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Histopathological Effect of Traces for Uranium on Cow Kidneys

Oula E. Hadi*, E.H. Altaee

Department of Pathology and Poultry Disease, College of Veterinary Medicine, University of Baghdad, Baghdad, Iraq.

Abstract | The pro-oxidant activity of uranium (U) is being evaluated in bovine kidneys, a tissue in which the toxic effects of this metal have been demonstrated. The study was conducted on several groups of grass-fed cows in different locations in Basra/Iraq. Histopathological examination of the kidneys revealed hemangiomatous transformation in cows with U in the kidney. Uranium levels were measured using a sodium iodide device, and samples were taken from the cows' kidneys, as they are the organs most affected by uranium. It was noted that if low concentrations of uranium were taken, there would be inflammation in the tissues, and animal might die, leading to degeneration, necrosis, and inflammation. However, in high doses, it leads to the occurrence of various tumors in the kidneys or the occurrence of clear cell carcinoma, Sarcomatoid type of renal cell carcinoma. The results indicate that the levels of uranium found in grass lead to the depletion of the antioxidant defense system in cows and stimulate oxidative stress in the kidneys. Although at current uranium doses, restraint stressors have rarely shown additive adverse effects, their potential impact has not been underestimated.

Keywords | Histopathological effect of Uranium, Cell carcinoma, Necrosis, Inflammation

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***Correspondence** | Oula E. Hadi, Department of Pathology and Poultry Disease, College of Veterinary Medicine, University of Baghdad, Baghdad, Iraq; **Email:** hsennaserh@yahoo.com
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INTRODUCTION

The earth's crust naturally contains uranium (Cuney, 2009). Its radioactivity and heavy metal toxicity make it one of the most severe pollution problems (Zou *et al*., 2011). Understanding the distribution and toxicity of uranium for humans and animals is crucial, especially in light of the rising amounts of uranium products being ingested or inhaled. Natural uranium comprises three isotopes including U234, U235, and U238. These isotopes differ in their radioactive properties but share similar chemical characteristics (ATSDR, 1999; Brugge *et al*., 2005).

One important method that uranium can contaminate animals with radionuclides is through their consumption of food, water, or soil (International Atomic Energy Agency, 2010). The known negative effects of uranium exposure from investigations and work-related exposures include chemically induced kidney toxicity, bladder damage, and lung cancer from exposure to radon, which is produced by radioactive decay (Chen *et al*., 2010).

Renal failure and injury to the proximal tubules may result from the location of the uranium accumulation in the tubules (Homma-Takeda *et al*., 2015). Moreover, numerous authors have shown that the liver (Souidi *et al*., 2005), the central nervous system (Lestaevel *et al*., 2005; Houpert *et al*., 2007), and the gastrointestinal tracts (Dublineau *et al*., 2007) are among the other biological targets of acute and chronic exposure to low uranium levels that have been shown to change.

Basrah Province is the main area in Iraq where uranium pollution is present. This study looked at the histopathological effects of uranium residues on cow kidney samples from the province of Basrah.

MATERIAL AND METHODS

Cow kidney samples (n=100) were collected from the Basrah governorate, and these samples were gathered from agricultural fields in the same governorate where the animals are breeding there and produced.

To achieve an equilibrium state between the mother radionuclide and her daughters, the samples were cut, grilled, and exposed to the sun for a while before being dried in an oven at 70 °C for the entire night. They were then ground into a fine powder and kept in Marinelli beakers for a month. Finally, they were analyzed using a gamma spectroscopy detector NaI (TI) spectroscopy system with a crystal dimension of (3×3).

Calculations

Activity concentration

Equation has been used to calculate the particular activity (Ahmed *et al*., 2013).

$$A\left(\frac{Bq}{Kg}\right) = \frac{NET}{E \times Ig \times m \times t}$$

Where t is the measurement period (86400 sec), A is the sample's specific activity, NET is the area under the peak, E is the detection efficiency, and Kg is the sample's mass in kilograms.

The study was conducted in four different locations in the city of Basrah, where Uranium concentrations were studied in the four locations. It was found that the concentrations of site N were 40 samples, site E was 20 samples, site W was 20 samples, and site S was 20 samples, according to Table 1 shown.

Table 1: Uranium concentrations were studied in the four locations of Basrah?

No.	Symbol	Uranium concentration (Bk/Kg)
1	N1	22.39±2.40
2	N2	22.90±2.37
3	N3	23.30±300
4	N4	23.30±3.01
5	N5	28.45±3.10
6	N6	28.50±3.09
7	N7	58.54±4.50
8	N8	58.54±4.59
9	N9	66.80±2.03
10	N10	66.81±2.00
11	N11	85.90±0.37
12	N12	85.92±1.70
13	N13	85.90±0.73
14	N14	67.99±4.60
15	N15	67.99±5.00
16	N16	17.19±0.70
17	N17	17.19±0.68
18	N18	17.19±0.70
19	N19	17.19±0.70
20	N20	22.90±2.37
21	N21	22.93±2.40
22	N22	22.93±2.00
23	N23	22.90±2.40
24	N24	17.19±0.70
25	N25	17.19±0.70
26	N26	17.19±0.70
27	N27	17.22±0.70
28	N28	17.22±0.70
29	N29	17.22±0.70
30	N30	17.22±0.70
31	N31	17.22±0.68
32	N32	17.22±0.68
33	N33	17.22±0.68
34	N34	19.69±9.72
35	N35	19.70±5.68
36	N36	19.70±5.68
37	N37	19.70±5.68
38	N38	19.69±9.72
39	N39	19.17±9.00
40	N40	17.22±0.70
41	E1	0.0±0.030
42	E2	0.44±0.20
43	E3	2.72±O.070
44	E4	0.33±0.021
45	E5	1.15±0.50
46	E6	78.8±20.7
47	E7	0.36±0.24
48	E8	0.07±0.031
49	E9	0.85±0.47
50	E10	14.95±3.600
51	E11	0.07±0.030
52	E12	0.06±0.31
53	E13	0.16±0.80

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No.	Symbol	Uranium concentration (Bk/Kg)
54	E14	0.61±038
55	E15	0.06±0.31
56	E16	0.06±0.31
57	E17	0.61±038
58	E18	0.61±038
59	E19	1.15±0.50
60	E20	1.15±0.50
61	W1	0.51±0.10
62	W2	2.19±0.10
63	W3	0.54±0.20
64	W4	2.93±0.14
65	W5	0.04±0.20
66	W6	5.74±0.21
67	W7	8.56±1.80
68	W8	8.43±0.33
69	W9	0.85±0.10
70	W10	10.03±2.50
71	W11	2.29±0.60
72	W12	6.71±1.70
73	W13	18.01±4.40
74	W14	64.81±17.00
75	W15	64.81±17.00
76	W16	64.81±17.00
77	W17	39.26±9.60
78	W18	39.26±9.60
79	W19	39.26±0.64
80	W20	39.26±0.64
81	S1	66.81±2.00
82	S2	39.26±0.64
83	S3	64.81±17.00
84	S4	60.81±17.01
85	S5	60.81±17.01
86	S6	64.81±17.00
87	S7	66.81±2.00
88	S8	85.92±1.70
89	S9	85.92±1.70
90	S10	33.92±1.22
91	S11	33.92±0.22
92	S12	21.15±0.50
93	S13	21.15±0.50
94	S14	21.15±0.55
95	S15	21.20±0.55
96	S16	22.20±0.50
97	S17	32.90±0.33
98	S18	32.90±0.33
99	S19	32.90±0.30
100	S20	30.22±0.22

Histopathological study

The tissue samples taken from the cow's kidney were preserved in a 10% formaldehyde solution for fixation before being routinely processed with a histokine. Tissue slices were embedded in paraffin blocks, sectioned with a microtome, stained with hematoxylin and eosin, and examined under a light microscope to record the histological changes (Neamah *et al*., 2019).

RESULTS AND DISCUSSION

As shown in Figure 1, cow's kidney's gross appearance reveals a proliferative, cortical, yellow orange to tan, well-circumscribed tumor that extends above the kidney's capsule surface and resembles clear cell carcinoma.

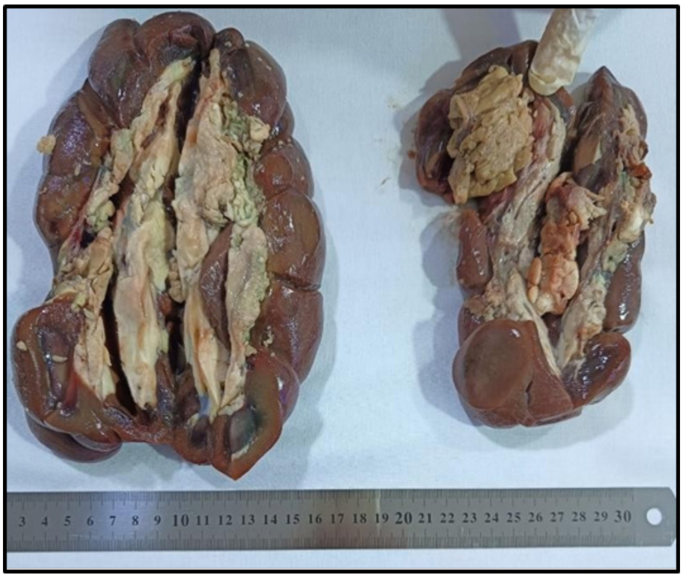

Figure 1: Clear cell carcinoma.

Tumor mode cells in renal cancer with clear cell appearance are transparent. Tiny blood arteries that supply the tumor with copious amounts of blood frequently divide the tumor cell clusters. Chromophobe renal cell carcinoma is the opposite pathological disorder. It is a solid tumor of pale, granular cells with noticeable borders. Lastly, reticular cytoplasm perinuclear halos and wrinkled hyperchromatic nuclei are also observed in renal cell cancer sarcomatoid, which exhibits cellular atypia and a loss of typical epithelial higcellularity.

Numerous short- and long-term studies have demonstrated the toxicity of uranium to both people and animals (Mahdi *et al*., 2018). It is widely acknowledged that the kidney is the primary organ at risk for damage from heavy metal poisoning, with the proximal convoluted tubules bearing most of the damage. Our goal is to ascertain whether uranium-induced kidney damage progresses in terms of histopathology research. In the kidney of a cow with decreased uranium content, we saw vacuolation of the renal tubules, lobulated glomeruli infiltrations with intestinal fibrosis, and inflammatory cell infiltrations (Figure 2) compared to the histological chacteristics of the control (Figure 1).

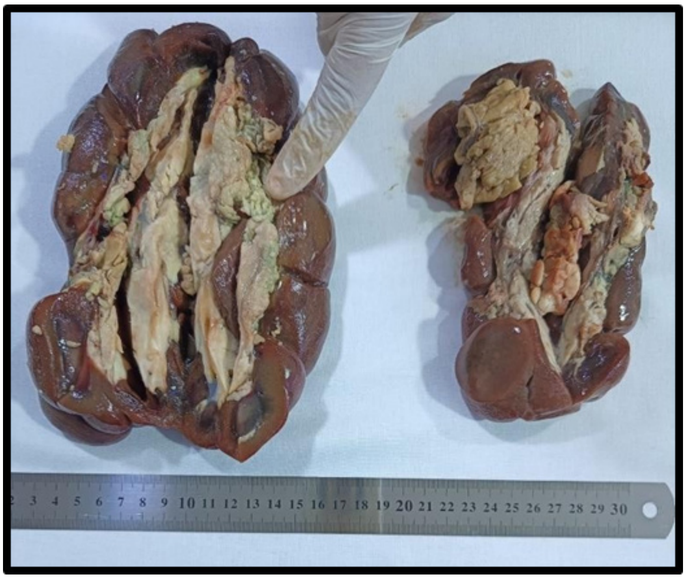

Figure 2: Sarcomatoied renal cell carcinoma.

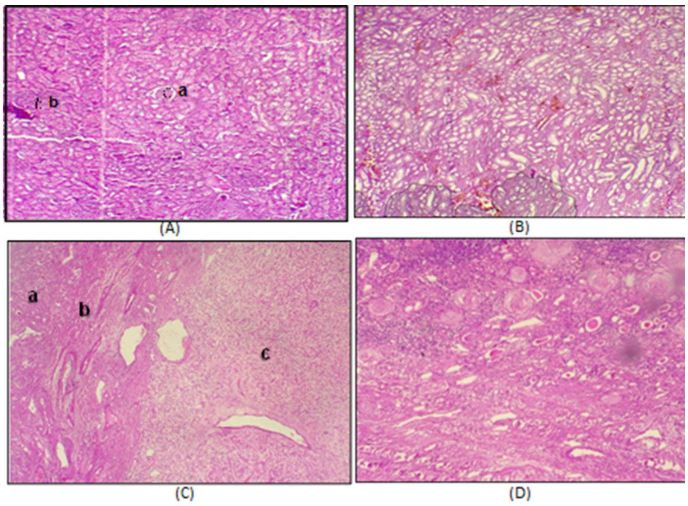

Figure 3: A: Normal Kidney tissue (a) glomerulus (b) renal tubules 4X, B: Nephritis of Kidney with inflammatory cell aggregation in low concentration of uranium 4X. C: (a) Normal kidney tissue. (b) area of fibrosis. (c) renal cell carcinoma 4X, D: Abnormal kidney with sclerosis of glomeruli renal tubules atrophy with collection of protein material in renal tubules in low concentration of uranium 4X.

Lesions showed signs of severe fibrosis and renal capsule invasion by mononuclear cells at higher concentrations. Many forms of renal cell cancers were discovered in areas with elevated uranium contents. The tumor in clear renal cell carcinoma comprises giant, spherical cells that join together to form enormous cell clusters. Many tumor cells had distinct cytoplasms or cell bodies, and the clusters of cells were frequently divided by microscopic blood veins that supplied the tumor with copious amounts of blood (Figure 3A). A solid tumor of granular pale cells with pronounced halos and wrinkled hyperchromatic nuclei was identified as chromophobe renal cell carcinoma. Sarcoma toid renal cell carcinoma also exhibited spindle cells, high cellularity, cellular atypia, and the absence of typical epithelial components.

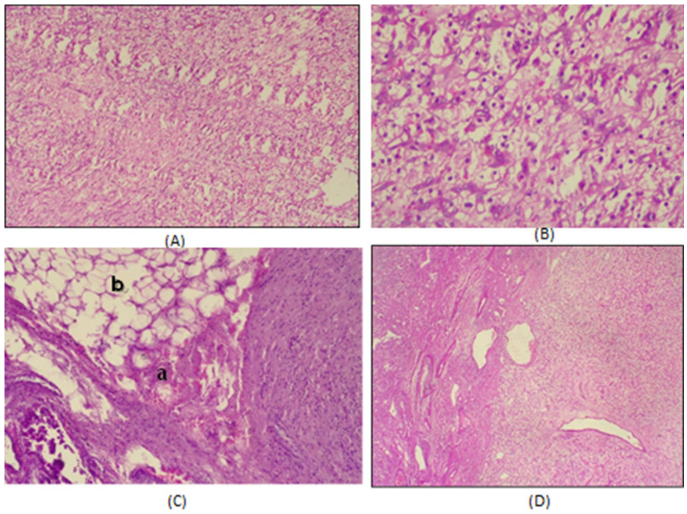

Figure 4: A: Clear cell carcinoma in kidney in high concentration of uranium 4X. B: renal cell carcinoma (a) clear cell cytoplasm with minimal pleomorphism (not high grade with thin (b) fibrovascular stroma and (c)infiltration of inflammatory cells in high concentration of uranium 40X. C: Fatty tissue invaded by renal cell carcinoma (a) tumor cell (b) fatty cell 4X. D: Renal cell carcinoma with sarcomatoied component (differentiation cell int connective tissue tumor sarcoma like) 4X.

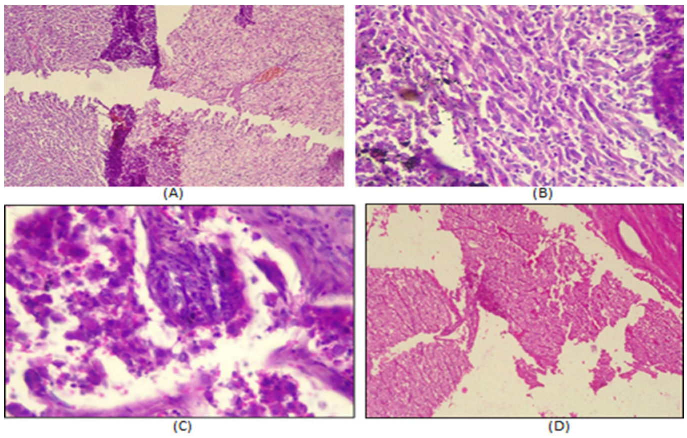

Figure 5: A: (a) clear cell carcinoma. (b) sarcomatoied carcinoma. B: Sarcomatoied renal cell carcinoma with (a) spindle cell with (b)hyperchromatic nuclei 10X. C: Sarcomatoied renal cell carcinoma with spindle cell with hyperchromatic nuclei 40X. D: Clear cell carcinoma of kidney in high concentration of uranium 4X.

Our research showed that uranium caused significant pathological alterations in cows kidneys. According to the research, exposure to uranium mainly affects the kidneys, bones, liver, lung, and central nervous system; nevertheless, the leading cause of death is renal insufficiency (Rozell *et al*., 2009; Al-Awadi and Alwan, 2014; Cheng *et al*., 2010). Following uranium injection, inhalation, or ingestion, inflammation is characterized as a harmful mechanism (Monleau *et al*., 2006; Weam *et al*., 2013; Orona and Tasat, 2012); nevertheless, there are few papers discussing its role in uranium nephrotoxicity (Zheng *et al*., 2015; I *et al*., 2018; Taulan *et al*., 2006). Despite the significant role, the inflammatory processes play a role in kidney injury (Ferenbach and Bonventre, 2015).

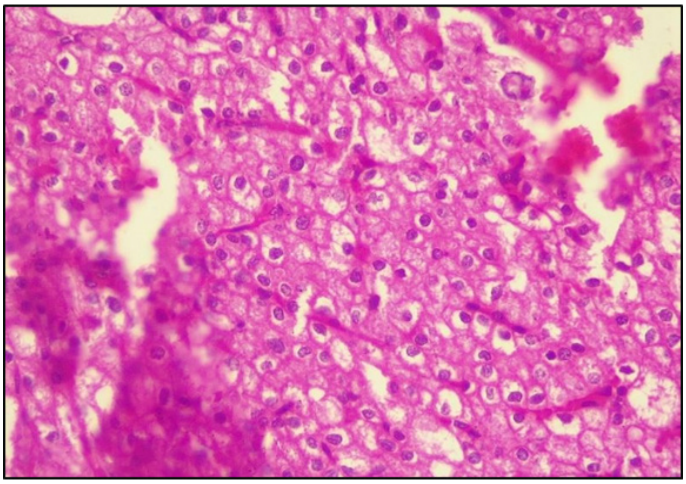

Figure 6: Clear cell carcinoma of kidney in high concentration of uranium 40X.

NF and KB activation was shown to elicit an inflammatory response in acutely exposed rats, and the transcriptome investigation (Taulan *et al*., 2006) observed the upregulation of three inflammatory genes, including osteopontin (opn), Pecam, and Gal-3, in mouse kidneys exposed to uranium. The inflammatory increase of intracellular and vascular cell adhesion molecules (ICAM) and VCAM generated by uranium (Bontemps *et al*., 2019) facilitates the recruitment of inflammatory cells to the kidney. The organ most vulnerable to uranium poisoning is the kidney, and it is widely known that uranium damages and malfunctions this organ, leading to either acute or chronic renal illness (UNSCEAR, 2016). Chronic oxidative stress, inflammation, DNA damage, and cell death are the leading causes of uranium-induced renal impairment (Guéguen *et al*., 2017; Haley *et al*., 1982; Diamond *et al*., 1989; Nada *et al*., 2011). Elevated urine glucose, protein, and electrolyte excretion indicate renal impairment (calcium, magnesium, sodium, potassium, and inorganic phosphate). Most likely due to decreased reabsorption from the proximal tubules or changed renal cell transport properties (Banday *et al*., 2008; Bontemps *et al*., 2019; Sánchez *et al*., 2001; Cappello and Macario, 2019).

Based on the exposure route and the molecule's solubility, uranium has been classified as carcinogenic in several experimental investigations. One description of carcinogenesis is as a step event (Asic *et al*., 2017). The first step involves the direct and indirect mutation of kidney cells' DNA (Yellowhair *et al*., 2018; Yazzie *et al*., 2003; Hamilton *et al*., 1997; Periyakaruppan *et al*., 2006; Wise *et al*., 2007), which turns them from healthy cells into possibly cancerous ones. After uranium exposure, DDR processes are presumably compromised, leading to an accumulation of nuclear DNA modification that facilitates their proliferation (Holmes *et al*., 2014; Saad *et al*., 2016; Adawiya *et al*., 2021).

CONCLUSIONS AND RECOMMENDATIONS

The effect of uranium present in the content of herbs fed to cows in different areas of the city of Basra was studied, and the health and tissue effects on the kidneys of cows fed on these herbs were studied. Uranium levels were measured using a sodium iodide device, and samples were taken from the cows' kidneys, as they are the organ most affected by uranium. If low concentrations of uranium are taken, there are cases of tissue inflammation, but in high doses they lead to the occurrence of various tumors in the kidneys. The study's findings suggest that uranium levels in herbs cause cows' antioxidant defense systems to weaken and increase oxidative stress in their kidneys.

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NOVELTY STATEMENT

Samples were taken from different locations using the latest methods and modern devices. The work was done in laboratories that have modern devices and technologies and keep pace with the modern era in analyzing site samples in the laboratory.

AUTHOR'S CONTRIBUTION

The authors of the manuscript collected the data, reviewed it, studied the biostatistical analysis, and wrote the manuscript. The authors also declare that they have approved the manuscript and approved its content.

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Data and materials

The respective authors will provide the datasets used in this study upon request.

Declarations

The College of Veterinary Medicine Clinic's Ethical Committee permitted the study to proceed in Basra City. The authors declare no competing interests.

Conflict of interest

The authors have declared no conflict of interest.

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