

Endocrine-disrupting chemicals and their adverse health effects: A review of current knowledge and the Nigerian situation

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ABSTRACT

Objective: Exposure of humans to certain natural or synthetic chemicals known as endocrine-disrupting chemicals (EDCs) can alter different levels of different endocrine functions ranging from synthesis to hormonal actions to metabolism. This disruption may have severe effects on human physiology and health. Some effects may be delayed, only manifesting across generations. The EDCs are ubiquitous in household, pharmaceutical, and industrial products; therefore, humans of all classes, ages, and sexes are readily exposed to several of them over a lifetime. Their harmful effects are believed to occur more in women and children. There is a growing concern among scientists and governments about the adverse effects of EDCs on humans. This has led to a steadily expanding body of research globally on the subject. However, studies investigating possible adverse health effects of EDCs in our country appear negligible. Also, there seems to be no coherent policy thrust from the government for regulating the introduction of EDCs into our environment. This narrative review aimed to provide an overview of the present scientific knowledge about EDCs and the relationships between them and public health and explore the attitude and experience of Nigerian researchers and policymakers about the emerging threat of EDCs and make recommendations for future research and policy direction.

Keywords: Endocrine disruptors, Humans, Hormones, Environmental pollutants, Public health, Nigeria

INTRODUCTION

Endocrine-disrupting chemicals (EDCs) are natural (endogenous or exogenous) or synthetic substances which influence one or more functions of the human endocrine system with consequent harmful health consequences (1). Although the term "endocrine disruptor" was coined in the early 1990s, it was formally introduced by the United States Environmental Protection Agency in 1996 (2, 3). There are over 84,000 such chemicals in various substances used in life and commercial activities, including plastics, fire retardants, pesticides, consumer products, and pharmaceutical agents (4-6). Being ubiquitous, humans of all classes, ages, and sexes are exposed to several of them per lifetime (4). Contact with these chemicals may occur through the soil, air, water, food, dust, fumes, breast milk, physical contact with certain household materials, or in utero through the transplacental spread. These chemicals are also absorbed through the gastrointestinal tract, the skin, etc (7).

Harmful effects of EDCs on human health appear to be related more to the duration (prolonged) of exposure and exposure to a combination of these chemicals than to the dosage exposed (8). These effects also appear to be transgenerational, occurring over two to three generations after exposure, as exemplified by diethylstilbestrol (1,9).

Examples of EDCs and their sources (1,7,10-12).

1. Persistent organic pollutants (POPs), e.g., polychlorinated biphenyls (PCBs) used in transformer and hydraulic fluids, in paints, oils, and some building materials; organochloride pesticides and polybrominated diethyl ether, also called brominated flame retardants (BFRs) used in furniture, carpet, and electronics

2. Phthalates are used widely in industrial chemicals and found in plastics, personal care products, food supplements, etc.

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3. Bisphenol A (BPA) found in plastics, epoxy resins, and thermal papers
4. Dioxin is a by-product of smelting, chlorine bleaching of paper, and chlorinated herbicide production
5. Parabens found in personal care products, pharmaceutical products, and food preservatives
6. Atrazine found in herbicides
7. Pyrethroids are found in contaminated water, soil and food.

EDCs disrupt the endocrine system by direct and indirect mechanisms that target different levels of the hypothalamic-pituitary-gonadal/thyroid/adrenal pathways. These disruptive effects include acting as hormone receptor agonists or antagonists, alteration of receptor expression, signal transduction, hormone synthesis, transport, storage, metabolism, and elimination of natural hormones from the body and causing epigenetic changes in DNA (2,3,13,14). The disruption of these hormones responsible for maintaining homeostasis, reproduction, development, and behavior may eventually result in harmful effects (1). There is growing concern among scientists, doctors, and governments about potential links between exposure to EDCs and various diseases resulting in different scientific bodies promoting the idea and warning that EDCs can have adverse health impacts (14). However, studies investigating possible adverse health effects of EDCs and the policy thrust about them in our society appear negligible.

This narrative review aimed to provide an overview of the present scientific knowledge about EDCs and the relationships between them and various human diseases and explore the attitude and experience of Nigerian researchers and policymakers about the emerging threat of EDCs and make recommendations for future research and policy direction.

Effects of EDCs on human health

The ability to reproduce and develop is directly related to an individual's endocrine system (1). Human health is under threat with the high prevalence of EDCs in the environment and the surge in the development of many endocrine-related disorders (15). Their resemblance to natural hormones enables them to mimic the actions of these natural substances in the body (16). For instance, while endogenous hormones bind to specific receptors to perform their endocrine functions, these EDCs disturb hormonal balance by activating or inactivating hormone receptors, thereby negatively affecting human development and health (14).

Humans are exposed to a wide array of these chemicals found in everyday products in their daily activities (14). Consequently, it is difficult to determine the total impact exposure to EDCs has on humans. However, scientific reviews and reports have documented impacts on reproduction (infertility, cancers, malformations), thyroid function, body metabolism and obesity, insulin and glucose homeostasis, and neurodevelopment (15). Also, exposure to these substances can occur without producing visible symptoms of any disease or with harmful effects manifesting at later ages and do not manifest in some people (3). The period in life when exposure to these chemicals occurs significantly affects the severity of its effect (3). Research has shown that developing fetuses and neonates are the most vulnerable to endocrine disruption. The EDCs may pose the greatest risk when organs and neural systems develop (3).

Also, exposure during these early formative periods confers the risk of adverse health effects that may last throughout a lifetime (5). Women and children are at the most significant risk of this public and environmental health hazard. These chemicals damage the anatomy and physiology of the female reproductive organs while children are in the rapid growth phase (3).

Over the last few years, some EDCs, otherwise known as obesogens, have had detrimental effects on the action of insulin, promoting weight gain and increasing the risk of type II diabetes.(3) Exposure to several toxicants like PCBs, OCPs, dioxins, BPA, and phthalates has been linked to the development of diabetes and related metabolic disorders (3). A relationship has also been established between the incidence of diabetes mellitus and chronic exposure to moderate and high ($\geq 150\mu\text{g As/l}$) inorganic arsenic (17). These exposures result in dysregulation of glucose homeostasis through insulin resistance and impaired glucose uptake (17). Apart from this endocrine toxicity, arsenic has been associated with cardiovascular diseases, skin and bladder cancer, stroke, and neurological effects (19).

In various studies, several exogenous agents were found to have metabolic, oestrogenic, anti-oestrogenic, and androgenic effects (3). Organochlorine pesticides (OCPs), due to their lipophilic nature and bioaccumulation potential, pose the greatest risk as EDCs in the environment (3). Reproductive toxicity resulting from the actions of one of the OCPs, dichlorodiphenyltrichloroethane (DDT), on follicle-stimulating hormone, oestrogen, and androgen receptors includes increased risk of infertility in both sexes, reproductive tract cancer in women, prostate and testicular cancer in men, menstrual disorders in women, low libido, early or delayed puberty in children and congenital disabilities of reproductive organs (3,14).

The EDCs such as BPA, phenols, and phthalates have been associated with premature births, miscarriages, and fetal developmental abnormalities in humans (3). The effects of exposure to diethylstilbestrol have been found to be trans and multigenerational, being seen in the children and grandchildren of exposed mothers (19). These effects include neuro-developmental disorders such as attention-deficit/hyperactivity disorder in children resulting in poor quality of life, low educational capacity, increased risk of obesity, poor morbidity and mortality health indicators, and even premature death in adulthood. This drug has also been linked to vaginal adenocarcinomas in female children of exposed females and hypospadias (abnormal opening of the urethra) in the grandsons and delayed menstrual regularity in their granddaughters (19).

Several EDCs such as propanil, triclosan, phenols, and phthalates impact the formation, function, and longevity of immune cells (4). The immature immune system is more vulnerable to EDCs (4). Maternal exposure to perfluorinated alkylate substances (PFASs) may produce immunotoxic effects in the child during the early developmental period (20). The PFASs are eliminated through breast milk; hence breast milk remains a major source of exposure in childhood. A prospective study among children 18 months to 5 years whose mothers were exposed to PFAS before birth shows an inverse association between prenatal exposure to PFAS and the serum vaccine-induced antibody concentrations against tetanus and diphtheria, resulting in diminished vaccination response (20). Similarly, a study by Dalsager et al. revealed a

higher incidence of high fever in children whose mothers' serum PFAS concentrations were elevated in early pregnancy (21).

Polychlorinated biphenyls (PCBs), one of the organochlorine pollutants that persist for a long time in the environment, have been reported to have neurotoxic, hepatotoxic, nephrotoxic, immunotoxic, carcinogenic, and cytotoxic effects in various human studies (3). Neuro-developmental deficits have been reported in neonates, infants, and school children exposed to PCBs (22). The PCBs have been shown to produce neurotoxic effects by activating the human thyroid hormone receptor transcription, resulting in the reduction of serum thyroid hormone levels. This interferes with the ability of the thyroid hormone to control neural development in growing children (22).

Lavender oil and tea tree oil, widely used oils, have been reported to potentially act as EDCs in girls and boys (23). These oils demonstrate estrogenic and anti-androgenic properties resulting in prepubertal disorders in adolescents. In boys, cases of abnormal breast development (prepubertal gynecomastia) following the use of these essential oil products have been recorded (24). In girls, premature breast development was observed (23). These abnormal breast growths disappeared with the discontinuation of these hygiene products.

The Nigerian situation

Several researchers have made efforts to study the impact of EDCs in Nigeria and bring attention to their adverse effects on the environment and the human population (25-27). However, a lot more needs to be done because the scope of the problem is not fully appreciated, or worse still, the existence of this public health concern remains unrecognized. Nigeria lacks the structures and policies needed to support the comprehensive studies that could provide the scientific basis to develop strategies for the necessary public health interventions (28).

Currently, Nigeria is making rapid progress in information and communication technology (ICT). Consequently, it has become Africa's most significant electrical and electronic waste (e-waste) dumping ground (26). These e-waste products contain EDCs harmful to humans and pose environmental hazards. (29,30). Nigeria has had an unfortunate history with the transboundary movement of hazardous wastes. Examples include the dumping in June 1988 of over 3,500 tonnes of toxic/harmful wastes originating from Italy in Koko, Delta State, and the massive shipment of container loads of e-waste into Nigeria in 2010 (31). Consequently, the Federal Government enacted the Harmful Waste Act (HWA) in 1988 and the adoption of the National Environmental (Electrical/Electronics Sector) Regulations in 2011.(31,32) However, the effectiveness of these regulatory laws is doubtful, as the importation of e-waste in Nigeria is still thriving (31).

Cosmetic products used by Black women and children have been demonstrated to contain EDCs associated with higher rates of diabetes, obesity, pre-term births, fibroids, early menarche, cancers, and infertility (33-36). In Nigeria, women have greater use of cosmetics and personal care products (PCPs) when compared with men (37). Therefore most of the adverse effects may predominantly affect this population and developing fetuses or infants at lower exposures (37). The government agency responsible for regulating cosmetic

products and certifying them safe and of good quality is the National Agency for Food and Drugs Administration and Control (NAFDAC) (38). However, despite all the agency's efforts, illicit trade in these cosmetic products still persists, hence the request that the National Assembly pass the Counterfeit Medical Product Bill to strengthen the war against offenders in the country (39).

There are many methods for waste disposal and management in Nigeria. However, the common waste disposal methods remain primitive and include open dumping, open burning, incineration, unregulated landfills, composting, and dumping into drain channels, streams, and rivers (40). These methods have raised concerns about leaching into the environment and endocrine-disrupting activities in wildlife and humans (41). Unfortunately, Nigeria has not invested adequately in modern waste management technologies such as recycling facilities or plants (40). Most public waste management agencies are poorly funded, understaffed and ill-equipped. However, a significant challenge for protecting and promoting a healthy environment favorable to life in Nigeria is that the constitution has rendered the constitutional provisions impossible to implement (40). In addition, Nigeria has failed to demonstrate the political will needed to amend the constitution in line with international standards flowing from the ratification of the African Charter (40).

Electrical and electronic waste, cosmetic products, and unregulated waste disposal, amongst many others, remain known sources of endocrine-disrupting chemicals (EDCs) and other hazardous substances in Nigeria and other LMICs. It may be argued that there is increased exposure to EDCs in Nigeria based on our records of poor legislation, ineffective regulation, and weak implementation. In 2011, South Africa became the first African country to regulate a substance as an EDC when it prohibited the use of infant feeding bottles containing Bisphenol A (BPA) (28). Unfortunately, the dumping of BPA baby bottles still occurs in Cameroon and Nigeria (42).

An African Conference on Health Effects of EDCs in South Africa recommended actions to reduce exposure to EDCs. These include the following: provision of appropriate training and education programs for individuals who use chemicals and products containing them; adoption of the precautionary principle; establishment of comprehensive biomonitoring programs; funding of additional epidemiology studies, including establishment of African birth cohorts; and increasing research on the impacts of EDCs on Africa's unique wildlife populations (28). These recommendations need serious consideration to help create awareness of the extent and seriousness of the EDCs in our environment and the need for practical, community-based interventions.

CONCLUSION

Since no comprehensive list of EDCs exists worldwide, there is a need for Nigerian researchers to design means of identifying EDCs present in our environment to define strategies to reduce or prevent their exposures and adverse health effects. We recommend further research to determine the scope of the problem of EDCs, especially their prevalence in our country. Infertility is increasing in Nigeria, and there's also an emerging trend of early puberty, especially in girls in our environment.

A link between these emerging trends and EDCs should also be explored in our society. Finally, further research is required to assess the knowledge and perception of the general public about EDCs, as this will guide policy formulation for community intervention.

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