Background: Although maternal hypothyroidism increases the risk of adverse neonatal and obstetric outcomes as well as lower IQ in children, the environmental determinants of maternal thyroid dysfunction have yet to be fully explored.

Objective: We aimed to examine associations between mid-pregnancy blood lead (BPb) and concomitant measures of thyroid function among participants in the Yugoslavia Prospective Study of Environmental Lead Exposure.

Methods: As part of a population-based prospective study of two towns in Kosovo—one with high levels of environmental lead and one with low—women were recruited during the second trimester of pregnancy, at which time blood samples and questionnaire data were collected. We measured concentrations of BPb, free thyroxine (FT4), thyroid-stimulating hormone (TSH), and thyroid peroxidase antibodies (TPOAb) in archived serum samples.

Results: Compared with women from the unexposed town, women from the exposed town had lower mean FT4 (0.91 ± 0.17 vs. 1.03 ± 0.16 ng/dL), higher mean TPOAb (15.45 ± 33.08 vs. 5.12 ± 6.38 IU/mL), and higher mean BPb (20.00 ± 6.99 vs. 5.57 ± 2.01 μg/dL). No differences in TSH levels were found. After adjustment for potential confounders, for each natural log unit increase in BPb, FT4 decreased by 0.074 ng/dL (95% CI: -0.10, -0.046 ng/dL), and the odds ratio for testing positive for TPOAb was 2.41 (95% CI: 1.53, 3.82). We found no association between BPb and TSH.

Conclusions: Prolonged lead exposure may contribute to maternal thyroid dysfunction by stimulating autoimmune to the thyroid gland.

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Introduction

The adverse effects of early childhood exposure to high levels of environmental lead are well established (Needleman and Landrigan 1991). In some but not all studies, higher prenatal lead exposure [blood lead (BPb) level, 10–20 μg/dL] is associated with a wide range of adverse pregnancy outcomes (Bellinger 2005), including shorter gestational lengths (Cantowwine et al. 2010); reduced birth weight (Bellinger et al. 1991; Gonzalez-Cossio et al. 1997), birth length, and head circumference (Hernandez-Avila et al. 2002); deficits in infant mental development (Gomma et al. 2002); and decreased child IQ (Schnaas et al. 2006; Wasserman et al. 1998, 2000). Elevated prenatal exposure to lead may be associated with adult-onset psychiatric disorders such as schizophrenia (Opler et al. 2004, 2008). Although mean BPb levels in the United States declined precipitously following the removal of lead from gasoline and most paint in the mid-1970s, the greatest decline in IQ among children occurs at the lowest levels of exposure (Lanphear et al. 2005), indicating that there may be no safe level of lead exposure (Bellinger 2008). In large areas of the world, where the mining, smelting, and refining of lead and the manufacture and recycling of lead-containing products such as batteries, computers, and solar panels are not closely monitored, lead poisoning is still a serious health concern for children. A recent episode of acute lead poisoning related to artisanal gold processing in a village in northernwestern Nigeria that killed 25% of the population < 5 years of age emphasizes the hazard that lead continues to pose in many places around the world (Dooyema et al. 2012).

A recent report on a U.S. national sample of more than half a million pregnant women found that 15.5% of those screened tested positive for either clinical [elevated thyroid-stimulating hormone (TSH)] or reduced free thyroxine (FT4) or subclinical [elevated TSH and normal FT4] hypothyroidism, far higher than previous estimates (Blatt et al. 2012). Prevalences in other parts of the world, especially developing countries where iodine deficiency is still a public health problem, have been found to be even greater (Mbah et al. 2011). Despite its high prevalence and negative outcomes, little is known about the predictors of clinical and subclinical gestational hypothyroidism aside from iodine deficiency. Maternal iodine intake must increase by 50% to fuel the increase in thyroid hormone production during pregnancy (Stagnaro-Green and Pearce 2013), and even mild to moderate first-trimester gestational iodine deficiency can lead to decrements in verbal IQ and reading ability in school-age children (Bath et al. 2013). Other variables reported to be associated with gestational hypothyroidism include larger maternal thyroid size, higher gravidity, higher prepregnancy body mass index (BMI) and increased fetal gestational age (Boas et al. 2009a; Mbah et al. 2011). Animal studies and studies of acute human exposure indicate that numerous chemicals interfere with thyroid hormone regulation and function (Boas et al. 2009b; Hartoft-Nielsen et al. 2011; Pearce and Braverman 2009). However, few studies assess the associations between persistent lower-dose environmental exposures on thyroid function, and even fewer consider these in pregnant women. The deleterious effect of gestational hypothyroidism on fetal brain development is well documented (de Escobar et al. 2004). Additionally, the presence of maternal thyroid peroxidase antibodies (TPOAb) during late gestation has been associated with reduced child IQ at 5 years of age even when controlling for postpartum thyroid dysfunction and maternal depression (Pop et al. 1995). Although untreated maternal thyroid dysfunction has been associated with a reduction of up to seven IQ points in school-age children (Haddow et al. 1999), results of studies in which mothers were treated have...
been inconsistent. Man and Serunian (1976) found lower psychological scores among 7-year-old children of mothers with inadequately treated prenatal hypothyroidism compared with the children of adequately treated and euthyroid women; and Lazarus et al. (2012) recently reported comparable mean IQ scores at 3 years of age among children whose mothers were randomized to be screened and, if necessary, treated for gestational hypothyroidism compared with children whose mothers were not screened or treated.

Building on previous occupational studies and on studies in small general population samples (Bledsoe et al. 2011; Dundar et al. 2006; Mbah et al. 2011; Tuppurainen et al. 1988), we hypothesized that maternal BPb might be associated with reduced thyroid function via one of three possible pathways. One potential mechanism involves iodine, adequate levels of which are essential for normal thyroid function. More than half a century ago, Slingerland (1955) demonstrated impaired uptake of iodine by fresh sheep thyroid tissue exposed to lead nitrate in solution. A subsequent study by Sandstead et al. (1979) of individuals exposed to lead in solution. A subsequent study by Sandstead et al. (1979) of individuals exposed to lead, showed impaired uptake of iodine by fresh sheep thyroid tissue exposed to lead nitrate in solution. A subsequent study by Sandstead et al. (1979) of individuals exposed to lead, showed impaired uptake of iodine by fresh sheep thyroid tissue exposed to lead nitrate.

To test these three potential pathways, we examined the associations between BPb and measures of FT4, TSH, and TPOAb in data collected during the Yugoslavia Prospective Study of Lead Exposure, Pregnancy Outcomes, and Child Development (Graziano et al. 1990). To our knowledge, this is the first study to explore the relationship between lead exposure and thyroid function in a sample of pregnant women.

Methods

Study population. Between May 1985 and December 1986, women in their second trimester of pregnancy were invited to participate in a study of pregnancy outcomes at their first prenatal visit to government clinics located at the centers of two towns in Kosovo. Details of the study design have been published previously (Factor-Litvak et al. 1991, 1999; Graziano et al. 1990; Wasserman et al. 1998). A total of 1,502 women were recruited: 602 from Mitrovica, a town with a lead smelter, refinery, and battery plant in which high BPb concentrations had been reported in both adults and children (Popovac et al. 1982); and 900 from Pristina, 25 miles to the south, where the primary source of environmental lead was gasoline (lead-based paint has been banned in Yugoslavia since 1922). Complete delivery data were available on 1,008 mother–infant pairs. Inclusion criteria for continuing in the study were giving birth to a single child between 18 and 44 weeks gestation who was free of major central nervous system defects or chromosomal abnormalities, and living within 10 km of the clinic. The 394 infants from Mitrovica with available cord blood BPb measures were then divided into three groups: < 15 μg/dL, 15–20 μg/dL, and > 20 μg/dL. Two groups of infants from Pristina were selected for follow-up: one group frequency-matched on BPb concentration to the group from Mitrovica with BPb < 15 μg/dL, and a second group matched on maternal and paternal education to the group from Mitrovica with BPb > 20 μg/dL. Of the resulting 711 infants invited to continue in the study, the parents of 541 consented. The sample for the present analyses included 291 women enrolled in mid-pregnancy who had adequate serum in storage to measure FT4, TSH, and TPOAb levels at the time of a follow-up study of prenatal thyroid function, lead, and child growth at 7 years of age (Lamb et al. 2008), and did not display overt hypothyroidism, defined as TSH > 2.5 μIU/mL and FT4 < 0.7 ng/dL, the latter cut-off value representing the lowest 5th percentile of the sample population (Stagnaro-Green et al. 2011) (Figure 1). This study was approved by the Columbia University Institutional Review Board (IRB) and by the “Komitetetik,” a National Institutes of Health–registered IRB at the University of Pristina, Kosovo. All women gave written informed consent before the study.

Data collection. At their first prenatal visit, pregnant women enrolled in this study were interviewed by trained bilingual (Serbo-Croatian and Albanian) interviewers who collected data on sociodemographic criteria, pregnancy and health history, and lifestyle variables. Fetal gestational age at interview ranged from 9 to 28 weeks, with a mean of 18 completed weeks. The nurses measured the women’s height and weight and obtained

![Figure 1. Recruitment and participation of study subjects. Abbreviations: CNS, central nervous system; SES, socioeconomic status.](image-url)
venous blood samples, which were refrigerated on site and transported on wet ice to Columbia University. After transport to Columbia, blood was stored at −20°C for several months until analyzed for lead, hemoglobin, erythrocyte protoporphyrin, and serum ferritin; samples with evidence of hemolysis were excluded. The remaining blood and serum was stored at −20°C and the thyroid measures were analyzed approximately 15 years after collection. Pilot data indicated that the values of FT4i, TSH, and TPOAb were in the range expected for women during mid-pregnancy.

**Blood lead.** Mid-pregnancy maternal serum samples were assayed for BPb according to methods described previously (Factor-Litvak et al. 1991). The Columbia laboratory participates in the Centers for Disease Control and Prevention (CDC) quality control program for BPb analyses and is certified by the Occupational Safety and Health Administration; during the course of the study, the intraclast correlation coefficient for agreement with CDC values for BPb was 0.95. All samples had BPb levels above the detection limit of 0.1 μg/dL.

**Maternal thyroid measures.** Maternal thyroid function during pregnancy was assessed using FT4i, TSH, and TPOAb, all of which have been shown to resist deterioration during freezing, storage, and thawing (Mannisto et al. 2007). FT4i and TPOAb were measured by a radioimmunoassay procedure, and TSH was measured using an IRMA procedure (all from ICN Biomedicals, Costa Mesa, CA). According to the technical specifications of the assay, TPOAb was characterized as slightly elevated if TPOAb levels were ≥ 10 IU/mL and < 20 IU/mL, moderately elevated if ≥ 20 IU/mL and < 100 IU/mL, and highly elevated if ≥ 100 IU/mL. For this study, all cases with slightly, moderate, or highly elevated TPOAb levels were considered positive. Euthyroid women with elevated TPOAb levels were considered at risk of hypothyroidism (Stagnaro-Green et al. 2011).

**Statistical analyses.** We natural log (ln)–transformed BPb, TSH, and TPOAb to meet assumptions of the statistical models and to reduce the influence of extreme values. Preliminary analyses evaluated potential confounding variables including maternal age, fetal gestational age at blood sample [because measures of thyroid hormone vary during the course of pregnancy (Glinoer 2000)], town (to account for unspecified geographic factors that might influence thyroid hormone level in pregnancy), anthropometric measures (maternal height, prepregnancy weight, and BMI), hemoglobin (Hgb), lifestyle characteristics (smoking, alcohol use, and coffee consumption), and sociodemographics (ethnicity, maternal education, parity, ratio of rooms to number of adults in household, and home ownership). Specifically, we used analysis of variance (ANOVA) to compare means of continuous outcome variables according to levels of categorical predictor variables. We calculated Spearman correlation coefficients to assess bivariate associations between continuous predictor and outcome variables. Multiple linear regression analysis was used to estimate covariate-adjusted associations between BPb and the continuous outcome measures of thyroid function, and logistic regression analysis to assess the relationship between BPb and the binary outcome measure TPOAb. Outcome-specific covariates were identified in preliminary analyses as variables associated with BPb and the specific outcome at p < 0.2. We also identified as covariates those found in previous studies to be associated with the outcome (Boas et al. 2009a; Mbah et al. 2011). We graphically examined the relationships between BPb and outcome measures and additionally ran our regression models substituting town for BPb as the main predictor variable. In sensitivity analyses restricted to Albanian women, associations between BPb and thyroid outcome measures were unchanged, indicating that ethnicity was not a major confounder (data not shown). We also found no difference when we included a quadratic term for fetal gestational age in our models and concluded that our results were not affected by a nonlinear association between gestational age and thyroid measures (data not shown). All statistical tests were two-tailed, with a significance level of 0.05. Data were analyzed using SAS® 9.2 statistical software (SAS Institute Inc., Cary, NC).

**Results**

At recruitment, the 291 subjects used in this analysis were similar to the 420 members of the cohort who did not meet the inclusion criteria in terms of age, education, number of prior live births, mid-pregnancy BPb and Hgb levels, and fetal gestation age at mid-pregnancy blood draw. Women from the two towns were comparable on all of these measures except for BPb levels. The only notable difference between those included and not included is that the distribution of ethnicities between the two towns, which had been comparable at the time of recruitment, was no longer comparable after loss to follow-up over the subsequent 7 years, likely due to migration during the mounting ethnic tensions in the late 1980s and early 1990s. In Pristina, the proportion of Albanian participants increased (from 59.0% in the original sample to 70.8% after loss to follow-up), the proportion of Serbian participants decreased (from 28.5% to 22.5%), and the proportion of other ethnicities decreased (from 12.5% to 6.8%), whereas in Mitrovica, the distribution did not change (53.4% vs. 54.9% Albanian, 28.65% vs. 27.1% Serbian, 18.0% vs. 18.1% other). In Mitrovica, those included had slightly higher mid-pregnancy BPb compared with those lost to follow-up (20.0 vs. 18.5 μg/dL), and among those included in the study, women in Mitrovica had slightly fewer prior live births compared with those in Pristina (mean, 1.4 vs. 1.7), but neither of these differences reached statistical significance (Table 1). Among the participants, we found highly significant differences between the two towns in both FT4i and TPOAb (p < 0.0001), but not in TSH (Table 2). Women from Mitrovica, who were more highly exposed to lead (mean

| Table 1. Participants compared with members of the Yugoslavia Prospective Study of Environmental Lead Exposure cohort lost to follow-up by child age 7 years. |
|-----------------|-----------------|-------------|-----------------|
| Characteristic | Included | Lost to follow-up | Included | Lost to follow-up |
| Maternal age (years) | 26.6 ± 4.7 | 26.7 ± 5.2 | 16.1–41.7 | 0.87 | 26.7 ± 4.5 | 26.1 ± 4.7 | 15.1–46.0 | 0.19 |
| Maternal education (years) | 9.2 ± 3.9 | 9.3 ± 3.8 | 0–17 | 0.099 | 9.8 ± 3.8 | 9.4 ± 4.0 | 0–17 | 0.29 |
| No. of prior live births | 1.7 ± 1.7 | 1.4 ± 1.6 | 0–9 | 0.87 | 1.5 ± 1.4 | 1.4 ± 1.5 | 0–9 | 0.93 |
| Mid-pregnancy BPb (μg/dL) | 5.6 ± 2.0 | 20.0 ± 7.0 | 1.6–41.3 | < 0.0001 | 5.8 ± 2.1 | 18.5 ± 7.9 | 1.7–43.4 | < 0.0001 |
| Gestational age at birth (days) | 276.2 ± 18.6 | 274.3 ± 18.1 | 195–333 | 0.38 | 274.6 ± 18.7 | 274 ± 18.1 | 164–308 | 0.87 |
| Gestational age at blood draw (days) | 132.7 ± 26.3 | 120.7 ± 26.8 | 61–192 | 0.001 | 134.9 ± 30.9 | 112.9 ± 25.8 | 47–220 | < 0.0001 |
| Maternal ethnicity | 0.0041 | | | | | | | |
| Albanian | 104 (70.8) | 79 (64.9) | 80 (48.5) | 134 (62.6) | 0.0041 | | | |
| Serbian | 33 (22.5) | 39 (31.7) | 56 (33.9) | 75 (32.9) | 0.61 | | | |
| Other | 10 (6.8) | 26 (18.1) | 29 (17.6) | 46 (18.0) | 0.79 | | | |

Values are mean ± SD or n (%). Included, women still enrolled in the study who had adequate serum in storage to measure thyroid hormone and antibody levels at the 7-year follow-up.

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BPb, 20.00 vs. 5.57 μg/dL), had lower mean 
FT4 (0.91 vs. 1.03 ng/dL) and higher mean 
TPOAb (15.45 vs. 5.12 IU/mL), both indicative 
of higher risk of gestational hypothyroidism. Of the 291 women in our sample, 
24 (8.25%) had FT4 levels < 0.7 ng/dL, the 
commonly used cutoff for hypothyroidism 
(Blatt et al. 2012), and 57 (19.59%) tested 
positive for TPOAb (≥ 10 IU/mL). Among 
those with positive TPOAb, 38 (66.67%) 
had slightly elevated levels (≥ 10 IU/mL 
and < 20 IU/mL), 13 (22.81%) had moder 
ately elevated levels (≥ 20 IU/mL and 
< 100 IU/mL), and 6 (10.53%) had highly 
elevated levels (≥ 100 IU/mL). Most strik 
tingly, the prevalence of elevated TPOAb 
(≥ 10 IU/mL) was nearly five times greater 
among women in Mitrovica compared with 
women in Pristina (32.64% vs. 6.80%) (data 
not shown).

In bivariate analyses (see Supplemental 
Material, Table S1), BPbs were significantly 
associated with town, ethnicity, maternal 
height, and fetal gestational age at blood draw. 
FT4 was significantly associated with ethnicity, 
maternal education, prepregnancy BMI, and 
crowded living conditions. TPOAb was 
significantly associated with smoking status. 

As expected, there was an inverse association 
between BMI and FT4. We also found that 
Albanians had higher mean FT4 than Serbians 
(0.99 ± 0.17 vs. 0.89 ± 0.16 ng/dL, respect 
ively), that those with no education had 
higher mean FT4 than those with any, and 
that there was a positive association between 
FT4 and adults per room. These results reflect 
associations between height and ethnicity 
(\( p < 0.01 \)), between ethnicity and education 
(\( p < 0.0001 \)), and between ethnicity and 
adults per room (\( p < 0.001 \)). In contrast to 
published findings of a protective relation 
ship between smoking and thyroid autoim 
munity (Belin et al. 2004; de Escobar et al. 
2004; Effraimidis et al. 2009), in our cohort 
smoking was associated with a higher mean 
TPOAb level. TSH was not significantly 
associated with any of the characteristics we 
selected as potential covariates.

Scatter plots between BPb and the three 
outcome variables, adjusted for potential confounders (Figure 2), suggest an inverse relationship between BPb and FT4 and a 
direct relationship between BPb and TPOAb, 
but no association between BPb and TSH.

| Table 2. Comparison of BPb and thyroid measures by town among study participants. |
|---|
| Town | BPb (μg/dL) | FT4 (ng/dL) | TSH (μIU/mL) | TPOAb (IU/mL) |
|---|---|---|---|---|
| Pristina | | | |
| \( n \) | 147 | 141 | 142 | 147 |
| Mean ± SD | 5.57 ± 2.01 | 1.03 ± 0.16 | 1.46 ± 0.68 | 5.12 ± 6.38 |
| Range | 1.60–18.60 | 0.67–1.79 | 0.20–4.14 | 1.00–66.33 |
| Mitrovica | | | |
| \( n \) | 144 | 138 | 136 | 144 |
| Mean ± SD | 20.00 ± 6.99 | 0.91 ± 0.17 | 1.46 ± 0.91 | 15.45 ± 33.08 |
| Range | 5.40–41.30 | 0.40–1.30 | 0.20–7.46 | 0.69–256.65 |
| \( p \)-Value (ANOVA) | < 0.0001 | < 0.0001 | 0.99 | 0.0002 |

Figure 2. Scatter plots of measured values for each outcome according to BPb (μg/dL). (A) FT4 adjusted for height, ethnicity, BMI, fetal gestational age, maternal education, adults per room. (B) TSH adjusted for hemoglobin, ethnicity, BMI, fetal gestational age, maternal age. (C) TPOAb adjusted for ethnicity, fetal gestational age, maternal age, adults per room.
**BPb was negatively associated with FT₄ and positively associated with TPOAb in both covariate adjusted and unadjusted models (p < 0.0001) (Table 3); no association was found between BPb and TSH. Controlling for potential confounders, for each log unit increase in BPb, FT₄ decreased by 0.074 ng/dL (95% CI: −0.10, −0.046 ng/dL). Using logistic regression to adjust for ethnicity, fetal gestational age, maternal age, and adults per room (a proxy measure for socioeconomic status), we found the estimated odds of testing positive for TPOAb to be 2.41 times greater for every log-unit increase in mid-pregnancy BPb (95% CI: 1.53, 3.82).

**Discussion**

The current study, an analysis of mid-pregnancy BPb compared with mid-pregnancy FT₄, TSH, and TPOAb levels, yielded a highly significant negative association between BPb and FT₄ and a highly significant positive association between BPb and TPOAb without any significant association between BPb and TSH. These results indicate that lead exposure may be a factor in reduced thyroid function, which has been suggested to increase the risk of poor obstetric outcomes (Ajmani et al. 2014; Casey et al. 2005; van den Boogaard et al. 2011) and lower IQ in children (Haddow et al. 1999; 2005; van den Boogaard et al. 2011) and observational studies, elevated TPOAb levels have been positively associated with exposure to organochlorines (Langer et al. 2008), polychlorinated biphenyls (Langer et al. 2007), and polyhalogenated biphenyls (Bahn et al. 1986). Studies using genetically predisposed mice have also shown bromine and bacterial lipopolysaccharides to be triggers of AT (Burek and Talor 2009).

Lead is known to affect the immune system, but in ways that are still not clearly understood (Dietert and Piepenbrink 2006). In _vitro_ and _in vivo_ studies in mice have suggested that lead initially skews T-lymphocyte response toward the Th (T helper) 2 pathway (Heo et al. 1998; McCabe and Lawrence 1991), increasing the risk of asthma and atopy, although a subsequent shift back to the Th1 pathway, observed in different mouse studies, could result in a predisposition to autoimmunity (Goebel et al. 2000). In a study of mice genetically predisposed to systemic lupus erythematosus, lead exposure triggered onset of the disease (Hudson et al. 2003). Lead has also been shown to stimulate production of autoantibodies against neural proteins in both rodent models and human occupational studies (El-Fawal et al. 1999; Waterman et al. 1992).

There are several limitations to our study of lead exposure and gestational thyroid dysfunction. The sample size, though large enough to produce robust findings when data from the two towns were combined, was not large enough to support statistically significant findings when analyses were stratified by town, even though the parameter estimates were similar in the combined and stratified models (see Supplemental Material, Table S2). Although the original study sample was selected to achieve broad representation across lead exposure levels and socioeconomic status, the current study relied on the

**Table 3. Unadjusted and adjusted regression coefficients (for FT₄, ln-transformed TSH, and ln-transformed TPOAb) and odds ratios (for TPOAb ≥ 10 IU/mL vs. < 10 IU/mL) for associations with ln-transformed mid-pregnancy blood lead concentrations, Pristina and Mitrovica combined.**

| Outcome          | Unadjusted | Adjusted |
|------------------|------------|----------|
|                  | R² (n)     | β OR (95% CI) | p-Value | R² (n)     | β OR (95% CI)* | p-Value |
| FT₄ (ng/dL)      | 0.11 (279) | −0.079 (−0.11, −0.052) | < 0.0001 | 0.25 (277) | −0.074 (−0.10, −0.046) | < 0.0001 |
| ln-TSH (μIU/mL)  | 0.0027 (279) | −0.012 (−0.008, 0.074) | 0.79 | 0.046 (276) | 0.026 (0.065, 0.12) | 0.58 |
| ln-TPOAb (IU/mL) | 0.075 (291) | 0.34 (0.20, 0.48) | < 0.0001 | 0.094 (291) | 0.31 (0.17, 0.46) | < 0.0001 |
| TPOAb ≥ 10 vs. < 10 IU/mL | 0.062 (291) | 2.51 (1.62, 3.39) | < 0.0001 | 0.074 (291) | 2.41 (1.53, 3.82) | 0.0002 |

*Model covariates: FT₄, height, ethnicity, BMI, fetal gestational age, maternal education, adults per room; TSH: hemoglobin, ethnicity, BMI, fetal gestational age, maternal age; TPOAb (continuous and dichotomous): ethnicity, fetal gestational age, maternal age, adults per room.
subsample for which we had mid-pregnancy thyroid measures. There is no reason to believe that such loss to follow-up would bias the biological relationships between PbP and thyroid outcome measures. Although it is possible that hormones may have degraded between the time between serum collection and analysis, we do not believe this was a major concern, because mean TSH levels are comparable to what would be expected in women during mid-pregnancy. Because thyroid-binding globulin may impede the reliability of FTx assays, it is preferable to use circulating total thyroxine as a measure of thyroid gland activity in pregnant women, because thyroid-binding globulin concentrations are elevated during pregnancy (Stagnaro-Green et al. 2011). Unfortunately, we did not have direct measures of total thyroxine and/or thyroid-binding globulin in our data. Finally, our data did not include mid-pregnancy urinary iodine measures, preventing us from definitively ruling out the possibility that lead causes gestational thyroid dysfunction by impairing uptake of iodine by the thyroid gland.

Conclusions

This study contributes unique information to our understanding of lead and gestational thyroid dysfunction. Our findings suggest that long-term lead exposure increases the risk of elevated TPOAb during pregnancy, adding to the growing literature on the environmental influences on AT. Although the results of this study are limited to pregnant women, future studies might extend them to examine the effect of prenatal lead exposure on TPOAb levels in children as well as on the development of postnatal hypothyroidism among the mothers.

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