Original Article

Blood Pressure Associated with Arsenic Methylation and Arsenic Metabolism Caused by Chronic Exposure to Arsenic in Tube Well Water*

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Abstract

Objective The effects of arsenic exposure from drinking water, arsenic metabolism, and arsenic methylation on blood pressure (BP) were observed in this study.

Methods The BP and arsenic species of 560 participants were determined. Logistic regression analysis was applied to estimate the odds ratios of BP associated with arsenic metabolites and arsenic methylation capability.

Results BP was positively associated with cumulative arsenic exposure (CAE). Subjects with abnormal diastolic blood pressure (DBP), systolic blood pressure (SBP), and pulse pressure (PP) usually had higher urinary iAs (inorganic arsenic), MMA (monomethylated arsenic), DMA (dimethylated arsenic), and TAs (total arsenic) than subjects with normal DBP, SBP, and PP. The iAs%, MMA%, and DMA% differed slightly between subjects with abnormal BP and those with normal BP. The PMI and SMI were slightly higher in subjects with abnormal PP than in those with normal PP.

Conclusion Our findings suggest that higher CAE may elevate BP. Males may have a higher risk of abnormal DBP, whereas females have a higher risk of abnormal SBP and PP. Higher urinary iAs may increase the risk of abnormal BP. Lower PMI may elevate the BP. However, higher SMI may increase the DBP and SBP, and lower SMI may elevate the PP.

Key words: Arsenic; Arsenic methylation; Arsenic metabolism; Blood pressure; Drinking water

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INTRODUCTION

Arsenic is a ubiquitous trace element that is widely distributed in the environment. Groundwater used for drinking in many countries of the world is contaminated by naturally occurring arsenic[1-2]. The toxicity of arsenic in drinking groundwater has become a major problem worldwide[3]. Epidemiological studies have suggested that long-term exposure to arsenic in drinking water

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is associated with skin lesions, peripheral vascular disease, hypertension, black foot disease, and a high risk of cancer including skin, lung, bladder, liver, and possibly kidney cancer[4-16].

In general, the toxicity of arsenic depends on the chemical forms in which it is present in the environment and in the organism[17]. Arsenic-related health effects are correlated with arsenic exposure dose and exposure duration, arsenic compounds, arsenic metabolism, and arsenic methylation capacity. Steinmaus et al. (2010) reported that inter-individual differences in arsenic metabolism played an important role in arsenic-related disease[18]. Ahsan et al. (2007) suggested that arsenic metabolism and differences in urinary arsenic metabolites and their joint distributions usually affected arsenic toxicity[19]. Higher MMA% (monomethylated arsenic), lower DMA% (dimethylated arsenic), or lower DMA/MMA in urine was correlated with skin lesions, skin cancer, bladder cancer, peripheral vascular disease, muscle cramps, and structural chromosomal aberrations in peripheral lymphocytes[20]. A negative relationship between arsenic metabolism efficiency and the risk of skin lesion has been observed[21]. Higher MMA% in urine carries a greater risk of skin lesions[22]. Yang et al. (2015) suggested that MMA may have a greater toxic effect on hyperkeratosis, whereas DMA and iAs (inorganic arsenic, including As^{III} and As^{V}) may have a greater toxic effect on depigmentation or pigmentation[23]. Subjects with skin lesions may have lower arsenic methylation capacity than those without skin lesions[24].

In recent years, a few studies have been conducted to investigate chronic arsenic toxicity via drinking water consumption associated with hypertension. The results supported a role of environmental arsenic exposure in hypertension[25-27]. The risk of hypertension was usually influenced by arsenic exposure, arsenic methylation capacity, and the profile of arsenic metabolites in the urine. Positive correlations between long-term arsenic exposure and increasing blood pressure (BP) were observed[28-29]. Cumulative arsenic exposure (CAE) was positively associated with the prevalence of hypertension. Meanwhile, higher MMA concentrations in the urine may increase susceptibility to hypertension. Lower DMA% may be correlated with increasing hypertension[30]. Li et al. (2015) suggested that inefficient arsenic methylation capacity was associated with hypertension[31]. Osorio-Yáñez et al. (2015) also revealed that early-life exposure to iAs was significantly associated with higher BP[32]. However, Islam et al. (2012) indicated an association between higher levels of arsenic in drinking water or duration of exposure and pulse pressure (PP), but not hypertension[33]. More evidence should be provided to support the relationship between arsenic exposure and hypertension.

Therefore, the relationships between arsenic exposure, arsenic metabolism, arsenic methylation capacity, and BP were investigated for a cohort from Inner Mongolia, China. The main objective of the present study was to analyze the BP associated with CAE. The risk factors of abnormal BP were also investigated.

METHODS AND MATERIALS

Study Area and Subjects

The study was conducted in Hanghou County of Inner Mongolia, China. Populations living in this area mainly rely on groundwater for drinking and domestic use. Arseniasis caused by consumption of drinking groundwater containing high levels of naturally occurring arsenic has been reported[34]. The lowest prevalence of skin lesions in females and males were 8.1% and 15.6%, observed in the < 20-year age group. This value increased to 59.3% in the 51–60-year age group of for males[23]. In the present study, the highest arsenic concentration in groundwater was 824.70 μg/L.

The study setting was home-based. Residents who had lived in the study area for more than 10 years were considered as eligible subjects. Residents who had consumed seafood in the past week and who were taking anti-hypertensive drugs were excluded. Pregnant and breastfeeding women were also excluded. Finally, 560 residents, including 399 (71.25%) females and 161 (28.75%) males, were selected as study subjects. The demographic characteristics of the study subjects are listed in Table 1. Informed consent was read and signed by all subjects before performing a detailed interview. Information about demographic characteristics, socioeconomic status, cigarette smoking and alcohol consumption history, dietary habits, type of work, medical history, and education level attained were obtained by well-trained interviewers using a structured questionnaire. The measurement of standing height and body weight were conducted by trained physicians. Body mass index (BMI) was computed as weight in kilograms divided by height in

square meters. The results are represented in Table 1. The present study was conducted according to the Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects.

Sample Collection

Approximately 50 mL first-morning void urine was obtained from each subject in 100 mL polypropylene tubes. A total of 560 urine samples were collected. The collected urine samples were immediately kept in an icebox. Within 8 h, all the urine samples were transferred to the Inner Mongolia Center for Endemic Disease Control and Research in Hohhot and stored at -20 °C in a low-temperature refrigerator. Then, the urine samples were kept in an icebox and transported to the Laboratory of Arsenic Analysis in the Institute of Geographic Sciences and Natural Resources Research, CAS (Beijing, China), and stored in a low-temperature refrigerator for further analysis. Similarly, 50 mL of groundwater from tube wells used for drinking were collected from each of the studied households. Each family had their own well. Tube well water was pumped for approximately 5 min to collect water at the tip of the tap, and samples were then collected. The water samples were stored in clean 100-mL bottles at -20 °C in a low-temperature refrigerator.

Blood Pressure (BP) Measurement

BP was measured by trained clinicians using the standard protocol recommended by the World Health rganization[35]. Each subject's BP was measured three times with a mercury sphygmomanometer in a sitting position after rest for at least 15 min. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were defined at the first and fifth Korotkoff sounds, respectively. The average value of the three measurements was taken as the proper value. An abnormal BP was defined as an average SBP ≥ 140 mmHg, or an average DBP ≥ 90 mmHg. PP was calculated by deducting DBP from SBP. A PP (pulse pressure) ≥ 55 mmHg was considered abnormal[36].

Sample Procedure

A high-performance liquid chromatography/ hydride generator (HPLC) was used to separate arsenic species in urine[37]. The concentrations of iAs, MMA, and DMA in urine samples were determined by inductively coupled plasma mass spectrometry (ICP-MS). Total arsenic content in drinking water was determined by HPLC and ICP-MS. The detection limit of this method for arsenic species was 1 ng. A standard reference material containing 1000 mg/L iAs, MMA, and DMA (National Center for Standard Reference Materials) was used to check the validity of urinary arsenic species measurement. The reliability of arsenic species determination was evaluated in terms of the analytical recovery rate for added arsenic species. The recovery rate was 83%-94% for iAs, 91%-97% for MMA, and 90%-102% for DMA.

Table 1. The Characteristics of the Study Subjects

Variables	The Arsenic Levels in Drinking Water			
	≤ 10 μg/L	10-100 μg/L	100-300 μg/L	> 300 μg/L
Age	38.24	39.60	34.69	39.21
Gender				
Female (*n* = 399)	79 (69.91%)	127 (83.01%)	115 (64.97%)	78 (66.67)
Male (*n* = 161)	34 (30.09%)	26 (16.99%)	62 (35.03%)	39 (33.33)
Smoking				
Smoker	39 (34.51%)	39 (25.49%)	61 (34.46%)	43 (36.75%)
Non-smoker	74 (65.49%)	114 (74.51%)	116 (65.54%)	74 (63.25%)
Alcohol				
Drinker	8 (7.08%)	13 (8.50%)	29 (16.38%)	21 (17.95%)
Non-drinker	105 (92.92%)	140 (91.50%)	148 (83.62%)	96 (82.05%)
BMI				
< 18.5	8 (7.08%)	4 (2.62%)	8 (4.52%)	9 (7.69%)
18.5-25	72 (63.72%)	109 (71.24%)	130 (73.45%)	63 (53.85%)
> 25	33 (29.20%)	40 (26.14%)	39 (22.03%)	45 (38.46%)

Statistical Methods

CAE was assessed for each subject according their detailed water consumption history, exposure duration (years), and the number of days each subject stayed at home in each year. Lifetime CAE was defined as $C \times W \times Y \times D/1000$ mg/L, where C is the arsenic concentration (μg/L) in the drinking water, W is the daily water consumption, Y is the exposure duration (years), and D is the number of days each subject stayed in the local home in each year.

Total arsenic concentration in urine (TAs) was the sum of arsenic metabolites, i.e., iAs + MMA + DMA. The arsenic methylation indices were defined as the percentages of respective arsenic species in urine. Therefore, the primary methylation index (PMI) was calculated as the ratio between MMA + DMA and TAs, and the secondary methylation index (SMI) was calculated as the ratio between DMA and MMA + DMA[38].

The Student's *t*-test and ANOVA were applied to evaluate the differences in urinary arsenic metabolites between the groups. A linear regression model was performed to analyze the relationships between BP (SBP, DBP, and PP) and CAE. Logistic regression models were further applied to estimate the multivariate-adjusted odds ratios (*OR*s) and their 95% confidence intervals (*CI*s) for the risk of abnormal BP. The models were constructed by the various arsenic metrics individually tested with adjustment for age, sex, BMI, etc.

In this study, all statistical analyses were performed using SPSS 18.0 software and Microsoft Excel 2007.

RESULTS

Blood Pressure

The BP, including SBP, DBP, and PP, is listed in Table 2. It can be seen that the DBP, SBP, and PP were significantly different among the age groups. The values usually increased with age. The SBP and DBP varied slightly between males and females, whereas males had obviously higher PP than females. The SBP, DBP, and PP were significantly increased with the BMI of the study subjects. The DBP was considerably higher for smokers than for non-smokers, and the values of SBP and PP were slightly higher for smokers. The DBP, SBP, and PP varied slightly between drinkers and non-drinkers. Moreover, the DBP, SBP, and PP were usually higher in subjects with skin lesions than in those without skin lesions. Among subjects exposed to different levels of arsenic in drinking water, the DBP and SBP varied greatly, while the PP varied slightly. Subjects who were exposed to arsenic levels in the range of 10-100 μg/L in drinking water had the highest DBP and SBP.

Arsenic Metabolites and Methylation

The concentrations and proportions of arsenic metabolites and the arsenic methylation capacity index are displayed in Table 3. The concentrations of iAs, MMA, DMA, and TAs in the urine of subjects with DBP higher than 90 mmHg were 59.32, 52.44, 228.08, and 339.44 μg/L, respectively, whereas the values for subjects with DBP lower than 90 mmHg were 49.97, 44.17, 187.55, and 281.09 μg/L, respectively. Similarly, subjects with SBP higher than 140 mmHg had higher urinary contents of iAs, MMA, DMA, and TAs than subjects with SBP lower than 140 mmHg. In addition, higher urinary concentrations of iAs, MMA, DMA, and TAs were observed for subjects with PP higher than 55 mmHg.

The table also shows that the iAs%, MMA%, and DMA% in urine varied slightly between subjects with abnormal BP (DBP and SBP higher than 90 and 140 mmHg, respectively) and with normal BP (DBP and SBP lower than 90 and 140 mmHg, respectively). Moreover, the iAs%, MMA%, and DMA% in urine were similar between subjects with normal and abnormal PP. The primary and secondary arsenic methylation capacity were slightly higher in subjects with abnormal PP than in those with normal PP, according to the PMI and SMI.

Relationships between Blood Pressure and Cumulative Arsenic Exposure

Figure 1 represents the relationships between blood pressure and cumulative arsenic exposure. The results indicated that positive correlations were observed between CAE and DBP, CAE and SBP, and CAE and PP.

ORs Estimates of Hypertension

The *ORs* for abnormal DBP, SBP, and PP for the concentrations and proportions of urinary arsenic speciation, arsenic methylation capacity, and skin lesion status are listed in Tables 4-6.

Table 4 shows that subjects with skin lesions had a higher risk of abnormal DBP than those without skin lesions (*OR*: 1.630, 95% *CI*: 1.082, 2.455). After

Table 2. Blood Pressure for the Study Subject

Items	DBP	SD	SBP	SD	PP	SD
Age						
< 30	76.82	7.67	120.32	9.99	43.52	5.56
30-50	84.91	11.35	129.07	16.06	44.16	8.19
> 50	89.93	14.57	137.64	22.40	48.09	10.93
P (ANOVA)	< 0.0001		< 0.0001		< 0.0001	
Gender						
Male	83.49	12.52	128.65	18.22	45.17	8.96
Female	83.66	11.06	127.12	14.28	43.73	6.46
P (*t*-test)	0.879		0.292		0.034	
BMI						
< 18.5	75.75	9.54	118.82	12.22	43.09	5.26
18.5-25	82.45	11.64	126.74	16.67	44.41	8.21
> 25	89.01	11.83	135.17	17.50	46.19	9.36
P (ANOVA)	< 0.0001		< 0.0001		0.025	
Smoking						
Y	85.44	10.90	129.99	15.71	44.79	8.23
N	82.79	12.49	127.51	17.69	44.74	8.38
P (*t*-test)	0.020		0.126		0.951	
Alcohol						
Y	84.84	9.21	129.10	13.20	44.19	6.90
N	83.37	12.43	128.10	17.63	44.83	8.50
P (*t* -test)	0.364		0.664		0.568	
Skin lesion						
With	85.28	11.83	129.99	17.75	44.91	9.12
Without	82.75	12.17	127.41	16.88	44.69	7.97
P (*t*-test)	0.022		0.100		0.773	
As content (μg/L)						
< 10	84.32	11.46	129.12	16.30	44.86	8.02
10-100	85.29	13.35	130.37	18.81	45.09	9.31
100-300	81.51	10.63	125.14	14.26	43.60	6.54
> 300	83.55	12.81	129.14	19.27	45.97	9.51
P (ANOVA)	0.034		0.033		0.105	

Table 3. Urinary Arsenic Metabolites and Methyllation Capacity Index of the Subjects

Variables	DBP			SBP			PP		
	> 90 mmHg	< 90 mmHg	*P*	> 140 mmHg	< 140 mmHg	*P*	> 55 mmHg	< 55 mmHg	*P*
iAs	59.32	49.97	0.195	54.80	51.50	0.668	56.48	51.60	0.612
MMA	52.44	44.17	0.210	49.95	45.17	0.472	45.65	46.16	0.950
DMA	228.08	187.55	0.075	221.47	191.04	0.274	208.00	195.56	0.683
TAs	339.44	281.09	0.091	325.76	287.11	0.350	310.12	292.67	0.705
iAs%	15.81	15.74	0.933	14.78	16.00	0.163	14.78	15.88	0.313
MMA%	13.89	14.13	0.613	13.57	14.19	0.214	13.91	14.09	0.781
DMA%	70.30	70.13	0.867	71.65	69.81	0.088	71.30	70.03	0.399
PMI	0.84	0.83	0.933	0.85	0.84	0.193	0.85	0.84	0.313
SMI	0.83	0.83	0.527	0.84	0.83	0.092	0.84	0.83	0.512

adjusting for gender, age, smoking, alcohol consumption and BMI, the *OR* was 0.881 (95% *CI*: 0.553, 1.403). The crude *ORs* (95% *CI*) of urinary concentrations of iAs, MMA, DMA, and TAs for the risk of abnormal DBP were 1.002 (0.999, 1.004), 1.002 (0.999, 1.005), 1.001 (1.000, 1.002), and 1.000 (1.000, 1.001), respectively. The *P* values of the trend were 0.1997, 0.187, 0.077, and 0.093. However, the adjusted *ORs* were 1.002 (0.999, 1.005), 1.001 (0.997, 1.004), 1.000 (0.997, 1.001), and 1.000 (1.000, 1.001), respectively. Moreover, the

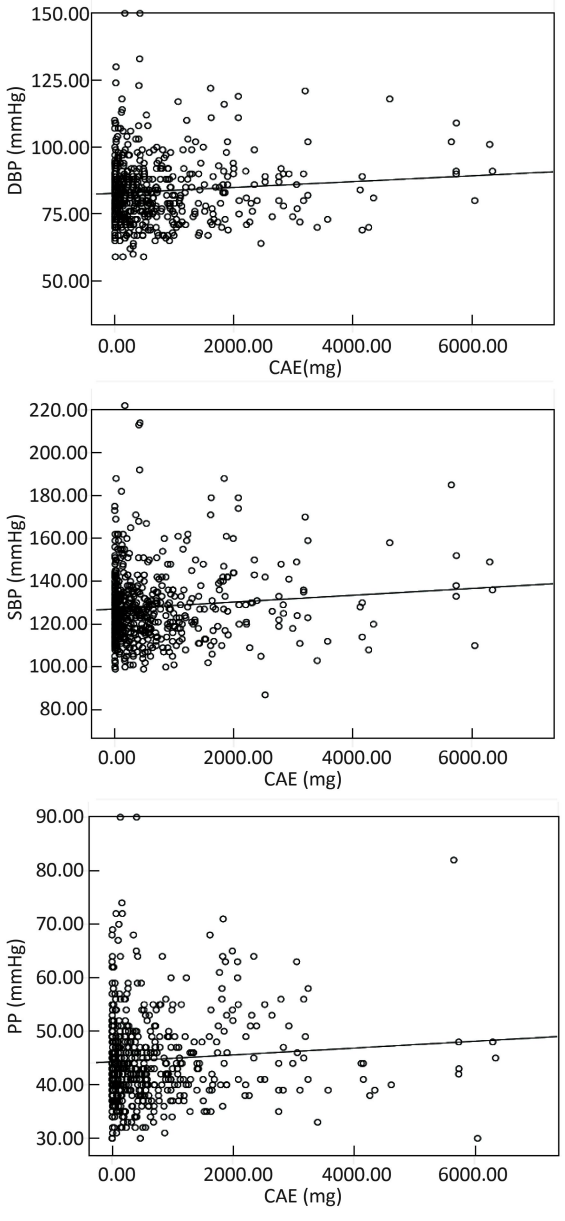

Figure 1. The relationships between blood pressure and cumulative arsenic exposure.

risk of abnormal DBP was positively related to iAs% (crude *OR*: 1.001, adjusted *OR*: 1.033), DMA% (crude *OR*: 1.002, adjusted *OR*: 0.989), and SMI (crude *OR*: 1.011, adjusted *OR*: 1.023).

Table 5 presents the *ORs* of arsenic metabolites for the risk of SBP. The table indicates that positive correlations were observed between SBP and skin lesions (crude *OR*: 1.774, 95% *CI*: 1.151, 2.735; adjusted *OR*: 0.931, 95% *CI*: 0.563, 1.541), iAs (crude *OR*: 1.001, 95% *CI*: 0.998, 1.003; adjusted *OR*: 1.002, 95% *CI*: 0.998, 1.005), iAs% (crude *OR*: 0.980, 95% *CI*: 0.953, 1.008; adjusted *OR*: 1.026, 95% *CI*: 0.996, 1.062), DMA% (crude *OR*: 1.020, 95% *CI*: 0.997, 1.042; adjusted *OR*: 0.996, 95% *CI*: 0.970, 1.023), PMI (crude *OR*: 1.020, 95% *CI*: 0.992, 1.050; adjusted *OR*: 0.974, 95% *CI*: 0.942, 1.008), and SMI (crude *OR*: 1.030, 95% *CI*: 0.995, 1.067; adjusted *OR*: 1.029, 95% *CI*: 0.988, 1.072).

The associations between PP and arsenic metabolites are listed in Table 6. The crude *ORs* for skin lesions, iAs, iAs%, PMI, and SMI were 1.046 (95% *CI*: 0.595, 1.837), 1.001 (95% *CI*: 0.997, 1.004), 0.982 (95% *CI*: 0.947, 1.017), 1.046 (95% *CI*: 0.595, 1.837), 1.019 (95% *CI*: 0.983, 1.056) and 1.014 (95% *CI*: 0.972, 1.059), while their adjusted *ORs* were 0.626 (95% *CI*: 0.334, 1.173), 1.003 (95% *CI*: 0.999, 1.006), 1.027 (95% *CI*: 0.990, 1.067), 0.973 (95% *CI*: 0.595, 1.837), and 0.993 (95% *CI*: 0.946, 1.044), respectively.

DISCUSSION

In this study, relationships between chronic arsenic exposure and BP were demonstrated. Subjects' BP was significantly elevated with increasing age and BMI. Subjects with skin lesions had higher SBP and DBP than those without skin lesions, indicating that SBP and DBP may be positively related to skin lesions. Therefore, subjects who suffer from skin lesions may have a higher risk of abnormal BP.

No positive relationships between SBP, DBP, and arsenic concentration in drinking water were found. However, the results of linear regression showed that the SBP, DBP, and PP were positively associated with CAE from drinking water. Higher CAE usually increased the SBP, DBP, and PP. Jiang et al. (2015) suggested that long-term arsenic exposure may accelerate the age-related increase in BP[29]. High CAE was positively associated with the prevalence of abnormal BP[30]. Osorio-Yañez et al. (2015) also revealed that long-term arsenic exposure significantly

increased DBP and SBP. Long-term arsenic exposure implied a higher level of CAE[32]. The results of the present study were consistent with previous studies.

DBP > 90 mmHg and SBP > 140 mmHg were defined as abnormal BP. PP > 55 mmHg was also considered as abnormal PP. The arsenic methylation capacity, arsenic concentrations, and percentages of arsenic metabolites in the urine of abnormal and normal BP subjects were compared. Higher urinary contents of iAs, MMA, and DMA were observed in subjects with abnormal BP, indicating that the subjects ingested higher amounts of arsenic. Total arsenic concentration in the urine was positively associated with DBP and SBP[32]. Subjects with abnormal BP usually had higher DMA%, whereas subjects with normal BP had higher iAs% and MMA%. Meanwhile, the PMI and SMI suggested that

Table 4. The Relationship between Urinary as Levels and DBP in Study Subjects

Variables	Crude *ORs*			Adjusted *ORs*		
	OR	95% *CI*	*P*	*OR*	95% *CI*	*P*
Gender	1.247	0.816, 1.906	0.307	2.316	1.225, 4.379	0.010
Age	1.075	1.055, 1.095	0.000	1.077	1.054, 1.100	0.000
Smoke	0.665	0.437, 1.013	0.058	1.642	0.916, 2.945	0.096
Alcohol	0.874	0.478, 1.601	0.663	1.430	0.662, 3.088	0.362
BMI	1.162	1.104, 1.223	0.000	1.110	1.054, 1.169	0.000
Skin lesions	1.630	1.082, 2.455	0.019	0.881	0.553, 1.403	0.594
iAs	1.002	0.999, 1.004	0.197	1.002	0.999, 1.005	0.216
MMA	1.002	0.999, 1.005	0.187	1.001	0.997, 1.004	0.761
DMA	1.001	1.000, 1.002	0.077	1.000	0.999, 1.001	0.437
TAs	1.000	1.000, 1.001	0.093	1.000	1.000, 1.001	0.410
iAs%	1.001	0.977, 1.025	0.933	1.033	1.003, 1.064	0.033
MMA%	0.989	0.949, 1.031	0.612	0.960	0.917, 1.006	0.087
DMA%	1.002	0.982, 1.022	0.865	0.989	0.966, 1.013	0.378
PMI	0.999	0.975, 1.023	0.933	0.968	0.940, 0.997	0.030
SMI	1.011	0.979, 1.043	0.516	1.023	0.986, 1.061	0.226

Table 5. The Relationship between Urinary as Levels and SBP in Study Subjects

Variables	Crude *ORs*			Adjusted *ORs*		
	OR	95% *CI*	*P*	*OR*	95% *CI*	*P*
Gender	0.607	0.367, 1.002	0.051	0.727	0.346, 0.971	0.400
Age	1.105	1.079, 1.131	0.000	1.107	1.079, 1.136	0.000
Smoke	0.744	0.474, 1.166	0.197	1.328	0.712, 2.477	0.372
Alcohol	1.161	0.584, 2.308	0.096	0.918	0.368, 2.289	0.854
BMI	1.169	1.108, 1.234	0.000	1.117	1.058, 1.179	0.000
Skin lesions	1.774	1.151, 2.735	0.009	0.931	0.563, 1.541	0.781
iAs	1.001	0.998, 1.003	0.668	1.002	0.998, 1.005	0.340
MMA	1.001	0.998, 1.004	0.472	1.000	0.997, 1.004	0.813
DMA	1.001	1.000, 1.001	0.211	1.000	0.999, 1.001	0.724
TAs	1.000	1.000, 1.001	0.295	1.000	1.000, 1.001	0.640
iAs%	0.980	0.953, 1.008	0.164	1.026	0.992, 1.062	0.129
MMA%	0.972	0.930, 1.016	0.214	0.955	0.907, 1.005	0.955
DMA%	1.020	0.997, 1.042	0.085	0.996	0.970, 1.023	0.758
PMI	1.020	0.992, 1.050	0.164	0.974	0.942, 1.008	0.129
SMI	1.030	0.995, 1.067	0.094	1.029	0.988, 1.072	0.167

the arsenic methylation capacity of subjects with abnormal BP was slightly lower than that of subjects with normal BP. Huang et al. (2007) found that subjects with hypertension had higher MMA% in urine and lower SMI than those without hypertension, indicating that arsenic exposure dose and arsenic methylation capacity impacts on the risk of hypertension[39]. Li et al. (2013) indicated that lower DMA% in urine may increase the risk of arsenic-induced hypertension[32]. In addition, Wang et al. (2011) revealed that arsenic methylation capacity may influence the incidence of hypertension[40]. However, Abhyankar et al. (2012) suggested that additional evidence should be obtained to evaluate the dose-response relationship between environmental exposure to arsenic and hypertension[25]. The evidence regarding the relationship between arsenic exposure and hypertension was limited in previous studies.

According to the results of logistic regression, positive correlations were observed between gender, age, smoking, alcohol consumption, BMI, and DBP. The results suggested that the risk of abnormal DBP was usually affected by gender, age, smoking, alcohol consumption, BMI, and DBP. Males had a higher risk of DBP than females. Higher contents of iAs and MMA in urine were associated with slightly increased DBP. iAs% and SMI were associated with DBP. Moreover, a negative correlation was found between PMI and DBP, whereas a positive relation was observed between DBP and SMI. The results indicated that lower primary arsenic methylation capacity may elevate the risk of high DBP.

The adjusted *ORs* suggested that gender was negatively associated with SBP. This indicated that males may have higher SBP than females. Smokers usually had a higher risk of high SBP than non-smokers and non-alcohol consumers. Age and BMI were positively correlated with SBP. Similarly, the concentration and percentage of iAs in urine were positively associated with SBP, indicating that a higher content of iAs and iAs% in urine increased the risk of high SBP.

The relationships between contents and percentages of arsenic in urine and abnormal PP were analyzed. The results suggested that the risk of abnormal PP was significantly higher for females than for males. Alcohol consumers usually had a higher risk of abnormal PP. BMI and age were positively correlated with the risk of abnormal PP. Moreover, higher iAs and iAs% in urine, as well as lower PMI and SMI, elevated the risk of abnormal PP, indicating that lower arsenic methylation capacity may increase the risk of abnormal PP.

Table 6. The Relationship between Urinary as Levels and PP in Study Subjects

Variables	Crude *ORs*			Adjusted *ORs*		
	OR	95% *CI*	*P*	*OR*	95% *CI*	*P*
Gender	0.327	0.152, 0.703	0.004	0.367	0.139, 0.971	0.044
Age	1.089	1.060, 1.118	0.000	1.084	1.054, 1.116	0.000
Smoke	0.753	0.431, 1.319	0.322	0.824	0.404, 1.679	0.594
Alcohol	2.746	0.835, 9.031	0.096	1.691	0.418, 6.838	0.461
BMI	1.079	1.025, 1.136	0.004	1.039	0.979, 1.104	0.208
Skin lesions	1.046	0.595, 1.837	0.876	0.626	0.334, 1.173	0.144
iAs	1.001	0.997, 1.004	0.612	1.003	0.999, 1.006	0.152
MMA	1.000	0.996, 1.004	0.950	1.000	0.996, 1.005	0.935
DMA	1.000	0.999, 1.001	0.682	1.000	0.999, 1.001	0.964
TAs	1.000	0.999, 1.001	0.705	1.000	1.000, 1.001	0.741
iAs%	0.982	0.947, 1.017	0.313	1.027	0.990, 1.067	0.156
MMA%	0.992	0.938, 1.049	0.781	0.998	0.938, 1.061	0.946
DMA%	0.992	0.938, 1.049	0.781	0.982	0.952, 1.013	0.251
PMI	1.019	0.983, 1.056	0.313	0.973	0.937, 1.010	0.182
SMI	1.014	0.972, 1.059	0.512	0.993	0.946, 1.044	0.793

In summary, age, gender, smoking, alcohol consumption, and higher BMI were usually associated with the risk of abnormal DBP, SBP, and PP. In terms of gender, males may have a higher risk of abnormal DBP, whereas females have a higher risk of abnormal SBP and PP. Higher iAs and iAs% in urine increased the risk of abnormal DBP, SBP, and PP. It appeared that iAs had a greater toxic effect on abnormal BP than MMA and DMA. Lower PMI was negatively related to higher DBP, SBP, and PP, suggesting that lower primary arsenic methylation capacity may elevate BP. In addition, a positive correlation was observed between SMI and DBP, and SMI and SBP, whereas a negative correlation was found between SMI and PP. This may indicate that higher secondary arsenic methylation capacity increases the risk of abnormal DBP and SBP, whereas lower secondary arsenic methylation capacity elevated the risk of abnormal PP.

CONCLUSIONS

Correlations among BP, arsenic exposure, and arsenic metabolism were investigated. The results revealed that BP was significantly influenced by gender, age, BMI, smoking, alcohol consumption, and BMI. DBP, SBP, and PP were positively correlated with CAE. Males may have a higher risk of abnormal DBP, whereas females may have a higher risk of abnormal SBP and PP. It seemed that iAs may have higher toxicity to abnormal BP than MMA and DMA. Lower primary arsenic methylation capacity may elevate BP. However, higher secondary arsenic methylation capacity may increase the risk of abnormal BP and SBP, whereas lower secondary arsenic methylation capacity may elevate the risk of PP.

CONFLICT OF INTEREST

We declare that we have no financial and personal relationships with other people or organizations.

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