

Article

Urinary Uranium Levels in Cancer Patients and Healthy Residents Living in Uranium Legacy-Affected Areas: A Comparative Study

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Abstract

Uranium is a naturally occurring radioactive heavy metal, and drinking water and food are the primary sources of non-occupational exposure for the general population. The aim of the present study was to evaluate urinary uranium concentrations among cancer patients and healthy residents living in uranium legacy-affected areas and to compare them with those of individuals residing in a region with a more favorable radiological environment, accounting for urinary creatinine levels. An observational human biomonitoring study was conducted among 80 adults divided into four groups ($n = 20$ each): cancer patients and healthy residents from the exposed area and cancer patients and healthy residents from the comparison area. Twenty-four-hour urine samples were analyzed for uranium using inductively coupled plasma mass spectrometry, and urinary creatinine was measured using the kinetic Jaffe method. Urinary uranium concentrations ranged from 0.01 to 1.30 $\mu\text{g/L}$, with the highest values observed in cancer patients from the exposed area. After creatinine adjustment, median uranium concentrations were 0.0974 $\mu\text{g/g creatinine}$ in exposed cancer patients, 0.0888 $\mu\text{g/g creatinine}$ in exposed healthy residents, 0.0515 $\mu\text{g/g creatinine}$ in comparison-area cancer patients, and 0.0607 $\mu\text{g/g creatinine}$ in comparison-area healthy residents. Significant differences were observed between exposed and comparison populations among both cancer patients ($p = 0.0066$) and healthy residents ($p = 0.0499$). Residence in the exposed area was positively associated with urinary uranium levels ($p = 0.292$, $p = 0.012$). These findings suggest higher internal uranium exposure among residents of uranium legacy-affected areas and support the use of urinary uranium as a biomarker of environmental exposure. This study contributes to the assessment of internal uranium exposure in residents of uranium legacy-affected areas, including both cancer patients and healthy residents. However, the findings should be interpreted as differences in exposure biomarkers and do not establish a causal relationship between uranium exposure and cancer.

Keywords: uranium; urine; creatinine; biomonitoring; cancer patients; environmental exposure



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1. Introduction

Uranium is a naturally occurring radioactive heavy metal widely distributed in the Earth's crust and present in soil, groundwater, surface water, air, plants, and food [1,2]. For the general population, food and drinking water are the principal sources of non-occupational exposure, whereas substantially higher exposure may occur in areas affected by mining, ore processing, combustion of uranium-bearing materials, or legacy waste deposits [3]. Environmental contamination from uranium-bearing sites may therefore lead to chronic low-level human exposure through contaminated water, locally grown food, and inhalation of contaminated dust [4].

Previous environmental assessments conducted in the Stepnogorsk area of Northern Kazakhstan have shown that settlements located near the Stepnogorsk Mining and Chemical Combine tailings area are characterized by several radiological factors relevant to potential chronic exposure. Aqsu, Zavodskoy, and Kvartsitka have been described as settlements located within approximately 5 km of the tailings area. Earlier radiological assessments in these settlements included measurements of ambient gamma dose rate, indoor and outdoor radon, radionuclide activity in water and soil, and scenario-based estimates of ingestion-related exposure through local water and food-chain pathways [5,6]. More recent groundwater investigations in mining-affected settlements also reported measurable radon concentrations in wells and boreholes, supporting the relevance of water-related exposure pathways in this region [7]. However, despite these environmental data, published human biomonitoring studies of non-occupational uranium exposure among residents of uranium legacy-affected settlements remain limited.

Biomonitoring of uranium in human biological media is an important approach for exposure assessment. Among available matrices, urine is considered one of the most informative indicators of recent internal uranium intake because a large proportion of absorbed uranium is excreted through the urinary pathway within the first days after exposure. Urinary uranium has therefore been used both in occupational monitoring and in environmental studies of potentially exposed populations [8].

At the same time, interpretation of urinary uranium depends on the sampling strategy and on urine dilution. Population studies often rely on spot urine because it is easier to collect, but 24 h urine provides a more integrated estimate of daily excretion. In a nationwide Swiss study based on 1393 adults, the median uranium excretion was 15 ng/24 h, and the 95th percentile was 67 ng/24 h, illustrating the usefulness of 24 h urine for estimating background population exposure [9]. For spot urine and creatinine-adjusted measurements, background population values are generally low. ATSDR summarized NHANES data for the general U.S. population and reported geometric mean urinary uranium levels in the range of 0.006–0.009 µg U/g creatinine or 0.005–0.010 µg U/L urine [10]. In a reference study from Warsaw, most values in non-exposed residents remained below the upper range expected for the general population, supporting the role of urinary uranium as a biomarker of background intake [11]. When spot urine is used, adjustment for urinary dilution becomes especially important. Creatinine remains the most widely used correction factor, and its strong association with urine osmolality has been demonstrated in a large human cohort, supporting its use to normalize urinary biomarker concentrations [12,13].

Previous environmental studies have shown that urinary uranium may increase in populations living in geochemically or technologically affected regions [14–16]. In a coal-mining area of Yili, Xinjiang, urine uranium concentrations ranged from 8.44 to 761.6 ng/L and were higher than reference values for unexposed populations, suggesting long-term environmental exposure, most likely associated with groundwater. Multimatrix studies from other regions have likewise demonstrated that uranium can be measured in urine, hair, nails, serum, water, soil, and food, although these matrices reflect different exposure

windows and may not always correlate closely with each other. Hair may better reflect longer-term intake, whereas urine is generally more responsive to recent exposure [17].

In Kazakhstan, uranium biomonitoring has already been applied in occupational settings. Previous studies of uranium workers at different stages of the nuclear fuel cycle reported measurable urinary uranium concentrations across exposed occupational groups and highlighted the need for continued biomonitoring and improved assessment of radiation-related exposure [18]. However, data on non-occupational uranium exposure among residents of uranium legacy-affected areas remain limited, especially when biological monitoring is combined with comparison groups living outside the affected area.

The present study was conducted as a human biomonitoring component within the broader assessment of potential health risks in uranium legacy-affected areas. Although radiation-related and uranium-associated environmental factors are relevant to cancer risk assessment, the present study was not designed to establish cancer causation or to estimate the risk of malignant neoplasms attributable to uranium exposure. Instead, urinary uranium was used as a biomarker of internal exposure, and cancer status was included to describe and compare biomonitoring profiles among residents with and without a previous cancer diagnosis.

The aim of the present study was to evaluate urinary uranium concentrations among cancer patients and healthy residents living in uranium legacy-affected areas and to compare them with those of individuals residing in a region with a more favorable radiological environment, accounting for urinary creatinine levels. The study was designed as a human biomonitoring study to assess whether residents of uranium legacy-affected areas have a higher internal uranium burden than residents of the comparison area, and whether this pattern is observed in both cancer patients and healthy residents. Cancer status was used as a subgroup characteristic to explore whether urinary uranium levels differed by disease status within the same residential area. The study was not designed to determine whether uranium exposure caused cancer.

2. Materials and Methods

2.1. Study Design, Study Area and Participants

This observational human biomonitoring study included 80 adult participants divided into four equal subgroups: cancer patients and healthy residents from the uranium legacy-affected area, and cancer patients and healthy residents from the comparison area. The sample size was determined by the exploratory nature of the study and the feasibility of recruiting participants who met all inclusion and exclusion criteria. Because this was an initial human biomonitoring study in a non-occupationally exposed population from uranium legacy-affected areas, no formal a priori power calculation was performed. Therefore, the study was intended to provide preliminary biomonitoring evidence and to generate hypotheses for larger future studies rather than to provide definitive risk estimates.

Cancer patients were recruited among residents with previously diagnosed malignant neoplasms. Recruitment was informed by previous regional epidemiological findings indicating that digestive tract cancers, respiratory and intrathoracic cancers, breast cancer, skin cancer, and malignancies of female reproductive organs were among the most frequent cancer localizations in the study area [19,20]. Eligible cancer patients were included if they met the residence criteria and agreed to provide 24 h urine samples. Because the present investigation was an exploratory human biomonitoring study and recruitment of eligible cancer patients was limited by feasibility and consent constraints, the cancer subgroups were not matched by cancer type. All cancer patients included in the study had completed their main anticancer treatment before urine sample collection, and none were receiving active chemotherapy, radiotherapy, or surgical treatment at the time of biological sampling.

Patients with kidney or urinary tract tumors were excluded to reduce the potential direct influence of urinary system malignancies on urinary biomarker excretion [20].

The exposed settlements were selected based on their location within the uranium legacy-affected Stepnogorsk area. Previous environmental assessments described Aqsu, Zavodskoy, and Kvartsitka as settlements located within approximately 5 km of the Stepnogorsk Mining and Chemical Combine tailings area [6]. In these settlements, earlier studies evaluated ambient gamma dose rates, indoor radon concentrations, water, soil, and food samples, and scenario-based radiation exposure pathways. These data provided the environmental context for classifying Aqsu and Zavodskoy as uranium legacy-affected settlements in the present biomonitoring study.

Akkol was selected as the comparison area because it is located outside the immediate uranium legacy-affected zone and has a more favorable radiological setting compared with the settlements located near the Stepnogorsk tailings area. Residence in Aqsu and Zavodskoy was used as a proxy indicator of potential long-term environmental exposure. However, individual-level measurements of uranium in drinking water, soil, dust, food, or air were not performed concurrently with urine sampling in the present study. Therefore, the exposure classification should be interpreted as area-based rather than as a direct quantitative assessment of individual environmental uranium exposure. The exposed population was recruited from Aqsu and Zavodskoy, both located in the uranium legacy-affected Stepnogorsk area. The comparison population was recruited from Akkol, which is located outside the immediate uranium legacy-affected zone and has a more favorable radiological setting. Thus, exposure classification in the present study was area-based. The geographic location of the uranium legacy-affected settlements, the comparison area, and the Stepnogorsk Mining and Chemical Combine tailings dump is shown in Figure 1.

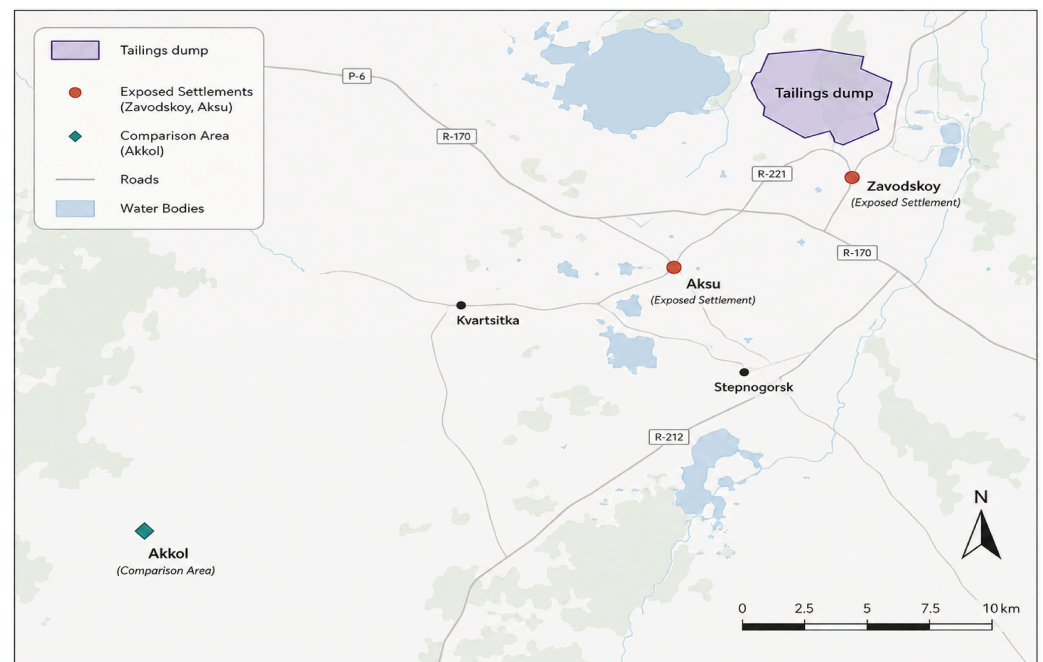


Figure 1. Map of the study area showing the exposed settlements (Zavodskoy and Aqsu), the comparison area (Akkol), and the location of the tailings dump.

Inclusion criteria were age above 18 years, permanent residence in the study settlement for at least 10 years, and voluntary informed consent to participate. Exclusion criteria were occupational exposure to ionizing radiation sources and acute diseases of the urinary tract. Occupationally exposed individuals were excluded to reduce potential confounding from

occupational radiation or uranium-related exposure. Participants with acute urinary tract diseases were excluded because such conditions may affect urine composition, renal and urinary excretion, and the interpretation of urinary biomarkers. The characteristics of the study participants are presented in Table 1.

Table 1. Characteristics of the study participants by study group.

Study Group	n	Age, Mean $\pm$ SD (Years)	Male, n (%)	Female, n (%)	Area of Residence	Disease Status
Cancer patients, exposed area	20	62.60 $\pm$ 9.76	8 (40.0)	12 (60.0)	Zavodskoy, Aqsu	Cancer
Healthy residents, exposed area	20	51.60 $\pm$ 9.30	9 (45.0)	11 (55.0)	Zavodskoy, Aqsu	Healthy
Cancer patients, comparison area	20	63.85 $\pm$ 12.88	5 (25.0)	15 (75.0)	Akkol	Cancer
Healthy residents, comparison area	20	54.05 $\pm$ 15.74	6 (30.0)	14 (70.0)	Akkol	Healthy

Data are presented as mean $\pm$ SD or n (%).

2.2. Urine Sampling and Transportation

For uranium determination, 24 h urine samples were collected in clean 2 L polyethylene containers. A 20 mL aliquot of each daily urine sample was then transferred into a sterile 30 mL plastic container and acidified with concentrated nitric acid to minimize uranium adsorption to the container walls and prevent sample degradation. All biological samples were coded and transported under cooled conditions to the Radiochemistry and Radiospectrometry Testing Laboratory of the Scientific Institute of Radiobiology and Radiation Protection, Astana Medical University. During transportation, the temperature did not exceed 4 °C. When transportation time exceeded 24 h, samples were stored at −20 °C until delivery [21].

2.3. Uranium Determination by ICP-MS

Urinary uranium analysis was performed according to ASTM C1844-24 using inductively coupled plasma mass spectrometry (ICP-MS) [22]. Before analysis, frozen samples were thawed for 2 h at room temperature (21 $\pm$ 4 °C). For sample preparation, 1 mL of urine was transferred into a 15 mL tube and mixed with 9 mL of 2% HNO₃. In addition, 100 μ L of thorium standard solution was added as an internal standard. Thus, the urine samples were diluted at a ratio of 1:10 before instrumental analysis. Samples were then centrifuged at 6000 rpm (4430 RCF) for 24 min, and the supernatant was transferred into labeled 18 mL vials. Uranium concentrations were measured using a quadrupole ICP-MS system (Agilent 7800, Agilent Technologies, Santa Clara, CA, USA) [14]. Certified standards and calibration solutions were used for quality control, including SRM 3164 material from NIST. The detection limit was 0.1 ng/L. Final uranium concentrations were calculated with the dilution factor taken into account. At least two replicate measurements were performed for each sample, and the final value was based on the mean of replicate measurements.

Although 24 h urine collection provides a more integrated estimate of urinary excretion than spot urine and reduces short-term dilution-related variability, creatinine adjustment was additionally applied to improve comparability between participants. This approach was used to account for residual differences in urine concentration and possible differences in completeness of 24 h urine collection. Urinary creatinine was also considered a quality-control indicator for the comparability of urine samples across study subgroups.

2.4. Determination of Urinary Creatinine

Urinary creatinine was determined in all participants in order to account for urine dilution and to normalize uranium concentrations. Creatinine was measured using the standard kinetic Jaffé method, based on the reaction of creatinine with picric acid in an alkaline medium with photometric detection of the resulting colored complex. Daily urine samples were used for creatinine determination. All biochemical analyses were performed in accredited clinical diagnostic laboratories operating in accordance with ISO 15189 quality standards. Creatinine values were expressed in mmol/L and were subsequently used to calculate creatinine-adjusted urinary uranium concentrations [23–25].

2.5. Statistical Analysis

Descriptive statistics were presented as mean $\pm$ standard deviation and as median with interquartile range (Q1–Q3), where appropriate. Both mean and median values were reported because urinary uranium concentrations showed skewed distributions and individual high values. The mean was retained to allow comparison with previous studies, whereas the median and interquartile range were used to provide a more robust description of central tendency and variability in non-normally distributed data. Because of the relatively small subgroup size and the non-normal distribution of several variables, between-group comparisons were performed using the two-sided Mann–Whitney U test. For the main pairwise comparisons of creatinine-adjusted urinary uranium concentrations, median differences with 95% confidence intervals and rank-biserial correlation coefficients were additionally calculated to provide measures of precision and effect size. Because the analyses were exploratory and hypothesis-generating, *p*-values were not adjusted for multiple comparisons and were interpreted cautiously. Correlations between creatinine-adjusted urinary uranium and demographic or clinical variables were assessed using Spearman's rank correlation coefficient. The correlation analysis was limited to variables available for all participants, including age, sex, cancer status, and area of residence. Sex, cancer status, and area of residence were coded as binary variables for exploratory non-parametric association analysis. Because these variables are nominal rather than ordinal, the resulting correlation coefficients were interpreted only as exploratory measures of association and not as evidence of an ordered dose–response relationship. Detailed data on smoking status, non-radiation occupational history, source of drinking water, dietary habits, kidney function parameters, socioeconomic status, and medication use were not systematically available for all participants. Therefore, these variables could not be included in the statistical analysis. Because of the small sample size and limited covariate availability, a fully adjusted multivariable regression model was not performed. A *p*-value below 0.05 was considered statistically significant.

2.6. Ethics

The study was conducted in accordance with bioethical principles, including protection of personal data, voluntary participation, and minimization of potential risks to participants. The study protocol was approved by the Local Bioethics Committee of NJSC Astana Medical University (Protocol No. 41, dated 5 November 2025). Written informed consent was obtained from all participants before inclusion in the study.

3. Results

3.1. Cancer Diagnosis/Localization and Treatment Status

The cancer subgroups included several broad cancer localization categories rather than a single targeted cancer type, reflecting previously reported regional cancer patterns

and the feasibility of recruiting eligible patients who agreed to provide 24 h urine samples (Table 2).

Table 2. Cancer diagnosis/localization categories and treatment status among cancer patients included in the study.

Characteristic	Cancer Patients, Exposed Area (n = 20)	Cancer Patients, Comparison Area (n = 20)
Digestive tract cancers	4 (20.0%)	3 (15.0%)
Respiratory and intrathoracic cancers	3 (15.0%)	2 (10.0%)
Breast cancer	6 (30.0%)	7 (35.0%)
Female reproductive organ cancers	5 (25.0%)	4 (20.0%)
Other malignant neoplasms	2 (10.0%)	4 (20.0%)
Total cancer diagnoses/localizations	20 (100%)	20 (100%)
Completed main anticancer treatment before urine sampling	20 (100%)	20 (100%)
Receiving active chemotherapy, radiotherapy, or surgical treatment at the time of urine sampling	0 (0%)	0 (0%)
Kidney or urinary tract tumors	0 (0%)	0 (0%)

Cancer diagnoses/localizations were grouped into broad clinical categories using available medical records. Recruitment of cancer patients was informed by previously reported regional cancer patterns, but the cancer subgroups were not matched by cancer type. All cancer patients had completed their main anticancer treatment before urine sampling, and none were receiving active anticancer treatment at the time of biological sample collection. Patients with kidney or urinary tract tumors were excluded from the study [26].

3.2. Urinary Creatinine Concentrations

Urinary creatinine concentrations were measured in all 80 participants to assess the comparability of urine samples and to account for the potential influence of urine dilution. Median creatinine concentrations were 14.55 mmol/L in cancer patients from the exposed area, 12.40 mmol/L in cancer patients from the comparison area, 12.30 mmol/L in healthy residents from the exposed area, and 12.35 mmol/L in healthy residents from the comparison area. Mean creatinine concentrations ranged from 11.95 ± 4.93 mmol/L in healthy residents from the comparison area to 14.60 ± 7.26 mmol/L in cancer patients from the exposed area.

No statistically significant differences were observed between exposed and comparison groups among cancer patients ($p = 0.405$) or among healthy residents ($p = 0.472$). Additional within-area comparisons between cancer patients and healthy individuals were also not statistically significant. The absence of statistically significant differences in urinary creatinine concentrations between the study subgroups supported the comparability of urine samples and allowed creatinine-adjusted uranium concentrations to be used as a complementary biomonitoring metric. Urinary creatinine and absolute urinary uranium concentrations across the study groups are summarized in Table 3.

Table 3. Urinary creatinine and absolute urinary uranium concentrations across study groups.

Study Group	n	Creatinine, mmol/L Mean $\pm$ SD	Creatinine, mmol/L Median (Q1–Q3)	Uranium, μ g/L Mean $\pm$ SD	Uranium, μ g/L Median	Uranium, μ g/L Min–Max
Cancer patients, exposed area	20	14.60 $\pm$ 7.26	14.55 (9.05–18.05)	0.18 $\pm$ 0.28	0.05	0.01–1.30
Cancer patients, comparison area	20	13.69 $\pm$ 6.16	12.40 (9.00–19.05)	0.03 $\pm$ 0.02	0.02	0.01–0.09
Healthy residents, exposed area	20	12.52 $\pm$ 3.08	12.30 (11.15–14.05)	0.05 $\pm$ 0.03	0.04	0.01–0.10
Healthy residents, comparison area	20	11.95 $\pm$ 4.93	12.35 (9.80–14.20)	0.04 $\pm$ 0.03	0.03	0.01–0.10

Values are presented as mean $\pm$ SD and median (Q1–Q3), where appropriate. Creatinine between-group comparisons: cancer patients, exposed vs. comparison, $p = 0.405$; healthy residents, exposed vs. comparison, $p = 0.472$.

3.3. Absolute Urinary Uranium Concentrations

Urinary uranium concentrations ranged from 0.01 to 1.30 μ g/L across the study population. The highest values were observed in cancer patients living in the exposed area, with a mean concentration of 0.18 $\pm$ 0.28 μ g/L, a median of 0.05 μ g/L, and a maximum of 1.30 μ g/L. In the comparison area, cancer patients had a mean uranium concentration of 0.03 $\pm$ 0.02 μ g/L and a median of 0.02 μ g/L. Among healthy participants, the mean concentration was 0.05 $\pm$ 0.03 μ g/L in the exposed area and 0.04 $\pm$ 0.03 μ g/L in the comparison area. Thus, in both cancer patients and healthy residents, uranium concentrations tended to be higher in the exposed settlements than in the comparison population. Median values remained low across all groups, whereas individual elevated concentrations were observed in the exposed area, particularly among cancer patients.

3.4. Creatinine-Adjusted Urinary Uranium Concentrations

After normalization to urinary creatinine, between-area differences in urinary uranium concentrations remained evident. Median creatinine-adjusted uranium concentrations were 0.0974 μ g/g creatinine in exposed cancer patients, 0.0515 μ g/g creatinine in comparison-area cancer patients, 0.0888 μ g/g creatinine in exposed healthy residents, and 0.0607 μ g/g creatinine in comparison-area healthy residents. The highest individual value was detected in cancer patients from the exposed area (0.8206 μ g/g creatinine), followed by healthy residents from the exposed area (0.4588 μ g/g creatinine). Mann–Whitney analysis showed statistically significant differences between exposed and comparison groups both among cancer patients ($U = 301$, $p = 0.0066$) and among healthy residents ($U = 273$, $p = 0.0499$). In contrast, Table 4B showed no significant difference between cancer patients and healthy residents within the exposed area ($U = 193$, $p = 0.8604$) or within the comparison area ($U = 161$, $p = 0.2977$). Median differences, 95% confidence intervals, and rank-biserial correlation coefficients for the main pairwise comparisons are presented in Table 4. These results suggest that the area of residence was more strongly associated with increased urinary uranium levels than cancer status in this cohort.

The distribution of creatinine-adjusted urinary uranium concentrations across the four study groups is shown in Figure 2. The box-and-whisker plot demonstrates variability within each subgroup and allows visualization of skewness and potential outliers.

Table 4. Creatinine-adjusted urinary uranium concentrations and pairwise comparisons.

(A) Descriptive Statistics								
Study Group	n	Mean, $\mu\text{g/g}$ Creatinine	SD	Median	Q1	Q3	Min	Max
Healthy residents, comparison area	20	0.0825	0.0895	0.0607	0.0247	0.0820	0.0121	0.3747
Cancer patients, comparison area	20	0.0549	0.0490	0.0515	0.0162	0.0725	0.0074	0.1938
Healthy residents, exposed area	20	0.1362	0.1141	0.0888	0.0544	0.1912	0.0256	0.4588
Cancer patients, exposed area	20	0.1839	0.2464	0.0974	0.0549	0.1503	0.0139	0.8206
(B) Pairwise Comparisons								
Comparison	U	p-Value	Median Difference	95% CI		Rank-Biserial Correlation		
Cancer patients: exposed vs. comparison area	301	0.0066	0.0458	0.0117–0.0921		0.505		
Healthy residents: exposed vs. comparison area	273	0.0499	0.0349	0.0014–0.0945		0.363		
Exposed area: cancer patients vs. healthy residents	193	0.8604	−0.0045	−0.0527–0.0463		−0.038		
Comparison area: cancer patients vs. healthy residents	161	0.2977	−0.0125	−0.0421–0.0118		−0.195		

U, Mann–Whitney U statistic; CI, confidence interval. Creatinine-adjusted urinary uranium concentrations are expressed as $\mu\text{g/g}$ creatinine. Pairwise comparisons were performed using two-sided Mann–Whitney U tests. Median differences are expressed as Hodges–Lehmann estimates with 95% confidence intervals. Rank-biserial correlation was used as an effect size measure. Statistical significance was set at $p < 0.05$.

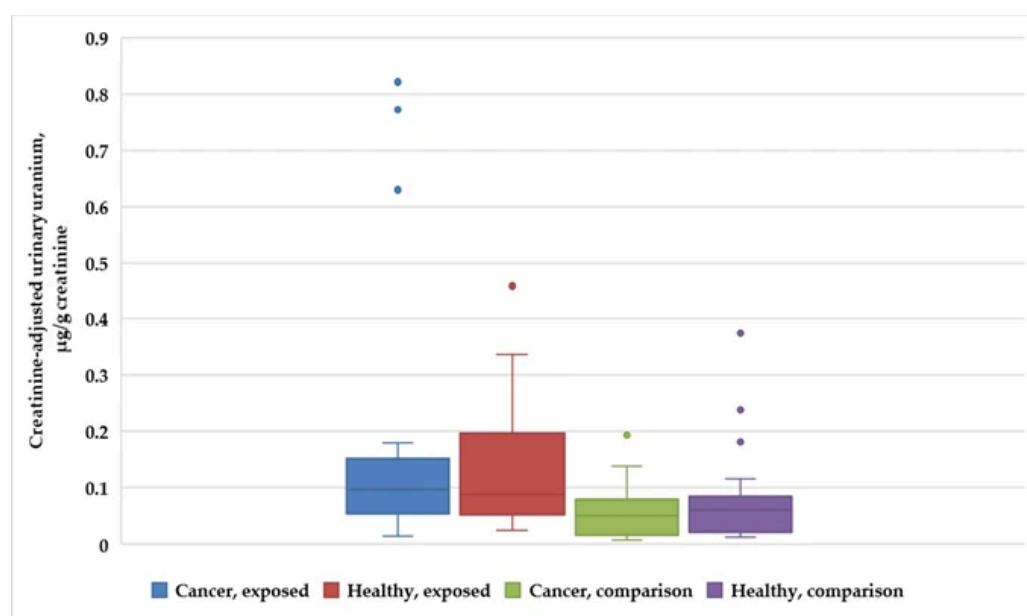


Figure 2. Box-and-whisker plot of creatinine-adjusted urinary uranium concentrations across the study groups. Boxes represent the interquartile range, horizontal lines indicate median values, whiskers show the range of non-outlier values, and individual points represent outliers.

3.5. Correlation Analysis

Spearman correlation analysis showed no statistically significant association between creatinine-adjusted urinary uranium and age ($\rho = 0.142$, $p = 0.223$), sex ($\rho = 0.092$, $p = 0.416$), or cancer status ($\rho = 0.081$, $p = 0.476$). However, a significant positive correlation was observed between urinary uranium and residence in the exposed area ($\rho = 0.292$, $p = 0.012$). This finding indicates an unadjusted association between area of residence and urinary uranium concentrations in the study population; however, the potential influence of unmeasured individual-level factors cannot be excluded.

4. Discussion

The present study demonstrated that urinary uranium concentrations were higher among residents of uranium legacy-affected areas than among the comparison population. After adjustment for urinary creatinine, significant between-area differences remained evident in both cancer patients and healthy residents, whereas no significant differences were observed between cancer patients and healthy individuals living within the same residential area. Furthermore, urinary uranium was positively correlated with residence in the exposed area but showed no association with age, sex, or cancer status. These findings suggest an association between area of residence and urinary uranium concentrations in this study population. However, this association should be interpreted as unadjusted because potentially relevant individual-level covariates were not included in the analysis.

Urinary uranium is widely accepted as a biomarker of internal uranium exposure because soluble uranium is predominantly eliminated through the kidneys. Nevertheless, interpretation of urinary uranium requires consideration of uranium toxicokinetics. Although urinary excretion mainly reflects recent internal exposure, a proportion of absorbed uranium is retained in mineralized tissues, particularly bone, where it may remain for prolonged periods and be gradually released during physiological bone remodeling. Consequently, urinary uranium reflects current internal exposure together with a limited contribution from previously retained uranium but should not be interpreted as a direct measure of cumulative body burden or lifetime exposure [27,28]. To reduce exposure misclassification, only individuals who had resided in the study area for at least 10 years were included, thereby increasing the likelihood that urinary uranium reflected long-term environmental residence rather than recent migration.

Our findings are consistent with previous human biomonitoring studies demonstrating elevated urinary uranium concentrations in populations living in environmentally affected areas. Similar observations have been reported in regions with uranium-rich groundwater, mining activities, or elevated natural background radiation, where urinary uranium has been shown to distinguish environmentally exposed populations from background populations [3,4,29]. Studies comparing different biological matrices have further demonstrated that urine primarily reflects recent internal exposure, whereas hair and nails may better represent longer-term accumulation [30–34]. These differences emphasize that urinary uranium should be interpreted as an indicator of current internal exposure rather than a surrogate measure of chronic body accumulation.

Several limitations should be considered when interpreting the present findings. Previous environmental investigations conducted in the same settlements documented elevated uranium concentrations in groundwater, increased radon activity, and enhanced radiation exposure among residents [6,7], providing relevant environmental context for the present study. However, individual-level measurements of uranium in drinking water, soil, dust, food, or air were not performed concurrently with urine sampling. In addition, detailed information on smoking, drinking-water source, occupational history, kidney function, diet, socioeconomic status, and medication use was unavailable and could not be incorporated

into the analysis. Consequently, the observed association between residential area and urinary uranium concentrations should be interpreted as an unadjusted association, and residual confounding cannot be excluded. The observed differences therefore cannot be independently attributed to residential location or to any specific environmental exposure pathway. Moreover, because the analyses were exploratory and hypothesis-generating, the reported *p*-values should be interpreted cautiously and should not be regarded as confirmatory evidence. The present study should therefore be regarded as an exploratory human biomonitoring investigation rather than an assessment of cancer risk.

5. Conclusions

Residents of uranium legacy-affected settlements exhibited higher urinary uranium concentrations than the comparison population. After creatinine normalization, median urinary uranium concentrations were 0.0974 µg/g creatinine in exposed cancer patients and 0.0888 µg/g creatinine in exposed healthy residents, compared with 0.0515 and 0.0607 µg/g creatinine, respectively, in the comparison area. Significant between-area differences were observed for both cancer patients (*p* = 0.0066) and healthy residents (*p* = 0.0499), whereas no significant differences were found between cancer patients and healthy individuals within the same residential area. Residence in the exposed area was the only variable significantly correlated with urinary uranium concentrations (*p* = 0.292, *p* = 0.012). These findings suggest that environmental conditions associated with uranium legacy-affected areas were more strongly associated with internal uranium exposure than with cancer status in this cohort. Although this study does not identify specific exposure pathways or establish causal relationships, it provides baseline human biomonitoring data for Kazakhstan and supports the application of urinary uranium, combined with creatinine adjustment, as a useful biomarker for assessing internal uranium exposure in populations residing near uranium legacy sites.

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Institutional Review Board Statement: The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Local Bioethics Committee of NJSC Astana Medical University (Protocol No. 41, dated 5 November 2025).

Informed Consent Statement: Written informed consent was obtained from all subjects involved in the study before participation and urine sample collection.

Data Availability Statement: The data presented in this study are not publicly available due to ethical and privacy restrictions related to individual-level biological and clinical information but may be available from the corresponding author upon reasonable request and with approval from the relevant institutional ethics committee.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

ICP-MS	Inductively coupled plasma mass spectrometry
SD	Standard deviation
Q1	First quartile
Q3	Third quartile

NIST National Institute of Standards and Technology
 ISO International Organization for Standardization

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