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Arsenic in drinking water and adverse birth outcomes in Ohio

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ABSTRACT

Background: Arsenic in drinking water has been associated with adverse reproductive outcomes in areas with high levels of naturally occurring arsenic. Less is known about the reproductive effects of arsenic at lower levels.
Objectives: This research examined the association between low-level arsenic in drinking water and small for gestational age (SGA), term low birth weight (term LBW), very low birth weight (VLBW), preterm birth (PTB), and very preterm birth (VPTB) in the state of Ohio.
Methods: Exposure was defined as the mean annual arsenic concentration in drinking water in each county in Ohio from 2006 to 2008 using Safe Drinking Water Information System data. Birth outcomes were ascertained from the birth certificate records of 428,804 births in Ohio from the same time period. Multivariable generalized estimating equation logistic regression models were used to assess the relationship between arsenic and each birth outcome separately. Sensitivity analyses were performed to examine the roles of private well use and prenatal care utilization in these associations.
Results: Arsenic in drinking water was associated with increased odds of VLBW (AOR 1.14 per μg/L increase; 95% CI 1.04, 1.24) and PTB (AOR 1.10; 95% CI 1.06, 1.15) among singleton births in counties where < 10% of the population used private wells. No significant association was observed between arsenic and SGA, or VPTB, but a suggestive association was observed between arsenic and term LBW.
Conclusions: Arsenic in drinking water was positively associated with VLBW and PTB in a population where nearly all (> 99%) of the population was exposed under the current maximum contaminant level of 10 μg/L. Current regulatory standards may not be protective against reproductive effects of prenatal exposure to arsenic.

1. Introduction

Arsenic is the 20th most common element in the Earth's crust and is a naturally occurring water contaminant in many regions of the world (IARC, 2004). The primary route of human exposure to arsenic is through contaminated drinking water, with additional contributions from contaminated food and air (Vahter, 2009; World Health Organization (WHO), 2011). While arsenic in drinking water has been classified as a Group 1 (known) carcinogen to humans (IARC, 2004) for bladder, lung, and skin cancers; the effect of chronic arsenic exposure through drinking water on fetal development is less well understood. Arsenic and its metabolites readily cross the placental barrier, and arsenic levels in cord blood are nearly as high as in maternal blood, demonstrating biologic plausibility for an association between exposure and fetal development (Concha et al., 1998; Hall et al., 2007). Currently, the maximum contaminant level (MCL) in drinking water set by the WHO and the USEPA is 10 μg/L, based on risk of cancers, cardiovascular diseases, and neurologic effects (40 C.F.R. § 141.62).

A growing body of epidemiologic research from regions with elevated arsenic levels in drinking water suggests that arsenic exposure during pregnancy is associated with reduced birth weight. In a cross-sectional study of pregnant women in Taiwan, women residing in areas

Abbreviations: AOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; CFR, Code of Federal Regulations; CWS, community water system; GEE, generalized estimating equations; IARC, International Agency for Research on Cancer; LMP, last menstrual period; LOD, limit of detection; MCL, maximum contaminant level; NHLBI, National Heart, Lung, and Blood Institute; ODH, Ohio Department of Health; PNC, prenatal care; PTB, preterm birth; SDWIS, Safe Drinking Water Information System; SES, socio-economic status; SGA, small for gestational age; term LBW, term low birth weight; USEPA, United States Environmental Protection Agency; USGS, United States Geological Survey; VLBW, very low birth weight; VPTB, very preterm birth; WHO, World Health Organization; WIC, Women, Infants, and Children

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of high drinking water arsenic (range, 0.15–590 μg/L) delivered infants with significantly lower mean birth weight than women in low arsenic areas (< 0.15 μg/L) (Yang et al., 2003). Similarly, a prospective cohort study comparing birth outcomes between two Chilean cities, one with a mean arsenic concentration in drinking water of 42 μg/L and one with an average arsenic concentration < 1 μg/L, found increased arsenic levels were associated with a 57 g reduction in birth weight (Hopenhayn et al., 2003). In a cohort of pregnant Bangladeshi women, a significant dose-response relationship between arsenic and birth weight, head circumference, and chest circumference was observed only for women with lower arsenic exposure (< 100 μg/L in urine) compared to those with higher arsenic exposures (≥100 μg/L) (Rahman et al., 2009). In a study of mothers and infants in Oklahoma, USA, Claus Henn et al. (2016) found that maternal urinary arsenic concentrations (median 0.3 μg/L) were significantly inversely related to birth weight and gestational length, although the fetal arsenic exposure was not solely from drinking water. In a cohort of 706 women and their infants in New Hampshire, USA, Gilbert-Diamond et al. (2016) found a significant decrease in birth weight from arsenic in drinking water and diet only among female infants born to overweight or obese mothers. The specific exposure window during pregnancy in which the fetus is most susceptible to the effects of arsenic is unknown, but one study of pregnant women in Bangladesh found a significant decrease in birthweight among women with higher arsenic exposure early in pregnancy (Huyck et al., 2007). Kwok et al. (2006), however, found no association between drinking water arsenic and birthweight among term infants born to women residing in three regions of Bangladesh with a range of exposures to arsenic through drinking water. In a prospective study of 122 pregnant women in Romania, Bloom et al. (2015) found a significant negative relationship between arsenic in drinking water and birthweight only among smokers.

Epidemiologic evidence of an association between arsenic in drinking water and preterm birth is inconsistent (Bloom et al., 2014). In a cross-sectional study of birth outcomes in Bangladesh, women who lived in an arsenic-affected village (mean arsenic in drinking water 240 μg/L, range 200–1371 μg/L) had significantly increased rates of spontaneous abortions, stillbirths, and preterm births compared to those in a "non-exposed" village (≤20 μg/L in drinking water) (Ahmad et al., 2001). Yang et al. (2003) found a non-significant increase in the odds of preterm birth among women in a high drinking water arsenic region compared to those in a low arsenic region. A study of adverse birth outcomes in Inner Mongolia did not detect an association of drinking water arsenic levels > 50 μg/L with preterm birth (Myers et al., 2010). In a sample of Chinese male infants, gestational age was significantly inversely related to arsenic in maternal blood (Xu et al., 2011). Preterm birth and reduced birthweight were spatially associated with higher levels of groundwater arsenic in New Hampshire, USA (Shi et al., 2015).

The majority of data on arsenic and birth outcomes are from populations with very high exposure, such as Bangladesh, West Bengal, China, and Argentina. Associations and dose-response relationships observed at high levels of exposure may not accurately reflect those at lower exposure. Less is known about reproductive health effects at low arsenic exposures (Quansah et al., 2015), such as those found in the Midwestern United States. The objective of this research was to examine the association between arsenic in drinking water and five birth outcomes; small for gestational age, term low birth weight, very low birth weight, preterm birth, and very preterm birth; in the state of Ohio where arsenic levels are relatively low.

2. Methods

2.1. Study population

This study used birth certificate data (from the 2003 revision of the U.S. Certificate of Live Birth) for births occurring in the state of Ohio between 2006 and 2008. Individual-level, de-identified birth certificate data for children born in Ohio was provided by the Ohio Department of Health (ODH).

2.2. Birth outcomes

The primary outcomes of interest in the study were small for gestational age (SGA), term low birth weight (term LBW), very low birth weight (VLBW), preterm birth (PTB), and very preterm birth (VPTB). SGA was defined as the smallest 10% of infants, according to birth weight, at each gestational age in the population (Wilcox, 2010). SGA status was calculated using sex- and gestational age-specific national birth weight references developed by Duryea et al. (2014). Term LBW was defined as an infant weighing < 2500 g at time of delivery among term infants (≥37 weeks gestation). An infant was considered VLBW if it weighed < 1500 g at time of delivery, regardless of gestational age. Preterm and very preterm births were defined as infants delivered prior to 37 and 32 weeks gestation, respectively. Gestational age was based on the reported last normal menstrual period (LMP). If the LMP was unknown, a clinical estimate of gestation was used. All birth outcomes were either reported directly on or were calculated from variables reported on the birth certificates.

2.3. Exposure assessment

The USEPA defines the legal limits of water contaminants and water testing schedules, as mandated in the Safe Drinking Water Act. The MCL for arsenic in drinking water is 10 μg/L (40 C.F.R. § 141.62). Public drinking water systems are required to monitor for arsenic every three years when using groundwater and annually when using surface water sources (40 C.F.R. § 141.23).

A total of 2968 arsenic measurements from 975 community water systems (CWS) in Ohio from 2006 to 2008 were obtained from the Ohio EPA Safe Drinking Water Information System (SDWIS). An annual measure of arsenic in drinking water was calculated for each of the 88 counties in Ohio as follows. First all measurements in each CWS providing drinking water in a county in a year were averaged, giving a CWS-year mean. Second, the CWS-year means in each county were averaged, weighted by the population served to control for the variable distribution network sizes of CWSs within a county. The resulting county-year mean was used as the exposure measure. The median number of CWSs in each county was 11, with a range from 3 to 54. The exposure measure assumed that each CWS serves only residents in the county in which the CWS office is located (Jones et al., 2014). The limits of detection (LODs) varied, but were typically 0.5 μg/L, and measurements below the LOD were equated with LOD/2. County-level population percentages of those using private well water were obtained from the Unites States Geological Survey (USGS) (USGS, 2015).

The arsenic exposure measures were linked with birth outcomes by the county and year(s) of gestation. If an infant's entire gestation fell within one calendar year, the county-year arsenic measure was assigned to the birth. If an infant's gestation spanned two calendar years, an average of the two annual estimates of arsenic was assigned to that birth, weighted by gestational months in each calendar year.

2.4. Covariates

The individual-level covariates were ascertained from the birth certificates and included infant sex, maternal age at birth, mother's race/ethnicity, maternal educational attainment, marital status, prenatal care (PNC) utilization, socioeconomic status, parity, cigarette use, and maternal pre-pregnancy body mass index (BMI). Maternal age was categorized as 10–19, 20–29, 30–39, and ≥40 years of age. Maternal race/ethnicity was defined as non-Hispanic white, non-Hispanic black, Hispanic, and other/unknown. Maternal educational attainment was categorized as less than a high school degree, high school degree, some