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Association of hypothyroidism with low-level arsenic exposure in rural West Texas

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ABSTRACT

It has been reported recently that a higher airborne arsenic level was correlated with higher urinary arsenic concentration and lower serum thyroxin level among urban policemen and rural highway workmen in Italy. The current study was to determine whether exposure to low-level arsenic groundwater (2–22 μg/L) is associated with hypothyroidism among 723 participants (118 male and 267 female Hispanics; 108 male and 230 female non-Hispanic whites, NHW) living in rural West Texas counties. Arsenic and iodine levels in their groundwater used for drinking and or cooking were estimated by the inverse distance weighted (IDW) interpolation technique. Groundwater arsenic was ≥ 8 μg/L in 36% of the subjects' wells while iodine concentration was <1 μg/L in 91% of their wells. Logistic regression analysis showed that arsenic in groundwater ≥ 8 μg/L and cumulative arsenic exposure (groundwater arsenic concentration multiplied by the number of years living in the current address) but not groundwater iodine concentration were significant predictors for hypothyroidism among Hispanics ($p<0.05$) but not NHW after adjusting for covariates such as age, gender, annual household income and health insurance coverage. The ethnic difference may be due to a marginally higher percentage of Hispanics ($p=0.0622$) who lived in areas with groundwater arsenic ≥ 8 μg/L compared with NHW. The prevalence of hypothyroidism was significantly higher in Hispanics or NHW of this rural cohort than the national prevalence. Measures should be taken to reduce arsenic in drinking water in order to prevent hypothyroidism in rural areas.

1. Introduction

Hypothyroidism affects a large number of Americans. The prevalence of hypothyroidism ranges from 3.7% (Aoki et al., 2007) to 4.6% (Hollowell et al., 2002) in the U.S. population 12 years of age or older. The prevalence increases with age in U.S. adults: 5.5% among those aged between 50 and 79 years of age, 10% in those >65 years of age (Skukor and Fleseriu, 2014), and 12.1% in those ≥ 80 years of age (Aoki et al., 2007). Also, gender difference exists: the prevalence in women was 2–11 times as high as in men in iodine replete areas (Gopinath et al., 2010; Vanderpump, 2011). Hypothyroidism is a risk factor for diabetes mellitus, infertility, obesity, cardiovascular diseases, osteoporosis, depression, and hyperlipidemia among others (Sharma et al., 2013; Garber et al., 2012; Hollowell et al., 2002). The main cause of hypothyroidism world-wide is iodine deficiency (Garber et al., 2012). Autoimmune disease is the second most common cause of hypothyroidism world-wide (Dubbs and Spangler, 2014) with the presence of serum thyroid antibody (Surks and Hollowell, 2007). In the United States, however, autoimmune thyroid disease (Hashimoto's thryoiditis) is the most common cause of hypothyroidism (Dubbs and Spangler, 2014).

Several lines of evidence indicate that exposure to arsenic not only causes cancers, cardiovascular diseases, diabetes etc. (Christoforidou et al., 2013; Wang et al., 2014; Chen et al., 2013; Moon et al., 2013), but also disrupts the endocrine system including thyroid hormone (Naujokas et al., 2013). Specifically, low-dose arsenic disrupts thyroid-hormone-related gene expression in cell cultures (Davey et al., 2008). In human studies, Meeker et al. (2009) reported that higher serum arsenic is correlated with higher thyroid-stimulating hormone (TSH) levels in a dose-dependent manner among 219 clients of an infertility clinic, although such patients may not represent the general population. The

Abbreviations: USEPA, United States Environmental Protection Agency; As, arsenic; TWDB, Texas Water Development Board; IDW, Inverse Distance Weighted

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increase in TSH is likely a feedback mechanism for decreased thyroid hormones (T_3 or T_4) due to arsenic toxicity because arsenic inhibits enzymes for the synthesis of thyroid hormones (Palazzolo and Jansen, 2008; Meeker et al., 2009). Recently, Ciarrocca et al. (2012) reported that higher airborne arsenic level was associated with higher urinary arsenic, lower serum T_4, and higher serum TSH levels among urban policemen and rural highway workmen in Italy. However, a potential association between exposure to arsenic in groundwater and hypothyroidism has not been studied, which this proposal intends to determine. Gong et al. (2014) have recently reported that 22% of the wells sampled from subjects of Project FRONTIER, which is an ongoing longitudinal epidemiological study on rural residents in West Texas, had a directly-measured arsenic level higher than the maximum contaminant level (MCL) 10 μg/L set by the U.S. Environmental Protection Agency (USEPA, 2014). Well water arsenic levels in the majority of the Project FRONTIER participants have been estimated, which gives us an opportunity to determine whether hypothyroidism is associated with higher groundwater arsenic even at the low-level exposure defined as <50 μg/L (Schmidt, 2014) and whether the prevalence of hypothyroidism in these rural counties is higher than that of the US general population. Arsenic at high- (>150 μg/L) or moderate- (50–150 μg/L) levels in drinking water (Schmidt, 2014) have been shown to cause many diseases such as cancer, cardiovascular diseases and diabetes (Christoforidou et al., 2013; Wang et al., 2014; Chen et al., 2013; Moon et al., 2013). Recent studies have demonstrated that arsenic at low-levels in drinking water also cause such diseases (Gong and O'Bryan, 2012; Heck et al., 2009; Tsuji et al., 2014). Thus, it is particularly of interest to know whether arsenic at low-dose would be associated with hypothyroidism in this rural cohort.

2. Methods

2.1. Participants

The participants were from Project FRONTIER (Facing Rural Obstacles to healthcare Now Through Intervention, Education & Research), an ongoing longitudinal epidemiological study on rural residents in West Texas counties, Cochran, Palmer, Bailey and Hockley (O'Bryant et al., 2009). These counties are at the border of or adjacent to a geographic hot spot for groundwater arsenic (i.e., above the MCL) in the southwest part of the Texas Panhandle Plains. Project FRONTIER employed the community based participatory research approach, partnering with local county leaders, churches, and social groups. Recruitment methods include flyers and mail-outs, community presentations, telephone calls, snowball and door-to-door visits (O'Bryant et al., 2009). Criteria for participation in Project FRONTIER have been described elsewhere (O'Bryant et al., 2009). Briefly, all individuals 40 years or older living in one of the four West Texas counties Cochran, Bailey, Hockley and Parmer (Fig. 1) were eligible to participate. Each participant underwent standardized medical examinations, clinical laboratory examinations, neurocognitive testing, and a comprehensive medical history interview. Additional information is collected from an informant.

The participants of the current study were selected from the total of 1211 subjects currently enrolled in Project FRONTIER based on the following criteria: (1) having made a consensus diagnosis for the presence or absence of hypothyroidism; (2) having complete information for age, gender, ethnicity, annual household income, obesity status, insurance coverage and low-density lipoprotein (LDL); (3) having groundwater arsenic and iodine levels estimated by the inverse distance weighted (IDW) interpolation method (Gong et al., 2014). A total of 723 participants (118 male and 267 female Hispanics: 108 male and 230 female non-Hispanic whites, NHW) met the above criteria and were selected for this study. Other ethnic groups were not included due to small sample sizes. Institutional Review Board (IRB) approval was obtained for Project FRONTIER with each participant (or caregiver) providing written informed consent.

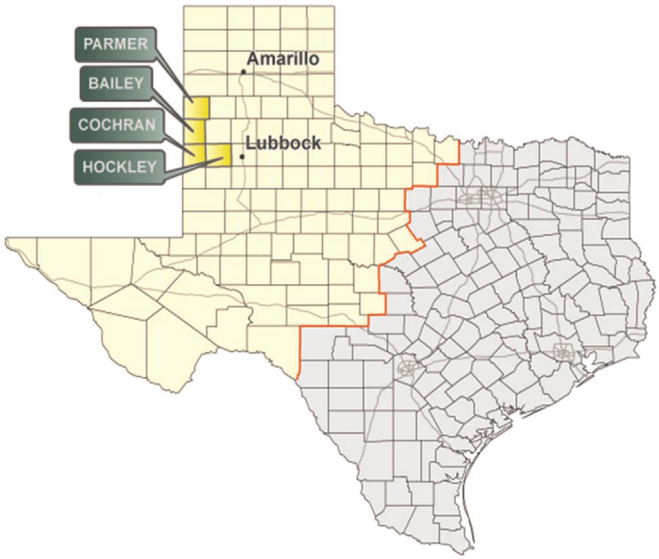

Fig. 1. Project FRONTIER Counties. Participants from Parmer, Bailey and Cochran are included in this study.

2.2. Diagnosis of hypothyroidism

Project FRONTIER has a Consensus Review Committee composed of clinicians and neuropsychiatric and other experts to make consensus diagnoses of diseases or health conditions. The diagnosis of hypothyroidism is based on (1) history of hypothyroidism made by subjects' doctors; (2) medications for treatment of hypothyroidism (excluding those due to surgery of Graves' disease); (3) blood tests results of free thyroxin ($T_4<5$ μg/L) and TSH >4.5 mIU/L (excluding secondary hypothyroidism); and (4) symptoms and signs. Symptoms and signs may include thin or brittle hair, dry skin, hypothermia, depression, peripheral edema, macroglossia, periorbital edema, and pretibial myxedema. These symptoms and signs are non-specific and were used only as supportive evidence. The T_4 and TSH ranges for the diagnosis of hypothyroidism made by subjects' doctors may vary (e.g. more stringent). Thus, if a subject did not meet the above criteria but had TSH >4.5 mIU/L then a diagnosis of hypothyroidism was made regardless of free T_4 levels in accordance with Aoki et al. (2007). There were two subjects with a history of goiters. One had a diagnosis of hypothyroidism and the other did not (with normal free T_4 and TSH levels).

2.3. Estimation of groundwater arsenic and iodine concentrations

We used the IDW interpolation technique to estimate groundwater arsenic and iodine concentrations. The estimated arsenic concentrations were correlated well with arsenic concentrations measured by the inductively coupled plasma mass spectrometry (ICP-MS) from well water samples donated by 198 subjects from our Project FRONTIER (Gong et al., 2014). All these subjects used well water for drinking and or cooking, including those who lived within their city limit. We obtained water quality reports from one of the cities, Morton (Cochran County), where public water supply is and has been from wells within the county