The relationship between Nephrotoxic Metals of cadmium, lead and mercury with Urinary Incontinence in Women

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Research Article

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Abstract

Purpose: Nephrotoxic metals of cadmium, lead and mercury are the common hazardous pollutants existing in surroundings. We examined the relationship between cadmium, lead and mercury with urgency urinary incontinence (UUI) and stress urinary incontinence (SUI) in women.

Materials and Methods: The women older than 20 years from the 2007-2016 National Health and Nutrition Examination Survey (NHNES) with the ascertained urinary incontinence through self-report were included. This study conducted the restricted cubic spline analysis to analyze characterize a dose-response relationship between a continuous exposure of different nephrotoxic metals and UUI and SUI.

Results: A total of 4,406 women were included in this study, with 2,624 (59.6%) were SUI and 3,177 (72.1) were UUI of the weighted population. The results of multivariate analysis indicated that age, race, marital status, body mass index (BMI) and nephrotoxic metals were risk factors for the odds of UUI and SUI. The odds ratio (OR; 95% confidence interval) of urinary incontinence were positively correlated with cadmium and lead in women. The OR of SUI increased with the increasing blood cadmium, possessing the maximum at 4 µg/L (2.18(1.34-3.58) overall). The odds of UUI increased with the blood and urinary lead, which reached the maximum at 7 µg/dL (2.03 (1.38-3.02) overall) and 5 µg/L (2.24 (1.34-3.75) overall) respectively.

Conclusions: Nephrotoxic metals of cadmium and lead were associated the odds of urinary incontinence in women. Excessive exposure to these metals will increase the OR of UUI and SUI in adult women.

Introduction

Urinary incontinence (UI) is a common disease with highly prevalent in women("Urinary Incontinence in Women," 2020) and defined as the involuntary loss of urine which affecting daily life(Lukacz et al., 2017). The types of UI were classified into stress urinary incontinence (SUI), urgency urinary incontinence (UUI) and mixed urinary incontinence according to the patient's clinical presentation(Muth, 2017). It was found that 17.1% of women aged ≥ 20 suffering from moderate to severe UI in the United States based a cross-sectional study(Wu et al., 2014). The incidence of UI increases with age and nearly 40% of elderly women worldwide are affected("Urinary Incontinence in Women," 2020). However, there were only 25% of affected women seeking treatment for UI and less than half of those received correspondingly effective treatment(Lukacz et al., 2017; Minassian et al., 2012). The underdiagnosed and undertreated of UI is an urgent problem for clinicians and there is lacking of an effective tool to break the plight.

Nephrotoxic metals of cadmium, lead and mercury are the common hazardous pollutants existing in surroundings and included in the lists of "Ten chemicals of major public health concern"(http://www.who.int/ipcs/assessment/public_health/chemicals_phc/en/). There were evidences proved that these metals have harmful effects on the function of the body(Orr & Bridges, 2017; Y. Sun et al., 2019). It was reported that nephrotoxic metals serving as biomarkers for the prediction of kidney stones(Y. Sun et al., 2019). Additionally, the cardiovascular events such as coronary heart diseases were proved to be related to the exposure of environmental nephrotoxic metals(Chowdhury et al., 2018). The oxidative stress was the recognized cause of nephrotoxicity and even low-dose exposures could be extremely damaging(Rana et al.,

2018). Although it is known that nephrotoxic metal exposure can impair organismal function, the relationship with UI has not been reported.

The objective of this study was to investigate whether there existing a relationship between nephrotoxic metal exposure and SUI/UUI in women according to the cross-sectional evidence from population-based National Health and Nutrition Examination Survey (NHNES). We hypothesized that nephrotoxic metal of cadmium, lead and mercury exposing would be associated with the odds of female SUI and UUI.

Materials And Methods

Study population

The demographic data included in the study originates from NHNES, a nationally representative stratified multistage survey of the resident noninstitutionalized US population. Participants will receive private questionnaires involve socioeconomics, diet and health at home or mobile examination centers. Simultaneously, examinations including medical, physiological and laboratory tests will be carried out. The specific survey methods and endpoint results have been reported in detail(Zipf et al., 2013).

We analyzed data from 5 consecutive NHANES 2-year survey cycles (2007–2008, 2009–2010, 2011–2012, 2013–2014, 2015–2016) which including the questionnaires involving urinary incontinence type and frequency. All the female participants aged 20 or older who responded to the survey questionnaire of “Kidney Conditions – Urology” were included in this cohort.

Nephrotoxic metal exposure

The exposure of nephrotoxic metals was tested by inductively coupled-plasma dynamic reaction cell-mass spectrometry. The independent variables included the nephrotoxic metals of cadmium, lead and mercury, which were all tested in blood and urine. Specimens from participants were processed, stored and transported to the Division of Environmental Health Laboratory Science, NCEH (National Center for Environmental Health) at CDC (Centers for Disease Control and Prevention) for analysis. All laboratory tests meet the 1988 Clinical Laboratory Improvement Act and the detailed quality assurances are listed in <https://www.cdc.gov/nchs/nhanes/index.htm>.

Urinary incontinence assessment

The primary outcome of the study was whether experiencing SUI or UUI in the past 12 months assessed by self-report. Participants would been asked the following two questions to decide the SUI (1) or UUI (2). “1) Have you leaked or lost control of even a small amount of urine with an activity like coughing, lifting or exercise? 2) Have you leaked or lost control of even a small amount of urine with an urge or pressure to urinate and you could not get to the toilet fast enough?” The assessment of UI by the self-reported questionnaire was proved as effective and reliable(Weinberg et al., 2015). The participants excluded from specific types of urinary incontinence (SUI or UUI) were considered non-cases.

Other clinical covariates

Age, race, marital status and education were included in this study as the covariates. The race was categorized as Non-Hispanic (white or black), Mexican American, Other Hispanic and Other. Marital status consisted of Married, Unmarried and Other. The education was classified as less than high school, high school or equivalent, college or above and other. The body mass index (BMI, kg/m²) was divided into non-obese (<30.0 kg/m²) and obese (≥30.0 kg/m²) using the World Health Organization criteria.

Statistical analysis

Restricted cubic spline was proved as an effective statistical analysis to characterize the dose-response relationship between continuous exposure and a special outcome (Desquilbet & Mariotti, 2010; Yaofei Sun et al., 2019). The relationship between the continuous nephrotoxic metals' exposure and the two kinds of UI was assessed by the restricted cubic spline with the three cutoffs in the 5th, 50th and 95th percentiles of the exposures. The estimated odds ratios (ORs) accompanied with 95% confidence intervals (95% CIs) of UI for different exposure values were measured using the procedure reported by Orsini and Greenland (Orsini & Greenland, 2011). The other clinical variables were respectively assessed by the Pearson chi-square test (for categorical variables) and the Student t-test (for continuous variables). All the results were adjusted for age, race, marital status, education and BMI. The exposure-response analysis was also proceeded by the age and BMI, which were found as prognostic factors for the UI (Almoussa & Bandin van Loon, 2018; Lukacz et al., 2017). This study included five 2-year cycles as the research subject to generate accurate prediction containing less sampling error. All the samples specific to the study of women who had proceed laboratory tests were retrieved from NHANES. The analyses in this study were conducted by Stata 12.0 and results were considered as statistically significant at 2-tailed $p < 0.05$.

Results

This study finally included 4,406 females. Among the weighted population 1,782 (40.4%) complained of SUI and 1,229 (27.9%) complained of UUI. Age was proved as a risk factor of UI ($p < 0.001$) and the average age for SUI/UUI were 52.65 ± 15.93 and 56.27 ± 16.73 years respectively, older than non-UI women. There were 997 (55.9%) women of SUI and 800 (65.1%) of UUI aged >50 years among the weighted SUI and UUI population respectively ($p < 0.001$). The Non-Hispanic white of different races accounted for the most among the two kinds of UI population ($p < 0.001$), 866 (48.6%) of SUI and 534 (43.4%) of UUI. Marital status showed the opposite trend of population distribution among the weighted SUI/UUI population ($p < 0.001$), which 913 (51.2%) married women reported as SUI and 618 (50.3%) unmarried women as UUI. The education level was also proved as the risk factor for the two kinds of UI and women with education level of college or above accounted for 946 (53.1%) in weighted SUI population ($p = 0.028$), 635 (51.7%) in UUI ($p = 0.020$). BMI was a predictive factor for UI ($p < 0.001$) and the SUI women with an average BMI of 30.56 ± 7.30 kg/m², which was 30.98 ± 7.68 kg/m² for UUI. The Non-obese females among the weighted two kinds of UI population were proved as the most part, 948 (53.2%) of SUI and 619 (50.4%) of UUI. The demographic of the included female population can be found in Table 1.

The nephrotoxic metals of cadmium and lead were proved as the risk factors of both SUI and UUI (Table 1, Fig. 1). It was found that blood and urinary cadmium were associated with the occurrence of UI and the population with SUI or UUI had higher levels of cadmium [blood: (0.43 ± 0.78 vs. 0.36 ± 0.63 , $p = 0.001$; 0.44 ± 0.74 vs.

0.37±0.67, p=0.002); urinary: (0.32±0.60 vs. 0.25±0.55, p<0.001; 0.36±0.64 vs. 0.24±0.54, p<0.001)]. Simultaneously, the results indicated that the blood and urinary lead were hazard factors for the suffering of SUI/UUI [blood: (1.35±1.25 vs. 1.23±1.06, p=0.001; 1.51±1.37 vs. 1.19±1.03, p<0.001); urinary: (0.53±1.42 vs. 0.44±0.83, p=0.008; 0.62±1.80 vs. 0.43±0.67, p<0.001)]. As for the mercury, there was no statistically significant difference between populations with SUI/UUI or not (p>0.05).

Among the included 4,406 females, the odds ratios of SUI/UUI were detailed described in Table 2 after adjustment of the nephrotoxic metal exposure. The ORs (95% CI) of UI were positively correlated with cadmium and lead in women. The OR of SUI increased with the increasing blood/urinary cadmium, possessing the maximum at 4 µg/L (2.18(1.34-3.58) overall) and 2.5 µg/L (1.41 (1.02-1.96) overall). As for the UUI, the same trends of OR were found and the maximum OR were 1.28 (1.15-2.09) at 4 µg/L, 1.62 (1.15-2.28) at 2.5 µg/L. The odds of UUI increased with the blood and urinary lead, which reached the maximum at 7 µg/dL (2.03 (1.38-3.02) overall) and 5 µg/L (2.24 (1.34-3.75) overall) respectively. The relationships between ORs of UI and nephrotoxic metal exposure were detailed shown in Fig. 2.

Additionally, we further analyzed the relationship between ORs of SUI/UUI and nephrotoxic metal exposure according to the subgroups of age and BMI, which were proved as the risk factors of UI. The trends of ORs between UI and nephrotoxic metal exposure among the population aged<50 years were described in Fig. 3. It was indicated that the ORs of SUI were positively correlated with blood/urinary lead and urinary mercury apart from the overall trends. However, the trends of ORs in the population aged≥50 years were different from the overall which were showed in Fig. 4. There were no obvious correlations except for the positive relationship of UUI' ORs and urinary lead/mercury. Based on the BMI, the population was divided into non-obese and obese subgroups. Among the non-obese subgroup, it was indicated that the ORs of UUI were negatively correlated with blood/urinary mercury (Fig. 5) which was different from the trends in obese subgroup (Fig. 6).

Discussion

This study firstly reveals the correlation between nephrotoxic metal exposure and two kinds of urinary incontinence in female. We detailed analyzed the relationship between the nephrotoxic metals of cadmium, lead, mercury and SUI/UUI based on five 2-year cycles from the NHANES database. It was founded that the levels of blood/urinary cadmium and lead were risk factors of the odds ratios of SUI/UUI in women. Simultaneously, there were further subgroups analyses according to age and BMI. The results showed that the higher level of nephrotoxic metals exposure of cadmium and lead were positively related with the higher ORs of SUI/UUI.

UI as one of the most common diseases in women has attracted widespread attention. It was reported that social isolation and psychological distress were the usual negative effects bring by UI, which also increased the risks of falls and fractures(Brown et al., 2000; E. Yang et al., 2018). The definition of SUI is the uncontrollable loss of urine due to the increased stress with physical activities and the occurrence is higher among young women("Urinary Incontinence in Women," 2020). As for UUI, it is the loss of urine at incorrect occasion and time with urgency and more common as female age("Urinary Incontinence in Women," 2020). There existed kinds of risk factors for UI in women, including age, BMI, injury and so on(Almoussa & Bandin van Loon, 2018; Nygaard & Shaw, 2016). The above evidence all indicated that UI is closely related to the

homeostasis imbalance and changes in indicators which reflect health levels may have a predictive effect on the occurrence of UI(Chughtai et al., 2019). Suffering from UI will not only seriously damage the living quality of the patient and subsequent individualized treatment will also add economic burden and life pressure on the patient(Wood & Anger, 2014). Therefore, it is extremely necessary to timely predict and prevent the occurrence of UI. We firstly detailed analyze the relationship between nephrotoxic metals and the occurrence of SUI/UUI, which contributing to formulate patient-centered prevention and treatment measures.

The exposure of nephrotoxic metals is the inevitable and extremely harmful process in daily life, just like decoration, smoking, drug and so on(Orr & Bridges, 2017; Rana et al., 2018; Y. Sun et al., 2019; B. Yang et al., 2018). To our knowledge, the perceptible effects of kinds of nephrotoxic metals are only toxic without biologic application(Bridges & Zalups, 2017; Satarug et al., 2020). It was reported that the exposure of nephrotoxic metals will increase the risk of kidney stones formation, acute/chronic kidney disease and even renal cancer(Kosiba et al., 2020; Orr & Bridges, 2017; Y. Sun et al., 2019). The nephrotoxic metals of cadmium is a prevalent environmental pollution toxic substances which mostly enriched in plants, aquatic and industrial products(Odabaei et al., 2004; Singh et al., 2015). Additionally, smoking is an important reason for the intake of metallic cadmium which nearly 1-2 μg of cadmium existing in most cigarettes(Orr & Bridges, 2017). And nearly 50% of the cadmium taken in by the body will be stored in the kidneys during the exposure(Thévenod, 2003), causing the un-recoverable renal dysfunction. Unexpectedly, the intake of cadmium approaching half safe intake according to guidelines may increase the risk of chronic kidney disease (CKD) by 73%(Satarug et al., 2020). The accumulation of cadmium in kidney can reduce glomerular filtration rate (GFR), result in polyuria and damage renal tubules(Orr & Bridges, 2017; Satarug et al., 2020). Simultaneously, the un-activated vitamin-D caused by excess renal cadmium would be the potential triggers of kidney stone formation(Johri et al., 2010; Orr & Bridges, 2017). However, the potential pathophysiological relationship between nephrotoxic metal cadmium exposure and UI has not been studied yet. In this study, we firstly analyze the retrospective data to reveal the relationship between UI and nephrotoxic metal exposure. Based on the accumulating form of renal cadmium and the subsequent kidney damage, smoking and polyuria may be the potential causes of SUI/UUI. Excessive smoking not only causes the accumulation of renal cadmium, but also damage the respiratory system causing chronic obstructive pulmonary emphysema (COPD), lung cancer and so on. And quitting smoking has been regarded as one of the lifestyle changes to improve UI(John, 2020). The polyuria caused by renal dysfunction can also lead to the occurrence of UI(Tyagi et al., 2017), which reminding clinician of alerting the diuretics in patients with CKD.

The nephrotoxic metallic lead usually exists as the compound with other substances in environment(Orr & Bridges, 2017). The lead compound usually as an industrial product mixed in gasoline, pipelines, batteries, paints and so on(Edwards & Prozialeck, 2009; Orr & Bridges, 2017). The interim safe intake level of dietary lead is 12.5 $\mu\text{g}/\text{L}$ defined by Food and Drug Administration (FDA) after the standard adjustment(Dolan et al., 2020). The nephrotoxic metallic lead has been proved to contain nerve, skeletal, renal toxicity and it was found that there was no threshold of the neurotoxicity caused by lead(Orr & Bridges, 2017; Satarug et al., 2020). Additionally, the lead poisoning is more common and more severe in children than adults(Orr & Bridges, 2017). The kidney is the primary organ for dietary lead accumulation due to the detoxification effect, which causing long-term irreversible renal toxicity of lead(Fowler & DuVal, 1991). Which had been studied well was that the exposure of nephrotoxic metallic lead would destroy glomerular development and cause renal dysfunction(Satarug et al., 2020). Another important pathological mechanism of metallic lead may origin from

the mitochondrial damage caused by oxidative stress and it was reported that the lead exposure contributing to the mitochondria permeability transition pore (MPTP)(Kerper & Hinkle, 1997; Simons, 1993). On the other hand, the lead ion (Pd^{2+}) could competitively inhibit the effect of Ca^{2+} in cell, which would lead to the disorder of cell function(Peng et al., 2002). The increase in oxidative stress and disorder of Ca^{2+} regulation caused by metallic lead may lead to chronic inflammation and abnormal muscle contraction, which can be regarded as the potential mechanism affecting the occurrence of UI.

As for nephrotoxic metallic mercury, it is mainly ingested by the human through food as the methylmercury (CH_3Hg^+)(Orr & Bridges, 2017). When the kidney exposing to the high dose of mercury, it can cause renal tubular damage and necrosis(Bridges & Zalups, 2017; Zalups & Ahmad, 2004). Just like lead, nephrotoxic metallic mercury can also cause mitochondrial damage and lead to disorder of cell function(Afsar et al., 2019). Simultaneously, the long-term exposure of mercury may destroy the renal function and decrease the GFR(Afsar et al., 2019; Bridges & Zalups, 2017). Different from the nephrotoxic metals of cadmium and lead, it was indicated that the level of blood or urinary mercury was not correlated with the occurrence of the UI. And it was only found that there were changes in the trend of UI occurrence in subgroups analysis. There is still lack of further evidence to confirm that nephrotoxic metallic mercury has an effect on the occurrence of UI.

In this study, we firstly revealed the relationship between nephrotoxic metals and the occurrence of SUI/UUI. It was found that nephrotoxic metallic cadmium and lead had a positive effect on the occurrence of SUI/UUI. However, this study still existed some limits as follows. Firstly, this study as a retrospective research has the possibility of existing bias. Secondly, the conclusion obtained from this retrospective study needs to conduct further multi-center prospective studies for verification. Thirdly, this study lacks in-depth research on potential pathological mechanisms of the correlation between the exposure of nephrotoxic metals and the occurrence of SUI/UUI.

Conclusion

This study firstly revealed the relationship between nephrotoxic metals exposure and the occurrence of SUI/UUI. Nephrotoxic metals of cadmium and lead were associated the odds of urinary incontinence in women. Excessive exposure to these metals will increase the OR of UUI and SUI in adult women. This will contribute to predict the SUI or UUI and assist clinicians to develop individualized prevention and treatment plans.

Declarations

Funding information

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Competing interests

The author reports no conflicts of interest in this work.

Ethical Statement

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study used previously collected deidentified data, which was deemed exempt from review by the Ethics Committee of the Tenth People's Hospital of Shanghai.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author, Bo Peng, upon reasonable request.

Author contributions

- (I) Conception and design: Jinliang Ni, Ziyi Li.
- (II) Administrative support: Yi Lu, Houliang Zhang, Jun Xie and Guangchun Wang.
- (III) Provision of study materials or patients: Yidi Wang, Jinbo Xie, Yifan Zhang.
- (IV) Collection and assembly of data: Weipu Mao, Keyi Wang and Bo Peng.
- (V) Data analysis and interpretation: Jinliang Ni, Ziyi Li.
- (VI) Manuscript writing: All authors.
- (VII) Final approval of manuscript: All authors.

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Tables

Table 1. Baseline characteristics of all patients in our study ^a.

Characteristic	Stress urinary incontinence (SUI)			Urge urinary incontinence (UI)		
	No	Yes	P value	No	Yes	P value
	No. (%)	No. (%)		No. (%)	No. (%)	
Total patients	2624 (59.6)	1782 (40.4)		3177 (72.1)	1229 (27.9)	
Age, y			<0.001			<0.001
Mean±SD	46.09±18.25	52.65±15.93	<0.001	45.83±17.12	56.27±16.73	<0.001
≤50	1558 (59.4)	785 (44.1)		1914 (60.2)	429 (34.9)	
>50	1066 (40.6)	997 (55.9)		1263 (39.8)	800 (65.1)	
Race			<0.001			<0.001
Non-Hispanic white ³	1043 (39.7)	866 (48.6)		1375 (43.3)	534 (43.4)	
Non-Hispanic black ⁴	605 (23.1)	268 (15.0)		580 (18.3)	293 (23.8)	
Mexican American ¹	422 (16.1)	323 (18.1)		541 (17.0)	204 (16.6)	
Other Hispanic ²	295 (11.2)	186 (10.4)		351 (11.0)	130 (10.6)	
Other ⁵	259 (9.9)	139 (7.8)		330 (10.4)	68 (5.5)	
Marital status			<0.001			<0.001
Married	1176 (44.8)	913 (51.2)		1551 (48.8)	538 (43.8)	
Unmarried	1223 (46.6)	738 (41.4)		1343 (42.3)	618 (50.3)	
Other	225 (8.6)	131 (7.4)		283 (8.9)	73 (5.9)	
Education			0.028			0.020
Less than high school	595 (22.7)	468 (26.3)		730 (23.0)	333 (27.1)	
High school or equivalent	558 (21.3)	367 (20.6)		664 (20.9)	261 (21.2)	
College or above	1471 (56.1)	946 (53.1)		1782 (56.1)	635 (51.7)	
Other	0 (0.0)	1 (0.1)		1 (0.1)	0 (0.0)	
BMI (kg/m ²)			<0.001			<0.001
Mean±SD	28.61±7.22	30.56±7.30	<0.001	28.79±7.08	30.98±7.68	<0.001
Non-obese	1668 (63.6)	948 (53.2)		1997 (62.9)	619 (50.4)	
Obese	956 (36.4)	834 (46.8)		1180 (37.1)	610 (49.6)	
Blood cadmium, µg/L (Mean±SD)	0.36±0.63	0.43±0.78	0.001	0.37±0.67	0.44±0.74	0.002

Urinary cadmium, $\mu\text{g/L}$ (Mean $\pm$ SD)	0.25 $\pm$ 0.55	0.32 $\pm$ 0.60	<0.001	0.24 $\pm$ 0.54	0.36 $\pm$ 0.64	<0.001
Blood lead, $\mu\text{g/dL}$ (Mean $\pm$ SD)	1.23 $\pm$ 1.06	1.35 $\pm$ 1.25	0.001	1.19 $\pm$ 1.03	1.51 $\pm$ 1.37	<0.001
Urinary lead, $\mu\text{g/L}$ (Mean $\pm$ SD)	0.44 $\pm$ 0.83	0.53 $\pm$ 1.42	0.008	0.43 $\pm$ 0.67	0.62 $\pm$ 1.80	<0.001
Blood mercury, $\mu\text{g/L}$ (Mean $\pm$ SD)	0.12 $\pm$ 0.56	0.13 $\pm$ 0.61	0.635	0.12 $\pm$ 0.60	0.11 $\pm$ 0.53	0.638
Urinary mercury, $\mu\text{g/L}$ (Mean $\pm$ SD)	0.58 $\pm$ 1.58	0.63 $\pm$ 1.81	0.320	0.59 $\pm$ 1.40	0.61 $\pm$ 2.23	0.724

^aFor categorical variables, P values were analyzed by chi-square tests. For continuous variables, the t-test for slope was used in generalized linear models.

Abbreviations: BMI, body mass index; SD, Standard deviation.

Table 2

Weighted odds ratio and 95% confidence intervals of urinary incontinence by levels of blood/urinary nephrotoxic metals levels, NHANES 2007–2016.

Characteristic	SUI				UUI			
Blood cadmium	1µg/L	2µg/L	3µg/L	4µg/L	1µg/L	2µg/L	3µg/L	4µg/L
Overall	0.99 (0.83- 1.18)	1.27 (1.04- 1.56)	1.67 (1.20- 2.32)	2.18 (1.34- 3.58)	1.05 (0.87- 1.28)	1.12 (0.90- 1.39)	1.20 (0.86- 1.67)	1.28 (1.15- 2.09)
Urinary cadmium	1µg/L	1.5µg/L	2µg/L	2.5µg/L	1µg/L	1.5µg/L	2µg/L	2.5µg/L
Overall	1.30 (1.08- 1.56)	1.33 (1.10- 1.63)	1.37 (1.07- 1.77)	1.41 (1.02- 1.96)	1.50 (1.24- 1.83)	1.54 (1.25- 1.90)	1.58 (1.21- 2.05)	1.62 (1.15- 2.28)
Blood lead	2µg/dL	4µg/dL	6µg/dL	7µg/dL	2µg/dL	4µg/dL	6µg/dL	7µg/dL
Overall	1.13 (0.98- 1.32)	1.15 (0.95- 1.40)	1.15 (0.84- 1.57)	1.15 (0.78- 1.69)	1.39 (1.19- 1.63)	1.65 (1.35- 2.02)	1.90 (1.38- 2.63)	2.03 (1.38- 3.02)
Urinary lead	2µg/L	3µg/L	4µg/L	5µg/L	2µg/L	3µg/L	4µg/L	5µg/L
Overall	1.15 (0.97- 1.37)	1.20 (0.97- 1.48)	1.25 (0.96- 1.62)	1.30 (0.94- 1.80)	1.44 (1.18- 1.76)	1.67 (1.27- 2.21)	1.93 (1.31- 2.86)	2.24 (1.34- 3.75)
Blood mercury	0.5µg/L	1µg/L	1.5µg/L		0.5µg/L	1µg/L	1.5µg/L	
Overall	1.06 (0.94- 1.18)	1.06 (0.94- 1.21)	1.07 (0.91- 1.25)		0.97 (0.86- 1.10)	0.96 (0.83- 1.11)	0.95(0.79- 1.14)	
Urinary mercury	1µg/L	2µg/L	4µg/L	6µg/L	1µg/L	2µg/L	4µg/L	6µg/L
Overall	1.05 (0.92- 1.21)	1.08 (0.89- 1.32)	1.10 (0.90- 1.35)	1.12 (0.88- 1.42)	1.00 (0.86- 1.15)	1.00 (0.81- 1.24)	1.02 (0.82- 1.28)	1.05 (0.81- 1.36)

Figures

Figure 1

The violin plot of nephrotoxic metals' impacts on urgency urinary incontinence (UUI) and stress urinary incontinence (SUI).

Figure 2

The dose–response analysis between blood/urinary nephrotoxic metals (cadmium, lead and mercury) and urgency urinary incontinence (UUI) and stress urinary incontinence (SUI) in the weighted population.

Figure 3

The dose–response analysis between blood/urinary nephrotoxic metals (cadmium, lead and mercury) and urgency urinary incontinence (UUI) and stress urinary incontinence (SUI) in the weighted population which aged ≤ 50 .

Figure 4

The dose–response analysis between blood/urinary nephrotoxic metals (cadmium, lead and mercury) and urgency urinary incontinence (UUI) and stress urinary incontinence (SUI) in the weighted population which aged >50 .

Figure 5

The dose–response analysis between blood/urinary nephrotoxic metals (cadmium, lead and mercury) and urgency urinary incontinence (UUI) and stress urinary incontinence (SUI) in the weighted population with the BMI as non-obese.

Figure 6

The dose–response analysis between blood/urinary nephrotoxic metals (cadmium, lead and mercury) and urgency urinary incontinence (UUI) and stress urinary incontinence (SUI) in the weighted population with the BMI as obese.