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Maternal Arsenic Exposure Associated With Low Birth Weight in Bangladesh

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Learning Objectives

- Summarize what previous population-based studies have shown about adverse effects of chronic exposure to arsenic in drinking water on health in general and on reproductive outcomes in particular.
- Identify correlations between mass spectrometric measurements of arsenic in specimens of maternal and newborn hair, maternal and newborn toenail, and drinking water; and between chronic arsenic exposure and birth weight.
- Compare the present findings, based on biomarkers of exposure to arsenic, with those of previous studies utilizing non-personal measurements.

Abstract

Objective: *To characterize the effects of maternal arsenic exposure on birth weight.* ***Methods:*** *Hair, toenail, and drinking water samples were collected from pregnant women ($n = 52$) at multiple time points during pregnancy and from their newborns after birth. Total arsenic was measured using inductively coupled plasma-mass spectrometry. The association between arsenic and birth weight was investigated using linear and logistic regression models.* ***Results:*** *Maternal hair arsenic measured early in pregnancy was associated with decreased birth weight ($\beta = -193.5 \pm 90.0$ g, $P = 0.04$). Maternal hair and drinking water arsenic levels measured at first prenatal visit were significantly correlated with newborn hair arsenic level ($\rho = 0.32$, $P = 0.04$ and $\rho = 0.31$, $P = 0.04$).* ***Conclusions:*** *Results suggest that maternal arsenic exposure early in pregnancy negatively affects newborn birth weight and that maternal hair provides the best integrated measure of arsenic exposure.* (J Occup Environ Med. *2007;49:1097–1104*)

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Inorganic arsenic is a by-product of coal combustion, as well as a naturally occurring water contaminant in many regions of the world. Elevated arsenic concentrations have been found in 781 of 1300 Environmental Protection Agency National Priorities List sites and in the drinking water of numerous countries including Australia, Argentina, Bangladesh, Chile, China, India, Mexico, Mongolia, Taiwan, Thailand, the United States, and Vietnam. Currently, an estimated 133 million people in Bangladesh are at risk of drinking water contaminated with arsenic.[1]

Epidemiologic studies have shown that chronic exposure to inorganic arsenic is associated with a number of adverse human health effects, including cancer of the skin, kidney, bladder, and lung, cardiovascular, pulmonary, peripheral vascular, and neurological disease, diabetes, hypertension, and chronic nonmalignant skin conditions.[2]

Although the reproductive toxicity of arsenic has been well documented in animal studies[3] and inorganic arsenic readily crosses the placenta, the effect of arsenic exposure on human reproductive outcomes has yet to be fully elucidated.[4–6] Population-based studies that examined the relationship between arsenic exposure and adverse pregnancy outcomes in humans found an association with spontaneous abortions, low birth weight, preterm delivery, stillbirths, or specific birth defects;[7–21] however, many of these studies did not assess individual exposure or control for confounders such as maternal age, diet, socioeconomic factors, and

other exposures. Moreover, these studies did not use biomarkers of exposure or assess exposure at multiple time points during pregnancy, which provides a more accurate assessment of exposure.

Hair and nails are useful biomarkers of arsenic exposure because arsenic has a high affinity for the sulfhydryl groups in these keratin-rich tissues.[22,23] Once bound to keratin, arsenic is isolated from metabolic activity. Thus, these tissues provide a record of cumulative past exposure, as well as serve as a proxy for internal dose. Despite these advantages, it is unknown which biomarker(s) are the best predictors of the effects of arsenic exposure on birth outcomes.

In this report, we examined the effects of maternal arsenic exposure on birth weight using pilot data from a cohort of pregnant women residing in an arsenic-endemic region of Bangladesh. We evaluated a panel of biomarkers, including arsenic measured in maternal and newborn hair and toenails, collected at different time points during pregnancy to determine which was most strongly associated with birth weight. This is the first report from an ongoing prospective study conducted in collaboration with Dhaka Community Hospital (DCH) in Bangladesh.

Materials and Methods

Site and Participant Selection

The pilot study was conducted between December 2004 and February 2005 in the Sirajdikhan Upazila of the Munshiganj District of Bangladesh, a region highly contaminated with arsenic. Fifty-one percent of more than 18,000 operational tube wells contain more than 50 μg/L of arsenic.[24] Of the 182 villages in Sirajdikhan, 42 were selected for inclusion in this study because they were accessible to the Sirajdikhan Community Clinic, a rural health care clinic operated by DCH, and because they had undergone arsenic mitigation activities, including arsenic-awareness programs and installation of safe drinking water sources. Arsenic mitigation was performed in collaboration with the United Nations Children's Emergency Fund between 2002 and 2005. Dates of installation and first public use of remediated water sources were not recorded; however, each participant in this study used the same drinking water source for at least 6 months before their pregnancy.

Subjects included in this study were pregnant women recruited through community meetings with health care workers from DCH. Women were eligible for the study if they were 18 years of age or older, had an ultrasound-confirmed singleton pregnancy of less than 28 weeks' gestation, used the same primary drinking water source for at least 6 months before becoming pregnant, planned to live at their current residence for the duration of the pregnancy, planned to continue prenatal health care with Sirajdikhan Community Clinic, and agreed to deliver at DCH or at home with a DCH-trained midwife. Of the 90 pregnant women identified through recruitment activities, 90 enrolled in the study (100%). Fifty-seven (63%) of those who enrolled were eligible to participate. Informed consent was obtained from all participants before enrollment. This study was approved by the Human Research Committees at the Harvard School of Public Health and DCH.

Study Procedures

Study procedures included questionnaire administration, ultrasound measurement, and sample collection performed at four time points during pregnancy. Trained study staff administered a detailed baseline questionnaire at enrollment (first prenatal visit) and a follow-up questionnaire at the second prenatal visit, typically around 28 weeks' gestation. These questionnaires ascertained information about diet, education, socioeconomic status, occupation, lifestyle habits, obstetrical, medical and family history, water use, and other exposures. Ultrasound measurements were collected at the first and second prenatal visits. Maternal hair, toenail, and drinking water samples were collected at the first prenatal visit and within 2 weeks after birth. These drinking water samples were collected from the same water source used by the participant for at least 6 months before pregnancy. Newborn measurements were collected at birth, and newborn hair and toenail samples were collected within 2 weeks after birth. Birth weight was measured using a scale that was precise to 50 g. All participants were provided with a free supply of prenatal vitamins that was refilled at each visit.

Hair and toenail samples were collected using titanium nitride scissors and stored in paper envelopes. External contamination was removed by sonication in a 1% Triton X-100 solution (Sigma-Aldrich, St. Louis, MO) for 20 minutes. Samples then were rinsed in demineralized water (Millipore Corporation, Billerica, MA), dried, weighed, and digested in Trace Select Ultra nitric acid (HNO_3) (Fisher Scientific, Pittsburgh, PA) at room temperature.[25] The resulting solution was diluted to 8% HNO_3 and analyzed following the method described by Amarasiriwardena et al.[26]

Standard reference material water (National Institute of Standards and Technology 1643d trace elements in water) (National Institute of Standards and Technology, Gaithersburg, MD) and certified human hair reference material (Shanghai Institute of Nuclear Research, Academia Sinica, China) were used to validate instrument performance and digestion method. The average percent recovery of National Institute of Standards and Technology 1643d and certified reference material hair was 88.7% (SD, 1.7%) and 83.2% (SD, 11.0%), respectively. Depending on the mass of the sample, the limit of detection (LOD) ranged from 0.001 to 0.09 μg/g for maternal hair samples, 0.03 to 1.11 μg/g for maternal nail samples, 0.001 to 0.08 μg/g for newborn hair samples, and 0.01 to 0.42 μg/g for newborn nail samples. All maternal samples and newborn nail

TABLE 1
Characteristics of the Study Population

Characteristic	Value
Age of mother (yr) (n = 52)	
Mean	24.0 ± 4.5
Range	18 to 38
Gestational age at first prenatal visit (wks) (n = 52)	
Mean	16.6 ± 4.8
Range	6.5 to 25
No. past pregnancies (n = 52)	
0	23 (44.2)
1	11 (21.1)
2	12 (23.1)
3	3 (5.8)
4	2 (3.9)
5	1 (1.9)
Mean	1.1 ± 1.3
Birth outcome (n = 52)	
Live births	49 (94.2)
Stillbirths	2 (3.9)
Not recorded	1 (1.9)
Birth gestational age (wks) (n = 49)	
Mean	39.9 ± 1.1
Range	35 to 42
Birth weight (g) (n = 49)	
Mean	2770 ± 420
Range	2000 to 3500
Sex of newborn (n = 49)	
Female	31 (63.3)
Male	18 (36.7)
Maternal weight gain during pregnancy (kg) (n = 49)	
Mean	6.18 ± 3.4
Range	−1 to 18
Activity level during pregnancy (n = 47)	
Sitting most of day	16 (34.0)
Standing stationary or half-day moving	19 (40.4)
Constantly moving or lifting	12 (25.5)
Illness reported during pregnancy (n = 45)	
Yes	19 (42.2)
No	26 (57.8)
Tetanus, measles, mumps, or rubella vaccination (n = 51)	
Yes	18 (35.3)
No	33 (64.7)
Tobacco or tobacco-like exposure (n = 52)	
Yes	30 (57.7)
No	22 (42.3)
Spouse education level (n = 52)	
Less than secondary	26 (50.0)
Secondary or higher	26 (50.0)

All data are shown as number (%) or mean ± standard deviation and range.

samples exceeded their respective limits of detection; however, two newborn hair samples had arsenic values below the LOD and were subsequently assigned half the LOD. Using these corrected values versus the raw values did not change the results.

Analysis Methods

Descriptive statistics (eg, means, medians, quartiles, and percentages) of demographic factors, arsenic levels, and other characteristics of the study population were calculated for all participants. Multivariate linear regression analyses were performed to assess the association between birth weight and biomarkers of maternal and newborn arsenic exposure. Additional covariates, including maternal age, spouse's education level, gestational age at first prenatal visit, number of past pregnancies, birth gestational age, sex of infant, activity level during pregnancy, illness reported during pregnancy, history of immunization, tobacco or tobacco-like exposure during pregnancy, and maternal weight gain during pregnancy, were evaluated in the models to determine if they influenced the effect of arsenic on birth weight. We considered a characteristic to confound the relationship between arsenic level and birth weight if deleting that variable from the model containing all other covariates resulted in a change of 10% or more in the regression estimate or standard error for birth weight. All final models were adjusted for gestational age at first prenatal visit, maternal weight gain, birth gestational age, and activity level during pregnancy. Because birth weight was measured in 50-g increments and birth weight data fell into six categories that were normally distributed, separate logistic regression analyses were performed using birth weight dichotomized at the median (<2750 g or ≥2750 g). Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Pearson's correlations evaluated the relationships between arsenic measured in maternal and newborn hair and nails. All analyses were conducted in SAS (SAS version 9.1; SAS Institute, Inc., Cary, NC).

Results

We recruited 57 eligible participants into our pilot study to determine the feasibility of conducting a large-scale prospective reproductive study in rural Bangladesh. Of these 57 participants, five discontinued participation in the study. We followed the pregnancy and births of the remaining 52 participants. Of these births, two were stillborn and one birth was not recorded. The remaining 49 were live births.

The characteristics of the study population are shown in Table 1. Approximate age of the participants ranged from 18 to 38 years with a mean age of 24 years (24.0 ± 4.5

TABLE 2
Arsenic Levels in Study Population

Biomarker	First Quartile	Second Quartile	Third Quartile	Fourth Quartile	Range
Drinking water at first visit (μg/L) (n = 52)	0.50	1.29	9.03	734.0	<1.0–734.0
Drinking water within 2 wks after birth (μg/L) (n = 50)	1.15	1.87	14.0	191.0	<1.0–191.0
Maternal hair at first visit (μg/g) (n = 51)	0.32	0.49	0.75	3.28	0.14–3.28
Maternal hair within 2 wks after birth (μg/g) (n = 47)	0.28	0.45	0.66	2.70	0.09–2.70
Maternal nail at first visit (μg/g) (n = 51)	0.58	0.92	2.24	6.15	0.19–6.15
Maternal nail within 2 wks after birth (μg/g) (n = 47)	0.40	0.73	1.56	8.04	0.19–8.04
Newborn hair within 2 wks after birth (μg/g) (n = 44)	0.04	0.10	0.19	0.78	<0.001–0.78
Newborn nail within 2 wks after birth (μg/g) (n = 42)	0.35	0.63	0.92	2.63	0.14–2.63

years). Fourteen women (27%) enrolled during their first trimester (≤12 weeks' gestational age) and 38 (73%) enrolled by 25 weeks' gestational age. Almost one-half of the study population had no prior history of pregnancy (n = 23, 44%). Participants gained an average of 6 kg (6.18 ± 3.4 kg) during pregnancy. Gestational age at birth ranged from 35 to 42 weeks with a mean value of 40 weeks (39.9 ± 1.1 weeks). Birth weight ranged from 2000 to 3500 g with a mean of 2770 g (2770 ± 420 g), and most newborns were female (n = 31, 63%). Forty-nine women (94%) reported taking their prenatal vitamins everyday, two (4%) reported taking them at least three times a week, and one (2%) reported not taking them at all.

Activity level during pregnancy was fairly evenly divided among the three categories with 16 women (34%) reporting sitting most of the day, 19 women (40%) reporting being on their feet all day but in a stationary position or spending half the day moving on their feet, and 12 women (26%) reporting being on their feet all day and constantly moving around or lifting objects. Only 18 participants (35%) had a history of any vaccination. The most common vaccination was tetanus (n = 17, 33%). Four women (8%) had been vaccinated against measles, three (6%) against mumps, and none against rubella. No participants smoked cigarettes, but 30 participants (58%) reported some tobacco or tobacco-like exposure: 29 participants (56%) reported environmental exposure to tobacco smoke, two (4%) reported chewing tobacco, and three (6%) reported chewing betel nuts. As most women in this population are not formally educated and do not work outside the home, spouses' education was considered a proxy for socioeconomic status. One-half of the study population (n = 26, 50%) had spouses with a secondary education or higher.

Arsenic levels in drinking water and in maternal and newborn nail and hair samples at two time points during the study are shown in Table 2. Of the 52 mother-newborn pairs in this study, 47 mothers provided both hair and nail samples at each time point. Hair and nails were collected from 45 and 43 newborns, respectively. Two newborn samples, one nail and one hair, were considered outliers and were excluded from the analyses because they had insufficient mass. Maternal and newborn arsenic levels in nails were higher than those in hair. Maternal hair and nail arsenic levels from the first prenatal visit were higher than those from the birth visit, although the difference between visits was larger for maternal nails than hair. Median newborn hair and nail arsenic levels were smaller than the maternal levels.

Correlations between maternal and newborn arsenic measurements, among hair, nail, and water measurements, and between arsenic levels measured during the first prenatal visit and at birth are shown in Table 3. Maternal hair arsenic level at the first prenatal visit was significantly correlated with maternal hair arsenic levels at birth ($\rho = 0.73$, $P < 0.001$) and with maternal nail arsenic level at first prenatal visit ($\rho = 0.63$, $P < 0.001$). Similarly, maternal nail arsenic level at birth was significantly correlated with maternal nail arsenic level at first prenatal visit ($\rho = 0.49$, $P < 0.001$) and with maternal hair arsenic level at birth ($\rho = 0.42$, $P = 0.003$). Newborn hair and nail arsenic levels showed a correlation of $\rho = 0.45$ ($P = 0.003$). Newborn nail arsenic level was not significantly correlated with maternal nail arsenic level at first prenatal visit ($\rho = -0.04$, $P = 0.80$) or with maternal nail arsenic level at birth ($\rho = 0.24$, $P = 0.12$). Newborn hair arsenic level was significantly correlated with maternal hair arsenic level at first prenatal visit ($\rho = 0.32$, $P = 0.04$), but not with maternal hair arsenic level at birth ($\rho = 0.25$, $P = 0.10$). Drinking water arsenic level at first prenatal visit was significantly associated with infant hair arsenic levels ($\rho = 0.31$, $P = 0.04$) and with maternal nail arsenic level at birth ($\rho = 0.72$, $P < 0.001$), but not with newborn nail or other maternal samples. Drinking water arsenic levels at birth were not significantly associated with any maternal or newborn arsenic levels.

In the multivariate linear regression analyses, we observed a statistically significant negative association between maternal hair arsenic levels at the first prenatal visit and newborn birth weight ($\beta = -193.5 \pm 90.0$,

TABLE 3
Correlation Between Maternal and Newborn Hair, Nail, and Water Arsenic Levels

	Maternal Hair 1	Maternal Hair 2	Maternal Nail 1	Maternal Nail 2	Newborn Hair	Newborn Nail	Water 1	Water 2
Maternal hair 1	1.00	0.73* ($P < 0.001$)	0.63* ($P < 0.001$)	0.43 ($P = 0.003$)	0.32* ($P = 0.04$)	−0.04 ($P = 0.82$)	0.23 ($P = 0.10$)	−0.08 ($P = 0.59$)
Maternal hair 2		1.00	0.49 ($P < 0.001$)	0.42* ($P = 0.003$)	0.25 ($P = 0.10$)	−0.02 ($P = 0.89$)	0.22 ($P = 0.13$)	0.02 ($P = 0.88$)
Maternal nail 1			1.00	0.49* ($P < 0.001$)	0.03 ($P = 0.84$)	−0.04 ($P = 0.80$)	0.23 ($P = 0.11$)	−0.02 ($P = 0.91$)
Maternal nail 2				1.00	0.30 ($P = 0.05$)	0.24 ($P = 0.12$)	0.72* ($P < 0.001$)	0.08 ($P = 0.58$)
Newborn hair					1.00	0.45* ($P = 0.003$)	0.31* ($P = 0.04$)	0.20 ($P = 0.19$)
Newborn nail						1.00	0.02 ($P = 0.88$)	0.16 ($P = 0.32$)
Water 1							1.00	0.10 ($P = 0.51$)
Water 2								1.00

*Statistically significant correlations of interest.

TABLE 4
Linear Regression Analysis of Maternal Hair Arsenic Level at First Visit (μg/g) and Birth Weight (g)

Model ($n = 43$)	Estimate	SE	P
Maternal hair at first visit	−193.5	90.0	0.04
Gestational age at first prenatal visit	35.6	11.0	0.003
Activity level during pregnancy	−130.5	78.0	0.10
Maternal weight gain	−25.4	18.5	0.18
Birth gestational age	193.1	51.4	<0.001

$P = 0.04$), indicating that for every 1 μg/g increase in arsenic, birth weight decreased by 194 g (Table 4). Birth gestational age and gestational age at first prenatal visit were positively associated with birth weight, whereas activity level during pregnancy and weight gain were negatively associated with birth weight. Maternal hair arsenic level at first prenatal visit explained 8.5% of the variation in birth weight, and overall, the model explained 42% of the variation in birth weight. Maternal nail arsenic level at first prenatal visit, maternal hair and nail arsenic levels at birth, and newborn nail and hair arsenic levels were not significantly associated with low birth weight.

In the logistic regression analyses, higher maternal hair arsenic levels at first prenatal visit, maternal hair arsenic level at birth, and maternal nail arsenic level at first prenatal visit were associated with lower birth weight, but the CIs included 1.0 (OR = 0.40, 95% CI = 0.12–1.35; OR = 0.45, 95% CI = 0.10–2.04; OR = 0.83, 95% CI = 0.48–1.42, respectively). Maternal nail arsenic level at birth and newborn nail and hair arsenic levels were not associated with birth weight (data not shown).

Conclusions

This is the first description of the effects of chronic arsenic exposure on birth outcomes using biomarkers of exposure collected at multiple time points from a prospective cohort of pregnant women exposed to a wide range of drinking water arsenic concentrations. Our results showed a negative association between maternal hair arsenic level at the first prenatal visit and birth weight after adjusting for relevant covariates. In addition, this pilot study established the feasibility of conducting a large-scale prospective reproductive study in rural Bangladesh.

Our observation that arsenic measured using biomarkers of exposure is inversely associated with birth weight strengthens the findings of an association between nonpersonal arsenic measurements and adverse birth outcomes found in previous studies in other populations. A prospective, ecological study in two Chilean cities reported that, after adjusting for confounders, newborns born in towns with higher arsenic concentrations in drinking water had lower birth weights of similar magnitude to those resulting from maternal exposure to second hand smoke and to benzene.[9] A modest risk of preterm delivery and a significant decrease in birth weight was found in an arsenic-exposed versus nonexposed region in Taiwan.[15] Four studies from Bangladesh have shown an association between exposure to arsenic in drinking water and adverse birth outcomes, including spontaneous abortion, stillbirth, preterm birth, infant death, or malformations.[12,17,20,21]

We did not find an association between birth weight and nail arsenic levels. In addition, maternal hair arsenic levels at the two time points were strongly correlated with each other, whereas maternal nail arsenic levels at the two time points were less strongly correlated. Similarly, newborn hair arsenic level was more

strongly correlated with maternal hair arsenic levels than was newborn nail arsenic level. Together, these data suggest that maternal hair may provide a better integrated measure of historical arsenic exposure. One centimeter of hair represents 1 month of exposure,[27] whereas approximately 100 days after exposure a dose of arsenic can be measured in the distal tip of a nail.[22,23,25] Although nail and hair sampling should theoretically measure the same duration of past arsenic exposure, it is likely that there was more variability in the nail data in our population. This variation may be because of women cutting their toenails more frequently than their hair over the course of pregnancy. Moreover, pooling nail clippings from all five toes introduces variability as the nail of the big toe grows more slowly than those of the smaller toes.

We did not find an association between birth weight and arsenic levels in drinking water. This may reflect the difference between measuring current arsenic exposure in water samples and past exposure in hair and nail samples. Although the study area is heavily affected by arsenic contamination, all villages that participated in the study had undergone arsenic mitigation activities, and all residents had access to at least one source of arsenic-free drinking water. Although many women had a personal tube well that was considered unsafe because it contained more than 50 μg/L of arsenic, as determined by Merck Arsenic Field Test Kits, 88% of the population used drinking water with less than 50 μg/L of arsenic at the time of enrollment. This percentage increased to 92% by the end of the study. Although women still reported using these contaminated tube wells for bathing and washing, almost all were using an alternative source of water for drinking and cooking purposes.

Although we found an association between birth weight and arsenic levels at first prenatal visit, we did not find an association between birth weight and arsenic levels at birth. In addition, maternal hair and nail arsenic levels at the first prenatal visit were more highly correlated than hair and nail arsenic levels at birth. Arsenic remediation may explain, in part, why the first samples were more strongly correlated with birth weight than the later ones. Alternatively, these data suggest the intriguing possibility that maternal arsenic is transferred early in pregnancy to the developing fetus. Although arsenic readily crosses the placenta, the timing and mechanism of transfer and the role of the placenta in mediating arsenic-related effects in the developing fetus are unknown and will require further investigation. Discerning the temporal pattern of exposure could be accomplished in future studies by segmenting hair into standard lengths and analyzing them separately to reconstruct exposure history.

One possible mechanism of reproductive toxicity from arsenic is through oxidative stress. In animal models, maternal exposure to reactive oxygen species (ROS) during pregnancy disrupts fetal growth.[28,29] Human placenta and fetus are vulnerable to toxic insult by ROS during pregnancy. Most ROS are membrane permeable and can readily cross the placenta.[30] Furthermore, the placenta is a mitochondria-rich organ, which may contribute a significant portion of free oxygen radicals.[31] In addition, many antioxidants such as ascorbic acid, tocopherol, β-carotenes, and Q10 coenzyme are also readily transferred across the placenta.[32] Elevated levels of serum lipid peroxidation markers have been shown in normal pregnant women, with concentrations peaking during the second trimester.[30,33,34] Disruptions in the oxidant-antioxidant balance favoring excessive oxidants may lead to pregnancy complications such as gestational diabetes, hypertension, or preeclampsia.[30,35–38] Finally, low birth weight has also been associated with a 40% increase in maternal oxidative stress levels measured at the 28th week of gestation.[39] However interesting and informative these experiments are, the precise mechanisms of arsenic toxicity vis-à-vis ROS remain unknown. Another biologically plausible explanation for adverse birth outcomes after arsenic exposure is epigenetic modification, ie, processes that may alter gene activity without changing DNA sequence and lead to modifications that can be transmitted to progeny cells.[40]

The positive association between gestational age at first prenatal visit and birth weight and the negative association between maternal weight gain and birth weight are unexpected. Because our study population does not represent a random sample, it is possible that women with higher-risk pregnancies are coming to medical attention sooner and, therefore, being enrolled in the study at an earlier gestational age than women with lower-risk pregnancies. Women with higher-risk pregnancies would be more likely to have lower birth weight infants. Prepregnancy birth weights were not consistently available for this pilot study, so maternal weight gain was substituted for body mass index. By using body mass index and the results of a semiquantitative nutritional questionnaire collected for the full analysis, we plan to clarify the relationship between maternal nutritional status and birth weight in this cohort.

Strengths of this study include a prospective study design and utilization of biomarkers of exposure, which reduces exposure misclassification. Remaining misclassification of exposure is likely to be randomly distributed. Incorporating both maternal and infant biomarkers collected at multiple time points allows us to better understand the transfer of arsenic from mother to child. Also, the study site is unique because it has a wide range of arsenic contamination among an ethnically and socially homogenous group of people, allowing for the evaluation of outcomes over a range of exposures.

Limitations of this study include small sample size and measurement of birth weight using a low-precision scale. Despite limited power of 68%, an association between arsenic exposure and birth weight was found in this study. Moreover, we will have adequate power and access to a higher precision scale in the larger cohort analysis. Another limitation is that our drinking water exposure assessment only captures current arsenic exposure. Finally, although we addressed major confounders of birth weight in these analyses, additional unidentified confounders may exist that could further clarify factors that influence birth weight.

In summary, this study shows a negative association between maternal arsenic exposure and birth weight. Analysis of data from the full cohort study will further elucidate the relationship between arsenic exposure and human pregnancy outcomes, fill important research gaps in our knowledge of the reproductive effects of arsenic toxicity, and help inform clinical and public health interventions.

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