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Subclinical renal tubular dysfunction in postmenopausal women exposed to low-level environmental cadmium

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Background and Aims: Environmental cadmium (Cd) exposure is a significant public health concern due to its cumulative toxicity and long biological half-life. Cd primarily targets the kidneys, particularly the proximal tubules, where it accumulates and contributes to progressive renal dysfunction. Chronic exposure, often through dietary intake or inhalation in Cd-polluted areas, is associated with both tubular and glomerular damage [1]. This study aimed to investigate the dose-response relationship between dietary Cd exposure and renal tubular damage in postmenopausal women aged 50 and above, chronically exposed to low levels of Cd through their diet.

Method: A cross-sectional study in 380 postmenopausal women was conducted to assess early kidney tubular damage. Urinary Cd concentrations were used to estimate the body burden of Cd, while urinary β2-microglobulin (β2MG) served as a biomarker of tubular proteinuria. Urinary Cd analyses were performed by Inductively Coupled Plasma Mass Spectrometry (ICP-MS) equipped with Quadrupole Ion Deflector. Creatinine was measured using the Alkaline Picrate method; calcium (Ca), by the automated colorimetric method and β2MG by chemiluminescence. Studied variables were adjusted to urinary creatinine (creat) to standardize results. A level of significance of 0.05 was used for all statistical comparisons and associations.

Results: The median age (interquartile range) of patients was 60.0 (56.0–65.3) years and for body mass index (BMI) was 27.0 (24.4–30.1) kg/m^2. All studied women were in the postmenopausal state. The median (interquartile range) for urinary Cd/creat was 0.30 (0.15–0.55) µg/g, and for β2-MG/creat was 90 (56–124) μg/g. Twenty-four women (6.3%) presented with a diagnosis of renal tubular damage, defined as a urinary β2-MG/creat ratio $\geq$300 μg/g. According to Brazilian reference ranges for urinary Cd[2], 36 women (9.5%) presented Cd levels above P95 reference level; these participants also showed significantly higher β2-MG/creat ($P = 0.002$) and urinary Ca/creat ($P = 0.036$) levels when compared to those under P95. Urinary Cd levels (ln-transformed) correlated positively with β2-MG ($r_s = 0.374$, $P = 6.8 \times 10^{-14}$; Fig. 1) and with Ca ($r_s = 0.261$, $P = 2.5 \times 10^{-7}$). Furthermore, by performing multiple linear regression analyses, in a fully adjusted model (for age, BMI, smoking and chronic medication), Cd/creat (ln transformed) was independently associated with urinary Ca/creat ($\beta = 1.229$, $P < 0.001$) and β2-MG/creat ($\beta = 1.399$, $P < 0.001$).

Conclusion: In postmenopausal women, urinary Cd is an independent predictor of urinary β2MG and urinary calcium, even when β2MG levels are within the 'normal' range. This finding supports the notion that low-level environmental exposure to Cd may adversely affect kidney health, contributing to subclinical tubular dysfunction.

Therefore, current thresholds for Cd exposure may underestimate the risk of renal dysfunction, particularly in vulnerable populations such as postmenopausal women. Enhanced monitoring and stricter environmental controls are warranted to mitigate the public health impact of Cd exposure.

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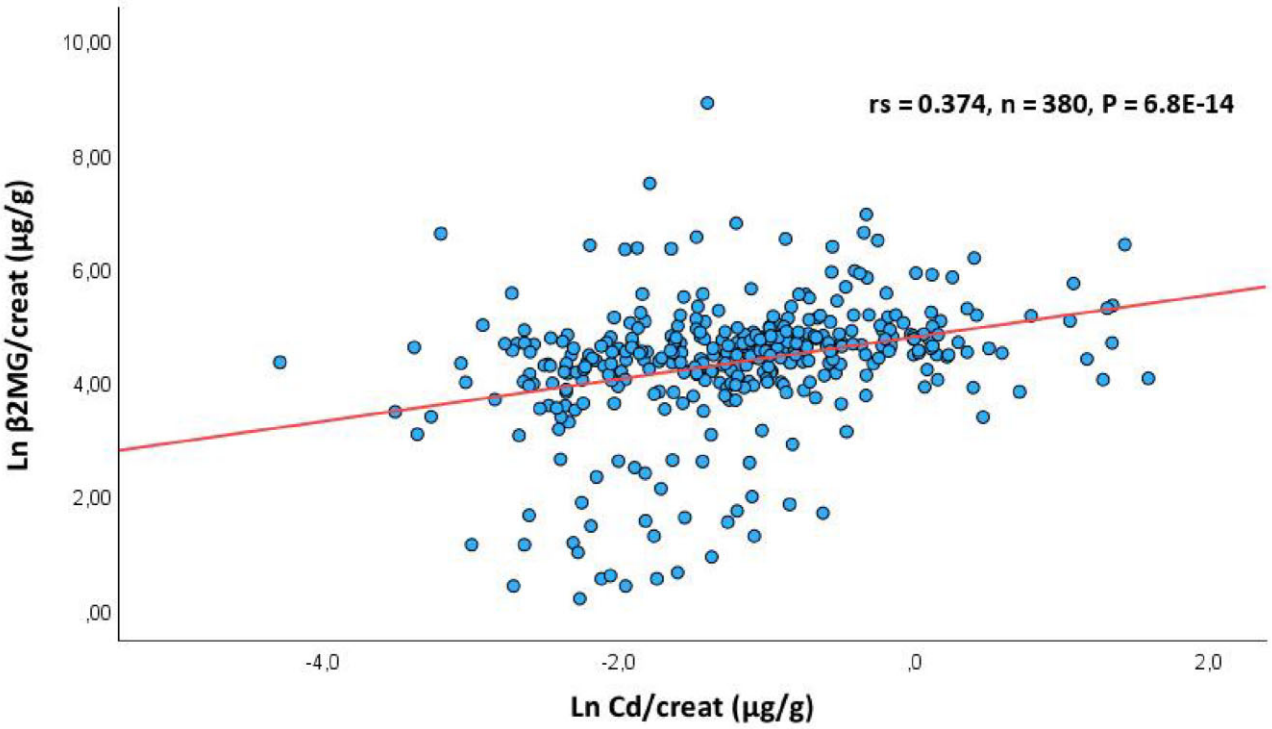

Figure 1: Correlation between urinary β2-microglobulin/creatinine (β2-MG/creat) and cadmium/creatine (Cd/creat) levels (variables ln-transformed) in postmenopausal women. r_s, Spearman's rank correlation coefficient; $P < 0.05$ was considered as statistically significant.

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