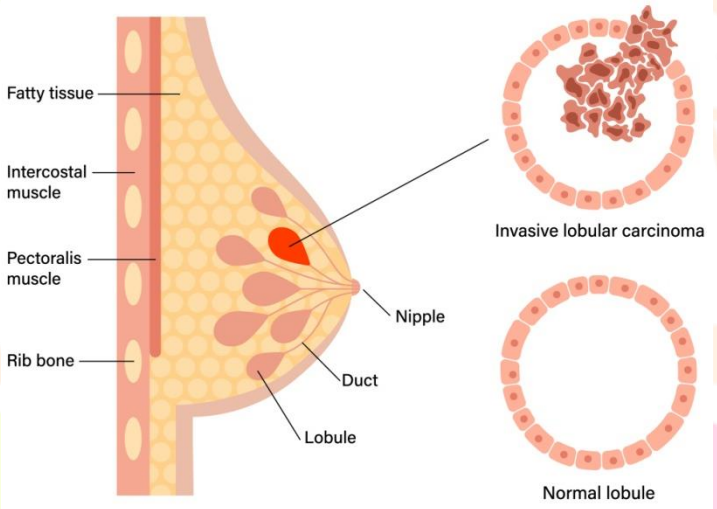

Figure 5: Invasive Breast Cancer

Frecuantly Occuring Breast Cancer

1.3.3 Lobular carcinoma in situ (LCIS)

commonly encountered in breast cancer is lobular carcinoma in situ, where the term “in situ” signifies that the cancerremain confined to its site of origin without spreading further. LCIS entails a significant proliferation of cells within the milk producing glands (lobules) of the breast.

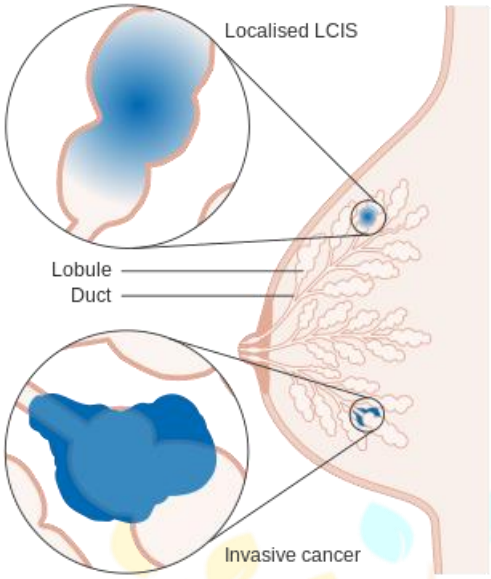

Figure 6: Invasive Breast Cancer

1.3.4 **Ductal carcinoma in situ** (DCIS)

DCIS, the prevalent form of non-invasive breast cancer, remain localized within the duct of the breast. Unlike invasive cancer, it not yet penetrate surrounding tissue. For instance, ductal comedocarcinoma is a subtype of DCIS. While confined to the ducts, DCIS does not typically metastasize to other parts of the body. Invasive lobular carcinoma (ILC) constitutes approximately 10% to 15% of breast cancer cases.

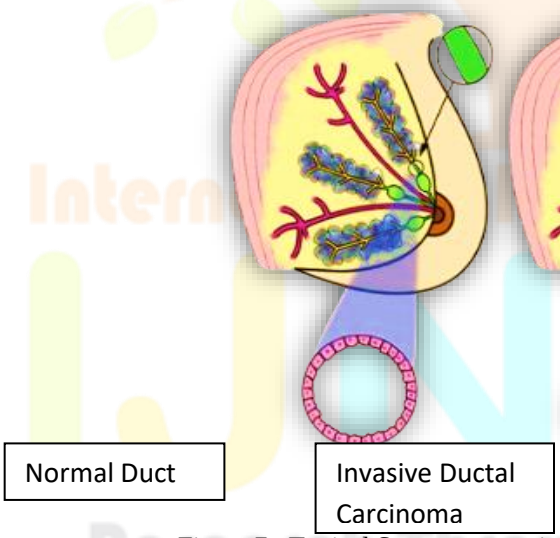

Figure 7 : Typical Structure associated with ductal carcinoma

1.3.5 **Infiltrating ductal carcinoma** (IDC)

IDC, often referred to as invasive ductal carcinoma, originates within the milk ducts of the breast. As it progresses IDC breaches the ductal wall and infiltrates the surrounding adipose tissue, potentially extending to other areas of the body. IDC stand as the most prevalent form of breast cancer, making up approximately 80% of all diagnosed cases.

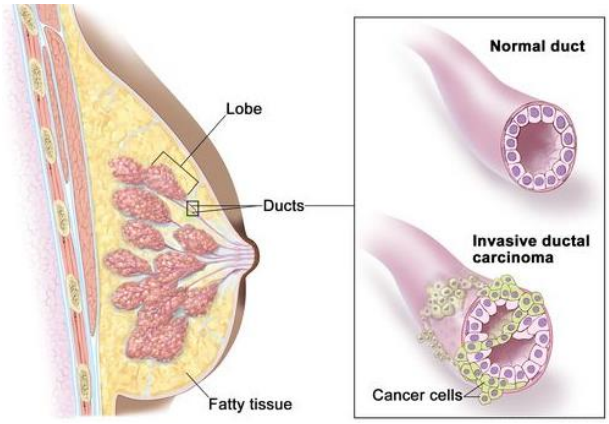

Figure 8: Infiltrating ductal carcinoma

Less commonly occurring Breast cancer

1.3.6 Medullary carcinoma

Medullary carcinoma is a type of invasive breast cancer characterized by a clearly defined boundary separating tumor tissue from normal tissue. This distinct boundary aids in its identification. Medullary carcinoma comprises a more 5% of all breast cancer cases.

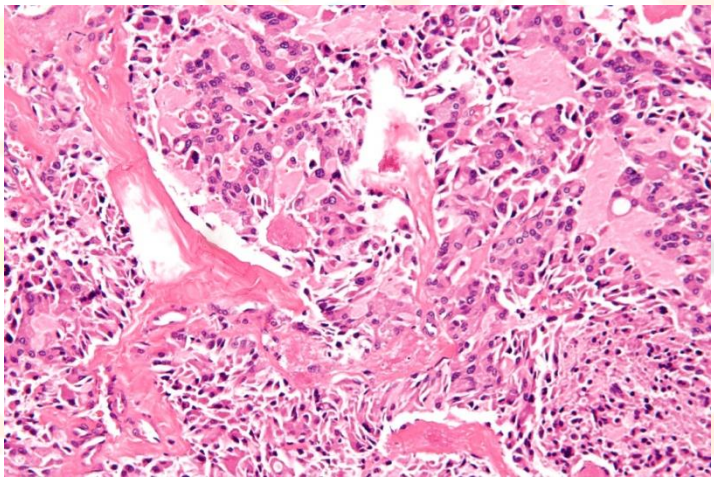

Figure 9: Medullary carcinoma

1.3.7 Mucinous carcinoma

Also know as colloid carcinoma, is an infrequent form of breast cancer arising from cancer cell that produce mucus. Patient diagnosed with mucinous carcinoma typically exhibits a more favorable prognosis compared to those with more prevalent types of invasive carcinoma.

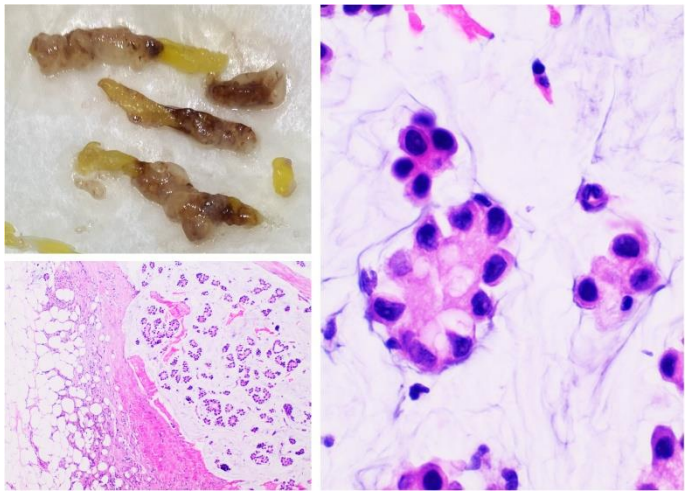

Figure 10: Mucinous carcinoma

1.3.8 Tubular carcinoma

Tubular carcinoma represent a distinct subtype of infiltrating (invasive) breast cancer. Patients diagnosed with tubular carcinoma typically experience a more favorable prognosis compared to those with more prevalent forms of invasive carcinoma. Tubular carcinomas constitute approximately 2% all of the breast cancer diagnoses.

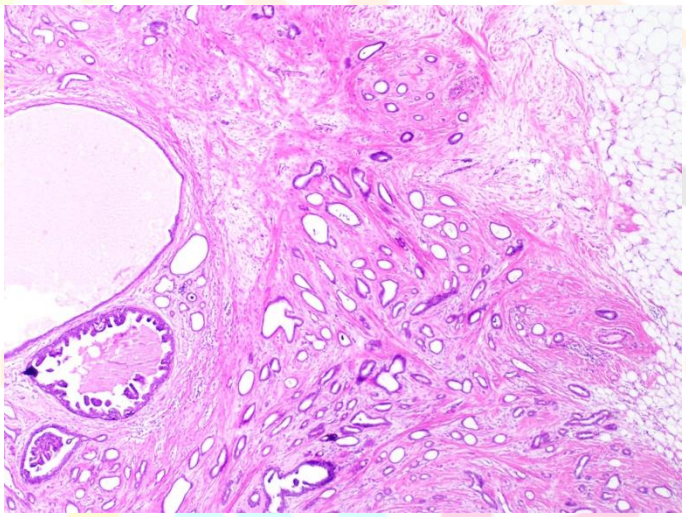

Figure 11: Tubular carcinoma

1.3.9 Inflammatory breast cancer:

Inflammatory breast cancer is characterized by visibly inflamed breast, often appearing red and warm, accompanied by dimples or thick ridges. This inflammation arises from cancer cells obstructing lymph vessels or channels in the skin over the breast. Despite its rarity norably aggressive and fast growing.

2. Causes of Breast cancer

2.1 Previous history of breast cancer

Women with a previous history of breast cancer face a heightened risk of developing breast cancer in their other breast.

2.2 Significant family history

A significant family history of certain types of cancer can elevate an individuals risk of developing breast cancer.

2.3 Genetic causes

Genetic factor play a major role in breast cancer risk, with family history serving as a significant indicator. The risk escalates if a close relative developed breast cancer at a young age, had a bilateral breast cancer, or if they a first degree relative (mother, sister, daughter). Additionally multiple second degree relative with breast cancer can also heighten the risk. Notably breast cancer in a male relative increasing the risk for all close female relatives. The abnormal genes BRCA1 and BRCA2 significantly raise breast cancer risk, with estimate suggesting a lifetime risk ranging from 40% to 85%. Women carrying the BRCA1 gene often develop breast cancer at a younger age.

2.4 Hormonal causes

Changes in hormone levels can influence the development of breast cancer. Factors such as irregular menstrual cycles, early pregnancy, hormonal replacement therapy, and the use of oral contraceptives may contribute to this risk.

2.5 Life style and dietary cause

A sedentary lifestyle and diet high in fat, especially among postmenopausal woman, can contribute to the risk of breast cancer. Additionally, obesity is identify as factor that may increase this risk. Alcohol consumption is another lifestyle factor linked to breast cancer, with risk escalating in proportion to the amount consumed. For instant, women who consume two to five alcoholic beverage per day face approximately one and a half times the risk of developing breast cancer compared nondrinkers.

2.6 Environmental cause:

Exposure to low doses of radiation over an extended period, such as in the case of profession like x-ray technicians, is associated with a slight elevation in the breast cancer among women.

3. Sign and symptoms

The primary indicator of breast cancer is often the discovery of a lump in the breast or armpit. Performing regular monthly breast self-exams (BSE) is effective methods to stay acquainted with changes in breast texture, size, cyclical fluctuation and skin condition. Other warning sign of breast cancer include swelling or a mass in the breast.

Other symptoms of breast cancer include swelling in the armpit, which indicates involvement of lymph nodes, as well as nipple discharge (clear and bloody), pain in the nipple, inverted (retraced) nipple, scaly or pitted skin on the nipple, persistent tenderness of the breast, and unusual breast pain or discomfort. In advanced stage (metastatic) the disease, additional symptoms may manifest, such as presence of underarm lymph nodes along with bone pain, shortness of breath, loss of appetite, headaches, and neurological pain or weakness.

4. Stages of breast cancer

Upon diagnosis, breast cancer is assigned a stage based on its level of advancement, aiding doctors in tailoring the most suitable treatment plan and providing a prognosis. Breast cancer stages are typically categorized broadly as either “in situ” (non-invasive) or “invasive’. “Furthermore, stages may be specified in detail and denoted be specified in detail and denoted by a numerical designation ranging from 0 to IV.

Table 1: Stages of breast cancer

Stage	Description
0	In situ carcinoma
I	The tumor measures less than ¾ inch (2 centimeters) in diameter and has not spread beyond the breast.
IIA	The tumor is ¾ inch or smaller in diameter and has spread to one to three lymph nod in the armpit, or microscopic amounts have spread to lymph nodes near the breastbone on the same side as the tumor, or both. Alternatively, the tumor is larger than ¾ inch but small 2 inch (5 centimeters) in diameter but has not spread beyond the breast.
IIB	The tumor is larger than ¾ inch but smaller than 2 inches in diameter, and it has spread to one to three lymph nodes near the breastbone on the same side as the tumor, or both. Alternatively, the tumor is larger than 2 inches in diameter but has not spread beyond the breast.
IIIA	The tumor is 2 inches or less in diameter and has spread to four to nine lymph nodes in the armpit or has enlarged at least one lymph node near the breastbone on the same side as the tumor. Alternatively, the tumor is large than 2 inches in diameter and has spread to up to nine lymph nodes in the armpit or to lymph nodes near the breastbone.
IIIB	The tumor has spread to the chest wall or skin, or it has caused breast inflammation (inflammatory breast cancer).

IIIC	The tumor can be any size and is accompanied by one of the following: it has spread to 10 or more lymph nodes in the armpit; it has spread to lymph nodes under or above collar bone; it has spread to lymph nodes in the armpit and has enlarged at least one lymph node near the breastbone on the same sides as the tumor, it has spread to four or more lymph nodes in the armpit, and microscopic amounts have spread to lymph nodes near the breastbone on the same side as the tumor.
IV	The tumor, irrespective of size, has metastasized to distant organs or tissue, such as the lunges or bones, or to lymph nodes distant distant the breast.

5. Risk Factors of Breast cancer

Table 2: Modifiable and Non-Modifiable risk factors of breast cancer

Non-Modifiable factors	Modifiable factors
Female sex	Hormonal replacement therapy
Older age	Diethylstilbestrol
Family history (of breast or ovarian cancer)	Physical activity
Genetic mutations	Overweight/obesity
Pregnancy and breastfeeding	Smoking
Menstrual period and menopause	Insufficient vitamin supplementation
Density of breast tissue	Excessive exposure to artificial light
Previous history of breast cancer	Intake of processed food
Non-cancerous breast cancer	Exposure to chemical
Previous radiation therapy	Other drug

6. Recent Advances in the Treatmrnt of Breast Cancer

Current Treatment Regimens

Triple negative breast cancer (TNBC) is more aggressive and difficult to treat than HR+ and HER2+ BC. Standard chemotherapy remains the mainstay of treatment for TNBC. Interestingly, TNBC is the BC subtype with the most complete response to chemotherapy (22%). However, their recurrence and metastasis rates are higher than those carrying non-TNBC tumor (67%). The median overall survival (OS) for patient with metastatic TNBC is about 9-12 mounth with conventional cytotoxic agents. The lack of ER,PR, and HER2 expression precludes the use of targeted therapies in advanced TNBC, and the only approved systemic treartment option is chemotherapy, usually taxanes, anthacycline, and platinum drugs, with or without bevacizumab, a recombinant humanized monoclonal antibody against vascular endothelial growth factor

(VEGF). Given the suboptimal treatment outcome with chemotherapy, new targrted therapies for TNBC are badly needed.

6.1 Novel Therapies

TNBC presents the greatest challenge among all breast cancer (BC) subtypes in terms of therapeutic option due to the absence of clearly defined molecular targets. There is an urgent need for the identification of new therapeutic targets and development of effective targeted agents.

Poly (ADP-ribose) Polymerase (PARP) Inhibitors

One of the singnificant breakthroughs in understanding the complex nature of TNBC is the discovry of a subset of sporadic TNBC that shares characteristics of homologous repair deficiency seen in BRCA1/2-mutated BC. To enhance treatment efficacy, drug combination regimens incorporating PARP inhibitors or the DNA- targeting platinum drug, carboplatin alongside standard chemotherapy have been proposed.

PARP enzymes play a role in repairing DNA single-strand breaks, while the BRCA1/BRCA2 genes encode tumor-suppressor proteins responsible for repairing DNA double-strand breaks through homologous recombination. Clinical trails have shown promising result with PARP inhibition in patient with germline BRCA1/BRCA2 mutation (gBRCA+) likely due to systhetic lethality resulting from unresolved DNA damage and replication arrest caused by the physical hindrance of DNA replication forks.

Olaparib has progressed the furthest in clinical development, demonstrating improved median progression free survival (PFS) and reduced risk od disease progression/death compared to standard chemotherapy in phase lll trials. Talazoparib, with its strong binding to DNA and traping of PARP-DNA complex, shows singnificant preclinical potency and promising antitumor activity as a single agent advanced gBRCA+BC.

While veliparib combined with carboplatin and paclitaxel did not extend PFS in gBRCA+BC, ongoing investigation are underway for its potential in advanced gBRCA+BC. Niraparib and rucaparib are also under investigation in advanced gBRCA+BC patient as monotherpy or in combination with chemotherapy.

Determining the use of PARP inhibition or carboplatin in TMBC typically involves assessing three DNA-based homologous recombination deficiency scores,which are closely linked to genetic defects in BRCA1/2. However, none of these agents effiectively treat all TNBC subtype, as TNBC can be further categorized into at least six subclasses, each with its distinct moilecular features and drug sensitivity. Identifying clinically relevant molecular biomarker of the drug responsiveness is crucial to refine this treatment approach.

Based on the provided information from your review paper, here is a structured discussion and conclusion for your paper.

7. Discussion

Breast cancer presents a significant global health challenge, with notable levels of morbidity and mortality. The prevalence of this disease underscores the urgent need for ongoing research and innovative approaches to treatment and prevention.

The review emphasizes the pivotal role of genetically modified mouse models and transplantation techniques in advancing our understanding of breast cancer metastasis. These models offer valuable insights into the intricate dynamics of cancer progression, aiding in the development of targeted therapies.

The classification of breast cancer into non-invasive and invasive types, further stratified by molecular subtypes like luminal A and luminal B, highlights the heterogeneous nature of the disease. This understanding is essential for customizing personalized treatment strategies based on specific biomarkers.

The discussion of risk factors, including non-modifiable factors such as genetic mutations and family history, along with modifiable factors like lifestyle choices and hormonal influences, underscores the multifaceted development of breast cancer. Environmental exposures and hormonal factors notably contribute, emphasizing the importance of preventive actions.

The review discusses promising advancements in breast cancer treatment, particularly for aggressive subtypes like triple-negative breast cancer (TNBC). Novel therapies such as PARP inhibitors and DNA-targeting platinum drugs offer new avenues for targeted treatment, especially in cases where traditional chemotherapy may be less effective.

7.1 **Challenges and Future Directions**

Despite significant progress, challenges remain in addressing the diverse molecular subtypes of breast cancer and overcoming treatment resistance. Further research is needed to identify biomarkers that predict treatment response and refine therapeutic approaches tailored to individual patients.

8. Conclusion

In conclusion, this review presents a comprehensive examination of breast cancer, encompassing its epidemiology, classification, risk factors, and recent therapeutic advancements. The utilization of genetically altered mouse models has played a pivotal role in elucidating critical aspects of breast cancer metastasis. The stratification of breast cancer into distinct subtypes underscores the significance of personalized medicine in treatment strategies. Emerging treatments such as PARP inhibitors show promising outcomes for aggressive breast cancer subtypes, emphasizing the ongoing importance of research in this area.

Looking ahead, efforts should concentrate on translating these research discoveries into clinical applications, refining early detection techniques, and tackling the challenges associated with treatment resistance. Collaborative interdisciplinary approaches will be crucial in furthering our comprehension of breast cancer and enhancing outcomes for patients globally.

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