Title: Chronic kidney disease of unknown aetiology in the US adult population: Evidence from NHANES

Background: Over the past two decades, a new form of chronic kidney disease (CKD) not linked to traditional risk factors such as diabetes and hypertension has emerged mainly in tropical, LMICs. CKD of unknown aetiology (CKDu) remains largely underexamined in high income nations like US, despite rising CKD rates not fully explained by traditional risk factors and accumulating evidence linking environmental exposures. This study estimated CKDu prevalence and evaluated associated risk factors among US adults.

Methods: We analysed data from 19,791 adults aged 20–80 years in NHANES 2003–2012. eGFR was calculated using the 2009 CKD–EPI equation. CKD was defined using KDIGO criteria. CKDu was defined as impaired renal function (eGFR <60 mL/min/1.73 $m^2$) in the absence of diabetes, hypertension or heavy proteinuria. Weighted logistic regression was used to assess associations between demographic, clinical, and environmental factors and CKDu.

Results: overall, 3,451 participants had CKD (13.6%, 95% CI 12.8–14.3). Among them, 747 (26.8%, 95% CI 24.3–29.4) were classified as suspected CKDu. In the subgroup of 11,288 adults without diabetes, hypertension or heavy proteinuria, 256 had CKDu (2.0%, 95% CI 1.7–2.4). Older age, race/ethnicity, current smoking, higher serum uric acid, elevated serum osmolality, and higher blood cadmium were independently associated with CKDu.

Conclusion: CKDu affects approximately 2% of US adults without traditional CKD risk factors. Although prevalence reaches 15–23% in some LMICs, the US prevalence is comparable to rates reported in several other regions, highlighting an under-recognized burden and the need to investigate environmental and occupational risk factors driving CKDu.

Keywords: Chronic kidney disease; CKDu; NHANES; prevalence; risk factors; United States