Ecotoxicology and Environmental Safety xxx (xxxx) xxxx

Contents lists available at ScienceDirect

Ecotoxicology and Environmental Safety

journal homepage: www.elsevier.com/locate/ecoenv

Maternal inorganic mercury exposure and renal effects in the Wanshan mercury mining area, southwest China

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ARTICLE INFO

Keywords:
Wanshan mercury mining area
Maternal
Inorganic mercury exposure
Renal function

ABSTRACT

This study evaluated the relationship between urine mercury (UHg) concentrations and renal function (serum creatinine (SCr) and blood urea nitrogen (BUN)) in delivery women in the Wanshan mercury (Hg) mining area. Leishan County was selected as the control area. 165 and 65 maternal samples were collected from the Wanshan and Leishan area, respectively. The geometric means of UHg concentrations were 1.09 and 0.29 μg/L in Wanshan and Leishan subjects, respectively. Significant differences ($p < 0.01$) of UHg were observed between the two populations, indicating the potential risks of inorganic Hg exposure in the Wanshan population. The median (interquartile range) values of SCr were 69.1 (12.5) μmol/L and 46.0 (11.0) μmol/L for the Wanshan and Leishan populations, respectively, indicating significant differences ($p < 0.01$) between the two groups. However, no significant differences among BUN values for the two groups were observed. A significant positive correlation ($r = 0.385$, $p < 0.001$) was observed between UHg concentration and SCr in the study population. The odds ratio (OR) value of UHg in Wanshan area was 9.29 times higher than that in Leishan area (95% confidence interval (CI): 3.58–24.1). The OR value of SCr decrease in patients with low UHg was 0.32 times higher than that in patients with high UHg (95% CI: 0.19–0.55). The OR value of SCr decrease in the population with fish consumption was 0.71 times higher than that of the population without fish consumption (95% CI: 0.58–0.88). In conclusion, maternal IHg exposure caused impaired renal function and fish consumption may play a role in preventing Hg-induced nephrotoxicity.

1. Introduction

Mercury (Hg) is a non-essential element in the human body. It exists mainly in three forms in the environment: elemental Hg, inorganic Hg (IHg), and organic Hg (especially for methylmercury (MeHg)). The toxicity of Hg varies with its chemical form, dose, and frequency of exposure. MeHg is neurotoxic to human beings, while IHg is mainly nephrotoxic (Bjørklund et al., 2017; Ha et al., 2017). Different forms of Hg enter the human body via different pathways. MeHg is mainly ingested by fish or rice consumption (Mergler et al., 2007; Feng et al., 2008), while elemental Hg and IHg are mainly ingested through the digestive and respiratory tracts (World Health Organization, 1990; World Health Organization, 1991).

IHg is mainly excreted from the human body via urine and feces (Nordberg et al., 2014). The kidney is the main target organ for the excretion and accumulation of IHg, causing different degrees of kidney damage. IHg mainly damages the proximal tubules and glomeruli (Stacchiotti et al., 2009). The half-life of Hg in urine is approximately 40–80 days (Nordberg et al., 2014). Urine Hg (UHg) concentrations can reflect the Hg level in the kidneys; therefore, it is often used to evaluate the recent exposure of IHg in the human body. The most commonly used indicators of renal function include serum creatinine (SCr), uric acid, blood urea nitrogen (BUN), cystatin C, beta-2 microglobulin, alpha-1 microglobulin, urinary microalbumin, urinary albumin, and glomerular filtration rate (Al-Saleh et al., 2012). SCr and BUN can be used as markers of renal toxicity in Hg environment exposure (Li et al., 2013). Previous studies have indicated the renal toxicity of IHg at occupational exposure (Frankol et al., 2005). However, regarding the effects of long-term low-dose exposure to IHg on human kidney function, there is a lack of human epidemiological research, especially for pregnant women who are more susceptible than the general population.

Wanshan Hg mine was the largest Hg mine in China and it was closed in 2001. Long-term, large-scale Hg mining and smelting activities have resulted in serious environmental Hg pollution to

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https://doi.org/10.1016/j.ecoenv.2019.109987
Received 26 September 2019; Received in revised form 12 November 2019; Accepted 17 November 2019

surrounding ecosystems (Feng et al., 2008; Feng and Qiu, 2008). Highly elevated Hg levels have been found in mine waste calcines (Qiu et al., 2005), surface water (Zhang et al., 2010a, 2010b), riparian soils (Qiu et al., 2005; Yin et al., 2016), and ambient air (Dai et al., 2012). In addition, Hg mining activities have caused serious Hg enrichment in rice and other agricultural crops in the range of 10.3–1160 ng/g (Horvat et al., 2003; Qiu et al., 2008), which exceed the National Permitted Limit for THg in foods in China (20 ng/g; National Health and Family Planning Commission (NHFPC) & China Food and Drug Administration (CFDA), 2017). Dietary intake is the main pathway of IHg exposure, which has caused impairment of renal function for local adults (Li et al., 2015).

In the present study, parturient women in the Wanshan area were selected as the research subject and parturient women in the Leishan area as the control group. The aim of the paper is to explore the possible impairment of IHg exposure on renal function in parturient women and the possible influencing factors. The results obtained in this study can be used for advising risk assessment and risk control of human IHg exposure in Hg polluted area.

2. Materials and methods

2.1. Study area and subjects

Two hospitals (Wanshan County People's Hospital and Chadian Town People's Hospital) in the Wanshan Hg mining area were selected. Chadian is a town belongs to Wanshan County, which is about 15 km to the county center. In addition, Leishan County People's Hospital, which is 170 km away from Wanshan, was selected as the control (Fig. 1).

Recruit criteria of the subjects included that they were parturient at the hospitals and had lived in the study area for more than 6 months. Exclusion criteria included those who suffered from nephropathy, liver disease, cardiovascular disease, and hepatitis b.

2.2. Sample collection

Morning urine samples (5 mL) from the pregnant women were collected in a clean polyethylene tube and 10% concentrated HNO_3 (pure grade) was added to the samples to prevent Hg loss. All samples were stored at 4 °C and were then returned to the laboratory for Hg analysis. Venous blood samples (5 mL) were collected from each participant in prepared vacuum tubes without anticoagulant. Serum samples were obtained immediately by centrifugation with 3000 rpm for 10 min. The ethics of this study was approved by the Affiliated Hospital of Guizhou Medical University. All participants had read, comprehended, and signed informed consent forms to join the study.

Questionnaires were designed to be used during face-to-face surveys. The survey included basic information regarding age, weight, occupation, participation in Hg mining activities, dental treatment, smoking and drinking habits, disease history, fish consumption, and daily consumption of local rice. After the survey, the completeness and accuracy of the data were evaluated. The dataset was built with EpiData 3.1 and the data were double inputted and checked.

2.3. Basic information

The average age, height, and body weight of the study subjects were 24.7 ± 4.7 years, 154.7 ± 3.9 cm, and 63.1 ± 7.4 kg, respectively, as shown in Table 1. No significant differences in age, height, or body weight were observed between the two groups.

2.4. Analytical methods

The urine samples were digested with HNO_3 in a water bath (95 °C) and UHg concentrations were measured by $SnCl_2$ reduction and cold vapor atomic fluorescence spectrometry (Li et al., 2015). SCr and BUN were analyzed by an automatic biochemical analyzer in the local hospitals.

Quality control consisted of method blanks, certificated reference materials, and blind duplicates. The limit of detection for UHg was 0.01 μg/L and the relative percentage difference was lower than 10% for UHg in duplicate samples. The determined UHg concentrations agreed with the certified values in certified reference materials (ZK020-1 and ZK020-2), and the recoveries averaged at 95.7% and 99.3%, respectively.

2.5. Data analysis

All data were analyzed using IBM SPSS 22.0 software for Windows. The data were first tested for normal distribution. If normal distribution existed, the characteristics of the data were described in mean ± standard deviation (SD) form. If the data were in normal distribution after log transformation, the geomean was used for the descriptive statistics. If the data were not in a normal distribution even after log transformation, the median (quartile) was used to represent the data. The Mann–Wilcoxon test was used to compare the differences between different groups, and the rank correlation analysis was used for correlation analysis. The study population was divided into four equal subgroups based on the UHg concentrations, the different levels of SCr and BUN between different subgroups were compared by F-test. Ordered logistic regression was used for multivariate analysis. The value of β represents the partial regression coefficient; the standard error represents the average error of the estimate; Wald χ^2 represents the effect of independent variable on dependent variable; OR is the odds ratio; The OR 95% CI means that there is a 95% probability that OR will fall within this range. In addition, independent variable includes age, occupation, education level, smoking, alcohol habits, use of whitening products, use of hair dye, tooth fillings and etc. The results of the statistical tests were considered statistically significant if $p < 0.05$.

3. Results

3.1. UHg

The geomeans of UHg concentration in the Wanshan and Leishan populations were 1.09 μg/L (n = 165) and 0.29 μg/L (n = 65), respectively, as shown in Fig. 2. The UHg concentration in the normal population should be less than 5 μg/L, as recommended by the United Nations Industrial Development Organization (United Nations Industrial Development Organization, 2003). In total, 15 people (9.1%) in the Wanshan area exceeded this recommended value of 5 μg/L; however, no person in the Leishan area exceeded this recommended value. Significant differences in UHg concentration were observed between the two groups ($p < 0.01$), indicating that Wanshan parturients were at risk of IHg exposure.

3.2. Renal function

The median values (interquartile range) of SCr in parturients from the Wanshan and Leishan area were 69.1 (12.5) and 46.0 (11.0) μmol/L, respectively. Significant differences in SCr levels were observed between the two groups ($p < 0.01$, Table 2). The reference value of SCr in normal people ranged from 44.0 to 80.0 μmol/L (Wan and Lu, 2015). There were 18 people in the Wanshan area (10.8%) and only 1 person in the Leishan area (1.5%) exceeding the reference value. The median (interquartile range) values of BUN in parturients in the Wanshan and Leishan areas were 5.3 (2.3) mmol/L and 5.7 (2.3) mmol/L, respectively. No significant difference in the BUN values was found between the two groups, and the reference value of BUN in normal people ranged from 1.7 mmol/L to 8.3 mmol/L (Wan and Lu, 2015). There were 17 people in the Wanshan (10.3%) and 3 people in the Leishan area (4.6%) exceeding the reference value.

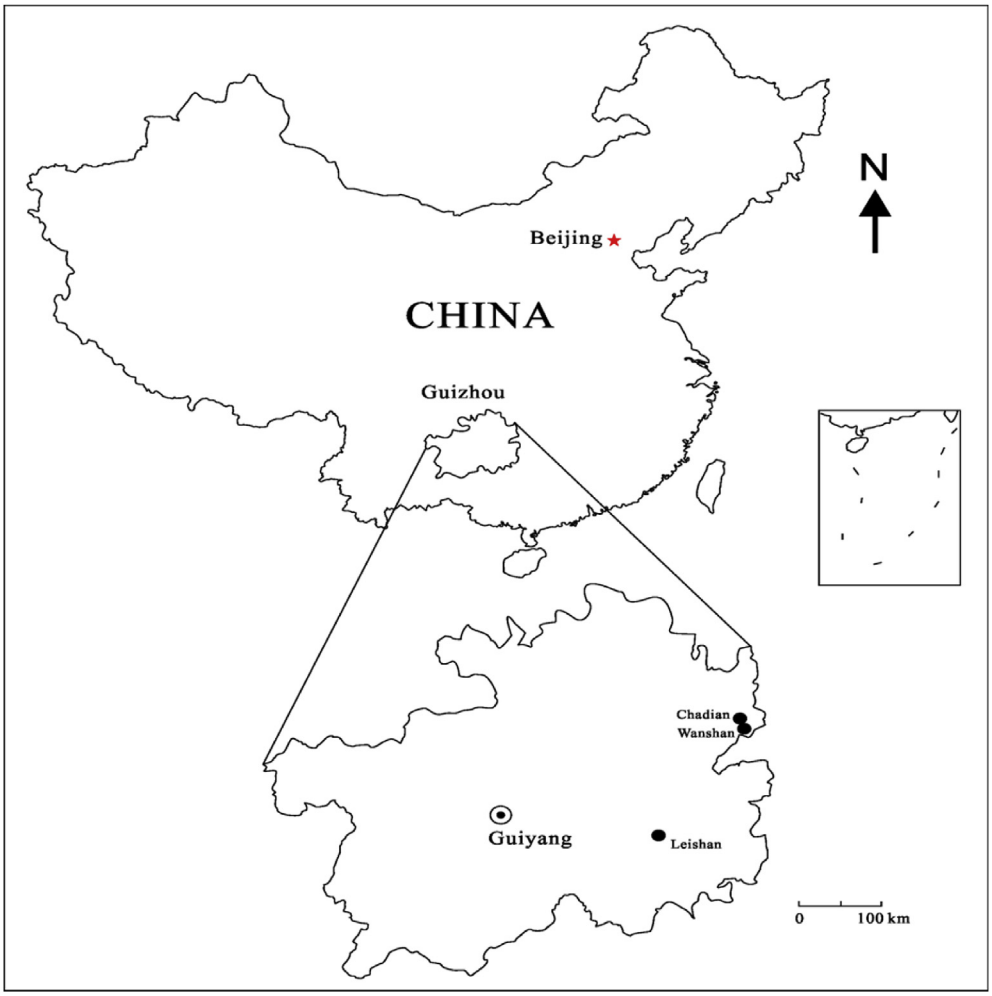

Fig. 1. Spatial location of three studied hospitals in Wanshan and Leishan County. Wanshan County People's Hospital and Chadian Town People's Hospital in the Wanshan County; Leishan County People's Hospital in Leishan County.

Table 1
Basic information of the study population (mean ± SD).

Site	n	Age (years)	Height (cm)	Body weight (kg)
Wanshan	165	24.7 ± 4.7	155.1 ± 4.2	62.3 ± 8.3
Leishan	65	25.1 ± 5.2	153.8 ± 3.8	64.9 ± 7.8
Total	230	24.7 ± 4.78	154.7 ± 3.9	63.1 ± 7.4

3.3. UHg and renal function

This study analyze the correlation relationships between UHg and renal function index (including SCr and BUN) in the study population. The rank correlation coefficient between UHg and SCr in the study population was 0.385, indicating a significant positive correlation ($p < 0.01$). However, no significant correlation was found between UHg and BUN ($rs = -0.099$, $p = 0.135$). To verify the renal effects resulting from IHg exposure, the study population was divided into four equal subgroups based on the UHg concentrations. The first group (Q1) is subgroup with UHg less than the 25th percentile; The second group (Q2) is subgroup with UHg between the 25th and 50th percentile; The third group (Q3) is subgroup with UHg between the 50th and 75th percentile; The fourth group (Q4) is subgroup with UHg higher than the 75th percentile. Then, the SCr and BUN levels in each quartile were compared (Fig. 3 and Fig. 4). The SCr levels in the third (Q3) and fourth quartiles (Q4) were significantly higher than those in the first quartile (Q1) and second quartiles (Q2) ($F = 15.521$, $p < 0.05$), confirming

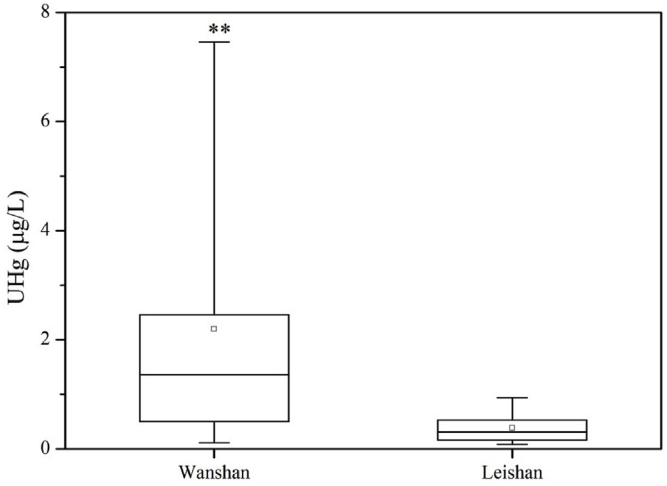

Fig. 2. Comparison of UHg between the Wanshan and Leishan groups. **, $p < 0.01$, compared with the Leishan area. Each box represents interquartile range (25th and 75th percentile), the band near the middle of the box is the 50th percentile (the median), and the whisker represents 5th and 95th percentile.

Table 2
Renal function of the study population.

Site	n	SCr (μmol/L)[a]	BUN (mmol/L)[a]
Wanshan	165	69.1 (12.5)*	5.3 (2.3)
Leishan	65	46.0 (11.0)	5.7 (2.3)
Total	230	64.3 (19.1)	5.5 (2.3)

*, $p < 0.01$, compared with the Leishan area.
[a] Data presented in median (interquartile range).

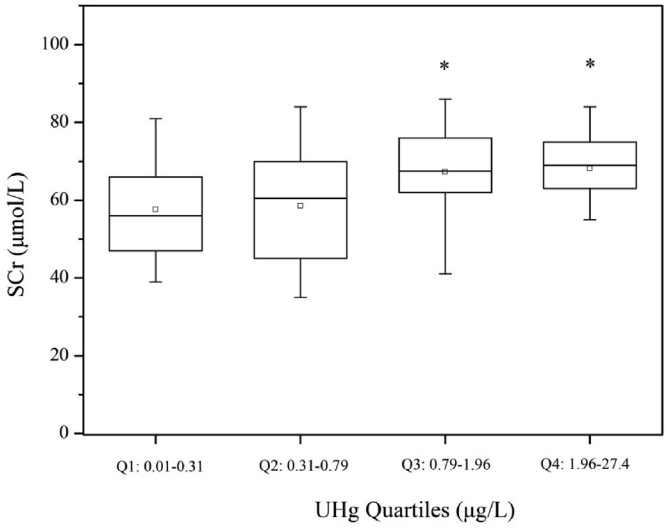

Fig. 3. Quartile analysis of serum creatinine (SCr) versus UHg in the study population. *, $p < 0.05$, compared with Q1. Each box represents interquartile range (25th and 75th percentile), the band near the middle of the box is the 50th percentile (the median), and the whisker represents 5th and 95th percentile.

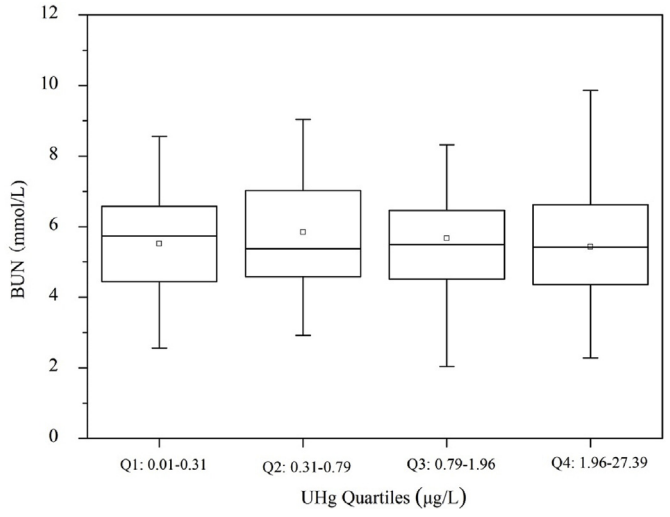

Fig. 4. Quartile analysis of blood urea nitrogen (BUN) versus UHg in the study population. Each box represents interquartile range (25th and 75th percentile), the band near the middle of the box is the 50th percentile (the median), and the whisker represents 5th and 95th percentile.

that IHg exposure led to increased SCr in the study population. However, no significant difference of BUN values was observed between different quartiles sorted by UHg concentrations (Fig. 4).

3.4. Influencing factors on UHg and renal function

The study population was divided into four groups according to the UHg and SCr levels, which were considered dependent variables. An ordered multi-classification logistic regression model was used for analysis. Age (divided into two groups according to the mean), occupation, education level, smoking and drinking habits, the use of whitening products, hair dye, and dental fillings were considered as independent variables (covariates). The results are shown in Table 3. The odds ratio (OR) value of UHg concentration in Wanshan area was 9.29 times higher than that in Leishan area (95% confidence interval (CI): 3.58–24.14). The OR value of UHg concentration in housewives and farmers was 4.45 times (95% CI: 1.33–14.89) and 4.29 times (95% CI: 1.31–14.06) higher than that in other occupations, respectively. The OR value of SCr decrease in patients with low UHg concentration was 0.32 times higher than that in patients with high UHg concentration (95% CI: 0.19–0.55); The OR value of SCr decrease in the population with fish consumption was 0.71 times higher than that of the population without fish consumption (95% CI: 0.58–0.88) as shown in Table 4.

4. Discussion

The geomean of UHg in parturients in the Wanshan area was 1.09 μg/L, which was significantly higher than that of the control group (0.29 μg/L) ($p < 0.01$). In addition, the OR (95% CI) value of UHg levels in the Wanshan group was 9.29 (3.58–24.1) higher than that of the Leishan group, indicating that the Wanshan population is at risk of IHg exposure.

Occupation has a significant impact on Hg exposure in the Wanshan area. Compared with other occupations, the OR (95% CI) values of UHg in farmers and housewives were 4.45 (1.33–14.89) and 4.29 (1.31–14.06) higher than that of other occupations, respectively. However, maternal occupations in the study group from the Wanshan area were not evenly distributed and more than 90% were housewives and farmers (Table 3). A long history of large-scale Hg mining and smelting activities has resulted in serious environmental Hg pollution in the Wanshan area. Residents may be exposed to Hg through their diet, breathing, and other pathways. Previous studies have indicated that agricultural crops cultivated in the Wanshan area could strongly accumulate Hg (Qiu et al., 2008) and the averages of THg concentration in rice and vegetables reached 51.6 and 143 ng/g, respectively (Feng et al., 2008), exceeding the national limits (20 ng/g for rice, 10 ng/g for vegetables) (National Health and Family Planning Commission (NHFPC) & China Food and Drug Administration (CFDA), 2017). Residents in Wanshan area generally live in a self-sufficient lifestyle and the consumption of local agricultural products is the main pathway of IHg exposure for these residents (Li et al., 2015).

Even large-scale Hg mining activities have ceased in the Wanshan area, the mine waste calcines and Hg-polluted soil can still continuously release large amounts of Hg to the atmosphere. In the rural area, coal and wood are the main heating and cooking fuels. The average of THg in Guizhou coal was measured at 0.53 mg/kg, which was significantly higher than the Chinese average (0.20 mg/kg) (Feng et al., 2002; Tang et al., 2017). Because of the high background values in the Wanshan area, the THg in the local wood was as high as 4.4 mg/kg (Zhang, 2015). Therefore, the coal and wood combustion processes will release large amounts of Hg, which can result in significant elevations of atmospheric Hg concentrations in the indoor environment (Li et al., 2015). Therefore, inhalation is another important pathway of IHg exposure for local populations.

IHg exposure can directly injure renal tubules in mice experiments, and degenerative changes of proximal convoluted tubules have been observed after 1 h in mice exposed to 100 mg/kg $HgCl_2$ (Zalups, 2001). Long-term low-dose Hg exposure can also affect the function of renal tubular re-absorption and lead to renal damage (Frankol et al., 2005). The SCr level is the most commonly used index for the clinical

Table 3
Multivariate logistic regression analysis for UHg in the study population.

Factor		n	β[a]	Standard error	Wald $\chi 2$[b]	p	OR[c]	OR 95%CI	
								Lower limit	Upper limit
Area	Wanshan	165	2.23	0.49	20.96	< **0.001**	9.29	3.58	24.14
	Leishan	65							
Smoking	No	227	0.04	1.87	0.00	0.985	1.04	0.03	40.45
	Once	2	−0.29	2.63	0.01	0.913	0.75	0.00	128.77
	< 10/day	1							
Drinking	Yes	53	−0.70	2.07	0.11	0.736	0.50	0.01	28.65
	No	177	−0.88	2.08	0.18	0.672	0.41	0.01	24.61
Use of whitening products	Yes	35	0.27	0.42	0.42	0.515	1.31	0.58	2.97
	No	195							
Occupation	Housewife	85	1.49	0.62	5.84	**0.016**	4.45	1.33	14.89
	Enterprise staff	4	1.39	1.62	0.74	0.391	4.01	0.17	95.77
	Worker	2	1.57	1.55	1.04	0.309	4.82	0.23	99.58
	Farmer	123	1.46	0.61	5.80	**0.016**	4.29	1.31	14.06
	Migrant worker	16							
Fish consumption	Yes	124	0.32	0.58	0.30	0.534	0.31	0.35	12.19
	No	106	0.46	0.57	0.66	0.585	1.37	0.01	4.30

[a] *Partial regression coefficient.*
[b] *Wald chi-square.*
[c] *Odds ratio.*

Table 4
Multivariate logistic regression analysis for SCr in the study population.

Factor		n	β[a]	Standard error	Wald $\chi 2$[b]	p	OR[c]	OR 95%CI	
								Lower limit	Lower limit
UHg	< $P50$	115	−1.14	0.28	16.94	< **0.001**	0.32	0.19	0.55
	≥ $P50$	115		.	.				
Fish consumption	Yes	124	−0.34	0.11	9.79	**0.002**	0.71	0.58	0.88
	No	106							
Smoking	No	227	1.33	1.87	0.51	0.475	3.79	0.10	147.53
	Once	2	−0.42	2.60	0.03	0.872	0.66	0.00	107.02
	< 10/day	1							
Drinking	Yes	53	−0.57	2.03	0.08	0.778	0.56	0.56	29.99
	No	177	−1.68	2.03	0.68	0.408	0.19	0.19	9.99
Use of whitening products	Yes	35	0.36	0.42	0.72	0.398	1.43	0.63	3.26
	No	195							
Occupation	Housewife	85	0.25	0.57	0.19	0.666	1.28	0.42	3.95
	Enterprise staff	4	−0.15	1.62	0.01	0.928	0.86	0.04	20.55
	Worker	2	1.37	1.46	0.88	0.348	3.94	0.22	69.20
	Farmer	123	0.09	0.55	0.03	0.872	1.09	0.37	3.20
	Migrant worker	16							

[a] *Partial regression coefficient.*
[b] *Wald chi-square.*
[c] *Odds ratio.*

evaluation of renal function. The increase of SCr is a sensitive biomarker for renal dysfunction. The present study found a significant positive correlation between UHg and SCr concentrations ($p < 0.01$). Quartile analysis of SCr with UHg concentrations also confirmed that IHg exposure led to increased SCr in the study population. The OR (95% CI) of SCr reduction was 0.32 (0.19–0.55) for those with low UHg concentrations compared with those with high UHg concentrations, confirming that IHg exposure in parturient women has resulted in elevations of SCr concentrations and impaired renal function (Li et al., 2013, 2015). Therefore, we can conclude that IHg exposure cause impairment of renal function in the study population.

The present study also showed that pregnant women with frequent fish consumption could antagonize the increase of SCr. The THg concentrations in fish collected from the Wanshan area were relatively low (with an average of 0.17 mg/kg), which were much lower than the national limit of 0.5 mg/kg (Qiu et al., 2009). However, fish meat is rich in n-3 unsaturated fatty acids and selenium (Se) (Li et al., 2010; Looi et al., 2016). Numerous studies have shown that n-3 fatty acids can reduce the inflammation of renal proximal tubular cells by activating peroxidase receptors (Li et al., 2005). In addition, Se is not only an antagonist to Hg toxicity (Li et al., 2016), but also a necessary trace element for human and an essential substance for maintaining the activity of many important enzymes in human body (Ralston, 2008; Rayman, 2012). In our previous study, we found that Wanshan residents revealed significantly elevated blood Se levels and dietary Se intake protected local residents suffering from Hg exposure (Li et al., 2015). Therefore, these nutrients digested during fish consumption can antagonize the impairment of IHg on renal function (Lin et al., 2014).

The UHg concentrations in parturients in the Wanshan area were significantly higher than those in the Leishan area and many parturients exceeded the limit set by UNIDO, which indicated risks of IHg exposure in the Wanshan population. An increase in UHg concentration can lead to an increased SCr concentration, confirming the damage to renal function caused by long-term low-dose IHg exposure. The results also showed that fish consumption could antagonize the impairment of IHg exposure on renal function in parturients.

5. Conclusions

In the present study, significant elevations of UHg and SCr in parturients in the Wanshan area were observed compared with those in the Leishan area, indicating the risks of IHg exposure and renal effects for the Wanshan population. The significant positive correlation between UHg and SCr confirmed that IHg exposure led to renal damage. The results provide important scientific guidelines for risk assessment and risk control of human Hg exposure in Hg polluted areas.

Author Contribution Statement

Chanchan Zhang: Methodology, Investigation, Data curation, Writing- Original draft preparation. Chunfang Gan: Methodology, Investigation, Data curation. Li Ding: Data curation. Min Xiong: Methodology, Investigation, Data curation. Aihua Zhang: Supervision. Ping Li: Conceptualization, Methodology, Supervision, Writing - review & editing.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

This study is funded by the National Natural Science Foundation of China (U1812403, 41622208, and 41573132), Key Laboratory of Environmental Pollution Monitoring and Disease Control, Ministry of Education, Guizhou Medical University (GMU-2017-HJZ-01), the Youth Innovation Promotion Association, Chinese Academy of Sciences (2017442), and the Chinese Academy of Sciences “Light of West China” Program.

References

Al-Saleh, I., Al-Sedairi, A., Elkhatib, R., 2012. Effect of mercury (Hg) dental amalgam fillings on renal and oxidative stress biomarkers in children. Sci. Total Environ. 431, 188–196.

Bjørklund, G., Aaseth, J., Olga, P., Alexandr, A., Anatoly, V., Margarita, G., Alexey, A., 2017. Molecular interaction between mercury and selenium in neurotoxicity. Coord. Chem. Rev. 332, 30–37.

Dai, Z.H., Feng, X.B., Sommar, J., Li, P., Fu, X.W., 2012. Spatial distribution of mercury deposition fluxes in Wanshan Hg mining area, Guizhou province, China. Atmos. Chem. Phys. 12, 5739–5769.

Feng, X.B., Li, P., Qiu, G.L., et al., 2008. Human exposure to methylmercury through rice intake in Wanshan mercury mining areas, Guizhou Province, China. Environ. Sci. Technol. 42, 326–332.

Feng, X.B., Qiu, G.L., 2008. Mercury pollution in Guizhou, southwestern China-an overview. Sci. Total Environ. 400, 227–237.

Feng, X.B., Sommar, J., Lindqvist, O., Hong, Y., 2002. Occurrence, emissions and deposition of mercury during coal combustion in the Province Guizhou, China. Water Air Soil Pollut. 139, 311–324.

Frankol, A., Budihna, M., Dodic-Fikfak, M., 2005. Long-Term effects of element al mercury on renal function in miners of the idrija mercury mine. Ann. Occup. Hyg. 49, 521–527.

Ha, E., Basu, N., Bose-O′, R., Mcsorley, E., Sakamoto, M., 2017. Current progress on understanding the impact of mercury on human health. Environ. Res. 152, 419–433.

Horvat, M., Natasa, N., Fajon, V., et al., 2003. Total mercury, methylmercury and selenium in mercury polluted areas in the province Guizhou, China. Sci. Total Environ. 304, 231–256.

Li, H., Ruan, X., Powis, S., et al., 2005. EPA and DHA reduce LPS-induced inflammation responses in HK-2 cells: evidence for a PPAR-gamma-dependent mechanism. Kidney Int. 67, 867–874.

Li, P., Du, B.Y., Chan, H.M., Feng, X.B., 2015. Human inorganic mercury exposure, renal effects and possible pathways in Wanshan mercury mining area, China. Environ. Res. 140, 198–204.

Li, P., Feng, X.B., Qiu, G.L., 2010. Methylmercury exposure and health effects from rice and fish consumption: a review. Int. J. Environ. Res. Public Health 7, 2666–2691.

Li, P., Li, Y., Feng, X.B., 2016. Mercury and selenium interactions in human blood in the Wanshan mercury mining area, China. Sci. Total Environ. 573, 376–381.

Li, Y., Zhang, B., Yang, L., Li, H., 2013. Blood mercury concentration among residents of a historic mercury mine and possible effects on renal function: a cross-sectional study in southwestern China. Environ. Monit. Assess. 185, 3049–3055.

Lin, Y.S., Ginsberg, G., Lin, J.W., Sonawane, B., 2014. Mercury exposure and omega-3 fatty acid intake in relation to renal function in the US population. Int. J. Hyg Environ. Health 217, 465–472.

Looi, L.J., Aris, A.Z., Haris, H., et al., 2016. The levels of mercury, methylmercury and selenium and the selenium health benefit value in grey-eel catfish (Plotosus canius) and giant mudskipper (Periophthalmodon schlosseri) from the Strait of Malacca. Chemosphere 152, 265–273.

Mergler, D., Anderson, A.H., Chan, H.M., et al., 2007. Methylmercury exposure and health effects in humans: a worldwide concern. Ambio 36, 3–11.

National Health and Family Planning Commission (NHFPC) & China Food and Drug Administration (CFDA), 2017. National Food Safety Standard, Tolerance Limit of Pollutants in Foods (In Chinese). GB2762-2017.

Nordberg, G., Fowler, B., Nordberg, M., 2014. Handbook on the Toxicology of Metals, fourth ed. Academic Press, Salt Lake City.

Qiu, G.L., Feng, X.B., Li, P., et al., 2008. Methylmercury accumulation in rice (Oryza sativa L.) grown at abandoned mercury mines in Guizhou, China. J. Agric. Food Chem. 56, 2465–2468.

Qiu, G.L., Feng, X.B., Wang, S.F., Shang, L.H., 2005. Mercury and methylmercury in riparian soil, sediments, mine waste calcines, and moss from abandoned Hg mines in east Guizhou province, Southwestern China. Appl. Geochem. 20, 627–638.

Qiu, G.L., Feng, X.B., Wang, S.F., et al., 2009. Mercury distribution and speciation in water and fish from abandoned Hg mines in Wanshan, Guizhou province, China. Sci. Total Environ. 407, 5162–5168.

Ralston, N., 2008. Selenium health benefit values as seafood safety criteria. EcoHealth 5, 442–455.

Rayman, M., 2012. Selenium and human health. Lancet 379, 1256–1268.

Stacchiotti, A., Morandini, F., Bettoni, F., et al., 2009. Stress proteins and oxidative damage in renal derived cell line exposed to inorganic mercury and lead. Toxicology 264, 215–224.

Tang, Z.W., Chai, M., Cheng, J.L., et al., 2017. Contamination and health risks of heavy metals in street dust from a coal mining city in eastern China. Ecotoxicol. Environ. Saf. 138, 83–91.

United Nations Industrial Development Organization, 2003. Protocols for Environmental and Health Assessment of Mercury Released by Artisanal and Small-Scale Gold Miners. ASM), Vienna UNIDO.

Wan, X.H., Lu, X.F., 2015. Diagnostics, eighth ed. People’s Medical Publishing House, Beijing.

World Health Organization, 1990. Environmental Health Criteria 101 - Methylmercury. WHO, Geneva.

World Health Organization, 1991. Environmental Health Criteria 118-Inorganic Mercury. WHO, Geneva.

Yin, R., Gu, C., Feng, X.B., Hu, N., 2016. Transportation and transformation of mercury in a calcine profile in the Wanshan Mercury Mine, China. Environ. Pollut. 219, 976–981.

Zalups, R., 2001. Molecular interactions with mercury in the kidney. Pharmacol. Rev. 52, 113–143.

Zhang, H., Feng, X.B., Larssen, T., et al., 2010a. Bioaccumulation of methylmercury versus inorganic mercury in rice (oryza sativa L.) grain. Environ. Sci. Technol. 44, 4499–4504.

Zhang, H., Feng, X.B., Larssen, T., et al., 2010b. Fractionation, distribution and transport of mercury in rivers and tributaries around Wanshan Hg mining district, Guizhou Province, Southwestern China: Part1-Total mercury. Appl. Geochem. 25, 633–641.

Zhang, P., 2015. Reconstruction Pollution History in Typical Mercury Pollutted Area by Dendrochemistry Technology. Master Thesis. Guizhou Normal University.