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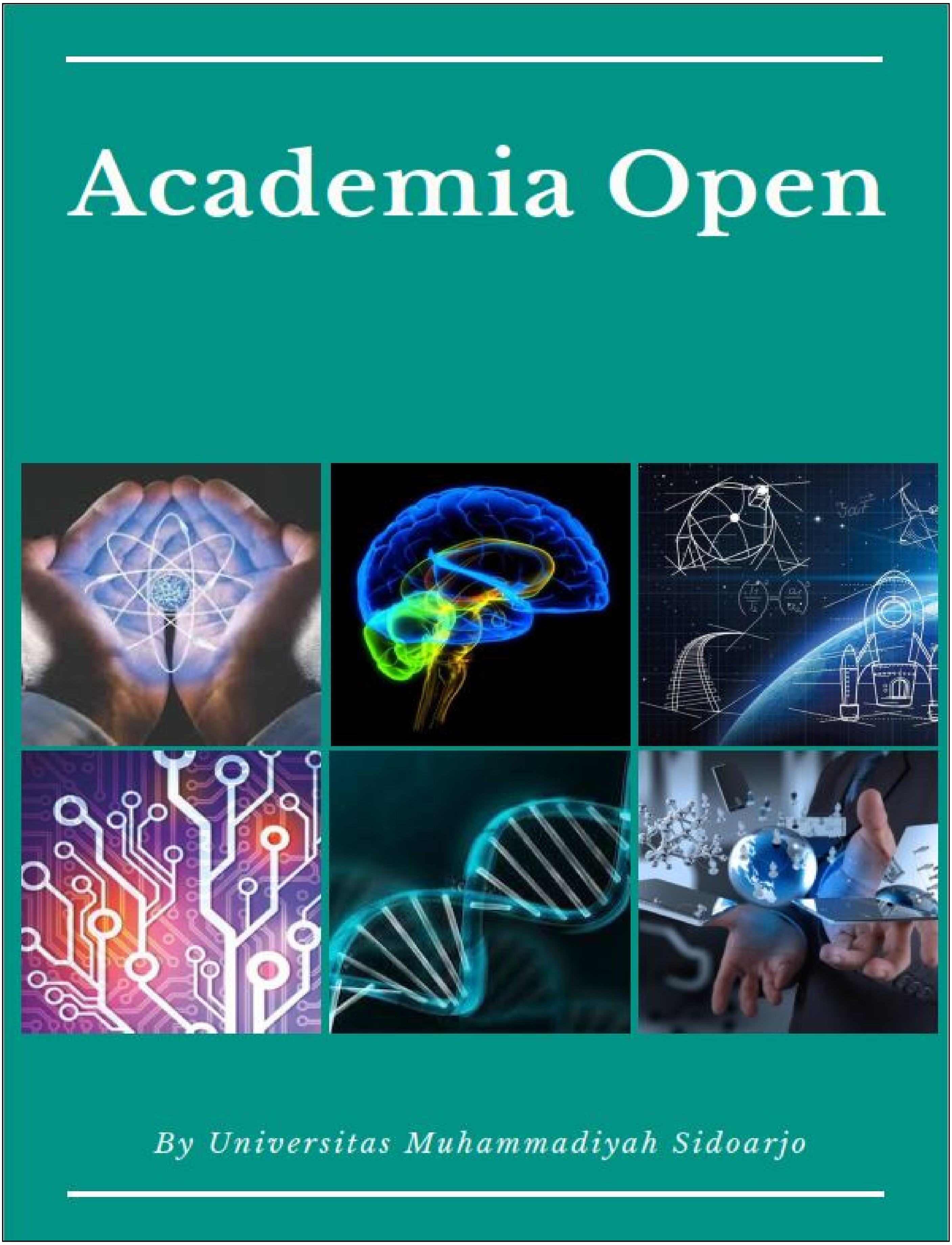

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Elevated Cadmium Drives Calcium Deficiency in Renal Failure Patients

Peningkatan Kadmium Menyebabkan Kekurangan Kalsium pada Pasien Gagal Ginjal

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Abstract

Background: Renal failure (RF) is a significant health issue with various etiological factors, including environmental toxins. **Specific Background:** Cadmium (Cd), a known toxic heavy metal, has been implicated in renal damage, while calcium (Ca) levels may also be affected. **Knowledge Gap:** The relationship between Cadmium and Calcium levels in RF patients, despite the well-established link between heavy metals and renal impairment, remains underexplored. **Aims:** This study aimed to evaluate changes in blood serum Cd and Ca levels in RF patients and investigate their correlation. **Methods:** The study, conducted in Iraq from July 2023 to February 2024, involved 150 participants, including 100 RF patients and 50 healthy controls, and used Flame Atomic Absorption Spectroscopy for analysis. **Results:** The mean Cd level was significantly higher in RF patients (2.30 µg/L) compared to controls (1.44 µg/L, $P < 0.05$). Conversely, the mean Ca level in RF patients was significantly lower (36.06 mg/dL) compared to controls (51.85 mg/dL, $P < 0.05$). A significant negative correlation between Cd and Ca levels was found ($P \leq 0.001$). **Novelty:** This study provides novel insights into the detrimental impact of elevated Cd levels on Ca status in RF patients. **Implications:** The study underscores the necessity of controlling Cd exposure and Ca levels in renal function (RF) management to mitigate its environmental impact on renal health.

Highlights:

1. Higher Cd Levels: Increased cadmium in RF patients.
2. Lower Ca Levels: Decreased calcium in RF patients.
3. Negative Correlation: Cadmium inversely affects calcium levels.

Keywords: Cadmium, Calcium, Renal Failure, Heavy Metals, Blood Serum

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Introduction

Heavy elements originate from industrial development, natural rock emissions, and the excessive use of chemical substances in human life. We cannot overlook the pollution caused by various automotive wastes [1]. These sources, combined with other processes that bring various benefits to humanity, can produce significant health dangers and environmental imbalances [2], [3]. Heavy metals may cause renal damage [4]; some studies suggest a direct relation between continuous heavy metal exposure and the worsening of renal failure disease [5].

Heavy metals are a group of elements whose levels are poorly defined in the human body. Some heavy metals, such as calcium and manganese, are necessary for the human body as they are essential for growth. In contrast, other elements like arsenic and lead are poisonous to the human body even at low levels [6].

Cadmium is a toxic heavy element that adversely affects the environment. Sources of environmental pollution include mining, metallurgical industries, plastic stabilizers, pigments, and nickel–cadmium batteries [7]. Significant sources of human intoxication are contaminated water, food, air, and cigarette smoke [8]. Cadmium poses an increasing threat to human health in many parts of the world due to continuous exposure [9]. Theoretically, cadmium can affect glucose metabolism by acting on various organs such as the adrenal glands, liver, and pancreas. Additionally, it may cause kidney damage, reproductive problems, and skeletal dysfunctions [10].

Calcium is one of the most many elements in the human body. It is an essential element obtained through dietary sources. Calcium is crucial for maintaining the human skeleton and teeth and assists in the functioning of nerves and muscles [11]. The requirement for calcium depends on the state of metabolism, and it is regulated by three primary mechanisms: bone turnover, renal absorption, and intestinal reabsorption [12].

Methods

The research was conducted in Babil Governorate. Blood samples were collected through venipuncture and placed in jet tubes, which were labeled with numbers assigned to the study participants to measure Cd and Ca levels. Initial approvals for the study protocol were obtained from volunteers who participated in the study. The questionnaire included data on medical history and exposure to sources of toxic elements such as smoking. The study was conducted between April 20, 2023, and March 25, 2024.

A total of 150 blood serum samples were collected, divided into two groups: 100 samples from RF patients and 50 samples from the control group (healthy individuals). The Flame Atomic Absorption Spectroscope (FAAS) was used to determine the levels of heavy elements in the blood samples of the participants [13]. Laboratory tests involved collecting blood in gel tubes without anticoagulants, followed by centrifugation at 3000 rpm for 20 minutes to separate the serum [14]. Twenty milliliters of the sample were injected into the electric oven, and the absorbance was measured and converted into concentrations [15]. The device automatically drew the parameters curve and extracted the slope equation.

Statistical Analysis

The data were analyzed using SPSS to examine the participants. The statistical difference between the measured elements in RF patients and the control group was determined by an independent sample t-test. Results were expressed as mean ± standard error, and $P < 0.05$ was considered statistically significant. The relationship between Cd and Ca concentrations in the RF group was determined by the Spearman correlation test. Results were expressed as R=0 (no association), R=1 (perfect positive correlation), or R=-1 (perfect negative correlation). The closer the value to 0, the weaker the correlation between the two groups.

Result and Discussion

A total number of 150 individual participated in this study, it is consisting of 70 males and 80 females, their age between 10 and 60 years old. Blood serum samples were obtained from 100 RF patients, and the control group included 50 healthy individuals. The general characteristics of serum heavy elements levels in patients and the control group are shown in Table 1.

Statistical Value	Cd Concentrations (ppb)		Ca Concentrations ×106 (ppb)	
	Patient Group	Control group	Patient Group	Control group
No. of Samples	100	50	100	50
Minimum	1.074	0.581	8.551	17.651
Maximum	6.671	2.736	56.360	93.653
Mean± Std. Error	2.30±0.261	1.44±0.105	36.06±11.230	51.85±17.498

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P- Value	0.010	0.000
Pearson correlation test	R= -0.026 with (p=0.856)	

Table 1. *Statistical Description of Cd and Ca Levels (ppb) in Serum Samples of the Study Groups*

Table 1 shows the minimum values of Cd and Ca levels in the RF group were (1.074 ppb) and (8.551 ppb), respectively. The maximum values of Cd and Ca levels in the RF group were (6.671 ppb) and (56360 ppb), respectively. Moreover, the mean values of Cd and Ca in the blood serum of RF patients were (2.30ppb) and (36.06), respectively.

Cd and Ca levels were different between RF patients and the control group ($p < 0.05$). Cd levels in RF patients were higher than control group significantly, while Ca levels in RF patients were lower than to the control group significantly.

The figure (1) shows that RF patients had higher Cd levels by about 0.61 compared to the control group, while RF patients had lower Ca levels by about 0.59 compared to the control group.

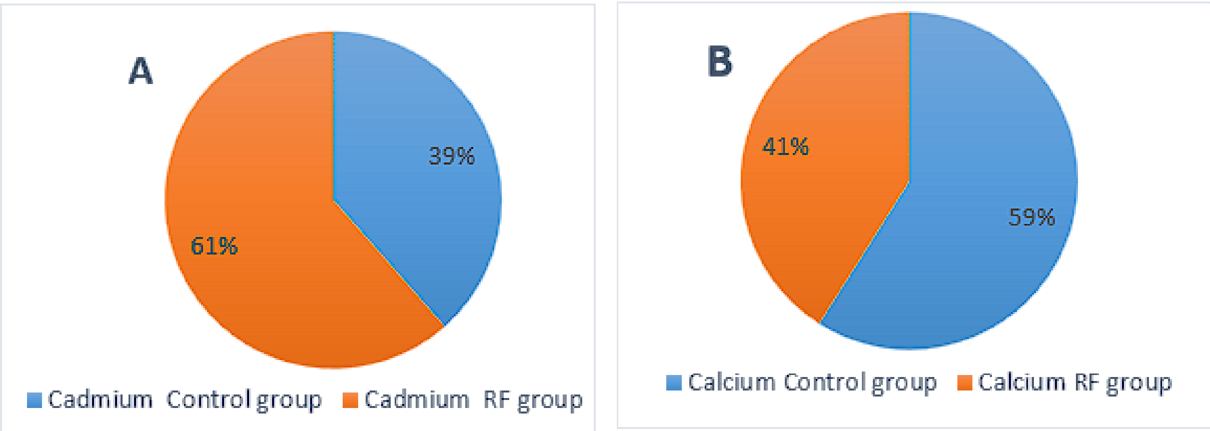

Figure 1. *Relation between (A) Cd and (B) Ca Levels in RF Group and Control Group*

As shown in Table 1, the relationship between Cd and Ca levels is inverse, where an increase in Cd levels corresponds to a decrease in Ca levels, indicating a negative relationship ($p < 0.05$).

The results show that continuous exposure to unintentional environmental levels of Cd is a significant cause of RF. Cd appears to be a determinant for the decrease in Ca levels, providing new evidence of the decrease in Ca levels with an increase in Cd levels in RF patients.

The relationship between Cd and Ca levels in blood serum in RF patients supports results from other studies, which have shown an effect on Ca excretion and renal function at high levels of Cd [16], [17]. Other studies have shown increased fractional secretion of Ca with rising Cd exposure, particularly in female [18]. Moreover, other studies have shown an increased prevalence of osteoporosis in Cd-exposed populations because Cd disturbs bone metabolism [19]. Our results present evidence for the effect of Cd on decreasing Ca levels, thus increasing the risk of RF and osteoporosis.

Tables 2 and 3 show the classification of RF patient samples according to age and smoking habits. The statistical differences between the measured elements for the RF patients were found using the One-Way ANOVA test.

Age (years)	Cd level (ppb)			Ca level (ppb)		
	Mean value± Std. Error	Min.	Max.	Mean value± Std. Error	Min.	Max.
(10-20)	0.79±0.076	0.58	0.99	50.90±1.51	47.97	56.36
(21-30)	1.20±0.035	1.12	1.31	43.15±0.834	41.01	45.63
(31-40)	1.46±0.046	1.34	1.59	37.27±1.44	33.38	40.58
(41-50)	1.81±0.035	1.74	1.94	28.60±1.51	25.55	32.38
(51-60)	3.56±0.781	2.28	6.42	20.41±0.946	17.65	22.52
P-value	0.001			0.001		

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Table 2. *Statistical Description of Cd and Ca Levels (ppb) by Age (years)*

There was a significant association ($p < 0.05$) between age and Cd and Ca levels in all participants. The level of Cd in the blood serum of RF patients significantly increased with age, while the level of Ca significantly decreased with age. Because cadmium like zinc in the periodic table, it can be replacing zinc, calcium and magnesium. It is depending on coordination chemistry, at many sites an ionic radius similar to Ca^{2+} allows for calcium replacement. Thus cadmium inside the cell is generally bound more strongly than calcium [20].

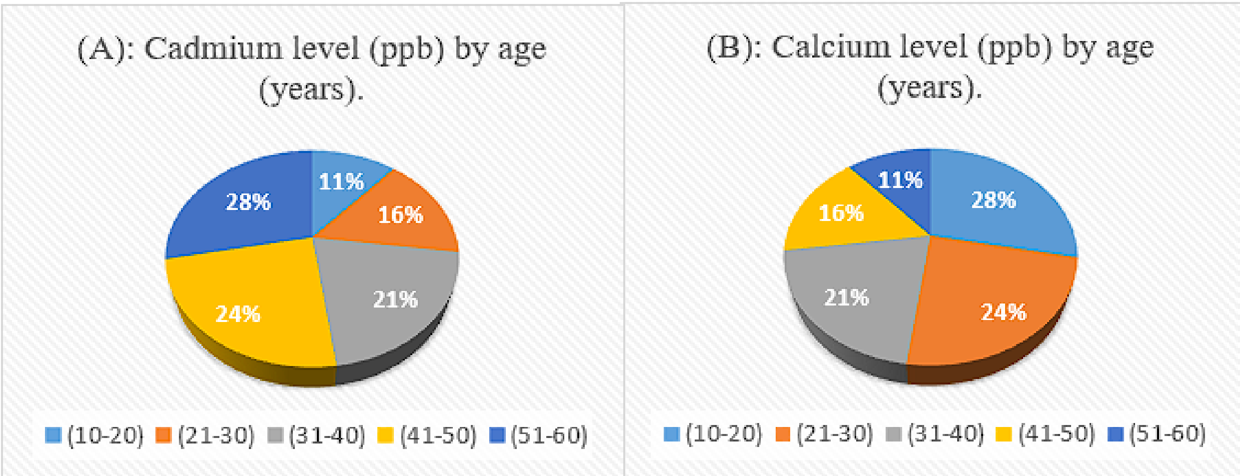

Figure 2. *Relation between (A) Cd and (B) Ca Levels in RF by Age*

The figure (2) shows that the Cd level in RF patients was about 0.11 ppb for those aged 10-20 years and then increased to the highest value of about 0.28 ppb for those aged 51-60 years. In contrast, the Ca level was about 0.28 ppb for those aged 10-20 years and then decreased to the lowest value of about 0.11 ppb for those aged 51-60 years.

Regarding smoking habits and their effect on RF, according to the period of smoking as the following (5-10), (11-15) and (16-20).

Smoking (years)	Ca level (ppb)			Cd level (ppb)		
	Mean value± Std. Error	Min.	Max.	Mean value± Std. Error	Min.	Max.
(5-10)	0.96±0.079	0.58	1.25	0.89±0.081	0.581	1.143
(11-15)	1.57±0.061	1.31	1.79	1.51±0.064	1.180	1.798
(16-20)	3.29±0.692	1.94	6.42	3.29±0.692	1.949	6.427
P-value	0.000			0.000		

Table 3. *Statistical Description of Cd and Ca Levels (ppb) According to Smoking Duration (Years)*

Smoking-related level of Cd and Ca levels vary by period of smoking in RF patients. The results showed that the Cd levels in smokers were significantly higher than those in non-smokers, while the Ca levels in smokers were significantly lower than those in non-smokers. Our findings provide evidence that one of the most important causes of increased Cd levels in RF patients is increased smoking habits with age, which greatly affects the decrease in Ca levels.

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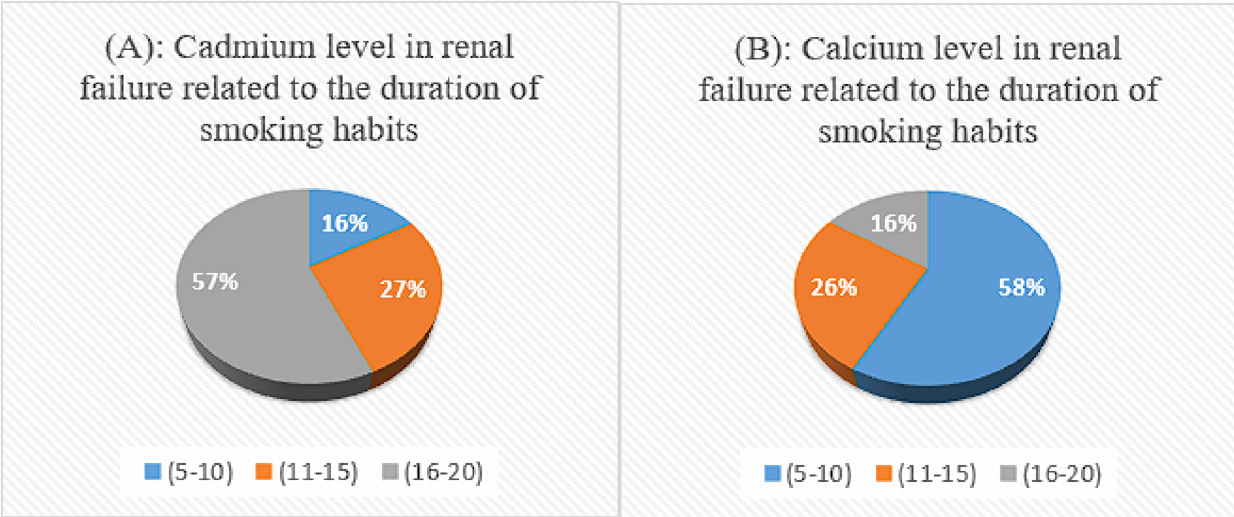

Figure 3. *Relation between (A) Cd and (B) Ca Levels in RF According to Smoking Duration (Years)*

The figure above shows that the Cd levels in RF patients were about 0.16 ppb for the (5-10) group of smokers and then increased to the highest value of about 0.57 ppb for the (16-20) group of smokers. In contrast, the Ca levels were about 0.58 ppb for the (5-10) years old group and then began to decrease, reaching the lowest value of about 0.16 ppb for the (51-60) group of smokers.

Conclusion

In conclusion, our study indicates that exposure to unintentional environmental levels of Cd can exacerbate RF. Moreover, Cd is a fundamental factor in the decrease of Ca levels. This study is significant as it provides new evidence that Cd can cause renal damage after high-level exposure. Health hazards from unintentional Cd exposure can be mitigated through the management and reduction of Cd emissions, as well as by monitoring blood serum Ca levels in all patients with RF.

References

1. . H. Srivastava, P. Saini, A. Singh, and S. Yadav, "Heavy Metal Pollution and Biosorption," in Biosorption Processes for Heavy Metal Removal, IGI Global, 2024, pp. 1-38.
2. . D.-M. Asiminicesei, D. I. Fertu, and M. Gavrilescu, "Impact of Heavy Metal Pollution in the Environment on the Metabolic Profile of Medicinal Plants and Their Therapeutic Potential," Plants, vol. 13, no. 6, p. 913, 2024.
3. . P. Saini, Biosorption Processes for Heavy Metal Removal, IGI Global, 2024.
4. . H. S. Budi et al., "Source, Toxicity, and Carcinogenic Health Risk Assessment of Heavy Metals," Reviews on Environmental Health, vol. 39, no. 1, pp. 77-90, 2024.
5. . Y. Zhang et al., "Exposure to Cadmium and Lead Is Associated with Diabetic Kidney Disease in Diabetic Patients," Environmental Health, vol. 23, no. 1, p. 1, 2024.
6. . G. I. Edo et al., "Environmental Persistence, Bioaccumulation, and Ecotoxicology of Heavy Metals," Chemistry and Ecology, vol. 40, no. 1, pp. 1-28, 2024.
7. . A. Ritambhara, S. Lamba, Deepika, and R. Prakash, "Cadmium in Environment—An Overview," in Cadmium Toxicity in Water: Challenges and Solutions, IGI Global, 2024, pp. 3-20.
8. . A. H. Jagaba et al., "Sources of Water Contamination by Heavy Metals," in Membrane Technologies for Heavy Metal Removal from Water, CRC Press, 2024, pp. 3-27.
9. . H. Zhu et al., "Assessment of Human Exposure to Cadmium and Its Nephrotoxicity in the Chinese Population," Science of The Total Environment, vol. 170488, 2024.
10. . M. Alemany, "The Metabolic Syndrome, a Human Disease," International Journal of Molecular Sciences, vol. 25, no. 4, p. 2251, 2024.
11. . P. Gupta and S. Badami, "Multiple Roles of Calcium in Maintaining Human Health," Clinical Endocrinology and Metabolism, vol. 3, no. 1, 2024.
12. . A. Staruschenko, R. T. Alexander, M. J. Caplan, and D. V. Ilatovskaya, "Calcium Signalling and Transport in the Kidney," Nature Reviews Nephrology, vol. 20, no. 1, pp. 1-15, 2024.
13. . F. Tamirat, W. D. Adane, M. Tessema, E. Tesfaye, and G. Tesfaye, "Determination of Major and Trace Metals in Date Palm Fruit (Phoenix dactylifera) Samples Using Flame Atomic Absorption Spectrometry and

Assessment of the Associated Public Health Risks," International Journal of Analytical Chemistry, vol. 2024, no. 1, p. 9914300, 2024.
14. . K.-N. Zhao et al., "Generation of Rapid and High-Quality Serum by Recombinant Prothrombin Activator Ecarin (RAPClot™)," Biomolecules, vol. 14, no. 6, p. 645, 2024.
15. . K. Debruille et al., "Portable IC System Enabled with Dual LED-Based Absorbance Detectors and 3D-Printed Post-Column Heated Micro-Reactor for the Simultaneous Determination of Ammonium, Nitrite, and Nitrate," Analytica Chimica Acta, vol. 1304, p. 342556, 2024.
16. . S. Satarug, "Is Chronic Kidney Disease Due to Cadmium Exposure Inevitable and Can It Be Reversed?," Biomedicines, vol. 12, no. 4, p. 718, 2024.
17. . S. M. Lang and H. Schiffl, "Smoking Status, Cadmium, and Chronic Kidney Disease," Renal Replacement Therapy, vol. 10, no. 1, p. 17, 2024.
18. . J. Song et al., "Predictors of Urinary Heavy Metal Concentrations Among Pregnant Women in Jinan, China," Journal of Trace Elements in Medicine and Biology, vol. 84, p. 127444, 2024.
19. . A. Cirovic, A. Cirovic, S. Yimthiang, D. A. Vesey, and S. Satarug, "Modulation of Adverse Health Effects of Environmental Cadmium Exposure by Zinc and Its Transporters," Biomolecules, vol. 14, no. 6, p. 650, 2024.
20. . G. F. Nordberg, A. Bernard, G. L. Diamond, J. H. Duffus, P. Illing, M. Nordberg, I. A. Bergdahl, T. Jin, and S. Skerfving, "Risk Assessment of Effects of Cadmium on Human Health (IUPAC Technical Report)," Pure and Applied Chemistry, vol. 90, no. 4, pp. 755-808, 2018.

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