International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 6s, 2025
https://www.theaspd.com/ijes.php

Evaluation of Cadmium and Calcium Levels in Blood Serum Samples of Beta-Thalassemia Patients

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Abstract
Weekly blood transfusions of beta-thalassemia patients lead to the accumulation of Iron; there are many studies about iron levels in blood beta-thalassemia patients, as well as other heavy metal levels. Few studies have examined the relationship between the a;mounts of heavy element Levels and β-thalassemia incidence. Therefore, the main goal of this study was to investigate the effect of Cadmium and Calcium Levels in beta-thalassemia patients and compare them with healthy control groups. The study involved 37 blood serum samples of Beta-thalassemia patients and 25 blood serum samples of the healthy control group. parameters included: sex, age, smoking status, and census. The blood Cadmium and Calcium levels were measured by flame atomic absorption spectrometry (FAAS). The results showed that the mean blood Cadmium level in beta-thalassemia patients is significantly higher than in the control group ($p<0.05$). Moreover, the mean blood Calcium level in beta-thalassemia patients is significantly lower than that of the control group. A statistically negative correlation between Cadmium and Calcium Levels was found in the beta-thalassemia patients ($r = -1.00$, $p<0.05$). This study revealed that Calcium deficiency is associated with higher blood Cadmium levels. In addition, there is no effect of age on Beta-Thalassemia, but there is a significant effect of smoking ($p<0.05$).The statistical comparison between the Cadmium and Calcium Levels of the patient and control groups was determined by the SPSS test with an Independent-Sample T-test. The Spearman correlation test was also used to determine the correlation between measured Cadmium and Calcium Levels for both groups.

Keyword*: Flame atomic absorption spectroscopy, Heavy elements, smoking habit, toxic metals and environmental.*

INTRODUCTION

Beta-thalassemia represents a significant genetic blood disorder characterized by impaired hemoglobin synthesis, resulting in chronic anemia that necessitates regular blood transfusions throughout the patient's life (Galanello & Origa, 2010). This condition disproportionately affects populations from Mediterranean, Middle Eastern, and Southeast Asian regions, presenting substantial health challenges related to transfusion-dependent complications. (Cao & Galanello, 2010) While iron overload due to frequent transfusions has been extensively researched, the relationship between beta-thalassemia and other trace elements remains insufficiently investigated despite their critical roles in physiological functions (Cappellini et al., 2014).

Cadmium (Cd) is a toxic heavy metal with no known beneficial biological role in humans. Environmental exposure occurs through contaminated food sources, industrial processes, and notably through tobacco smoke (Järup & Åkesson, 2009; Jarup, 2003). Once absorbed, cadmium has a remarkably long biological half-life of 10-30 years, accumulating primarily in the kidneys and liver (Bernard, 2008). Prolonged cadmium exposure has been linked to kidney dysfunction, bone demineralization, and increased cardiovascular disease risk (Järup et al., 1998). For thalassemia patients with already compromised hematological status, elevated cadmium levels may compound existing health complications (Marcon et al., 2018).In contrast, Calcium (Ca) is an essential mineral vital for numerous physiological processes, including bone formation, muscle contraction, nerve transmission, and blood coagulation (Del Valle et al., 2011). Calcium homeostasis is meticulously controlled by the coordinated functions of parathyroid hormone, vitamin D, and calcitonin (Peacock, 2010). Disruptions in calcium metabolism can lead to significant health issues, such as osteoporosis, tetany, and heart arrhythmias

(Yadav et al., 2024). Calcium shortage in beta-thalassemia patients may result from dietary insufficiencies, malabsorption, or interactions with other elements, thereby complicating the clinical presentation of the disorder (Soliman et al., 2023).

Increasing data suggests a substantial link between cadmium and calcium metabolism. Cadmium can disrupt calcium absorption and utilization by competing for shared binding sites on transport proteins and enzymes (Thévenod, 2009). This interaction may provide significant challenges in beta-thalassemia, as emerging research indicates an inverse correlation between cadmium and calcium levels in patients' blood (Shazia et al., 2012). Elevated cadmium levels may alter calcium homeostasis, leading to deficits that complicate the therapeutic management of these individuals.

Patients with beta-thalassemia may exhibit distinct vulnerability to trace element imbalances owing to several reasons. The fundamental pathophysiology comprises inefficient erythropoiesis, hemolysis, and heightened intestinal iron absorption (Sadiq et al., 2024). Moreover, routine blood transfusions inject external components into the bloodstream, potentially disrupting the balance of endogenous trace elements (Xie et al., 2022). Chelation therapy, frequently utilized to address iron overload, may influence other elements via non-specific binding (Kontoghiorghes et al., 2020).

Prior studies have mostly concentrated on the management of iron overload in beta-thalassemia, while other trace metals and minerals have received comparatively less scrutiny (Pinto and Forni, 2020). Few studies have shown changes in zinc, copper, and selenium levels in thalassemia patients (Şahin et al., 2021), although thorough examinations of cadmium and calcium levels in this demographic are still lacking.

Environmental and lifestyle factors additionally affect elemental profiles in thalassemia patients. Smoking markedly elevates cadmium exposure (Whitfield et al., 2010), thus exacerbating dangers linked to heavy metal buildup in this susceptible demographic. Comprehending these connections is crucial for formulating comprehensive management strategies (Zakaria et al., 2021)

This study seeks to examine cadmium and calcium concentrations in the blood serum of beta-thalassemia patients relative to healthy controls utilizing flame atomic absorption spectrometry (FAAS). We aim to elucidate the potential toxicological effects of cadmium and nutritional status concerning calcium in this population by analyzing correlations among these elements and accounting for variables such as age, gender, and smoking status. This knowledge may enhance personalized clinical treatments, nutritional guidelines, and lifestyle adjustments for beta-thalassemia patients, thereby improving health outcomes and quality of life.

MATERIALS AND METHODS

Ethical approval: All procedures used in this study were reviewed and approved by The Scientific Committee of Al-Najaf Technical Institute and done under the guidelines of Al Zahraa Educational hospital, Iraqi ministry of Health, in Najaf Governorate and was secured prior to study commencement. Informed consent was obtained from all participants.

This study analyzed serum cadmium (Cd) and calcium (Ca) levels in β-thalassemia patients compared to age- and sex-matched healthy controls in Najaf Governorate, Iraq. A prospective cohort study was conducted, involving 37 β-thalassemia patients (ages 11–59) undergoing regular weekly blood transfusions and 25 healthy controls (ages 11–40) without indications of anemia or iron shortage.

Blood samples (3 mL) were collected via venipuncture from each participant following a 12-hour overnight fast before scheduled transfusions for the β-thalassemia cohort. Samples were collected during routine visits between March 1 and April 1, 2025, to Al Zahraa hospital affiliated Iraqi ministry of Health, in Najaf Governorate. Serum separation was achieved via centrifugation (3000 rpm for 20 minutes) of samples

collected in serum separator tubes. Cadmium and calcium concentrations were determined using flame atomic absorption spectroscopy (FAAS). A 20 µL aliquot of serum was directly aspirated into the FAAS instrument for absorbance measurement and subsequently converted to concentration values.

Data regarding medical history, including smoking status (a potential source of Cd exposure), were collected via structured interviews. Statistical analysis was performed using SPSS software. Independent samples t-tests were utilized to compare Cd and Ca levels between the β-thalassemia and control groups. One-way analysis of variance (ANOVA) assessed the influence of age on Cd and Ca concentrations, while Spearman's rank correlation coefficient was employed to evaluate the correlation between Cd and Ca levels within each group. Statistical significance was established at $p < 0.05$. Sixty-two serum samples, comprising 37 β-thalassemia patients and 25 healthy controls, were studied.

RESULTS

Comprehensive results are displayed in [Table 1]. The approach utilized stringent sample collecting and processing processes, guaranteeing the reliability and validity of the acquired data. FAAS, a recognized analytical method, precisely measured Cd and Ca concentrations. The statistical analyses were judiciously chosen to answer the unique study issues, facilitating a rigorous interpretation of the findings. The research complied with recognized ethical standards, ensuring the rights and welfare of all participants were protected. The study's shortcomings, such as the limited sample size and the possibility of confounding variables, must be acknowledged when interpreting the findings. Future investigations utilizing bigger sample sizes and a more thorough evaluation of potential confounding variables are advised to clarify the link between β-thalassemia, Cd, and Ca homeostasis.

The average concentrations of Cd and Ca in the blood serum of β-thalassemia patients were (3.642±0.568 ppb) and (35.233±2.170 ppb), respectively, while the average concentrations of Cd and Ca in the blood serum of the control group were (31.766±0.242 ppb) and (35.233±2.170 ppb), respectively. The cadmium level in β-thalassemia patients was considerably elevated compared to the control group, whereas the calcium level in β-thalassemia patients was dramatically diminished relative to the control group, with a $p < 0.05$ in both instances.

Table 1: Statistical description of Cd and Ca levels (ppb) in serum samples of the study groups.

Statistical Value	Cd Concentrations Patient Group (ppb)	Cd Concentrations Control group (ppb)	Ca Concentrations Patient Group (ppb)	Ca Concentrations Control group (ppb)
No. of Samples	37	25	37	25
Mean± Std. Error	3.642±.568	1.766±.242	35.233±2.170	48.645±3.496
P-value	0.012		0.000	
Pearson correlation test	R= -1.00 with (p=0.000)			

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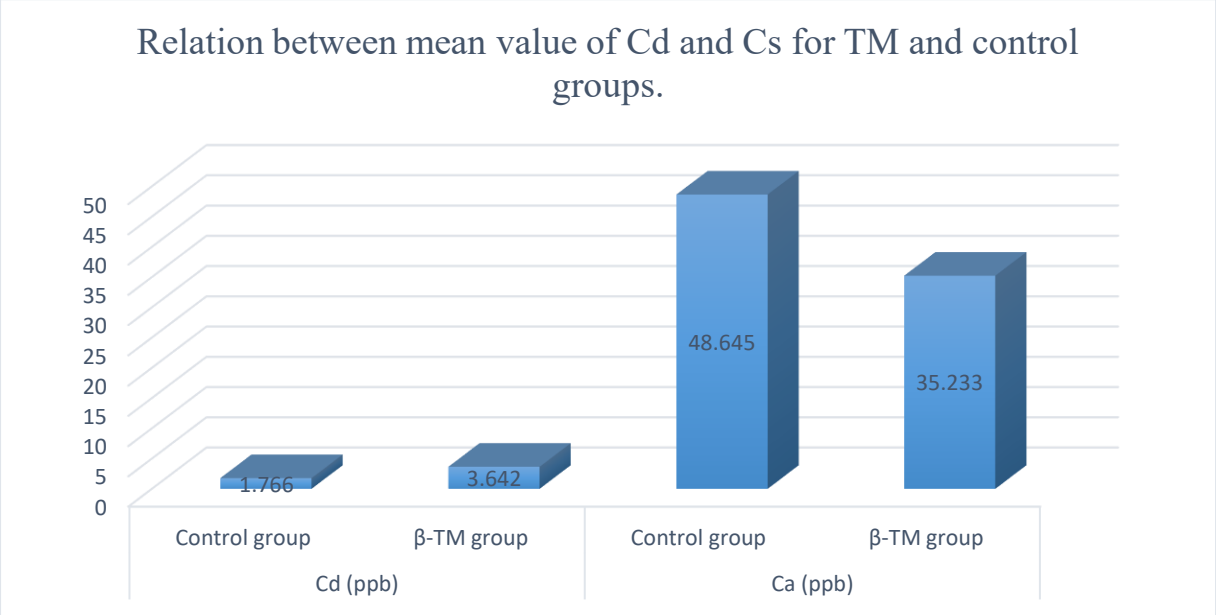

Fig. 1: The patient and control groups' mean Cd and Ca levels.

The average Ca level in blood serum samples of β-thalassemia patients is lower than that of the control group due to people's exposure to Cd-accumulating material used in their jobs.

Table (2) shows the mean values of Cd and Ca levels in blood serum samples for each patient group and their relation to age.

Age (years)	Mean value± Std. Error of Cd level (ppb)	Mean value± Std. Error of Ca level (ppb)
(11-20)	3.044±2.157	37.247±13.818
(21-30)	3.147±2.422	36.350±13.695
(31-40)	3.889±3.330	34.613±14.702
(41-50)	4.972±6.016	32.337±14.675
(51-60)	3.160±2.047	35.351±12.146
P-value	0.800	0.963

Figure 2 shows that the mean value of Cd level increases from 11 years of age to 41-50 years, but it decreases at 51-60 years ($p>0.05$). Adversely, the mean value of Ca level decreases from 11 years of age to (41-50) years, but it increases at (51-60) years ($p>0.05$). So, statistically, no effect was observed for age on Cd and Ca levels.

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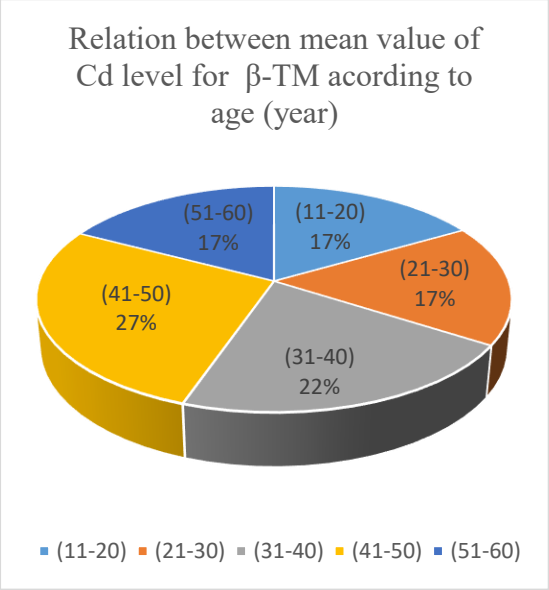

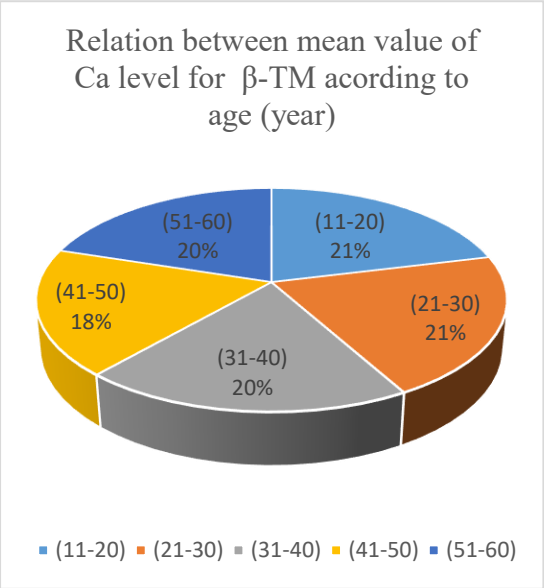

The table (3) shows the mean values of Cd and Ca levels in blood serum samples for each patient group and their relation to smoking.

Smoking habit	Mean value± Std. Error of Cd level (ppb)	Mean value± Std. Error of Ca level (ppb)
Smoking	5.217±3.940	33.446±14.413
Non-Smoking	2.149±2.100	36.925±12.094
P-value	0.005	0.431

The table (3) shows the mean Cd and Ca levels in blood serum samples for each patient group and their relation to smoking.

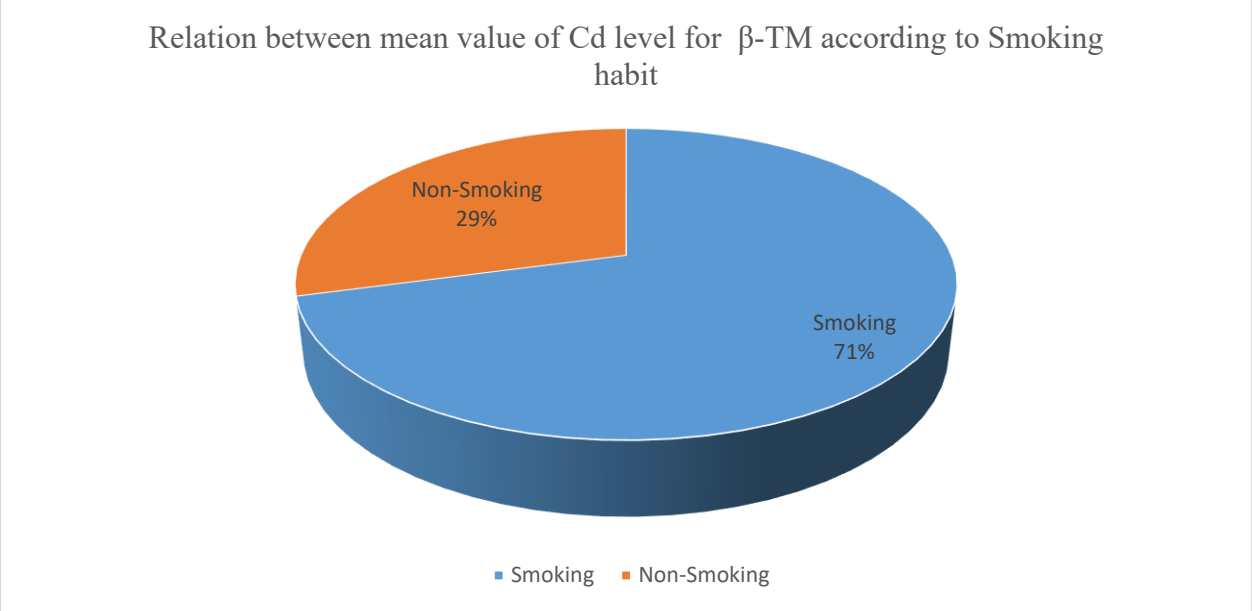

Figure (3) shows that the mean value of Cd level increases at Beta-Thalassemia Patients ($p<0.05$) and the mean value of Ca level decreases at Beta-Thalassemia Patients ($p<0.05$).

Figure (3) shows that the mean value of Cd level increases at Beta-Thalassemia Patients ($p<0.05$) and the mean value of Ca level decreases at Beta-Thalassemia Patients ($p<0.05$). So, there was a significant effect observed for smoking on Cd and Ca levels, which means that the smoking patients are exposed to Cd accumulation as a result of continuous smoking habits. In a previous study, the increase in Cd levels was associated with increased smoking. The increased level of Cd in the serum was similar to many conditions that cause diseases, such as anemia.

DISCUSSION

Heavy Metal Toxicodynamics and Micronutrient Deficiency in Beta-Thalassemia

Beta-thalassemia major represents a lifelong transfusion-dependent hematologic disorder, where routine blood infusions, although life-saving, introduce significant risks of metabolic imbalance. Most prevailing studies have primarily emphasized iron overload in thalassemia. However, this study provides a pivotal shift by investigating lesser-discussed but equally influential trace elements—**cadmium (Cd)** and **Calcium (Ca)**—highlighting their opposing serum behaviors and implications for clinical outcomes.

1. Cadmium Accumulation and Toxic Burden

The study observed significantly elevated cadmium concentrations in the blood serum of beta-thalassemia patients (mean: 3.642 ± 0.568 ppb) compared to healthy controls (1.766 ± 0.242 ppb; $p = 0.012$). This elevation is deeply concerning. Cadmium, a non-essential and highly toxic heavy metal, accumulates in vital organs and impairs cellular functions, particularly in the kidneys, bones, and cardiovascular system. The bioaccumulation of cadmium over time, given its half-life of up to 30 years, exacerbates the oxidative and inflammatory milieu that already afflicts thalassemia patients, thereby accelerating end-organ damage.

2. Calcium Deficiency and Physiological Vulnerability

Conversely, Calcium, an essential macro-mineral, showed a statistically significant deficiency in thalassemia patients (mean: 35.233 ± 2.170 ppb) compared to controls (48.645 ± 3.496 ppb; $p < 0.001$). Calcium is critical in bone health, neuromuscular coordination, and coagulation pathways—all systems heavily taxed in thalassemic pathophysiology. Its depletion is likely driven by multiple mechanisms, including:

- Increased cadmium interference with intestinal calcium absorption (competitive inhibition).
- Enhanced renal calcium excretion due to tubular damage.
- Possible dietary insufficiencies or impaired vitamin D metabolism are commonly reported in chronic diseases.

3. Toxicological Interplay: Cadmium-Calcium Axis

The most striking statistical finding is the **perfect inverse correlation** between cadmium and calcium levels in patients ($r = -1.00$, $p < 0.05$). This correlation underscores a direct antagonistic relationship. Cadmium mimics Calcium and competes for its transporters, displacing it in physiological systems and blocking its bioavailability. This dynamic contributes to calcium depletion and promotes cadmium retention, creating a vicious cycle of toxicity and deficiency. This interaction has profound implications in thalassemia management, especially in preventing bone demineralization, neuromuscular disturbances, and cardiac instability.

4. Smoking as a Contributing Factor

The study further identifies **smoking** as a statistically significant contributor to increased cadmium levels ($p = 0.005$), supporting existing literature that tobacco smoke is a primary cadmium source. Smokers with

thalassemia displayed cadmium levels over double those of non-smokers (5.217 vs. 2.149 ppb), amplifying their toxic burden. Interestingly, while calcium levels were also lower in smokers, the statistical difference was insignificant ($p = 0.431$), suggesting that smoking's effect on Calcium may be indirectly mediated through cadmium or systemic inflammation.

5. Age and Sex Influence

The study found no significant age-related differences in cadmium or calcium levels ($p > 0.05$), indicating that accumulation and depletion are more likely tied to environmental exposures (e.g., smoking) and disease-related metabolic alterations rather than age-dependent physiological changes. Sex distribution was not highlighted in the detailed analysis, indicating a potential area for future research.

CONCLUSION

Our investigation revealed an inverse relationship between cadmium and calcium levels in patients with beta-thalassemia, highlighting significant variances in the levels of these heavy elements. Elevated cadmium levels were associated with reduced calcium levels, contributing new insights into the trace element imbalances prevalent in this population. We recommend regular monitoring of serum calcium levels in all patients diagnosed with beta-thalassemia major, coupled with prompt measures such as oral calcium supplements and smoking cessation to alleviate the symptoms. This study demonstrates increased blood cadmium levels in persons with β-thalassemia. The findings highlight a crucial interaction between the accumulation of hazardous metals, such as cadmium, and the regulation of critical trace elements in the development of this condition. This requires a comprehensive, eco-conscious, precision medicine strategy for the management of β-thalassemia. A comprehensive understanding and focused intervention regarding this intricate interplay of elemental interactions is likely to markedly boost clinical results and improve the overall quality of patient care. Additional study is necessary to clarify the mechanisms underlying cadmium accumulation and to investigate new therapeutic approaches to reduce cadmium toxicity and enhance essential element balance in β-thalassemia patients. This entails examining the influence of genetic predisposition, environmental exposure, and compromised detoxification mechanisms on the measured cadmium load. Creating innovative diagnostic instruments that accurately measure hazardous and necessary element concentrations will be vital for tailored therapy approaches and enhanced patient classification.

Acknowledgements

I would like to express my great thanks to Al-Najaf technical institute affiliated with Al-FuratAl-Awsat technical university, and the head of the Thalassemia Center in Al Zahra Hospital, Dr. Ahmed Mirza, and I am heartily indebted to the head of optometry, Dr. Hyder A. Ali, and Dr. Amin Al-Waili, who assisted me during my research. I must not forget to acknowledge deep Gratitude to my friend Dr. Bassam Abdulameer Al-Madany.

Conflict of interest:

The authors declare no conflict of interest**.**

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