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Mercury and selenium interactions in human blood in the Wanshan mercury mining area, China

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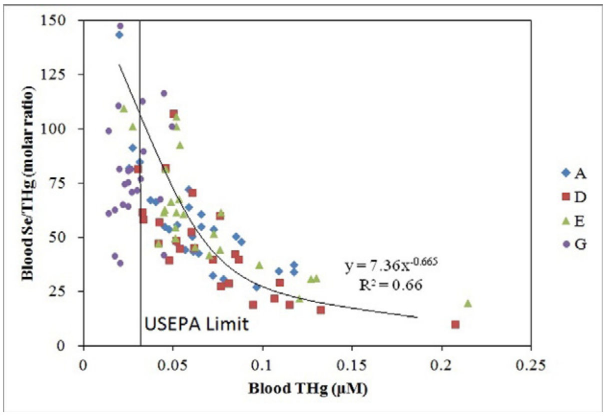
HIGHLIGHTS

- Residents living close to the mine waste heaps were exposed to Hg, Se, and As.
- 80.2% of blood THg level exceeded 5.8 μg/L and the blood Se levels were at the range of safe level.
- Rice consumption contributed 72.6% of total Se intake.
- The blood Se: THg and Se: MeHg molar ratio were higher than 1 and Se protected local residents suffering from Hg exposure.

GRAPHICAL ABSTRACT



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ABSTRACT

Human blood mercury (Hg), selenium (Se) and other trace element levels were investigated in the Wanshan mercury mining area. Residents living near the mine waste heaps had significantly elevated blood Hg, Se and arsenic (As) levels, which indicates the impact from Hg mining and smelting activities. Rice samples showed high Se levels, as 72.6% of total Se intake comes from rice consumption. The means of the Se:total Hg (THg) and Se:methyl Hg (MeHg) molar ratios were 60.7 ± 27.1 and 110 ± 53.6 respectively. Blood Se:Hg molar ratios were negatively correlated with blood Hg levels. 80.2% of the study population had blood THg levels that exceeded the 5.8 μg/L regulation level set by the USEPA, which indicated the risk of Hg exposure. On the other hand, the blood Se levels were within a safe-level range, and dietary Se intake protected local residents who suffered from Hg exposure.

1. Introduction

Humans may be exposed to both essential and toxic elements in food, air, soil and drinking water. In the general population, dietary

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intake is the main source of these essential and toxic elements. Tolerable intake levels have been set for many toxic elements in food, and recommended daily intakes have been established for nutrients. Concentrations of these essential and toxic elements in blood and urine can serve as good biomarkers of on-going exposure or body burden. Blood concentrations can reveal selenium (Se), methylmercury (MeHg) and lead (Pb) exposure (Cornelis et al., 1996).

MeHg is a potent toxicant (ATSDR, 1999; NRC, 2000; USEPA, 1997). The nervous system is the primary target organ for MeHg poisoning (Clarkson, 2002). In the general population, MeHg exposure occurs primarily through consumption of fish and marine mammals, which poses a particular challenge to public health because of its nutritional benefits. The maximum MeHg level in fish recommended by the Joint FAO/WHO Food Standards Programme CODEX Committee on Contaminants in Foods is 1.0 μg/g for predatory fish and 0.5 μg/g for other fishery products.

However, inconsistency of MeHg toxicity observed in different populations is commonly attributed to possible effects of dietary modulation. Most attention has been paid to the three major epidemiological studies on the development of children from New Zealand, the Faroe Islands and Seychelles, but the results of the three studies differed (Kjellstrom et al., 1986, 1989; Grandjean et al., 1997, 1998; Myers et al., 1995, 2003). A wide variety of foods and nutrients can alter MeHg metabolism and detoxify MeHg. Therefore, dietary information is important to examine the effects of MeHg exposure (Chapman and Chan, 2000). Selenium (Se) has protective effects observed in animal studies and has received the most attention as a potential protector against MeHg toxicity. Chen et al. (2006) found that Se may bind Hg through the selenol group, and its antioxidative properties help eliminate reactive oxygen species induced by Hg. Li et al. (2012b) confirmed that supplementation of organic Se significantly increased Hg excretion and protected against oxidative damage in Hg miners. Se can also decrease the oxidative stress induced by MeHg in rat brains (Sakamoto et al., 2013).

The Wanshan Hg mine was the largest Hg mine in China. Large scale Hg mining activities have resulted in serious Hg contamination of the local environment (Qiu et al., 2005). Hg and Se were the main metallogenic elements, while As, Sb, Pb and Zn were mineralization-associated elements (Hua and Cui, 1995). Rice can bio-accumulate high levels of MeHg in mercury (Hg) mining areas in Guizhou, Southwestern China (Horvat et al., 2003; Qiu et al., 2008; Zhang et al., 2010a). Rice consumption, rather than fish consumption, is the main route of human MeHg exposure in the Wanshan Hg mining area (Feng et al., 2008), Guizhou Province (Zhang et al., 2010b) and even inland areas of southern China (Li et al., 2012a). Se, Zn and Cd pollution was also observed in stream waters and rice paddy fields in the Wanshan Hg mine (Sovik et al., 2011; Zhang et al., 2014a).

This study is designed to evaluate levels of blood trace elements (Mn, Fe, Cu, Zn, As, Se, Cd, Hg, Pb) in the population of the Wanshan Hg mining area. Efforts were made to identify possible pathways of Se intake and its interaction with Hg.

2. Materials and methods

2.1. Study area

The Wanshan Hg mine was selected for this study. It is located in the eastern part of Guizhou Province and was the largest Hg mine in China. Large scale Hg mining was operated in the area for >50 years before the closure of mining activities in 2001, resulting in serious Hg contamination to the local environment.

Wanshan County consists of 5 towns, namely Wanshan, Huangdao, Xiaxi, Aozhai and Gaolouping and covers an area of approximately 338 km^2. The population in 2012 Wanshan County was 68,000, and the rural population constituted about 80% of the total population. The local economy is undeveloped, and the Per Capita Gross Domestic Product was 14,914 RMB (US Dollar 2400) in 2011, which was about half of the national average in China at that time.

2.2. Sample collection

Sampling was conducted in December 2012. A total of four sites in Xiaxi and Aozhai (A, D, E and G) were selected to survey in this study (Fig. 1). Descriptive statistics of the study population and rice consumption information are shown in Table 1. Participants were recruited based on the criteria that they had been local residents for >3 months. The recruitment strategy in the survey was to recruit 10–20% of the entire population at each site. All the participants participated voluntarily. The recruitment period lasted two days. A questionnaire was also conducted to obtain basic information on age, body weight, occupation, history of involvement of artisanal Hg mining activity, dental fillings, smoking and alcohol drinking habits, illness and the amount of daily rice consumption.

Venous blood samples (5 mL) were collected from each participant in prepared Ethylenediaminetetraacetic acid (EDTA) vacuum tubes. Blood samples were refrigerated at 4 °C during storage and kept on ice during shipping to the laboratory and then stored at −20 °C until analysis. Raw rice samples were collected from each participating household.

The present study obtained ethics approval from the Institute of Geochemistry, Chinese Academy of Sciences. All participants signed an informed consent lease before any data were obtained.

2.3. Analytical methods

Trace elements (Mn, Fe, Cu, Zn, As, Se, Cd, Hg, Pb) in the blood were determined by inductively coupled plasma mass spectrometry (Thermo Elemental X7, USA) after dilution with 0.1% HNO_3, 0.1% 2-mercaptoethanol and 0.1% Triton-X 100 (Wang et al., 2010). This method simplifies sample pretreatments with detection limits of 0.01–0.1 μg/L for all the elements. The determined trace element concentrations agreed with the certified values in certified reference materials (Seronorm Trace Elements Whole Blood L-2), and the recoveries were between 92.2% and 113% (Table 2). The relative percentage difference was lower than 10% for trace elements in blood duplicate samples.

The blood MeHg concentrations were adopted from our previous study (Li et al., 2015a). MeHg in the blood samples were digested using a KOH-methanol/solvent extraction technique and then measured using aqueous ethylation, purge, trap and GC-CVAFS detection (Brooks Rand MERX).

Total Se concentrations in the rice samples were determined by hydride generation atomic fluorescence spectrometry (AFS920, Jitian, China) following the procedure described in Zhu et al. (2008).

2.4. Calculation of modeled blood Se

A one compartment steady-state pharmacokinetic model was used to predict blood Se concentrations (Chien et al., 2003). The model for estimating turnover time is:

$$\tau = CpV_D/IF \qquad (1)$$

where τ is the reciprocal of the biological decay constant of Se (17 days, Mahapatra et al., 2001); Cp is the steady state concentration of Se in blood (μg/L); V_D is the apparent volume of blood in the body (estimated at 5.5 L); I is the Se intake through ingestion (μg/day), which can be obtained from multiplying the Se concentration in the rice by the amount of daily rice ingestion; and F is the uptake fraction into the blood through ingestion (estimated at 50%).

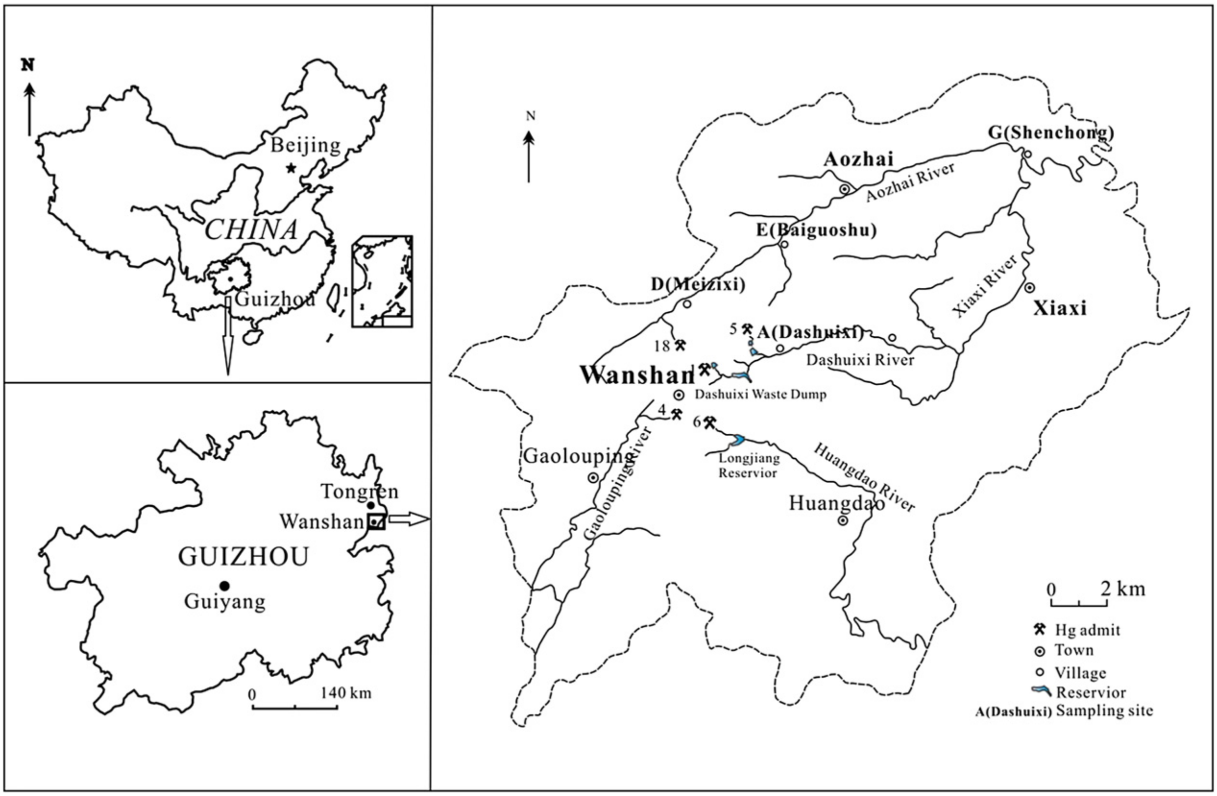

Fig. 1. Location of sampling sites in the Wanshan Hg mining area.

2.5. Data analysis

All data were analyzed by SPSS (Version 19, IBM, USA). The data were tested for normal distribution by the Kolmogorov-Smirnov test. If they were not normally distributed, the data were log transformed for further statistical analysis. The characteristics of the data are described in Mean ± Standard Deviation (SD) for normal distribution and Geometric mean for log normal distribution. Mean values of the data at different sites were compared using Analysis of Variance (ANOVA). Results of the statistical tests were considered statistically significant if $p < 0.05$.

3. Results and discussion

3.1. Trace elements profile

Concentrations of blood trace elements at different sites are summarized in Table 3. Site G was considered the control site in this study, and its blood trace element levels were comparable with those obtained from other control areas (Wu et al., 1996; Li et al., 2006; Lin, 2010; Zhang et al., 2011; Li et al., 2012c; Li et al., 2014; Zhang et al., 2015).

As shown in Table 3, the means of blood As, Se, THg and MeHg concentrations at sites A, D and E were significantly higher than those at site G (Table 3). Blood As levels at three sites (A, D and E) were also higher than the values determined by Li et al. (2012c) in the control area. Additionally, the average of blood Se at sites A, D and E were 243, 219 and 274 μg/L respectively, which were considerably higher than the value of 157 μg/L at site G and the value of 143 μg/L obtained at the background area (Wu et al., 1996). For blood THg and MeHg levels, our previous study indicated that the residents at site A, D and E, who are located in the upstream region, were seriously exposed to both IHg and MeHg, and the results showed a similar trend of reduction with increasing distance from the point-source of Hg contamination within the two catchments (Li et al., 2015a, 2015b).

The means of blood Fe, Cu and Mn concentrations at site A were significantly higher than those at site G, which resulted from Mn smelting in the upstream region. There were no significant differences between blood Pb, Zn and Cd concentrations among sites A, D, E and site G.

Hg and Se were the main mining elements in the Wanshan Hg mine, and As, Sb, Pb and Zn were the main mineralization-associated elements. Hg, Se and As significantly correlated with each other and were the main pollutants. High blood As, Se, THg and MeHg concentrations at site A, D and E resulted from environmental pollution caused by Hg

Table 1
Descriptive statistics of the study population and rice consumption information.

Site	Name	Population	n	Male	Female	Age (years)	Weight (kg)	Rice source			Rice ingestion rate (g/d)
								Local	Market	Mix	
A	Dashuixi	100	27	12	15	49.9 ± 12.8	54.6 ± 8.8	19	6	2	354 ± 110
D	Meizixi	150	25	11	14	54.9 ± 17.2	50.3 ± 9.6	25	0	0	436 ± 150
E	Baiguoshu	150	25	13	12	50.4 ± 15.2	58.4 ± 12.9	25	0	0	376 ± 142
G	Shenchong	200	24	13	11	52.3 ± 9.30	55.5 ± 8.6	17	7	0	500 ± 177
Total			101	49	52	51.8 ± 13.9	54.7 ± 10.4	86	13	2	416 ± 155

Table 2
List of determined value and recovery of trace elements in Seronorm Trace Elements Whole Blood L-2.

Elements	Determined value (μg/L)	Certified value (μg/L)	Recovery (%)
Mn	34.2	31.4	109%
Fe	306,000	332,000	92.2%
Cu	1270	1340	94.8%
Zn	7444	7100	105%
As	15.9	14.1	113%
Se	154	161	95.7%
Cd	5.31	5.01	106%
Hg	16.8	17.0	98.8%
Pb	333	337	98.8%

mining activities. In this study, we focused on Hg and Se exposure and their interactions.

3.2. Exposure route of Hg and Se

The local population had different exposure pathways of MeHg and inorganic Hg (IHg). Consumption of rice is the main route of human MeHg exposure (Feng et al., 2008), but both rice and vegetable consumption contributed to IHg exposure for local residents (Li et al., 2015b).

In this study, a significant positive correlation was found between blood Se and THg concentrations ($r^2 = 0.16$, $p < 0.001$) and between blood Se and MeHg concentrations ($r^2 = 0.087$, $p < 0.01$).

A comparison of rice Se concentrations at the different sites is shown in Fig. 2. The averages of the rice Se concentrations were 66.0 ± 19.7, 235 ± 156, 643 ± 496, 175 ± 151 ng/g for sites A, D, E and G respectively. The average of all the rice samples was 242 ± 277 ng/g with a geometric mean of 145 ng/g, which was significantly higher than the Guizhou average of 32.3 ng/g (Chen et al., 2002) and the national average of 25 ng/g (Li et al., 2005). Since rice is not considered a Se-enriched plant, high Se concentrations found in the study area may be the result of high Se concentrations in the soil. For populations that eat less fish (1.2 g/d for local residents), cereal may be the dominant Se source for humans. The mean Se concentration of regular rice in China was 25 ng/g, which is regarded as extremely low Se-containing rice (Chen et al., 2002; Zhen et al., 2008). Rice is the staple food for inhabitants in South China, and the contribution to Se intake from rice products is estimated to be 7.5–12.5 μg per day if the mean rice consumption of an adult was 300–500 g.

The modeled blood Se concentrations were calculated based on Se intake from rice consumption. A significant correlation ($r = 0.35$, $p < 0.001$) was observed between the modeled and the measured blood Se for all participants. Based on the slope of the regression equation (0.726), rice consumption contributed to 72.6% of total Se intake. These findings were comparable to results obtained by Zhang et al. (2014a, 2014b), which showed that rice (43%), meat (40%) and vegetables (8%) comprised the main routes of Se intake for Wanshan local residents.

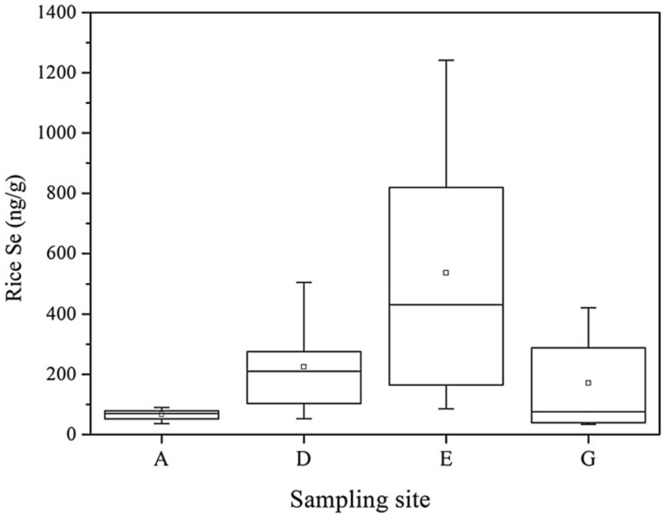

Fig. 2. Comparison of rice Se concentrations at different sites. Each box represents the interquartile range (25th and 75th percentile), the band near the middle of the box represents the 50th percentile (the median) and the whiskers represent the 5th and 95th percentiles.

3.3. Hg-Se interaction

Se:Hg molar ratio was considered an important value for risk assessment (Peterson et al., 2009; Sormo et al., 2011), which suggested that Se:Hg molar ratios above 1 indicate substantial protection against adverse Hg affects. MeHg-cysteine accounts for <1% of MeHg in whole blood (Clarkson and Magos, 2006); however, MeHg-cysteine can cross blood-brain barriers (Simmons-Willis et al., 2002; Clarkson and Magos, 2006), making it neurotoxic.

In this study, the means of the Se:THg and Se:MeHg molar ratios in human blood were 60.7 ± 27.1 and 110 ± 53.6 respectively. All blood samples had Se:THg and Se:MeHg molar ratios >10, which indicated less MeHg neurotoxicity. The major form of Se in blood is seleno-cysteine, which could form a stronger complex with MeHg than cysteine (Chen et al., 2006; Khan and Wang, 2009) and could make MeHg less available and less able to cross blood-brain barriers.

Fig. 3 showed Se:Hg molar ratios as a function of Hg molar concentrations in human blood. The Se:THg molar ratios negatively correlated with THg ($r = 0.68$, $p < 0.01$) while the Se:MeHg molar ratios negatively correlated with the MeHg levels ($r = 0.64$, $p < 0.01$). This significant negative correlation was also observed in dolphin blood (Hong et al., 2012), bird tissues (Burger et al., 2013), commercial fish from New Jersey and Illinois, USA (Burger and Gochfeld, 2013) and saltwater fish from the Aleutians Islands (Burger et al., 2012). The results indicated

Table 3
Statistical results of human blood trace elements at different sites (Mean ± SD, (Geomean)).

Element	A (n = 27)	D (n = 25)	E (n = 25)	G (n = 24)	Reference value	Threshold acceptable limit
Mn (μg/L)	10.1 ± 7.89 (8.26)[b]	8.38 ± 6.67 (7.04)	7.33 ± 2.60 (6.82)	5.88 ± 2.22 (5.52)	4.89 ± 2.67[d]	
Fe (mg/L)	433 ± 63.4 (429)[a]	396 ± 67.3 (390)	406 ± 54.1 (402)	364 ± 58.3 (360)	419 ± 43.5[e]	
Cu (μg/L)	798 ± 97.7 (793)[c]	763 ± 103 (756)	746 ± 106 (739)	732 ± 104 (725)	802[f]	
Zn (mg/L)	5.70 ± 1.01 (5.62)	5.46 ± 0.55 (5.43)	5.52 ± 0.87 (5.45)	5.91 ± 0.86 (5.85)	4.67[f]	
As (μg/L)	8.08 ± 1.13 (8.00)[a]	7.16 ± 0.66 (7.13)[a]	6.78 ± 0.55 (6.76)[a]	5.78 ± 0.63 (5.74)	5.48 ± 3.49[g]	
Se (μg/L)	243 ± 58.8 (237)[a]	219 ± 72.7 (209)[b]	274 ± 71.8 (265)[a]	157 ± 61.0 (149)	143.1 ± 47.8[h]	
Cd (μg/L)	3.03 ± 1.80 (2.55)	2.18 ± 2.28 (1.59)	2.57 ± 1.98 (2.12)	2.46 ± 1.54 (2.30)	2.44[i]	5[l]
THg (μg/L)[j]	12.5 ± 5.33 (11.4)[a]	14.7 ± 7.85 (13.1)[a]	13.9 ± 8.27 (12.3)[a]	5.28 ± 1.99 (4.95)		5.8[m]
MeHg (μg/L)[j]	6.73 ± 3.64 (5.87)[b]	7.93 ± 4.13 (7.00)[a]	6.64 ± 3.36 (5.99)[b]	3.83 ± 1.60 (3.56)		
Pb (μg/L)	49.2 ± 13.5 (47.3)	54.7 ± 18.7 (51.7)	48.8 ± 19.1 (45.4)	47.7 ± 14.5 (45.8)	46.2[k]	100[n]

a, $p < 0.001$, b, $p < 0.01$, c, $p < 0.05$, compared with G. d, Li et al., 2006; e, Zhang et al., 2011; f, Zhang et al., 2015; g, Li et al., 2012c; h, Wu et al., 1996; i, Lin, 2010; j, data from Li et al., 2015a, 2015b; k, Li et al., 2014; l, ACGIH, 1991; m, NRC, 2000; n, MOH, 2006.

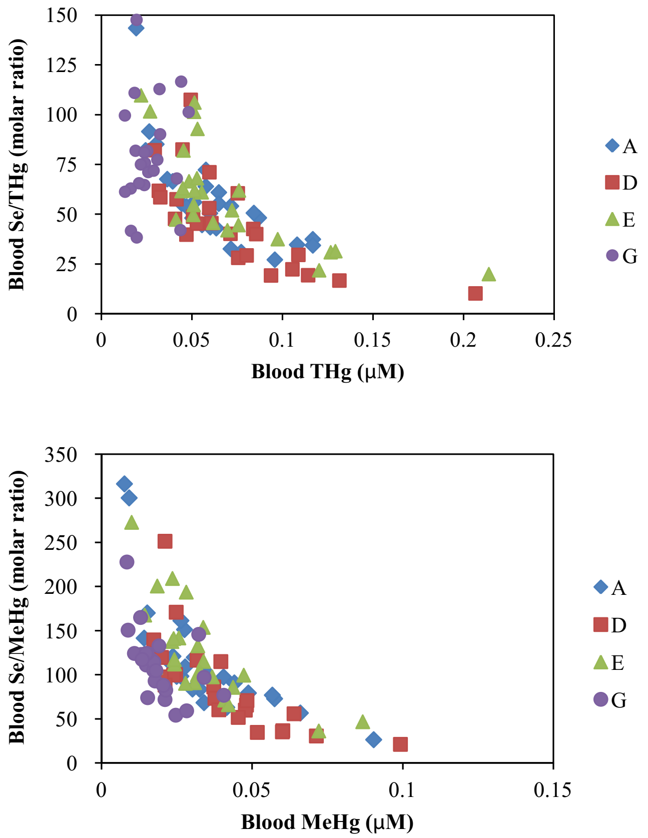

Fig. 3. Relationship between THg, MeHg and Se/Hg molar ratios in the blood.

that the Se:Hg molar ratio is an important index for Hg-Se interaction, and Se can attenuate the adverse effects induced by MeHg exposure.

3.4. Risk assessment

The blood THg level of 5.8 μg/L recommended by USEPA has been adopted for risk assessment of MeHg exposure on the developing fetus. In this study, 80.2% (81/101) of the study population had blood THg levels exceeding 5.8 μg/L, which indicated the study populations were at risk of Hg exposure.

The recommended dietary allowance (RDA) of Se for adults is 55 μg/day, and the tolerable upper limit (UL) of Se intake for adults is 400 μg/day in the USA (ATSDR, 1996). Modeled minimum and maximum blood Se levels were 85 and 618 μg/L respectively. Generally, the blood Se levels for the study populations were within a safe-level range.

Zhang et al. (2014a, 2014b) proposed a new criterion for Se/Hg exposure assessment, which is based on Se-Hg interactions and considers not only the toxicological consequences of Hg exposure but also the benefits and/or adverse effects of Se intake. The benefit-risk ratio (BRR) indicates health benefits if $1 < \text{BRR} < 1 + \nabla\text{Se}/\text{PDI}_{\text{Hg}}$, or it indicates health risks if $\text{BRR} < 1$ or $\text{BRR} > 1 + \nabla\text{Se}/\text{PDI}_{\text{Hg}}$ (∇Se represents a threshold value for Se poisoning which considers the protective effects from Hg exposure; PDI_{Hg} represents the probable daily intake of Hg). We calculated the index of BRR for all study populations, and all BRR indicates health benefits. The results indicated that dietary Se intake may protect local residents who suffer from Hg exposure in the Wanshan Hg mining area.

4. Conclusions

Residents living near the mine waste heaps revealed significantly elevated blood Hg, Se and As levels. Rice samples in the study area showed high Se levels, and rice consumption contributed to 72.6% of the total Se intake. 80.2% of the study population had blood THg levels exceeding 5.8 μg/L set by USEPA, which indicated that the study populations were at risk of Hg exposure. The blood Se levels were within a safe-level range, and dietary Se intake may protect local residents who suffer from Hg exposure.

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