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Does the metal content in soil around a pregnant woman's home increase the risk of low birth weight for her infant?

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Abstract

Low birth weight (LBW) is associated with a number of maternal environmental exposures during pregnancy. This study explored the association between soil metal concentrations around the home where the mother lived during pregnancy and the outcome of LBW. We used a retrospective cohort of 9,920 mother–child pairs who were insured by Medicaid during pregnancy and lived in ten residential areas, where we conducted soil sampling. We used a grid that overlaid the residential areas and collected soil samples at the grid intersections. The soil was analyzed for the concentration of eight metals [arsenic (As), barium (Ba), chromium (Cr), copper (Cu), lead (Pb), manganese (Mn), nickel (Ni), and mercury (Hg)], and we then used Bayesian Kriging to estimate the concentration at the actual maternal addresses, since we had the GIS coordinates of the homes. We used generalized additive modeling, because the metal concentrations had nonlinear associations with LBW, to develop the best fitting multivariable model for estimating the risk of LBW. The final model showed significant associations for female infants, maternal smoking during pregnancy, non-white mothers, Cu, and As with LBW. The As variable was nonlinear in relation to LBW, and the association between higher concentrations of As with LBW was strong

($p = 0.002$). We identified a statistically significant association between soil concentrations of arsenic around the home of pregnant women and an increased risk of LBW for her infant.

Keywords

Arsenic; Copper; Geocoding maternal residence

Introduction

Low birth weight (LBW) is a much studied outcome of pregnancy since it is associated with infant morbidity and mortality and it can be measured precisely (Bernstein et al. 2000; Doctor et al. 2001). LBW refers to infants who weigh less than 2 500 g, or 5.5 pounds, at birth. Many exposures during pregnancy have been associated with the outcome of LBW including maternal substance use, including tobacco, and maternal illnesses (e.g., infections, hypertension). Fetal exposure to lead (Pb), mercury (Hg), and arsenic (As) have been associated with other adverse child outcomes (Shirai et al. 2010; Lin et al. 1998; Ahmad et al. 2001; Hopenhayn et al. 2003; Yang et al. 2003). In the research regarding chemical exposures, maternal blood levels, samples from the umbilical cord, infant blood, or maternal urine during pregnancy are used to measure concentrations. These approaches do not elucidate the origin of the metal (Rahman et al. 2009); therefore, some studies also use questionnaires to measure expected sources of the exposure, including fish consumption (Hg), residence proximal to coal burning plants (Hg and As), and water source (Davis et al. 2009; Aelion et al. 2009a, b). Epidemiologic studies that show associations between environmental exposure to chemicals in soils and adverse child outcomes suggest that hand-to-mouth contamination and skin absorption of soil tracked into homes cross the placenta during some stages of gestation (Wasserman et al. 1994; Mejía et al. 1997; Tong et al. 1998; Mielke et al. 2007; Vahter 2009; Davidson et al. 2006).

The effect of low-level exposure to metals in soil during pregnancy is an important topic for the USA and other developed countries, where high levels are rarely reported. Low-dose exposures to metals such as cadmium (Cd) and lead (Pb) are associated with LBW (Shirai et al. 2010; Odland et al. 1999). Our study focuses on maternal pregnancy exposure to low concentrations of eight metals [arsenic (As), barium (Ba), chromium (Cr), copper (Cu), lead (Pb), manganese (Mn), nickel (Ni), and mercury (Hg)] in soil proximal to maternal residences and the association of these metals with LBW in their infant.

Methods

This is a retrospective cohort study of 9,920 pregnant women and their newborn children who were insured by South Carolina Medicaid from January 1, 1996 through December 31, 2002, and resided in one of ten residential study areas during pregnancy. These women were identified through their Medicaid billing records, and they were followed through pregnancy and delivery using merged reimbursement files for the mothers and children and the birth certificates. We excluded twins and other multiples and children with an identified birth defect or known cause of a disability. We included all singleton live births that were insured

by South Carolina Medicaid during the study period; therefore, we captured pregnant women living below 185 % of the federal poverty level.

Ten study areas were selected for study throughout South Carolina, in rural, suburban, and urban neighborhoods. The study sites were chosen based on having at least 800 births in the 6-year period, within a 100-km² area, as described in previous publications (Zhen et al. 2008). Addresses were obtained from a Medicaid eligibility file for the sixth month of pregnancy, since this was the month with the highest enrollment, and these addresses were geo-coded using ArcGIS version 9.3. To maintain confidentiality about maternal residences, the soil sampling was done using a grid laid over the surface area and the intersections of the grid lines were used to identify sampling locations. The soil was sampled after the period in which the pregnancy occurred, at 5-cm depth, 1.0–3.0 km apart, and it was analyzed for each metal by an independent analytical laboratory (Pace Analytical, Huntersville, NC) (Aelion et al. 2008, 2009a, b). In order to estimate the soil metal concentrations at the known maternal addresses, we used data from approximately 100 nodes per area to do Bayesian Kriging and statistical methods including variable transformation (Aelion et al. 2009b; Diggle et al. 1998; Diggle and Ribeiro 2007; Cressie 1993; Ribeiro and Diggle 2001; Kim et al. 2009).

The dependent variable in this analysis was birth weight less than 2,500 g (LBW), as recorded on the birth certificate. The covariates were infant, maternal, and neighborhood characteristics obtained from the birth certificate and the Medicaid billing file (Table 1). The infant characteristics were sex and weeks of gestation (greater than 36 weeks, 28–36 weeks, and less than 28 weeks). The maternal covariates were maternal age (less than 18 years, 18–34, and greater than 34 years), maternal race (non-Hispanic white, non-Hispanic black, and all others), number of prior births (parity: 0, 1, 2, and 3 or more), and tobacco and alcohol use (yes or no). Neighborhood characteristics obtained from the census block group for each mother were the density per square mile and the median age of housing in the block group where the mother resided during the sixth month of pregnancy. Finally, we assessed the univariable relationship between the eight metals and LBW, as shown at the bottom of Table 1. We showed the variability in the concentrations throughout our study sites using the interquartile range (IQR), which is the difference between the third and the first quartile values, i.e., Q3–Q1.

The hypothesis for this study was there is an inverse relationship between concentrations of metals in soil proximal to maternal residence during pregnancy associated with infant birth weight. Thus, we expected higher concentrations of soil metals would be associated with lower birth weight. We explored the association between the concentration of each metal with the risk of LBW using the multivariable generalized additive model (GAM) (Hastie and Tibshirani 1990; Wood 2006). GAM allowed us to use variables that do not have a linear relationship between the metal and the LBW outcome. We used a binary response variable LBW (<2,500 vs. 2,500 or more grams at delivery) and assumed it followed a Bernoulli distribution with $P(\text{LBW} = 1) = p$. The covariates ($\{X_j\}_{j=1, \dots, m}$) included both mother, child, and neighborhood covariates and the Kriged concentration for soil chemicals. A semi-

parametric model, $\text{logit}(p_i) = \alpha_0 + \sum_{j=1}^s \alpha_j x_{ij} + \sum_{j=s+1}^m f_j(x_{ij})$, $i = 1, \dots, n$, $j = 1, \dots, m$, was used, where n is the sample size, m is the total number of predictors, and the first s predictors was assumed to be linearly associated with $\text{logit}(p)$ by parameter α (parametric terms). The “mgcv” package in R was used for the GAM model fitting, since this allowed both the linear and nonlinear terms to be in the model (Wood 2006).

Results

Table 1 shows the infant, maternal, neighborhood, and soil metal concentrations values for the 9,920 mother–child pairs included in the study. The LBW babies were more likely to be female and delivered at less than 36 weeks gestation. The mothers of LBW infants were more likely to be less than 18 or over 34 years of age at the time of birth, non-white, have three or more children, smoke and use alcohol during pregnancy, compared to the normal weight infant mothers. The metal concentrations for the LBW and normal birth weight groups are the Kriged estimates at the location where the mother lived during pregnancy. The value for As was statistically significantly higher for the LBW babies compared to the normal weight infants.

Table 2 shows the final adjusted multivariable model. Female infants, maternal smoking, mothers who are not non-Hispanic whites, and soil concentrations of Cu and As were statistically significantly associated with LBW (Table 2). The multivariable model identified a negative coefficient for Cu, indicating that higher levels of soil concentration of Cu were associated with a lower likelihood of LBW. The As variable is a spline function since it was nonlinear; the association between As and LBW was positive and strong ($p = 0.002$), showing that higher levels of As were associated with higher odds of LBW.

Discussion

The study question for this research was does the metal content of soil around a pregnant woman’s home increase the risk of LBW for her infant? We identified a statistically significant association between arsenic in soil near the maternal residence during pregnancy and the outcome of LBW. This finding has not been previously reported although there are reports of arsenic, lead, and mercury in soil and the adverse child outcome of intellectual disability (Liu et al. 2010; McDermott et al. 2011). We also found a negative association between Cu in soil and LBW, which is contrary to a report in the literature that shows low levels of Cu in maternal blood has been associated with LBW (Uriu-Adams et al. 2010). Clearly this finding should be further investigated in subsequent work. The other covariates associated with LBW were previously reported in the literature including female infants, maternal non-white race, and smoking during pregnancy (Cunningham et al. 2010).

This study has a number of limitations. We did not directly measure metal concentrations in soil around the mother’s home; instead we used estimates from sampling in the neighborhood and statistical methods to predict the level at the residence. In addition, the soil sampling occurred after the pregnancy and deliver of the child. The estimate of soil half-life for inorganic chemicals, including As, Ca, Cr, Pb, Hg, and Ni, are all 1.0×10^8 (or

100,000,000 days) so if the soil is not replenished, the concentration measured after pregnancy is a good estimate of the concentration during the sixth month of pregnancy (Blaisdell et al. 2003). Finally, the study was conducted among low-income families, since we used Medicaid-funded births in South Carolina and we used the address from the sixth month of pregnancy since this was the month with the highest enrollment. The literature does identify seasonality as a risk factor (Zahran et al. 2013); however, it does not provide evidence of a gestational month of greatest vulnerability to metal exposure, and it is possible that the in utero month of exposure could be a contributing factor to the risk of LBW.

One of the biggest strengths of this study is the large sample size and the use of birth weight from the birth certificate, which provides complete data and ample power for the analyses. We studied 9,920 children who lived in the ten areas where we did soil sampling. Another strength was our use of Kriging to get estimates of the metal concentration for the maternal address. This is an innovative way to estimate exposure since surface soils accumulate long-lived contaminants deposited from air and applied to soils over time, and metals are generally long-lived and environmentally stable. People track soil and dust from outside their homes, it accumulates on floors inside the home, and studies confirm that metals in soils are bioavailable to humans (Zota et al. 2011). Our study adds to the literature that now reports studies that report measured blood levels of Pb in children exposed to metal-contaminated soils and drinking water (Calderón et al. 2001) and As in urine of individuals exposed to As from drinking water and soil (Mielke et al. 2007; Carrizales et al. 2006; Factor-Litvak et al. 1999; Zahran et al. 2011; Thornton et al. 1990; Hinwood et al. 2004; Hwang et al. 1997).

Additional epidemiologic study in different geographic and socioeconomic groups is needed to assess the generalizability of our findings. In addition, basic science and translational research are needed to provide a better understanding of the potential mechanism(s) whereby soil metal concentration may impact infant growth. An understanding of the mechanisms underlying the observed association is necessary to determine the clinical significance of the findings and to develop effective preventive interventions for women who are, or desire to become pregnant.

Conclusion

We identified a positive statistically significant association between arsenic in soil near the maternal residence during pregnancy and the outcome of LBW and a negative association between copper in soil and LBW. This finding suggests the metal content of soil around a pregnant woman's home can impact the risk of LBW for her infant.

Acknowledgments

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Table 1

Characteristics of the mother–child pairs and soil metal levels, by LBW status

	Low birth weight <2,500 g (n = 1,146)	Normal birth weight ≥ 2,500 g (n = 8,774)	Odds ratio ^a (low vs. normal)
Infant characteristics			
Infant gender			
Boy	528	4,554	1.00
Girl	617	4,221	1.26 (1.11, 1.43)
Weeks of gestation			
>36	453	7,632	1.00
28–36	579	727	13.42 (11.61, 15.51)
<28	48	4	202.17 (72.58, 563.10)
Maternal characteristics			
Mother's age			
<18	362	2,370	1.27 (1.11, 1.45)
18–34	739	6,139	1.00
>34	44	266	1.38 (0.99, 1.91)
Mother's race			
Non-Hispanic white	222	2,738	1.00
Other	923	6,034	1.89 (1.62, 2.20)
Parity			
0	334	2,724	0.91 (0.78, 1.05)
1	169	1,450	0.86 (0.72, 1.04)
2	139	875	1.18 (0.96, 1.44)
3 or more			
Tobacco use			
No	923	7,342	1.00
Yes	222	1,433	1.23 (1.05, 1.44)
Alcohol use			
No	1,119	8,668	1.00
Yes	24	88	2.11 (1.34, 3.33)
Neighborhood characteristics			
Density			
Population/sq. mile	3,014.31	2,732.32	1.00 (1.00, 1.00)
Median age of houses in years	48.0	45.0	1.00 (1.00, 1.00)
Metal concentrations in soil in mg kg ⁻¹ (interquartile range: quartile 3–quartile 1) ^b			
Arsenic (As) (IQR: 2.56)	3.47	3.25	1.04 (1.02, 1.07)
Barium (Ba) (IQR: 51.26)	50.40	49.77	1.00 (1.00, 1.00)
Chromium (Cr) (IQR: 117.79)	19.13	18.95	1.00 (0.99, 1.01)
Copper (Cu) (IQR: 13.34)	17.88	17.14	1.00 (1.00, 1.00)
Lead (Pb) (IQR: 62.89)	85.45	72.28	1.00 (1.00, 1.00)

	Low birth weight <2,500 g (n = 1,146)	Normal birth weight ≥ 2,500 g (n = 8,774)	Odds ratio ^a (low vs. normal)
Manganese (Mn) (IQR: 195.83)	179.77	180.49	1.00 (1.00, 1.00)
Nickel (Ni) (IQR: 43.21)	4.58	4.57	1.00 (0.98, 1.02)
Mercury (Hg) (IQR: 0.03)	0.09	0.10	0.87 (0.70, 1.07)

^aCrude odds ratio, when there is only one predictor in the model

^bOdds ratio for 1 unit change in metal concentration

Table 2

GAM for association between metals and infant LBW

Variables	Low versus normal birth weight		
	Coefficient estimate	Standard error	<i>p</i> value
Infant sex (female vs. male)	0.235	0.064	<0.001
Maternal smoking during pregnancy (yes vs. no)	0.548	0.087	<0.001
Mother's race (other vs. non-Hispanic white)	0.811	0.087	<0.001
Neighborhood density	0.000	0.000	0.342
Copper in soil	−0.006	0.003	0.036
	Estimated degrees of freedom	Chi-sq	<i>p</i> value
Arsenic in soil (smooth term As)	3.876	16.71	0.002