Comparison of hypertension and diabetes mellitus prevalence in areas with and without water arsenic contamination

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Background: Arsenic (As), one of the most significant hazards in the environment affecting millions of people around the world is associated with several diseases including cancers, Diabetes Mellitus (DM) and Hypertension (Htn). Drinking water contaminated with inorganic arsenic (iAs) is the primary route of exposure. This study was conducted to determine the difference in the prevalence of DM and Htn in areas with different levels of water contamination of As. **Materials and Methods:** In this analytic ecologic study, after measurement of As level in drinking water in all urban regions of Qazvin Province (Islamic Republic of Iran), two cities with As level of 20-30 μg/L and two with the As level <5 μg/L were selected as exposed and unexposed groups, respectively. Measuring the prevalence of above-mentioned diseases in the 30-60 year-old population of the said regions as total sampling, the results were statistically analyzed and compared. **Results:** The mean prevalence of Htn in exposed and unexposed areas were 7.09% and 3.73%, respectively and for DM were 4.53% and 1.99% in the said groups, respectively. There was a positive correlation between As level and Htn ($P < 0.001$) and between As level and DM ($P < 0.001$). **Conclusion:** High level of As in drinking water, even in the range of 20-30 μg/L has a relationship with increased prevalence of DM and Htn.

Key words: Arsenic, diabetes mellitus, drinking water, hypertension, prevalence

INTRODUCTION

Arsenic (As), one of the most significant hazards in the environment affecting millions of people around the world, is associated with several diseases. Drinking water contaminated with inorganic arsenic (iAs) is the primary route of exposure.[1] Natural groundwater As-contamination and the sufferings of people as a result has become a crucial water quality problem in many parts of the world. Most As compounds are odorless and tasteless and readily dissolve in water, which creates an elevated health risk. Ingesting food or water containing more than 0.01 mg/L of iAs is harmful to the body while an iAs content exceeding 60 mg/L can be fatal.[2] iAs exists in two valence states: iAs (III) and iAs (V), which trivalent As species are more toxic than pentavalent species, and organic forms are more toxic than inorganic forms. The metabolism of As almost certainly contributes to the adverse health effects seen in populations exposed to iAs.[3]

Arsenic exposure appears to be associated with the development of type II diabetes mellitus (DM). Chronic As exposure affects pancreas through damaging insulin secreting β-cells leading to insufficient insulin secretion, possibly through increased oxidative stress. This exposure also affects the liver and interfering with normal glucose metabolism leads to insufficient energy production. All of these consist the factors leading to DM in susceptible individuals.[4] Epidemiologic studies in Taiwan, Bangladesh and Sweden have demonstrated a diabetogenic effect of As.[5] Incidence and prevalence studies have found a dose-response relationship between exposure to As in drinking water and the risk of diabetes.[4]

Likewise, studies have found that As exposure increases the risk of developing hypertension (Htn). A study of Htn in Bangladesh found a dose-effect relationship between levels of As in drinking water and the prevalence of Htn; for a 50 mcg/L concentration of As in water, the risk of Htn was doubled when compared with unexposed individuals.[6] Recent evidence suggests that early life exposures to As may play a significant role in the onset of chronic adult cardiovascular diseases.[7]

This study was carried out to determine the difference in prevalence of DM and Htn in areas with different levels of water contamination with As.

MATERIALS AND METHODS

In this analytic ecologic study, 55 samples of drinking water of 55 different urban areas in Qazvin Province

(a province in North-West of Iran) were obtained to be measured for the level of As and this was carried out in the reference Laboratory of the Health Faculty of Tehran University of Medical Sciences and Health Services. Laboratory analysis was performed by means of the device of Inductively Coupled Plasma-Optical Emission Spectroscopy, model of Spectro arcos, made by Spectro Company in Germany. All water samples were obtained simultaneously in summer of 2010. Based on the "Iranian national water standards" considering the 5th revision of standards (No. 1053) about the physical features of drinking water (ICS[International Classification for Standards]: 13.060.020),[8] the permissible drinking water As the level is deemed ≤10 μg/L, which is consistent with the latest World Health Organization standards[9] as well, two urban areas with drinking water As level of more than twice of the maximum permissible level were selected as exposed areas and two other urban areas with less than half level of maximum permissible level (i.e., < 5 μg/L) were selected as unexposed groups. Selection of exposed and unexposed areas was with regard to the obtained results of water samples, which we assessed for As level as mentioned above. Two selected exposed areas were Mahmoodabad and Abegarm, with water As levels of 22.5 and 29.0 μg/L, respectively. Otherwise, two unexposed areas included Khorramdasht and Sharifieh, both with water As levels of 4.0 μg/L.

As a total sampling screening, all individuals in the age range of 30-60 years old, with the history of living of at least 5 years in the area, in the four cities of exposed and unexposed areas were screened for DM and Htn, by the health staffs of the regional health centers. Screening for DM was based on measuring fasting blood sugar (FBS) by means of Pars-Azmoon kits through, which the FBS ≥126 mg/dL in two separated tests was considered DM[10] and screening of Htn was through three separated times measuring blood pressure regarding all aspects of correct measurement and after resting for at least 15 min by means of ALPK2 mercurial device and expert health staffs through which the average of systolic and diastolic pressures equal to or more than 140 mmHg and 90 mmHg,[11] respectively were considered Htn.

Registered results were analyzed statistically by STATA software and $P < 0.05$ was considered significant. Logistic regression and correlation analyses were conducted to identify any association between variables.

RESULTS

Out of 15069 screened populations, including 6769 male and 8300 female in exposed and unexposed cities, 371 individuals (M:150, F:221) had Htn in exposed areas. On the other hand, there were 367 found hypertensive patients (M:140, F:227) in unexposed regions and the mean prevalence of Htn in exposed areas was 7.09% compared to 3.73% of the population in unexposed areas [Figure 1].

The details of distribution of Htn among exposed and unexposed populations and sex groups are shown in Table 1.

Positive correlation for Htn and DM between exposed and unexposed regions showed significant P value of less than 0.001 [Table 2].
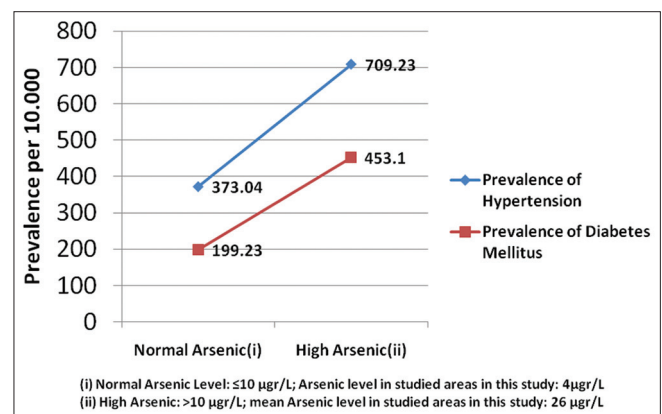

Figure 1: Comparison of prevalence (per 10,000) of hypertension and diabetes mellitus in two areas with normal and increased levels of arsenic in drinking water

Table 2: Correlation between arsenic and diseases (hypertension, diabetes mellitus) in total of population and each gender

Variables	Arsenic (total)	Arsenic	
		Male	**Female**
Hypertension	0.074	0.137	0.029
P value	0.001	0.001	0.009
Diabetes	0.065	0.087	0.047
P value	0.001	0.001	0.001

Table 1: Comparative mean prevalence of Htn and DM per 10,000 of exposed and unexposed population to high arsenic level of drinking water

Total screened			Known cases of Htn		Prevalence of Htn per 10,000		Known cases of DM		Prevalence of DM per 10,000	
15,069	Exposed population:5231	M:1633 F:3598	371	M:150 F:221	709.23	M:18.55 F:614.23	237	M:74 F:163	453.06	M:453.15 F:453.02
	Un-exposed population:9838	M:5136 F:4702	367	M:140 F:227	373.04	M:272.58 F:482.77	196	M:65 F:131	199.22	M:126.55 F:278.60

Htn=Hypertension; DM=Diabetic mellitus; F=Female; M=Male

Table 3: Logistic regression

Disease	Parameter	Co-efficient	SD error	T	P	95% CI
Hypertension	Arsenic	0.033	0.0038	8.67	0.001	0.025-0.04
	Gender	−0.0049	0.0036	−1.35	0.176	−0.012-0.002
	Constant	0.0399	0.0029	13.88	0.001	0.034-0.045
Diabetes mellitus	Arsenic	0.022	0.003	7.19	0.001	0.016-0.028
	Gender	−0.008	0.003	−2.69	0.007	−0.014 −0.002
	Constant	0.026	0.002	11.25	0.001	0.021-0.03

Htn=Hypertension; DM=Diabetic mellitus; CI=Confidence interval; SD=Standard deviation

The number of found patients of DM was 237 (M:74, F:163) in exposed population while there were 196 (M:65, F:131) in unexposed individuals. The mean prevalence rates of DM in exposed and unexposed regions were 4.53% and 1.99%, respectively [Figure 1].

Logistic regression showed that exposure to As and gender (women) had a positive effect on diabetes. Logistic regression also showed that exposure to As had a positive effect on Htn [Table 3].

DISCUSSION

Based on the results of this study, high level of As in drinking water, even in the range of 20-30 μg/L could affect the prevalence of Htn and DM significantly with $P < 0.001$ for both said diseases, comparing unexposed areas.

In similar studies, Rahman *et al.*, found a dose-effect relationship between levels of As in drinking water and the prevalence of Htn in Bangladesh that for a 50 μgr/L concentration of As in water, the risk of Htn was doubled when compared with unexposed individuals.[6]

Chien-Jen Chen *et al.*, studied 382 men and 516 women residing for long-term in villages where arseniasis was hyperendemic and found a 1.5-fold increase in age-and sex-adjusted prevalence of Htn compared with residents in non-endemic areas. The higher the cumulative As exposure, the higher prevalence of Htn was. This dose-response relation remained significant after adjustment for age, sex, DM, proteinuria, body mass index, and serum triglyceride level. The results suggested that long-term As exposure could induce Htn in humans.[12] Both studies confirmed our findings on the correlation of drinking water As level with Htn.

In another study, Chen *et al.*, evaluated the association between As exposure from drinking water and blood pressure using the baseline data of 10,910 participants in Bangladesh. A time-weighted well As concentration (TWA) based on current and past use of drinking wells was derived. Odds ratios for high pulse pressure (≥55 mmHg) by increasing TWA quintiles (≤8, 8.1-40.8, 40.9-91.0, 91.1-176.0, and 176.1-864.0 μg/L) were 1.00 (referent), 1.39 (95% confidence interval [CI]: 1.14, 1.71), 1.21 (95%

CI: 0.99, 1.49), 1.19 (95% CI: 0.97, 1.45), and 1.19 (95% CI: 0.97, 1.46). Regarding their results among participants with a lower than average dietary intake level of B vitamins and folate, the odds ratios for high pulse pressure by increasing TWA quintiles were 1.00 (referent), 1.84 (95% CI: 1.07, 3.16), 1.89 (95% CI: 1.11, 3.20), 1.83 (95% CI: 1.09, 3.07), and 1.89 (95% CI: 1.12, 3.20), the odds ratios for systolic Htn suggested a similar, but weaker association and no apparent associations were observed between TWA and general or diastolic Htn. They concluded that the effect of low-level As exposure on blood pressure is nonlinear and may be more pronounced in persons with lower intake of nutrients related to As metabolism and cardiovascular health.[13]

On the other hand, epidemiologic studies carried out in Taiwan, Bangladesh, and Sweden demonstrated a diabetogenic effect of As. This link has been observed in people drinking contaminated well water in Taiwan (Lai *et al.*, 1994; Tseng *et al.*, 2000, 2002) and Bangladesh (Rahman *et al.*, 1998, 1999), and in people working in copper smelters (Rahman and Axelson, 1995) and art glass industry (Rahman *et al.*, 1996) in Sweden.[5,14-20] Navas-Acien *et al.*, (2008) investigated the association of As exposure as measured in urine, with the prevalence of type 2 diabetes in a representative sample of US adults. Regarding the results of this study the prevalence of type 2 DM was 7.7%. after adjustment for risk factors and markers of seafood intake, participants with type 2 diabetes had a 26% higher level of total As (95% CI: 2.0-56.0%) than participants without type 2 DM. Total urine As was associated with increased prevalence of type 2 DM.[21]

Diaz-Villasenor *et al.*, confirming the association of chronic exposure to high concentrations of As in drinking water with increased risk for developing type 2 DM, through two separated researches defined its pathophysiologic mechanisms as impairing pancreatic β-cell functions, particularly insulin synthesis and secretion and directly effect in glucose homeostasis through the impairment of the expression of genes related to DM type 2. Regarding their conclusions, As affects insulin sensitivity in peripheral tissue by modifying the expression of genes involved in insulin resistance and shifting away cells from differentiation to the proliferation pathway. In the liver As disturbs, glucose

production, whereas in pancreatic beta-cells As decreases insulin synthesis and secretion and reduces the expression of antioxidant enzymes. The consequences of these changes in gene expression include the reduction of insulin secretion, induction of oxidative stress in the pancreas, alteration of gluconeogenesis, abnormal proliferation and differentiation pattern of muscle and adipocytes as well as peripheral insulin resistance.[22,23]

Otherwise, Chen *et al.*, found no association between As exposure from drinking water and DM, in their study in Bangladesh. In their study, which had showed results different from ours and many other similar studies, the researchers assessed the association between drinking water with As concentration <300 μg/L in different ranges of 0.1-8, 8-41, 41-91, 92-176 and ≥177 μg/L and some variables including total urinary As, or the composition of urinary As metabolites, glucosuria and HemoglobinA1c (HbA1c) level.[24] This difference may be due to a different type or valence state of present As in their water.

Regarding the results of this study and similar researches, we suggest routinely measurement of As level in drinking water in all urban and rural areas, especially where the incidence and prevalence of DM and Htn are high. This can lead to some interventions such as using appropriate treatment devices; through filtration processes, ion exchange, electrodialysis reversal and other appropriate methods to decrease As in drinking water to the desirable level by the related responsible organizations.

Limitations of the study

One of the most important limitations of our study was no As speciation because of laboratory limitations and its high expense. Although the health guidelines are based on total As concentrations, this speciation could help in assessment the results regarding the valence states. Since, we had selected similar case and control areas, in the socio-economic situation and life-style and because of the large number of sampling, we could ignore some other variables such as family history of diseases, body mass index in cases, life-style variables, occupation, net duration of As exposure, age and sex distributions and so on. Furthermore, this was an ecological study and we could not assess any association between individuals to establish strength of association. So, to avoid ecological fallacy, we analyzed data by correlation and regression. We suggest other researchers to design cohort study for further more evaluations.

ACKNOWLEDGMENTS

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