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UNRAVELLING THE COMPLEX INTERPLAY: ENVIRONMENTAL MIXTURES AND BREAST CANCER RISK

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Abstract

Background. Globally, breast cancer ranks as the fourth most frequent reason for mortality when it comes to fatalities from cancer. The worrisome increases in rates of occurrence and death observed during the previous thirty years or more can be linked to several factors, such as changes in risk factor profiles, advancements in cancer registration, and the development of more effective detection technology. A strong association exists between the progression of metastasis and the mortality rate in breast cancer, with environmental pollutants seemingly contributing to this phenomenon. This association prompts a significant inquiry into the mechanisms that regulate the formation of metastases due to environmental and chemical contaminants. The impact of pollutants and chemical substances on communication pathways, which are essential for the growth and spread of tumor cells, among the numerous possible risk factors is gaining increasing focus. **Material and Methods.** Scientific research on environmental variables and additional factors linked to breast carcinoma was located and reviewed using engines such as the PubMed database, the MEDLINE database the Scopus database, and Google Scholar, among others, with search terms like “Breast Cancer”, “Risk components”, “Chemical exposures”, “Environmental toxic exposure”, “Disease progression”, “Bisphenol-A”, “Heavy metallic materials”, and “Food preparations”. **Results.** This literature aimed to present a thorough overview of the existing data on the impact of environmental and chemical toxins on breast cancer and as a result, a significant relationship between these toxins and breast cancer and its metastatic potential was discovered in more depth. **Conclusion.** In Conclusion, breast cancer's complexity demands a holistic approach encompassing genetic, environmental, and early detection strategies. Advancements in stem cell biology and gene identification enhance our understanding. Yet, dissemination remains a key challenge. Environmental toxins play a significant role, necessitating further epidemiological and molecular investigations to mitigate breast cancer's global impact.

Key words: pathogenesis, risk factor, breast cancer, Bisphenol A, chemical exposures, environmental mixtures.

ОБЪЯСНЕНИЕ СЛОЖНОГО ВЗАИМОДЕЙСТВИЯ: ЗАГРЯЗНЕНИЕ ОКРУЖАЮЩЕЙ СРЕДЫ ТОКСИЧНЫМИ ВЕЩЕСТВАМИ И РИСК РАЗВИТИЯ РАКА МОЛОЧНОЙ ЖЕЛЕЗЫ

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Аннотация

Актуальность. Во всем мире рак молочной железы занимает 4-е место среди наиболее частых причин смертности от рака. Тревожный рост заболеваемости и смертности, наблюдающийся в последние 30 и более лет, может быть связан с несколькими факторами, такими как изменения в профилях факторов риска, достижения в регистрации рака и разработке более эффективных технологий обнаружения

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рака. Существует тесная связь между прогрессированием метастазов и уровнем смертности от рака молочной железы, причем, по-видимому, этому явлению способствует загрязнение окружающей среды. Эта связь побуждает к серьезному исследованию механизмов, которые регулируют образование метастазов, вследствие влияния загрязнения окружающей среды. Среди многочисленных возможных факторов риска, способствующих росту и распространению опухолевых клеток, все большее внимание уделяется влиянию химических веществ, загрязняющих окружающую среду. **Материал и методы.** Научные исследования окружающей среды и факторов, связанных с раком молочной железы, были проанализированы с использованием таких баз данных, как PubMed, MEDLINE, Scopus и Google Scholar, с поисковыми запросами: «Рак молочной железы», «Компоненты риска», «Химическое воздействие», «Токсическое воздействие на окружающую среду», «Прогрессирование заболевания», «Бисфенол-А», «Тяжелые металлы» и «Приготовление пищи». **Результаты.** Целью обзора литературы было представить тщательный анализ существующих данных о влиянии экологических и химических токсинов на рак молочной железы, и в результате была обнаружена значительная связь между этими токсинами и раком молочной железы и его метастатическим потенциалом. **Заключение.** Злободневность проблем, связанных с раком молочной железы, требует комплексного подхода, включающего исследование генетических, экологических факторов и стратегию раннего выявления. Достижения в области биологии стволовых клеток и идентификации генов расширяют наше понимание. Тем не менее диссеминация опухолевых клеток остается ключевой проблемой. Экологические токсины играют значительную роль и требуют дальнейших эпидемиологических и молекулярных исследований для снижения глобального бремени рака молочной железы.

Ключевые слова: патогенез, фактор риска, рак молочной железы, Бисфенол А, химические воздействия, токсины окружающей среды.

Introduction

Worldwide, cancer of the breast took its toll on approximately 2.3 million women; in the year 2022, it was responsible for 666 103 fatalities [1]. Gender, age, estrogen, family history, genetic mutations, and way of life are risk factors [2] but as we look more closely at the risk factors, we discover that pollutants in the environment and chemicals may have a role in the etiology and the development of breast carcinoma. This is consistent with the alarming fact that over the past three decades, death rates have increased and the disease is becoming more common. As the fourth most prevalent cause of cancer-related fatalities worldwide at this time, breast cancer requires a comprehensive understanding of its complexity [1, 3, 4].

Carcinogenesis is a complex process that can occur in any cell, tissue, or organ and result in a variety of cancers. It is characterized by six major hallmarks. Apoptosis avoidance, an infinite proliferative potential, increased angiogenesis, resistance to anti-growth signals, induction of self-growth signals, and the menacing potential to spread are among the distinguishing features. The combination of environmental factors and genetic predispositions drives this complex process of pathological changes. Breast cancer has become a prominent case among the various cancers, offering a difficult obstacle as well as a chance for early intervention [5, 6].

In this review, we go deeper into the intricate details of breast cancer pathogenesis and the fundamental mechanisms of carcinogenesis that are impacted by pollutants in the environment. An extra layer of complexity is produced by widespread exposure to these toxins, which are found in everyday items like plastics and pesticides. Upon closer examination of these contributing factors, we find a few toxic substances that appear to have an impact on the development and course of breast cancer. These comprise persistent organic pollutants (POPs) and endocrine disruptors, which affect the invasion and metastatic processes of breast cancer. Environmental contaminants are still in the atmosphere and keep negatively affecting human well-being even after their prohibition for many years owing to health hazards. The change from epithelium to mesenchymal tissue, cancer-stemness, and a number of other mechanisms have been identified. These mechanisms are associated with the formation of cancer metastases and chemotherapy resistance, and they may be targets for pollutants [4, 6]. This review will highlight various toxins and their impact on breast cancer. A graphical representation of risk factors that this review is highlighting is shown in Figure 1.

1. Exposure to Organic Pollutants

1a. PCBs, also known as polychlorinated biphenyls

In the first decade of the 1980s, polychlorinated biphenyls, also called PCB became prevalent in electrical devices and production methods until they were eventually restricted worldwide because of health hazards. Their environmental persistence poses risks of exposure to the broader public through a variety of sources, including consumer products, work environments, ambient air, and diet. This is true even after the ban was implemented. High-grade breast cancer tumors and an overall poor prognosis for breast cancer have been linked to PCBs, specifically 105 and 118 [7, 8].

Between 2000 and 2023, several associations between PCB concentrations and breast cancer predictive variables, recurrence, and survival were examined in epidemiological studies. PCB concentrations in serum

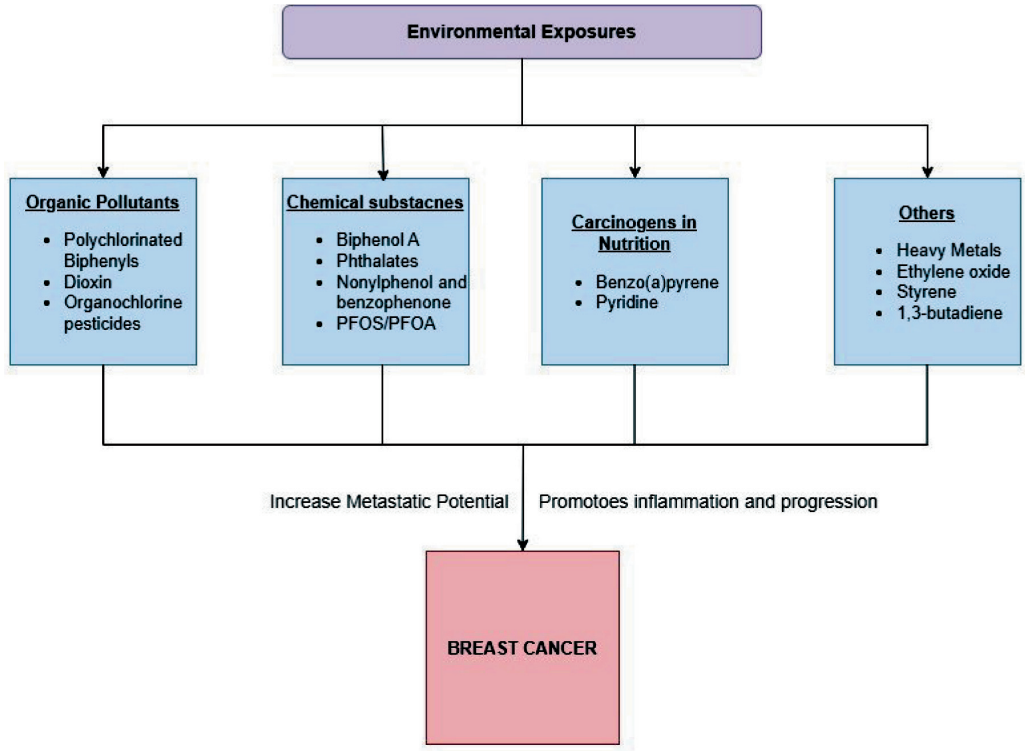

Fig. 1. A graphical representation of various factors affecting breast cancer. Note: created by the authors
Рис. 1. Схема влияния различных факторов на возникновение рака молочной железы. Примечание: рисунок выполнен авторами

and breast adipose tissue were measured during the time of diagnosis [9–12]. In some studies, a higher amount of PCB 153 present was linked to a greater likelihood of lymph node involvement; however, larger research studies failed to consistently replicate these findings. A higher chance of developing breast carcinoma recurrence was linked to the total amount of 14 PCBs, according to a case-control study. Moreover, the entire quantity of twenty-seven PCBs was linked to a higher probability of breast cancer-related fatalities, particularly in individuals who had tumors that tested favorable for the hormone estrogen [10–12].

Through Rho-associated kinase (ROCK) stimulation, PCBs—PCB 104 in particular—increase breast carcinoma cell migration and tumor growth, according to in vitro research [13]. Furthermore, it was recently demonstrated that human vascular endothelial cells exhibit inflammation-promoting responses when confronted with PCBs., which compromises the endothelium barrier's ability to function. Furthermore, it was discovered that PCB 104 promoted the excessive expression of Vascular endothelial growth factor (VEGF), which resulted in endothelial hyperpermeability and disease-causing cells' movement through the endothelium. This process contributed to the metastasis of tumors [11–13]. The phosphatidylinositol 3-kinase (PI3K) pathway was activated to mediate this process, indicating a possible mechanism for PCB-induced metastasis. Additionally, it was demonstrated that PCB 104 triggers Janus kinase 3 (JAK3) as well as the receptor for epidermal growth factor, or EGFR, respectively, which raises the amount of matrix metalloproteinase-3 (MMP-3) and quickens the trans-endothelial displacement of tumor cells. Twenty-two studies, including nested and case-control designs, assessed PCB levels, predominantly from blood or adipose tissue. Elevated PCB 99, 105, and 183 levels correlated with increased breast cancer risk (OR 1.43, 2.05, 1.57). PCB 118 and 138 also elevated risk, albeit with high heterogeneity. Other PCBs showed no significant association [11]. So, when everything is taken into account, these findings show the complicated connection between PCBs and the earliest stages, development, and dissemination of cancer of the breast, providing novel insights into potential therapies [10–13].

1b. Dioxin

Among its many functions within the etiology of carcinoma of the breast, 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD) is a potent carcinogen and aryl hydrocarbon receptor (AHR) agonist. According to the latest clinical research, the presence of adipose tissue TCDD quantities has been linked with a greater probability of metastasis to lymph nodes, especially in those with an average body mass index of ≥25 kg/m² (OR=4.48, 95 % confidence interval (CI)=1.32–20.71) [14, 15]. Even though the function of AHR in malignancy remains highly contentious, dioxin, a potent tumor booster, has shown evidence of potential protective properties against the development of breast carcinoma [15]. Dioxin serves as an AHR ligand which

inhibits ERα communication as well as may mitigate the effects of the estrogen hormone on growth in both culture conditions in vitro as well as in in vivo studies. In addition, regardless of the ER situation, the TCDD inhibits dissemination, invasion, as well as colonies generation by cancerous breast cells through blocking the AHR communication route while upsetting the CXCL12/CXCR4 axis as well [16]. In xenograft models, TCDD inhibits metastasis in vivo by roughly 50 % while having no effect on the growth or growth of carcinoma-like cells in the tumor. Dioxin, however, may cause epithelial-mesenchymal transition, increased migration, and mitochondrial dysfunction, according to conflicting studies. To understand the contextually dependent pro- as well as anti-cancer properties of AHR stimulants and inhibitors, deeper mechanistic studies are necessary [14–16].

1c. Organochlorine pesticides

Due to their persistent environmental effects, organochlorine pesticides (OCPs) were used for a variety of purposes throughout the world but were outlawed both in Europe and the USA [8, 17]. Still, in some areas, they are present and contaminate soil and food. Studies on epidemiology have connected the advancement of breast cancer to OCPs such as dichlorodiphenyltrichloroethane (DDT) and dichlorodiphenyldichloroethane (DDE). A higher chance of involvement of lymph nodes and larger tumors is correlated with DDE exposure [8, 10]. Increased blood levels of OCP are linked to a lower overall survival rate, and exposure to dieldrin is associated with a higher mortality rate in tumors that are ER-positive. According to study findings, DDT has the potential to cause the estrogen and androgen proportion to be disrupted, which could lead to the expansion of hormone-dependent cancerous breast cells. This could happen via a non-genomic ER signaling route [8, 17]. DDT levels were examined in twenty-eight case-control and eight nested case-control studies. The results showed a positive correlation between the risk of breast cancer and DDT (OR: 1.22; 95 % CI: 1.03–1.45). Likewise, there was a noteworthy rise in risk for DDE (OR: 1.15; 95 % CI: 1.01–1.30) [8].

In MCF7 cells, the common organochlorine pesticide hexachlorobenzene (HCB) stimulates cell division and opens the insulin-like growth factor I (IGF-I) signaling route. Twelve case-control and two nested case-control studies investigated hexachlorobenzene (HCB) levels, with variable sample sources. The overall odds ratio (OR) for the highest versus lowest HCB levels was 1.06 (95 % CI: 0.68–1.65), indicating no significant association. Heterogeneity persisted across sample types [10, 18]. Additionally, it initiates the c-SRC/HER1/STAT5b as well as HER1/ERK1/2 routes, and these result in AhR-dependent differentiation in cells of MDA-MB-231 [8, 17, 18]. Within 5 μM, the chemical HCB increases the MMP2/9 expression, discharge, as well and movement, accordingly, this facilitates the invasion of cells via the non-genomic AhR gene and HER1/EGFR routes, which stimulate c-Src in full effect. In living cells, HCB promotes lung dissemination, increases its protein levels of MMP9 along with MMP2, initiates signaling processes, and promotes growth underneath the skin despite the presence of tumor receptors for hormones [8, 17]. In MDA-MB-231 cells, AHR/TGF-β1 communication and TGF-β1 engagement are investigated. The following implies that ERK1/2 transcription seems exclusively associated with HCB-induced cell mobility whilst HCB plays a role within Epithelial-mesenchymal transition (EMT) via the channels of Jun N-terminal kinase (JNK)a p38, and SMAD3. When everything is considered, HCB-mediated Smad3 stimulation may be regulated by c-SRC and AhR, connecting them to EMT. The results obtained imply the fact that the correlation between oral contraceptives notably HCB, and the onset of breast carcinoma could entail intricate channels of signaling [8, 18].

2. Interaction with substances which are chemical in nature

2a. The influence of bisphenol A on human health

Food containers often include the chemical bisphenol A (BPA), a foreign estrogen used in resins composed of epoxy and plastics made of polycarbonate which contributes to exposure to the atmosphere. Studies reveal links among bisphenol A (BPA) as well as several health issues, including diabetes, heart disease, cancer, and inflammation. BPA-exposed breast cancer cells exhibit a potent gene expression profile connected to unfavorable outcomes in studies. [19, 20], proving that BPA has an estrogenic effect. Low BPA levels significantly boost growth in the number of estrogen receptor-positive (ER+) cells due to stimulating genes that support the development of the cell period and minimizing genes that prevent cell proliferation [21]. While the chemical BPA serves as a low-affinity ligand for the receptor for estrogen, it prevents the cytotoxic impact of chemotherapy on breast cancer cells that are both ER-positive and ER-negative at environmentally significant doses. This antagonistic relationship also involves other estrogen receptors, including estrogen-related receptor γ (ERRγ) as well as G-protein-coupled receptor 30 (GPR30). BPA induces invasion and migration of breast cancer cells via a GPR-dependent pathway. Additionally, it triggers the activation of ERRγ, which raises Matrix metalloproteinase (MMP) articulation and promotes invasion of cells through ERK1/2 and AKT signaling [21, 22]. Additionally, the chemical BPA induces FAK, ERK2 as well as SRC, which promotes cell movement and amplifies the activity of NFκB and AP-1 DNA linking by means of an ERK2 along with SRC based routes. These results highlight the complex role which the chemical BPA plays in the emergence of cancers of the breast and immunity to treatment with chemotherapy

through a variety of channels of signaling, highlighting the demand for more investigation [20–22].

2b. The consequences of Phthalates on human health

Phthalates are ubiquitous industrial chemical contaminants used as polymers as well as in a variety of everyday items. Examples of these contaminants include di(2-ethylhexyl) phthalate (DEHP), di(n-butyl) phthalate (DBP), and butyl benzyl phthalate (BBP) [23]. These drugs might trigger disruptions to the hormonal system. Data indicates that in cancerous breast cells, these contribute to enhanced neoplasm movement, spread, and expansion of cells. In carcinoma of the breast, phthalates such as BBP and DBP foster the synthesis of histone deacetylase 6 (HDAC6) via the ER alpha, EGFR, and PKA/AP2a route. The following consequently sets off a chain reaction of messages including β-catenin, GSK3β as well as AKT, that display vimentin [23, 24]. Phthalates induce the aryl hydrocarbon receptor (AHR) within ER negative breast carcinoma tissues known to be as MDA-MB-231, which in turn initiates the cycle of The AMP system (cAMP)-CREB1-PKA signaling processes. The origin of stimuli can be traced down to a non-genomic route. Likewise, phthalates turn on the receptors known as peroxisome proliferator-activated (PPARs), which could aid in MCF7 differentiation. Phthalates also affect a drug called tamoxifen vulnerability by preventing positive ER cells of MCF-7 from experiencing cell death brought upon by tamoxifen. Furthermore, Urinary phthalate metabolites, mono-benzyl phthalate (MBzP) and mono-2-isobutyl phthalate (MiBP), were found to be passively correlated with breast cancer in nine studies involving 7820 cases (OR=0.73, 95 % CI: 0.60–0.90; OR=0.75, 95 % CI: 0.58–0.98). Nevertheless, no significant correlation was found between bisphenol A (BPA), mono-ethyl phthalate (MEP), mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono-2-ethylhexyl phthalate (MEHP), mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP), mono-(3-carboxypropyl) phthalate (MCPP), and mono-butyl phthalate (MBP) [23]. The outcomes illustrate the requirement for further studies by indicating that phthalates might possess a bearing on the occurrence of cancer in women and the rise in resistance to cancer therapies [23–25].

2c. The repercussions of nonylphenol and benzophenone on human health

Nonylphenol (NP) and benzophenone-1 (BP1) a pair renowned for hormonal halting substances put out from a variety of manufacturing processes, show estrogen-like reactions in human beings on breast cancer cells from MCF-7 that display ER. According to an analysis, BP1 and NP therapy (at 10-5–10-7 M) increased MCF-7 cell proliferation in a way akin to the effects of 17-beta-estradiol (E2), with ICI-182,780, an ER antagonist, attenuating the responses. [26]. MCF-7 cell migration was also induced by BP1, NP, and E2, in a manner similar to that of E2. ERα-dependent changes in gene expression associated with dissemination and the spread included a decrease within p21 and a spike within cyclin D1 and cathepsin D, which were hampered by ICI-182,780. In contrast, BP1 increased the growth of BG1 ovarian cancer cells that expressed ER in xenograft mouse models. These findings demonstrate the xenoestrogenic impact of BP1, suggesting a potential role in the genesis of breast cancer by stimulating the proliferation of tumor cells that express ER through ER signaling channels [25, 26].

2d. Per- and poly-fluoroalkyl substances, or PFOS/PFOA consequences

Perfluorooctanoic acid (PFOA), like perfluorooctane sulfate (PFOS) and perfluoroalkyl acids (PFAAs), are used frequently because of their ability to repel water and may be endocrine disruptors that contribute to breast cancer. The human breast epithelial cells MCF10 were exposed to PFOA (50–100 μM) and PFOS (1–10 μM) both of which showed tumorigenic activity [27]. These substances promoted cell proliferation by altering the cell cycle, raising cyclin D1, CDK4/6, and lowering p27 levels. Due to their ability to promote cell invasion and migration, both substances may have a part in the course of carcinoma of the breast evolution. The mechanism of action suggests that PFAAs may act on breast epithelial cells through PPARα, as opposed to ER [27, 28]. Perfluoroalkyl substances (PFAS) exposure and breast cancer risk were examined in eleven studies. Elevated but statistically insignificant risk estimates were observed for perfluorooctanoic acid (PFOA), perfluorooctanesulfonic acid (PFOS), perfluorodecanoic acid (PFDA), perfluorohexanesulfonic acid (PFHxS), and perfluoroheptanoic acid (PFHpA). On the other hand, the risk estimates for perfluorononanoic acid (PFNA), perfluoroundecanoic acid (PFUnDA), perfluoro-n-tridecanoic acid (PFTrDA), and perfluorododecanoic acid (PFDoDA) were reduced; only PFDoDA was statistically significant (OR: 0.69; 95 % CI: 0.50–0.95) [29].

3. Exposure to carcinogens in the nutrition

Common genetically toxic cancer-causing agents in human nutrition are 2-amino-1-methyl-6-phenylimidazo [4,5-b] pyridine (PhIP) along with benzo(a) pyrene (BaP), which can be generated by inadequate process of combustion as well as animal products processing, accordingly. One kind of synthetic aromatic petroleum-based substance is called BaP, while PhIP is a heterocyclic amine. Both tobacco smoke and a range of foods contain these toxins.

3a. Effect of Benzo(a)pyrene

The mammary cancer-causing agent baP significantly increases the shift in MDA-MB-231 cell movement. Following being induced by vomitoxin, COX-II gets blocked by NS398 to enhance spread

and demonstrate COX-II engagement. Exposure to BaP increases the production of PGE2, the quantity of COX-II protein content, and the COX-II cells by a factor of 46. Two AHR antagonists, resveratrol and alpha-naphthoflavone, prevent BaP-induced spread and connect it to the AHR pathway. BaP causes cell movement via the lipoxygenase- and Src-dependent route that affects breast carcinoma growth and spread rather than initiation in cells of MDA-MB-231 via activation of SRC, FAK, and ERK2 [30]. Prooxidant BaP causes a rise in reactive oxygen species (ROS), and this, in turn, drives MMP activity and expression respectively, ERK signaling, and MCF7 as well as MDA-MB-231 cell movement and invasion. Cumulative exposure to BaP in a mouse model stimulates the growth and dissemination of tumors, suggesting that it participates in multiple phases of the incurable cascade in the course of breast cancer evolution [31].

3b. Pyridine containing amino-1-methyl-6-phenylimidazo [4,5-B]

Rats can develop cancer from cooked meat-derived genetically toxic PhIP, as well as human breast epithelial cells (MCF10A) can develop cancer in the laboratory at physiologically feasible levels. The characteristics that the study gradually developed that are associated with cancer include development, movement, invasion, tumor formation with dissemination, decreased growth factor reliance, anchorage-independent growth, affected acinar conformity, as well as a rise in how many stem cells there are. Reduced transcription of E-cadherin, accordingly, elevated NOX-1 along with ROS, ERK channel stimulation, enhanced H-RAS expression, and elevated HIF-1α, SP1, aldehyde dehydrogenase activity, MMP-9, MMP-2 as well as TNF-α are among the few molecular changes. In contrast, ICI 182,780, an antiestrogen, reverses the dose-dependent increases in migration and invasion observed in MCF7 and T47D following PhIP treatment. PhIP-induced pervasive phenotype is associated with elevated levels in cathepsin D, cyclooxygenase-2, or matrix metalloproteinase activity [32].

4. Contact with Toxic Metals

Decreased transcription of ER-alpha or PR and a higher level of, p-53, 06 methylguanine DNA methyltransferase, HER2/neu as well as Ki67 are among the poor molecular prognostic variables linked to higher concentrations of hazardous metals (Iron, Copper, Zinc, the metal lead, Chrome, and the nickel) in breast tumors that are malignant. A relationship exists among the increase in pathological DNA methylation and toxic metal buildup, indicating that treatment sensitivity is decreased and breast cancer progression is accelerated. The trace element amounts of the metal zinc, copper, iron, as well as calcium are higher in neoplastic breast tissues, and these values are statistically correlated with prognostic factors [21, 33]. Extended exposure to cadmium stimulates breast cancer cells' movement as well as spread via the TGIF/MMP2 signaling pathway. In contrast, tungsten amplifies the metastasis of breast cancer by altering the tumor microenvironment. Metal-induced epigenetic dysregulations may play a part in shaping up CSC-like cells and carcinogenicity, all these links warrant further research in this particular area [34, 35].

5. Ethylene oxide

Ethylene oxide (EtO) and breast cancer may be related in dose-response, according to a retrospective analysis conducted on a cohort of sterilant workers in Swedish medical equipment plants. In comparison to those with the lowest cumulative exposure, women with medium exposure showed an elevated incidence rate ratio (IRR) of 2.76 (95 % CI 1.20–6.33), and those with the highest cumulative exposure showed an IRR of 3.55 (95 % CI 1.58–7.93) [36]. Peplonska et al. on the other hand, found no difference in the odds of having been exposed to EtO before versus after (odds ratio [OR], 0.9; 95 % CI: 0.6–1.4) in their extensive occupational survey [37]. Numerous studies have looked into potential links between working in healthcare settings and breast carcinoma, including being exposed to ethylene oxide, chemical solvents, medications, late-night work hours, and radiation from ionizing sources. Studies on medical professionals, female nurses, and even male health and social workers (8 exposed cases) showed positive correlations. According to a study by Peplonska et al. female nurses working in specialty hospitals had a greater probability of developing breast tumors (OR=2.2; 95 % CI: 1.1 – 4.6), but this was not the case for all registered nurses [38].

6. Styrene and 1,3-butadiene

In the rubber industry, occupational exposure to styrene and butadiene was primarily measured in one study, while others relied on job titles or estimated exposure to different agents. Women with the largest overall contact with butadiene as well as styrene in a northwestern group of 8 rubber material manufacturing facilities showed raised cancer-related fatalities (OR for styrene, 1.5; 95 % CI: 0.6–3.4; OR 1,3 butadiene, 1.9; 95 % CI: 0.8–4.4), compared to those with no contact [39]. The correlation between styrene and 1,3 butadiene in this industry prevented the modeling of independent effects. Limited control for breast cancer risk factors is a concern, given the comparison with the general population. Additional evidence from the rubber industry demonstrated a significant trend in breast cancer mortality across quartiles of cumulative exposure to aromatic amines in a rubber tire manufacturing plant. Job title studies generally showed positive but nonsignificant findings for work in plastic and rubber product manufacturing, including in a male cohort. However, one study found no increased risk for rubber and plastics manufacturing work [40].

Conclusion

In conclusion, breast cancer is still a major global health concern that necessitates a multimodal strategy that includes environmental risk factors, genetic knowledge, and early detection. Our knowledge about the development and resistance to drugs mechanisms behind breast carcinoma has improved as a result of studies upon stem cell biology and gene identification. Even though biological and chemotherapy prevention methods are becoming increasingly sophisticated, It is imperative to acknowledge that dissemination is a primary factor contributing to the substantial mortality rate linked to breast tumors and that toxins could potentially be involved at a more fundamental level. Environmental contaminants have been connected to the invasion, progression, and breast cancer's chemoresistance. As described in our review these toxins including toxic metals, persistent organic pollutants, and chemical exposures from consumer products are at the forefront and require even more epidemiological studies to enhance our understanding thus, further investigation through these epidemiological and molecular studies is required to fully understand the complex interactions between xenobiotics in the breast cancer exposome. Understanding the full impact of environmental factors on breast cancer is critical to improving public health and lowering the global burden of this complex disease as we work toward effective prevention and treatment modalities.

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