Environmental Research 272 (2025) 121181

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Review article

A review of the occurrence and distribution of Per- and polyfluoroalkyl substances (PFAS) in human organs and fetal tissues

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ARTICLE INFO

Keywords:
Per- and polyfluoroalkyl substances (PFAS)
Human exposure
Internal organs
Placenta
Fetal tissues

ABSTRACT

This review synthesizes current evidence on PFAS concentrations across human organs and tissues, excluding blood matrices. Literature search was conducted using PubMed, Web of Science, and Scopus. The earliest reported study on the topic measured PFOS, PFOSA, PFOA, and PFHxS levels in human liver and serum, showing mean liver concentrations of 18.8 ng/g and a liver-to-serum ratio of 1.3:1 for PFOS. Subsequent research extended these findings to other organs, with measurements in pooled samples indicating organ-specific accumulation patterns. PFOS was predominant in liver, kidney, and lung, while PFOA was more prominent in bone. Pathological conditions, such as liver disease, have shown to influence PFAS distribution, with diseased tissues exhibiting altered accumulation patterns. On the other hand, the occurrence of PFAS in fetal and placental tissues demonstrated that these compounds cross the placenta, although fetal exposure levels were significantly lower than maternal levels. Tissue-specific accumulation has been reported, with liver and lung showing higher concentrations compared to other fetal tissues. Associations between PFAS levels in the placenta and birth outcomes indicated potential sex-specific effects, including reduced birth weight in male infants exposed to higher PFOS levels. This review highlights important differences in the detection frequencies and concentrations of PFAS across organs and the specific studies. These variations are attributed to differences in analytical methods, sample characteristics, and exposure sources. The findings underscore the need for standardized methodologies and further research to better understand PFAS distribution in human tissues and their potential health impacts, particularly during critical developmental stages.

Abbreviations

EFSA	European Food Safety Authority
EtFOSAA	Ethylperfluorooctanesulfonamidoacetic acid
FHEA	Perfluorohexyl ethanoic acid
PFAS	Per- and polyfluoroalkyl substances
PFBA	Perfluorobutanoic acid
PFBS	Perfluorobutanesulfonic acid
PFC	Perfluorinated compounds
PFCA	Perfluoroalkyl carboxylic acids
PFDA	Perfluorodecanoic aci
PFDoDA	Perfluorododecanoic acid
PFDS	Perfluorododecane sulfonate
PFHpA	Perfluoroheptanoic acid
PFHpS	Perfluoroheptanesulfonic acid
PFHxA	Perfluorohexanoic acid
PFHxS	Perfluorohexanesulfonic acid
PFNA	Perfluorononanoic acid
PFOA	Perfluorooctanoic acid
PFOPA	Perfluorooctylphosphonic acid
PFOS	Perfluorooctane sulfonate
PFOSA	Perfluorooctanesulfonamide
PFPeA	Perfluoropentanoic acid
PFSA	Perfluorosulfonic acids
PFTeDA	Perfluorotetradecanoic acid
PFTrDA	Perfluorotridecanoic acid
PFUnDA/ PFUnA	Perfluoroundecanoic acid
POPs	Persistent organic pollutants
8:2 Cl-PFESA	2-[(8-Chloro-1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-hexadecafluorooctyl) oxy]-1,1,2,2-tetrafluoroethanesulfonic acid

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1. Introduction

Per- and polyfluoroalkyl substances (PFAS) are a diverse group of synthetic organofluorine compounds characterized by their exceptional chemical stability and unique properties, including resistance to heat,

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https://doi.org/10.1016/j.envres.2025.121181
Received 18 January 2025; Received in revised form 12 February 2025; Accepted 18 February 2025
Available online 19 February 2025

water, and oil (Glüge et al., 2020; Habib et al., 2024). While these properties have led to a widespread use of PFAS in industrial applications and consumer products, growing evidence suggests significant environmental and health concerns (Rekik et al., 2024). The environmental persistence and bioaccumulative potential of these compounds have emerged as critical issues among the thousands of existing PFAS (Payne et al., 2024; US EPA, 2024a,b). Human exposure occurs through multiple pathways, including contaminated drinking water, food consumption, consumer products, and occupational exposure (Domingo, 2012; Domingo and Nadal, 2017, 2019; Brase et al., 2021). Upon entering the body, PFAS demonstrate distinct pharmacokinetic behavior that differs from traditional persistent organic pollutants (POPs) (Jian et al., 2018; Deepika et al., 2022). Unlike lipophilic POPs, which accumulate in fatty tissues, PFAS show strong affinity for proteins, particularly serum albumin and liver fatty acid-binding proteins (Li et al., 2021; Zhao et al., 2023). This protein-binding mechanism facilitates their retention in protein-rich organs (Starnes et al., 2024).

In recent years, various investigations have identified several potential health effects associated with PFAS exposure (Sunderland et al., 2019; Jane et al., 2022; Panieri et al., 2022). These include: a) endocrine system disruption, particularly affecting thyroid function through interference with hormone transport proteins (Coperchini et al., 2021, 2024; Zheng et al., 2023), b) immunological effects, including decreased antibody production following vaccination (Abraham et al., 2020; Crawford et al., 2023) and altered immune responses (Ehrlich et al., 2023), c) developmental impacts, with prenatal exposure potentially leading to reduced birth weight and altered developmental trajectories (Blake and Fenton, 2020; Hall et al., 2022), d) reproductive health concerns (Fenton et al., 2021; Green et al., 2024), and e) potential carcinogenic effects, particularly for specific compounds like PFOA and PFOS (Zahm et al., 2024), which have been associated with increased risks of kidney and testicular cancer (Bartell et al., 2021; Steenland and Winquist, 2021; Pesonen and Vähäkangas, 2024).

Studies focused on specific human organs and tissues have reported that PFAS can mean a threat to kidney health (Stanifer et al., 2018), being linked to an impaired renal function, with a decrease in the estimated glomerular filtration rate (Liang et al., 2023). PFAS have been associated with both acute and chronic kidney disease (CKD) because the kidneys are a primary target organ involved in the excretion of PFAS (Ferrari et al., 2019, 2021). Recently, Xie et al. (2022a) assessed the potential association between serum concentrations of 18 PFAS and renal function parameters of teenagers living near a Chinese fluorochemical industrial plant. A significant association was found between the increase in the levels of PFOA and PFHpA, and an increasing risk of CKD. However, no significant correlation was noted between the levels of other PFAS and CKD. Positive correlations between urinary PFAS concentrations and key small kidney molecules have been also reported by He et al. (2023), who investigated the adverse health effects of 23 PFAS on the human kidney via urine metabolomics. A positive association between PFOA and CKD was also recently found by Haruna and Obeng-Gyasi (2024). On the other hand, human hepatotoxicity of PFAS has been also evidenced in observational investigations by the associations of these compounds and markers of liver injury (Costello et al., 2022), as well as through *in vivo* and *in vitro* studies (Maerten et al., 2024). Although brain is not a predominant tissue for accumulation of PFAS, these compounds can enter and accumulate in brain at varying levels, which may cause adverse effects on brain functions and behavior (Cao and Ng, 2021; Starnes et al., 2022). In turn, bone is another tissue that can result affected by PFAS (Khosrojerdi et al., 2024). In a representative sample of the USA population, it was found that the levels of PFAS in serum were associated with lower bone mineral density, mainly limited to women, a gender in which osteoporosis was also related with PFAS exposure (Khalil et al., 2016). Moreover, concentrations of PFOS, PFOA, PFHxS, and PFNA in maternal serum samples collected during pregnancy, were associated with inverse effects on bone size and mass in British girls at 17 years of age (Jeddy et al., 2018). Adverse effects on bone health were also found by Xiong et al. (2022), who reported an association between the serum levels of PFOS, PFOA, PFHxS, and PFNA with lower bone mineral density in USA adolescents (12–19 years). In a same line, recently Wei et al. (2024) suggested that exposure to PFAS during childhood and adolescence could affect future bone health, increasing the risk of osteoporosis in the adulthood.

The bioaccumulation of PFAS in human organs and tissues represents a pressing public health concern. Comprehensive biomonitoring of PFAS is critical for understanding their widespread presence, environmental persistence, and associated health risks. While blood/serum are widely used as primary biomonitoring matrices (Göckener et al., 2020; Belay et al., 2025; Taucare et al., 2024; Megson et al., 2025), breast milk is also a valuable indicator (LaKind et al., 2023; González and Domingo, 2024). Additionally, non-invasive matrices such as urine, hair, and nails have shown promise for exposure assessment (Comito et al., 2023). However, a systematic search in major scientific databases highlights a significant lack of data on PFAS concentrations in internal human organs and tissues beyond blood-based matrices. Given the increasing concerns about human exposure to PFAS, it is basic to determine their tissue-specific distribution and to establish quantitative correlations between internal organ concentrations and blood, serum, or plasma levels. This review aims to address this gap by critically analyzing and synthesizing the existing literature on PFAS concentrations in human organs and tissues.

2. Search strategy

The scientific databases Scopus, Web of Science, and PubMed were utilized to identify articles relevant to the main topic of this review. All searches were conducted on October–December 2024. The search included all publications cited in these databases, without restrictions on the publication date. The following keywords and their combinations were used to perform the search: *perfluorinated compounds, PFC, perfluoroalkyl substances, polyfluoroalkyl substances, PFAS, human organs, human tissues, brain, liver, lungs, kidneys, bone, spleen, adipose tissue, placenta, fetal organs*. This approach ensured a comprehensive collection of literature pertinent to the distribution of PFAS in human organs and tissues.

3. Concentrations of PFAS in internal human organs and tissues (other than blood)

According to the databases used for preparing this review, the first study reporting the concentrations of PFC/PFAS in human internal organs/tissues, excluding blood, was conducted by Olsen et al. (2003). These researchers measured the levels of PFOS, PFOSA, PFOA and PFHxS in samples of human serum and liver from 30 non-occupationally exposed individuals. Samples from postmortem donors were obtained over an 18-month period through the International Institute for the Advancement of Medicine (IIAM, PA, USA). Half of the donors in the study exhibited liver PFOS levels below the limit of quantification (LOQ) of 4.5 ng/g. Among all samples, the mean PFOS concentration in the liver was 18.8 ng/g, with values ranging from <LOQ to 57.0 ng/g. The corresponding mean PFOS concentration in serum was 17.7 ng/mL. For the 23 paired liver and serum samples, this translated to an average liver-to-serum concentration ratio of 1.3:1. The liver to serum concentration ratios could not be calculated for PFOSA, PFOA, and PFHxS because most liver samples and many serum samples were <LOQ. More specifically, only one liver sample (6.3 ng/g) could be quantified for PFOSA, two for PFOA (25 and 47.0 ng/g), and three for PFHxS, (1.4, 5.6 and 8.2 ng/g). All other donors showed liver concentrations < LOQ (range: <3.4-<18.5 ng/g). The results of that study suggested that the liver to serum ratio of PFOS would be comparable to that reported in a previous toxicological investigation carried out by Seacat et al. (2002) in cynomolgus monkeys. Maestri et al. (2006) developed an analytical method to determine the concentrations of PFOA and PFOS in pooled postmortem samples of various organs and tissues belonging to seven

non-occupationally exposed individuals of Northern Italy. For PFOA and PFOS, the results (ng/g) were the following: liver (3.1, 13.6), kidney (3.5, 6.4), adipose tissue (1.4, 1.7), brain (0.5, 1.3), basal ganglia (0.3, 1.2), hypophysis (2.0, 7.6), thyroid (2.3, 3.1), gonads (1.9, 3.4), pancreas (1.3, 3,5), lung (3.8, 7.9), and skeletal muscle (0.6, 1.0). That was a very preliminary study, in which only one pooled sample was analyzed for PFOA and PFOS. In an extensive interesting review on exposure assessment of PFC for the general population of Western countries, Fromme et al. (2009) presented the knowledge (at that time) of the PFC levels in indoor and ambient air, house dust, drinking water and, while human biomonitoring data of PFC concentrations in blood, breast milk, and human tissues were also reviewed. Regarding human internal organs, the studies by Olsen et al. (2003) and Maestri et al. (2006) were discussed, while the results of a pilot study performed in Germany (Völkel et al., 2007) were also included. In that pilot study, the concentrations of PFOS and PFOA were measured in ten samples of liver of deceased German individuals. The mean PFOS and PFOA levels were 17.9 ng/g (range: 1.6–45.4 ng/g) and 1.8 ng/g (range: 0.5–3.5 ng/g), with percentages of detection of 100% and 90%, respectively.

Yeung et al. (2013) analyzed concentrations of 12 PFAS in liver and serum samples collected from liver transplant patients. The study participants suffered from severe hepatic conditions, including hepatocellular carcinoma, cirrhosis caused by hepatitis C infection, and acute liver failure. Diseased liver tissue samples (n = 66) were obtained from the liver tissue bank at the Victorian Liver Transplant Unit, Austin Health, Melbourne, Australia, with control liver tissues (n = 9) collected from cancer patients during liver resection surgery. PFOS and PFOA were detected in all liver samples at ranges of 0.375–42.5 ng/g ww, and 0.101–2.25 ng/g ww, respectively. More than 90% had detectable concentrations of PFHxS (range: <0.034–1.85 ng/g ww) in diseased livers compared to a less percentage (22%) of control livers. In turn, EtFOSAA, PFNA and PFDA were detected in most control and diseased samples, with concentrations ranges of <0.034–1.85 ng/g ww, <0.034–1.23 ng/g ww, and <0.034–0.765 ng/g ww, respectively. In contrast, the levels of PFDS, PFPeA, and PFHxA in liver were not detected (<0.168 ng/g ww). It was concluded that pathological changes in diseased livers might alter the distribution of PFAS in that tissue. In another more recent study aimed at determining the occurrence and distribution of PFAS in livers of patients with liver cancer, Liu et al. (2021) measured the levels of 21 PFAS in samples of tumor liver (TL) and non-tumor liver (NL) obtained from a hospital in Guangzhou, China. The highest detection frequencies (DF) (>92.7%) corresponded to these compounds: PFHxA, PFNA, PFUnA, PFHxS, PFHpS, and PFOS. In general, for all analyzed PFAS, the DF were comparable in NL and TL samples, except for PFOA, PFTrDA, and PFTeDA, whose DF in TL samples were higher than those found in the NL samples. The highest mean levels in NL samples corresponded to PFOS (22.2 ng/g dw), PFBA (8.43 ng/g dw) and PFHpS (61.13 ng/g dw), while in TL samples PFOS (22.4 ng/g dw), PFBA (6.55 ng/g dw) and PFHpS (6.37 ng/g dw), as well as PFOPA (6.61 ng/g dw) showed also the highest concentrations among all the analyzed PFAS. The concentration ranges of the ∑21 PFAS in the TL and NL samples were 5.70–303 ng/g, and 4.08–240 ng/g, respectively.

In relation to other internal organs, in Pavia, Italy, Pirali et al. (2009) determined the concentrations of PFOA and PFOS in thyroid tissues of 28 patients undergoing surgery for malignant and benign thyroid disorders. The objective of that study was to establish if there was a relationship between the levels of PFOA and PFOS, and the clinical, biochemical, and histologic phenotype of the patients. The potential relationship between tissue and serum levels of both compounds was another goal of the study. PFOA and PFOS could be detected in all analyzed samples, being their median (range) concentrations 2.0 ng/g (0.4–4.6 ng/g) and 5.3 ng/g (2.1–44.7 ng/g), respectively. The levels of PFOA and PFOS in thyroid were independent on the underlying thyroid disease, while their serum concentrations were significantly higher than those in the correspondent thyroid specimens. On the other hand, Kärrman et al. (2010) determined the levels of 12 PFCs in human liver samples collected postmortem in Catalonia, Spain. PFHxS, PFOS, PFNA, PFDA, and PFUnDA were detected in all samples, while PFOA was detected in 50% of the samples. The mean concentrations (ng/g ww) of these six PFCs were, in decreasing order: 26.6, 1.45, 0.85, 0.73, 0.71, and 0.50, for PFOS, PFUnDA, PFDA, PFNA, PFOA and PFHxS, respectively. By far, PFOS showed the highest levels, ranging between 9.67 and 52.13 ng/g ww. The relationships between these concentrations in human liver and those in blood samples were estimated using levels of human blood previously measured in individuals living in the same area (Ericson et al., 2007). Liver/serum ratios of 1.7:1, 1.4:1, and 2.1:1 were found for PFOS, PFDA, and PFUnDA, respectively. Among the studies on the accumulation of PFAS in human tissues, one of the most complete and exhaustive was carried out by Pérez et al. (2013), who measured the concentrations of 21 PFAS in 99 samples of autopsy tissues (bone, brain, liver, lung and kidney) collected in Tarragona County (Catalonia, Spain). All samples contained detectable levels of at least two of the 21 analyzed PFAS, with varying accumulation patterns across tissues. Liver and brain showed similarities, as did also kidney and lung. In liver, PFHxA, PFOS, and FHEA were the most prevalent, with median concentrations of 68.3, 41.9, and 16.7 ng/g, respectively. PFOS was found in 90% of samples, while PFOA was detected in 45%. In brain, PFHxA was the most predominant, being present in all samples (range: 10.1–486 ng/g). PFOS was detected in only 20% (median: 1.9 ng/g), while PFOA was absent. The highest PFAS accumulations were found in lung, with median concentrations of 807 and 207 ng/g, for PFBA and PFHxA, respectively. PFOS was found in most samples, while PFOA contributed significantly despite being detected in fewer samples. In kidney, PFBA was predominant (263 ng/g), with notable but lower levels of PFDoDA and PFDA. PFOS also showed high concentrations (55.0 ng/g). Bone had the lowest PFAS burdens, being PFOA the main contributor (median: 20.9 ng/g), while PFOS was not detected. In summary, PFHxA showed the highest concentrations in brain and liver, whereas the highest median levels of PFBA were found in kidney and lung. In turn, PFOA was the predominant compound in bone, while PFOS primarily accumulated in lung, liver, and kidney, being its levels in bone and brain notably low. That study showed, for the very first time, the accumulation of certain short chain PFC, such as PFBA and PFHxA, in human tissues.

Data on the accumulation of PFAS in bone is very limited. Koskela et al. (2017) performed a study aimed at measuring PFAS in human femoral bones, and how PFOA could affect human osteoclasts and osteoblasts. Bone bank samples (18) and bone tissue biopsies of a single cadaver were analyzed for the concentrations of PFOA, PFNA, PFDA, PFUnA, PFDoA, PFHxS and PFOS. Neither PFOA, nor PFOS, were found in femur, tibia and fibula from the cadaver. However, PFNA was detected in all three long bones (0.85, 0.47 and 0.19 ng/g ww in femur, tibia and fibula, respectively). In turn, the mean concentrations of PFAS from human femoral head samples measured from trabecular bone (given in ng/g dw) and bone marrow (given in ng/g ww) were the following: PFOA (0.15 and 0.44), PFNA (0.63 and 0.17), PFDA (0.03 and 0.04), PFUnA (0.07 and 0.02), PFHxS (0.03 and 0.07) and PFOS (0.89 and 0.70). These results were complemented with *in vitro* studies, which allowed to conclude that PFAS were present in bone, having the potential to affect human bone cells partly.

To test the hypothesis that glioma could be used as an indicator of the brain distribution of exogenous substances, Xie et al. (2022b) carried out a study, in which the levels of 17 PFAS were measured in samples (n = 26) of brain glioma tissues of patients in a Hospital of Guangzhou, China. The DF ranged between 8% for 8:2Cl-PFESA and 85% for PFOS, PFBS and PFDoA had the highest and lowest median levels, 0.77 and 0.10 ng/g ww, respectively, being those of PFOS and PFOA, 0.49 and 0.30 ng/g ww, respectively. The median concentration of ∑PFAS was 2.9 ng/g ww (range: <0.05−51 ng/g ww). Glioma was an effective indicator for monitoring PFAS in brain, as the results were similar to those previously reported in autopsy brain tissues of healthy subjects (Pérez et al.,

2013). On the other hand, it has been reported that PFBA, an ubiquitous PFAS, has a short half-life in blood with low serum/plasma levels (EFSA, 2020), but relatively high levels in internal organs such as lung and kidneys (Pérez et al., 2013). To verify the previous results of Pérez et al. (2013) with PFBA, Abraham et al. (2021) measured the levels of that compound in human samples of lung (n = 7) and kidney (n = 9), using a different method of quantification. Samples were collected from tumor patients, and obtained from Biopredic International (Rennes, France). The concentrations range of PFBA were 0.08–0.24 ng/g, and 0.04–0.19 ng/g in lung and kidney tissues, respectively, results that -especially for lung-were considerably lower than those previously reported by Pérez et al. (2013). It was concluded that the analysis of PFBA in tissues could have a notable dependence of the instrumental quantification and even a potential contamination of the samples. According to PubMed, Web of Science, and Scopus, the most recent study on the occurrence of PFAS in human blood and internal organs was conducted by Nielsen et al. (2024). These researchers measured the levels of PFHxS, PFOA, PFOS, and PFNA in samples of blood and five organs (liver, kidneys, lungs, spleen, and brain) collected from 19 medicolegal autopsies of subjects residing in Southern Denmark. In liver, kidneys and lung the DF were 90–100% of the samples, in spleen the DF were somewhat lower for PFHxS (55%) and PFNA (28%), while in brain cortex the DF ranged between 0% for PFHxS and 2.8% for PFOS. The highest concentrations (ng/g ww) corresponded to PFOS (liver: 6.277, lungs: 3.031, kidneys: 2.174, spleen: 1.392, and brain cortex: 0.334). In that study, the authors also established the correlation between the levels found in blood samples with those detected in the analyzed organs. Tissue concentrations correlated well with the blood levels, except for PFHxS, which showed weaker correlations, particularly for kidney, while PFOA correlated less well for spleen and liver. Based on the correlations between the levels of PFAS found in blood and various target organs, it was concluded that the blood concentration of PFAS would be an appropriate exposure biomarker to measure exposure to these compounds.

A comprehensive summary of the aforementioned studies is provided in Table 1.

Table 1
Occurrence and concentrations of PFAS in human organs and tissues.

Country	PFAS Included in the Study	Organs and Tissues Analyzed	Highlights	Reference
USA	PFOS, PFOSA, PFOA, PFHxS	Liver	PFOS detected in liver with mean concentration of 18.8 ng/g. Liver-to-serum PFOS concentration ratio was 1.3:1. Liver levels for PFOSA, PFOA, and PFHxS mostly below LOQ.	Olsen et al. (2003)
Italy	PFOA, PFOS	Liver, kidney, adipose tissue, brain, basal ganglia, hypophysis, thyroid, gonads, pancreas, lung, skeletal muscle	Preliminary study with pooled samples. PFOA and PFOS detected in multiple organs. Highest concentrations found in liver and lung.	Maestri et al. (2006)
Germany	PFOS, PFOA	Liver	Mean PFOS and PFOA concentrations in liver were 17.9 ng/g and 1.8 ng/g, respectively. PFOS detected in all samples, PFOA in 90%.	Völkel et al. (2007)
Australia	PFOS, PFOA, PFHxS, EtFOSAA, PFNA, PFDA	Diseased and control liver tissues	PFOS and PFOA detected in all liver samples. Diseased livers had higher PFHxS detection rates than control livers. Pathological changes may alter PFAS distribution.	Yeung et al. (2013)
China	21 PFAS, including PFOS, PFHxA, PFNA, PFUdA, PFBA	Tumor liver (TL) and non-tumor liver (NL)	High detection frequency for PFOS, PFHxA, and PFNA. Concentration ranges of ∑21 PFAS in TL and NL were 5.70–303 ng/g and 4.08–240 ng/g, respectively.	Liu et al. (2021)
Italy	PFOA, PFOS	Thyroid	PFOA and PFOS detected in all samples. Median thyroid concentrations were 2.0 ng/g for PFOA and 5.3 ng/g for PFOS.	Pirali et al. (2009)
Spain	PFHxS, PFOS, PFNA, PFDA, PFUnDA	Liver	PFOS detected in all liver samples with mean concentration of 26.6 ng/g.	Kärrman et al. (2010)
Spain	21 PFAS, including PFOS, PFHxA, PFBA, PFOA	Liver, brain, lung, kidney, bone	PFHxA and PFBA showed the highest median concentrations in liver and lung, respectively. PFOS accumulated most in lung, liver, and kidney, while PFOA predominated in bone.	Pérez et al. (2013)

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4. Concentrations of PFAS in human placenta and fetal organs

As above commented, the first scientific report on the occurrence of PFC/PFAS in human internal organs was published at the beginning of the current century (Olsen et al., 2003) (see Table 2). Since then, the results of a rather limited number of studies on that topic have been published. On the other hand, data on tissue concentrations in human placenta and fetal organs were not available until the last decade, when Mamsen et al. (2017) measured the levels of PFOS, PFOA, PFNA, PFUnDA and PFDA in samples of placenta and fetal organs obtained of legal abortions performed in Danish hospitals. Thirty-four samples of placenta and 108 fetal organs were collected, together with 24 blood samples. The highest concentrations (ng/g) of PFAS in placenta corresponded to PFOS (1.3), followed by PFOA (0.23), PFNA (0.14), PFDA (0.10) and PFUnDA (0.06), with a similar order also observed in fetal organs: mean levels of 0.60, 0.17, 0.09, 0.08, and 0.06 ng/g, respectively. Interestingly, it was found that placental concentrations of PFOS, PFOA, PFNA, and PFUnDA were approximately 11–15% of the levels detected in the maternal circulation, being the concentrations even lower in the fetal organs (5–13% of maternal levels). Thus, fetal exposure to these PFAS was 7–20 times lower than maternal exposure. In a subsequent study related with the previous one (Mamsen et al., 2017), Mamsen et al. (2019) determined the levels of PFOS, PFOA, PFNA, PFDA, PFUnA, and PFHxS, in samples of human embryos, fetal organs (liver, lung, heart, central nervous system, and adipose tissue), their corresponding placentas, as well as maternal serum, which were obtained from elective pregnancy terminations and cases of intrauterine fetal death. PFOS, followed by PFOA and PFNA, were the most detected PFAS in placenta with DF of 93%, 82%, and 83%, respectively, while in fetal organs the DF were 76%, 70% and 53%, respectively. Liver and

Table 1 (*continued*)

Country	PFAS Included in the Study	Organs and Tissues Analyzed	Highlights	Reference
Finland	PFOA, PFOS, PFNA, PFDA, PFUnA	Bone (femur, tibia, fibula, femoral head)	PFOS and PFOA not detected in a cadaver long bones. PFNA detected in all samples, with femur having the highest concentration.	Koskela et al. (2017)
China	17 PFAS, including PFOS, PFBS, PFDoA, PFOA	Brain glioma tissues	Median PFOS and PFOA concentrations were 0.49 and 0.30 ng/g, respectively. Glioma was used as an indicator of PFAS distribution in brain.	Xie et al. (2022)
Denmark	PFOS, PFHxS, PFOA, PFNA	Liver, kidney, lung, spleen, brain cortex	PFOS had highest concentrations across organs. Weak correlations between blood and tissue levels for PFHxS and PFOA in spleen and liver were found.	Nielsen et al. (2024)

Table 2
Summary of available studies on the concentrations of PFAS in human placenta and fetal tissues.

Country	PFAS Included in the Study	Tissues Analyzed	Highlights	References
Denmark	PFOS, PFOA, PFNA, PFDA, PFUnDA	34 human placental samples and 108 fetal organs	PFAS were transferred from mother to fetus. PFOS showed the highest concentrations in both placenta and fetal tissues.	Mamsen et al. (2017)
Denmark	PFOS, PFOA, PFNA, PFDA, PFUnDA, PFHxS	Placenta, human embryos and fetal tissues (liver, lung, heart, CNS, adipose tissue)	All PFAS passed the placenta and deposited to embryo and fetal tissues.	Mamsen et al. (2019)
USA	PFOS, PFOA, PFNA, PFDA, PFBA, PFPeA, PFHxA, PFHpA, PFBS, PFHxS, GenX	Placenta	PFOS, PFOA, PFNA and PFDA were the most abundant. PFOS levels linked to reduced birth weight in male infants.	Hall et al. (2022)

lung, followed by adipose tissue, heart and central nervous system, were the organs/tissues with the highest levels of these compounds. In both, placental and fetal tissues, PFOS showed the highest concentrations (placenta: median 1.24 ng/g, range 0.45–3.87 ng/g; fetal tissues: median 0.83 ng/g, range 0.19–12.61 ng/g), followed by PFOA (placenta: median 0.3 ng/g, range 0.15–0.99 ng/g; fetal tissues: median 0.49 ng/g, range 0.15–3.62 ng/g). In turn, the levels of PFNA, PFDA, and PFUnA in all placental and fetal tissues were below 0.73 ng/g. Based on these findings. Mamsen et al. (2017, 2019) stated that PFAS could cross the placenta and accumulate in embryonic and fetal tissues, therefore emphasizing the need for risk assessments of PFAS exposure during pregnancy. On the other hand, to assess the associations between the concentrations of PFAS in placenta with birth outcomes, the levels of 11 PFAS were measured in samples of placenta collected from women living in central North Carolina, USA (Hall et al., 2022). The DF ranged between 0% for PFPeA and PFHpA, and percentages between 96 and 100% for PFNA (100%), PFOS (99%), PFOA (98%) and PFDA (96%). Only these four compounds could be quantified, with median values of 0.95, 0.27, 0.11 and 0.06 ng/g ww, for PFOS, PFOA, PFNA and PFDA, respectively. Sex-specific differences were observed between PFAS exposure and birth outcomes, with higher PFAS concentrations identified in nulliparous pregnancies. Specifically regarding PFOS, elevated placental levels of this compound were linked to reduced birth weight relative to gestational age in male infants, whereas in female infants, higher PFOS exposure was associated with increased birth weight.

5. Discussion and conclusions

The exhaustive search in three scientific databases of the accumulation of PFAS/PFC in human internal organs and tissues (excluding blood) detected only 17 papers on the topic. Unfortunately, the studies reported in these papers are not comparable. Firstly, there are notable differences in the specifically measured PFAS. While some researchers determined the concentration of an only compound: PFOS (Olsen et al., 2003), PFBA (Abraham et al., 2021), or just in a couple of PFAS, basically PFOS and PFOA (Maestri et al., 2006; Pirali et al., 2009; Koskela et al., 2017), other investigators measured the levels of various compounds, being Pérez et al. (2013) who measured the highest number of PFAS (21). Another important difference is also the analyzed organs and tissues. While some researchers analyzed samples of an only tissue: liver (Olsen et al., 2003; Kärrman et al., 2010; Liu et al., 2021), bone (Koskela et al., 2017), or thyroid (Pirali et al., 2009), other investigators determined the levels of PFAS in various organs and tissues (Maestri et al., 2006; Pérez et al., 2013; Nielsen et al., 2024). Additionally, the number of samples analyzed varied greatly across studies, highlighting the overall limited data available for specific tissues (see Table 1). For example, some studies relied on pooled samples or small sample sizes, which may limit the generalizability of the findings. Anyhow, it is evident that data on the actual levels of PFAS in human organs and tissues, other than blood/serum/plasma is certainly limited. Based on the information here reviewed, lungs seem to be a tissue showing high PFAS levels (Pérez et al., 2013; Nielsen et al., 2024). However, for PFOS and PFOA, the two PFAS, for which more data are available, there is a trend to accumulate mainly in liver and bone, respectively. In liver, the concentration of PFOS was higher than that of PFOA (Maestri et al., 2006; Kärrman et al., 2010; Pérez et al., 2013; Nielsen et al., 2024), which in turn was higher than the concentrations of PFNA and PFDA (Pérez et al., 2013), or very similar to that of PFNA (Nielsen et al., 2024). While the 21 analyzed PFASs were found in all tissues (Pérez et al., 2013), in the recent study by Nielsen et al. (2024), only PFOS, PFNA, PFOA and PFHxS were quantified.

The heterogeneity in analytical methods used across studies also means a challenge for data comparison. Some studies used older methods with lower sensitivity, while others used more advanced techniques. Among these, SPE-UHPLC-HRMS allows the detection of a wider range of PFAS at lower concentrations (Belay et al., 2025). The choice of extraction and cleanup methods, as well as the calibration standards used, can also significantly impact the accuracy and reliability of the results. Recent advances in analytical techniques have led to more reliable and comprehensive PFAS analysis in human tissues. High-resolution mass spectrometry (HRMS), coupled with liquid chromatography (LC), offers improved sensitivity and selectivity for quantifying a broad range of PFAS, including emerging compounds. Isotope dilution methods are also crucial for correcting matrix effects and ensuring accurate quantification (US EPA, 2024a,b). Online solid-phase extraction (SPE) coupled with LC-MS/MS provides efficient sample

cleanup and preconcentration, enhancing sensitivity and reducing matrix interferences (Belay et al., 2025; US EPA, 2024a,b). However, standardization of analytical protocols is still needed to ensure comparability across different laboratories and studies.

Regarding the occurrence of PFAS in placenta and fetal tissues, the studies reviewed provide critical insights into the presence and impact of these compounds in human placenta and fetal tissues. PFAS, mainly PFOS, PFOA, PFNA, PFDA, and PFUnDA, can cross the placenta, although at reduced concentrations compared to maternal blood levels. Maternal exposure levels are generally 7–20 times higher than those found in fetal tissues, highlighting a degree of protection offered by the placental barrier. However, even these reduced levels raise concerns due to the bioaccumulative nature of PFAS and their potential adverse health effects. In fetuses, among examined organs, liver and lungs showed the highest PFAS accumulation, suggesting a potential organ-specific affinity or vulnerability. The relatively high DF for PFOS, PFOA, and PFNA found in placental and fetal tissues indicate widespread exposure, although concentrations vary. Hall et al. (2022) found sex-specific impacts of PFAS exposure, with elevated placental PFOS levels associated with reduced birth weight in male infants, and increased birth weight in female infants, emphasizing potential gender-based physiological differences in response to PFAS. The above results underline the ability of PFAS to accumulate in fetal tissues, raising concerns about their developmental and health impacts. The presence of PFAS in critical organs during early development -even at low concentrations-required further investigations.

In summary, the findings reported in the reviewed studies underscore the need for stricter regulation of PFAS exposure, particularly among pregnant populations. The widespread detection of specific PFAS highlights the importance of global initiatives to minimize environmental and human exposure to these chemicals. Advancing the understanding of PFAS accumulation mechanisms and their associated health impacts is essential for mitigating risks and establishing effective regulatory policies and remediation strategies.

Declaration of competing interest

The author declare the following financial interests/personal relationships which may be considered as potential competing interests: The sole author of this manuscript, José L. Domingo, Rovira i Virgili University Faculty of Medicine and Health Sciences, Reus, Spain is currently a Member of the Editorial Board of ENVIRONMENTAL RESEARCF

Data availability

Data will be made available on request.

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