Lead and Cadmium Level in Biological Samples of Kidney Failure Patients in AL-Diwaniyah Governorate, Iraq

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***Abstract*—Renal failure occurs when the kidneys become unable to filter waste products and excess fluids from the blood in an effective way. It can be caused by many medical problems such as diabetes, and hypertension. Exposure to heavy elements is another causative factor. Fifteen patients with chronic renal disease on dialysis were involved in the study (12 males and 3 females) aged between 26 and 74. Complete medical history was taken from all. The control group involved eight healthy adults aged between 33 and 47. Serum and urinary lead and cadmium before and after dialysis (for patients) were taken and once for control, samples were analyzed by using an atomic absorption spectrophotometer. Results for Lead show that by comparing pre-dialysis to post-dialysis state, there was a significant reduction in mean serum lead (Pb) from 0.04±0.04 to 0.01±0.01, respectively (p = 0.011), which becomes nearly similar to the control group. For urinary samples, there was a significant reduction in mean urinary lead (Pb) from 0.88±0.95 to 0.22±0.37, respectively (p = 0.010), which also becomes nearly similar to the control group. For Cadmium by comparing pre-dialysis to post-dialysis state, there was no significant reduction in mean serum cadmium (Cd) from 0.03±0.05 to 0.00±0.00, respectively (p = 0.086), which becomes nearly similar to the control group. And for urinary samples, there was a significant reduction in mean urinary cadmium (Cd) from 0.02±0.03 to 0.01±0.01, respectively (p = 0.010).**

***Keywords*—Renal failure, Cadmium (Cd), Lead (Pb), Iraq**

I. Introduction

Kidney disease has been considered one of the utmost neglected chronic diseases. The risk of it is seen across people of all ages and variable socio-economic status. Consequently, studies directed at those populations are necessary to properly evaluate the burden of renal disease globally. Numerous causes have been related with the pathogenesis of kidney failure with diabetes and hypertension on the top of the list [1].

Impaired renal function is a precursor for chronic kidney disease which is a serious public problem in new eras, and associated with a decrease in work productivity among those living with the disease. It is known to have a well-known link with many environmental factors such as many medications like (NSAIDs, and Aminoglycoside) and food such as high sodium and high phosphorous diet [2, 3].

Heavy metal exposure from environmental sources such as drinking water has been implicated in the occurrence of chronic kidney disease in various situations [4].

Lead is dominant in industries, chiefly those including batteries, dyes, and pipes. Deposits of industrial practices and old lead-based paints can pollute soil and water. Cadmium is found in industrial places, mainly in battery manufacturing, and in regions with high pollution such as soil, with additional dietary sources such as contaminated food and water [4].

Heavy elements in the periodic table have high atomic weight and high density. Most of them are present in the biosphere, they are present in the soil, water, and rocks, and are often released to the surroundings by many commercial and industrial sources. The toxicity of these elements has been known for decades. However, some are beneficial in nature and vital to humans such as zinc, copper, and manganese [5].

Many elements are toxic such as (lead, thallium, and cadmium), are considered common industrial products that substantially pollute the environment [6].

Generally, heavy metals that are naturally occurring in the environment and are vital for survival may become hazardous if accumulate in the organisms. Some of these elements are mercury, Cadmium, arsenic, nickel, copper, and Lead [7].

Cadmium is usually released into the atmosphere as a result of man-made or industrial activities. Both humans and animals are exposed to it but in different way [8].

Cadmium can cause aquatic pollution by absorption, industrial waste, and sediments. Humans can be poisoned with it by ingesting food, drinking water, or breathing air rich in those heavy metals [8].

Regarding lead, it is a non-biodegradable substance. It is available in nature in very small quantities. Its availability is increasing now because of manufacturing, fossil fuel, and mining [9].

It's toxic to humans if its level exceeds optimum, the children are considered the highest risk group [9].

Cadmium-induced nephrotoxicity can be presented with many symptoms such as phosphaturia, aminoaciduria, Fanconi-like syndrome, renal tubular acidosis, hypercalciuria, and renal failure [10, 11].

Lead has a great deteriorating effect on many organs functions such as the brain and kidneys. It has an influence on renal function that chronic lead nephropathy can be presented as interstitial fibrosis, glomerulonephritis, and renal failure [12].

Lead (Pb) and Cadmium (Cd) are heavy metals that have no biological role in the human body [13, 14]. They are two of ten environmental pollutants that carry major public health hazards by WHO (World Health Organization) [15].

Pb and Cd can be accumulated in the body because there is no excretory mechanism to aid their elimination, as a result, the tissue level of these two elements increases with age [16, 17].

The most vulnerable tissues for Cd and Pb accumulation are kidneys, brain, and bones, making them more liable to toxic effects, in addition to many other tissues and organs [17, 18].

Many long-term effects of chronic exposure to Cd and Pb result in distinct pathologies and diseases in nearly all organs [19].

The study aims to know the level of cadmium and lead in chronic renal disease patients, comparing it with healthy people and to determine the effect of dialysis on these levels which can help us in early detection and management.

II. Literature Review

Numerous studies have investigated the relationship between renal function and exposure to toxic elements such as lead and cadmium. Jin *et al.* [20], found that chronic cadmium exposure is linked to renal dysfunction, while Muntner *et al.* [21] ,demonstrated a significant association between blood lead levels and chronic kidney disease (CKD) prevalence. Åkesson *et al.* [22], observed that even low-level cadmium exposure can lead to a decline in glomerular filtration rate (GFR) among Swedish women. Morales *et al.* [23] noted that higher blood levels of lead and cadmium were associated with early markers of renal damage in children.

In alignment with these studies, the current research shows elevated levels of cadmium and lead in patients with chronic renal disease prior to dialysis, attributed to the kidneys' inability to excrete accumulated trace elements due to insufficiency. Consistent with Tasneem *et al.*'s [23], post-dialysis results indicate a significant reduction in lead and cadmium levels in serum and urine, though the reduction in serum cadmium was not statistically significant. This highlights the role of dialysis in reducing trace element levels. However, this outcome contrasts with findings from Atieh Makhlough *et al.* [24] , who reported an increase in serum lead levels post-dialysis, and other studies indicating that cadmium and lead levels may rise after dialysis. This discrepancy underscores the need for further investigation into the levels of these elements in dialysate fluid.

III. Patients and Methods

Fifteen patients with chronic renal disease on dialysis were involved in the study (12 were male and 3 were female) aged between 26 and 74. The control group involves eight healthy persons (4 males and 4 females).

Patients' characteristics were evaluated in Table 1, all of them had GFR<15 ml/min/1.73 m^2.

The study was conducted from the first of November to the first of January. All patients involved in the study were visitors to the dialysis unit at AL-Diwaniyah Teaching Hospital in Al-Qadisiyah governorate in the south of Iraq, control group was healthy volunteers.

A complete history was taken from all of them regarding name, age, residency duration of illness, and dialysis duration, Verbal consents were obtained. Blood and urine samples were obtained from all (before and after dialysis for the diseased group and single time in control) and samples were sent to the laboratory for analysis.

Assessing serum and urine levels of cadmium and lead classically includes complex analytical methods. Urine Samples are collected in unpolluted, metal-free dishes, and stored frozen for longer storage. Six ml of urine was taken with the addition of 3 ml of nitric acid HNO_3(69%).

While for serum samples we collect blood via proper anticoagulants (EDTA) in metal-free tubing, we centrifuge samples to isolate the serum. These are stored in freezing for long storage.

Analysis of samples done by Atomic Absorption Spectrophotometer (AA-700)-Shimadzu Japan.

For urine samples, the flame atomic absorption spectroscopy (FAAS) technique can be used for assessing lead and cadmium in urine. We dilute the samples with a modifier (nitric acid) to lessen possible interference.

A digestion step is performed, this classically involves adding a concentrated acid (e.g., nitric acid) for digestion and then heating the sample to break down organic matter.

A series of calibration standards was prepared with identified concentrations of lead and cadmium.

Setting Up the flame instrument and choosing the appropriate lamp for the metal being analyzed (lead or cadmium) was done, with adjustment of the instrument settings to include the wavelengths fir to the metals. We use the calibration standards to generate a calibration curve we aspirate the diluted samples into a flame and measure the absorbance of each sample at the exact wavelength.

Graphite furnace spectroscopy is used for serum samples. We formulate standards and samples through dilution to diminish interference. The sample was injected into the furnace to be atomized and the absorption of lead and cadmium was measured at their corresponding wavelengths.

We use the calibration curve to quantify the concentration of lead and cadmium in the urine and serum samples. We compare the measured values to known reference values.

The selected wavelength for cadmium is 228.8nm while for lead it is 283.3 nm. The calibration curves were as follows;

Precision and Accuracy of the Atomic Absorption Spectrophotometer (AAS) for Lead and Cadmium Analysis was ensured by multiple readings of each sample that yield an approximate similar result. While the accuracy is highly dependent on the calibration process. Standard solutions of known concentrations are used to make a calibration curve, to which the sample readings are matched.

Table 1. Patient's characteristics

No.	age	gender	residency	duration of illness	clinical presentation
1	53	male	urban	12 y	anemia, heart failure
2	63	male	urban	8y	anemia, hypertension
3	54	female	urban	6y	dyslipidemia
4	37	male	urban	10 mo.	anemia
5	58	male	urban	2y	hypertension, diabetes
6	26	male	urban	3.5y	anemia
7	49	female	urban	4y	edema, anemia
8	74	male	urban	1 y	anemia, hypertension
9	60	male	urban	8 mo.	edema, anemia
10	41	male	urban	8 mo.	anemia
11	33	male	urban	1.5y	anemia, edema
12	68	male	urban	1.5y	hypertension, diabetes
13	63	male	urban	2y	anemia, hypertension
14	60	male	urban	3y	hypertension
15	73	female	urban	2 mo	hypertension, anemia

IV. Result and Discussion

A. Demographic Characteristics of Patients Enrolled in This Study

The current study included 15 patients of whom there were 3 females (20.0 %) and 12 males (80.0%) and the male-to-female ratio was 4:1, as shown in Fig. 1 and Table 2. The mean age of all enrolled patients was 54.13±14.43 years and the age range was between 26 and 74 years. The duration of illness was ranging between 2 months and 12 years and the mean duration was 3.12±3.27 years. Based on residence, all patients were from urban areas. The study included also 8 control subjects. There was a significant difference in mean age (p = 0.022), but no significant difference in gender proportions between groups (p = 0.311).

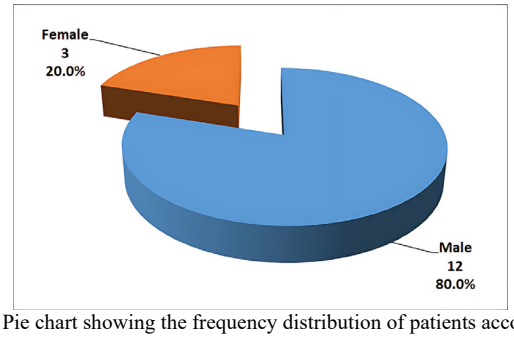

Fig. 1. Pie chart showing the frequency distribution of patients according to gender.

B. Comparison of Mean Serum and Urinary Lead (Pb) and Cadmium (Cd) Elements before and after Dialysis

A comparison of mean serum and urinary lead element (Pb) before and after dialysis is shown in Table 3. By comparing pre-dialysis to post-dialysis state, there was a significant reduction in mean serum lead (Pb) from 0.04±0.04 to 0.01±0.01, respectively (p = 0.011), as shown in Fig. 2, which becomes nearly similar to the control group. By comparing pre-dialysis to post-dialysis state, there was a significant reduction in the mean urinary lead (Pb) from 0.88±0.95 to 0.22±0.37, respectively (p = 0.010), as shown in Fig. 3, which becomes nearly similar to the control group.

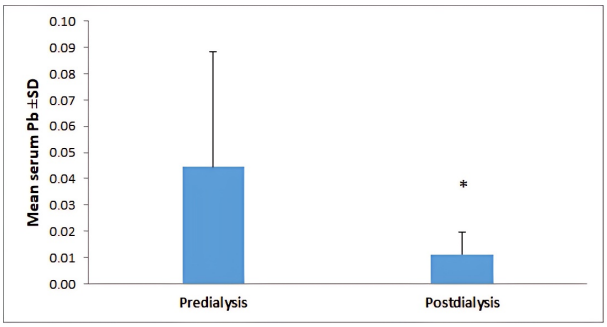

Fig. 2. Bar chart showing comparison of mean serum lead element (Pb) before and after dialysis to control group.

By comparing pre-dialysis to post-dialysis state, there was no a significant reduction in mean serum cadmium (Cd) from 0.03±0.05 to 0.00±0.00, respectively (p = 0.086), as shown in Fig. 4, which becomes nearly similar to the control group. By comparing pre-dialysis to post-dialysis state, there was significant reduction in mean urinary cadmium (Cd) from 0.02±0.03 to 0.01±0.01, respectively (p = 0.010), as shown in Fig. 5 and Table 4.

Table 2. Demographic characteristics of patients enrolled in this study

Characteristic	Patients group n = 15	Control group n = 8	p-value
Age (years)			
Mean± SD	54.13±14.43	41.00±5.10	0.022 I *
Range	26–74	33–47	
Gender			
Male, n (%)	12 (80 %)	4 (50 %)	0.311 Y
Female, n (%)	3 (20 %)	4 (50 %)	NS
Duration of illness (years)			
Mean± SD	3.12±3.27	---	---
Range	2 months -12 years	---	
Residence			
Urban	15 (100.0 %)	8 (100.0 %)	
Rural	0 (0.0 %)	0 (0.0 %)	

SD: standard deviation; I: independent sample t-test; Y: Yates correction test; NS: not significant; *: significant at $p \leq 0.05$

Table 3. Comparison of mean serum and urinary lead element (Pb) before and after dialysis

Characteristic	Control group	Pre-dialysis	Post-dialysis	P1 Pre-versus control	P2 Pre-versus post
Serum lead (Pb)					
Mean± SD	0.01±0.01	0.04±0.04	0.01±0.01	0.057 I NS	0.011 Pa *
Range	0–0.03	0.01–0.16	0–0.04		
Urinary lead (Pb)					
Mean± SD	0.19±0.23	0.88±0.95	0.22±0.37	0.059 I NS	0.010 Pa **
Range	0–0.51	0.02–3.49	0–1.13		

SD: standard deviation; Pa: paired t-test; I: independent sample t-test; NS: not significant; *: significant at $p \leq 0.05$; **: significant at $p \leq 0.01$

Table 4. Comparison of mean serum and urinary cadmium element (Cd)

Characteristic	Control group	Pre-dialysis	Post-dialysis	*P1* Pre-versus control	*P2* Pre-versus post
Serum cadmium (Cd)					
Mean± SD	0.00±0.00	0.03±0.05	0.00±0.00	0.204 I NS	0.086 Pa NS
Range	0–0.01	0–0.2	0–0		
Urinary cadmium (Cd)					

Mean± SD	0.05±0.04	0.02±0.03	0.01±0.01	0.114 I NS	0.025 Pa *
Range	0–0.11	0–0.08	0–0.03		

SD: standard deviation; Pa: paired t-test; I: independent sample t-test; NS: not significant; *: significant at $p \leq 0.05$; **: significant at $p \leq 0.01$

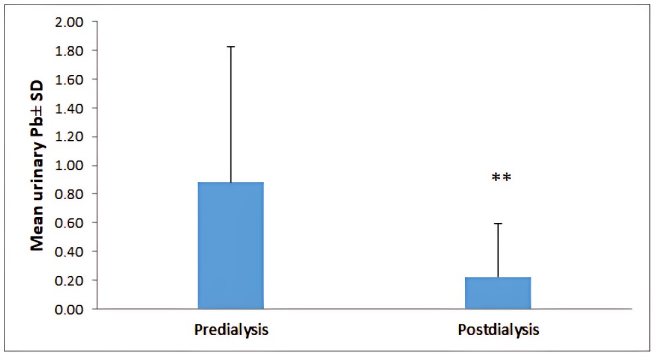

Fig. 3. Bar chart showing comparison of mean urinary lead element (Pb) before and after dialysis to control group.

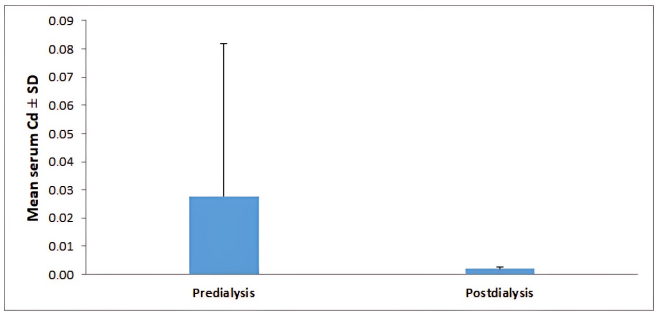

Fig. 4. Bar chart showing comparison of mean serum cadmium element (Cd) before and after dialysis to control group.

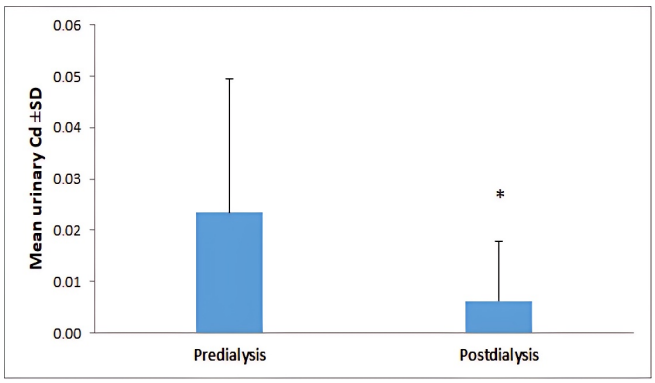

Fig. 5. Bar chart showing comparison of mean urinary cadmium element (Cd) before and after dialysis to control group.

In our study, we evaluate both serum and urinary levels of cadmium and lead in patients with chronic renal failure on hemodialysis (pre-dialysis and post-dialysis assessment) while samples obtained once in control.

Measuring sources of cadmium and lead in the study population may involve many steps such as:

1. The use of air sampling devices to collect airborne particles.
2. Water samples are collected from various sources.
3. Soil and dust samples collection.
4. Biomonitoring with (blood, urine, hair, and nail samples)
5. Dietary evaluation and assessment by food sample collection
6. testing household items such as ceramics and paint, and testing some products such as toys and cosmetics

In AL-Diwaniya, exposure to cadmium can typically be related to Agricultural Sources, such as the use of fertilizers, which contaminate soil and crops and lead to food contamination (vegetables, cereals, seafood). Water contamination cannot be forgotten. It is also considered air Pollution from emitted from burning fossil fuels is also a possibility.

Lead poisoning is common in older buildings as deteriorating paints can produce lead dust and in buildings near roadways, another important source is contaminated water from lead pipes use. Lead poisoning also can be the result of the use of traditional cosmetics and medicines.

Our study of cadmium and lead in chronic renal failure patients faces many challenges and limitations as getting a sufficiently large and diverse sample of CRF patients can be difficult which can limit the generalization of the findings.

Another problem is with the accurate assessment of long-term exposure which requires detailed historical data, misclassification of exposure history can result in bias. In addition, individual variances in the absorption, metabolism, and excretion of these metals can vary broadly. Many other factors, such as age, gender, and co-existing medical illnesses, can affect both metal exposure and renal function.

Numerous studies have explored the association between renal function and exposure to lead and cadmium. At this point the current study can be compared with international and local studies through the following:

The levels of toxic elements were elevated in all patients and were decreased post dialysis to a value nearly consistent with that of control, which may be secondary to the presence of another source of exposure causing accumulation such as environment, diet, job, and tobacco smoking. This result was consistent with the Tasneem study in which significant difference between patients and control at pre-dialysis sampling [23].

There is a raised level of both elements in all samples of patients (pre-dialysis values) may be explained by the inability of the kidneys to excrete accumulated amounts of trace elements secondary to insufficiency as explained by A. Makhlough *et al*. [24].

The elevated levels of cadmium and lead in chronic renal disease are also reported by Takesh M and Keiichi [25]. and by ANA N. *et al.* [26].

A new survey conducted in Iraq has established that lead and cadmium levels are significantly greater in patients with renal failure compared to healthy individuals [27].

The limitations of this study are the small number of patients involved and the lack of their past detailed biochemical background.

More robust statistical tests can be performed in the future with a larger patient sample and more detailed history with proper evaluation of renal function tests at study time to assess the correlation between the heavy metal level and (the clinical and laboratory results). It can also be done A more comprehensive study of each contamination source for the population, with proper testing methods on long-term effects, and correlate that with clinical and laboratory results to define the impact of that on the population.

V. Conclusion

In this study patients with renal failure exhibit elevated levels of lead and cadmium. These metals are nephrotoxic and can accumulate in the body due to impaired renal excretion. For lead by comparing pre-dialysis to post-dialysis state, there was a significant reduction in mean urinary and serum lead (Pb) which becomes nearly similar to the control group. For cadmium by comparing pre-dialysis to post-dialysis state, there was no significant reduction in mean serum cadmium (Cd), which becomes nearly similar to the control group while for urinary cadmium, there was a significant reduction in mean urinary cadmium (Cd).

While dialysis helps manage the symptoms and metabolic imbalances of kidney failure, its effect on heavy metal detoxification is not ideal. Patients on dialysis remain at risk for continued heavy metal accumulation, which can cause further damage to the kidneys and overall health. Regular monitoring of heavy metal levels in dialysis patients is also recommended to lessen the ongoing risks. Shortly, we will try to be involved in longitudinal studies to track lead and cadmium levels over time in kidney disease patients undergoing different treatment regimens (e.g., dialysis vs. non-dialysis) to assess long-term exposure effects and variability.

Conflict of Interests

The authors declare no conflict of interest.

Author Contributions

WS collected and prepared biological samples from patients for measurement, and measurements were performed with the assistance of KH in the Advanced Nuclear Physics Laboratory, Department of Physics, College of Education, University of Al-Qadisiyah. WS wrote the paper, extracted, and interpreted the results, and cited the sources with the assistance of KH.

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