Longitudinal analysis reveals early-pregnancy associations between perfluoroalkyl sulfonates and thyroid hormone status in a Canadian prospective birth cohort

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Abstract

Serum perfluoroalkyl acids (PFAAs) have been linked to disruption of maternal thyroid hormone homeostasis, but results have varied between studies which we hypothesized was due to timing of the thyroid hormone measurements, variability in PFAA isomer patterns, or presence of other stressors. In a longitudinal study design, we investigated the time-dependency of associations between PFAA isomers and thyroid hormones during pregnancy and post-partum while considering thyroid peroxidase antibody (TPOAb) status and mercury (Hg) coexposure. In participants of a prospective Canadian birth cohort (n=494), free thyroxine (FT4), free triiodothyronine (FT3), thyroid stimulating hormone (TSH) and TPOAb were quantified in maternal plasma collected in each trimester and 3-months postpartum, and 25 PFAAs (15 linear and 10 branched) and Hg were quantified in samples collected during the second trimester. Perfluorohexane sulfonate (PFHxS) and total branched isomers of perfluorooctane sulfonate (PFOS) were positively associated with TSH in mixed-effect models, with strongest associations early in gestation. Throughout pregnancy and post-partum, PFHxS was inversely associated with FT4, consistent with elevated TSH, while Hg was inversely associated with FT3. In TPOAb-positive women, negative associations were found between PFUnA and FT4, and 1m-PFOS and TSH, supporting previous studies that thyroid disorder could increase susceptibility to PFAA-mediated hormone dysregulation. Hg did not confound associations but was a significant interaction term, revealing further positive associations between PFOS isomers (Σ3m+4m-PFOS) and TSH. Higher perfluoroalkyl sulfonate exposures were associated with higher TSH and/or lower FT4, strongly suggestive that PFHxS and branched PFOS isomers are risk factors for subclinical maternal hypothyroidism. Isomer-specific analysis is important in future studies, as crude measures of 'total-PFOS' masked the associations of branched isomers. A concerning result was for PFHxS which had consistent negative associations with FT4 at all time points and a positive association with TSH in early pregnancy when fetal development is most sensitive to disruption.

Keywords: Perfluoroalkyl acids, Perfluoroalkyl sulfonates, Perfluoroalkyl carboxylates, Thyroid hormones, Pregnancy Longitudinal study design