

## Role of xenoestrogens and endocrine disrupting chemicals on the occurrence of breast cancer and female reproductive disorders

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Increased urinary concentrations of Polycyclic Aromatic Hydrocarbons (PAHs) and their metabolites are associated with increased risk of some reproductive disorders. The toxicity of PAHs, dioxins and other endocrine disrupting chemicals (EDCs) are exclusively mediated through Aryl hydrocarbon Receptor (AhR). AhR overexpression contributes to the loss of normal ovarian function in polluted environments but its expression level in breast cancer and female reproductive disorders has remained unclear. We aimed in the present study to demonstrate the potential role of environmental factors with estrogenic activities in tumor etiology by focusing on the role of aryl hydrocarbon receptor (AhR) which mediates the effects of many environmental endocrine disruptors and contributes to the loss of normal ovarian function in polluted environments. This case control study which was conducted on breast cancer, breast fibroadenoma and uterine leiomyoma aimed also to compare the differential levels of AhR and its interactions with other fundamental genes (ER, AR, PgR) in breast, uterine and ovarian tissues. In each group of patients 138 cases who underwent surgery from June 2009 to June 2012 were matched with 138 controls by age and hospital records. AhR overexpression was detected in 87% of epithelial cells of young breast cancer patients which was comparable with breast fibroadenoma. Living near PAHs generating factories and dioxins caused increased risk of premenopausal breast cancer ( $p=0.001$ ,  $OR=4.8$ ). Adiposity and abnormal weight gain after 18 years were considered as the other background factors, which may contribute to the levels of endogenous and exogenous estrogens via food intakes. Direct and indirect exposure to cigarette smoke ( $p=0.005$ ,  $OR=1.43$ ) was considered as a weak risk factor without association with AhR levels in breast cancer. AhR was significantly overexpressed ( $p=0.034$ ,  $OR=1.667$ ) in uterine leiomyoma and this overexpression was correlated with living in Tehran [ $p=0.04$ ,  $OR=16(1.216-210.58)$ ], smoking [ $P=0.04$ ,  $OR=2.085(1.29-3.371)$ ], living near PAHs producing companies [ $p=0.007$ ,  $OR=2.22(1.256-3.926)$ ] and eating grilled meat [ $P=0.042$ ,  $OR=1.28(1.92-3.842)$ ]. This study contributes to the understanding of the effects of EDCs on AhR levels as well as women's health and point out possible risk factors for the development and growth of female reproductive disorders in Tehran in comparison to some other cities of Iran.