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The transfer of per- and polyfluoroalkyl substances (PFAS) from mother to child: Comparison between maternal and cord blood in an Italian cohort

Arianna Fornasari [a], Maria Sech [a], Elena Piva [b], Luca Morini [c], Fabio Vaiano [d], Viola Seravalli [e], Anna Seidenari [f], Jacopo Lenzi [g], Giuliana Simonazzi [f], Paolo Fais [a], Jennifer P. Pascali [a,*]

[a] Unit of Legal Medicine and Forensic Toxicology, Department of Medical and Surgical Sciences, University of Bologna, Via Irnerio 49, Bologna 40126, Italy
[b] dtoLABS, Via Pozzuoli, 13C/13D, Spinea, VE 30038, Italy
[c] Unit of Legal Medicine and Forensic Toxicology, Department of Public Health, Experimental and Forensic Medicine, University of Pavia, Italy
[d] Unit of Forensic Toxicology, Department of Health Sciences, University of Florence, Florence 50121, Italy
[e] Unit of Obstetrics and Gynecology, Department of Health Science, University of Florence, Florence, Italy
[f] Unit of Obstetrics and Gynecology, Department of Medical and Surgical Sciences, University of Bologna, Via Massarenti 9, Bologna, Italy
[g] Biostatistics, Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy

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ABSTRACT

Per- and polyfluoroalkyl substances (PFAS) are persistent synthetic pollutants associated with multisystemic toxicity, including endocrine disruption and developmental risks. While maternal-fetal transmission has been documented, significant gaps remain regarding the fetal burden of emerging and short-chain alternatives. This study quantified 23 PFAS in paired maternal and cord blood samples from 120 women recruited in Italy, between 2024 and 2025 during the ELENA project (Early Life Exposure to per- and polyfluoroalkyl substaNces (PFAS) and HeAlth risks). Analysis was performed using LC-HRMS to evaluate the single and total PFAS burden after solid-phase extraction. PFAS were detected in 99.04% of maternal and 84.8% of cord blood specimens. Legacy compounds, PFOS (99.0%), PFOA (83.7%), and PFHxS (78.8%), were the most prevalent in maternal samples. Significant associations were found between the regular use of processed food and higher levels of maternal 6:2FTS and PFHpS. While the median sums of PFAS in maternal and cord blood were 1.19 ng/mL and 0.49 ng/mL respectively, nearly 30% of women and 3% of cord blood exceeded the 2 ng/mL NASEM threshold associated with potential health risks. In general, when comparing the observation frequencies and concentration of the compounds in paired samples, the kinetic barrier of placenta has been confirmed, with no selective accumulation. The calculated Transplacental Transfer Efficiency (TTE) values suggested that chemical structure significantly dictates fetal burden. These results highlight the urgent need for biomonitoring approaches and targeted strategies to reduce maternal exposure to legacy and emerging PFAS to protect fetal development.

1. Introduction

PFAS are a large family of synthetic compounds introduced in the 1940s which are characterized by a fully or partially fluorinated carbon chain of various lengths. Since their discovery, they have been incorporated in multiple everyday products in non-stick coatings, water-repellant textiles, grease-repellant paper, technical fabrics, cosmetics and food packaging. Their widespread use together with their persistence has led to environmental contamination in thousands of sites in the U.S. and Europe. Nevertheless, considering that sensitive analytical methods for PFAS detection in complex specimens became available only in the 2010s, estimates of global contamination and human burden are likely to be underestimated [1]. Humans are exposed to these compounds via inhalation of air and dust, dermal absorption, and ingestion of contaminated water and food. While inhalation and dermal absorption account for most occupational exposure, ingestion represents the leading source of exposure for the general population. Furthermore, pre- and perinatal exposure has been documented, with maternal-fetal transmission occurring through placental transfer and breastfeeding [2,3].

Human biomonitoring is essential for assessing actual exposure levels [4]. Consequently, the National Academies of Sciences, Engineering, and Medicine (NASEM) published clinical guidelines in 2022 establishing threshold values for total PFAS in human serum [5,6] correlated with varying degrees of health risk and specific clinical

* Corresponding author.
E-mail address: jennifer.pascali@unibo.it (J.P. Pascali).

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follow-up requirements. NASEM defined serum PFAS levels below 2 ng/mL as unlikely to be associated with adverse health effects, whereas levels ≥ 20 ng/mL were linked to a heightened risk. Intermediate levels (2–20 ng/mL) were identified as having potential adverse effects, particularly for sensitive populations. Numerous studies [7] have documented PFAS as multisystemic toxicants. Indeed, PFAS exposure is associated with endocrine disruption, altered lipid metabolism, immunotoxicity, hepatotoxicity, nephrotoxicity, and carcinogenicity, with IARC specifically classifying PFOA and PFOS as carcinogenic [8]. Pregnancy and the fetal period represent critical windows of bioaccumulation, during which exposure to environmental contaminants can pose unique and disproportionate risks to both maternal and neonatal health. PFAS exposure during pregnancy [9] has been linked to gestational diabetes, gestational hypothyroidism, and hypertensive disorders, including preeclampsia. Exposure during the fetal stage has been demonstrated to interfere with pregnancy maintenance, fetal development, and long-term health outcomes in offspring such as risk of metabolic syndrome, including obesity, dyslipidemia, hypertension, and impaired glucose regulation. The underlying mechanisms include altered thyroid function, interference with steroid hormone metabolism, modulation of peroxisome proliferator-activated receptors (PPARs), and disruption of placental development. The placenta, essential for nutrient and xenobiotic transport, is also a vulnerable target. PFAS cross the placental barrier via transporters, potentially disrupting trophoblast invasion, angiogenesis, and placental homeostasis [10], potentially harming fetal growth. Despite the growing body of evidence linking PFAS exposure to adverse neonatal outcomes, significant gaps remain in our understanding of maternal-fetal toxicokinetics. Current literature has predominantly focused on a narrow subset of legacy compounds, such as PFOA and PFOS, often overlooking the complex mixture of emerging and short-chain alternatives that now characterize modern human exposure. Furthermore, while the placenta is recognized as a key interface, the transplacental transfer efficiency (TTE) of many newer PFAS congeners remains poorly characterized, particularly regarding how carbon chain length and functional groups influence their partitioning between maternal and cord blood. In this context, we hypothesized that TTE is heavily dictated by functional groups rather than just carbon chain length, expecting lower transfer for PFSAs than PFCAs due to the stronger albumin binding affinity of sulfonic groups. Direct quantification in matched cohorts is therefore essential, especially in Europe where recent cord blood data remain scarce. To address these limitations, the ELENA project (Early Life Exposure to per- and polyfluoroalkyl substaNces (PFAS) and HeAlth risks) aimed to i) quantify a broad profile of 23 PFAS, including legacy, emerging, and short-chain compounds in matched maternal and umbilical cord blood samples to provide a map of prenatal exposure; ii) determine the transplacental transfer efficiency (TTE) for each compound, identifying structural determinants that facilitate or hinder fetal exposure; iii) evaluate the cumulative human burden in relation to the 2022 NASEM clinical guidelines, assessing whether current exposure levels in our cohort reach the thresholds associated with heightened health risks for the maternal-fetal unit. The multi-level hypothesis driving the design of this study posits that the gestational barrier is partially permeable to environmental pollutants, resulting in the detectable presence of both legacy and emerging PFAS in fetal cord blood. Under this framework, maternal lifestyle and dietary habits, such as the regular consumption of processed foods or fish, are hypothesized to significantly drive and elevate the maternal body burden of specific PFAS congeners. Finally, it is hypothesized that a compound's unique chemical structure fundamentally dictates its Transplacental Transfer Efficiency (TTE), with sulfonic acids exhibiting lower fetal transfer than carboxylic acids due to their stronger binding affinities to maternal serum proteins. By expanding the analytical window to 23 compounds, this research seeks to provide a more accurate estimation of the "hidden" PFAS burden and establish a scientific basis for targeted clinical monitoring and risk assessment during the critical window of gestation.

2. Materials and methods

2.1. Sample collection

Pregnant women were enrolled before term delivery at the Sant'Orsola Hospital in Bologna (Italy) and at the Careggi Hospital in Florence (Italy) in the period between November 2023 and February 2025. The study was approved by the Ethical Committee of Alma Mater Studiorum – University of Bologna (protocol number CE AVEC: 718/2023/Sper/AOUBo). Women were excluded if they were younger than 18 years. Positive blood and/or urine tests for alcohol or drug use were considered exclusion criteria. All subjects provided written informed consent and completed a questionnaire concerning lifestyle and dietary habits.

Maternal blood was collected by venipuncture. Both maternal and cord blood samples were collected in polypropylene EDTA vials soon after delivery, stored at −20°C until analysis, and analyzed as whole blood.

2.2. Materials

All analytes (> 98% purity) and mass labeled standards used as surrogate and injection standards were from Wellington Laboratories (Guelph, Ontario, Canada). Chemical names and information about isotope-labelled analogues are reported in Table 1 of Supplemental Information (SI). Sixteen isotopically labelled internal standards (surrogates) were added to the samples before extraction in known amounts to

compensate for analyte losses and matrix effects during the extraction process. Mass-labelled PFOA, PFBA and PFOS (chemical purities > 98% and isotopic purities of > 99%) were used as injection standards. They were added to the purified extracts before injection to monitor instrument stability and precision of the injection. Reference solution for accurate mass measurement was obtained from Agilent Technologies (Santa Clara, CA, USA). Target perfluoroalkyl analytes were prepared at serial dilutions of 0.05, 0.1, 0.25, 1, 2.5, and 5 ng/mL in water/methanol (90/10, v/v) for calibration; working solutions of isotopically labelled compounds and injection standards were prepared at the concentration of 250–1000 ng/mL and 10–30 ng/mL respectively, in methanol (for details on surrogate and injection standards see Table 1 in SI). Methanol, acetonitrile and formic acid 98–100% (all LC–MS grade) were supplied by Merck (Darmstadt, Germany). Water for mobile phase was produced by Sartorius Arium mini apparatus (Goettingen, Germany). Ammonium acetate was provided by Sigma-Aldrich (St.Louis, MO, USA). WAX polymer (150 mg, 6 mL) cartridges were also from Agilent Technologies.

2.3. Sample preparation and LC-HRMS analysis

0.5 mL of blood was added with 2.5 μL of mass labeled standard working solution (final concentration 3.13–12.5 ng/mL) and 1 mL of acetonitrile. Mechanical agitation was performed for 30 s by vortexing (IKA, Staufen, Germany). Samples were then centrifuged at 4500 rpm for 5 min and the supernatant was collected and purified by weak anion exchange SPE according to the method previously developed and validated [11]. QC samples for quality assurance testing were prepared at the concentration of 0.5 and 1.0 ng/mL and were processed with samples for each batch. Analyses were carried out in a 1290 Infinity II LC coupled to 6546 quadrupole time-of-flight mass spectrometer (Q-TOF) (Agilent Technologies, Santa Clara, USA) via ESI source. Chromatographic separations were performed in a Poroshell EC-C18 column (2.1 ×100 mm, 1.9 μm), (Agilent Technologies) at 40°C. An LC C18 column (EclipsePlus -C18, 3.0 ×50 mm 1.8 μm) was placed downstream of the pump to delay any perfluorinated interferents possibly originating from the fluidic system. Analyses were carried out in 20 mM ammonium acetate in water (mobile phase A) and methanol (mobile phase B), both containing 0.1% formic acid (v/v) under gradient (see Table 2 in SI).

Flow rate was 0.250 mL/min. The injected volume was 5 μL. The Q-TOF instrument was set in negative acquisition mode, mass scan was set in the range 100–1000 *m/z* at a rate of 3 spectra/sec. Data analysis was performed by the Masshunter software (version B.10.1, Agilent Technologies). Quantification was achieved by using isotope dilution technique to account for matrix effects and adjust for any losses during sample preparation. PFAS concentrations were above the LOQ (see Table 2 of SI). Compounds detected but not quantified were counted for detection frequency and as LOQ/$\sqrt{2}$ for the average calculation. When present, branched isomers were quantified together with linear isomers. For details on method performances obtained during validation tests, the readers are referred to the Table 3 in SM.

2.4. Statistical analysis

Categorical variables were summarized as counts and percentages, while numerical variables, including PFAS concentrations, were described using mean, standard deviation (SD), median, interquartile range (IQR), and full range (min–max). Body mass index (BMI) was classified using World Health Organization (WHO) categories. Normality of PFAS concentration distributions was assessed using the Shapiro–Wilk W and Shapiro–Francia W′ tests, together with visual inspection of normal quantile plots. The Shapiro–Wilk test showed significant departures from normality for all PFAS concentration variables evaluated in maternal and cord blood (W range: 0.3330–0.8861; all $p < 0.001$). Shapiro–Francia results were consistent overall, with significant departures from normality in most evaluable variables (W′ range: 0.3639–1.0000; p-value range: <0.001–0.772). Normal quantile plots of the main PFAS variables further showed clear deviations from normality, including right-skewed distributions, zero inflation, and extreme values. Accordingly, associations between maternal blood PFAS concentrations and maternal characteristics were assessed using rank-based methods: the Wilcoxon rank-sum test for dichotomous variables, the Kruskal–Wallis test for categorical variables with more than two levels, and Spearman's rank correlation coefficient for continuous variables. Analyses were repeated for all individual PFAS and for total, carboxylic, sulfonic, short-chain, and long-chain PFAS concentrations. Exact p-values were computed for Wilcoxon and Spearman statistics using randomization and Monte Carlo permutation methods, respectively. All p-values, including those from Kruskal–Wallis tests, were adjusted for multiple comparisons using the Simes–Benjamini–Hochberg procedure to control the false discovery rate (FDR) [12]. Correlations between PFAS concentrations in maternal blood and cord blood were assessed using Spearman's rank correlation coefficient and illustrated using scatter plots. In cases of twin pregnancies (n = 2), PFAS concentrations in the corresponding paired samples (cord blood and maternal blood) were averaged before computing correlation coefficients. All analyses were conducted using Stata 18 (StataCorp. 2023. Stata Statistical Software: Release 18. College Station, TX: StataCorp LLC). A two-sided significance level of 0.05 was adopted.

3. Results and discussion

The study involved the recruitment of 120 women aged between 21 and 50 years in the period November 2023 and February 2025. Paired samples were collected from maternal blood and cord blood; the gestational age of the participants ranged from 30 weeks + 5 days to 40 weeks + 4 days. Participants were from two distinct geographical areas: 78 participants were from the Sant'Orsola Hospital in Bologna and 42 from the Careggi Hospital in Florence.

3.1. Results of PFAS in maternal blood and correlation with geographical area and lifestyle

Analysis on blood material confirmed the presence of the pollutants in 99.04% of the samples; only one sample (0.96%) was negative for the tested PFAS. In most participants, the number of retrieved molecules was > 2 up to 6, in particular 57.2% of samples were characterized by 2 up to 4 compounds, and 32.8% of samples had 1 or fewer detected PFAS. Only one sample tested positive for up to 8 different analytes. Mean and median of the sum of all PFAS in maternal blood was 2.09 ng/mL and 1.19 ng/mL respectively, concentrations ranged from 0.08 to 15.32 ng/mL. The most frequently detected PFAS were PFOS, PFOA, and PFHxS, detected respectively in 99%, 83.7%, and 78.8% of the samples, followed by PFBS found in 38.50% and PFNA in 33.7% of the samples (Fig. 1). In Table 1, the concentration range, mean, median, and standard deviation of the four most frequently detected compounds in maternal samples are reported. These compounds account for 57% of total PFAS, with a combined concentration of 1.19 ng/mL compared to 2.09 ng/mL for total PFAS. PFOS concentrations were found to be threefold higher, in terms of both mean and median values, compared to the other compounds analyzed. PFAS were also evaluated based on functional group and C-F chain length. PFAS compounds with a C-F chain length shorter than 5 atoms were present in 38.5% of samples, whereas those with 5 or more C atoms were found in 99% of cases, making them significantly more prevalent. PFAS were also studied on the basis of their functional group, sulfonic acids (SO_3) were present in 99% of samples, whereas carboxylic acids (COOH) were detected in 84.6%, with the long-chain sulfonic acids being the most represented (Fig. 2). The majority (70.2%) of the women presented a total concentration of the sum of all analyzed molecules below 2 ng/mL, 29.8% had a value between 2 and 20 ng/mL, while no participants exceeded the 20 ng/mL high-risk NASEM threshold (Fig. 3).

In our cohort, 76% of participants lived in urban areas with significant qualitative and quantitative differences in PFAS profile according to geographical position (see Fig. 4), 66% of participants consumed organic food and 55% processed food daily. Water consumption was mainly from plastic bottles (66%); 36% of participants consumed fish ≥ 2 times per week. Water-repellent textiles were used by 57% of participants. Smoking habits (no smoking in 73%) and body mass index (BMI < 25 in 55% cases) were also recorded. Gestational pathologies such as hypertension/preeclampsia, gestational diabetes and low birth weight were also investigated, but no significant associations or patterns were observed. Significant associations were found for 6:2FTS and PFHpS and regular use of processed food, FDR-adjusted p-values 0.008. In all other cases poor or absent associations were observed. No statistically significant association was found between the sum of PFAS and frequent fish consumption (> twice/week) but higher values of PFAS, especially for sulfonic acids congeners were observed (Fig. 5). When comparing lifestyle habits, specifically fish consumption, the use of ready-to-eat products, and the use of water-repellent textiles, with the total PFAS burden in maternal blood, a trend emerged for fish consumption. The percentage of samples exceeding the 2 ng/mL threshold was nearly double in cohorts with higher exposure habits compared to those with lower consumption levels (Fig. 6).

3.2. Results of PFAS in cord blood and comparison with maternal blood

PFAS were present in 84.80% of the cord blood specimens, 15 samples tested negative for all investigated PFAS. The most frequently detected molecules were PFOS (66.7%), PFOA (65.7%), and PFHxS (40.4%), followed by PFNA in 27.3% (Fig. 1). PFOS concentration ranged from 0.00 to 8.52 ng/mL (mean 0.54 ng/mL, median 0.35 ng/mL, SD 1.06 ng/mL), PFOA from 0.00 to 2.06 ng/mL (mean 0.26 ng/mL, median 0.19 ng/mL, SD 0.31 ng/mL), PFHxS from 0.00 to 1.33 (mean 0.14 ng/mL, median 0.10 ng/mL, SD 0.20 ng/mL), and PFNA from 0.00 to 1.8 ng/mL (mean 0.25 ng/mL, median 0.18 ng/mL, SD 0.31 ng/mL) (table2). When comparing total PFAS concentrations in maternal and fetal/cord blood, it was observed that maternal blood consistently showed higher total concentrations of these substances, both in terms of mean and median values, with a greater variability (Table 2). Only 3% of cord blood samples, compared with 29.8% of

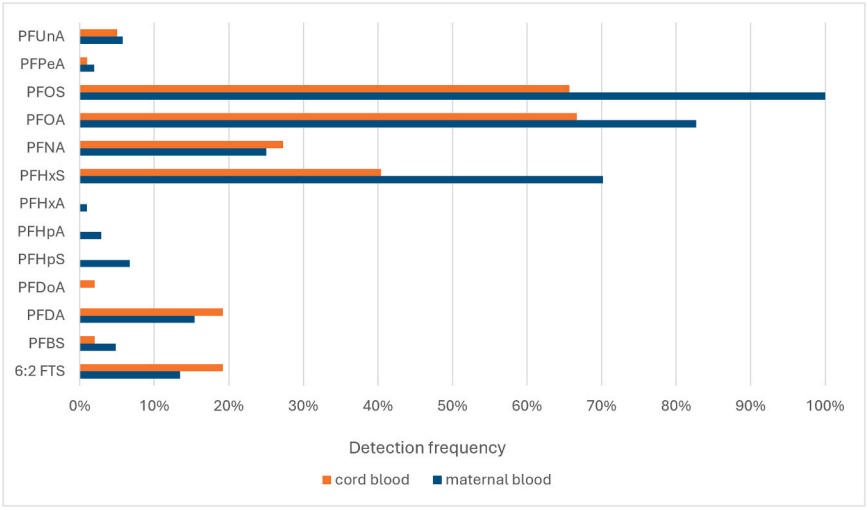

Fig. 1. Occurrence (Detection Frequency) of PFAS in maternal and cord blood.

Table 1
Range, mean, median and SD (standard deviation) of the PFAS most frequently detected in maternal blood.

Analyte	Range (ng/mL)	MEAN (ng/mL)	MEDIAN (ng/mL)	SD (ng/mL)
PFOS	0.00 – 8.80	1.10	0.70	1.41
PFOA	0.00 – 3.20	0.35	0.25	0.25
PFHxS	0.00 – 1.54	0.19	0.13	0.25
PFNA	0.00 – 1.48	0.10	0.00	0.24

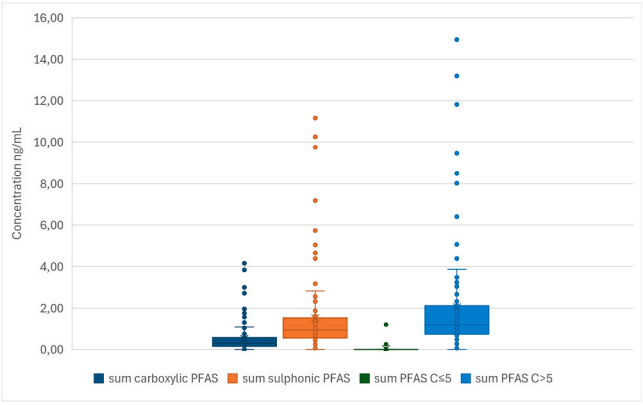

Fig. 2. PFAS were also evaluated based on functional group and C-F chain length in maternal blood.

maternal samples, had total PFAS concentrations above 2 ng/mL. In general, when comparing the detection frequencies of the various compounds in maternal and cord blood, it is noted that compounds highly represented in maternal blood, such as PFOS, PFOA, PFHxS, and PFNA, were also the most represented in fetal blood (Fig. 7). Cord blood samples also showed the presence of PFDA and 6:2 FTS. Transplacental Transfer Efficiency (TTE) was calculated for the most prevalent PFAS and 6:2FTS due to its peculiar chemical structure, as the ratio between cord blood and maternal blood concentrations. Only paired maternal-cord blood values were considered (Table 3). All calculated TTE values were below 1, specifically PFHxS had a mean of 0.55 (median 0.48), PFOA 0.58 (0.51), PFNA 0.61 (0.68), PFOS mean 0.35 (0.36), and 6:2FTS 0.41 (0.25).

In the present study the near-total prevalence of PFAS in maternal blood (99.04%), with a median sum of PFAS of 1.19 ng/mL, underscores

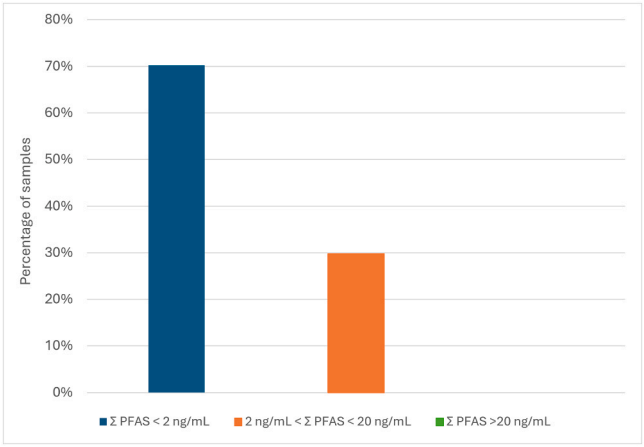

Fig. 3. Total PFAS concentrations in maternal blood according to NASEM concentrations limits.

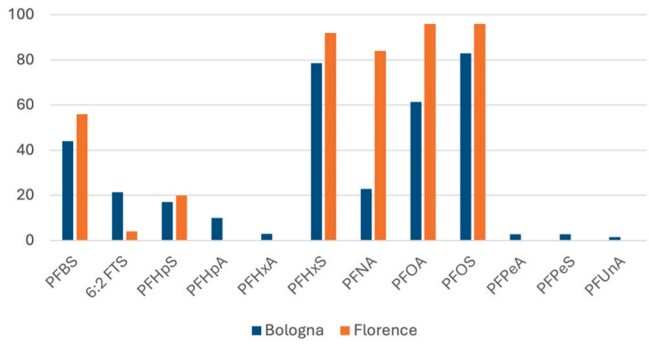

Fig. 4. Geographical differences in PFAS presence.

the widespread environmental contamination in the monitored regions of Bologna and Florence. Our findings confirm that "legacy" compounds, specifically PFOS (99.00%), PFOA (83.7%), and PFHxS (78.8%), remain the primary contributors to the human chemical burden. The significantly higher prevalence of long-chain (C > 5) sulfonic acids (99%) compared to carboxylic acids (84.6%) suggests a higher persistence or greater bioaccumulation potential of sulfonated congeners in this population. Regarding the fetal unit, the study confirms the detection of

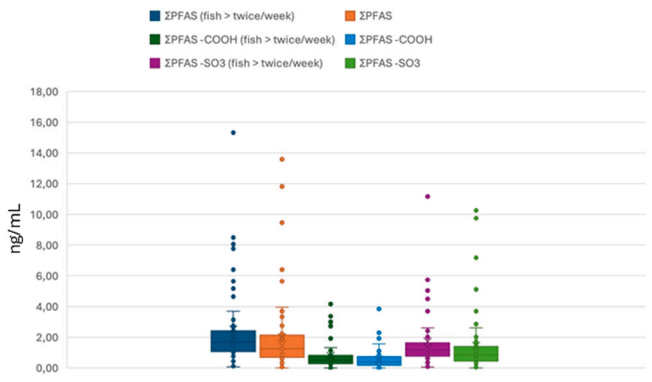

Fig. 5. ΣPFAS, ΣPFAS COOH, and ΣPFAS SO_3 for women consuming fish < twice/week versus ≥ twice/week.

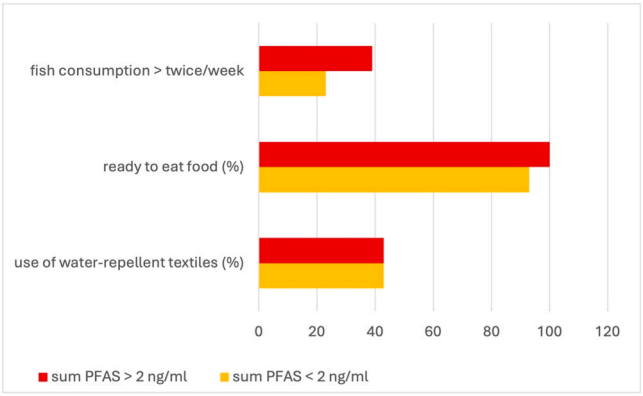

Fig. 6. Sum of PFAS according to lifestyles habits.

Table 2
Range, mean, median and SD (standard deviation) of the most frequently detected PFAS in cord blood.

Analyte	Range (ng/mL)	MEAN (ng/mL)	MEDIAN (ng/mL)	SD (ng/mL)
PFOS	0.00 – 8.52	0.54	0.35	1.06
PFOA	0.00 – 2.06	0.26	0.19	0.31
PFHxS	0.00 – 1.33	0.14	0.10	0.20
PFNA	0.00 – 1.80	0.25	0.18	0.31

PFAS in 84.8% of cord blood specimens, proving that the placenta is at least partially permeable to some of these toxicants. While maternal blood consistently showed higher total concentrations and greater variability than cord blood, the fetal unit was clearly not protected from exposure. A key finding was the higher detection frequency (DF) of emerging congeners like 6:2 FTS and PFDA in cord blood, with 6:2 FTS detected in 20% of samples. The absence of short chain PFAS in cord blood may reflect maternal concentrations near the LOQ. However, certain compounds with lower occurrence and concentration in maternal blood, such as PFHpS (mean 0.05 ng/mL), PFHpA (mean 0.06 ng/mL), and PFHxA (mean 0.04 ng/mL), were notably absent in fetal blood, confirming the possible role of the placenta as a kinetic barrier. Transplacental Transfer Efficiency (TTE) analysis revealed values > 0.5 for PFHxS, PFOA and PFNA, whereas PFOS and 6:2FTS showed values < 0.5. Finally, the study did not find any statistically significant or interesting patterns linking PFAS levels to any of the specific gestational pathologies already described in literature, such as hypertension, pre-eclampsia, gestational diabetes, and low birth weight [13–16].

The detection frequency in this cohort is comparable to a Danish study [17] conducted on maternal sera of 216 women during 2018–2021, which highlighted PFOS > PFOA > PFHxS > PFNA. The concentrations of PFOS, PFOA, PFHxS, and PFNA retrieved were of the same order of magnitude as other European or Canadian studies involving pregnant women [18], where data for single PFAS in serum/blood were in the range of a few ng/mL. In contrast, a study by Marks and colleagues [19] on British maternal serum from 1991 to 1992 reported median concentrations at least one order magnitude higher. This observed difference may be explained by the adoption of increasingly restrictive European regulations in recent decades, including the 2006 REACH framework, which restricted PFOS production and use [20]; the 2008 Stockholm Convention listing PFOS as a persistent organic pollutant (POP) [21]; and subsequent phase-outs of PFOA under the 2017 Amsterdam Declaration [22] and EU restrictions effective from 2020 [23]. These measures have led to substantial reductions in environmental [24] and human PFAS burdens across Europe, as evidenced by temporal trend studies showing declines of legacy PFAS in serum levels over the past 20–30 years [24]. When comparing with other regions [25,26], differences in PFAS profiles in cord blood were evident, e.g., PFDA, PFUnDA, and PFHpA detected in a lower percentage of cord blood samples in our study or not detected at all, though PFOA, PFOS, PFNA, and PFHxS remained the most frequently detected congeners globally.

Regarding the Transplacental Transfer Efficiency (TTE), PFAS showed a clear structure-dependent behavior, closely linked to their binding affinity for human proteins, particularly liver fatty acid–binding protein (L-FABP) and serum albumin [27]. Our findings confirm that functional groups significantly influence placental passage, as evidenced by higher TTEs for perfluorocarboxylic acids (PFCAs) (PFNA mean 0.61; PFOA mean 0.58) compared to perfluorosulfonic acids (PFSAs) (PFHxS mean 0.56; PFOS mean 0.35). This hierarchy is consistent with the observations documented in previous studies [28,29], which attributed this disparity to the stronger binding affinity of sulfonic groups to maternal serum albumin, a mechanism that effectively limits the free fraction available for fetal transfer. The higher TTE observed for PFNA (C9) relative to PFOA (C8) is suggestive of transfer efficiency influenced by chain length in carboxylates congeners [28,30]. The observed sulfonate order (PFHxS > PFOS) also matches the chain-length dependency patterns identified within the PFSA group [28]. Regarding the maternal-fetal transfer of emerging substitutes, while a recent meta-analysis suggested an elevated efficiency for 6:2 FTS [31], our data indicated a different behavior. Whereas legacy compounds showed comparable concentrations between maternal and cord blood, 6:2 FTS displayed a marked differential distribution (TTE value 0.41). This suggests that its transfer capacity remains moderate, a behavior similar to long-chain sulfonates as suggested by broader structural reviews [28]. Overall, our TTE values (0.35–0.61) fall within the ranges reported for whole blood matrices [28,32]; in these matrices, the higher maternal neonatal hematocrit differences compared to serum-based studies naturally result in lower TTE ratios, validating the consistency of our analytical approach with established blood partitioning dynamics.

In the context of this study, lifestyle and dietary habits played a significant role in determining the total PFAS burden. A significant association was identified between the regular consumption of processed food (55% of the cohort) and higher levels of 6:2 FTS and PFHpS ($p = 0.008$). 6:2 FTS is a fluorotelomer used as an alternative to legacy PFAS, often discussed in studies on plastic food-contact-materials (FCMs) [33]. These data suggest that particular attention should be paid to lifestyle during reproductive age. Regarding clinical risk, the majority of samples (70.2%) fell below the 2 ng/mL threshold established by the 2022 NASEM guidelines. However, nearly 30% of women exhibited levels between 2 and 20 ng/mL, a range associated with potential adverse health effects in sensitive populations and where guidelines recommend encouraging PFAS exposure reduction during pregnancies in case a source has been identified.

The detection of emerging alternatives in cord blood samples

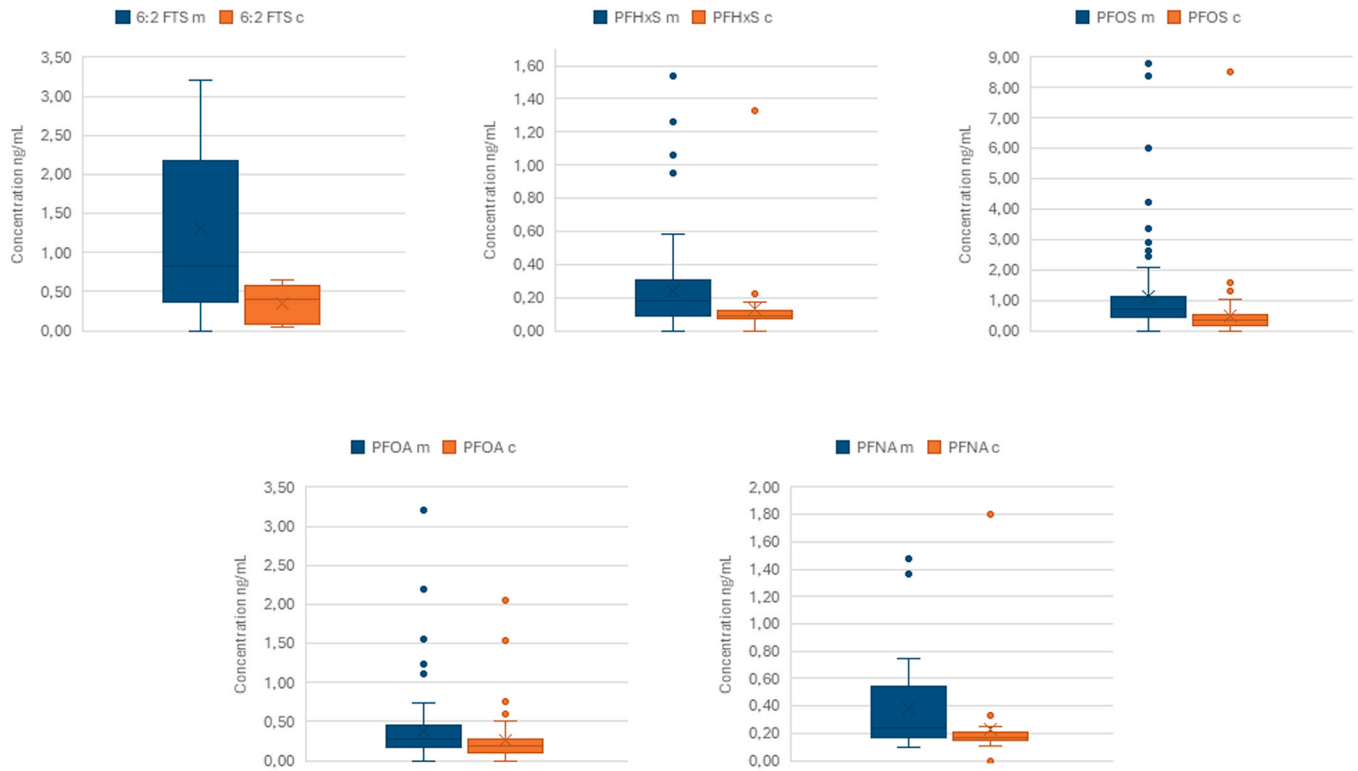

Fig. 7. PFAS different concentrations between maternal (m) and cord (c) blood.

Table 3
Transplacental transfer efficiency (TTE) mean and median values for the most detected compounds and 6:2FTS.

Analyte	TTE (mean)	TTE (median)
PFOS	0.35	0.36
PFOA	0.58	0.51
PFHxS	0.55	0.48
PFNA	0.61	0.68
6:2FTS	0.41	0.25

suggests they successfully reach the fetal compartment, potentially posing new, uncharacterized risks to development. The fact that only 3% of cord blood samples exceeded the 2 ng/mL threshold, compared to 29.8% of maternal samples, suggested that while transfer occurs, the placenta may act as a partial kinetic barrier, confirmed also by the calculated TTE, resulting in lower absolute concentrations in the fetus.

The observed TTE values suggested that chemical structure, specifically the difference between sulfonic (PFSA) and carboxylic (PFCA) groups, significantly dictates fetal burden. This highlights the need to move beyond simple carbon chain length when modeling exposure. Questions remain regarding the "hidden" burden of short-chain alternatives (PFHpA, PFHxA) that were absent in fetal blood. Furthermore, recent data on PFAS concentrations in cord blood from European populations are scarce, as most studies relying on maternal concentrations to infer prenatal exposure [34–36]. There is a clear need for wider multicenter studies and longitudinal monitoring to elucidate the long-term health implications of PFAS exposure.

A major strength of this study is that it represents one of the first European cohorts to profile 23 legacy and emerging in paired maternal-cord samples. However, the scientific power of comparing these concentrations with literature is restricted, as PFAS burdens vary across populations due to differences in geography and sampling timeframe. The limitation is that our data reflected blood concentrations rather than serum levels, which better facilitated the comparison with paired maternal-cord blood samples, but limited the comparison with studies based on serum analysis. It should be noted that whole blood concentrations are typically approximately two-fold lower than serum due to hematocrit partitioning; for these reasons, direct comparisons of absolute concentrations with serum-based studies should be interpreted with caution. Moreover, potential confounders (age, parity, BMI) were not adjusted for, which represents a major limitation and may have contributed to the null findings for gestational pathologies.

The small number of twin pregnancies (n = 2) within our cohort represents a sensitivity limitation, preventing a robust assessment of transplacental transfer dynamics specific to multiple gestations. Probably due to the relatively small sample size or to sampling bias, the study did not identify statistically significant patterns linking PFAS levels to specific gestational pathologies. Furthermore, since the analyses exploring the associations between maternal characteristics and PFAS concentrations did not account for potential confounding variables (such as maternal age, parity, and pre-pregnancy BMI), these specific findings should be considered exploratory, as residual confounding from these maternal factors cannot be entirely excluded.

4. Conclusions

This study demonstrated near-ubiquitous PFAS contamination in an Italian cohort, dominated by legacy long-chain sulfonic acids but featuring emerging alternatives. Maternal concentrations remained predominantly below the 2 ng/mL threshold for heightened health risks; however, this level was exceeded by nearly one in three women, highlighting a subgroup whose exposure falls into a range that requires closer attention. Key findings of this study underscored transplacental transfer, with fetal levels consistently lower but still significant, especially for emerging alternatives like 6:2 FTS. The association between processed food consumption and specific congeners underscored the role of lifestyle in exposure.

These results contribute to filling critical gaps in PFAS maternal-fetal transfer and cord blood data, though larger longitudinal studies are

essential to elucidate the health implications of this ongoing exposure.

CRediT authorship contribution statement

Maria Sech: Formal analysis, Data curation. **Elena Piva:** Methodology, Formal analysis, Data curation. **Morini Luca:** Resources, Methodology. **Vaiano Fabio:** Resources, Methodology. **Simonazzi Giuliana:** Resources. **Paolo FAIS:** Project administration, Funding acquisition. **Pascali Jennifer P.:** Writing – review & editing, Validation, Supervision, Methodology, Investigation. **Fornasari Arianna:** Formal analysis, Data curation. **Seidenari Anna:** Resources. **Seravalli Viola:** Data curation. **Lenzi Jacopo:** Formal analysis, Data curation.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jpba.2026.117637.

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