



Association Between Heavy Metals and Type 2 Diabetes Mellitus

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ABSTRACT

Type 2 diabetes mellitus (T2DM) is a multifactorial metabolic disorder influenced by environmental and physiological factors, including exposure to toxic heavy metals. This study aimed to evaluate the association between blood levels of lead (Pb), cadmium (Cd), and copper (Cu) and T2DM, as well as their relationship with kidney function parameters. A case-control study was conducted on 118 participants, including 92 patients with T2DM and 26 healthy controls. Blood concentrations of Pb, Cd, and Cu were measured using flame atomic absorption spectrometry (FAAS), along with urea and creatinine levels. Statistical analysis was performed using independent samples t-test and Pearson correlation coefficient. The results showed significantly higher levels of Pb and Cd in T2DM patients compared to controls ($p < 0.001$), while Cu levels were significantly higher in controls ($p < 0.05$). Urea and creatinine levels were elevated in the diabetic group, indicating impaired renal function. Significant positive correlations were observed between heavy metal levels and biochemical parameters. In conclusion, elevated levels of Pb and Cd are associated with T2DM and may contribute to renal dysfunction. Monitoring heavy metal exposure may be useful for early detection and management of diabetes-related complications.

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1. INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from insulin resistance and impaired insulin secretion. It represents a major global health concern due to its increasing prevalence and association with serious complications such as cardiovascular diseases, neuropathy, and kidney dysfunction [1], [2]. The rising incidence of T2DM has been linked to multiple factors, including lifestyle changes, obesity, genetic predisposition, and environmental influences [3].

In recent years, increasing attention has been given to environmental pollutants, particularly heavy metals, due to their potential role in metabolic disorders. Heavy metals such as lead (Pb), cadmium (Cd), and copper (Cu) are widely distributed in the environment and can enter the human body through food, water, and air [4], [5]. These metals can accumulate in biological systems and induce oxidative stress, disrupt enzymatic functions, and interfere with glucose metabolism [6], [7].

Several studies have reported a possible association between heavy metal exposure and the development of T2DM. Elevated levels of Pb and Cd have been observed in individuals with diabetes compared to healthy controls, suggesting their contribution to insulin resistance and β -cell dysfunction [8], [9]. Moreover, exposure to multiple metals has been linked to an increased risk of diabetes and metabolic disturbances [10], [11]. Although copper is an essential trace element, abnormal levels have been associated with oxidative damage and poor glycemic control in diabetic patients [12], [13].

Despite these findings, the relationship between heavy metal exposure and T2DM remains not fully understood, particularly in regions with varying environmental conditions. Therefore, further investigation is required to clarify this association and its implications for public health.

Therefore, this study aims to evaluate the levels of selected heavy metals (Pb, Cd, and Cu) in patients with T2DM compared to healthy individuals, and to investigate their relationship with fasting blood glucose and kidney function parameters. It is hypothesized that elevated levels of heavy metals (Pb, Cd, and Cu) are significantly associated with alterations in fasting blood glucose and kidney function parameters in patients with type 2 diabetes mellitus.

2. METHODS

This study was designed as a case-control study conducted to evaluate the levels of selected heavy metals in patients with type 2 diabetes mellitus (T2DM) compared to healthy individuals. A total of 118 participants were included in this study, consisting of 92 patients diagnosed with T2DM and 26 healthy controls. The samples were collected from the National Center for Diabetes Treatment and Research.

The remaining blood samples were collected in acid-washed tubes prepared with diluted nitric acid and rinsed with deionized water to avoid contamination [14]. Samples were stored at -20°C until analysis. Blood concentrations of lead (Pb), cadmium (Cd), and copper (Cu) were determined using flame atomic absorption spectrometry (FAAS) (Analytik Jena, Germany). The method is based on the absorption of light by free metallic atoms in the gaseous state, where the absorbance is directly proportional to the concentration of the element in the sample.

The instrument was operated under optimized conditions according to the manufacturer's instructions. Specific wavelengths were selected for each element (Pb: 217.0 nm, Cd: 228.8 nm, Cu: 324.8 nm). Calibration curves were constructed using standard solutions of known concentrations. All measurements were performed in triplicate to ensure accuracy. Blanks and quality control samples were included to minimize contamination and ensure the reliability of the results.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 22.0 (IBM Corp., USA) and Microsoft Excel 2010. Continuous variables were expressed as mean $\pm$ standard deviation (SD). Data were tested for normality using the Shapiro–Wilk test prior to analysis. Differences between groups were assessed using the independent samples t-test. Pearson correlation coefficient was used to evaluate the relationships between heavy metal concentrations (Pb, Cd, and Cu) and biochemical parameters (fasting blood glucose, urea, and creatinine). A p-value of less than 0.05 was considered statistically significant.

3. RESULTS & DISCUSSION

3.1 Comparison Between Male Patients and Controls.

As shown in Table 1, a comparison was made between male patients with type 2 diabetes mellitus (T2DM) and healthy controls in terms of fasting blood glucose, age, body weight, and blood levels of lead (Pb), cadmium (Cd), and copper (Cu).

Fasting blood glucose levels were significantly higher in T2DM patients compared to controls (226.45 ± 98.91 vs. 99.40 ± 4.60 mg/dL, $p < 0.05$), indicating poor glycemic control among diabetic patients. In addition, both mean age and body weight were significantly higher in the patient group compared to controls ($p < 0.05$), suggesting that increasing age and higher body weight are associated with an increased risk of T2DM [2],[3],[15].

Regarding heavy metals, blood levels of Pb, Cd, and Cu were significantly elevated in T2DM patients compared to healthy controls ($p < 0.05$). Pb levels were markedly higher in patients (569.99 ± 208.05 $\mu\text{g/L}$) compared to controls (378.20 ± 275.63 $\mu\text{g/L}$). Similarly, Cd and Cu levels were also significantly increased in the diabetic group.

These findings are consistent with previous studies that reported a significant association between heavy metal exposure and diabetes mellitus [9],[10],[16]. The elevated levels of Pb and Cd may contribute to oxidative stress and pancreatic β -cell dysfunction, leading to impaired insulin secretion [4], [17]. In addition, alterations in Cu levels may reflect disturbances in antioxidant defense mechanisms and metabolic regulation [12], [18]. Overall, these results support the hypothesis that heavy metal accumulation plays an important role in the development and progression of T2DM among male patients.

Table 1. Comparison of Clinical Parameters and Heavy Metal Levels between Male T2DM Patients and Healthy Controls.

Parameter	Groups	N	Mean ± SD
Fasting Sugar(mg/dL)	Patient	55	226.454±98.913 *
	Control	10	99.400±4.599
Age (years)	Patient	55	51.181±16.787 *
	Control	10	29.600±7.026
Weight(kg)	Patient	55	82.527±20.218 *
	Control	10	66.500±12.747
Pb(µg/l)	Patient	55	569.998±208.047*
	Control	10	378.196±275.626
Cd(µg/l)	Patient	55	5.264±1.536*
	Control	10	3.691±2.766
Cu(µg/l)	Patient	55	888.563±119.844*
	Control	10	573.127±63.960

*Indicates a significant difference at $p < 0.05$

3.2 Comparison Between Female Patients and Controls

As shown in Table 2, a comparison was made between female patients with type 2 diabetes mellitus (T2DM) and healthy controls in terms of fasting blood glucose, age, body weight, and blood levels of lead (Pb), cadmium (Cd), and copper (Cu). Fasting blood glucose levels were significantly higher in T2DM patients compared to controls (226.43 ± 92.66 vs. 94.69 ± 10.73 mg/dL, $p < 0.05$), indicating poor glycemic control among diabetic females. In addition, both age and body weight were significantly higher in the diabetic group compared to controls ($p < 0.05$), suggesting that increasing age and higher body weight are associated with an increased risk of T2DM [2],[3],[15].

Regarding heavy metals, Pb and Cd levels were significantly elevated in T2DM patients compared to controls ($p < 0.05$). Pb levels were markedly higher in patients (631.86 ± 142.57 µg/L) compared to controls (85.12 ± 12.53 µg/L). Similarly, Cd levels were increased in the diabetic group (5.29 ± 0.92 µg/L) compared to controls (1.55 ± 0.40 µg/L).

These findings are consistent with previous studies that reported a strong association between Pb and Cd exposure and diabetes mellitus [9],[10],[16]. The elevated levels of these metals may contribute to oxidative stress, pancreatic β -cell dysfunction, and impaired insulin activity [4], [17].

In contrast, Cu levels were significantly higher in the control group compared to T2DM patients ($p < 0.05$), although considerable variability was observed among control values. This variation may be attributed to the essential role of copper as a trace element involved in antioxidant defense mechanisms and metabolic regulation [12], [18], as well as possible environmental or dietary factors.

Overall, these results indicate that Pb and Cd accumulation is strongly associated with T2DM, whereas Cu levels may exhibit a different pattern depending on physiological and environmental conditions.

Table 2. Comparison of Clinical Parameters and Heavy Metal Levels between Female T2DM Patients and Healthy Controls.

Parameter	Groups	N	Mean ± SD
Fasting Sugar(mg/dL)	Patient	37	226.432±92.661 *
	Control	16	94.687±10.731
Age (years)	Patient	37	50.162±12.781 *
	Control	16	36.875±9.287
Weight(kg)	Patient	37	81.810±18.339 *
	Control	16	64.937±10.122
Pb(µg/l)	Patient	37	631.857±142.566 *
	Control	16	85.122±12.531
Cd(µg/l)	Patient	37	5.290±0.922 *
	Control	16	1.546±0.398
Cu(µg/l)	Patient	37	927.586±116.967 *
	Control	16	2220.551±5647.210

*Indicates a significant difference at $p < 0.05$

3.3 Comparison Between Female Patients Aged Over 30 Years and Controls

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As shown in Table 3, a comparison was made between female patients with type 2 diabetes mellitus (T2DM) aged over 30 years and healthy controls in terms of fasting blood glucose (FBG), age, body weight, kidney function parameters, and heavy metal levels.

Fasting blood glucose levels were significantly higher in T2DM patients compared to controls (213.87 ± 77.19 vs. 94.38 ± 10.25 mg/dL, $p < 0.05$), indicating poor glycemic control in the diabetic group. In addition, both age and body weight were significantly higher in T2DM patients compared to controls ($p < 0.05$), suggesting that aging and increased body weight are associated with the development and progression of T2DM [2],[3],[15].

Regarding kidney function, urea levels were significantly elevated in T2DM patients compared to controls ($p < 0.05$), suggesting impaired renal function. However, creatinine levels did not show a significant difference between the two groups, which may indicate that renal impairment is still at an early stage and may be more sensitively detected through urea levels [19].

Concerning heavy metals, Pb and Cd levels were significantly higher in T2DM patients compared to controls ($p < 0.05$). Pb levels were markedly elevated in patients (642.58 ± 142.83 µg/L) compared to controls (86.61 ± 12.28 µg/L), while Cd levels were also increased in the diabetic group (5.28 ± 0.89 µg/L) compared to controls (1.53 ± 0.42 µg/L).

These findings are consistent with previous studies that reported a strong association between Pb and Cd exposure and diabetes and its complications [9], [10],[16]. The elevated levels of these metals may contribute to oxidative stress, cellular damage, and impaired insulin function [4], [17].

In contrast, Cu levels were significantly higher in the control group compared to T2DM patients ($p < 0.05$), with considerable variability observed among control values. This variation may be attributed to the essential role of copper in antioxidant defense systems and metabolic regulation [12], [18], as well as environmental or dietary factors affecting its levels.

Overall, these results support the hypothesis that Pb and Cd accumulation is associated with T2DM and early renal impairment, whereas Cu levels may follow a different biological pattern depending on physiological and environmental factors.

Table 3. Comparison of Clinical Parameters, Kidney Function, and Heavy Metal Levels Between Female T2DM Patients and Healthy Controls Aged Over 30 Years

Parameter	Groups	N	Mean $\pm$ SD
Fasting Sugar(mg/dL)	Patient	33	213.870 $\pm$ 77.189*
	Control	13	94.381 $\pm$ 10.250
Age(years)	Patient	33	53.301 $\pm$ 9.305 *
	Control	13	39.612 $\pm$ 7.950
Weight(kg)	Patient	33	81.319 $\pm$ 14.811 *
	Control	13	65.693 $\pm$ 10.617
Urea(mg/dl)	Patient	33	27.361 $\pm$ 10.179*
	Control	13	21.92 $\pm$ 4.42
Creatinine(mg/dl)	Patient	33	0.66 $\pm$ 0.18
	Control	13	0.52 $\pm$ 0.10
Pb (µg/l)	Patient	33	642.584 $\pm$ 142.830 *
	Control	13	86.612 $\pm$ 12.279
Cd (µg/l)	Patient	33	5.2751 $\pm$ 0.89 *
	Control	13	1.533 $\pm$ 0.4245
Cu(µg/l)	Patient	33	928.617 $\pm$ 119.811 *
	Control	13	2535.031 $\pm$ 2422.004

*Indicates a significant difference at $p < 0.05$

3.4 Comparison Between Female Patients with Body Weight <70 kg

As shown in Table 4, a comparison was made between female patients with type 2 diabetes mellitus (T2DM) and healthy controls with body weight less than 70 kg in terms of fasting blood glucose (FBG), age, body weight, kidney function parameters, and heavy metal levels.

Fasting blood glucose levels were significantly higher in T2DM patients compared to controls (262.57 ± 149.43 vs. 93.55 ± 12.09 mg/dL, $p < 0.05$), indicating poor glycemic control in the diabetic group. In addition, age was significantly higher in T2DM patients compared to controls ($p < 0.05$), while body weight showed no

significant difference between the two groups, which is consistent with the weight-based classification of this subgroup [3],[15].

Regarding kidney function, urea levels were significantly elevated in T2DM patients compared to controls ($p < 0.05$), suggesting impaired renal function. However, creatinine levels did not show a significant difference between the two groups, indicating that renal impairment may still be at an early stage [15].

Concerning heavy metals, Pb and Cd levels were significantly higher in T2DM patients compared to controls ($p < 0.05$). Pb levels were markedly elevated in patients ($607.58 \pm 115.67 \mu\text{g/l}$) compared to controls ($88.96 \pm 11.99 \mu\text{g/l}$), while Cd levels were also increased in the diabetic group ($4.66 \pm 0.90 \mu\text{g/l}$) compared to controls ($1.53 \pm 0.25 \mu\text{g/l}$).

These findings are consistent with previous studies demonstrating the association between heavy metal exposure and metabolic dysfunction in T2DM [9],[10],[16]. The elevated levels of Pb and Cd may contribute to oxidative stress, cellular damage, and impaired insulin activity [4], [17].

In contrast, Cu levels were significantly higher in the control group compared to T2DM patients ($p < 0.05$). This pattern may be attributed to the essential role of copper in antioxidant defense mechanisms and metabolic regulation [12], [18], as well as environmental or dietary factors affecting its levels.

Overall, these findings are consistent with previous results, demonstrating elevated Pb and Cd levels in T2DM patients, whereas Cu exhibits a different biological pattern depending on physiological and environmental conditions.

Table 4. Comparison of Clinical Parameters, Kidney Function, and Heavy Metal Levels Between Female T2DM Patients and Healthy Controls with Body Weight <70 kg

Parameter	Groups	N	Mean $\pm$ SD
Fasting Sugar(mg/dL)	Patient	7	262.571 $\pm$ 149.428 *
	Control	11	93.5454 $\pm$ 12.086
Age(years)	Patient	7	52.714 $\pm$ 20.229 *
	Control	11	36.545 $\pm$ 8.948
Weight(kg)	Patient	7	61.285 $\pm$ 6.237 *
	Control	11	59.090 $\pm$ 5.04
urea(mg/dl)	Patient	7	31.28 $\pm$ 8.052 *
	Control	11	21.091 $\pm$ 4.903
Creatinine(mg/dl)	Patient	7	0.7 $\pm$ 0.2
	Control	11	0.48 $\pm$ 0.07
Pb ($\mu\text{g/l}$)	Patient	7	607.583 $\pm$ 115.670*
	Control	11	88.957 $\pm$ 11.992
Cd ($\mu\text{g/l}$)	Patient	7	4.656 $\pm$ 0.901 *
	Control	11	1.527 $\pm$ 0.2529
Cu($\mu\text{g/l}$)	Patient	7	951.924 $\pm$ 42.600 *
	Control	11	800.909 $\pm$ 121.198

*Indicates a significant difference at $p < 0.05$

Additionally, urea levels were generally elevated in T2DM patients, whereas creatinine levels did not show consistent significant differences between groups.

4. LIMITATIONS

This study has several limitations. The relatively small sample size may limit the generalizability of the findings. In addition, differences in age and body weight between patients and controls may act as potential confounding factors. The case-control design does not allow for establishing causal relationships between heavy metal exposure and T2DM. Future studies with larger sample sizes and multivariate analysis are recommended to confirm these findings.

5. CONCLUSION

The findings of the present study indicate that demographic factors, including gender, age, and body weight, are associated with variations in fasting blood glucose levels and the concentrations of selected heavy metals in the blood. Patients with type 2 diabetes mellitus (T2DM) exhibited significantly higher levels of lead (Pb) and cadmium (Cd) compared to healthy controls, suggesting a strong association between heavy metal exposure and metabolic disturbances.

A significant relationship was observed between the concentrations of Pb, Cd, and Cu and fasting blood glucose levels, indicating their possible role in the progression of T2DM and its related complications. In addition, the measured levels of these metals exceeded internationally recommended limits in most samples, highlighting potential health risks associated with chronic exposure.

These findings suggest that monitoring heavy metal levels may be useful for the early detection and management of diabetes-related complications. Further studies with larger sample sizes are recommended to confirm and better clarify these associations.

Publication Ethics

Ethical Approval

This study was conducted in accordance with accepted ethical research standards and the principles of human subject protection. Ethical and administrative approval was obtained from the National Diabetes Center (NDC), Baghdad Governorate, Approval Ref. No. 6122025NDC, prior to data and sample collection. No harmful, invasive, or experimental procedures were performed at any stage of the study.

Informed Consent

Verbal informed consent was obtained from all participants before blood sample collection. Participants were fully informed about the objectives of the study, the type of samples to be collected, and the confidentiality of their personal information. All collected data were used exclusively for scientific and research purposes.

Authors' Contributions

All authors contributed equally to the study design, sample collection, laboratory analyses, data interpretation, and manuscript preparation. All authors reviewed and approved the final version of the manuscript prior to submission.

Conflict of Interest

The authors declare that there are no conflicts of interest related to the publication of this research.

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Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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