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RESEARCH ARTICLE

Analyzing the role of soil and rice cadmium pollution on human renal dysfunction by correlation and path analysis

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Abstract The aim of this study was to investigate the role of soil and rice pollution on human renal dysfunction. The participants were 97 inhabitants (46 men and 51 women) who are aged 50 to 60 years old and have been living in Xiaogan (Hubei, China) from birth. We collected samples of soil, rice, and urinary correspondingly. Urinary N-acetyl-β-D-glucosaminidase (NAG) and β-2-microglobulin (β_2MG) were used as indicators of renal dysfunction, and urinary cadmium (U-Cd) was used as indicator of total internal cadmium exposure. We made a hypothesis that soil cadmium concentration (S-Cd) and rice cadmium concentration (R-Cd) could be used as indicators of environmental cadmium exposure. Correlation and path analysis were used to estimate the relationships among the levels of rice cadmium (R-Cd), soil cadmium (S-Cd), urinary cadmium (U-Cd), and renal damage indicators (NAG and β_2MG). Our results showed that there was positive significant relationship between S-Cd (R-Cd, U-Cd), and U-NAG (U-β_2MG). The standard multiple regression describing the relationship between S-Cd (R-Cd, U-Cd) and U-NAG was $Y_1 = 1.26X_1–6.53X_2 + 9.32$, where Y is U-NAG, X_1 is U-Cd, X_2 is S-Cd. The equation of U-β_2MG was $Y = 49.32X_1 + 3085.99X_2 + 143.42$, where Y is U-$\beta_2$MG, X_1 is U-Cd, X_2 is R-Cd. It is obvious that the effect of S-Cd and R-Cd on NAG or U-β_2MG cannot be ignored. Through our study, we can find that the effects of S-Cd on renal health even as significant as R-Cd. To protect people from the damage of cadmium pollution, it is vital to monitor the situation of soil and rice cadmium pollution.

Keywords Soil · Rice · U-Cd · U-Nag · U- β_2MG correlation analysis · Path analysis

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Introduction

Cadmium (Cd) is a toxic non-essential element in human body (Ezaki et al., 2003; Ke et al. 2015a; Uraguchi and Fujiwara, 2012). Cd exists in a refractory sulfide form with low content in the environment which usually does little harm to human body. However, with the increasing exploitation and cadmium use, cadmium pollution and influence of human health often had been reported in recent decades. The most severe consequence of cadmium pollution was Itai-itai disease happened in the 1950s in Japan(Zhang, Du, Zhai, and Shang, 2014). It is well known that kidney is one of the main target organs of cadmium exposure (Suwazono et al., 2011) (Osawa et al., 2001). Cadmium can enter into body through dieting or other routes, then accumulates mainly in the kidney. At high levels, it can reach to a critical threshold which can lead to serious kidney disease. For example, it could lead to the dysfunction of glomerular and tubular (Jarup and Akesson 2009; Staessen et al. 1994).

Currently, environmental cadmium pollution is more severe in some countries such as China, Japan and

Thailand (Nishijo et al. 2014; Nogawa et al. 2004; Swaddiwudhipong et al. 2010) (Jin et al. 2004). In China, cadmium pollution in soil and rice is widely spread. Decades ago, approximate 133 km^2 of soil in China was contaminated by Cd (Xu Liangjiang et al. 2011). Some provinces such as Hunan, Jiangxi, and Hubei reached the level of production of "cadmium rice." According to the investigation of the USA and the European Union, about 82~94 % of cadmium in the environment depositing in the soil resulted in significant increasing of cadmium content in the crops. Many scientists agreed that diet is the main source of Cd intake (Akerstrom, Sallsten, Lundh, and Barregard, 2013) (Osawa et al., 2001) and Cd in rice is the most influential factor of daily dietary Cd intake among general population (Ikeda, Ezaki, Tsukahara, and Moriguchi, 2004) (Uraguchi and Fujiwara, 2012). Cadmium in soil is a risk for human health due to its accumulation in food and feed crops. There is an increasing belief that soil plays an important role in feed and food supplying of the biological chain which delivers safe and high-quality products to consumers. Hence, Cd exposure in rice and soil is a critical determinant of Cd exposure in the general China population. Long-term exposure to environmental cadmium shows a strong association with renal dysfunction. To protect people from the adverse health effects by Cd exposure, it is extremely important to determine the critical threshold of Cd exposure.

At present, most studies focused on estimating the relationship between U-Cd (urinary cadmium) and renal effect indicators as well as the benchmark dose of U-Cd. Several studies demonstrated the importance of estimating the relationship between cadmium concentration in rice and those three renal indicators (Nogawa et al. 2015; Osawa et al. 2001). However, studies on soil cadmium pollution risk assessment were rare. And none of these studies employed the method of path analysis to compare the relative importance of R-Cd (cadmium concentration in rice), S-Cd (cadmium concentration in soil) and U-Cd to U-NAG and U-β_2MG. And to our knowledge, none of them got the data of R-Cd, S-Cd, U-Cd and renal health indicators correspondingly. In our previous studies, we reported levels of urinary Cd from different cadmium pollution areas in China (Ke et al. 2015b). Through correlation analysis and regression analysis, we found that there was positive correlation between U-Cd and U-NAG or U-β_2-MG. We also established a dose-response relation between U-Cd and indicators of health effects (NAG and β_2-MG). The highlights of this study were we employed correlation and path analysis to evaluate and compare the relationship between exposure indicators (R-Cd, S-Cd and U-Cd) and renal health indicators (NAG, β_2MG). Besides that, we collected all the samples (urinary, rice and soil) correspondingly. As far as we know, it is the first study in this research field to conduct a cross- sectional study.

Our research objective was to explore the role of soil cadmium and rice cadmium pollution on renal dysfunction. We used path analysis to improve our hypotheses that the S-Cd and R-Cd could be used as indicators of environmental cadmium exposure. The structure of our overall conceptual model was based on results from previous investigations of relationships among S-Cd, R-Cd, U-Cd, U-NAG, and U-β_2MG (Shao et al. 2007; Wallin et al. 2014). This would help to discover the importance of soil and rice cadmium pollution on human renal health and the assessment of soil cadmium pollution.

Materials and methods

Study area and participants

The city studied in our research is Xiaogan, located in the northeast of Hubei province, is an important agricultural region of China (Ke et al. 2015c). The local people produced rice as their staple food. A total of 5 villages were selected and there were no significant differences among these villages. The participators in this study were consisted of 46 men and 51 women who have been living in the same hamlets from birth in those 5 villages. All of the subjects aged 50 to 60 years and mainly subsisted on local-grown rice. They are mainly engaged in farming for occupation. The subjects were requested to complete a self-made questionnaire as date demographics of all the participants. Participants who were possibly occupational exposed to Cd or other heavy metals were excluded. Furthermore, participants with genetic kidney diseases were also excluded.

Sampling and chemical analysis

All the rice samples were collected from the participants' households by quartering method. Soil samples were collected from the area producing the investigated rice by five points sampling method. The rice and soil cadmium concentration was determined according to the standard method. Rice and soil cadmium were measured by Atomic Absorption Spectrometry as reported in previous studies (Ke, Cheng, Zhang, Hu, et al., 2015). Finally, we got soil, rice, and urinary samples from 97 residents. The morning urine samples were collected from them and placed in −20 °C until analysis. All containers were treated with acid before use. Each sample was divided into small portions after collection to measure U-NAG, U-β_2MG, U-Cd and creatinine (cr) levels. The detailed measurement procedures were previously reported (Ke, Cheng, Zhang, Jia, et al., 2015). All urinary parameters were adjusted for the creatinine concentration. U-Cd was expressed as μg/g cr, U-NAG was expressed as U/g cr and U- β_2MG was expressed as μg/g cr.

Statistical analysis

Microsoft 2013 Excel (Microsoft Corporation, USA) was used to establish database of survey data and the experimental results. SPSS 17.0 for Windows (SPSS Inc., Chicago, IL, USA) was used to conduct the statistical analyses. *t* test showed the distribution of S-Cd, R-Cd, U-Cd, U-NAG, and U-β_2MG obeyed log-normal distribution characteristic. The geometric mean, mean and prevalence of S-Cd, R-Cd, U-Cd, U-NAG, and U-β_2MG values were calculated. The maximum allowable concentration (MAC) of S-Cd was 0.6 mg/kg(pH > 7.5) according to GB15618-1995. The maximum allowable concentration (MAC) of R-Cd was 0.2 mg/kg according to GB 2762-2012. The ratio of S-Cd (R-Cd) that exceeded the corresponding MAC was used to reflect the station of local cadmium pollution. The cut-off value of U-β_2MG was 1000 μg/g cr. The cut-off value of U-Cd was 5 μg/g cr. The cut-off value of U-NAG was 17 U/g. The relationship between and among the levels of R-Cd, S-Cd, U-Cd, and indicators of renal damage was estimated by regression and path analysis. Correlation analysis was used to study whether there is some kind of interdependent relationship between variables, and to explore its related and associated degree. Path analysis can be used to not only study the relationship between variables but also give a reason for the importance of the results.

The correlation coefficient was decomposed into direct effects and indirect effects by path analysis, so that the relative importance of the factors on the result is revealed. Between a dependent variable y and various independent variables x_i (i = 1,2,3,...,n) in interrelated systems, there is a linear relationship whose regression equation is:

$$Y = b_0 + b_1x_1 + b_2x_2 + \ldots + b_nx_n \quad (1)$$

The measured values are substituted into formula (1), and equations are built and solved by the principle of least squares, then the path coefficients (p_yx_i) are obtained. The path coefficient is the standard partial regression coefficient of the variable, indicating the relative importance of the variables to the result.

Normal matrix equations can be built using formula (1) by mathematical transformation:

$$\begin{bmatrix} 1 & r_{x_1x_2} & \cdots & r_{x_1x_n} \\ r_{x_2x_1} & 1 & \cdots & r_{x_1x_n} \\ \vdots & \vdots & \ddots & \vdots \\ r_{x_nx_1} & r_{x_nx_2} & \cdots & 1 \end{bmatrix} \begin{bmatrix} \rho_{yx_1} \\ \rho_{yx_2} \\ \vdots \\ \rho_{yx_n} \end{bmatrix} = \begin{bmatrix} r_{x_1y} \\ r_{x_2y} \\ \vdots \\ r_{x_ny} \end{bmatrix} \quad (2)$$

In Eq.(2), r_{xixj} is the correlation coefficient between x_i and x_j, r_{xiy} is the correlation coefficient between x_i and y, p_{yxi} is the direct path coefficient of xi to y. Pyxi is obtained by solving Eq.(2):

$$P_{yx_i} = b_i\frac{\sigma_{x_i}}{\sigma_y} \quad (3)$$

In Eq.(3), b_i is the partial regression coefficient, σ_{xi} is the standard deviation of x_i, σ_y is the standard deviation of y, and $r_{xiyj}p_{yxj}$ is the indirect path coefficient of x_i via x_j to y.

Results

We collected urine samples from 97 subjects (46 men, 51 women), including 35 smokers and 62 non-smokers. Through *t* test, men and women were examined simultaneously, sex did not affect the level of U-Cd, U-NAG and U-β_2MG ($P > 0.05$). There were significant differences between smokers and non-smokers except U-NAG ($P < 0.01$). Therefore, we only distinguished the smoking status.

After the detection of all the samples, the level of S-Cd and R-Cd was calculated. The results were shown in Table 1. The level of S-Cd ranged from 0.21 to 1.94 mg/kg with a mean (SD) value of 0.76(0.38) mg/kg. And about 57.7 % soil samples' cadmium concentration exceeded its MAC ($P < 0.01$). R-Cd values ranged from 0.01 to 0.29 mg/kg with a mean (SD) value of 0.15(0.06) mg/kg, about 17.53 % rice samples' cadmium concentration exceeded its MAC ($P < 0.01$). Our previous study in Xiaogan showed that the mean (SD) level of R-Cd was 0.149 (0.058) mg/kg and about 17.5 % soil sample cadmium concentration exceeded the MAC. The results of the present research were consistent with our previous researches (Ke, Cheng, Zhang, Hu, et al., 2015), supporting the reliability of the present results.

Table 2 showed the values of U-Cd, U-NAG, and U-β_2MG. The mean value of U-Cd was 8.42 ± 6.21 μg/g cr (range: 1.04 to 27.51 μg/g cr, prevalence: 62.86 %) and 5.23 ± 4.35 μg/g cr (range: 0.17 to 28.52 μg/g cr, prevalence: 40.32 %) in smokers and non-smokers, respectively. The mean value of U-NAG was 13.32 ± 8.93 U/g cr (range: 2.05 to 42.63 U/g cr, prevalence: 34.29 %) and 11.86 ± 7.03 U/g cr (range:0.87 to 36.72 U/g cr, prevalence: 20.97 %) in smokers and non-smokers, respectively. The mean value of U-β_2MG was 1027.45 ± 804.04 μg/g cr (range: 78.96 to 2815 μg/g cr, prevalence: 40.00 %) and 857.71 ± 651.73 μg/g cr (range: 48.84–3453.65 μg/g cr, prevalence: 30.65 %) in smokers and non-smokers, respectively. It was obvious that mean

Table 1 Statistical analyses of Cd concentration in soil and rice

Sample	N	GM	Mean ± SD	Range	Median	MAC	Ratio that exceeded
		mg kg^{-1}	mg kg^{-1}	mg kg^{-1}	mg kg^{-1}	mg kg^{-1}	The MAC (%)
Soil	97	0.68	0.76 ± 0.38[a]	0.21–1.94	0.66	0.6	57.73 %
Rice	97	0.13	0.15 ± 0.06[a]	0.01–0.29	0.144	0.2	17.53 %

GM geometric mean, *SD* standard deviation, *MAC* maximum allowable concentration

[a] Extremely significant compared to maximum allowable concentration ($p < 0.01$)

values of smokers were significantly higher than those of non-smokers.

It can be seen from Table 3 that on the whole, S-Cd ($r = 0.407$, $P < 0.01$), R-Cd ($r = 0.306$, $P < 0.01$) and U-Cd ($r = 0.587$, $P < 0.01$) had significant correlation with U-NAG. And S-Cd also had significant correlation with R-Cd ($r = 0.466$, $P < 0.01$) and U-Cd ($r = 0.847$, $P < 0.01$). R-Cd ($r = 0.582$, $P < 0.01$) had significant correlation with U-Cd. In addition, Table 4 showed that S-Cd ($r = 0.365$, $P < 0.01$), R-Cd ($r = 0.466$, $P < 0.01$) and U-Cd ($r = 0.514$, $P < 0.01$) had significant correlation with U-β_2MG. And S-Cd also had significant correlation with R-Cd ($r = 0.466$, $P < 0.01$) and U-Cd ($r = 0.847$, $P < 0.01$). R-Cd ($r = 0.582$, $P < 0.01$) had significant correlation with U-Cd. In a word, no matter for smokers or non-smokers, S-Cd, R-Cd, and U-Cd had significant correlation with U-NAG and U-β_2MG. And S-Cd, R-Cd, and U-Cd may have some effects on each other.

From correlation analysis, we can speculate that excessive cadmium content in the soil can lead to a significant increasing cadmium content in rice. There was positive association between U-Cd and R-Cd, which demonstrated that Cd exposure from rice was a critical determinant of Cd exposure. Furthermore, S-Cd, R-Cd, and U-Cd had significant correlation with U-NAG and U-β_2MG. It may indicate that S-Cd, R-Cd, and U-Cd have effects on human renal health.

The correlation coefficients only represented the closeness of the relationship between S-Cd, R-Cd, U-Cd, U-NAG, and U-β_2MG. From correlation analysis, we know there were significant relationships among S-Cd, R-Cd, U-Cd, and U-NAG, U-β_2MG. S-Cd, R-Cd, U-Cd could affect each other mutually. Therefore, in order to reveal the true relationship between S-Cd, R-Cd, U-Cd, and U-NAG, U-β_2MG, the direct and indirect effects of S-Cd, R-Cd, U-Cd on U-NAG, U-β_2MG were investigated using path analysis. The results of path analysis were shown in Table 5–6.

Table 5 showed the standard multiple regression equation of the U-NAG and U-β_2MG. For total population, the standard multiple regression equation of the U-NAG was $Y = 1.26X_1–6.53X_2 + 9.32$, where Y was U-NAG, X_1 was U-Cd, X_2 was S-Cd. The equation of the U-β_2MG was $Y = 49.32X_1 + 3085.99X_2 + 143.42$, where Y was U-$\beta_2$MG, X_1 was U-Cd, X_2 was R-Cd. For smokers, the equation of U-NAG was $Y = 0.77X + 6.83$, where Y was U-NAG, X was U-Cd. The equation of U-β_2MG was $Y = 50.12X_1 + 5008.61X_2–230.20$, where Y was U-$\beta_2$MG, X_1 was U-Cd, X_2 was R-Cd. For non-smokers, the equation of

Table 2 Descriptive statistics of U-Cd, U-NAG, and U-β_2MG

	S	Num	Range	Mean ± SD	GM	M	C	Prevalence
U-Cd(μg/g)	Y	35	1.04–27.51	8.42 ± 6.21[a]	6.5	7.71	5	62.86 %
	N	62	0.17–28.52	5.23 ± 4.35[a]	3.77	4.31		40.32 %
	ALL	97	0.17–28.52	6.38 ± 5.3	4.59	4.83		48.45 %
U-NAG(-U/g)	Y	35	2.05–42.63	13.32 ± 8.93	10.5	11.39	17	34.29 %
	N	62	0.87–36.72	11.86 ± 7.03	9.8	10.28		20.97 %
	ALL	97	0.87–42.63	12.39 ± 7.76	10.05	10.503		25.77 %
U-β_2MG(-μg/g)	Y	35	78.96–2815	1027.45 ± 804.04[a]	732.64	753.15	1000	40.00 %
	N	62	48.84–3453.65	857.71 ± 651.73[a]	619.67	764.47		30.65 %
	ALL	97	48.84–3453.65	921.97 ± 72.89	658.27	760.89		34.02 %

By correlation analysis, the correlation coefficients between S-Cd, R-Cd, U-Cd, U-NAG and U-β_2MG were calculated. Meanwhile, the direct and indirect correlation coefficients between and among them were obtained from path analysis. S-Cd and R-Cd were cadmium exposure materials in environment. Urinary Cd concentration was an accepted indicator of Cd body burden and kidney accumulation. U-Cd and U-β_2MG were biomarkers of kidney effects

S smoking, *Y* yes, *N No*, *N* number, *SD* standard deviation, *GM* geometric mean, *M* median, C criterion

[a] Significant difference between smokers and non-smokers($P < 0.01$)

Table 3 The correlation coefficients (*r*) among S-Cd, R-Cd, U-Cd, and U-NAG

	Total				Smokers				Non-smokers			
	S-Cd	R-Cd	U-Cd	U-NAG	S-Cd	R-Cd	U-Cd	U-NAG	S-Cd	R-Cd	U-Cd	U-NAG
S-Cd	–	0.466[a]	0.847[a]	0.407[a]	–	0.510[a]	0.928[a]	0.451[a]	–	0.391[a]	0.735[a]	0.348[a]
R-Cd	0.466[a]	–	0.582[a]	0.306[a]	0.510[a]	–	0.541[a]	0.097	0.391[a]	–	0.583[a]	0.432[a]
U-Cd	0.847[a]	0.582[a]	–	0.587[a]	0.928[a]	0.541[a]	–	0.536[a]	0.735[a]	0.583[a]	–	0.643[a]
U-NAG	0.407[a]	0.306[a]	0.587[a]	–	0.451[a]	0.097	0.536[a]	–	0.348[a]	0.432[a]	0.643[a]	–

U-β2MG. And S-Cd, R-Cd, and U-Cd may have some effects on each other

[a] Indicates statistical significance at 0.01 level

U-NAG was Y = 1.04X + 6.41, where Y was U-NAG, X was U-Cd. The equation of U-β_2MG was Y = 66.23X + 511.32, where Y was U-β_2MG, X_1 was U-Cd, X_2 was R-Cd.

Each coefficient was the direct path coefficient of each factor in the equation. The indirect correlation coefficient between each factor was obtained by multiplying direct path coefficient by the correlation coefficient between each factor.

The standardized direct and indirect effect of S-Cd, R-Cd, and U-Cd on U-NAG and U-β_2MG was presented in Table 6. The direct effect reflected the sole impact. As we can see from Table 6 that for total population, the direct effect of U-Cd on U-NAG was 0.86 and the indirect effect of U-Cd on U-NAG through S-Cd was −0.27. The direct effect of S-Cd on U-NAG was −0.32; however, the indirect effect of S-Cd on U-NAG through U-Cd was 0.73. As we had already mentioned that the simple correlation coefficient between S-Cd and U-NAG was about 0.41($P < 0.01$). So we could conclude that S-Cd had great effect on U-NAG. Moreover, the simple relation coefficient between R-Cd and U-NAG was about 0.31($P < 0.01$). But R-Cd as a variable was rejected from this path analysis model. It may because that the data of R-Cd was not fit very well in this model. It did not mean R-Cd have no effect on U-NAG. In some ways, this results indicated that compared to U-Cd and S-Cd, the effect of R-Cd on U-NAG was not significant.

For general people, the direct effect of U-Cd on U-β_2MG was 0.37 and the indirect effect of U-Cd on U-β_2MG through R-Cd was 0.15. The direct effect of R-Cd on U-β_2MG was 0.25 and the indirect effect of R-Cd on U-β_2MG through U-Cd was 0.31. The simple correlation coefficient between S-Cd and U-β_2MG was 0.37($P < 0.01$). But S-Cd as a variable was rejected from this path analysis model. For smokers, the results about the direct and indirect effect of U-Cd and R-Cd on U-β_2MG were similar. Although S-Cd was rejected from this path analysis model, its effects could not be ignored for the reason that it has significant relationship between U-β_2MG.

Discussion

In our previous study, we collected urinary samples from seven provinces of China and investigated the cadmium pollution situation of rice in five provinces including the Hubei province. However, we did not get the data of soil. In the current research, we collected the samples of soil, rice and urine correspondingly. As far as we know, this is the first time the cadmium concentration in soil and rice was used as indicators of environmental cadmium exposure. There are three advantages of our study: first, we investigated the cadmium pollution from soil to human. Second, we collected all samples correspondingly, even though it was quite hard to achieve. Last, for the first time, we adopted the path analysis to estimate the relationship between indicators of environmental cadmium exposure (soil, rice, and urinary cadmium) and human renal dysfunction.

Our research collected the samples of soil, rice and urinary correspondingly from Xiaogan, Hubei province, which is an

Table 4 The correlation coefficients between S-Cd, R-Cd, U-Cd, and U-β_2MG

	Total				Smokers				Non-smokers			
	S-Cd	R-Cd	U-Cd	U-β_2MG	S-Cd	R-Cd	U-Cd	U-β_2MG	S-Cd	R-Cd	U-Cd	U-β_2MG
S-Cd	–	0.466[a]	0.847[a]	0.365[a]	–	0.510[a]	0.928[a]	0.474[a]	–	0.391[a]	0.735[a]	0.231
R-Cd	0.466[a]	–	0.582[a]	0.466[a]	0.510[a]	–	0.541[a]	0.553[a]	0.391[a]	–	0.583[a]	0.395[a]
U-Cd	0.847[a]	0.582[a]	–	0.514[a]	0.928[a]	0.541[a]	–	0.573[a]	0.735[a]	0.583[a]	–	0.442[a]
U-β_2MG	0.365[a]	0.466[a]	0.514[a]	–	0.474[a]	0.553[a]	0.573[a]	–	0.231	0.395[a]	0.442[a]	–

[a] Indicates statistical significance at 0.01 level

Table 5 The regression coefficient (*r*) of path analysis

	Dependent	Model	Un-standardized coefficients			Standardized coefficients		
	Variable			β	Std. error	Bata	*t*	sig
	NAG	1	constant	6.90	1.01		6.9	0.00
Total			U-Cd	0.86	0.12	0.59	7.07	0.00
		2	Constant	9.32	1.53		6.10	0.00
			U-Cd	1.26	0.22	0.86	5.58	0.00
			S-Cd	−6.53	3.14	−0.32	−2.08	0.04
	β_2MG	1	Constant	478.63	97.77		4.895	0.00
			U-Cd	68.99	11.81	0.51	5.84	0.00
		2	Constant	143.42	170.121		.843	0.00
			U-Cd	49.32	14.19	0.37	3.48	0.00
			R-Cd	3085.99	1296.38	0.25	2.38	0.02
Smokers	NAG	1	Constant	6.834	2.200		3.106	.004
			U-Cd	0.77	0.21	0.54	3.65	0.00
	β_2MG	1	Constant	402.647	192.250		2.094	0.044
			U-Cd	74.16	18.46	0.57	4.02	0.00
		2	Constant	−230.20	348.24		−.66	.513
			U-Cd	50.12	20.84	0.39	2.40	0.02
			R-Cd	5008.61	2346.60	0.34	2.13	0.04
Non-smokers	NAG	1	Constant	6.41	1.083		5.92	0.00
			U-Cd	1.04	0.16	0.64	6.51	0.00
	β_2MG	1	Constant	511.32	117.68		4.35	0.00
			U-Cd	66.23	17.36	0.44	3.82	0.00

important agricultural region of China and its local people produced rice as their staple food. According to our results, about 57.7 % soil samples exceeded the MAC of cadmium. Zhang et al. made an investigation about the soil cadmium pollution of one province of China. In their research, the over-limit ratio of S-Cd was 52.38 % (Zhang et al., 2014). Chen et al. made a research about the relation of cadmium concentration in vegetable soil to cadmium contamination in vegetables of Northern Guizhou. About 90 % of the vegetable soil exceeded the MAC (Chen et al. 2012). Rice, an important staple food for nearly half of the world's population, is a major source of Cd intake (Cheng et al., 2006; Watanabe et al. 2004). It is well known that the outbreak of Itai-Itai was because of the long-term consumption of cadmium contaminated rice. About 17.53 % rice samples in our research exceeded the MAC of cadmium. These results were consistent with our previous research results. Our previous research showed that there were more than 18 % rice samples in Xiaogan, Hubei, exceeded the MAC of R-Cd. And the highest over-limit ratio (41.1 %) was observed in Hezhang. It was obvious that the cadmium pollution of soil and rice were quite serious in China.

The correlation analysis showed that there were significant relationships among S-Cd, R-Cd, U-Cd, U-NAG, and U-β_2MG; in addition, S-Cd, R-Cd, and U-Cd could affect each other mutually. Path analysis demonstrated that when U-NAG was used as the dependent variable, U-Cd and S-Cd had significant direct and indirect effects on it. When U-β_2MG was used as dependent variable, U-Cd and R-Cd had significant effects on it. The correlation between S-Cd

Table 6 Direct (DE) and indirect (IE) effects of S-Cd, R-Cd, and U-Cd on NAG and β_2MG

	Independent variable	dependent variable	Correlation coefficient	Direct effect	Indirect effect		
					U-Cd	R-Cd	S-Cd
Total	U-Cd	NAG	0.59	0.86	–	–	−0.27
	S-Cd		0.41	-0.32	0.73	–	–
	U-Cd	β_2MG	0.51	0.37	–	0.15	–
	R-Cd		0.47	0.25	0.31	–	–
Smoker	U-Cd	β_2MG	0.57	0.39	–	0.19	–
	R-Cd		0.55	0.34	0.21	–	–

and indicators of human renal health such as U-NAG and U-β_2MG has been carried out in some researches (Kobayashi et al. 2008) (Brus et al. 2002; de Vries et al. 2007; Franz et al. 2008; Linden et al., 2003). And some researches showed that rice cadmium pollution could cause significant damage to human body health (Ikeda et al., 2004; Kobayashi et al. 2009a) (Kobayashi et al. 2002; Osawa et al. 2001). For instance, Koichi first reported a highly positive correlation between R-Cd and urinary concentrations of indicators of renal dysfunction (Nakashima et al. 1997). The relationship between cadmium polluted rice and occurrence of renal tubular dysfunction was also recently determined by Etsuko Kobayashi et al. (Kobayashi et al. 2009b). So we hypothesized that S-Cd and R-Cd are the main factors of cadmium exposure in environment and human renal health would be subjected to them. In our study, there was a highly positive correlation between S-Cd and U-NAG and U-β_2MG. Furthermore, S-Cd also had significant relationship with R-Cd and U-Cd. Correlation analysis showed that there was significant relationship between R-Cd and U-Cd, U-NAG and U-β_2MG. Those results implied that cadmium pollution in soil could does harm to human renal health by producing cadmium-rice or other crops. The control of the accumulation of Cd from soil is an important food-safety issue.

Since the correlation coefficients between S-Cd, R-Cd, and U-Cd on U-NAG and U-β_2MG were highly positive and there was relationship between S-Cd, R-Cd and U-Cd, path analysis can be used to identify the significance of the partial regression coefficient and gradually remove non-significant factors. Through path analysis, after deleting redundant independent variables from the equations, more simplified equations for U-NAG and U-β_2MG were obtained: the standard multiple regression equation of U-NAG was $Y1 = 1.26X_1–6.53X_2 + 9.32$, where Y was U-NAG, X_1 was U-Cd, X_2 was S-Cd. The equation of U-β_2MG was $Y = 49.32X_1 + 3085.99X_2 + 143.42$, where Y was U-$\beta_2$MG, X_1 was U-Cd, X_2 was R-Cd. From the above equations, we can find that the effects of soil and rice pollution could not be ignored. In recent decades, soil heavy metal pollution has become an imperative environmental issue. Among various heavy mental elements, cadmium (Cd) is identified as an extremely significant pollutant because of its high transfer rate from soil to plants and strong bio-toxicity (Lane et al., 2015). Excessive Cd uptake can enter the human body through the food chain, threatening health, especially for children and pregnant women. Many studies showed that soil Cd was a major source of human Cd intake (Satarug et al. 2009). Zhang believed that in the control of other factors, soil cadmium levels had a considerable impact on urinary cadmium level (Y. Zhang, Wang, and Ma, 2014). In order to study whether the cadmium pollution of heavy metals in soil had impact on the local population kidney damage, Huang made a risk assessment of some indexes such as U-Cd and NAG. They found soil cadmium pollution was a greater risk of health hazards to human health (Wang et al. 2015).

We should notice that rice roots have strong ability to adsorb heavy metals in soil. Some previous epidemiological studies of Japan indicated that in non-polluted areas Cd from rice accounted for 30–40 % of the daily Cd intake in non-polluted areas(Ikeda et al., 2004), while in some polluted areas, higher contribution of up to 70 %. Thus, Cd exposure from rice is a critical determinant of Cd exposure. The earliest studies dated back to 1973 for the relationship between renal dysfunction and cadmium concentration in rice in the Jinzu River in Japan(Watanabe et al. 2002). In 2001, Osawa made a retrospective study on the relation between renal dysfunction and cadmium concentration in rice. The study showed that the increasing of the cadmium content in rice can lead to a significant rise of the indicators which means the increasing of the cadmium content in rice can lead to kidney damage (Osawa et al., 2001). In addition, in 2009, Etsuko Kobayashi et al. also conducted a research to explore the relationship between cadmium content in rice and renal tubular damage.

Conclusion

In conclusion, this study first used the correlation analysis and path analysis to analyze whether S-Cd and R-Cd could have negative influence on renal health. Our research results showed that S-Cd and R-Cd played important roles in U-NAG and U-β_2MG emission. So essentially, cadmium pollution in soil and rice cause damage to human body health. We suggested we should adopt S-Cd and R-Cd as indicators of cadmium environmental exposure and we should take stringent regulatory measures to the cadmium content in soil and rice. However, we have to admit that on the base of our research, we cannot know which one is more applicable to indicate cadmium environmental exposure and assess the related human renal dysfunction. On the one hand, from correlation analysis, we know there were significant relationships among S-Cd, R-Cd, U-Cd, and U-NAG, U-β_2MG. S-Cd, R-Cd, U-Cd could affect each other mutually. On the other hand, through path analysis, we found that compared to S-Cd, the effect of R-Cd on U-NAG was not significant. However, when we took U-β_2MG as the bio-marker, the effect of S-Cd was not significant compared to S-Cd. The future research should focus on the risk assessment of S-Cd and R-Cd.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

Akerstrom M et al (2013) Associations between urinary excretion of cadmium and proteins in a nonsmoking population: renal toxicity or normal physiology? Environ Health Perspect 121(2):187–191. doi:10.1289/ehp.1205418

Chen XJ et al (2012) Study on Soil Environmental Quality Based on Fuzzy Comprehensive Evaluation—A Case Study of Liwu Copper Area in Jiulong County. Research of Soil & Water Conservation 19(1):130–133

Cheng F et al (2006) Cadmium and lead contamination in japonica rice grains and its variation among the different locations in southeast China. Sci Total Environ 359(1–3):156–166. doi:10.1016/j.scitotenv.2005.05.005

de Vries W et al (2007) Critical soil concentrations of cadmium, lead, and mercury in view of health effects on humans and animals. Rev Environ Contam Toxicol 191:91–130

Etsuko K, Yasushi S, Mirei D, Ryumon H, Teruhiko K (2009a) Influence of Consumption of Cadmium-Polluted Rice or Jinzu River Water on Occurrence of Renal Tubular Dysfunction and/or Itai-itai Disease. Biological Trace Element Research 127(3):257–268

Ezaki T et al (2003) Analysis for threshold levels of cadmium in urine that induce tubular dysfunction among women in non-polluted areas in Japan. Int Arch Occup Environ Health 76(3):197–204. doi:10.1007/s00420-002-0390-9

Franz E et al (2008) A chain modeling approach to estimate the impact of soil cadmium pollution on human dietary exposure. J Food Prot 71(12):2504–2513

Ikeda M et al (2004) Dietary cadmium intake in polluted and non-polluted areas in Japan in the past and in the present. Int Arch Occup Environ Health 77(4):227–234. doi:10.1007/s00420-003-0499-5

Jarup L, Akesson A (2009) Current status of cadmium as an environmental health problem. Toxicol Appl Pharmacol 238(3):201–208. doi:10.1016/j.taap.2009.04.020

Jin T et al (2004) Environmental epidemiological study and estimation of benchmark dose for renal dysfunction in a cadmium-polluted area in China. Biometals 17(5):525–530

Kobayashi E, Suwazono Y, Dochi M, Honda R, Nishijo M, Kido T et al (2008) Estimation of benchmark doses as threshold levels of urinary cadmium, based on excretion of β 2 -microglobulin in cadmium-polluted and non-polluted regions in japan. Toxicology Letters 179(2):108–112

Kobayashi E, Yasushi S, Mirei D, Ryumon H, Teruhiko K (2009a) Influence of Consumption of Cadmium-Polluted Rice or Jinzu River Water on Occurrence of Renal Tubular Dysfunction and/or Itai-itai Disease. Biological Trace Element Research 127(3):257–268

Kobayashi E, Yasushi S, Mirei D, Ryumon H, Teruhiko K (2009b) Estimation of Benchmark Rice Cadmium Doses as Threshold Values for Abnormal Urinary Findings with Adjustment for Consumption of Jinzu River Water. Bulletin of Environmental Contamination and Toxicology 83(1):102–107

Kobayashi E, Yasushi O, Yasushi S, Teruhiko K, Koji N (2002) Dose-response relationship between total cadmium intake calculated from the cadmium concentration in rice collected from each household of farmers and renal dysfunction in inhabitants of the Jinzu River basin, Japan. Journal of Applied Toxicology 22(6):431–436

Ke S et al (2015a) Body burden of cadmium and its related factors: a large-scale survey in China. Sci Total Environ 511:649–654. doi:10.1016/j.scitotenv.2015.01.014

Ke S et al (2015b) Estimation of the benchmark dose of urinary cadmium as the reference level for renal dysfunction: a large sample study in five cadmium polluted areas in China. BMC Public Health 15:656. doi:10.1186/s12889-015-2021-x

Ke S et al (2015c) Cadmium contamination of rice from various polluted areas of China and its potential risks to human health. Environ Monit Assess 187(7):408. doi:10.1007/s10661-015-4638-8

Lane EA, Canty MJ, More SJ (2015) Cadmium exposure and consequence for the health and productivity of farmed ruminants. Research in Veterinary Science 101:132–139

Nakashima K, Kobayashi E, Nogawa K, Kido T, Honda R (1997) Concentration of cadmium in rice and urinary indicators of renal dysfunction. Occupational and Environmental Medicine 54(10): 750–755

Nishijo M et al (2014) Risk assessment for Thai population: benchmark dose of urinary and blood cadmium levels for renal effects by hybrid approach of inhabitants living in polluted and non-polluted areas in Thailand. BMC Public Health 14:702. doi:10.1186/1471-2458-14-702

Nogawa K et al (2004) Environmental cadmium exposure, adverse effects and preventive measures in Japan. Biometals 17(5):581–587

Nogawa K et al (2015) Benchmark dose of cadmium concentration in rice for renal effects in a cadmium-polluted area in Japan. J Appl Toxicol 35(1):24–28. doi:10.1002/jat.2982

Osawa T et al (2001) A retrospective study on the relation between renal dysfunction and cadmium concentration in rice in individual hamlets in the Jinzu River basin, Toyama prefecture, Japan. Environ Res 86(1):51–59. doi:10.1006/enrs.2001.4248

Satarug S, Scott HG, Sens MA, Sens DA (2009) Cadmium, Environmental Exposure, and Health Outcomes. Environmental Health Perspectives 118(2):182–190

Shao B et al (2007) Application of benchmark dose (BMD) in estimating biological exposure limit (BEL) to cadmium. Biomed Environ Sci 20(6):460–464

Staessen JA et al (1994) Renal function and historical environmental cadmium pollution from zinc smelters. Lancet 343(8912):1523–1527

Suwazono Y et al (2011) Application of the hybrid approach to the benchmark dose of urinary cadmium as the reference level for renal effects in cadmium polluted and non-polluted areas in Japan. Environ Res 111(2):312–314. doi:10.1016/j.envres.2010.11.013

Swaddiwudhipong W et al (2010) Correlations of urinary cadmium with hypertension and diabetes in persons living in cadmium-contaminated villages in northwestern Thailand: a population study. Environ Res 110(6):612–616. doi:10.1016/j.envres.2010.06.002

Uraguchi S, Fujiwara T (2012) Cadmium transport and tolerance in rice: perspectives for reducing grain cadmium accumulation. Rice (N Y) 5(1):5. doi:10.1186/1939-8433-5-5

Wallin M et al (2014) Low-level cadmium exposure and effects on kidney function. Occup Environ Med 71(12):848–854. doi:10.1136/oemed-2014-102279

Wang L, Xiangfen C, Hongguang C, Chen F, Wang J, Zhao X, Lin C, Xiao P (2015) A review of soil cadmium contamination in China including a health risk assessment. Environmental Science and Pollution Research 22(21):16441–16452

Watanabe T et al (2004) Gender-related difference, geographical variation and time trend in dietary cadmium intake in Japan. Sci Total Environ 329(1–3):17–27. doi:10.1016/j.scitotenv.2004.03.010

Watanabe Y, Etsuko K, Yasushi O, Yasushi S, Teruhiko K, Koji N (2002) Relationship between cadmium concentration in rice and renal dysfunction in individual subjects of the Jinzu River basin determined using a logistic regression analysis. Toxicology 172(2):93–101

Xu L et al (2011) Research progress of bioremediation technology of cadmium polluted soil. J Nanjing Norm Univ (Natural Science Edition) 34(01):102–106

Zhang WL et al (2014) Cadmium exposure and its health effects: a 19-year follow-up study of a polluted area in China. Sci Total Environ 470-471:224–228. doi:10.1016/j.scitotenv.2013.09.070