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HEAVY METAL CONTAMINATION IN DRINKING WATER: CONNECTION TO CHRONIC KIDNEY DISEASE RISK

Original Research

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ABSTRACT

Background: Heavy metal contamination in drinking water is a growing global public health concern, especially in rural and resource-limited regions. Chronic exposure to nephrotoxic metals such as lead, cadmium, and arsenic is increasingly recognized as a significant environmental risk factor for chronic kidney disease (CKD). In areas lacking proper water regulation and infrastructure, such exposures can lead to serious long-term health consequences and increased disease burden in vulnerable populations.

Objective: To evaluate the concentration of heavy metals in drinking water and investigate their association with CKD among adults living in rural regions of Pakistan.

Methods: A cross-sectional quantitative study was conducted involving 250 adult participants (52% male, 48% female; mean age 45.8 ± 13.4 years) from rural communities with known environmental exposure. Water samples from participants' households were collected and analyzed for lead, cadmium, arsenic, and mercury using inductively coupled plasma mass spectrometry (ICP-MS). Renal function was assessed using serum creatinine, estimated glomerular filtration rate (eGFR), and urine albumin-to-creatinine ratio (UACR). Clinical and demographic data, including smoking status and comorbidities, were collected through structured interviews and medical records. Logistic regression analysis was performed to determine associations between heavy metal levels and CKD, adjusting for age, gender, smoking, and existing health conditions.

Results: Lead levels exceeded WHO limits in 87% of water samples (mean: 0.72 mg/L), cadmium in 75% (0.15 mg/L), arsenic in 81% (0.098 mg/L), and mercury in 64% (0.006 mg/L). A total of 23 participants (9.2%) met clinical criteria for CKD. Lead exposure showed the strongest association with CKD (AOR: 2.85; 95% CI: 1.75–4.61; $p<0.001$), followed by cadmium (AOR: 2.40; $p=0.002$) and arsenic (AOR: 1.92; $p=0.018$). Mercury exposure was not statistically significant (AOR: 1.45; $p=0.168$).

Conclusion: High levels of lead, cadmium, and arsenic in rural drinking water are significantly associated with increased risk of CKD. These findings highlight the urgent need for water safety regulation and environmental health interventions in affected regions.

Keywords: Arsenic, Cadmium, Chronic Kidney Disease, Drinking Water, Environmental Exposure, Lead, Mercury.

INTRODUCTION

Heavy metals, typically defined by a specific density of 5 g/cm³ or greater, are known environmental pollutants with significant implications for human health. Among the most toxic of these are mercury, lead, arsenic, and cadmium, though other metals such as antimony, chromium, nickel, copper, and zinc are also recognized for their hazardous biological effects (1). These metals commonly enter water systems through both point sources—such as agricultural runoff, industrial discharges, and wastewater treatment plants—and non-point sources, including widespread pesticide use and diffuse industrial waste (2). Water pollution, now a global crisis, is linked to the deaths of approximately 14,000 people each day due to its hazardous health effects (3). With increasing industrialization and anthropogenic activity, heavy metals accumulate in aquatic systems, and once a critical concentration is reached, their toxicity can become pronounced in both ecological and human health contexts (4). The association between environmental heavy metal exposure and human disease was first highlighted during pollution-related disasters in Japan in the 1950s (5). The International Agency for Research on Cancer (IARC) has classified several heavy metals, including arsenic, cadmium, inorganic lead compounds, nickel, and chromium, as carcinogenic to humans (6). Arsenic exposure is linked to malignancies of the skin, lungs, bladder, colon, and kidneys, while cadmium is associated with prostate and renal cancers. The World Health Organization (WHO) has set the maximum safe limit of arsenic in drinking water at 10 µg/L; however, in several areas of Pakistan, particularly in Sindh and Punjab, levels have been reported as high as 50 µg/L or more (7). Notably, Manchar Lake in Sindh exhibits arsenic concentrations up to 158 µg/L, exceeding WHO guidelines by over fifteenfold (8). For cadmium, the WHO recommends a tolerable concentration of 0.003 mg/L in drinking water, yet measurements in regions such as Khyber Pakhtunkhwa have reached levels as high as 0.21 mg/L (9). Lead, another potent toxicant, is known to induce severe neurological outcomes, including coma, convulsions, and renal failure, and is particularly dangerous for children (10). Alarming concentrations of lead—up to 4.7 mg/L—have been detected in drinking water in Azad Jammu and Kashmir, significantly surpassing the WHO limit of 0.01 mg/L (11).

Arsenic toxicity manifests in dermatological conditions such as skin lesions, keratosis, and melanosis, which affect up to 30–40% of populations residing near Manchar Lake (12,13). Lead exposure in Karachi has been correlated with neurobehavioral and psychological disturbances, particularly in children with elevated blood lead levels (14,15). Cadmium, when excessively accumulated in children, is associated with osteotoxic effects and increased urinary calcium excretion (16). One of the more concerning long-term health outcomes linked to heavy metal exposure is chronic kidney disease (CKD), a progressive condition with high global burden (17). While traditional risk factors for CKD include diabetes, hypertension, obesity, and smoking, environmental nephrotoxins such as lead, cadmium, and mercury have emerged as significant contributors, particularly in populations experiencing chronic low-dose exposures (18). Cadmium has been shown to induce renal tubular damage in experimental animal models even at low concentrations (19), while lead is implicated in causing albuminuria, nephropathy, and mitochondrial swelling in renal tubular cells (20). Elevated levels of nickel, copper, and cadmium have also been associated with proteinuria and renal dysfunction (21). Despite growing evidence of nephrotoxic effects from heavy metals, limited research exists linking environmental contamination of drinking water with CKD prevalence in Pakistan. Addressing this gap, the present study aims to assess the concentration of heavy metals in drinking water across selected regions and investigate their potential association with clinical markers of CKD. The findings are intended to inform policy frameworks for water safety and public health by aligning water quality standards with WHO guidelines and supporting targeted interventions for mitigating environmental health risks.

METHODS

This quantitative cross-sectional study aimed to explore the association between heavy metal contamination in drinking water and the risk of chronic kidney disease (CKD) in adults. A total of 250 participants were included, selected from both urban and rural communities situated in regions previously identified to have potential heavy metal contamination in water sources. Participants were eligible if they were aged 18 years or older, consumed local drinking water as their primary source of hydration, and provided informed consent. Individuals with a known history of congenital kidney disorders, those on dialysis, or who had undergone kidney transplantation were excluded to reduce confounding effects. Ethical approval for the study was obtained from the institutional review board (IRB), and informed written consent was obtained from all participants prior to enrollment. Participants were evaluated through a combination of

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medical record review and structured interviews to assess general health status, lifestyle factors, and any prior diagnoses of CKD or other comorbidities such as diabetes and hypertension. Drinking water samples were collected from 10 geographically diverse households within the study regions, chosen based on their proximity to potential sources of environmental pollution, including industrial discharge and agricultural runoff. These samples were analyzed for concentrations of lead, arsenic, cadmium, and mercury using Inductively Coupled Plasma Mass Spectrometry (ICP-MS), a sensitive and precise method for detecting trace elements in environmental matrices.

Each participant underwent clinical assessment to evaluate renal function. Blood samples were collected to measure serum creatinine, which was used to calculate the estimated glomerular filtration rate (eGFR) using the CKD-EPI formula. Urine samples were analyzed to determine the albumin-to-creatinine ratio (ACR). CKD was defined according to established international criteria: an eGFR of less than 60 mL/min/1.73 m² and/or an ACR greater than 30 mg/g persisting for more than three months. Descriptive statistics, including means and standard deviations, were used to summarize demographic data, levels of heavy metals in water samples, and renal function markers among participants. Inferential statistical analysis was conducted using multivariate regression models to examine the relationship between heavy metal exposure and the presence of CKD. Adjustments were made for potential confounding factors, including age, sex, smoking status, hypertension, diabetes, and body mass index. All analyses were conducted using standard statistical software with a significance level set at $p<0.05$.

RESULTS

A total of 250 participants were included in the study, comprising 130 males (52%) and 120 females (48%). All participants were residents of rural regions with a documented history of water contamination. The mean age was 45.8 ± 13.4 years, with 48% falling in the 31–50 year age group, followed by 32% over the age of 50 and 20% aged between 18–30 years. Among the participants, 24% reported being smokers, while 34% had at least one comorbidity such as hypertension or diabetes. Analysis of drinking water samples from participants' households revealed elevated levels of several heavy metals. The mean concentration of lead was found to be 0.72 mg/L, significantly exceeding the WHO permissible limit of 0.01 mg/L in 87% of the samples. Cadmium levels averaged 0.15 mg/L, with 75% of samples above the 0.003 mg/L WHO limit. Arsenic was detected at a mean concentration of 0.098 mg/L, with 81% of samples surpassing the guideline value of 0.01 mg/L. Mercury concentrations, while lower, still exceeded the WHO limit of 0.001 mg/L in 64% of cases, with a mean value of 0.006 mg/L. Clinical findings demonstrated evidence of impaired kidney function among the participants. The mean serum creatinine level was 1.3 ± 0.47 mg/dL, slightly above the normal reference range of 0.6–1.2 mg/dL. The average estimated glomerular filtration rate (GFR) was 62.4 ± 18.3 mL/min/1.73m², indicating reduced renal function in a significant portion of the sample. Additionally, the mean urine albumin-to-creatinine ratio (UACR) was markedly elevated at 201 ± 140 mg/g, compared to the normal threshold of <30 mg/g. Based on standard clinical diagnostic criteria, 23 individuals (9.2%) were diagnosed with chronic kidney disease (CKD). Multivariate logistic regression analysis identified a statistically significant association between exposure to specific heavy metals and the likelihood of CKD. Lead exposure demonstrated the strongest association, with an adjusted odds ratio (AOR) of 2.85 (95% CI: 1.75–4.61; $p<0.001$). Cadmium exposure was also significantly associated with CKD (AOR: 2.40; 95% CI: 1.38–4.16; $p=0.002$), followed by arsenic (AOR: 1.92; 95% CI: 1.12–3.28; $p=0.018$). Although mercury exposure showed a trend toward increased risk (AOR: 1.45; 95% CI: 0.85–2.47), it did not reach statistical significance ($p=0.168$).

Table 1: Demographic Characteristics of Participants

Variable	Category	Frequency	Percentage (%)
Gender	Male	130	52.0
	Female	120	48.0
Area Type	Rural	250	100.0
Age Group	18–30 years	50	20.0
	31–50 years	120	48.0
	>50 years	80	32.0
Smoking Status	Smoker	60	24.0
	Non-Smoker	190	76.0
Comorbidities	Yes	85	34.0
	No	165	66.0

Table 2: Heavy Metal Concentration in Drinking Water Samples

Heavy Metal	Mean Concentration (mg/L)	WHO Limit (mg/L)	% Samples Exceeding WHO Limit
Lead	0.72	0.01	87%
Cadmium	0.15	0.003	75%
Arsenic	0.098	0.01	81%
Mercury	0.006	0.001	64%

Table 3: Clinical Kidney Markers Among Participants

Parameter	Mean ± SD	Normal Reference Range
Serum Creatinine (mg/dL)	1.3 ± 0.47	0.6 – 1.2
GFR (mL/min/1.73m²)	62.4 ± 18.3	>90
Urine Albumin-to-Creatinine Ratio (mg/g)	201 ± 140	<30
CKD Diagnosed (%)	23 participants	-

Table 4: Association Between Heavy Metal Exposure and CKD Risk

Heavy Metal	Adjusted Odds Ratio (95% CI)	P-Value	Interpretation
Lead	2.85 (1.75–4.61)	<0.001	Strong association
Cadmium	2.40 (1.38–4.16)	0.002	Statistically significant
Arsenic	1.92 (1.12–3.28)	0.018	Statistically significant
Mercury	1.45 (0.85–2.47)	0.168	Not statistically significant

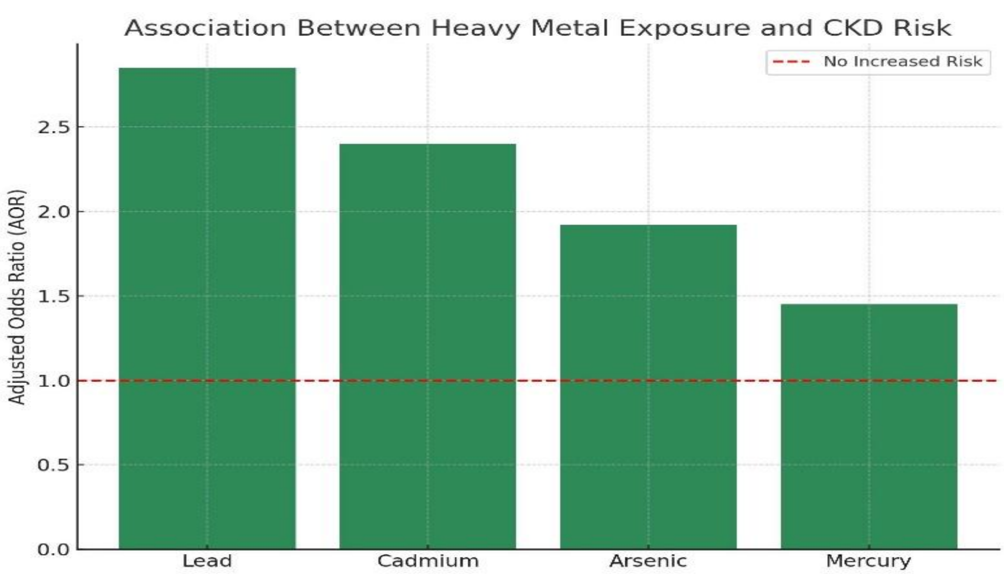

Figure 1 Association Between Heavy Mental Exposure and CKD Risk

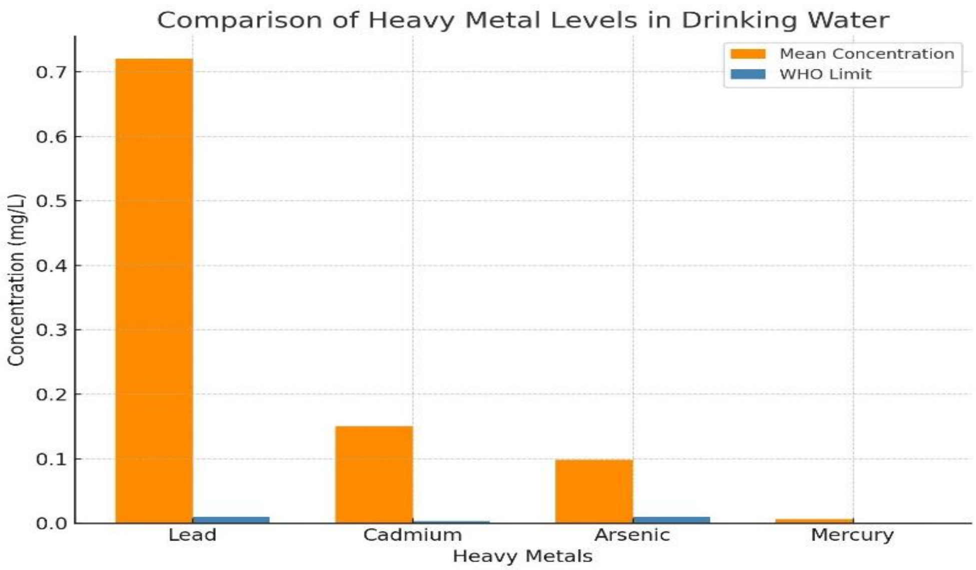

Figure 2 Comparison of Heavy Mental Levels in Drinking Water

DISCUSSION

The present study investigated the burden of heavy metal contamination in drinking water and its association with chronic kidney disease (CKD) among rural populations in Pakistan. The findings revealed that the concentrations of lead, cadmium, and arsenic in household water supplies frequently exceeded World Health Organization (WHO) permissible limits, with a notably high prevalence of impaired renal function among exposed individuals. These results reinforce the growing global concern regarding the nephrotoxic effects of environmental pollutants and underscore the vulnerability of rural communities where water quality monitoring is minimal or absent. Lead was the most prominent contaminant, exceeding WHO limits in 87% of the water samples and showing the strongest association with CKD. The adjusted odds ratio (AOR) of 2.85 for lead exposure aligns with previous findings that identified lead as a potent nephrotoxin associated with albuminuria, glomerular dysfunction, and tubular damage (20-22). Proteinuria and reduced glomerular filtration rate (GFR) have also been reported in populations with elevated blood lead levels (23), which supports the renal implications observed in the current cohort. The consistency across studies strengthens the validity of lead's role in progressive kidney injury, particularly in resource-limited settings. Cadmium, detected above WHO limits in 75% of water samples, was also significantly linked to CKD (AOR 2.40). Cadmium's renal toxicity has been well-documented in experimental and epidemiological literature, particularly for its role in tubular injury, calcium metabolism disruption, and long-term renal accumulation due to its prolonged biological half-life (24). The use of inductively coupled plasma mass spectrometry (ICP-MS) in this study enabled accurate quantification of cadmium at low concentrations, addressing a critical challenge in assessing chronic exposure, and adding methodological strength to the findings.

Arsenic was detected in concentrations above WHO guidelines in 81% of samples, with a corresponding AOR of 1.92 for CKD risk. Prior environmental health research has linked chronic arsenic exposure with nephrotoxicity, reduced GFR, and other systemic complications including cardiovascular disease, dermatological lesions, and malignancies (25). The present findings echo this evidence and point toward a broader pattern of health deterioration under prolonged exposure to inorganic arsenic in drinking water. In contrast, mercury, although elevated in 64% of samples, did not show a statistically significant association with CKD in this analysis. This outcome diverges from earlier findings suggesting mercury-induced renal pathologies such as membranous nephropathy (24,25). The observed non-significance in this study may be attributed to relatively lower average concentrations, reduced bioavailability, or inter-individual variation in susceptibility. This highlights that not all heavy metals exhibit uniform nephrotoxic profiles and emphasizes the need for exposure-specific risk assessments. A major strength of this study lies in its exclusive focus on rural communities, where

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populations often lack access to safe drinking water and regulatory oversight is minimal. This population-based approach contributes valuable data to the limited body of research addressing environmental contributors to CKD in low-resource settings. Furthermore, the study's application of robust laboratory techniques, adjustment for key confounders, and detailed clinical profiling add to its scientific rigor.

However, several limitations must be acknowledged. The cross-sectional design inherently limits the ability to infer causality. The reliance on single-time water sampling, while pragmatic, does not capture temporal fluctuations in exposure. Additionally, the study did not assess other potential environmental or occupational exposures, such as agricultural pesticide use or dietary intake, which may have contributed to kidney impairment. The lack of participant-specific water sampling further limits the precision of exposure attribution. A broader geographic sampling frame and inclusion of biomarker analyses, such as urinary heavy metal levels, would enhance the validity of future research. Despite these constraints, the findings strongly suggest a public health imperative to monitor and mitigate heavy metal contamination in drinking water supplies, particularly in underserved rural populations. The association between environmental exposure and renal disease observed in this study adds to the growing evidence base supporting environmental health interventions. Longitudinal cohort studies, incorporating repeated exposure assessments and biomarker validation, are recommended to further elucidate the causal pathways and long-term health consequences of chronic low-dose exposure to heavy metals.

CONCLUSION

This study concludes that the presence of elevated levels of lead, cadmium, and arsenic in drinking water is significantly associated with an increased risk of chronic kidney disease among rural populations in Pakistan. These findings emphasize the pressing need for effective regulatory oversight, routine monitoring of water quality, and community-based public health interventions. By drawing attention to environmental exposures as critical yet often overlooked contributors to kidney disease, this research underscores the importance of integrating environmental health into national kidney disease prevention and water safety policies.

AUTHOR CONTRIBUTION

Author	Contribution
Kirsh Kumar	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Sajan Sarang	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Hina Qasim Memon	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Anchal Kumari	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Hira Jamil	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Abdul Razzaque Nohri*	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

REFERENCES

1. Yang J, Lo K, Yang A. Trends in Urinary and Blood Cadmium Levels in U.S. Adults with or without Comorbidities, 1999-2018. Nutrients. 2022;14(4).
2. Danziger J. Synergistic susceptibility to environmental lead toxicity in chronic kidney disease. Curr Opin Nephrol Hypertens. 2024;33(5):543-50.

3. Nigra AE, Navas-Acien A. Racial Inequalities in Drinking Water Lead Exposure: A Wake-Up Call to Protect Patients with End Stage Kidney Disease. J Am Soc Nephrol. 2021;32(10):2419-21.
4. Lin CJ, Shih HM, Wu PC, Pan CF, Lin YH, Wu CJ. Plasma selenium and zinc alter associations between nephrotoxic metals and chronic kidney disease: Results from NHANES database 2011-2018. Ann Acad Med Singap. 2023;52(8):398-410.
5. Mishra M, Nichols L, Dave AA, Pittman EH, Cheek JP, Caroland AJV, et al. Molecular Mechanisms of Cellular Injury and Role of Toxic Heavy Metals in Chronic Kidney Disease. Int J Mol Sci. 2022;23(19).
6. Danziger J, Willetts J, Larkin J, Chaudhuri S, Mukamal KJ, Usvyat LA, et al. Household Water Lead and Hematologic Toxic Effects in Chronic Kidney Disease. JAMA Intern Med. 2024;184(7):788-96.
7. Yin G, Xin M, Zhao S, Zhao M, Xu J, Chen X, et al. Heavy metals and elderly kidney health: A multidimensional study through Enviro-target Mendelian Randomization. Ecotoxicol Environ Saf. 2024;281:116659.
8. Win-Thu M, Myint-Thein O, Win-Shwe TT, Mar O. Environmental cadmium exposure induces kidney tubular and glomerular dysfunction in the Myanmar adults. J Toxicol Sci. 2021;46(7):319-28.
9. Farkhondeh T, Naseri K, Esform A, Aramjoo H, Naghizadeh A. Drinking water heavy metal toxicity and chronic kidney diseases: a systematic review. Rev Environ Health. 2021;36(3):359-66.
10. Satarug S, Vesey DA, Gobe GC. Dose-Response Analysis of the Tubular and Glomerular Effects of Chronic Exposure to Environmental Cadmium. Int J Environ Res Public Health. 2022;19(17).
11. Smereczański NM, Brzóska MM. Current Levels of Environmental Exposure to Cadmium in Industrialized Countries as a Risk Factor for Kidney Damage in the General Population: A Comprehensive Review of Available Data. Int J Mol Sci. 2023;24(9).
12. Yin G, Zhao S, Zhao M, Xu J, Ge X, Wu J, et al. Complex interplay of heavy metals and renal injury: New perspectives from longitudinal epidemiological evidence. Ecotoxicol Environ Saf. 2024;278:116424.
13. Medgyesi DN, Mohan S, Bangia K, Spielfogel ES, Spaur M, Fisher JA, et al. Community Water Trihalomethanes and Chronic Kidney Disease. JAMA Netw Open. 2025;8(7):e2518513.
14. Gao H, Zhu N, Deng S, Du C, Tang Y, Tang P, et al. Combination Effect of Microcystins and Arsenic Exposures on CKD: A Case-Control Study in China. Toxins (Basel). 2023;15(2).
15. Shi X, Wang X, Zhang J, Dang Y, Ouyang C, Pan J, et al. Associations of mixed metal exposure with chronic kidney disease from NHANES 2011-2018. Sci Rep. 2024;14(1):13062.
16. Kuo PF, Huang YT, Chuang MH, Jiang MY. Association of low-level heavy metal exposure with risk of chronic kidney disease and long-term mortality. PLoS One. 2024;19(12):e0315688.
17. Wei Y, Lyu Y, Cao Z, Zhao F, Liu Y, Chen C, et al. Association of low cadmium and mercury exposure with chronic kidney disease among Chinese adults aged ≥80 years: A cross-sectional study. Chin Med J (Engl). 2022;135(24):2976-83.
18. Haruna I, Obeng-Gyasi E. Association of Combined Per- and Polyfluoroalkyl Substances and Metals with Chronic Kidney Disease. Int J Environ Res Public Health. 2024;21(4).
19. Doccioli C, Sera F, Francavilla A, Cupisti A, Biggeri A. Association of cadmium environmental exposure with chronic kidney disease: A systematic review and meta-analysis. Sci Total Environ. 2024;906:167165.
20. Aaseth J, Alexander J, Alehagen U, Tinkov A, Skalny A, Larsson A, et al. The Aging Kidney-As Influenced by Heavy Metal Exposure and Selenium Supplementation. Biomolecules. 2021;11(8).
21. CANPOLAT Ö. THE GLOBAL PROBLEM: WATER POLLUTION AND HEAVY METALS-A. Research And Evaluations In Agriculture, Forestry And Aquaculture. 2023 Dec:119.
22. Talema A. Causes, negative effects, and preventive methods of water pollution in Ethiopia. Quality Assurance and Safety of Crops & Foods. 2023 Apr 1;15(2):129-39.
23. Tsai HJ, Hung CH, Wang CW, Tu HP, Li CH, Tsai CC, Lin WY, Chen SC, Kuo CH. Associations among heavy metals and proteinuria and chronic kidney disease. Diagnostics. 2021 Feb 11;11(2):282.
24. Danziger J, Willetts J, Larkin J, Chaudhuri S, Mukamal KJ, Usvyat LA, Kossmann R. Household Water Lead and Hematologic Toxic Effects in Chronic Kidney Disease. JAMA Intern Med. 2024 Jul 1;184(7):788-796.
25. Gao Z, Wu N, Du X, Li H, Mei X, Song Y. Toxic Nephropathy Secondary to Chronic Mercury Poisoning: Clinical Characteristics and Outcomes. Kidney Int Rep. 2022 Mar 18;7(6):1189-1197.