Deteriorating Women's Health Due to Rising Exposure to Per and Polyfluoroalkyl Substances (PFAS): A Review

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Abstract. A major class of water pollutants emerging as a threat to human health, particularly women's health, is Per-and-poly-fluoroalkyl substances (PFAS). PFAS belongs to a group of fluorine-containing frequently used synthetic chemicals in consumers and products manufactured by industries. The major concern linked to PFAS is that they exhibit bioaccumulation potential as their perfluorocarbon moieties do not degrade or degrade extremely slowly when exposed to natural elements. The reason PFAS has been termed **"forever chemicals**." These chemicals are disposed of in aquatic bodies via improper disposal methods, PFAS also build or concentrate in the aquatic environment because they are persistent. These chemicals further enter the human food chain via drinking water. Consumption of PFAS by women leads to catastrophic health effects such as disruption of reproductive functions, development of fetal irregularities in pregnancy, alteration of hormone secretions, menstrual cyclicity irregularities, etc. They have even been linked to life-threatening diseases, such as the development of cancer in women. In this study, we have reviewed the existing research works available to understand the alarming consequences of PFAS on female health and the various challenges being faced due to inadequate treatment and management of these chemicals. Further, the scope of developing mathematical models for studying the extent of the harmful effects of PFAS on women's health as well as devising proper management and disposal practices, is discussed in this paper.

Keywords*:*Women's Health, Per and Polyfluoroalkyl Substances, Water Pollution, Reproductive Health, Forever Chemicals

1 Introduction

Because of the toxicity and longevity in the environment, the wherewithal for bioaccumulation, and the potential for detrimental health effects, PFASs have recently attracted more and more attention on a global scale [1]. They are highly fluorinated surfactants that have been employed in the manufacturing of electronics, fluoropolymers, clothing, carpet and fabric protection coatings, and food packaging, among other industrial uses and manufactured goods [2]. Perfluoro octane sulfonic acid, C8F17SO3H (PFOS), and perfluorooctanoic acid, C7F15COOH (PFOA), are the two PFASs that are most frequently created and found in the environment. Water, sediment organisms, and air are only a few of the environmental compartments where PFASs have been found [3][4]. Industry, governments, scientists, and even the public have all expressed severe concerns about PFAS.The C8-based chemicals PFOS and PFOA are often the dominant components, and it has been found in a variety of aquatic matrices consisting of lakes, rivers, groundwater, snow, and rain [5][6]. The degradation products of PFAS can be highly resistant to various processes breaking it down and are freely mobile in air, water, and soil [7][8]. PFAS has detrimental effects on women's health. Exposure to PFAS can disrupt reproductive health by causing menstrual irregularities, reducing fertility, and increasing the risk of miscarriage and preterm birth [9]. PFAS can also interfere with hormonal balance, potentially leading to hormonal imbalances and an increased risk of hormone-related cancers such as breast and ovarian cancer [10][11]. Additionally, PFAS exposure may weaken the immune system in women, making them more susceptible to infections and potentially impacting autoimmune conditions [12][13].

2 Sources Of Per and Polyfluoroalkyl Substances (PFAS)

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The main ways that PFAS pollutants enter soil and water habitats are by the release of Aqueous Film Forming Foam (AFFF), discharge from sewage treatment plants and garbage, and toxic waste like activated sludge [14].
The sources of all these effluents are given below.

- **Fire training/fire response sites:**

During the stages of these chemicals' preservation, preparation, usage, and post-use cleanup, PFAS can enter the aquatic and terrestrial habitats as a significant point source [15]. Additionally, AFFF-contaminated water from temporary ponds that were utilized for fire training activities may leak lower or overflow laterally, which might represent a significant diffused source of contamination in the neighborhood [16]. Numerous countries, namely the United States and Australia, have claimed that the use of AFFF at airports, training grounds for the fire service, and defense institutions also contaminated the land and groundwater. Ninety sites are currently being investigated in Australia regarding PFAS contamination brought on by the regular usage of AFFF.Similar to this, there are roughly 26,000 PFAS-affected places within America, and as a result, over six million people are exposed to contaminated drinking water [17]. The affected areas are found around and close to defense establishments in Australia and the USA, where AFFF is utilized for training or fire extinguishing [18].

- **Wastewater effluents:**

Recycling plants, sewage treatment, public garbage dumps, and organic wastes are the main sources of PFAS pollution of both water and soil. Low concentrations of PFAS compounds found in household wastewater can eventually assemble in biosolids at municipal wastewater treatment facilities [19]. In recent years, Australian biosolids have been shown to contain several PFAS chemicals, including PFOA and PFOS. Total PFAS concentrations in household sludge were found to range between 55 and 3370 ng/g in the United States, according to Higgins et al. (2005). According to estimates, the total amount of PFAS in biosolids in the USA was estimated to be roughly 2749-3450 kg per year, and about 1375-2070 kg of PFAS were applied to agricultural land.[15] PFAS can infiltrate the drainage system via different commercial sources, such as the production of PFAS, fluoropolymers, and AFFF. Because traditional sewage and effluent treatment procedures cannot effectively remove these resistant molecules from the system, the PFAS problem occurs in sewage sludge [20].

- **Landfill leachate:**

Household garbage composed of materials with repellent and stain-resistant coverings (such as rugs) may leak PFAS compounds when disposed of in a dump [21]. Because of this, PFAS can migrate laterally to surrounding landmasses or leach into the groundwater via contaminated garbage residues if the right liner is not present. When discarded in wastes alongside wastewater effluents, industrial effluents such as clothes, building supplies, and protective coatings can be a pervasive producer of PFAS and other related chemicals. Long-chain PFAAs were discovered in landfills where the aforementioned waste types were dumped [22]. Short-chain PFAS compounds may outnumber large ones in the effluents of previous dumpsites, according to Knutsen et al. This is due to the fact that these chemicals are released from a wide range of commercial and domestic wastes. The difficulty in removing such PFAS contaminants from water highlights the issue of PFAS pollution in surface and underground resources around the world from waste sites. This adds to the overall challenges of sludge treatment techniques [23].

3 PFAS In Human Population

The human population has been exposed to PFAS from a number of sources, such as food consumption, water intake, air and dust, and consumer products [24]. Daily human exposures to PFAS by oral ingestion, inhalation, and skin contact result from its ubiquitous manufacture, use in everyday household and commercial items, incorrect disposal, and resistance to degradation. Intake of food is frequently the main source of PFAS openness, especially PFOS and PFOA [25]. Among all food items, typically, fish and shellfish have the highest PFAS contents and the number of times it is realized. Dairy products, eggs, drinks, and vegetables are additional food items that may include PFAS [26]. However, food at times absorbs PFAS contamination by means of transference from packaged foods or production since PFAS are used as water-resistant and greasy coatings for food-contact items and non-stick kitchenware [27]. The most common human intake of PFAS is through potable water. It has been identified in a number of investigations in samples of drinking water from various countries [28].

4 Effect of PFAS on Women's Health

PFAS exposure during pregnancy can increase the risk of complications such as preterm birth, low birth weight, and preeclampsia·[29]. This outcome might be brought on by more PFAS levels in breast milk as well as PFAS placental transfer. Studies comparing maternal and cord blood show that a mother can convey a lot of (40 percent or over) levels of her toxic levels of PFAS to a child by transfer of the placenta, and this occurs for each reproductive year [30]. These results suggest that the physiologic burden of PFAS in women is significantly influenced by pregnancy and may be related to changes in excretion patterns, placental transfer, and blood loss that occur during pregnancy [31].

Compared to moms, breastfeeding considerably raises PFAS measurements in newborns [32]. Since research has indicated the level of PFAS, particularly PFOA, and PFOS, is more in those women who have not breastfed, breastfeeding may also be a significant way for post-partum women to eliminate PFAS [33].
According to Colles et al., moms who have breastfed in the past or who have had children for a longer period of time tend to have reduced cord plasma or blood levels of certain PFAS than others [34]. Increased blood PFAS levels have been observed in infants and young children who were breastfed, even those who lived in locations where PFAS contamination was known [35]. The development of the mammary glands may be affected by PFAS, although breastfeeding is one of the key functions of the breast that may be affected [36]. In one of the earliest studies examining the harmful impacts of PFOA on physically vulnerable rats, reduced body weight and high death rate were observed which, depends on dosage, and subsequent research revealed that this was because the mammary glands' ability to produce milk was not fully developed. PFOS reduces messengerRNA and prolactin-family hormone levels in the blood in a dose-dependent manner, according to other studies looking at how it affects prolactin-family hormone concentrations [37]. Women's prolactin-family hormone levels and indicators of lactational function can be assessed following PFAS exposure.

Exposure to PFAS may alter how the mammary gland develops and have an impact on breastfeeding, in addition to raising the risk of breast cancer[38]. A study that looked at the correlation of PFAS contamination and breast cancer risk among women under 50 in Taiwan found a connection between being exposed to PFHxS and PFOS and the likelihood of developing breast cancer with estrogen receptor positivity. Mancini et al. have also identified relationships between exposure to PFOS or PFOA and breast cancers that express estrogen, progesterone, or both receptors [39].

Through the thyroid and the control of thyroid hormone, PFAS may alter breast tissue in an unstudied but plausible manner. Under typical circumstances, the pituitary gland produces TSH to promote thyroid peroxidase's production of T3 and T4when there is a lack of thyroid hormone. Since autoimmune thyroid disease is frequently linked with TPO-Abs levels in the blood that can be detected,TPO-Abs, which are antibodies to thyroid peroxidase, shouldn't be seen in the blood of healthy people. Investigating PFAS-induced changes in the function of the thyroid is crucial because healthy thyroid hormone regulation is necessary for the reproductive system to function normally. Furthermore, its traditional function in lactation, the thyroid axis also modifies thyroid hormone levels may fluctuate causing unfavorablevariations in other reproductive hormones, irregular menstruation,and even female infertility [40].

PFAS can impair HPGA function and interfere with hormone control throughout the body, in addition to having an effect on endocrine organs directly. Normal endocrine processes, including women's menses cycles, the release of hormones, reproductive health, and stability of the body, depend heavily on the neuroendocrine system, in particular the HPGA. Hormones like follicle-stimulating hormone (FSH), estrogen, luteinizing hormone (LH), progesterone, and gonadotropin-releasing hormone (GnRH), whose cyclical release is unaffected by PFAS exposure, are secreted in a manner necessary for HPGA modulation of the olestras cycle in rats. In a study on the frequency of PFOS exposure, individuals in the highest category showed more PFOS deposition in the hypothalamus compared to all other brain regions, which is important considering that hypothalamic modulation of hormones is essential in sexual behaviors. Additionally, PFOS-treated animals had an increase in the number of atretic follicles in their ovary, indicating that these chemicals have the potential to affect normal ovarian functions such as follicular development and ovulation after long-term exposure. Both of these investigations provide credence to the idea that PFAS, in particular PFOS, may affect the control of the neuroendocrine system and regular reproductive functions.

5 Exposure of Infants to PFAS

Infants are exposed to PFASs before and after birth through the placenta, breast milk, water, packed foods, formula milk, and many other ways, which will bring a negative impact on their bodies and overall activities. Infants and young children may be more susceptible to exposure due to increased hand-to-mouth activity. Some of the adverse effects of PFAS on infants are discussed below.

Several studies have reported correlations between PFAS exposure during fetal development and changes in infants' cardio-metabolic features, as well as additional correlations between babyhood serum PFAS and changed blood lipid profiles. Of particular note are the correlations between umbilical cord
blood triglycerides and PFOA. Further research has linked prenatal exposure to PFAS to a rise in child obesity [41].

Newborn child's lower immune response to vaccinations has been linked to PFAS contamination. Toddlers who were immunized against tetanus and diphtheria at a young age and who were exposed to PFAS had decreased antibody levels when tested at ages below 7. Adolescents also showed reduced levels of antibodies in a similar fashion [42].
Some have looked at a mother's PFAS levels during pregnancy and the frequency of illnesses in early childhood, such as ear infections, respiratory problems, chickenpox, etc. High adolescent illnesses are linked to higher mother serum PFAS levels as well as likely pregnant contamination [43].

Peroxisome Proliferator Activating Receptors, or PPARs, are critical nuclear sensors found in the placenta that are targeted by PFAS, making the growing fetus sensitive to the impacts of abnormal placental function.[44] Interfering with angiogenesis is an additional putative route for placental alteration.[45] However, this could be subsequent to PFAS-induced PPAR stimulation.[46] Lower birth weights have been associated with greater parental serum levels of certain PFAS, but consequences appear to vary depending on the newborn's sexual identity.[47] Angiogenesis interference and placental effects adequacy may be the reason or a contributing factor in these findings.[48] Genetic variations, which may improve certain women's placentas' ability to transport risky substances to the fetus, are another susceptibility. It will be necessary to conduct additional research in this area to fully understand any changes in birthweight or other consequences among female and male newborns.[49]

Even though it has been found in newborn rice cereal, there hasn't been much research on PFAS in foodstuffs especially made for newborns and toddlers. Since almost every newborn in the United States ingests one or both baby formula and baby food, more research on PFAS is required [50].

6 Conclusion

Within almost six decades since their introduction and usage, PFAS compounds have benefited our society in certain ways, but they have also caused grave environmental and human health concerns.
The scientific understanding of PFAS behaviors has only been observed to have an effect on living organisms and people recently, and it has largely been concentrated on a small number of PFAS compounds like PFOA or PFOS. Because a large number of populations do intake water that contains PFAS worldwide, a causal relationship could have negative public health effects. The relationships between PFAS exposure and menstrual abnormalities in biological research is constrained by methodological issues.
Exposure to PFAS has been associated with increased risks of various cancers, reproductive issues, hormonal disruption, weakened immune function, developmental problems in children, and potential damage to the liver and kidneys. Minimizing exposure to PFAS is crucial for protecting human health. Moreover, to examine the effect of PFAS on female health, there hasn't been much work done on mathematical models that incorporate PFAS and their harmful health effects. But we urgently need mathematical models to forecast the harm they will do and the levels that should be kept in water for various situations and compounds to ensure good human health. Compared to experimental data, this strategy is more affordable. As a result, evolving research as well as mathematical modelling analysis in this area shall predict the harm that PFAS would cause to women's health as well as aid scientists in creating strategies to prevent the use of these chemicals.

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