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Letter to the Editor

Association between Renal Dysfunction Biomarkers and Low Levels of Cadmium Burden in Populations Exposed to Environmental Cadmium

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Dear Editor-in-Chief

Cadmium is one of the heavy metal pollutants that causes nephrotoxicity and carcinogenicity in workers of occupational exposure (1). Since cadmium can be released into the atmosphere, and thus widely distributed in the environment, non-occupational exposure of cadmium is ubiquitous in general population in china (2) as well as all over the world (3). However, the association between renal dysfunction and low cadmium burden is still questionable (4, 5).

In this study, we examined cadmium toxicity from a new perspective of non-occupational patients suffering from renal dysfunction. Eighty two patients with renal dysfunction, who enrolled at the Yangpu Hospital in the year of 2017 and characterized as urine albumin/creatinine ratio≥30 mg/g creatinine (6), were included in the patient cohort, and 74 time-matched subjects were served as the control cohort.

Fasting blood samples were collected for determination of blood lead (Bpb), cadmium (Bcd), creatinine (CREA), urea nitrogen (BUN), uric acid (URCA), and cystatin C (CysC). Spot midstream urine samples were analyzed for cadmium (Ucd), albumin (ALB), β_2-microglobulin (BMG), N-acetyl-β-D-glucosaminidase (NAG), and retinol binding protein (RBP).The cadmium and lead were detected by using an atomic absorption spectrophotometer (ZEEnit700P, Analytikjena), while renal dysfunction biomarkers were detected by using an automatic biochemical analyzer (Dimension RXL MAX，SIEMENS).

All the urinary biomarkers were normalized to urinary creatinine. Data were analyzed using SPSS version 20.0 (Chicago, IL, USA). Values below the LOD were considered negative and given an arbitrary value of LOD/√2. Median (P_{50}) and interquartile range (P_{25}-P_{75}) were used for data with skewed distribution. Mean ± standard deviation was used for data with normal distribution. The Mann-Whitney U test was used for parameter comparisons between groups. A Spearman correlation analysis was conducted to evaluate bivariate associations between variables.

The investigation was in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the hospital.

A comparison of cadmium level was made between the patient cohort and the control cohort. As shown in Table 1, urinary cadmium level in the patient cohort was much higher than in the control cohort. No differences were noted for

levels of blood lead or blood cadmium between the two cohorts. Conversely, the subjects were divided into high cadmium (HC) group and low cadmium (LC) group based on the median of 0.76 µg/g creatinine. Fifty one nephropathy patients and 27 healthy individuals were in the high cadmium group, 31 nephropathy patients and 47 healthy individuals were in the low cadmium group. Table 2 shows the results of different biomarkers. No difference was noted for uric acid between the two groups.

Moreover, using Spearman Correlation Analysis, urinary cadmium was positively correlated with all the renal dysfunction biomarkers, and that the correlations were significant.

Table 1: Cadmium and lead exposure in the patient and control cohorts

Cohort	*Numbers*	*Ucd (µg/g creatinine) ***	*Bpb(µg/L)*	*Bcd(µg/L)*
Patient cohort	82	1.09(0.50,3.77)	23(15,39)	0.8(0.4,2.5)
Control cohort	74	0.40(0.19,1.24)	24(15,36)	1.1(0.7,2.3)
p value		<0.001	0.798	0.067

Note: Ucd, urinary cadmium; Bpb, blood lead; Bcd, blood cadmium. ***P*<0.001.
Data are presented as 'Median (P_{25},P_{75})'. We used the Mann-Whitney U test for parameters comparison

Table 2: Biomarkers of renal function in the HC and LC groups

Biomarkers	*Unit*	*Low cadmium group (n=78)*	*High cadmium group (n=78)*	*P value*
CREA*	µmol/L	71(61-86)	80(61-151)	0.044
URCA	µmol/L	338(282-411)	384(300-468)	0.069
BUN*	mmol/L	5.5(4.1-7.1)	6.1(4.8-12.2)	0.012
CysC**	mg/L	0.8(0.6-1.1)	1.1(0.8-2.0)	<0.001
ALB**	mg/g [a]	10.3(3.3-136.3)	332.8(9.7-1368.6)	<0.001
BMG**	mg/g [a]	0.2(0.1-0.3)	0.6(0.3-4.3)	<0.001
NAG**	U/g [a]	5.5(2.8-17.1)	31.3(12.7-58.4)	<0.001
RBP**	mg/g [a]	0.4(0.2-2.2)	4.9(0.7-10.9)	<0.001

Note: [a]urinary biomarkers were expressed as per gram of urinary creatinine. **P*<0.05;***P*<0.001.
Data are presented as 'Median (P_{25}-P_{75})'. The Mann-Whitney U test was used for parameters comparison

Therefore, this study demonstrated that even a low cadmium burden was positively associated with renal dysfunction in general urban patients, cadmium maybe an important risk factor in renal dysfunction.

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Conflicts of interest

The authors declare no conflict of interest.

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