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Environmental Exposure to Breast Cancer: Study Narrative Review, How to Prevent in Indonesia?

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A B S T R A C T

The environment is one of the factors in the epidemiological triad as the concept of the emergence of a disease, including breast cancer which is the global burden. Globally, WHO declared breast cancer to have 2.26 million new cases per year in 2020, with the mortality rate climbing to 685,000. In Indonesia, breast cancer has the highest incidence rate for women, with 1.4 per 1000 population in 2013 growing to 1.79 per 1000 people in 2018. This review aims to describe environmental exposure factors that have the potential to cause breast cancer. The review study used the narrative review method with a screening process of 28 articles used. Environmental exposures that become potential occurrences of breast cancer are divided into 4, exposure to pesticides, exposure to household chemicals, exposure to food packaging, and exposure to air pollution which have different pathophysiologies for each exposure. Exposure to chemicals such as DDE and DDT in pesticides that have been proven to be carcinogenic and are still used in Indonesia. Exposure to chemicals from household chemicals such as PCBs, Benzophenone, and Phthalates in some household appliances are also carcinogenic substances. The use of BPA, BaP, and 2-Amino-1-Methyl-6-Phenylimidazo [4,5-B] pyridine in food packaging trigger breast cancer. Exposure to cigarette smoke or smoking behavior, consumption and evaporation of alcohol, as well as exposure to $PM_{2.5}$ are air pollutants that are at risk of causing breast cancer. How to prevent it, we can use biopesticide, bioplastic, change a healthy lifestyle and replace fossil fuels into biofuels.

Kata kunci:

Kanker Payudara
Paparan Pestisida
Paparan Bahan Kimia Rumah Tangga
Paparan Kemasan Makanan
Gaya Hidup

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A B S T R A K

Lingkungan merupakan salah satu faktor dalam triad epidemiologi sebagai konsep munculnya suatu penyakit, termasuk kanker payudara yang menjadi beban global. Secara global, WHO menyatakan kanker payudara memiliki 2,26 juta kasus baru per tahun pada tahun 2020, dengan angka kematian meningkat menjadi 685.000. Di Indonesia, kanker payudara memiliki angka kejadian tertinggi pada wanita, dengan 1,4 per 1000 penduduk pada tahun 2013 tumbuh menjadi 1,79 per 1000 orang pada tahun 2018. Tinjauan ini bertujuan untuk mendeskripsikan faktor paparan lingkungan yang

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berpotensi menyebabkan kanker payudara. Kajian review menggunakan metode narrative review dengan proses screening sebanyak 28 artikel yang digunakan. Paparan lingkungan yang menjadi potensi terjadinya kanker payudara dibagi menjadi 4, paparan pestisida, paparan bahan kimia rumah tangga, paparan kemasan makanan, dan paparan polusi udara yang memiliki patofisiologi yang berbeda untuk setiap paparan. Paparan bahan kimia seperti DDE dan DDT pada pestisida yang telah terbukti bersifat karsinogenik dan masih digunakan di Indonesia. Paparan bahan kimia dari bahan kimia rumah tangga seperti PCB, Benzophenone, dan Phthalates di beberapa peralatan rumah tangga juga merupakan zat karsinogenik. Penggunaan BPA, BaP, dan 2-Amino-1-Methyl-6-Phenylimidazo[4,5-B]pyridine dalam kemasan makanan memicu terjadinya kanker payudara. Paparan asap rokok atau perilaku merokok, konsumsi dan penguapan alkohol, serta paparan PM2.5 merupakan polutan udara yang berisiko menyebabkan kanker payudara. Cara mencegahnya, kita bisa menggunakan biopestisida, bioplastik, mengubah gaya hidup sehat dan mengganti bahan bakar fosil menjadi biofuel.

INTRODUCTION

The five types of cancer that are the biggest problems in the world are lung cancer, liver cancer, stomach cancer, colorectal cancer and breast cancer. According to the data from the Global Cancer Observatory in 2018, there are 18.1 million new cases per year, with the mortality rate climbing to 9.6 million. From these statistics, it can be determined that breast cancer is a disease with a rather high mortality rate, particularly among women (InfoDATIN, 2019).

The World Health Organization (WHO) in 2020 declared that breast cancer is cancer that often occurs globally.(WHO, 2021) The International Agency for Research on Cancer (IARC) projects more than 2.26 million new cases, with an annual increase of 12% and a death toll of 685.000 in 2020. Breast cancer is one of the global burdens and a major public health problem in women caused by many factors (Lei, Zheng, Zhang, & Wang, 2021).

The incidence of breast cancer is higher in developed countries than developing countries, but the mortality rate is higher in developing countries. In Western Europe, the incidence of breast cancer reaches more than 90 new cases per 100,000 women per year, while in East Africa it is 30 new cases per 100,000 women per year and the breast cancer mortality rate in the two countries is almost the same, which is around 15 per 100,000 cases (WHO, 2021).

According to the Ministry of Health of the Republic of Indonesia (Kemenkes RI), breast cancer will be the most frequent cancer among women in 2020. Breast cancer is now one of the most frequent kinds of cancer in women, with a very high frequency in all nations worldwide (InfoDATIN, 2019; WHO, 2021). Cancer is quite common in Indonesia. According to data published by the Indonesian Ministry of Health's Directorate of Prevention and Control of Noncommunicable Diseases (2020), breast cancer has the highest incidence rate for women, with 1.4 per 1000 population in 2013 growing to 1.79 per 1000 people in 2018 (Kesehatan, Penanggulangan, & Nasional, n.d.).

According to the Indonesian Association of Surgical Oncology Specialists, the incidence of breast cancer in Indonesia is predicted to be 8,625 cases in 2017, with 82 percent of them being in an advanced stage. This is related to women's unwillingness to undergo early tests. Early detection of breast cancer offers for a greater possibility of long-term survival, or the ability to live longer after being diagnosed with cancer.(InfoDATIN, 2019)

Breast cancer have multifactorial cause, but is often associated with environmental factors (pesticides exposure, household materials exposure, packaged food exposure), foods containing carcinogens age, genetic factors, poor diet or lifestyle, reproductive factors such as menstruation, hormonal factors are exposure to steroid hormones, intrinsic risk factors are hereditary or genetically related menopause, age for giving birth to first child, breastfeeding, and family planning.(Maria, Sainal, & Nyorong, 2017) When the body's immunity decreases, the person concerned is susceptible to falling ill both physically and mentally which can lead to the risk of the emergence of malignant cells (cancer).(Kesehatan et al., n.d.; Maria et al., 2017; Salam, Sukohar, & Bakri, 2019).

Epidemiological investigations found that the likelihood of passive smoking for breast cancer far outweighs the risk of developing a history of active smoking, and exposure to chemicals such as DDT, DDE, POPs, and carciogen.(Basnet, Dhital, & Rakshit, 2022; Koual et al., 2020) Nearly all known types of cancer appear gradually, both as defects build up in cancer cells and in their daughter cells. Every cell that replicates has the possibility of defects (mutations), unless there is a proper prevention and repair of defects. The defect may persist and will be passed on to daughter cells and the body usually protects against cancer by various means or methods, such as apoptosis, the presence of helper molecules (DNA polymerase), and cell aging (Huedo-Medina, Ballester, & Johnson, 2013).

Exposure to the chemical DDE in pesticides had a 1.95 times (OR = 1.95, 95% CI = 1.10, 3.52) risk of cancer in the family history (P. Olaya-Contreras, J. Rodríguez-Villamil, H.J. Posso-Valencia, 1998). PCBs 105 chemical exposure had a 3.17 times risk (OR = 3.17, 95% CI = 1.51, 6.68) and PCBs 108 had a 2.31 times risk (OR = 2.31, 95% CI = 1.11, 4.78) in a family history of BC sufferers. Furthermore, this article will discuss further environmental exposures that have a risk for the incidence of BC (K.J. Aronson, Miller, & Woolcott, 2000).

Exposure to various environmental chemicals present in everyday items may raise the chance of acquiring cancer, according to growing epidemiological data and a better knowledge of the pathways linking toxicants to cancer formation. Several studies have lately highlighted concerns about the role of low-dose exposure to environmental

contaminants in cancer start and progression, indicating that these chemicals may increase cancer invasion and metastasis (Woolcott et al., 2001). As a result, the goal of this review is to highlight the key results about the involvement of environmental pollutants in the development of invasion and metastasis in breast cancer, as well as their relationship(s) with chemoresistance (Salam et al., 2019).

Lack of public awareness of healthy living behavior and lack of public knowledge about the dangers of breast cancer are the main problems in overcoming it. As a result, most patients are found at an advanced stage and difficult to treat.(Krishnan, Stathis, Permuth, Tokes, & Feldman, 1993) Therefore, preventive measures are needed so that breast cancer cases are reduced or breast cancer sufferers do not experience complications, especially for people who lack knowledge and are afraid to check their disease to the nearest health service (Kesehatan et al., n.d.)(Maria et al., 2017).

METHOD

This study uses a review method with the type of narrative review. Narrative review aims to identify exposure to environmental factors that can potentially cause breast cancer. Sources of scientific articles are obtained from several databases and there are no standard or protocols in the collection of article narrative reviews.(Huedo-Medina et al., 2013) Articles used as reviews have inclusion criteria, such as: have environmental variables that are related to or have a risk of breast cancer, can be accessed in full and do not use the review method. From the results of the article inclusion criteria, the total articles used were 28. Therefore, article screenings as below figure 1.

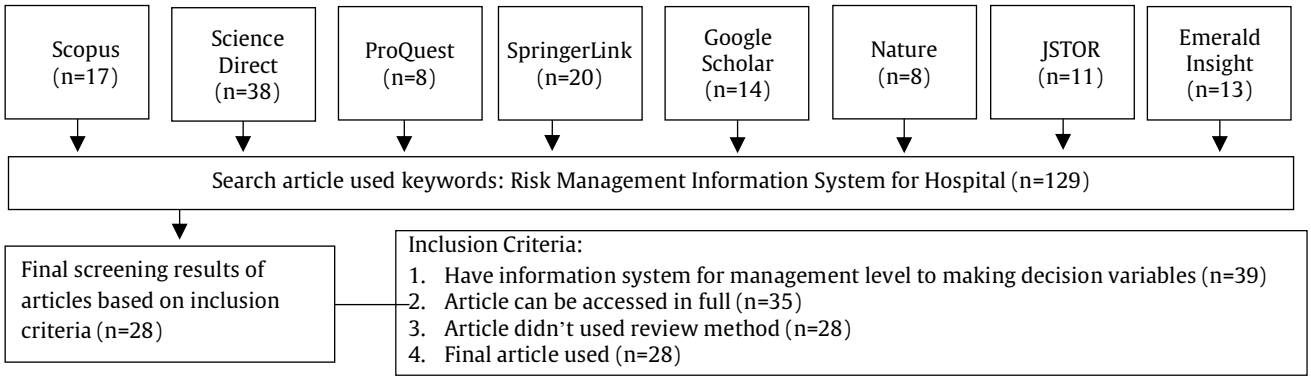

Figure 1. Flow Chart Screening Article

Table 1. Result Synthesis Matrix

No	Main Idea	Similarities of Research Findings
1	Pesticide Exposure(Iwasaki et al., 2008; Koual et al., 2020; Woolcott et al., 2001)	The results of existing research indicate that pesticide exposure can affect breast cell proliferation by acting as estrogen mimics or by interfering with pathways leading to increased breast cell proliferation which may affect breast cancer risk.
2	Household Chemicals Exposure (Chen & Chien, 2014; Demers et al., 2002; Francisco et al., 2016; Hsieh et al., 2012; S. J. In, Kim, Go, Hwang, & Choi, 2015; Y. K. In, Soon, & Moon, 2004; Koual et al., 2020; Lü, Huang, Huang, & Cai, 2019; Rumph et al., 2022; Woolcott et al., 2001)	The results of existing research indicate that household chemical exposure can affect breast cell by accumulating evidence that Polychlorinated biphenyls (PCBs), Benzophenone, and Phthalates exposure raises the risk of a variety of health issues, including obesity, low birth weight, diabetes, endometriosis, polycystic ovary syndrome, and breast cancer.
3	Food Packaging Exposure (Choudhary, Sood, Donnell, & Wang, 2012; Guo et al., 2015; S. J. In et al., 2015; Keri et al., 2007; Krishnan et al., 1993; Lauber & Gooderham, 2011; Lee et al., 2012; Miller, Holloway, & Foster, 2005; Oral, Erkekoglu, Kocer-Gumusel, & Chao, 2016; Park et al., 2013)	The results of existing research indicate that breast cancer can be caused by exposure to Bisphenol with a gene expression profile that is indicative of tumor aggressiveness and is related with poor clinical outcomes in breast cancer patients, Benzo(a)pyrene which is the mammary carcinogen in rodents, and it also helps to make breast cancer more likely in humans, and 2-amino-1-methyl-6-phenylimidazo [4,5-b] Pyridine as a carcinogen generated from cooked food.
4	Air Pollution ("Breast Cancer," n.d.; Calle, Miracle-mcmahill, Thun, & Heath, 1994; Lu et al., 2014; Manjer et al., 2000; Meng, Gao, Goldberg, Rosen, & Fan, 2000; Miller et al., 2005; Shin, Sánchez-Velar, Sherr, & Sonenshein, 2006; Susan & John, 2001; Terry et al., 2019; Y. Wang, Xu, Ke, & Luo, 2017; White, O'Brien, Niehoff, Carroll, & Sandler, 2019; M. Xu et al., 2016)	Breast cancer can be triggered by pollutant polycylic armocatic carbons such as cigarette smoke which has a high chemical level can spread to all organs of the body and can develop into various diseases, including breast cancer. In addition, 7,12-Dimethylbenz(a) anthracene (DMBA) and alcohol consumption may accelerate the growth and aggressiveness of pre-existing breast cancers through a variety of possible pathways. $PM_{2.5}$ pollutants can impact breast cancer developing in women living in areas with high traffic-related pollutants.

RESULTS AND DISCUSSION

The results of filtering 28 articles explained that environmental exposure was classified into 4 groups, namely, pesticides, household chemicals, food packaging and air pollution. Pesticide exposure is caused by the use of chemicals that are harmful and proven to be carcinogenic. Exposure to household chemicals comes from household appliances made from hazardous plastic chemical polymers. Exposure to food packaging is sourced from food and beverage containers used made from plastic polymers which are dangerous and carcinogenic. Air pollution is also evident in the incidence of breast cancer, sourced from cigarettes, alcohol consumption and evaporation, as well as $PM_{2.5}$ pollutants. A clearer description is presented in table 1.

Exposure to pesticides with the active ingredients dichlorodiphenyldichloroethane (DDE) and dichlorodiphenyltrichloroethane (DDT) which are included in the Organochlorine group (OCPs). Exposure to household chemicals that have the potential for breast cancer comes from chemicals Polychlorinated biphenyls (PCBs), Benzophenone, and Phthalates. Exposure to chemicals in food packaging such as Bisphenol A (BPA), Benzo(a)pyrene (BaP) and 2-Amino-1-Methyl-6-Phenylimidazo [4,5-B]pyridine. Air pollution such as exposure to cigarette smoke, or smoking behavior, alcohol consumption, and exposure to $PM_{2.5}$ pollutants are toxic materials that can potentially cause breast cancer.

Pesticide Exposure

Organochlorine Pesticides (OCPs)

A group of pesticides known as organochlorine pesticides (OCPs) are synthetic organic compounds that are used as insecticides, herbicides, termites, and fungicides in both agricultural and residential settings around the world. Despite the fact that they are illegal in the United States and Europe, they are nevertheless employed in certain nations and continue to contaminate food and soils due to their long-term persistence in the environment. According to epidemiological study, OCPs such as dichlorodiphenyldichloroethane (DDE) and dichlorodiphenyltrichloroethane (DDT) may change critical pathways linked in breast cancer development and have an influence on BC prognosis and survival.(Woolcott et al., 2001)

DDT and DDE are found in the environment and can affect breast cell proliferation by acting as estrogen mimics or by interfering with pathways leading to increased breast cell proliferation which may affect breast cancer risk. DDE and PCBs, two chemicals that are found in breast cancer patients' blood, have been found to rise in blood levels in several studies. Because pesticides often have estrogen in them, it is thought that the process of cell growth will speed up.(Koual et al., 2020)

DDT helps hormone-dependent breast cancer cells grow by changing the balance of estrogen and androgen and blocking the androgen signaling pathway, which slows growth in hormone-responsive breast cancer cells, according to the limited experimental evidence we have.

For example, DDE exposure has been connected to a dose-dependent increased relative risk of lymph node involvement and a larger tumor, while a recent study found that higher OCPs levels in the blood were linked to a worse overall survival rate. In those with ER-positive cancers, exposure to dieldrin (another organochlorine pesticide) was connected to an increased risk of mortality.(Iwasaki et al., 2008)

Household Chemicals Exposure

Polychlorinated biphenyls (PCBs)

In the early 1980s, most countries banned PCBs because they were bad for people's health. PCBs are a group of aromatic compounds that were used in a lot of industrial and electrical applications. Because PCBs are long-lasting in the environment, they can get into the general population through food, air, work, and consumer goods (as with POPs). High-grade breast tumors and poor outcomes for patients who have them are thought to be caused by PCBs, which are thought to be linked to PCBs.(Francisco et al., 2016; Koual et al., 2020; Woolcott et al., 2001)

In addition, more and more evidence shows that the direct bond among cancerous cells and endothelial cells is a critical step in the process of becoming metastatic. It has been shown that PCBs can make vascular endothelial cells more active, which makes the endothelial barrier less effective. PCBs make human vascular endothelial cells more oxidatively stressed, which causes them to become more inflammatory. The genes for monocyte chemoattractant protein-1 (MCP1), E-SELECTIN, intracellular adhesion molecule-1 (ICAM-1), and vascular endothelial cell adhesion molecule-1 (VECAM-1) have been up. These genes have a greater chance of causing breast cancer.(Demers et al., 2002; Lü et al., 2019; Rumph et al., 2022)

Benzophenone / Nonylphenol

A chemical known as benzophenone-3 and nonylphenol, which are emitted by a variety of industrial products (lubricating oil additives, laundry detergents, and emulsifiers). They are environmental chemicals that may harm people by interacting with the endocrine system. An investigation of the impact of estrogen receptors on the development and spread of MCF-7 human breast cancer cells.(S. J. In et al., 2015)

BP-3 is a popular chemical in sunscreen and a variety of other consumer goods. However, it is also suspected of being an endocrine disruptor (EDC). The endocrine system secretes hormones that play a critical role in regulating many vital body activities. There is accumulating evidence that EDC exposure raises the risk of a variety of health issues, including obesity, low birth weight, diabetes, endometriosis, polycystic ovary syndrome, and breast cancer.(Park et al., 2013)

Phthalates

Many synthetic compounds, such as phthalates, may be present in the environment. Phthalates are used in the production of plastic products such as food wrappers and cosmetics. Plasticizers include phthalates such as butyl benzyl phthalate, di(n-butyl) phthalate (DBP), and di (2-ethylhexyl) phthalate (DEHP).(Y. K. In et al., 2004)(Oral et al., 2016) They are considered to be endocrine disruptors, and they have been demonstrated to accelerate cell growth. Phthalates are also suspected to contribute to the development and dissemination of breast cancer cells as well as tumor growth and spread by up-regulating histone deacetylase 6. (HDAC6).(Chen & Chien, 2014; Hsieh et al., 2012)

Food Packaging Exposure

Pesticide residues may be found in many commercially grown fruits, vegetables, and cereal crops. Furthermore, because of their resistance to degradation, persistence in the

environment, and bioaccumulation inside the food chain, many chemicals are categorized as persistent organic pollutants (POPs).(Salam et al., 2019) They have been illegal in most countries for decades due to human health concerns. Chemicals continue to accrue in soils, sediments, air, and biota due to their long half-lives. These compounds continue to be ingested by humans in a number of ways.

Bisphenol A (BPA)

BPA is a xenoestrogen that occurs naturally in polycarbonate and epoxy resins. The major source of contamination for the regular populace is the food packaging sector. Numerous studies have been done to ascertain the potential for adverse effects of BPA exposure on human health, owing to its widespread presence in the environment and estrogenic activity both in vivo and in vitro.(Keri et al., 2007; Krishnan et al., 1993; Oral et al., 2016) They think that BPA is strongly linked to a variety of diseases, including diabetes, cardiovascular disease, inflammatory disease, and cancer. Numerous investigations have shown that BPA has a function in cancer growth and treatment resistance.(Krishnan et al., 1993; Lee et al., 2012)

Bisphenol A was initially identified as a pro-estrogenic chemical. Breast cancer cells exposed to BPA have been shown to exhibit a gene expression profile suggestive of tumor aggressiveness, which is associated with poor health outcomes in women with breast cancer. BPA, on the other hand, is a low-affinity ligand for estrogen receptors and has been shown to inhibit the cytotoxic effects of multiple chemotherapeutics (doxorubicin, cisplatin, and vinblastine) in both ER-alpha-positive and negative breast cancer cells, independent of the classical hormone receptors, by increasing the expression of anti-apoptotic proteins. These cell types express alternative estrogen receptors, such as G-protein-coupled receptor 30 (GPR30) and members of the estrogen-related receptor family.(Keri et al., 2007; Krishnan et al., 1993; Lee et al., 2012; Oral et al., 2016)

Benzo(a)pyrene (BaP)

People who consume BaP can get breast cancer, and it also makes it more likely for rodents to get cancer. They were more likely to get into. People who took Vomitoxin, which makes people more likely to get sick, also made the cells more likely to invade. People who took NS398, which makes people less likely to get sick, took both. A study says COX-II may play a role in the effects of BaP, but it's not clear how.(Guo et al., 2015)

Additionally, the scientists demonstrated that BaP stimulates the expression of v3 integrin on the cell surface and the production of metalloproteinase (MMP)-2 and MMP-9. Guo et al. demonstrated in another work that BaP's pro-oxidant qualities (increased ROS generation) activated the ERK signaling pathway, which stimulates MMP expression and activity in MCF7 and MDA-MB-231 cells.(Castillo-Sanchez, Villegas-Comonfort, Galindo-Hernandez, Gomez, & Salazar, 2013; Miller et al., 2005) As a result, cell migration and invasion were facilitated. In a mouse model, cumulative BaP exposure results in enhanced tumor development and metastasis to the liver and lung. Taken together, our findings indicate that BaP may operate on many phases of the metastatic cascade and contribute to the development of breast cancer.(S. J. In et al., 2015; Miller et al., 2005; Park et al., 2013)

2-Amino-1-Methyl-6-Phenylimidazo [4,5-B]pyridine

2-amino-1-methyl-6-phenylimidazo [4,5-b] Pyridine (PhIP) is a carcinogen derived from cooked beef that induces cancers in the colon, prostate, and mammary glands in rats. PhIP has also been proven to be carcinogenic in vitro utilizing human breast epithelium MCF10A cells at physiologically relevant micro to nanomolar levels. In this investigation, there were more and more indicators that carcinogenesis was taking place. Less dependency on growth factors, anchorage-independent growth, acinarconfigurational disruption, growth, migration, and invasion were among the indicators seen. There were also greater populations of stem-like cells..(Choudhary et al., 2012; Lauber & Gooderham, 2011)

Air Pollution Exposure

Cigarette Smoke

Cigarette smoke can increase the risk of breast cancer because it contains chemicals in high concentrations that can cause breast cancer. Toxins in cigarette smoke can spread to all organs of the body and can develop into various diseases, including breast cancer.(Miller et al., 2005) In this case, passive smoking will have a more dangerous impact on the body due to direct exposure to toxins in cigarette smoke. Unlimited proliferation will result in the development of breast cancer. Cigarette smoke (tobacco) contains a carcinogenic substance that is harmful to the body, namely Polycyclic Aromatic Hydrocarbons (PAHs), which can increase the risk of breast cancer.(Calle et al., 1994; Manjer et al., 2000)

The presence of cigarette smoke, which is made up of a complex combination of over 4,000 different chemicals, including free radicals and oxidants in high concentrations, causes a loss in lung function, which may lead to breast cancer. When carbon monoxide, ammonia, or tar are breathed via the respiratory tract, the production of reactive oxygen species (ROS) by macrophages and neutrophils causes an increase in oxidant load in the lungs. Furthermore, cigarette smoke lowers plasma antioxidant capacity, which is linked to a reduction in sulfhydryl/glutathione (GSH) protein.(Susan & John, 2001) GSH deficiency leads to an increase in lipid peroxidase and transcription of proinflammatory cytokine genes, resulting in lung congestion.

Several research have been conducted to discover which cigarette smoke compounds, out of over a hundred potential carcinogens, may contribute to increased BC metastasis. Cigarette smoke contains ligands for acetylcholine receptors (AHRs) as well as nicotine, the primary addictive component of cigarettes. Evidence from in vitro studies employing cell cultures, in vivo studies on rodents, and human studies, including epidemiological studies, indicate that nicotine, on its own, may stimulate a range of processes necessary for cancer development.(Calle et al., 1994) Nicotinic acetylcholine receptors also play a role in cell growth and angiogenesis, morphological changes, and resistance to apoptosis in lung cancer cell lines that have been exposed to nicotine.(Calle et al., 1994; Miller et al., 2005; Susan & John, 2001)

7,12-Dimethylbenz(a) Anthracene

7,12-Dimethylbenz(a) anthracene (DMBA) can also make cells grow and angiogenesis, cause morphological changes that suggest a migratory, invasive phenotype, and make cells resistant to apoptosis in lung cancer cell lines through the

nicotinic acetylcholine receptors. It can also cause breast cancer.(Chen & Chien, 2014; Shin et al., 2006)

Alcohol

Accumulating data suggests that alcohol consumption may accelerate the growth and aggressiveness of pre-existing breast cancers through a variety of possible pathways. Alcohol may enhance cancer cell motility by reorganizing the cytoskeleton and promoting cancer cell invasion through breakdown and rebuilding of the extracellular matrix.(S. Wang et al., 2012) Alcohol may potentially enhance tumor angiogenesis by activating pro-tumor cytokines and chemokines.(M. Xu et al., 2016)

In addition, alcohol may increase the number of cancer stem cells, which affects how neoplastic cells work, how aggressive they are, and how well they respond to treatment. Alcohol may be broken down in mammary tissues and breast cancer cells, which can cause reactive oxygen species (ROS) and oxidative stress to happen. A member of the epidermal growth factor receptor (EGFR) family, called ERBB2, is linked to the growth of tumors caused by alcohol.(Lu et al., 2014; Meng et al., 2000; Y. Wang et al., 2017)

$PM_{2.5}$

$PM_{2.5}$ pollutants can impact the development of breast cancer in women living in areas with high traffic-related pollutants.("Breast Cancer," n.d.; Terry et al., 2019) The results of Niehoff's research show that PM2.5 can have the effect of changing the histological characteristics of breast tissue and as an early diagnosis of carcinogenic mechanisms on the risk of breast cancer caused by exposure to air pollution. The research sample was taken from 1,930 women's breast issues with various demographics.(Niehoff et al., 2020)

How to Prevent Environmental Exposure?

Biopesticide

Biopesticide is the use of biologically active ingredients in the composition of pesticides.(Basnet et al., 2022) Biopesticides are safer for public health and the environment. The active ingredients that can be used are microbial, which is a diversity of microorganisms from algae, bacteria, fungi, viruses, and protozoa. Biopesticides target to kill pests precisely and will not harm other organisms and are environmentally friendly.

In India, the application of biopesticides has been marketed and used even the demand for biopesticides is higher than chemical pesticides. The marketing of biopesticides in India is categorized into biofungicides, bioherbicides, and bioinsecticides.(Arakere, Jagannath, Krishnamurthy, Chowdappa, & Konappa, 2022) Biofungicides can use microorganisms such as *Trichoderma viridae* and *T. harzianum*, *Fusarium proliferatum*, *Pseudomonas fluorescens*, *Bacillus subtilis*, *B. pumilus*, *Ampelomyces quisqualis,* etc; bioherbicides can use biologically agent species from *Mycoherbicides* such as *Lasiodiplodia pseudotheobromae*, *Neoscytalidium novaehollandiae*, *Macrophomina phaseolina*, *Phoma macrostoma*, *Sclerotinia minor*, *Chondrostereum purpureum*, *Colletotrichum gloeosporioides f. sp. aeschynomene*, *Phytophthora palmivora,* etc.(Berestetskiy, 2021) the active ingredient that is often used in bioinsecticides is *Bacillus thuringiensis var. kurstaki*, *Beauveria bassiana*, *Verticillium lecanii*, *Metarhizium anisopliae*, *Paecilomyces lilacinus*, etc.

Bioplastics Food Packaging and Household Materials

The use of plastic as food packaging and household appliances poses a major risk to health, one of which can trigger breast cancer. To prevent this problem, it is necessary to substitute chemical plastics into bioplastics. Bioplastics are made up of biodegradable polymers such as PLA (Polylactic acid), PHA (Polyhydroxyalkanoates), starch blends, PBS (Polybutylene succinate), PBAT (Polybutylene adipate terephthalate), and etc, making up 55% of the bioplastic polymers produced worldwide.(Shaikh, Yaqoob, & Aggarwal, 2021)("Market – European Bioplastics e.V.," n.d.) Bioplastics have been used in various sectors such as packaging, electronic equipment, automotive, construction, agriculture, electroplating, etc. The Indonesian government, through *Badan Pengawas Obat dan Makanan* (The Food and Drug Administration), can apply bioplastic assessment as a component of food industry certification assessment. Biodegradable polymers can be modified to stabilize temperatures for fruit and vegetable storage.(Mangaraj, Yadav, Bal, Dash, & Mahanti, 2019)

Lifestyle changes and fuel substitution

Smoking behavior and alcohol consumption can cause many diseases, one of which is breast cancer. The prevention thing that can be done is to change the behavior of not smoking or not being exposed to cigarette smoke, then not consuming alcohol or replacing it with drinking water or fruit and vegetable juices. Changes in behavior can only be done by individuals who already have awareness, it will be difficult to change behavior in individuals who do not have sufficient awareness.

Fossil is a fuel that is not environmentally friendly, the emissions produced can be in the form of pollutants such as $PM_{2.5}$ and other traffic-related pollutants as a factor in breast cancer. To prevent this problem, it can be done in two ways, first by changing behavior such as not using motorized vehicles or cycling to travel short distances, using masks that meet standards when traveling outside the house and planting trees in the house area. These are ways to reduce air pollutants produced by burning fossil fuels.

The second way is to substitute fossil fuels into biofuels. Biofuel or biofuel is one of the fuels produced from biological raw materials to produce green energy.("Direktorat Jenderal EBTKE - Kementerian ESDM," n.d.) Algae are non-flowering plants, can be found in light or dark green in wetlands and contain chlorophyll. Algae can be used in various sectors, one of which is the energy sector. Algae has characteristics such as absorbing CO_2, did not require a large area for cultivation and has a high lipid content. Lipids in algae can be used as biofuels with a conversion method, which converts vegetable oils into biofuels. Algal carbohydrates, namely bioethanol and biobutanol, can be used as additional compositions in the production of biofuels. Algae species Chlamydomonas reinhardtii (21% lipid, 48% sugar), Spirulina platensis (8% lipid, 60% sugar) and Chlorella sp. (19% lipid, 56% sugar) from several studies can be used as biofuel feedstock.(Demirbas & Fatih Demirbas, 2011; L. Xu, Cheng, & Wang, 2018)

CONCLUSIONS AND SUGGESTION

The environment is one of the factors in the epidemiological triad as the concept of the emergence of a disease, including breast cancer which is the global burden.

Exposure to chemicalssuch as DDE and DDT in pesticides that have been proven to be carcinogenic and are still used in Indonesia. Exposure to chemicals from household chemicals such as Polychlorinated biphenyls (PCBs), Benzophenone, and Phthalates in some household appliances are also carcinogenic substances. The use of Bisphenol A (BPA), Benzo(a)pyrene (BaP), and 2-Amino-1-Methyl-6-Phenylimidazo [4,5-B] pyridine in food packaging triggers breast cancer. Exposure to cigarette smoke or smoking behavior, consumption and evaporation of alcohol, as well as exposure to PM2.5 are air pollutants that are at risk of causing breast cancer. Efforts to prevent environmental exposure are to switch from chemical pesticides to biopesticides with safe biological active ingredients. The change of plastic chemical polymers into bioplastic polymers can be a solution to the problem of household chemicals exposure and food packaging exposure. Behavior change by limiting smoking and alcohol consumption and switching from fossil fuels to biofuels.

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