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A COMPREHENSIVE REVIEW ON UNDERSTANDING BREAST CANCER'S ORIGINS AND RISK FACTORS

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ABSTRACT

Background: Breast cancer is a highly prevalent malignancy among women globally, with complex origins that involve genetic, environmental, and lifestyle factors. This review presents an analysis of the primary risk factors associated with breast cancer development, encompassing genetic mutations, hormonal influences, environmental exposures, and lifestyle factors such as diet, physical activity, and reproductive history. This study reviews the background of breast cancer research, focusing on the development of knowledge regarding its pathogenesis and the interaction between inherited genetic mutations, including BRCA1 and BRCA2, and acquired risk factors. **Methodology:** The methodology involved a systematic review of the existing literature, which included epidemiological studies, clinical trials, and molecular research. Peer-reviewed articles published in the last two decades were identified through key database searches to analyze trends in risk factor identification and their correlation with breast cancer incidence. Attention was focused on the role of biomarkers and genetic screening in identifying high-risk individuals. **Future perspectives**: Future perspectives include the potential for innovative prevention strategies, such as personalized risk assessments informed by genetic and molecular profiles, alongside targeted interventions that consider both modifiable and non-modifiable risk factors. The review highlights the necessity for ongoing investigation into the socioeconomic and cultural factors associated with breast cancer risk, alongside the

promise of novel therapies, including immunotherapy and gene editing, in decreasing breast cancer incidence and enhancing patient outcomes. **Conclusion**: comprehending the origins and risk factors of breast cancer is essential for enhancing early detection and prevention strategies. This review provides a comprehensive overview of existing knowledge and potential future directions in addressing this widespread disease.

KEYWORDS: Breast Cancer, Ductal, Lobular, Risk Factors, Metastatic, Stages, Family, Woman.

1. INTRODUCTION

The breast, designed for milk production during lactation, is made up of lobules that generate milk and are linked to ducts that go to the nipples. Cells that are present in lobules and ducts in the fibrous and adipose tissue of the breast are often the cause of breast cancer. Males do not have a physiological need for milk production, so although their breast anatomy is similar to that of females, male breasts do not have specialized lobules. **Figure.1.**[1]

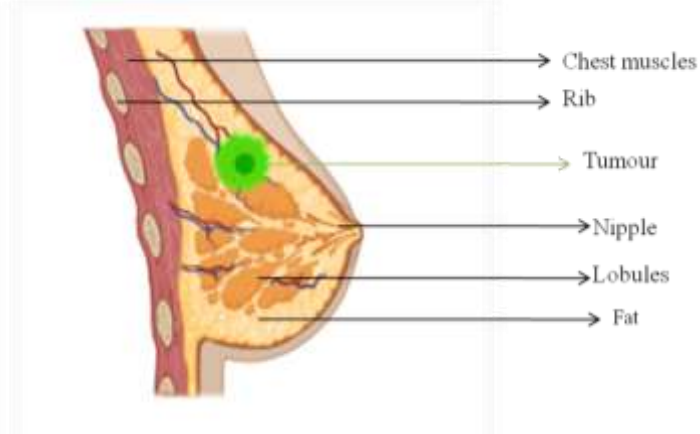

Figure 1: Representation of breast anatomy and breast cancer.[1]

Breast cancer (BC) is a disorder in which abnormal breast cells multiply uncontrollably and form tumors'. If left untreated, tumors can grow throughout the body and kill you. Breast cancer is the most common carcinoma in females and the major cause of cancer-related deaths in women worldwide.[1] Breast cancer is regulated by both high-frequency genes (e.g., BRCA1, BRCA2, p53, PTEN, ATM, NBS1, and LKB1) and low-frequency genes (e.g., CYP genes, GSTs, alcohol/metabolism genes, DNA repair genes, and cell signaling molecules). HER-2/neu antigen over expression has been demonstrated in a variety of human cancers, such as cancers of the breast, ovaries, lungs, stomach, and mouth.[2] According to the World Health Organization (WHO), cancer is the main or second most common cause of death

before the age of 70 in 112 of 183 countries. Additionally, it ranks third or fourth in an additional 23 nations.[3] Breast cancer accounts for around 25% of all cancer cases and 15% of all cancer-related deaths among women.[4] In contrast, breast cancer affects both men and women. Male breast carcinomas account for 0.8–1% of all breast cancers.[5,6]

1.1 Epidemiology of Breast Cancer

According to the World Health Organization (WHO), malignant neoplasms constitute the highest global burden for women, accounting for 107.8 million Disability-Adjusted Life Years (DALYs), 19.6 million of which are caused by breast cancer.[7] Breast cancer is the most often diagnosed cancer among women globally, with 2.26 million [95% UI, 2.24–2.79 million] new cases in 2020.[8] In the United States alone, breast cancer is estimated to account for 29% of all new malignancies in women.[9] According to the 2018 GLOBOCAN statistics, age-standardized incidence rates (ASIR) of breast cancer are highly and favorably related to the Human Development Index (HDI).[10] According to 2020 statistics, the ASIR was the greatest in very high HDI nations (75.6 per 100,000), while it was more than 200% lower in medium and low HDI countries (27.8 per 100,000 and 36.1 per 100,000, respectively).[8] In addition to being the most frequent, breast cancer is the top cause of cancer mortality in women globally. Globally, breast cancer caused 684,996 deaths [95% UI, 675,493-694,633] at an age-adjusted rate of 13.6/100,000[8] although industrialized nations had the greatest incidence rates, Asia and Africa accounted for 63% of all fatalities in 2020.[5] Most women who acquire breast cancer in a high-income nation will survive; the converse is true for women in the majority of low- and middle-income countries.[11] Considering into account the clinical extent of breast cancer, 5-year survival rates were 89.6% for localized and 75.4% for regional cancer in areas with developed health care (Hong Kong, Singapore, and Turkey). In less developed nations (Costa Rica, India, the Philippines, Saudi Arabia, and Thailand), the survival rates for localized and regional breast cancer were 76.3% and 47.4%, respectively.[12] Breast cancer incidence and mortality rates have risen during the past three decades. Between 1990 and 2016, breast cancer incidence more than quadrupled in 60/102 countries (e.g., Afghanistan, Philippines, Brazil, Argentina), while fatalities doubled in 43/102 countries (e.g., Yemen, Paraguay, Libya, Saudi Arabia).[13] According to current forecasts, by 2030, the global number of new cases diagnosed will be 2.7 million per year, with 0.87 million fatalities.[14]

1.2 Molecular Pathophysiology

Breast cancer can develop as a result of genetic abnormalities and DNA damage brought on by estrogen exposure. Alpha (α) and beta (β) estrogen receptors (ERα and ERβ) are the two types of estrogen receptors in humans.[15] ERα generally occurs in the breast gland, uterus, ovary (meningeal cells), bone, male reproductive organs (testis and epididymis), prostate (stroma), liver, and adipose tissue. ERβ is mostly present in the prostate epithelium, bladder, ovary (granulose cells), colon, adipose tissue, and immune system.[16] The significance of ERβ in carcinogenesis is still debated; however, the ERα protein has been identified as a key player. Activation of ERα by estrogen is usually assumed to be responsible for enhanced proliferation in breast tumors', while numerous studies indicate that the presence of ERβ has an anti-proliferative impact.[16] The expression of estrogen receptor alpha (Erα) is increased in triple-negative breast cancer (TNBC). ERβ1 is the form of the ERβ receptor that suppresses tumor growth, while ERβ2 and ERβ5 exhibit pro-tumor activity.[17]

2. CLASSIFICATION OF BREAST CANCER

2.1 Histological Classification

Invasive breast cancers (IBC) are a broad category of tumors with varying clinical presentation, behavior, and appearance. The World Health Organization (WHO) differentiates at least 18 distinct histological breast cancer types. In triple-negative breast cancer (TNBC), estrogen receptor alpha (Erα) expression is negative. The ERβ1 version of the ERβ receptor acts as a tumor suppressor, whereas ERβ2 and 5 demonstrate pro-oncogene activity in TNBC.[18] Invasive breast cancer of no special type (NST), formerly known as invasive ductal carcinoma is the most frequent subgroup (40–80%).[19] This type is diagnosed by default as a tumor that does not fit into one of the histological special categories.[18] Approximately 25 percent of invasive breast tumors' have different development patterns and cytological markers, hence, they are recognized as particular subtypes (e.g., invasive lobular carcinoma, tubular, mutinous A, mutinous B, neuroendocrine).[19] Molecular categorization In invasive breast cancer, mRNA gene expression levels can be used to distinguish molecular subtypes from histological subtypes. Perou et al. discovered four molecular subtypes using microarray gene expression data on a sample of 38 breast tumors' in 2000. Luminal, HER2-enriched, basal-like, and normal breast-like.[21] The typical breast-like subtype has now been removed, as it is likely to indicate sample contamination by normal mammary glands. The Cancer Genome Atlas Project (TCGA) analyzed over 300 primary tumors (at the DNA, RNA, and protein levels) and integrated them into biologically homogeneous groupings. The

consensus clustering validated the separation of four major breast cancer intrinsic subtypes based on mRNA gene expression levels (Luminal A, Luminal B, HER2-enriched, and basal-like).[22] In 2007, an integrated investigation of human and mouse mammary tumors' revealed the fifth intrinsic subtype—Claudin-low breast cancer.[23]

2.2 HER-2 Enriched Breast Cancer

10–15% of breast tumors' are HER2-enriched. It is distinguished by the strong expression of HER2 and the lack of ER and PR. This subtype mostly expresses genes and proteins linked to proliferation (e.g., ERBB2/HER2 and GRB7), rather than luminal and basal gene and protein clusters.[24,25] There is also evidence of APOBEC3B-mediated mutagenesis in the HER2-enriched subtype. APOBEC3B is a subclass of APOBEC cytidine dreaminess that cause cytosine mutation biases and serve as a source of mutation clusters.[26,27] HER2-enriched tumors' develop faster than luminal malignancies and had the poorest prognosis of any subtype prior to the discovery of HER2-targeted treatments. Importantly, the HER2-enriched subtype is not synonymous with clinically HER2-positive breast cancer, as many ER-positive/HER2-positive tumors' fall into the luminal B category. Furthermore, around 30% of HER2-enriched tumors' are identified as clinically HER2-negative using immune-histochemistry (IHC) or fluorescence in situ hybridization (FISH) techniques.[28]

2.3 Luminal Breast Cancer

Luminal breast cancers are ER-positive tumors', accounting for over 70% of all instances of breast cancer in Western countries.[29] Luminal-like malignancies most typically show as IBC with no distinct subtype, however they may sometimes differentiate into invasive lobular, tubular, invasive cribriform, mutinous, and invasive micro papillary carcinomas.[30,31] The luminal A and B subtypes of luminal-like tumors, which have different clinical outcomes, are distinguished by two main biological processes: proliferation-related pathways and luminal-regulated pathways.[32] Luminal tumors are distinguished by the presence of estrogen receptors (ER) or progesterone receptors (PR) and the lack of HER2. In this subtype, ER transcription factors activate genes whose expression is indicated by the luminal epithelium lining the mammary ducts.[33] It also exhibits decreased expression of genes associated with cell growth.[34] Luminal B tumors have a higher grade and a worse prognosis than subtype A. They are ER-positive and may also be PR-negative or HER2-positive. It also contains the strong expression of proliferation-related genes (e.g., MKI67 and AURKA).[35,36,37]

2.3 Triple Negative Breast Cancer (TNBC)

Triple-Negative Breast Cancer (TNBC) is a diverse group of breast cancers that are ER-negative, PR-negative, and HER2-negative. They account for around 20% of all breast cancers. TNBC is more prevalent among women under 40 years of age and African-American women.[28] The majority (approximately 80%) of breast cancers arising in BRCA1 gremlin mutation are TNBC, while 11–16% of all TNBC harbor BRCA1 or BRCA2 gremlin mutations. TNBC tends to be biologically aggressive and is often associated with a worse prognosis.[38] The most common histology seen in TNBC is infiltrating ductal carcinoma, but it may also present as modularly-like cancers with a prominent lymphocytic infiltrate; metaplastic cancers, which may show squamous or spindle cell differentiation; and rare special type cancers like adenoid cystic carcinoma (AdCC).[39,40] The phrases basal-like and TNBC are sometimes used interchangeably; however, not all TNBC are basal. TNBCs may be split into six subgroups based on gene expression profiling: basal-like (BL1 and BL2), mesenchymal (M), mesenchymal stem-like (MSL), immune-modulator (IM), luminal androgen receptor (LAR), and an undetermined group (UNS).[41,42]

2.4 Claudin Low Breast Cancer

Claudin-low (CL) breast cancers have a poor prognosis since they are mostly ER-negative, PR-negative, and HER2-negative. CL tumors' represent 7–14% of all invasive breast cancers.[30] All other poor-prognosis categories (Luminal B, HER2-enriched, and Basal-like) and Claudin-low tumors' had similar survival rates. Genes involved in cell-cell adhesion, such as occluding, E-cadherin, and Claudin 3, 4, and 7, have lower expression levels in the CL subtype. These tumors also show stem cell-like gene expression patterns and substantial expression levels of epithelial-mesenchymal transition (EMT) genes.[43,44]

2.5 American Joint Committee on Breast Cancer Classification

The AJCC staging system, which incorporates grading, immune-histochemical biomarkers, and structural disease progression, serves as a baseline tool for estimating the expected outcome of breast cancer patients. Since its establishment in 1977, the American Joint Committee on Cancer (AJCC) has developed a globally recognized staging system based on anatomic findings: tumor size (T), nodal status (N), and metastases. However, gene expression profiling has revealed multiple molecular subtypes of breast cancer.[45] The eighth edition of the AJCC staging manual (2018) presents a new predictive staging method for breast cancer that, in addition to morphological criteria, recognizes molecular variables.[46]

These factors—ER, PR, HER2, grade, and multigame assays are suggested in practice to characterize the prognosis.[47,48] The recent upgrade to breast cancer staging using biologic markers enhanced outcome prediction when compared to previous staging based only on morphological aspects of the disease. The validation studies involved the reassessment of the Surveillance, Epidemiology, and End Results (SEER) database (n = 209,304, 2010–2014) and the University of Texas MD Anderson Cancer Centre database (n = 3327, years of treatment, 2007–2013), according to the 8th edition AJCC manual, which proved the more accurate prognostic information. **Figure.2.**[49,50]

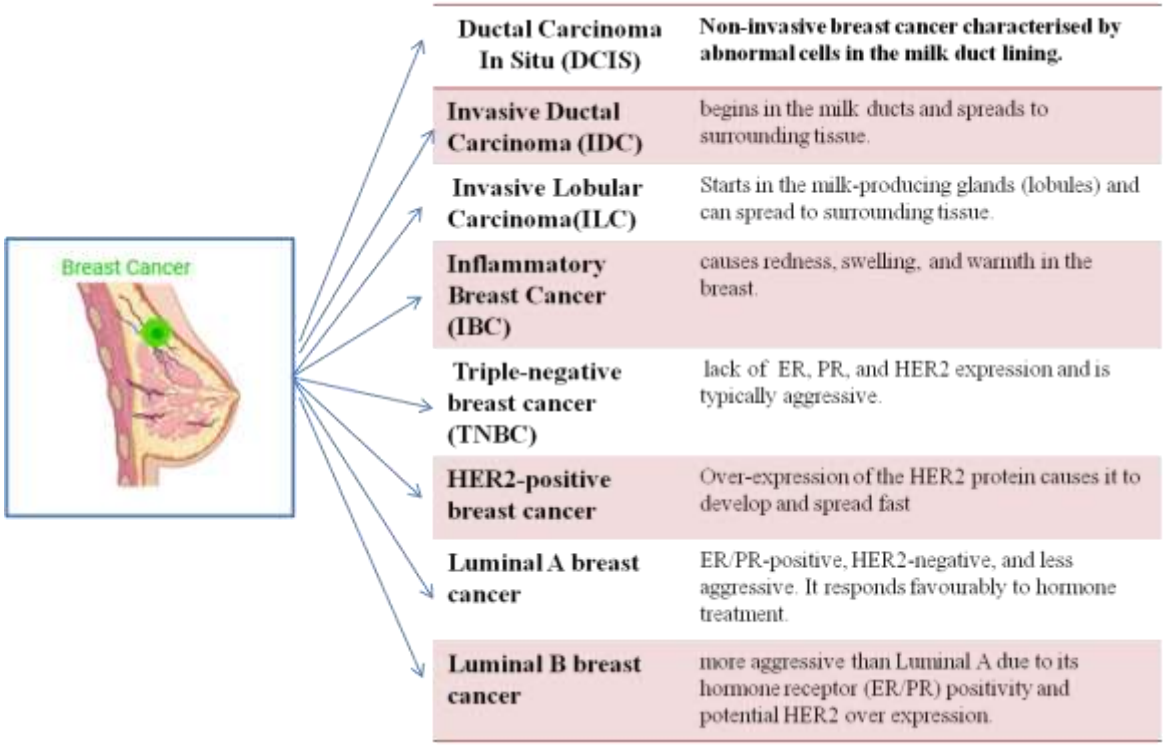

Figure 2: Representation of main types of breast cancer.

3. Stages of Breast Cancer

Breast cancer is staged utilizing the T, N, and M categorizations with Tumour (T): The size and biomarkers of the primary breast tumour. Node (N): Lymph node involvement, including location, size and extent. Metastasis (M) is the presence of cancer cells that have migrated to distant bodily locations. **Firure.3.**[51]

Stage 0 refers to cancer that is limited to the breast ducts and has not spread to the surrounding tissue.[51]

Stage IA refers to a small, invasive tumour that has not migrated to the lymph nodes.[18]

Stage IB: Tumour that has progressed to lymph nodes with a diameter more than 0.2 mm but less than 2 mm is classified as stage IB. There may be no sign of a tumour in the breast, or the tumour is 20 mm or less in size.[51]

Stage IIA

Although there is no tumour in the breast, the cancer has spread to one to three maxillary lymph nodes. It hasn't spread to other areas of the body. The tumour has spread to one to three auxiliary lymph nodes that are 20 mm or smaller. The tumour is larger than 20mm but less than 50mm in diameter and has not spread to the auxiliary lymph nodes.[51]

Stage IIB

The tumour has spread to 1–3 axillary lymph nodes and is bigger than 20 mm but not 50 mm. The tumour is larger than 50 mm, but has not spread to the lymph nodes in the axilla.[51]

Stage IIIA

The cancer has spread to 4-9 axillary or internal mammary lymph nodes, depending on tumour size. It has not spread to other bodily parts. A tumour larger than 50 mm that has spread to one to three axillary lymph nodes is categorised as Stage IIIA.[51]

Stage IIIB

The tumour has spread to the chest wall, the breast has swelled or ulcerated, or it is categorised as inflammatory breast cancer. It may have progressed to up to nine axillary or internal mammary lymph nodes. It has not spread to other bodily parts.[51]

Stage IIIC: Tumour that has progressed to ten or more lymph nodes in the axillary, internal mammary, or behind the clavicle but has not migrated to other regions of the body.[51]

Stage IV (metastatic)

The tumour may have spread to other organs, including the bones, lungs, brain, liver, distant lymph nodes, and chest wall.[51]

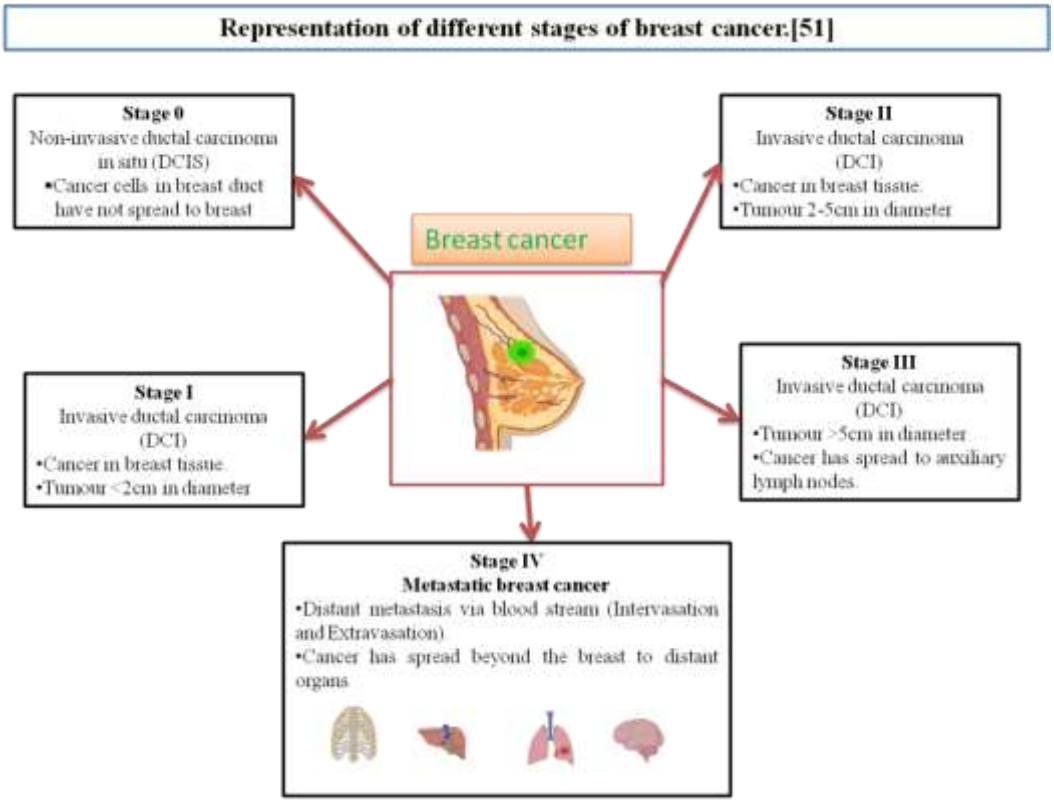

Figure 3: Representation of different stages of breast cancer.[51]

4. Risk Factors of Breast Cancer

It is crucial in general health screening for women to detect traits connected to a higher risk of developing breast cancer. The number of risk factors for breast cancer is enormous, including both modifiable and non-modifiable variables. **Table. 1.**[52]

Table 1: These variables work together to increase a person's risk of developing breast cancer.[52]

Non- modifiable risk factors	Modifiable risk factors
Female sex	Hormonal replacement therapy
Older age/ Age factor	Physical activity
Family history	Overweight obesity
Genetic mutations	Alcohol consumption
Ethnicity	Smoking
Pregnancy and breast feeding	Insufficient vitamin supplementation
Density of breast tissue	Excessive exposure to artificial light
Previous history of breast cancer	Exposure to chemicals
Previous radiation therapy	Other drugs

4.1 NON- MODIFIABLE RISK FACTORS

4.1.1 Female Sex

Female sex is one of the biggest risk factors for breast cancer, mostly due to higher hormonal stimulation. Unlike males, who have low estrogen levels, women have breast cells that are highly sensitive to hormones (especially estrogen and progesterone) and any disturbances in their equilibrium. Circulating estrogens and androgens are positively related to a higher risk of breast cancer.[53] Premenopausal and postmenopausal women have a greater risk of breast cancer due to changes in the physiological levels of endogenous sex hormones; the Endogenous Hormones and Breast Cancer Collaborative Group has also confirmed similar findings.[54,55] Men account for fewer than 1% of all breast cancer cases. Breast cancer in males, on the other hand, is an uncommon illness that is usually more advanced when diagnosed than in women. Men's average age at diagnosis is around 67. The key variables that raise a man's risk of breast cancer are older age, BRCA2/BRCA1 mutations, higher estrogen levels, Klinefelter syndrome, family history of breast cancer, and radiation exposure.[55]

4.1.2 Older Age/ age Factor

At present, almost 80% of patients with breast cancer are over the age of 50, while more than 40% are over the age of 65.[56] This malignant tumor is uncommon for this age group, but because of its aggressive nature, it still poses a significant clinical and social burden. Research has shown that higher histological malignancy, restricted expression of steroid receptors, frequent over expression of HER-2 receptors, or the molecular subtype "basal-like" (also called "triple negative") are frequently associated with breast cancer in young women.[57] Furthermore, the incidence of breast cancer in premenopausal women is increasing—within 30 years, it has nearly doubled.[58]

4.1.3 Family History

A family history of breast cancer is a substantial risk factor for developing breast cancer. Approximately 13–19% of patients diagnosed with breast cancer report a first-degree family suffering from the same ailment.[59] Additionally, the risk of breast cancer grows dramatically with the rising number of first-degree relatives affected; the risk may be much higher when the affected relatives are under 50 years old.[60,61,62] The rates of breast cancer are much greater in all individuals with a family history, regardless of age. This association is caused by epigenetic modifications and environmental variables that could act as triggers.[63] An

increased risk of breast cancer may result from a family history of ovarian cancer, particularly in cases where BRCA1 and BRCA2 mutations are present.[64]

4.1.4 Genetic Mutations

Apparently, a tiny proportion of breast cancer cases (5–10%) are hereditary. The most well-known genetic alterations linked to this malignancy are abnormalities in the BRCA1 and BRCA2 genes.[65] The BRCA1 gene, which is situated on chromosome 17, is a suppressor gene that produces a nuclear protein that is responsible for genome stability. This protein, together with the products of other suppressor genes, signal transduction genes, and DNA damage detecting genes, forms a protein complex that binds to RNA polymerase II and interacts with histone de-acetylene, altering transcription, DNA repair, and recombination processes. The BRCA1 protein, along with the BRCA2 gene product, which is also a suppressor gene located on chromosome 13, is notably active in the repair of double DNA strand breaks by homologous recombination.[66] Mutations in these genes occur in just 3–5% of breast cancer patients. Nonetheless, these patients ought to be a part of the preventative program because of the high frequency of BRCA1/BRCA2 genes. The expected 10-fold increased risk of breast cancer in carriers of the BRCA1/BRCA2 mutation is observed.[67] Aside from the higher risk of breast cancer, bearers with such mutations are also more likely to develop ovarian cancer. A considerable variety of DNA repair genes that can interact with BRCA genes, such ATM, PALB2, BRIP1, or CHEK2, have been shown to be implicated in the development of breast carcinogenesis; nevertheless, they are characterized by a lesser penetrance (moderate degree) compared to BRCA1 or BRCA2.[68,69]

4.1.5 Hormonal and Reproductive Risk Factors

Many research investigations have proven a strong link between endogenous hormone exposure—especially estrogen and progesterone—and an increased risk of breast cancer in women. As a result, the occurrence of certain events such as pregnancy, nursing, first menstruation, and menopause, as well as their length and accompanying hormonal imbalance, are critical in terms of possible carcinogenic events in the breast microenvironment. The first full-term pregnancy at an early age (particularly in the early twenties) and a subsequent rising number of births are connected with a lower risk of breast cancer.[70] Furthermore, pregnancy has preventive benefits against future cancer. However, protection was detected during the 34th pregnancy week and was not proven for pregnancies lasting 33 weeks or fewer.[71] Women with a history of preeclampsia during pregnancy or children born from a

preeclampsia pregnancy had a decreased chance of getting breast cancer.[72] Deregulated hormone levels during preeclampsia, including increased progesterone and decreased estrogen levels, as well as insulin, cortical, insulin-like growth factor-1, androgens, human chorionic gonadotropin, corticotrophin-releasing factor, and IGF-1 binding protein levels that are outside of physiological ranges, have a protective effect against breast carcinogenesis. Breastfeeding for a longer period lowers the risk of both ER/PR-positive and -negative malignancies.[73]

4.1.6 Density of Breast Tissue

Breast tissue density varies throughout one's life; nonetheless, professional practice has defined numerous classifications such as low-density, high-density, and fatty breasts. Women with lower body mass indices who are younger, pregnant, nursing, or undergoing hormone replacement therapy are known to have larger breasts.[74] In general, higher breast tissue density corresponds with higher breast cancer risk; this pattern is evident both in premenopausal and postmenopausal females.[75] Tissue from the breast for density screening was offered as a potential, non-invasive, and rapid tool for rational monitoring of females at elevated risk of cancer.[76]

4.2. MODIFIABLE FACTORS

4.2.1 Alcohol Consumption

Several studies reveal a link between alcohol intake and an increased risk of breast cancer.[77,78] This reliance is caused by a variety of processes, including alcohol, which increases the quantity of estrogen in the blood by blocking their metabolism in the liver and accelerating the conversion of androgens to estrogen. Furthermore, it inhibits the immune system and DNA repair activities, which may promote cellular proliferation and migration. Finally, alcohol's metabolites are carcinogenic substances.[79] It is believed that every 10 g of pure alcohol consumed each day increases the risk of breast cancer by 9%.[80]

4.2.2 Diet

Multiple studies have been conducted to investigate the effect of nutrition on cancer development. The link between a diet high in saturated fats, especially those from animals, and the risk of getting colon cancer is clear.[81] On the other hand, studies indicate that the association between food and the risk of breast cancer is not totally consistent. Dandamudi et al. examined systematic research published between 2013 and 2017. Ten of the seventeen papers assessed investigated the effect of an "unhealthy" diet on breast cancer risk. The diet

in question comprised sweetened soft drinks, processed fruit juices, red and processed meats, hardened fats, saturated fats, salted food (chips, chips, peanuts), refined grains, and sweetened products (sweets, desserts).[81] Excessive use of the aforementioned goods was found to be significantly associated with an increased risk of breast cancer, although not all of the reviewed research supported this finding. This association was particularly concerned about the overindulgence in saturated fats, salt, and red and processed meat.[82] This in-depth investigation also found that a diet rich in vegetables, fruits, fish, legumes, oils, and vegetable oils lowers the incidence of breast cancer.[82]

4.2.3 Smoking

Smoking tobacco carcinogens are delivered to breast tissue, increasing the likelihood of alterations in oncogene and suppressor genes (especially p53). Thus, both active and passive smoking considerably contribute to the activation of pro-carcinogenic events.[84] Additionally, prolonged smoking history and smoking before the first full-term pregnancy are additional risk factors that are more prominent in females with a family history of breast cancer.[85,86]

4.2.4 Obesity

Obesity is one of the risk factors for developing breast cancer, as established by several research investigations. Jiralerspong and Goodwin conducted a pooled study of various papers that examined the link between obesity and breast cancer prevalence in premenopausal and postmenopausal women. This study discovered that both overweight and obesity increased the chance of getting breast cancer, specifically steroid-receptor-expressed breast cancer, in postmenopausal women who did not use hormone replacement therapy.[87,88] Obesity promotes the process of cancer through several mechanisms. Overdeveloped adipose tissue is a source of numerous cytokines, chemokines, and endocrine factors, in particular proangiogenic and promitogenic leptin, which affects the immune environment of the described tissue.[89] Obese women are less likely than normal-weight women to undergo breast reconstruction, and those who do face greater surgical problems. Systemic chemotherapy and hormone treatment work less well in obese women. Obese women have a higher chance of local recurrence than women of normal weight. Obese women who survive breast cancer experience considerably reduced cancer treatment effectiveness.[90]

4.2.5 Other Drugs

Antibiotics, antidepressants, statins, antihypertensive medicines (e.g., calcium channel blockers, angiotensin II-converting enzyme inhibitors), and NSAIDs (including aspirin, ibuprofen) may also be possible risk factors for breast cancer.[91,92]

Method

The authors investigated a wide range of literature databases, including MEDLINE, EMBASE, Pub Med, Web of Science, and Google Scholar, to collect all available data. To learn about recent kinds, stages, risk factors, and current status of breast cancer.

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