

## Association of renal tubular injury and bone resorption induced by exposure to cadmium of inhabitants living in a polluted area, mae sot district, Tak province, Thailand

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**Objective:** To determine the correlation of cadmium(Cd) concentrations, renal tubular injury markers( $\beta^2$ -microglobulin,  $\beta^2$ MG, and N- acetyl- $\beta$ -D-glucosaminidase, NAG), and the bone resorption marker (deoxypyridinoline, DPD) in the urine samples of residents in a Cd contaminated area, Mae Sot district, Tak province, Thailand. **Methods:** Four hundred and two morning urine samples were selected for analysis of renal tubular injury and bone resorption markers from subjects aged over 50 years old, who had high urinary Cd ( $>5\mu\text{g/g}$  creatinine, Cr). The urinary Cd was analyzed by atomic absorption spectrometry,  $\beta^2$ MG was determined by EIA (GLAZYME  $\beta^2$ MG- EIA) and NAG was measured by colorimetric assay (NAG test Shionogi). The cut-off values to determine renal tubular injury were  $>1,000\mu\text{g/gCr}$  for  $\beta^2$ MG and  $>8$  units/gCr for NAG. Free urinary DPD was measured by competitive enzyme immunoassay (Metra™ DPD EIA). Cut-off values for bone resorption increment were 5.4 and 7.6 nmol/mmol Cr for males and females, respectively. All of the data were analyzed and computed for the Partial Correlation Coefficients.

**Results:** Table 1 shows the mean and or with S.D of age, and renal and bone dysfunction marker concentrations of the study subjects. High concentrations of NAG and  $\beta^2$ MG were significantly correlated to Cd concentrations, but DPD was not (Table 2). The results showed that renal tubular injury may be induced by high Cd exposure, however, the reason why  $\beta^2$ MG inversely correlated to the DPD in males is unclear. The prevalence of high DPD subjects was 19.23% (males) and 26.83% (females), reflecting an increase of bone resorption. When we computed according to kidney tubular injury marker levels, the prevalence of high DPD subjects was significantly increased in females with  $\text{NAG}>8$  units/gCr ( $\chi^2=10.936$ ,  $p=0.001$ ), but not significantly among male subjects ( $\chi^2=1.743$ ,  $p=0.187$ ) when compared to the low NAG subject group ( $\text{NAG}\leq 8$  units/gCr). **Conclusion:** The bone resorption marker was increased among these inhabitants and the association between bone resorption and renal tubular injury has been clearly shown. Our data illustrate evidence supporting the assumption that bone dysfunction induced by high Cd exposure is an indirect effect mediated by kidney tubular injury. Surveillance of kidney and bone dysfunction progression among high Cd exposed inhabitants is necessary and must be continued to prevent severe Itai Itai disease.

Table 1 Mean and standard deviation of age, renal tubular injury markers ( $\beta^2$ MG, NAG), bone resorption marker (DPD) and urinary cadmium concentration (UCd) of the study subjects (n=402)

Characteristics	Male (n=156)			Female (n=246)		
	Mean $\pm$ S.D.	Min	Max	Mean $\pm$ S.D.	Min	Max
Age <sup>a</sup> (years)	63.97 $\pm$ 8.78	50.0	88.0	61.12 $\pm$ 8.03	50.0	85.0
$\beta^2$ MG ( $\mu\text{g/gCr}$ )	577.31 $\pm$ 10.28	10.0	118,850.2	264.99 $\pm$ 7.60	10.0	146,217.7
NAG (units/gCr)	5.28 $\pm$ 1.80	1.4	35.9	5.22 $\pm$ 1.86	0.9	41.4
UCd ( $\mu\text{g/g}$ )	6.37 $\pm$ 2.22	0.6	106.4	6.37 $\pm$ 2.02	0.9	38.8
DPD (nmol/mmol Cr)	3.79 $\pm$ 1.64	0.7	19.3	5.90 $\pm$ 1.60	0.8	26.1

<sup>a</sup>Arithmetic mean±S.D., others are geometric mean and S.D.

Table 2 Partial Correlation Coefficient controlling the age (>50 years old) of Mae Sot inhabitants, Tak province, Thailand, computed with parameters of bone resorption marker, renal tubular injury markers and urinary cadmium concentrations

	$\beta_2$ MG		NAG		UCd	
	Male	Female	Male	Female	Male	Female
DPD	-0.180*	-0.120	0.010	0.105	-0.109	0.038
UCd	0.216**	0.278***	0.309***	0.295***		

$\beta_2$ MG = urinary  $\beta_2$ -microglobulin, NAG = N-acetyl- $\beta$ -D-glucosaminidase, UCd = urinary cadmium

DPD = urinary deoxypyridinoline, \*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.0001