DIVERGENT ASSOCIATIONS OF BLOOD AND URINE CADMIUM LEVELS WITH KIDNEY FUNCTION

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Background and Aims: Cadmium is nephrotoxic at high exposure levels. Lower level exposure is widespread but data on kidney impact at these levels are scarce. In the 1999-2006 National Health and Nutrition Examination Survey (NHANES), higher blood cadmium levels were related to reduced estimated glomerular filtration rate (eGFR; <60 mL/min/1.73 m^2). Our aim was to compare urine and blood cadmium with reduced eGFR in NHANES 1999-2008.
Methods: We included 6,231 NHANES 1999-2008 participants aged ≥ 20 years who had blood and urine cadmium available. eGFR was estimated using the Modification of Diet in Renal Disease (MDRD) equation.
Results: Geometric mean blood and urine cadmium and MDRD eGFR levels were 0.40 µg/L, 0.26 µg/g creatinine, and 86.8 ml/min/1.73 m^2, respectively. Blood and urine cadmium levels were correlated (r_s = 0.60). After adjustment, the odds ratio (95% CI) for reduced eGFR comparing the 75th to the 25th percentile of blood cadmium levels was 1.44 (1.15, 1.82). In contrast, for urine cadmium, the corresponding odds ratio (95% CI) was 0.47 (0.34, 0.66). Without adjustment for urine creatinine, the odds ratio was 0.97 (0.81, 1.16).
Conclusions: In this large, representative sample of US adults, blood and urine cadmium, although correlated, were associated in opposite directions with eGFR. Both dose measures reflect environmental exposure although blood cadmium incorporates current exogenous exposure and endogenous exposure from body burden. Potential mechanisms for these unexpected findings include the impact of adjusting urine cadmium for urine dilution with urine creatinine which is significantly associated with eGFR in this population; an impact of renal filtration on cadmium excretion; cadmium-related hyperfiltration with urine cadmium dose; and alterations in metal excretion due to protein binding. Prospective epidemiologic studies and experimental studies are needed to understand these cross-sectional findings.