Cadmium-Exposed Population in Mae Sot District, Tak Province: 2. Prevalence of Renal Dysfunction in the Adults

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Background: *In 2004, 7,697 cadmium-exposed persons aged 15 years and older in Mae Sot District, Tak Province, Thailand, were screened for urinary cadmium levels and 554 cases (7.2%) had ≥ 5 μg/g creatinine.*
Objective: *The present study reported the prevalence of renal dysfunction among those with high urinary cadmium (≥ 5 μg/g creatinine).*
Material and Method: *The study persons were interviewed and examined for detection of renal dysfunction. Venous blood and second morning urine were obtained from each subject for microscopic analysis and biochemistry measurements.*
Results: *Of the 527 examined persons, 14.2% had urinary β_2-microglobulin excretion between 300 and 999 μg/g creatinine, and 19.9% contained ≥ 1,000 μg/g creatinine. About 21.1% had serum creatinine concentrations between 1.1 and 1.4 mg/dl and 4.2% contained ≥ 1.5 mg/dl. Low glomerular filtration rate (GFR < 60 ml/min/1.73 m^2 body surface area) was present in 16.9% of the study persons. Of the persons surveyed, 75.3% had the fractional excretion of phosphate > 5% and 24.7% contained the fractional excretion of potassium > 10%. The overall prevalence rates of hypertension and urinary stones in the study population were 31.3% and 8.9%, respectively. Excretion of urinary β_2-microglobulin significantly increased with increasing urinary cadmium levels. Both increased serum creatinine and decreased GFR appeared to be associated with increasing urinary cadmium although the difference was not statistically significant. There were no significant associations between urinary cadmium levels and excretion of urinary protein, urinary calcium, hypertension, and urinary stones.*
Conclusion: *Excessive exposure to cadmium might produce renal dysfunction among the present study population. Increased urinary excretion of β_2-microglobulin is a good indicator of renal tubular dysfunction among persons with excessive cadmium exposure.*

Keywords: *Cadmium, Urine, Environmental exposure, Renal dysfunction, Thailand*

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For people in the general environment, the major route of cadmium exposure is via food. Increase in soil cadmium content generally results in an increase in the uptake of cadmium by plants. Agricultural crops grown in cadmium-contaminated areas have been found to contain elevated cadmium content compared with normal levels[1,2]. Human cadmium exposure via food in contaminated areas can therefore be many times above normal intakes and long-term oral exposure may lead to cadmium toxicity. Urinary excretion of cadmium is a good indicator of excessive cadmium exposure and body burden[1-6]. Several studies have shown that the kidney is the main target organ for chronic cadmium exposure[1-7]. The nephrotoxic effects are characterized by tubular dysfunction and tubular cell damage. An early sign of tubular dysfunction is demonstrated by increased urinary excretion of low molecular weight proteins. The renal effects of cadmium causing proteinuria may progress and lead to increased blood creatinine, decreased glomerular filtration rate (GFR),

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and end-stage renal disease[1-7]. There is controversy as to whether the urinary cadmium threshold for preventing cadmium nephropathy is 5 or 10 μg/g creatinine[2,3]. The American Conference of Governmental Industrial Hygienists biological exposure index for urinary cadmium is 5 μg/g creatinine[3].

In Mae Sot District, Tak Province, Thailand, the paddy fields receiving irrigation from the two creeks and crops grown in the areas were found to contain markedly elevated cadmium levels during the surveys in 2001-2004[8-11]. Both creeks passed through a zinc rich area where the zinc mine had been actively operated for more than 20 years. Since most of the residents living in these contaminated areas consumed rice grown locally, they were at risk of chronic cadmium toxicity. Of the 7,697 cadmium-exposed persons 15 years and older surveyed in 2004, 554 cases (7.2%) had urinary cadmium levels ≥ 5 μg/g creatinine[12]. This report presented the prevalence of renal dysfunction among those 554 persons with high urinary cadmium.

Material and Method

All persons who contained urinary cadmium levels ≥ 5 μg/g creatinine during the survey in 2004[12] were the subjects of the present study. Health education about cadmium toxic effects and the benefits of the screening assessment for detection of renal dysfunction were provided to the target persons. They were asked about history and treatment of hypertension, diabetes, urinary stone, and renal diseases by trained health workers.

Blood pressure was measured twice on the right arm in a sitting position and the average was recorded. Hypertension was defined as diastolic pressure ≥ 90 mmHg and/or systolic pressure ≥ 140 mmHg or receipt of current antihypertensive medication. Diabetes was defined as receipt of current anti-diabetic treatment.

Venous blood was collected from each participant and sent to the laboratory of Mae Sot General Hospital within 2 hours of collection for analysis of complete blood counts and serum biochemical parameters. The samples were measured by using the auto-analyzers (Coulter HmX and Beckmann Synchron CX3, Beckman Coulter, Fullerton, CA, USA, and Konelab 30, Thermo Electron Corporation, Vantaa, Finland). The laboratory of the hospital has been certified for clinical chemistry analysis by the National External Quality Assessment Scheme in Clinical Chemistry, Thailand Ministry of Public Health, and by the External Quality Assessment in Clinical Chemistry, Faculty of Medical Technology, Mahidol University. Estimation of GFR was calculated from the serum creatinine with the MDRD equation[13].

A 30-ml sample of second morning urine was obtained from each subject. One 3-5 ml aliquot from each urine sample was kept frozen (-20°C) for analysis of β_2-microglobulin within 1 month after collection. Prior to the storage, one drop of 0.5N sodium hydroxide was added to those showing the pH of 5 or below to adjust the urine pH of 6-8 for prevention of further degradation of β_2-microglobulin in an acid condition. Urinary β_2-microglobulin content was determined by using the enzyme immunoassay by the Department of Biochemistry, Faculty of Medicine Siriraj Hospital, Mahidol University. The remaining urine samples were forwarded to the laboratory of Mae Sot General Hospital within 2 hours of collection for microscopic analysis and biochemistry measurements. The fractional excretion of calcium, phosphate, and potassium was calculated according to the formula[14,15], *i.e.* fractional excretion of calcium =

$$\frac{(\text{urine calcium concentration})/(\text{plasma calcium concentration})}{(\text{urine creatinine concentration})/(\text{plasma creatinine concentration})} \times 100\%$$

Persons who had a history of a urinary stone, hematuria, and/or high serum creatinine (≥ 1.5 mg/dl) were screened for the presence of urinary stone by X-ray and ultrasonography.

The distributions of variables, including urinary and blood markers, were expressed in percentages of the study persons. The arithmetic or geometric mean and standard deviation were used to summarize the renal markers for each group of persons. The geometric mean was used when the logarithms of the observations were more likely to distribute normally than the observations themselves. The Chi-square test was used for comparison of proportions and analysis of variance or the Kruskal-Wallis test was used for comparison between means.

Results

Of the 554 persons who had urinary cadmium levels ≥ 5 μg/g creatinine, 527 cases (95.1%) were screened for renal dysfunction. The remaining persons were absent and could not be contacted during the assessment survey.

Age, sex, and smoking status

About 30.2% of the 527 respondents were 60 years and older (Table 1). The male to female ratio was about 0.6:1. About half (48.0%) of them were current smokers. Of the 527 respondents, 352 cases (66.8%)

Table 1. Age, sex, and smoking status of the cadmium-exposed persons aged 15 years and older who had urinary cadmium ≥ 5 μg/g creatinine, Mae Sot District, Tak Province

	Urinary cadmium (μg/g creatinine)								p-value
	5-10		10.1-20		> 20		Total		
	No.	%	No.	%	No.	%	No.	%	
Total	352		131		44		527		
Age (years)									
< 30	17	4.8	10	7.6	1	2.3	28	5.3	0.28*
30-44	109	31.0	32	24.4	8	18.2	149	28.3	
45-59	123	34.9	47	35.9	21	47.7	191	36.2	
≥ 60	103	29.3	42	32.1	14	31.8	159	30.2	
Mean ± SD**	51.0 ± 13.9		51.3 ± 13.9		53.8 ± 11.6		51.3 ± 13.7		0.36***
Sex									
Male	123	34.9	55	42.0	17	38.6	195	37.0	0.35
Female	229	65.1	76	58.0	27	61.4	332	63.0	
Smoking status									
Never	135	38.4	46	35.1	20	45.5	201	38.1	0.79
Former	47	13.4	20	15.3	6	13.6	73	13.9	
Current	170	48.3	65	49.6	18	40.9	253	48.0	

* Comparison between proportions
** Arithmetic mean ± standard deviation
*** Comparison between means

Table 2. Urinary excretions of β_2-microglobulin, protein, and calcium among the study persons by level of urinary cadmium

	Urinary cadmium (μg/g creatinine)								p-value
	5-10		10.1-20		> 20		Total		
	No.	%	No.	%	No.	%	No.	%	
Total	352		131		44		527		
β_2-microglobulin (μg/g creatinine)									
< 300	237	67.3	90	68.7	20	45.5	347	65.8	0.015
300-999	53	15.1	14	10.7	8	18.2	75	14.2	
≥ 1,000	62	17.6	27	20.6	16	36.4	105	19.9	
Mean ± SD*	129.1 ± 12.9		224.4 ± 10.0		693.4 ± 11.9		170.6 ± 12.6		<0.01
Protein (mg/g creatinine)									
< 200	157	44.6	61	46.6	12	27.3	230	43.6	0.22
200-1,000	169	48.0	59	45.0	28	63.6	256	48.6	
> 1,000	26	7.4	11	8.4	4	9.1	41	7.8	
Mean ± SD*	249.2 ± 2.5		255.4 ± 2.6		307.0 ± 2.3		255.4 ± 2.5		0.36
Calcium (mg/g creatinine)									
< 200	297	84.4	106	80.9	34	77.3	437	82.9	0.37
200-1,000	52	14.8	25	19.1	9	20.5	86	16.3	
> 1,000	3	0.9	0	0.0	1	2.3	4	0.8	
Mean ± SD*	90.2 ± 2.4		101.0 ± 2.3		115.6 ± 2.8		94.7 ± 2.4		0.36

* Geometric mean ± standard deviation

had urinary cadmium levels between 5 and 10 μg/g creatinine, 131 cases (24.9%) were between 10.1 and 20 μg/g creatinine, and 44 cases (8.3%) had cadmium concentrations > 20 μg/g creatinine. There were no significant differences between these 3 groups in the distributions of age, sex, and smoking status.

Urinary excretion of β_2-microglobulin, protein, and calcium

Of the 527 examined persons, 75 cases (14.2%) had urinary β_2-microglobulin excretion between 300 and 999 μg/g creatinine, and 105 cases (19.9%) had ≥ 1,000 μg/g creatinine (Table 2). Persons whose urinary cadmium exceeding 20 μg/g creatinine significantly had the highest proportion of those having β_2-microglobulinuria ≥ 1,000 μg/g creatinine. The geometric mean level of urinary β_2-microglobulin significantly increased with increasing urinary cadmium levels. There were no significant associations between urinary cadmium levels and excretion of urinary protein and calcium in the study persons.

The present study revealed that 54.5% (98/180) of the persons with high urinary β_2-microglobulin excretion remained to have normal serum creatinine (≤ 1.0 mg/dl). The proportions were 73.3% (55/75) among those with β_2-microglobulin excretion 300-999 μg/g creatinine and 41.0% (43/105) among those with ≥ 1,000 μg/g creatinine.

Blood markers

About 21.1% of the study persons had serum creatinine concentrations between 1.1 and 1.4 mg/dl

Table 3. Blood biochemistry analyses among the study persons by level of urinary cadmium

	Urinary cadmium (μg/g creatinine)								p-value
	5-10		10.1-20		> 20		Total		
	No.	%	No.	%	No.	%	No.	%	
Total	352		131		44		527		
Creatinine (mg/dl)									
≤ 1.0	270	76.7	97	74.0	27	61.4	394	74.8	0.07
1.1-1.4	69	19.6	30	22.9	12	27.3	111	21.1	
≥ 1.5	13	3.7	4	3.1	5	11.4	22	4.2	
Mean ± SD*	0.96 ± 0.32		0.98 ± 0.37		1.08 ± 0.47		0.97 ± 0.34		0.16
Glomerular filtration rate (ml/min/1.73 m^2 body surface area)									
< 30	4	1.1	2	1.5	2	4.5	8	1.5	0.17
30-59	52	14.8	19	14.5	10	22.7	81	15.4	
≥ 60	296	84.1	110	84.0	32	72.7	438	83.1	
Potassium (mEq/l)									
< 3.5	128	36.4	41	31.3	24	54.5	193	36.6	0.02
≥ 3.5	224	63.6	90	68.7	20	45.5	334	63.4	
Mean ± SD*	3.64 ± 0.54		3.75 ± 0.52		3.47 ± 0.38		3.66 ± 0.53		<0.01
Calcium (mg/dl)									
< 8	15	4.3	7	5.3	0	0.0	22	4.2	0.47
8-10	321	91.2	115	87.8	42	95.5	478	90.7	
> 10	16	4.5	9	6.9	2	4.5	27	5.1	
Mean ± SD*	8.9 ± 0.7		8.9 ± 0.7		9.0 ± 0.6		8.9 ± 0.7		0.39
Phosphate (mg/dl)									
< 3.0	192	54.5	63	48.1	22	50.0	277	52.6	0.42
≥ 3.0	160	45.5	68	51.9	22	50.0	250	47.4	
Mean ± SD*	3.0 ± 1.3		3.0 ± 1.0		3.0 ± 0.7		3.0 ± 1.2		0.74
Bicarbonate (mEq/l)									
≤ 22	92	26.1	27	20.6	20	45.5	139	26.4	<0.01
> 22	260	73.9	104	79.4	24	54.5	388	73.6	
Mean ± SD*	23.6 ± 2.8		23.7 ± 2.7		23.0 ± 2.5		23.6 ± 2.8		0.15

* Arithmetic mean ± standard deviation

and 4.2% contained ≥ 1.5 mg/dl (Table 3). The mean level of serum creatinine slightly increased with increasing urinary cadmium. Of the study persons, 83.1% remained to express GFR of ≥ 60 ml/min/1.73 m^2 body surface area. Persons whose urinary cadmium exceeding 20 μg/g creatinine had the lowest proportion of those expressing GFR ≥ 60 ml/min but the differences between the 3 subgroups were not statistically significant.

About one-third (36.6%) of the study persons had serum potassium levels < 3.5 mEq/l and 26.4% had serum bicarbonate ≤ 22 mEq/l. Persons whose urinary cadmium exceeding 20 μg/g creatinine significantly had the highest proportion of those with low serum potassium and bicarbonate. Of the study persons, 4.2% had serum calcium < 8 mg/dl and 52.6% had serum phosphate < 3.0 mg/dl. There were no significant differences between the 3 subgroups in the distributions of serum calcium and phosphate.

Only 1.3% of the study persons had the fractional excretion of calcium > 5%. The mean level of the fractional excretion of calcium increased with increasing urinary cadmium. About 75.3% of the surveyed persons had the fractional excretion of phosphate > 5% and 24.7% contained the fractional excretion of potassium > 10%. The distributions of the fractional excretions of phosphate and potassium in the 3 subgroups of cadmium levels were comparable.

Of the 37 persons with serum bicarbonate < 20 mEq/l, only one had proximal renal tubular acidosis. This case had hypokalemia, high urinary β_2-microglobulin, high fractional excretion of potassium and phosphate, and high urinary cadmium. There were 2 additional cases who presented with distal renal tubular acidosis.

The overall prevalence rates of hypertension and diabetes in the present study population were 31.3% and 3.4%, respectively. Urinary stones and anemia were presented in 8.9% and 45.4% of the study persons, respectively. There were no significant differences between the 3 subgroups in the prevalences of hypertension, diabetes, urinary stone, and anemia.

Discussion

In general, cadmium excretion in urine increases with age, being female, and level of smoking[1-6]. Similar findings were observed in the cadmium-exposed persons living in these contaminated areas when the analysis included all levels of urinary cadmium[12]. However, the present study suggested that among those with high urinary cadmium levels (≥ 5 μg/g creatinine), these 3 variables

Table 4. Fractional excretions of calcium, phosphate, and potassium among the study persons by level of urinary cadmium

	Urinary cadmium (μg/g creatinine)								p-value
	5-10		10.1-20		> 20		Total		
	No.	%	No.	%	No.	%	No.	%	
Total	352		131		44		527		
Fractional excretion of calcium (%)									
< 1	165	46.9	51	38.9	15	34.1	231	43.8	0.10
1-5	183	52.0	79	60.3	27	61.4	289	54.8	
> 5	4	1.1	1	0.8	2	4.5	7	1.3	
Mean ± SD*	1.30 ± 1.41		1.42 ± 1.08		1.94 ± 2.38		1.38 ± 1.45		0.05
Fractional excretion of phosphate (%)									
< 1	10	2.8	6	4.6	4	9.1	20	3.8	0.23
1-5	76	21.6	28	21.4	6	13.6	110	20.9	
> 5	266	75.6	97	74.0	34	77.3	397	75.3	
Mean ± SD*	9.7 ± 8.9		10.4 ± 13.6		14.4 ± 19.4		10.3 ± 11.5		0.33
Fractional excretion of potassium (%)									
≤ 10	269	76.4	96	73.3	32	72.7	397	75.3	0.71
> 10	83	23.6	35	26.7	12	27.3	130	24.7	
Mean ± SD*	8.6 ± 7.6		9.0 ± 8.1		11.3 ± 13.2		8.9 ± 8.4		0.92

* Arithmetic mean ± standard deviation

Table 5. Prevalence of hypertension, diabetes, urinary stone, and anemia among the study persons by level of urinary cadmium

	Urinary cadmium (μg/g creatinine)								p-value
	5-10		10.1-20		> 20		Total		
	No.	%	No.	%	No.	%	No.	%	
Total	352		131		44		527		
Hypertension									
Yes	107	30.4	42	32.1	16	36.4	165	31.3	0.71
No	245	69.6	89	67.9	28	63.6	362	68.7	
Diabetes									
Yes	11	3.1	5	3.8	2	4.5	18	3.4	0.85
No	341	96.9	126	96.2	42	95.5	509	96.6	
Urinary stone									
Yes	28	8.0	14	10.7	5	11.4	47	8.9	0.54
No	324	92.0	117	89.3	39	89.6	480	91.1	
Anemia*									
Yes	155	44.0	59	45.0	25	56.8	239	45.4	0.27
No	197	56.0	72	55.0	19	43.2	288	54.7	

*Hemoglobin < 13 g/dl in males or < 12 g/dl in females

might contribute less significant influence on cadmium concentrations.

The authors' findings revealed that a significant proportion of the study persons with high urinary cadmium levels had abnormal renal measurements, including β_2-microglobulinuria, proteinuria, high fractional excretion of phosphate, hypokalemia, and low GFR. However, aging might have some effects on these findings since urinary cadmium and some renal markers such as β_2-microglobulinuria were found to increase with increasing age. Increased excretion of β_2-microglobulin has been widely used as an early indicator of renal tubular dysfunction and follow-up studies have shown that the proteinuria may be irreversible, particularly among persons whose β_2-microglobulin exceeding 1,000 μg/g creatinine, even after cessation of exposure[1-5,16-18]. The present survey revealed that about one-fifth of the study persons excreted β_2-microglobulin ≥ 1,000 μg/g creatinine. β_2-microglobulinuria increased significantly with increasing urinary cadmium. Moreover, among those with high β_2-microglobulin excretion, a significant proportion of them remained to have normal serum creatinine. These findings suggested the potential benefit of urinary β_2-microglobulin measurement for excessive cadmium exposure and early evidence of renal tubular dysfunction among cadmium-exposed persons.

An increase in urinary calcium level has been reported in some populations exposed to cadmium but not in others[1-6,19]. Hypercalciuria was not prevalent in the presented exposed persons and was not significantly associated with urinary cadmium. Low urinary calcium excretion might partly be due to low calcium intake, which was very common in rural Thailand[20]. Perhaps, collection of 24-hour urine may be warranted to determine the true occurrence of hypercalciuria in the study population.

Serum creatinine and GFR were used to indicate the severity of chronic kidney disease in our survey. The prevalence of GFR < 60 ml/min (chronic kidney disease stages 3-5) in our cadmium-exposed population (16.9%) was much higher than those reported in one adult Thai population (6.3%) and the US population (4.7%)[21,22]. Both increased serum creatinine and decreased GFR in the present study population appeared to be associated with increasing urinary cadmium although the difference was not statistically significant. These findings implicated that cadmium, in more severe cases, might produce a combination of tubular and glomerular dysfunctions.

Some epidemiologic studies have shown positive association between hypertension and body cadmium levels but some have found no association[1-3,23-25]. In the present population with

high levels of urinary cadmium, there was no significant correlation between hypertension and cadmium concentrations. Further studies are needed to examine those with low urinary cadmium levels for comparison.

An increased prevalence of urinary stones has been observed in workers occupationally exposed to cadmium[26-29]. Possibly, this is related to the increased urinary excretion of calcium, secondary to kidney damage. The present study revealed no association between urinary stones and urinary cadmium. However, the prevalence of urinary stones in the study persons might be underestimated since the authors screened only those who had a history of passing a stone, hematuria, and/or chronic kidney disease. Further investigations of measurement of other relevant biomarkers and clinical examination may be useful to determine association between cadmium accumulation and an increased frequency of urinary stone formation.

Although increases in incidences of tubular and glomerular dysfunctions have been identified among cadmium-exposed residents in numerous epidemiologic studies, including the present survey, no bio-markers are specific indicators of cadmium toxic effects. The present report found some medical conditions in the survey persons with elevated levels of renal markers. Some renal conditions such as hypokalemic periodic paralysis and endemic distal renal tubular acidosis, which are common in Thailand[30-32], may partly contribute to renal dysfunction among the study persons. The authors suggest that further investigations for possible detection of other potential causes of renal dysfunction should be carried out individually among those cadmium-exposed persons with abnormal renal markers, which may lead to appropriate case management.

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การได้รับสารแคดเมียมในประชากรอำเภอแม่สอด จังหวัดตาก: 2. ความชุกของความผิดปกติของไตในผู้ใหญ่

พิสิฐ ลิมปธนโชติ, วิทยา สวัสดิวุฒิพงศ์, ปราณี มหาศักดิ์พันธ์, สมยศ กรินทราทันต์

ภูมิหลัง: *จากการตรวจปัสสาวะในประชากรอายุ ≥ 15 ปี ที่อาศัยอยู่ในพื้นที่ที่มีการปนเปื้อนของสารแคดเมียมในดินและพืชผลการเกษตร ในอำเภอแม่สอด จังหวัดตาก ในปี พ.ศ. 2547 รวม 7,697 ราย พบว่า 554 ราย มีระดับแคดเมียมในปัสสาวะ ≥ 5 ไมโครกรัมต่อกรัมครีเอตินิน*

วัตถุประสงค์: *รายงานนี้ได้นำเสนอความชุกของความผิดปกติของไตในผู้ที่มีระดับแคดเมียมในปัสสาวะสูง ≥ 5 ไมโครกรัมต่อกรัมครีเอตินิน ดังกล่าว*

วัสดุและวิธีการ: *กลุ่มประชากรตัวอย่างได้รับการสัมภาษณ์ และตรวจประเมินความผิดปกติของไต โดยการเก็บตัวอย่างเลือดและปัสสาวะตรวจทางห้องปฏิบัติการ เพื่อประเมินการทำงานของไต*

ผลการศึกษา: *จากประชากรที่สำรวจได้รวม 527 ราย พบว่าร้อยละ 14.2 มีระดับบีตาทูไมโครโกลบูลินในปัสสาวะ 300-999 ไมโครกรัมต่อกรัมครีเอตินิน และร้อยละ 19.9 มีระดับ ≥ 1,000 ไมโครกรัมต่อกรัมครีเอตินิน ส่วนระดับครีเอตินินในเลือดพบว่าร้อยละ 21.1 และ 4.2 มีระดับครีเอตินินในเลือด 1.1-1.4 และ ≥ 1.5 มิลลิกรัมต่อเดซิลิตร ตามลำดับ ร้อยละ 16.9 มี glomerular filtration rate (GFR) < 60 มิลลิลิตรต่อนาทีต่อ 1.73 ตารางเมตรของพื้นที่ผิวกาย ร้อยละ 75.3 ของประชากรที่สำรวจมีการขจัดฟอสเฟตทางปัสสาวะ > 5% และร้อยละ 24.7 มีการขจัดโปแตสเซียมทางปัสสาวะ > 10% จากการศึกษาพบความชุกของโรคความดันโลหิตสูงและนิ่วในทางเดินปัสสาวะร้อยละ 31.3 และ 8.9 ตามลำดับ กลุ่มประชากรที่มีระดับแคดเมียมในปัสสาวะสูงกว่า จะพบมีระดับบีตาทูไมโครโกลบูลินในปัสสาวะและค่าครีเอตินินในเลือดสูงขึ้น ส่วน GFR มีแนวโน้มลดลง จากการศึกษาไม่พบความสัมพันธ์ระหว่างระดับแคดเมียมในปัสสาวะกับระดับโปรตีนในปัสสาวะ ระดับแคลเซียมในปัสสาวะ ความดันโลหิตสูง และนิ่วในทางเดินปัสสาวะ*

สรุป: *ประชากรที่สัมผัสสารแคดเมียมมากกว่าปกติอาจทำให้มีความผิดปกติทางไตเพิ่มขึ้น การขับบีตาทู-ไมโครโกลบูลินในปัสสาวะสามารถใช้เป็นตัวบ่งบอกความผิดปกติของไตในระยะแรกที่ดีได้*