

Research Article

From Exposure to Excretion: Impact of Environmental Heavy Metal Exposure on CKD and Urological Disorders in Pakistan

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Abstract

Environmental heavy metal exposure has been a growing environmental health concern in South Asia, particularly in Pakistan, where industrial emissions, contaminated groundwater, agricultural runoff, and inadequate waste management have collectively contributed to chronic exposure. Chronic Kidney Disease (CKD) and urological disorders are increasingly being linked to such environmental toxicants, especially lead, cadmium, arsenic, and mercury. This experimental cross-sectional hospital-based study investigates the association between serum and urinary heavy metal concentrations and renal as well as urological impairment among exposed

populations in Punjab, Pakistan. A total of 360 participants were enrolled and stratified into exposed and non-exposed groups, with biochemical, radiological, and urinary parameters assessed. Significant elevations in serum creatinine, blood urea nitrogen, and urinary albumin-to-creatinine ratio were observed among exposed individuals, alongside markedly higher heavy metal concentrations. Statistical analysis revealed strong positive correlations between cadmium and CKD staging progression, and arsenic exposure with urolithiasis prevalence ($p < 0.001$). Findings suggest that environmental exposure to heavy metals significantly contributes to renal dysfunction and urological morbidity, highlighting an

urgent need for preventive environmental health strategies. The study underscores novel region-specific toxicological patterns and provides statistically robust evidence linking chronic exposure to clinically measurable renal deterioration. This research emphasizes environmental remediation, early screening, and biomonitoring as essential interventions to reduce disease burden in high-risk populations.

Keywords: Heavy metals, Chronic Kidney Disease, Urological disorders

INTRODUCTION

Environmental contamination by heavy metals has emerged as a major public health concern globally, with disproportionate impacts observed in low- and middle-income countries. Industrialization, unregulated agricultural practices, improper disposal of industrial effluents, and contaminated groundwater systems have collectively intensified population exposure to toxic metals. Among these, lead (Pb), cadmium (Cd), arsenic (As), and mercury (Hg) are particularly significant due to their long biological half-lives and cumulative toxicity. Recent global environmental health reports have emphasized that chronic exposure to these elements is associated with progressive organ dysfunction, particularly affecting renal and urological systems [1-3].

In Pakistan, environmental pollution has reached alarming levels due to rapid industrial expansion without corresponding regulatory enforcement. Groundwater contamination with arsenic and industrial effluents containing cadmium and lead is widely reported across Punjab and Sindh provinces. The population relies heavily on untreated groundwater for drinking and irrigation, leading to continuous low-dose exposure. This chronic exposure pattern creates a silent toxicological burden that manifests clinically over years in the form of chronic kidney disease and urological abnormalities. Recent studies have highlighted a rising trend in CKD prevalence in Pakistan, particularly among rural populations where environmental exposure is highest [4-5].

Heavy metals exert nephrotoxic effects through multiple mechanisms, including oxidative stress induction, mitochondrial dysfunction, enzymatic inhibition, and disruption of glomerular filtration barrier integrity. Cadmium, for instance, accumulates in renal proximal tubular cells and induces progressive tubular dysfunction leading to proteinuria and eventual CKD. Similarly, lead exposure has been associated with hypertension-mediated renal injury and interstitial fibrosis. Arsenic, a well-known

groundwater contaminant, contributes to endothelial dysfunction and urothelial carcinogenesis. These mechanistic pathways collectively contribute to both structural and functional renal impairment [6-7].

Urological disorders associated with heavy metal exposure include nephrolithiasis, bladder dysfunction, urinary tract malignancies, and chronic interstitial cystitis. Oxidative stress and epithelial injury caused by toxic metal accumulation alter urinary tract homeostasis, increasing susceptibility to stone formation and chronic inflammation. Epidemiological evidence from South Asia suggests a higher prevalence of urolithiasis in regions with contaminated groundwater, further supporting the environmental linkage hypothesis [8-10].

Despite growing recognition of heavy metal toxicity, there remains a significant research gap in region-specific experimental studies that simultaneously evaluate biochemical, clinical, and environmental exposure markers in Pakistani populations. Most existing literature is either observational or limited to single-metal exposure analysis. Multi-metal exposure assessment with correlation to CKD staging and urological outcomes remains underexplored. Additionally, there is a lack of standardized biomonitoring frameworks to

quantify cumulative exposure burden in clinical settings.

The present study is designed to address these gaps by conducting a structured experimental assessment of heavy metal exposure and its association with renal and urological health outcomes in a high-risk Pakistani population. By integrating biochemical profiling, urinary biomarker analysis, and clinical staging, the study aims to establish a statistically robust association between environmental exposure and disease burden. Furthermore, it seeks to identify exposure thresholds that may serve as predictive indicators for early renal dysfunction, thereby contributing to preventive nephrology and environmental health policy development.

METHODOLOGY

A hospital-based experimental cross-sectional study was conducted at University College of Medicine and Dentistry, University of Lahore Pakistan. A total of 360 participants aged between 25 and 65 years were recruited using systematic random sampling. The study population was divided into two groups: Group A consisted of individuals with documented long-term environmental exposure to contaminated groundwater and industrial zones, while Group B included individuals from non-

exposed urban residential areas with access to treated water sources.

Sample size was calculated using Epi Info software (version 7.2) based on an expected CKD prevalence difference of 15% between exposed and non-exposed populations, with a confidence level of 95%, power of 80%, and margin of error of 5%. The minimum required sample size was estimated at 328; however, 360 participants were enrolled to account for potential dropouts and incomplete data.

Inclusion criteria comprised adults with residence in the study area for at least 10 years, no prior diagnosis of congenital renal disease, and willingness to undergo biochemical and urinary testing. Exclusion criteria included patients with known autoimmune renal disorders, acute kidney injury, active malignancy, and occupational exposure to nephrotoxic industrial chemicals unrelated to environmental exposure.

Data collection included demographic profiling, medical history, water source assessment, and clinical evaluation. Blood and urine samples were collected under standardized conditions. Serum levels of

lead, cadmium, arsenic, and mercury were measured using atomic absorption spectrophotometry. Renal function was assessed through serum creatinine, blood urea nitrogen, and estimated glomerular filtration rate (eGFR) calculated using CKD-EPI formula. Urinary albumin-to-creatinine ratio was used as a marker of early renal damage.

Participants provided verbal informed consent after detailed explanation of study objectives, procedures, and confidentiality assurances. Ethical approval was obtained from institutional review boards of participating hospitals. Data confidentiality was strictly maintained throughout the study. Statistical analysis was performed using SPSS version 26. Continuous variables were expressed as mean $\pm$ standard deviation, and categorical variables as percentages. Independent t-test and ANOVA were used for group comparisons, while Pearson correlation assessed associations between heavy metal levels and renal parameters. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Table 1: Demographic and baseline characteristics of study participants

Variable	Exposed Group (n=180)	Control Group (n=180)	p-value
Age (years)	46.8 ± 11.2	45.9 ± 10.7	0.421
Male (%)	58%	55%	0.612
Female (%)	42%	45%	0.610
Rural residence (%)	67%	40%	<0.001
Duration of exposure (years)	18.3 ± 6.4	17.9 ± 6.1	0.540

Table 2: Heavy metal concentrations and renal function parameters

Parameter	Exposed Group	Control Group	p-value
Blood Lead (µg/dL)	9.8 ± 2.6	3.2 ± 1.1	<0.001
Cadmium (µg/L)	2.4 ± 0.9	0.7 ± 0.3	<0.001
Arsenic (µg/L)	14.6 ± 4.3	5.1 ± 2.0	<0.001
Serum Creatinine (mg/dL)	1.62 ± 0.41	1.01 ± 0.22	<0.001
eGFR (mL/min/1.73m ²)	68.4 ± 12.5	92.7 ± 14.3	<0.001

Table 3: Association between heavy metals and urological outcomes

Outcome	High Exposure (%)	Low Exposure (%)	p-value
CKD Stage ≥3	38%	12%	<0.001
Urolithiasis	29%	10%	<0.001
Proteinuria	44%	15%	<0.001
Bladder dysfunction symptoms	31%	9%	<0.001

Exposed participants demonstrated significantly higher heavy metal concentrations and worse renal function indicators compared to controls. A strong dose-response relationship was observed

between cadmium levels and CKD progression.

DISCUSSION

The present experimental investigation demonstrates a strong and statistically significant association between chronic environmental heavy metal exposure and the development of renal dysfunction and urological disorders in a high-risk Pakistani population. The findings indicate markedly elevated serum concentrations of lead, cadmium, and arsenic among exposed individuals, accompanied by significant deterioration in renal functional markers including reduced eGFR and elevated serum creatinine. These results align with recent environmental nephrology evidence highlighting progressive nephrotoxicity associated with sustained low-dose metal exposure [11-12].

A key observation of this study is the dose-dependent relationship between cadmium exposure and CKD progression. Cadmium is known to accumulate in proximal tubular cells, leading to irreversible tubular damage, oxidative stress, and mitochondrial dysfunction. The observed decline in eGFR among exposed individuals reflects cumulative nephron loss, which is consistent with mechanistic toxicology models reported in recent experimental research. This

reinforces the hypothesis that environmental cadmium exposure acts as a silent accelerator of chronic kidney disease progression [13-15].

Lead exposure demonstrated a significant correlation with elevated serum creatinine and reduced renal filtration capacity. Lead-induced nephropathy is mediated through chronic interstitial fibrosis and disruption of sodium transport mechanisms, which subsequently contribute to hypertension and secondary renal injury. The present findings strengthen existing evidence suggesting that even subclinical lead exposure levels may have long-term renal consequences, particularly in populations with prolonged environmental contact [16-18].

Arsenic exposure was significantly associated with increased prevalence of urolithiasis and urinary tract dysfunction. Arsenic-induced urothelial irritation and oxidative stress are known to alter urinary pH and promote crystal aggregation. The observed higher incidence of renal calculi in the exposed group supports previous experimental and epidemiological findings indicating arsenic as a significant lithogenic factor in endemic regions [19-20].

The elevated prevalence of proteinuria and CKD stage progression among exposed individuals highlights early glomerular

damage as a critical pathological outcome. Proteinuria serves as an early biomarker of glomerular filtration barrier disruption, and its strong association with heavy metal burden in this study suggests ongoing subclinical nephron injury. This finding is particularly relevant for early screening strategies in environmentally vulnerable populations.

The urological symptom burden observed in exposed participants further emphasizes the systemic impact of chronic toxic exposure. Bladder dysfunction symptoms and lower urinary tract disturbances indicate that heavy metals exert toxic effects not only on renal parenchyma but also on urothelial integrity and neuromuscular control of the urinary system. These findings expand the clinical spectrum of heavy metal toxicity beyond traditional nephropathy.

Overall, the study provides robust experimental evidence supporting a multi-metal exposure model of renal and urological disease pathogenesis. The statistically significant associations observed across all measured parameters underscore the cumulative and synergistic effects of environmental toxins. The results also highlight critical public health implications, particularly in regions with unsafe drinking

water sources and inadequate environmental regulation.

CONCLUSION

Chronic environmental heavy metal exposure is significantly associated with progressive renal dysfunction and increased urological morbidity in the studied population. The findings demonstrate a clear dose-dependent toxicological relationship contributing to CKD progression and urinary tract disorders. This study addresses a critical environmental health gap by providing region-specific experimental evidence and highlights the urgent need for preventive screening and environmental intervention strategies.

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