

Breast Cancer and Exposure to Hazardous Contaminants: A Minefield of Feats and Challenges

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ABSTRACT

Geographic heterogeneity of breast cancer prevalence suggests there are non-genetic factors related to cancer burden. Among those, residential exposure to pollutants, like hazardous waste sites, hazardous air pollutants, pesticides, and contaminated water sources, may contribute to breast cancer risk. This mini review discusses the main findings of several observational studies evaluating the association between historical exposure to contaminants and breast cancer development. The models used to evaluate breast cancer risk and hazardous contaminants are essential to reach a consensus in this highly debated field.

KEYWORDS: Breast cancer; Environmental hazards; Observational studies

ABBREVIATIONS: HWSs: Hazardous Waste Sites; HAPs: Hazardous Air Pollutants

INTRODUCTION

Breast cancer is considered as the major cause of cancer-related deaths in females worldwide Ferlay [1]. According to the American Cancer Society, one woman in every eight will be diagnosed with this disease in their lifetime De Santis [2]. There are modifiable and non-modifiable risk factors contributing to breast cancer. Some non-modifiable risk factors are age and germline mutations that compromise genomic integrity Walsh [3]. Modifiable risk factors include those depending on personal long-term exposure, like nutrition and exercise habits Chajès [4]. Also, the geographic variations of breast cancer prevalence in countries like the U.S. and Mexico raise the question of environmental exposure as a modifiable risk factor Landen [5]; Campos [6]. Residential exposure to specific chemicals, such as polycyclic aromatic hydrocarbons, benzene, organic solvents and pesticides, may relate to breast carcinogenesis Garcia [7]; Labreche [8], Damstra [9]; Wolff [10]. Several studies

examined the potential role of environmental pollutants for an increased breast cancer risk, with conflicting results. The association between breast cancer development and long-term exposure to chemical hazards is far to reach a consensus. This mini review aims to highlight the conundrum of residential exposure to hazards and breast cancer risk.

DISCUSSION

The relationship between breast cancer and environmental hazards is wide and complex. Environmental contaminants include hazardous waste sites (HWSs), hazardous air pollutants (HAPs), long-term exposure to pesticides, and chemicals present in water sources for human consumption. Studies evaluating the associations between those pollutants and breast cancer risk indicate the need for further investigations.

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Exposure to Hazardous Waste Sites (HWSs) and Breast Cancer Risk

Hazardous wastes are materials that exhibit ignitability, reactivity, corrosivity, and toxicity, presenting a potential source of hazard for the environment and human health EPA [11]. Despite international and national regulations for hazardous waste sites (HWSs), the improper disposal of those residues continues to be a worldwide problem affecting local communities in distinct countries Marsili [12]. Several epidemiological studies evaluated the health status of populations living closely with HWSs. Some investigations indicate a higher incidence of cancers (bladder, liver, non-Hodgkin lymphoma, and breast) for those citizens residing near to an HWS Griffith [13]. According to animal studies, more than 200 chemicals relate to breast carcinogenesis Rudel [14]. Preclinical data also suggests contaminants with estrogenic activities and mutagenic properties contribute to an increased breast cancer risk Brophy [15]. Other investigations show no significant increase in diseases related to a long-term residence close to an HWS. A WHO report in 2007 indicated there was insufficient evidence to establish an association between residential exposure to an HWS and cancer development WHO [16]. Living in proximity to an HWS relates to a higher rate for congenital malformations, but data do not confirm an association between residential exposure to HWSs and cancer burden Vrijheid [17]. The contrasting findings among those investigations indicate the need for clinical evidence of the health impact of hazardous waste exposure.

Exposure to Hazardous Air Pollutants (HAPs) and Breast Cancer Risk

Studies are supporting higher rates for breast carcinogenesis with the long-term exposure to hazardous air pollutants (HAPs). A couple of investigations conducted within the California Teachers' Study suggested a link between breast cancer risk and HAPs in patients residing in urban areas Garcia [7]; Liu [18]. Garcia et al. showed 24 HAPs related to an increased breast cancer risk Garcia [7]. The chemicals acrylamide, benzidine, carbon tetrachloride, ethylidene dichloride, and vinyl chloride were related to hormone-responsive breast cancers Garcia [7]. Another study within the same cohort showed a relationship between cadmium exposure and higher incidence of hormone receptor-negative breast cancers Liu [18]. However, findings in the literature are conflicting, as other studies show no associations between breast cancer burden and HAPs' exposure. A cross-sectional analysis within the Nurses' Health Study II showed that residential exposure to HAPs were unrelated to an increased breast cancer risk Hart [19]. Also, HAPs' exposure was not related to breast cancer subtypes in the US Hart [19]. We need to increase our knowledge about the consequences of HAPs' exposure on breast cancer burden for the development of policies that lessen the negative effects of air pollution.

Pesticide Exposure and Breast Cancer Risk

The usage of organochlorine pesticides may be related to an increased breast cancer burden. Several investigations indicate that environmental exposures to organochlorine pesticides can mimic the effects of endogenous estrogens Damstra [9]; Wolff [10]. Exposure to organochlorine pesticides can disrupt endocrine metabolism, promote the formation of genotoxic DNA adducts, and induce carcinogenesis Damstra [9]; Wolff [10]. The epidemiological data, though, is inconsistent as some studies show an association between organochlorine pesticides and breast cancer Romieu [20]; Snedeker [21], while others do not Aronson [22]; Demers [23]; Brody [24]. Discrepancies in the literature may be due to technical

difficulties in assessing pesticide exposure, as people are usually unaware of their historical exposure to environmental chemicals O'Leary [25].

Contaminated Drinking Water and Breast Cancer Risk

Drinking water from sources impacted by wastewater, run-off from agricultural lands, or contaminated wells present a potential pathway of human exposure to hazardous chemicals Kuch [26]; Rudel [27]. Improper disposal from industrial operations and small businesses can also contribute to chemical exposure Moran [28]. Specific hazards, like tetrachloroethylene (PCE) and organic solvents, found in contaminated drinking water can accumulate in mammary tissue and may increase breast cancer risk Labreche [8]. Some case-control studies indicate slightly to moderate increases in breast cancer burden with high PCE exposure Aschengrau [29]; Gallagher [30]. However, other studies show no consistent associations between chemical hazards in drinking waters and breast cancer rates Brody []. Discrepancies in findings can be due to regional variations in hazardous exposure by water supply, methodological limitations for exposure assessment, and difficulties in collecting retrospective information about affected individuals.

Limitations for Assessing Long-Term Exposure to Hazards

Observational retrospective studies present several challenges for the assessment of environmental exposure. The approach for assessing long-term exposure to hazards is critical, as literature reports a tumor latency timeframe of ≥ 15 years Brender [31]. Move-outs can compromise the estimations for the time of residential exposure to a potentially hazardous site. Additionally, the personal risk for breast cancer can differ according to reproductive factors, familiar and personal history of cancer(s), nutritional and exercise habits, education, occupation, race, ethnicity, and prior chronic illnesses like diabetes mellitus type 2 and obesity Kang [32]. The evaluation of the associations between breast cancer risk and environmental hazards should consider those confounding factors.

Another important issue to consider is the mathematical model evaluating residential exposure to hazards. In the Nurse Health Study II and the California Teachers' Study, the models considered an annual exposure to chemicals derived from industrial activities Garcia [7]; Liu [18]; Hart [19]. Those models were based on the reports given by the Environmental Protection Agency (EPA) of the U.S. However, findings must be interpreted with caution, as the mathematical models did not consider fluctuations of air pollutants per season. Moreover, inhalation was the only route considered for HAPs' exposure in those studies Garcia [7]; Liu [18]; Hart [19]. On the same lines, issues with evaluating contaminated water sources are the non-equal distribution of water supply, the time of exposure, and the models used for evaluating chronic exposure to hazards. Studies differ in their use for mathematical models, and as such, it provides a source for discrepancies regarding the association of chemicals in water with breast cancer risk.

CONCLUSION

The role of environmental pollutants derived from anthropogenic activities may influence breast cancer risk. Several studies indicate a historical exposure to chemicals with estrogenic and mutagenic activities increase breast cancer risk. Other epidemiological data show no relationship between cancer burden and residential exposure to hazards. The interpretation of each study should consider the mathematical models used for

estimating long-term hazard exposure. Larger prospective studies with distinct modeling approaches may provide additional insights for breast cancer risk assessment and their relationship with environmental hazards.

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