Association of Urinary Arsenic and Sleep Disorder in the U.S. Population: NHANES 2015-2016

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Research Article

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Abstract

Arsenic is a known carcinogen and neurotoxin and is found in the natural earth crust. Arsenic exposure can develop depression, memory dysfunction, and neurodegenerative disorder. The mechanism of arsenic toxicity on the nervous system is not known. There is a lack of research on the association between arsenic exposure and sleep disturbance in humans. This study aims to investigate the relationship between six types of urinary speciated arsenic exposure and sleep disturbance in adults from the general population using the National Health and Nutrition Examination Survey (NHANES) 2015–2016 dataset. Sleep disturbance was measured using self-reported questionnaires, asking participants if they had ever told a doctor they had trouble sleeping. We utilized multivariate logistic regression analysis using complex survey procedures to examine the association between six types of urinary arsenic concentration and trouble sleeping. The total sample included 1,611 adults who were 20 years and older. Of the study participants, 30.0% had trouble sleeping. Urinary arsenous acid was associated with an increased odds of had trouble sleeping [odds ratio: 1.47 (95% confidence interval 1.02–2.11). The other five types of urinary speciated arsenic (arsenic acid, arsenobetaine, arsenocholine, dimethylarsinic acid, monomethylarsonic acid) were not associated with a sleep disorder.

Introduction:

Arsenic is an element that occurs naturally in the Earth. Chronic arsenic exposure can occur through drinking water or dietary sources; arsenic exposure can lead to non-carcinogenic and carcinogenic health effects (Rahman et al., 2018). Arsenic exposure has been associated with impaired immune responses, causing an increased susceptibility to disease in humans (Rahman et al., 2020a). The International Agency for Research on Cancer (IARC) declared arsenic as a type 1 carcinogen. In addition to skin cancer, skin conditions are the most common external presentation of arsenic toxicity. The most prominent cancers include lung, skin, liver, kidney, and bladder cancer. Other health conditions caused by chronic arsenic exposure include impaired intellectual function, hypertension, ischemic heart disease, restrictive pulmonary disease, diabetes mellitus, non-cirrhotic portal fibrosis, and peripheral vascular disease (Rahman et al., 2018).

Arsenic exposure commonly occurs through water contamination and dietary sources. Common dietary sources include grape and apple juice, rice cereal, brown and white rice, beer, and wine (Nachman et al., 2017). Epidemiological evidence shows that arsenic concentrations in drinking water over the Environmental Protection Agency (EPA) maximum allowable concentration of 10 µg/L are associated with detrimental human health effects (Mayer & Goldman, 2016). Private wells in the U.S. are not regulated by the EPA and can lead to exposures > 10 µg/L (Sanders et al., 2012). Once exposed, arsenic can metabolize to inorganic and organic arsenic; inorganic arsenic is known to be acutely toxic to humans (Jomova et al., 2011). Inorganic arsenic is metabolized to form monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA). Organoarsenics, including arsenobetaine, arsenocholine, and arsenosugars, are less harmful to human health than inorganic arsenics; common exposures are through seafood consumption (Choi et al., 2009).
Arsenic has been linked to sleep disorders. In the United States (U.S.), among adults, one form of arsenic was associated with leg jerks and wake-up at night while sleeping (Shiue, 2017). Sleep loss and sleep disorders are common but often overlooked health issues. Public health consequences can include morbidity, mortality, accidents, injuries, reduced family well-being, reduced functioning, and reduced quality of life. Inadequate or insufficient sleep is linked with development of chronic diseases such as cardiovascular disease, hypertension, diabetes, anxiety, depression, alcohol use, obesity, and endocrine, immune, and nervous system disorders in adults and children (Rahman et al., 2020b; Scinicariello et al. 2017; Guo et al., 2016). Sleep deprivation has been associated to the prefrontal cortex's actions, including creative, divergent, and innovative aspects of cognition and cognitive systems that rely on emotional data (Killgore, 2010; Van Cautera et al., 2008).

Only a few studies have investigated the relationship between arsenic and sleep disturbance, and these studies reported conflicting findings (Lilis et al., 1985; Shiue, 2017). Lilis et al. (1985) found that arsenic exposure was associated with depression, memory problems, and paresthesia in copper smelter workers, but was not significant for sleep disturbances. Shiue (2017) observed an association between trimethylarsine oxide and sleep disturbance defined as leg jerk and wake-up at night while sleeping, but no association with other forms of speciated arsenic. Chronic sleep deprivation is increasingly common; 37.1% of the U.S. general population is estimated to have short sleep duration (Scinicariello et al., 2017). Over the previous 50 years, average sleep duration in adolescents and adults has decreased by 1.5-2 hours per night (Van Cautera et al., 2008). Both arsenic exposure and sleep disorders can lead to chronic disease and severe health conditions.

**Study Aim:**

The association between arsenic and sleep disorders in the U.S. is unknown. Only a few studies to our knowledge have investigated the association between urinary speciated arsenic exposure and trouble sleeping, a type of sleep disorder, using a population-based dataset.

**Methods:**

**1.1 Study Population**

The National Health and Nutrition Examination Survey (NHANES) is a national survey assessing the health and nutritional status of children and adults in the U.S. (National Center for Health Statistics, 2017). Urinary arsenic samples were collected in participants aged 18 years and older who met the one-third subsample selection criteria. To oversample adult smokers, participants 18 years and older who were not in the one-third subsample but who smoked at least 100 cigarettes in their entire lifetime were included (CDC, 2018b). For sleeping disorders, participants aged 16 years and older were sampled by NHANES (CDC, 2018a). In our study, only participants aged 20 years and older were included in the data analysis. Demographic data for the NHANES study is included in the "2015-2016 Demographics File" (CDC, 2017a). We restricted the sample to only individuals who had no missing data on the independent
(speciated arsenic) and dependent (trouble sleeping) variables, and depression, a key confounder in this study (n=1,611).

1.2 Urinary Arsenic Assessment

The NHANES 2015-2016 "Speciated Arsenics - Urine - Special Sample (UASS_I)" dataset was used in this analysis. Samples were collected at Mobile Examination Centers (MECs) and sent to the Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, GA, for analysis. Detailed information on the laboratory procedures conducted by NHANES can be found in the "Arsenics - Speciated - Urine Laboratory Procedure Manual." Samples were analyzed for the following types of speciated arsenic and corresponding lower level of detection (LLOD): urinary arsenous acid 0.12 µg/L, urinary arsenic acid 0.79 µg/L, urinary arsenobetaine 1.16 µg/L, urinary arsenuocholine 0.11 µg/L, urinary dimethylarsinic acid (DMA) 1.91 µg/L, urinary and monomethylarsonic acid (MMA) 0.20 µg/L (CDC, 2018b).

1.3 Sleep Disorder Assessment

The NHANES 2015-2016 "Sleep Disorders (SLQ_I)" dataset was used in this analysis. Questions were asked in the home by interviewers using a Computer-Assisted Personal Interview (CAPI) system. Several questions related to sleep patterns were asked, including usual sleep time on weekdays or workdays, usual wake time on weekdays or workdays, sleep hours, how often participants snore, snort, or stop breathing, if participants have ever told a doctor, they had trouble sleeping, and how often they feel overly sleepy during the day (CDC, 2018a). In our study, to determine if the participant had a sleep disorder, we used the NHANES variable SLQ050 (ever told a doctor or other health professional that you had trouble sleeping).

1.4 Covariates

We included covariates from social and demographic factors such as gender (male, female), race/ethnicity (Mexican American, other Hispanic, Non-Hispanic White, Non-Hispanic Black, Other Race-Including Multi-Racial), highest level of education (less than high school, high school graduate/GED or equivalent, some college or A.A. degree, college graduate or above), marital status (married, widowed/divorced/separated, never married, living with partner), family poverty-to-income ratio (<130%, 130% - 350%, >350%), moderate physical activity (yes, no), cotinine, BMI (underweight, normal weight, overweight, obese), and depression (yes, no). For demographic variables used in Table 1, the following data files were used: 2015-2016 Body Measures (BMX_I), Physical Activity (PAQ_I), Cotinine and Hydroxycotinine - Serum (COT_I), Mental Health - Depression Screener (DPQ_I), and Demographic Variables (DEMO_I). Other data files utilized in this study are Albumin and Creatine (ALB_CR_I), Arsenic Total Urine Special Sample (UTASS_I), and Speciated Arsenics-Urine Special Sample (UASS_I).

Creatinine (mg/dL), antimony (ug/L) and total urinary arsenic (ug/L) were all defined as continuous variables. Serum Cotinine (COT_I), a valid marker, was used to adjust for smoking. BMI was categorized
as underweight <18.5, normal weight 18.5-24.9, overweight 25-29.9, and obese ≥30 (CDC, 2003). Moderate physical activity was assessed by questionnaire, which asked participants, “In a typical week do you do any moderate-intensity sports, fitness, or recreational activities that cause a small increase in breathing or heart rate such as brisk walking, bicycling, swimming, or volleyball for at least 10 minutes continuously?”. The responses were yes and no (CDC, 2017b). The poverty-to-income ratio (PIR) is determined annually using the poverty threshold determined by U.S. Department of Health and Human Services. PIR is the annual household income divided by the poverty threshold, categorized by < 130%, 130–350%, and >350% (Bailey et al. 2017). The Patient Health Questionnaire (PHQ-9), a nine-question screening tool, was used to assess for depression. The questionnaire determines the frequency of depression symptoms with a score placed on the frequency of each symptom over the previous 2 weeks. Scores range from 0 to 3 as follows: 0: “not at all,” 1: “several days,” 2: “more than half the days,” or 3: “nearly every day.” The maximum score is 27; depression was defined as a score of ≥ 10.

1.5 Statistical Analyses

Survey design procedures were used to create weighted analysis, which incorporated sampling design stratification and clustering procedures. To assess the distribution of participants’ demographic and socioeconomic status by trouble sleeping, descriptive statistics were used. Percentages were reported for the categorical predictors, and medians with interquartile ranges were written for the continuous variables. A bar-chart of the median levels of the six speciated urinary arsenic examined was plotted. The Wilcoxon-Mann-Whitney test was used to determine the differences between the underlying distributions of age, serum cotinine, creatinine, antimony and total urinary arsenic by trouble sleeping. In contrast, the chi-square test was utilized to assess the relationship between the categorical covariates and trouble sleeping.

Unadjusted logistic regression was used to compute odds ratios (ORs) and 95% confidence intervals (95% CI) for the association between urinary arsenic and sleep disorders. Multivariate logistic regression was used to calculate the 95% CI for the exposure-disease relationship of interest and ORs; potential confounders were controlled. Each independent arsenic variable had individual models run. In the bivariate analysis, confounders controlled for in the analyses that were significantly associated with trouble sleeping included race/ethnicity, age, serum cotinine, and depression. All analyses were computed using SAS® (version 9.4, Cary, NC) with p-value < 0.05 considered statistically significant.

Results:

We analyzed data on 1,611 participants aged ≥ 20 years. In Table 1, we present the distribution of participants’ sociodemographic and health-related characteristics by trouble sleeping. Most of the study participants were Non-Hispanic White (65.4%) and married (53.3%). Approximately 31.9% were at least college graduates, 47.9% were involved in moderate physical activity, 38.5% had a family poverty-to-income ratio >350%, and 40.8% were obese. Almost one-third of the participants had a sleep disorder (30.0%), and only 7.0% were depressed. Of all the highlighted sociodemographic and health-related
factors, only age, race/ethnicity, and depression were statistically significantly associated with trouble sleeping. Individuals with a sleep disorder were more likely to be older, Non-Hispanic White, have higher serum cotinine, and be depressed.

Table 2 shows the distribution of select participants’ laboratory measures by trouble sleeping. There was a reasonable proportion of individuals at or above the detection limit and below the lower detection limit except for urinary arsenic acid. Only 1.9% of the participants had a level at or above the detection limit. Serum cotinine and urinary arsenous acid were the only measures that were significantly associated with trouble sleeping. Individuals with a sleep disorder were more likely to have higher serum cotinine and urinary arsenous acid below the lower detection limit. In Figure 1, we present the median levels of all the urinary arsenic examined. Urinary arsenous acid and urinary arslenocholine had the lowest medians of 0.08µg/L, while urinary dimethylarsinic acid had the highest median of 1.35 µg/L.

Table 3 shows the unadjusted odds ratios (OR), adjusted odds ratios (AOR), and 95% confidence intervals (95% CI) of the association between arsenic and trouble sleeping. Of all the urinary arsenic examined, only urinary arsenous acid (µg/L) was associated with a significantly higher risk of trouble sleeping in both the unadjusted and adjusted models. In the adjusted model, urinary arsenous acid (µg/L) was associated with a 47% higher odds of trouble sleeping (adjusted odds ratio (AOR: 1.47, 95% CI: 1.02, 2.11). Depression and age were the only covariates that were significantly associated with trouble sleeping in all the adjusted models (data not presented).

Discussion:

Our study assessed the association between speciated arsenic exposure and the risk of developing a sleep disorder among 1,611 US adults ages ≥ 20 years. We defined sleep disorder as trouble sleeping and found an association between high levels of urinary arsenous acid and sleep disorders. Other forms of speciated urinary arsenic were not associated with a sleep disorder. Previous studies investigated the relationship between arsenic and sleep troubles in the US population using NHANES datasets and occupational workers (Shiue, 2017; Lilis et al., 1985). Shiue (2017) conducted a study on the association between several environmental chemicals, including arsenic, and sleep disorders. The author found that trimethylarsine oxide was associated with wake-up at night and leg jerks while sleeping but did not find an association between other forms of speciated arsenic. Although Shiue (2017) analyzed NHANES data, the 2005–2006 dataset included different sleep variables compared to our study using the 2015–2016 NHANES dataset. In addition, the 2005–2006 dataset included trimethylarsine oxide, whereas the 2015–2016 dataset only included the other six speciated arsenics. Therefore trimethylarsine oxide was not available for analysis in our study. Lilis et al. (1985) determined that arsenic contributed relatively little to the total number of reported symptoms by copper smelter workers. However, there was an association between arsenic exposure and symptoms other than sleep disturbances including memory problems, depression, and paresthesia (Lilis et al., 1985). In another study among subjects with chronic arsenic exposure and arsenic-related skin lesions, sleep quality measured using the Pittsburgh Sleep Quality Index (PSQI) was not associated with hair arsenic concentration, pigmenary changes, or hyperkeratosis.
Furthermore, Mukherjee et al. (2003) studied neuropathy in arsenic toxicity from groundwater contamination in India. The neuropathic pain often interfered with patient’s activities of daily living, including causing insomnia. Both groups of arsenicosis patients studied, from different villages of India, identified sleep disorders (Mukherjee et al., 2003).

In our study, a positive statistical association was found between urinary arsenous acid, an inorganic type of arsenic acid, and sleep disturbance. Arsenic is metabolized to arsenous acid leading to trivalent arsenicals that bear higher cytotoxicity and genotoxicity than pentavalent analogs (Szekeres et al., 2018). Arsenous acid is an inorganic form of arsenic. Once ingested by humans, it is methylated to MMA and then to DMA (Steinmaus et al., 2009). The most prominent cause of health issues related to arsenic exposure are inorganic arsenicals (Kuivenhoven & Mason, 2020). Caldwell et al. (2009) determined that DMA and arsenobetaine contributed to the greatest amount the total urinary arsenic level in participants, using NHANES 2003–2004 data. Arsenous acid was detected in 4.6% of the participants (Caldwell et al., 2009).

Behavioral factors such as smoking, alcohol consumption, obesity, income, and marital status have been associated with sleep disorders (Grandner et al., 2015; Liu et al., 2013). Liu et al. (2013) determined a significant difference in BMI among participants with no sleep issues and participants with sleep disorders, with the average BMI lower for those with no sleep disorders compared to those with a sleep disorder. In our bivariate analysis, there was no significant difference in trouble sleeping among BMI categories (underweight, normal weight, overweight, obese). Grandner et al. (2015) found that a higher percentage of females had an insufficient sleep as compared to males. Sleep disturbance increased as income increased; those with some college and college had increased insufficient sleep measured by the number of days of insufficient sleep (Grandner et al., 2015). Our study did not find a significant difference among gender, education, marital status, poverty-to-income ratio (PIR), or activity level in those with sleep disorders and those without. However, there was a significant difference in race and ethnicity among those with sleep disorders. Ram et al. (2010) found using NHANES data that Hispanics and Whites reported longer sleep duration as compared to Blacks. Blacks had significantly higher rates of sleep apnea compared to Hispanics, but Whites had higher rates of sleep apnea than both Blacks and Hispanics (Ram et al., 2010). In this current study, non-Hispanic Whites had the highest rate of trouble sleeping, while Hispanics had the lowest.

In our study, we used the 2015–2016 NHANES population as a representative sample of the US population. Arsenic exposure was assessed through NHANES laboratory data using urine samples. Six types of speciated urinary arsenic were measured, and sleep disorder was assessed using self-reported questionnaire data. Studies on the adverse effects of arsenic and sleep disorders and other neurological deficits are recommended to understand how arsenic may affect sleep in humans.

**Strengths And Limitations:**
In our study, to determine the population with sleep disorders, we used the NHANES variable “ever told a doctor you had trouble sleeping.” This does not ensure that the subjects were given a medical diagnosis or had confirmation with clinical testing, but rather the patient self-reported a sleep issue. In addition, NHANES chooses the subjects and oversamples participants ≥ 60 years, Hispanics, and African Americans, resulting in a different sample composition than the entire US. We analyzed a cross-sectional survey, limiting us from determining a temporal association between arsenic and sleep disorders. Our study was the first to find a positive association between urinary arsenous acid and sleep disorders, defined by trouble sleeping, using NHANES data. The NHANES dataset provides a sampling of the US population, allowing us to apply our findings to a large population.

**Conclusion:**

Identifying factors that may affect sleep health is critical in preventing sleep disorders and their health effects. Our study found that urinary arsenous was significantly associated with sleep disorders in the US population. Due to the significant health consequences of sleep disorders, more studies, especially prospective studies, are recommended to investigate the role of arsenic toxicity in sleep disorders.

**Declarations**

**Ethics approval and consent to participate:** This study uses only secondary data analyses without any personal information identified using statistical data from the NHANES website, no further ethical approval for conducting the present study is required.

**Consent to Participate:** Consent was given by all the authors

**Consent for publication:** Consent was given by all authors.

**Authors’ contributions:** Humairat H. Rahman conceptualized the study and contributed to the introduction and discussion. Korede K. Yusuf conducted data analysis and contributed to the drafting of the paper. Danielle Niemann contributed to the methods section and drafting of the paper. All authors read and approved the final manuscript.

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**Competing interests:** The authors declare that they have no conflicts of interest.

**Availability of data and material:** NHANES data is secondary data provided by the CDC to the public (CDC/National Center for Health Statistics, 2020).

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Tables
Table 1
Selected demographic and health-related characteristics of the study sample by trouble sleeping status
NHANES 2015–2016

| Variable                        | Overall | Trouble Sleeping | No Trouble Sleeping | P-value |
|---------------------------------|---------|------------------|---------------------|---------|
| **Age (years)***                | 28.3    | 28.2             | 28.6                | < 0.001 |
| Gender                          | 0.09    |                  |                     |         |
| Male                            | 49.8    | 25.9             | 74.1                |         |
| Female                          | 50.2    | 29.5             | 70.5                |         |
| **Race/ethnicity**              |         |                  |                     | < 0.001 |
| Hispanic                        | 31.2    | 23.1             | 76.7                |         |
| Non-Hispanic White              | 34.1    | 34.4             | 5.6                 |         |
| Non-Hispanic Black              | 20.3    | 26.6             | 73.4                |         |
| Other Race- Including Multi-Racial | 14.4    | 23.3             | 76.7                |         |
| **Highest level of education**  | 0.14    |                  |                     |         |
| Less than high school           | 23.3    | 25.1             | 74.9                |         |
| High school graduate/GED or equivalent | 22.0    | 25.4             | 74.7                |         |
| Some college or AA degree       | 28.9    | 32.9             | 67.1                |         |
| College graduate or above       | 25.8    | 26.2             | 73.8                |         |
| **Marital Status**              | 0.11    |                  |                     |         |
| Married                         | 51.4    | 26.5             | 73.6                |         |
| Widowed/Divorced/Separated      | 20.1    | 35.2             | 64.8                |         |
| Never married                   | 17.9    | 25.6             | 74.4                |         |
| Living with partner             | 10.6    | 22.9             | 77.1                |         |
| **Family poverty-to-income ratio** | 0.56    |                  |                     |         |
| <130%                           | 37.2    | 28.1             | 72.0                |         |

*Median and interquartile range reported for continuous variables. P-values in bold are statistically significant at < 0.05.
| Weighted percentages (%) |
|---------------------------|
| 130–350%                  | 37.6 | 26.0 | 74.1 |
| >350%                     | 25.3 | 29.7 | 70.3 |
| **Moderate activity**     |      |      | 0.52 |
| Yes                       | 39.4 | 30.3 | 69.7 |
| No                        | 60.6 | 25.9 | 74.1 |
| **BMI**                   |      |      | 0.50 |
| Underweight               | 1.9  | 26.7 | 73.3 |
| Normal weight             | 24.8 | 26.9 | 73.1 |
| Overweight                | 33.3 | 25.1 | 74.9 |
| Obese                     | 40.0 | 30.1 | 69.9 |
| **Depressed**             |      |      | <0.001|
| Yes                       | 7.0  | 74.3 | 25.7 |
| No                        | 93.0 | 26.7 | 73.3 |

*Median and interquartile range reported for continuous variables. P-values in bold are statistically significant at < 0.05.
Table 2
Selected laboratory measures of the study sample by trouble sleeping status NHANES 2015–2016

| Variable                          | Overall n (%) | Trouble Sleeping n (%) | No Trouble Sleeping n (%) | P-value |
|-----------------------------------|---------------|------------------------|---------------------------|---------|
| Cotinine level (ng/ml)*           | 0.03 (4.53)   | 0.03 (52.30)           | 0.03 (2.06)               | 0.035   |
| Creatinine, urine (mg/dL)*        | 100.38 (105.93) | 97.55 (103.87)      | 102.64 (107.28)           | 0.929   |
| Antimony (µg/L)*                  | 0.04 (0.06)   | 0.04 (0.06)            | 0.04 (0.06)               | 0.9371  |
| Urinary arsenic, total (µg/L)*    | 5.57 (8.78)   | 5.50 (9.08)            | 5.65 (8.56)               | 0.755   |
| Urinary Arsenous acid (µg/L)      | < 0.001       |                        |                           |         |
| At or above detection limit       | 46.8          | 24.3                   | 75.7                      |         |
| Below lower detection limit       | 53.1          | 35.1                   | 24.9                      |         |
| Urinary Arsenic acid (µg/L)       | 1.9           | 34.5                   | 65.5                      | 0.5171  |
| At or above detection limit       | 1.9           | 34.5                   | 65.5                      |         |
| Below lower detection limit       | 98.1          | 29.9                   | 70.1                      |         |
| Urinary Arsenobetaine (µg/L)      | 0.2736        |                        |                           |         |
| At or above detection limit       | 45.3          | 31.8                   | 68.2                      |         |
| Below lower detection limit       | 54.7          | 28.5                   | 71.5                      |         |
| Urinary Arsenocholine (µg/L)      | 0.3500        |                        |                           |         |
| At or above detection limit       | 14.5          | 32.5                   | 67.5                      |         |
| Below lower detection limit       | 85.5          | 29.6                   | 70.4                      |         |
| Urinary Dimethylarsinic acid (µg/L) | 0.231        |                        |                           |         |
| At or above detection limit       | 66.7          | 29.3                   | 70.6                      |         |
| Below lower detection limit       | 33.2          | 31.4                   | 68.6                      |         |
| Urinary Monomethylarsonic acid (µg/L) | 0.053         |                        |                           |         |
| At or above detection limit       | 53.1          | 27.9                   | 72.0                      |         |

*Median and interquartile range reported for continuous variables. P-values in bold are statistically significant at < 0.05.
**Weighted percentages (%)**

| Below lower detection limit | 46.9 | 32.3 | 67.7 |

*Median and interquartile range reported for continuous variables. P-values in bold are statistically significant at < 0.05.*

**Table 3**

Unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (CI) of the association between arsenic and trouble sleeping NHANES III 2015–2016

| Speciated Urinary Arsenic                      | OR (95% CI)       | AOR (95% CI)    |
|------------------------------------------------|-------------------|-----------------|
| Urinary Arsenous acid (µg/L)                   | 1.69 (1.22, 2.32) | 1.47 (1.02, 2.11) |
| Urinary Arsenic acid (µg/L)                    | 0.81 (0.42, 1.59) | 1.35 (0.57, 3.17) |
| Urinary Arsenobetaine (µg/L)                   | 0.85 (0.63, 1.16) | 0.93 (0.65, 1.33) |
| Urinary Arsenocholine (µg/L)                   | 0.87 (0.65, 1.18) | 0.76 (0.51, 1.11) |
| Urinary Dimethylarsinic acid (µg/L)            | 1.10 (0.92, 1.32) | 1.15 (0.88, 1.51) |
| Urinary Monomethylarsonic acid (µg/L)          | 1.23 (0.97, 1.56) | 1.24 (0.93, 1.67) |

OR: Unadjusted odds ratio; AOR-adjusted odds ratio; CI: confidence interval. Estimates in bold are statistically significant at p-value < 0.05. Adjusted for age, serum cotinine (smoking status), race/ethnicity and depression.

**Figures**
Figure 1

Median Speciated Urinary Arsenic Levels of the study sample (µg/L), NHANES 2015–2016