THE PRESENCE OF ENDOCRINE DISRUPTING CHEMICALS (EDCS) AND SUSCEPTIBILITY TOWARDS COVID-19

Abstract

From the last two-three decades exposure of such unwanted substances known as "Endocrine-disrupting chemicals (EDCs)" are increased. These substances are responsible for inviting many acute and chronic diseases, which adversely interfere metabolic and reproductive system. These substances act via mimicking the hormonal action. Also, it interferes with glucose haemostasis and causes such diseases like diabetes, gestational diabetes and also affects male and female reproductive system, cardiovascular system. Because of having these diseases individual increases the possibility for such more diseases like coronavirus disease COVID-19. In the presented study different exposure sites of EDCs and susceptibility towards the COVID-19 has been described.

Keywords: Endocrine-disrupting chemicals (EDCs), COVID-19, Immunity, Susceptibility.

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I. INTRODUCTION

In the past few years, mankind has achieved its highest in medical science field, and many more is yet to be achieved, simultaneously. And with these benefits, there are a number of consequences as well. We are witnessing many anthropogenic events. The ratio of adverse health outcomes has been increasing, and medical science and researchers are striving to find the cures and causes of such diseases, simultaneously. As pollution and population are increasing, such chemicals or exogenous substances are playing a major role in causing these adverse to deleterious health effects. These substances are called "Endocrine-disrupting chemicals (EDCs)" [1, 2]. And risks from infectious diseases like Coronavirus disease (COVID-19) by the SARS-CoV-2 virus (severe acute respiratory syndrome-corona virus-2) is increasing as well.

EDCs are "exogenous substances, that may be natural or synthetic, which interact with the endocrine system of the living entity and further alter the hormonal function; results in adverse health effects in particular and in their offspring also". These substances are ubiquitous, they are present in plasticizers, by-products, pollutants, pesticides and hormones including natural and synthetic. These disruptors lead to impairment in the endocrine system and according to the Endocrine Society, such disrupting chemicals contribute to various diseases including obesity, diabetes, PCOS, and cancer [2]. Coronavirus disease (COVID-19) refers to the novel coronavirus disease that emerged in last months of 2019. It has been believed that coronavirus has been exposed from the Huanan seafood market of Wuhan China and identified as a zoonotic disease that emerged from bats. [3]. A study conducted in patients who suffered from pneumonia by visiting this place shows that 48.8% of patients had comorbidities including diabetes, CVD, and hypertension. And condition got severe as they had to be shifted to the intensive care unit. [4].

Being lipophilic in nature these substances are easily accumulated in adipose tissue and causes unbalanced adipogenesis. This irregular adipogenesis results in high number of adipocytes. And as a result of the dysfunction of adipocytes BMI ratio (body mass index) increases. Normal, range is from 18.5 to 24.9. Where as a BMI ≥25 kg/m2 is considered to be overweight, and a BMI ≥30 kg/m2 is classified as obese [5, 6, 7].

EDCs include synthetic chemicals including industrial solvents, lubricants, and by-products i.e., polychlorinated biphenyls, polybrominated biphenyls, plasticizers-phthalates, bisphenols and its derivatives-BP-A(bisphenol-A), BP-E(bisphenol-E), BP-S(bisphenol-S), pesticides, and fungicides including Methoxychlor, DDT (dichlorodiphenyltrichloroethane), pharmaceutical agents- DES (diethylstilbesterol), cosmetic material-parabens. Such phenolic compounds include phenolic EDCs, such as nonylphenol-di-ethoxylate, and nonylphenol-mono-ethoxylate. 4-nonylphenol, 4-tert-octylphenol, and 4-cumylphenol Other EDCs include perchlorate, triclosan, perfluoroalkyl (PFAS), and dioxins. Some natural chemicals include phytoestrogen, and genistein coumestrol [8, 9].

II. POSSIBLE SOURCES OF EDCs

A vast study has been going on finding the possible exposure sites of EDCs since late 90s. In the year 1993 this topic was studied in humans and animals [10]. Some of the major disrupting chemicals that interferes with humans are Bisphenol-A, phthalates, perfluoroalkyl

(PFAS), and Triclosan, DDT (dichlorodiphenyltrichloroethane), vinclozolin, and DES. EDCs are being exposed at every phase of life from birth to later upcoming stages of life. An investigation conducted by group of scientists in Malaysia in order to determine the EDCs in drinking water from two different sources including tap water and river water showed that total 14 EDCs were detected. Among them bisphenol was found in all the 165 sources [11].

1. **BPA (Bisphenols):** Bisphenols are one of the most prominently found chemicals. It was 1st discovered in 1891, and around 40 years later it was used as a pharmaceutical ingredient as an artificial estrogen in 1930. Also known as xenoestrogen. Afterward, it was used in polycarbonate plastics, water bottles, food cans [12, 13]. These chemicals are ubiquitous and their sources are electrical devices- transformers, capacitors, motors, bushings, regulators, switches, hydraulic oil, fluorescent lights ballasts, plastic, fiberglass and many more [9]. For BPA, major site of action is steroid hormones, PPAR pathways and RXR pathway. As studies show BPA are responsible for causing deleterious effects during pregnancy, in obesity and in postnatal stages also. Way of exposure on EDCs are breathing direction, transdermal root, placenta, breast milk [14]. A study conducted in Seoul, South Korea in which analysis of presence of BPA was checked in the pregnant women, around 300 women have participated in this study in order to check the levels of BPA in different stages. This study showed that different ways of BPA exposure include maternal serum, urine, breast milk, and placenta. In which profusely BPA was detected [15]. Several experimental evidences are available that shows the detrimental effect of BPA; such experiments are carried out in rodents, mammals and different animals in order to check adverse effects of BPA [16, 17, 18, 19, 20].

2. **Phthalates:** Sources of phthalates includes plastic products, pacifiers, bottle nipples, teethers. Cosmetics, personal care product such as nail polish, hair spray, perfumes, soaps, vinyl products, medical devices i.e.- catheters, IV tubes and blood bags. Such these sources are exposed to human body via ingestion, inhalation, dermal absorption or may be blood transfusion [21]. Phthalates are present in the following products: cosmetics, infant items such lotions, powders, soaps, and teethers; toys, aromatic items like candles, cleaners, and air fresheners; medical equipment like tubes, and blood bags; pharmaceutical enteric coatings; and art products. Exposure to phthalates is associated with male genital abnormalities, decreased sperm counts, endometriosis, and obesity [22]. Numerous studies have been conducted in order to find the deleterious effects of phthalates caused on mammals including rodents and humans . As described sources of phthalates are medical instruments so infants and unborn are at high risk from these disruptors. Phthalates are classified in Carcinogenic, Mutagenic, and Reprotoxic compounds by the European Chemicals Agency [23].

3. **PCBs (Polychlorinated Biphenyles):** In the United States PCB production was started in 1926 afterward in 1977 United States Congress banned the production of PCBs [24]. Theoretically up to 209 different congeners are possible but in commercial products, not all 200 have been found [25]. In this duration, PCBs were used in daily life at various places but later on, their harmful effects were observed they got eliminated. Being lipophilic in nature, these chemicals are stored in the environment as well as in the human body, especially in adipose tissues [26]. PCBs are classified as carcinogens according to the International Agency of Research on Cancer, these chemicals are hydrophobic and accumulate in high lipid-containing tissues [27].

III. HOW EDCs PLAY A ROLE IN LOWERING IMMUNITY

Having an optimum immunity level is the most prioritized thing nowadays, and susceptibility to the disease SARS-CoV-2 increases because of having low immunity levels. Scientists have almost discovered the possible pathways by which this virus is infecting us. World Health Organization has mentioned that chemicals adversely affect to the innate and adaptive immune responses in the individual and lowers immunity, as immunity level decreases our body becomes more vulnerable to diseases [28] i.e., COVID-19.

As different pathways take place in our body with regular mechanisms in this routine activity EDCs interfere via (1) altering hormone synthesis or transport or lysis, (2) acting as an agonist or antagonist, (3) brings epigenetic alteration, (4) interfering with signal transduction pathway, and (5) cell cycle regulation and pathway interference. As EDCs come in the contact with the living entity it attacks on the nuclear receptors of the hormones as well as intracellular receptors of the hormones. Thus, metabolic and reproductive the major hormones are adversely affected by EDCs [29, 30].

Table 1: EDCs and their Effects on Targeted Organ System

No.	EDCs	Affecting system- Intracellular Receptors[ICR] and Nuclear Receptors [NR]	Effects	References
1.	BPA	NR- Female reproductive system	Decreases cell viability, alters gene, cell cycle progression and mitosis also reduces aromatase expression and causes ovarian cancer.	[31, 32, 33]
		NR- Male reproductive system	Decreased sperm morphology and density.	[34, 35]
		ICR- Glucagon	Alters hormone transport across cell membranes. It is observed that in adult male mice cells which secrete glucagon, in such cells BPA blocks the calcium signaling (glucose induced).	
2.	phthalates	A case study	Traces were detected in the 75□ infants.	[37]

3.	Triclosan	NR-Female reproductive system	Adversely affects luteal cell progesterone levels and ovary function.	[38, 39]
		A case study	Prenatal exposure brings alteration in the reproductive system.	
		NR-Male reproductive system	The steroidogenesis pathway is affected and causes prostate cancer in male and breast, ovarian cancer in female.	
4.	PCB	NR-Male reproductive system	Decreases sperm count.	[40]
5.	Imidazoline	ICR-Insulin	Alters the ions to enhance insulin secretion.	[41]
6.	Tolylfluanid	ICR-Insulin	Alters signal transduction in hormone responsive cell by damaging the insulin action by insulin signaling in primary rodent & human adipocytes through a reduction in insulin receptor substrate-1 levels.	[42]

IV. INCREASED RISK OF COVID-19 FROM EDCs

As mentioned in the Table 1, EDCs causes adverse effects in male reproductive systems via altering androgen activity by bringing carcinogenic effects in the reproductive organs as well as in female reproductive system. Also, they interfere with pancreatic hormones responsible for glucogenesis and gluconeogenesis thus causing an imbalance in glucose homeostasis which results in diabetes. Indefinite level chronic exposure of EDCs is responsible for many chronic diseases such as thyroid dysfunction, diabetes, obesity, cancer and cardio vascular disease, and the people having this disease are highly susceptibility for infectious disease like COVID-19 [43].

Some of the EDCs are classified as obesogens, which raises the global issue of obesity [44]. Among all the EDCs categories BPA has maximum deleterious effects as it's related to the diabetes mellitus, polycystic ovary syndrome, and cancer [45].

The ultimate responses to these diseases are hormonal imbalance, obesity, decreased immunity and high susceptibility. All these comorbidities are involved the COVID-19 [46].

V. CONCLUSION

In conclusion, it's been proved that EDCs, COVID-19 and different morbidities are associated together in order to cause a disease also solely they are enough to cause deleterious health effects but their combination makes the situation worse. Also, the linking agent between such dangerous diseases needs to be controlled that is EDCs. Their constant exposure from neonatal to postnatal levels and further in the later stages needs to be controlled. We strictly have to focus on the minimal EDCs exposure to inhibit such diseases like COVID-19.

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