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# Heavy Metal Exposure and Chronic Kidney Disease of Unknown Origin (Ckdu): An Emerging Environmental Nephropathy

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***Abstract***
*Background: Chronic kidney disease of unknown origin (CKDu) is increasingly recognized as a public health concern in agricultural and industrial regions. Emerging evidence suggests that environmental exposure to heavy metals may play a critical role.*
***Objective****: To evaluate the association between heavy metal exposure (lead, cadmium, arsenic) and CKDu in patients attending a tertiary care hospital.*
***Methods****: A cross-sectional study was conducted between January 2024 and March 2025 involving 120 CKDu patients. Serum and urinary heavy metal levels were measured and compared to age- and sex-matched controls. Demographic, occupational, and clinical data were also collected.*
***Results****: Mean blood lead and urinary cadmium levels were significantly higher in the CKDu group compared to controls ($p < 0.01$). A strong correlation was found between duration of occupational exposure and severity of kidney dysfunction ($r = 0.71$). Arsenic exposure was observed predominantly in patients using unregulated groundwater.*
***Conclusion****: Chronic exposure to environmental heavy metals is significantly associated with CKDu. This finding highlights the need for environmental surveillance, early screening, and regulatory intervention in vulnerable populations.*
***Keywords****: Chronic kidney disease, heavy metals, CKDu, environmental nephropathy, lead, cadmium, arsenic*

## INTRODUCTION

Chronic Kidney Disease (CKD) is an escalating global health concern, contributing significantly to morbidity and mortality across both developed and developing nations. A particularly troubling subset of this disease, termed Chronic Kidney Disease of Unknown Origin (CKDu), has been increasingly identified in populations lacking conventional risk factors such as diabetes mellitus or long-standing hypertension. CKDu is predominantly seen in agricultural and industrial communities, especially in tropical regions, where environmental and occupational exposures are believed to contribute significantly to disease onset.

Among the suspected etiological agents, heavy metals such as lead, cadmium, and arsenic have drawn substantial attention due to their established nephrotoxic effects. These elements, often encountered in agricultural settings through fertilizers, pesticides, or contaminated groundwater, accumulate in the body over time, potentially leading to renal dysfunction. South India, with its widespread agricultural activity and reliance on untreated groundwater, presents a unique context for studying the environmental underpinnings of CKDu.

This study was undertaken with the primary objective of evaluating the association between chronic exposure to heavy metals—specifically lead, cadmium, and arsenic—and the occurrence of CKDu. We hypothesized that individuals with CKDu would exhibit significantly elevated levels of these heavy metals compared to healthy controls, particularly among those with long-term occupational exposure and groundwater consumption. The study also aimed to correlate the extent of exposure with markers of renal dysfunction, thereby strengthening the evidence for causality.

## MATERIALS AND METHODS

This was a cross-sectional observational study conducted over a 15-month period, from January 2024 to March 2025, at the Department of General Medicine and Nephrology, Sree Balaji Medical College and Hospital, Chennai. The study protocol received approval from the institutional ethics committee, and informed consent was obtained from all participants.

**Study Population:** A total of 120 patients diagnosed with CKDu and 60 healthy, age- and sex-matched controls were enrolled. CKDu was defined by an estimated glomerular filtration rate (eGFR) of less than 60 mL/min/1.73 $m^2$ in the absence of known causes such as diabetes mellitus, chronic hypertension, or glomerulonephritis.

**Inclusion Criteria:** - Age between 20 to 60 years - eGFR < 60 mL/min/1.73 $m^2$ - No history of diabetes or chronic hypertension

**Exclusion Criteria:** - Acute Kidney Injury - Known etiology for CKD (e.g., polycystic kidney disease, lupus nephritis)

**Data Collection:** A detailed clinical history was obtained, including occupational exposure, duration of employment, and source of drinking water. Physical examination findings and laboratory investigations, including serum creatinine, urinary protein levels, and eGFR, were documented. Heavy metal exposure was assessed using: - Blood Lead levels via Inductively Coupled Plasma Mass Spectrometry (ICP-MS) - Urinary Cadmium and Arsenic levels, standardized to urinary creatinine

**Statistical Analysis:**

Data were analyzed using SPSS version 26. Continuous variables were expressed as mean ± standard deviation and compared using the independent t-test. Categorical variables were analyzed using the chi-square test. Pearson's correlation coefficient was used to determine the relationship between duration of occupational exposure and renal function parameters. A p-value < 0.05 was considered statistically significant.

**Results**

Demographics and Clinical Features are summarized in Table 1.

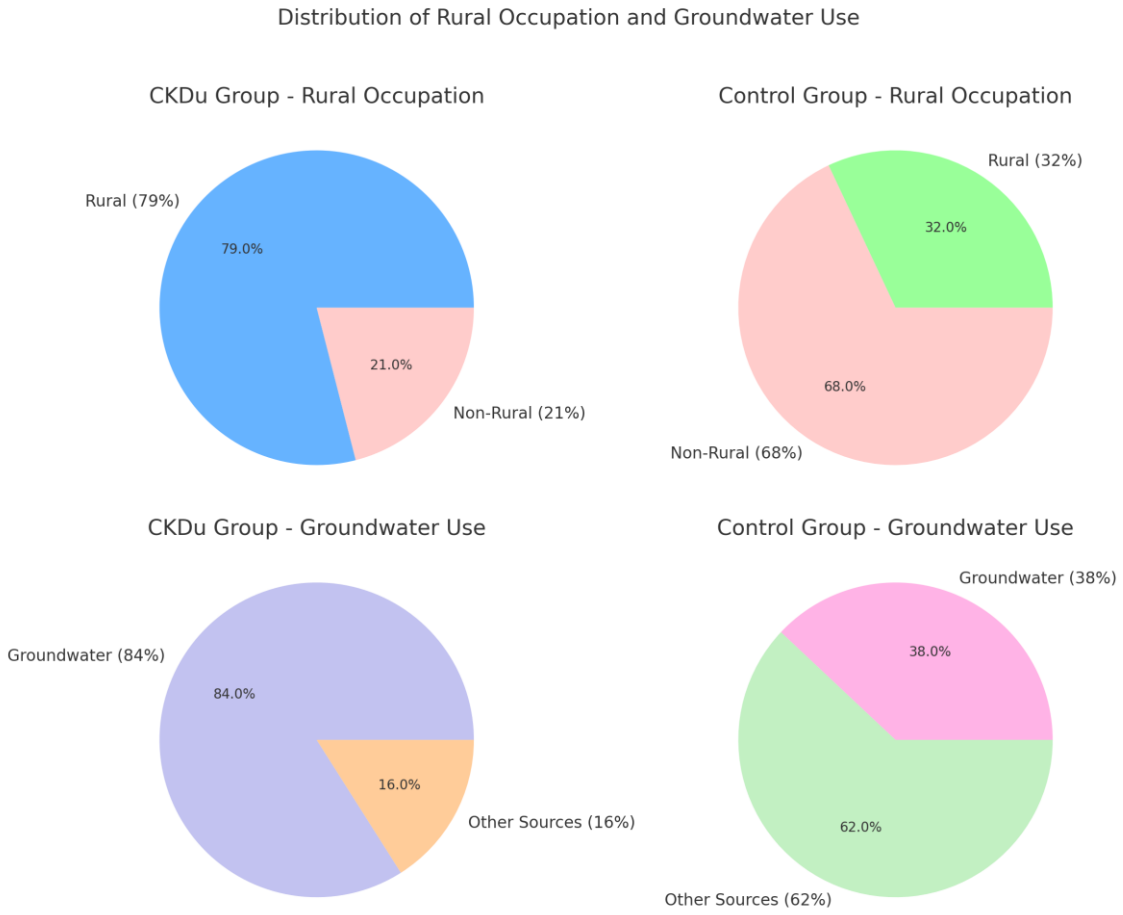


Figure 1: Distribution of rural occupation and groundwater use among CKDu patients and controls.

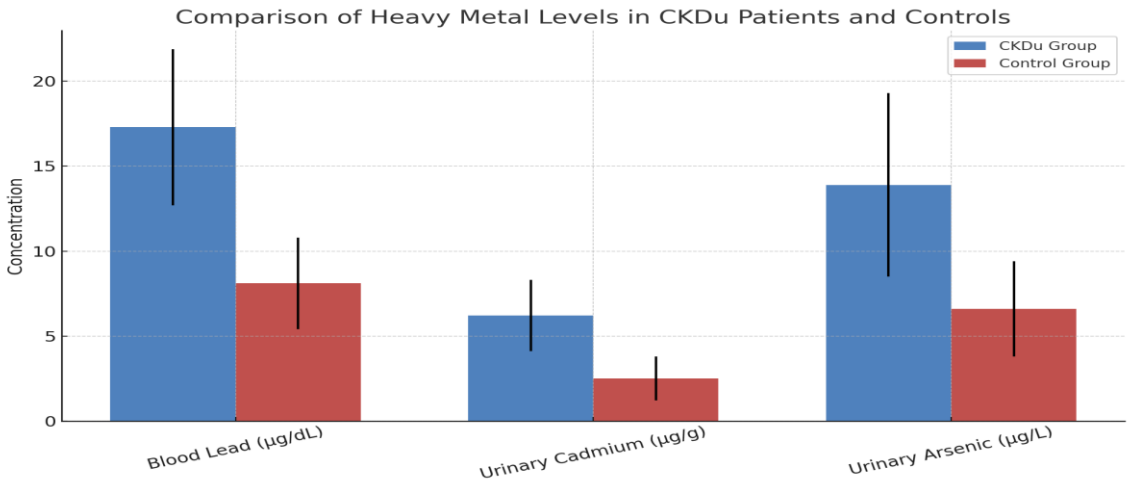


Figure 2: Comparison of heavy metal levels in CKDu patients and controls.
Figure 3: Correlation between duration of occupational exposure and serum creatinine ($r = 0.71$, $p < 0.001$).

## DISCUSSION

This study provides evidence linking chronic exposure to environmental heavy metals and CKDu. Elevated blood lead and urinary cadmium levels in CKDu patients suggest nephrotoxic bioaccumulation. The correlation between occupational exposure duration and kidney dysfunction strengthens the causal argument.

Arsenic, mainly from groundwater, was also elevated, consistent with regional geological contamination. These findings underscore the need for public health measures, including safer water practices, protective occupational measures, and environmental regulation.

## CONCLUSION

The present study provides compelling evidence supporting the role of environmental heavy metal exposure in the pathogenesis of CKDu. Patients diagnosed with CKDu demonstrated significantly higher levels of blood lead and urinary cadmium and arsenic when compared to healthy controls. These findings were most pronounced in individuals engaged in rural occupations and those reliant on untreated groundwater, highlighting potential routes of chronic exposure.

Moreover, a strong positive correlation was observed between the duration of occupational exposure and serum creatinine levels, underscoring the dose-dependent nephrotoxicity of these metals. These results underscore the urgent need for multidisciplinary intervention, including public health surveillance, environmental regulation, and educational campaigns on safe agricultural and water practices.

Addressing CKDu requires not only clinical management but also systemic changes aimed at reducing environmental hazards. Early screening of at-risk populations, stringent regulation of agrochemicals, and ensuring access to safe drinking water are critical steps in mitigating the burden of this emerging environmental nephropathy in affected regions.

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**Conflicts of Interest**

None declared.

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