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Consumption of arsenic-contaminated drinking water and anemia among pregnant and non-pregnant women in northwestern Romania ☆

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ABSTRACT

Anemia is a global health problem. To evaluate the impact of low-moderate water arsenic exposure (mostly <10 μg/L) on anemia, we conducted a cross-sectional study of 217 Romanian women. The adjusted prevalences for 'any' anemia (prevalence proportion ratio (PPR)=1.71, 95% CI 0.75–3.88) and pregnancy anemia (PPR=2.87, 95% CI 0.62–13.26) were higher among drinking water arsenic exposed women than among unexposed women. These preliminary data underscore the need for a more definitive study in this area.

1. Introduction

Anemia is a global problem with negative impacts on human health, including increased risks of maternal and child mortality and adverse effects on cognitive and physical development (Allen, 2000). Despite the high prevalence, particularly in regions that also experience groundwater arsenic contamination (WHO, 2008), few epidemiologic studies have investigated the impact of arsenic exposure on anemia. There is even less evidence on the risk of anemia in pregnant women consuming arsenic-contaminated drinking water, particularly in association with low-moderate levels (<50 μg/L) which are found in large regions around the world (Amini et al., 2008). To date, three epidemiologic studies investigated the risk of anemia related to high-level exposure to arsenic via drinking water in arsenic-endemic regions of Bangladesh and West Bengal, India (Heck et al., 2008; Majumdar et al., 2009; Merrill et al., 2012). Only one epidemiologic study, conducted in Chile, focused on anemia in pregnancy and a potential link to moderate level arsenic exposure (Hopenhayn et al., 2006). To address the existing data gap concerning low-moderate drinking water arsenic exposure and anemia, we conducted an exploratory, cross-sectional investigation among women enrolled in a study recently completed in northwestern Romania. This area is recognized for geogenic contamination of underground drinking water, with low to moderate concentrations (Neamtiu et al., 2015).

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2. Material and methods

Participants included pregnant women 18–44 years of age and residing in Timis County, Romania recruited between December 2011 and January 2013. Participants ($n=297$) were initially recruited to a case-control study of drinking water arsenic exposure and pregnancy loss. A detailed description of the recruitment strategy is provided elsewhere (Bloom et al., 2014). Briefly, we enrolled 150 women receiving treatment for incident spontaneous pregnancy loss of 5–20 weeks completed gestation as case participants, and 150 women receiving routine prenatal care for ongoing pregnancies matched to case participants by gestational age (±1 week) as controls ($n=3$ participated first as a control and then as a case). The participants completed a physician-administered study questionnaire, including detailed questions concerning demographics, lifestyle factors, and medical, reproductive, residential, and occupational histories. All women provided written informed consent and the study protocol was approved by the Institutional Review Boards of the Emergency County Hospital in Timisoara, Romania and the University at Albany, U.S.

The current study outcome was defined as self-report of having ever received a clinician diagnosis of anemia. We used questionnaire data to further qualify cases as 'pregnancy anemia' and 'non-pregnancy anemia'. 'Pregnancy anemia' was defined as a reported diagnosis during the study pregnancy or within one year of a reported previous pregnancy; all other diagnoses were defined as 'non-pregnancy anemia'. To preclude exposure measurement misclassification associated with residential mobility we restricted cases to women who received the anemia diagnosis while residing in their current residence, from which we collected drinking water samples (i.e., $n=67$ excluded).

We reconstructed drinking water exposure histories based on questionnaire data weighted by arsenic measured in drinking water. The details of water collection and arsenic determination are provided elsewhere (Bloom et al., 2014). In brief, we collected water samples from reported residential sources into arsenic free containers and used a method based on hydride generation-atomic absorption spectrometry for arsenic determination. The limit of detection (LOD) was 0.5 μg/L; to preclude bias we did not impute values below the LOD (Schisterman et al., 2006). Average arsenic concentration was calculated as the mean of arsenic determinations made in up to two residential drinking water sources. To focus on exposures 'common' in our study population, we excluded $n=13$ extreme outliers from further analysis; observations more than three interquartile ranges above the 75th %tile of the sample distribution (Kitchens, 1998).

We characterized the overall distributions for participants' demographics, lifestyle factors, and arsenic exposure, and compared them by anemia status. We used Poisson regression models with robust variance estimation to assess prevalence proportion ratios (PPRs) and 95% confidence intervals (CI) for associations between arsenic exposure and anemia, adjusted for cigarette smoking and education as confounders based on the literature. We also considered the influence of self-reported continuous maternal pre-pregnancy body mass index (BMI) and self-report of having ever received a physician diagnosis of kidney disease, by entering them as covariates in the models. We first defined qualitative exposure as 'unexposed' (0 μg/L) and use of residential water sources with 'any' arsenic contamination (>0 μg/L). We next categorized average arsenic exposure in a semi-quantitative scale as 'unexposed' (0 μg/L), 'low exposure' (>0–5 μg/L), and 'moderate exposure' (>5 μg/L), using a cut-off value equal to half the 10 μg/L World Health Organization drinking water standard (WHO, 2011). We also tested the P for trend by entering semi-quantitative arsenic exposure as an ordinal variable into Poisson regression models.

To assess the impact of participants recall and exposure misclassification associated with time since diagnosis, we conducted a sensitivity analysis by restricting the study sample to participants diagnosed with anemia during the study pregnancy. To help guide a future investigation, we determined the sample size required for detecting adjusted associations at $P<0.05$ with 80% statistical power. All statistical analyses were conducted using SAS v.9.3 (SAS Institute, Cary, NC) and we used PASS 12.0 (NCSS LLC, Kaysville, UT) to determine sample size. Statistical significance was defined as $P<0.05$ for a two-tailed test.

3. Results

The current analysis included $n=217$ with an anemia diagnosis while living in the study residence or without history of anemia, and with average drinking water arsenic concentration less than 15 μg/L. A total of 25 women reported a history of clinician-diagnosed anemia while residing in the study household, 192 did not (Table 1). Overall, more women with a history of anemia lacked a high school degree, never smoked cigarettes, and had a history of kidney disease than women without anemia, although the differences were not statistically significant. Women with and without anemia had similar BMI and similar duration residing at the study address. Compared to women without anemia, women with anemia had higher drinking water arsenic concentrations (median= 1.46 vs. 0.10 μg/L; $P=0.080$). The concentration was particularly high in 10 women with pregnancy anemia (median=3.34 μg/L).

Table 1
Characteristics of study participants, by anemia status.

Characteristics	Anemia ($n=25$)	No anemia ($n=192$)	P-value
Education, n (%)			
Less than high school	7 (28.0)	41 (21.4)	0.752
High school	8 (32.0)	66 (34.4)	
University	10 (40.0)	85 (44.3)	
Cigarette smoking, n (%)			
Never	19 (76.0)	129 (67.2)	0.374
Ever	6 (24.0)	63 (32.8)	
Kidney disease, n (%)			
No	20 (83.3)	177 (92.2)	0.149
Yes	4 (16.7)	15 (7.8)	
Maternal body max index, median (25th, 75th %tile) kg/m^2	22.1 (20.4, 23.0)	22.0 (20.1, 24.6)	0.808
Duration of residence at study address, median (25th, 75th %tile) Years	9 (3, 18)	8 (3, 21)	0.383
Age at diagnosis, median (25th, 75th %tile) Years	23 (20, 26)	–	–
Time since diagnosis, median (25th, 75th %tile) Years	6 (0, 12)	–	–
Average arsenic concentration, median (25th, 75th %tile) μg/L	1.46 (0, 3.61)	0.10 (0, 2.39)	0.080

Note: Mann–Whitney U and χ^2 tests used to compare continuous and categorical variables, respectively.

Table 2 presents unadjusted and multivariable-adjusted regression results. The effect estimate for 'any' anemia suggested a