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Variability of perfluoroalkyl substance concentrations in pregnant women by socio-demographic and dietary factors in a Spanish birth cohort

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ABSTRACT

Background: Prenatal exposure to perfluoroalkyl substances (PFAS) might affect child health; but maternal determinants of PFAS exposure are unclear. We evaluated the socio-demographic and dietary factors of prenatal PFAS concentrations in a Spanish birth cohort.

Methods: We analyzed perfluorohexanesulfonic acid (PFHxS), perfluorooctanesulfonic acid (PFOS), perfluorooctanoic acid (PFOA), and perfluorononanoic acid (PFNA) in 1216 plasma samples collected during the 1ST trimester of pregnancy (2003–2008). We used multivariable linear regressions to assess the geometric mean (GM) ratios of PFAS concentrations by socio-demographic and dietary factors. We used analysis of variance (ANOVA) to assess the variability of PFAS concentrations by maternal factors.

Results: GM PFAS concentrations ranged from 0.55 ng/mL for PFHxS to 5.77 ng/mL for PFOS. Women born outside of Spain had lower PFAS concentrations (e.g. GM ratio for PFHxS 0.53[95%CI: 0.46, 0.60] than Spanish women. PFHxS and PFOA concentrations were higher in mothers from the regions of Sabadell (2.13[1.93, 2.35] and 1.73[1.60, 1.88], respectively) and Valencia (1.40[1.28, 1.54] and 1.42[1.31, 1.53], respectively) than Gipuzkoa. PFOA and PFNA concentrations decreased with parity (≥2 children: 0.79[0.67, 0.94] and 0.82[0.68, 0.99], respectively). Younger women (i.e. <25 years) had lower PFHxS (0.73[0.62, 0.86]) and PFOS (0.85[0.75, 0.96]) concentrations than older women. PFHxS and PFOA concentrations were lower in women who previously breastfed for >6 months compared to those who never breastfed (0.79[0.67, 0.94] and 0.82[0.71, 0.95], respectively). High intake of fish and shellfish during pregnancy (i.e. ≥5.6 servings/week) was associated with 11% (1.11[1.04, 1.18]) higher PFOS concentrations than the lowest intake group. Our ANOVA models explained 26% to 40% of PFAS concentrations variability.

Conclusions: Prenatal PFAS concentrations were mainly determined by maternal country of birth, region of residence, previous breastfeeding and age. Fish and shellfish intake also contributed to PFOS and PFOA concentrations.

Abbreviations: ANOVA, Analysis of variance; BMI, Body mass index; CI, Confidence interval; FFQ, Food frequency questionnaire; GAM, Generalized additive model; GM, Geometric mean; HPLC-MS/MS, High performance liquid chromatography–tandem mass spectrometry; INMA, Environment and Childhood Project (*INfancia y Medio Ambiente*); IQR, Interquartile range; LOQ, Limit of quantification; LOD, Limit of detection; PFAS, Perfluoroalkyl substances; PFBS, Perfluorobutane sulfonate; PFHxS, Perfluorohexane sulfonate; PFOS, Perfluorooctane sulfonate; PFOA, Perfluorooctanoate; PFNA, Perfluorononanoate; SD, Standard deviation.

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1. Introduction

Perfluoroalkyl substances (PFAS), such as perfluorohexane sulfonate (PFHxS), perfluorooctane sulfonate (PFOS) perfluorooctanoate (PFOA) and perfluorononanoate (PFNA), are manmade contaminants that are extensively used in industrial and commercial applications, including non-stick cookware, personal care products and as water or stain repellents for food packaging (Buck et al., 2011; Casals-Casas and Desvergne, 2011; Stahl et al., 2011). PFAS have a high affinity to serum albumin and have been detected ubiquitously in human blood samples (Salvalaglio et al., 2010). Their human biological half-lives are of three to seven years (Olsen et al., 2007). Early-life exposure to PFAS is suspected to induce developmental toxicity, and possibly affect the neurodevelopment, reproductive and immunological function in the offspring (Corsini et al., 2014; Lau et al., 2004). PFAS can cross the placental barrier as they have been detected in cord blood samples (Inoue et al., 2004; Manzano-Salgado et al., 2015; Zhang et al., 2013). Because placental transfer is the main route of fetal exposure to PFAS, many birth cohort studies have assessed maternal PFAS concentrations (Fei et al., 2007; Needham et al., 2011; Ode et al., 2013). PFAS concentrations can be influenced by many socio-demographic and dietary factors but there is no consensus as to which factor may be more relevant for PFAS concentrations during pregnancy (Brantsæter et al., 2013; Halldorsson et al., 2008; Ode et al., 2013; Sagiv et al., 2015).

Several socio-demographic factors may be associated with PFAS concentrations. PFAS concentrations were different by country of birth in studies assessing different ethnical backgrounds, e.g. Swedish (Ode et al., 2013), USA and Peruvian (Calafat et al., 2006b). Higher PFAS concentrations have been associated with smoking habit in pregnant and non-pregnant USA women (Jain, 2013; Sagiv et al., 2015), with being nulliparous (Brantsæter et al., 2013; Halldorsson et al., 2008) with shorter breastfeeding periods (Fei et al., 2010; Sagiv et al., 2015) and with older maternal age (Sagiv et al., 2015). Moreover, diet seems to be one of the main sources of PFAS exposure in the general population (Haug et al., 2010; Pérez et al., 2014; Domingo et al., 2012a; Vestergren and Cousins, 2009). Fish and shellfish are of special concern because higher PFAS concentrations have been detected worldwide compared to other food items (Domingo, 2012; Pérez et al., 2014). Yet the studies looking at what is the contribution of fish to PFAS exposure are either of small sample size or in non-pregnant populations or, have assessed PFAS in food items instead of in human biological samples. Also other dietary sources, e.g. red meat, snacks and animal fats, have been positively associated with PFAS blood concentrations (Halldorsson et al., 2008). Drinking water has also been associated with increased levels of PFAS especially with PFOA but the majority of studies were carried out near contaminated settings (Hölzer et al., 2008; Mondal et al., 2012; Schwanz et al., 2016) where PFAS exposure is higher than for the general population.

Moreover, the two main studies assessing the role of maternal socio-demographic or dietary determinants of PFAS concentrations during pregnancy (Halldorsson et al., 2008; Sagiv et al., 2015) used samples taken before or during the year 2002 when PFOS was not yet phased out (EPA, 2000). Studies with samples from more recent years are needed to assess the role of the maternal socio-demographic and dietary factors in influencing more recent PFAS concentrations during pregnancy. Thus we studied the socio-demographic and dietary factors that influence maternal PFAS concentrations during 2003–2008 in a Spanish birth cohort from Mediterranean and Atlantic areas.

2. Material and methods

2.1. Study population

We used data from the INMA (*INfancia y Medio Ambiente*, *Environment and Childhood*) birth cohort study including three Spanish regions: Gipuzkoa, Sabadell and, Valencia. During 2003–2008, a total of 2122 pregnant women in these regions were recruited in their first ultrasound visit (first trimester). The inclusion criteria was: to be resident of one of the regions, to be 16 years old or older, to have a singleton pregnancy, to give birth in the hospital of reference; to have no language barrier and to not have used an assisted reproduction program. Women who agreed to participate provided blood samples and completed self-reported questionnaires on socio-demographic and dietary factors during the first trimester of pregnancy. Further details on the recruitment and follow-up are described elsewhere (Guxens et al., 2012). We analyzed PFAS in 1243 women that had available plasma samples. For this study we only included 1216 women that had complete data on socio-demographic and dietary factors (Supplementary Fig. S1). Our study was approved by the regional ethical committees of each cohort and all participating women signed written informed consent before beginning the study (Guxens et al., 2012).

2.2. PFAS determination

Maternal plasma samples collected at around 12 weeks of pregnancy (mean: 12.3; standard deviation (SD): 5.7; range: 4.1–41.7 weeks) were aliquoted in 1.5 mL criotubes and stored at −80 °C until their analysis at the Institute for Occupational Medicine, RWTH Aachen University, (Aachen, Germany), as previously described (Manzano-Salgado et al., 2015). Briefly, plasma concentrations of perfluorobutane sulfonate (PFBS), PFHxS, PFOS PFOA and PFNA were determined by column-switching liquid chromatography coupled (Agilent 1100 Series HPLC apparatus) with tandem mass spectrometry (Sciex API 3000 LC/MS/MS system in ESI-negative mode) according to a modified protocol described by Kato et al. (2011). The between day imprecision for the spiked bovine samples ($n = 42$) ranged from 6.4% for PFOA (4.0 ng/mL) to 12.6% for PFHxS (0.4 ng/mL). The between day imprecision ranged from 8.7% for PFHxS (0.7 ng/mL) to 11.1% for PFNA (0.7 ng/mL). The limit of quantification (LOQ) determined as a signal-to-noise-ratio of 6 in the vicinity of the analytes, was 0.2 ng/mL for PFHxS, PFOS and PFOA and 0.1 ng/mL for PFNA. The limit of detection (LOD) was LOQ/2.

2.3. Socio-demographic and dietary characteristics

We assessed the following maternal socio-demographic characteristics through a questionnaire completed by the mothers in the first trimester of pregnancy: country of birth (Spain or other), region of residence (Gipuzkoa, Sabadell and, Valencia), type of residence zone (urban, sub-urban, and rural), education (university, secondary and, primary or less education), social class (professionals and managers, skilled manual/non-manual and, semi-skilled/unskilled), parity (0, 1 and, ≥2), age (in years), any previous breastfeeding (none, short term [<4 months], long term [4–6 months] and, very long term [>6 months]), pre-pregnancy body mass index (BMI) (underweight, normal weight, overweight and, obese) and, smoking at the beginning of pregnancy (none, 1–10 cigarettes/day and, >10 cigarettes/day).

We assessed dietary factors in the first trimester of pregnancy using a semi-quantitative food frequency questionnaire (FFQ) of 101 food items (Vioque et al., 2013). The FFQ asked women about the average intake (quantity and frequency) of a food item during the previous three months of pregnancy. The frequency categories ranged from "never or <once per month" to "≥6 times/day" with a total of 9 frequency categories. We used the frequency intake of each food item to estimate the average servings per week. We then grouped food items into the following groups: total fish and shellfish (i.e. fatty fish, lean fish and, shellfish), total meats (i.e. white meat, red meat and, processed meat), eggs, dairies, cereals and pasta, fruits and vegetables, vegetable oil and, tap water intake (Vioque et al., 2013).