How to Cite:
Darwish, K. M., Nada, S. Z., & Kazar, S. H. (2022). Association between lead poising and chronic kidney disease in a sample of Iraqi population. *International Journal of Health Sciences*, *6*(S2), 11697–11705. https://doi.org/10.53730/ijhs.v6nS2.8125

Association between lead poising and chronic kidney disease in a sample of Iraqi population

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***Abstract*---**High environmental exposure to lead is associated with kidney failure, but the effect of low-level environmental exposure has not been well studied. Objective : The aim of the study was to evaluate the blood lead levels in the serum of patients with renal failure and compare it with those in the control group, as well as to verify its relationship with kidney function. Subjects and Method : The study included 87 people, their ages ranged (17-72 years), 45 of them were diagnosed with chronic kidney disease, while 32 of them were diagnosed with good health. Samples were collected from December 2022 to May 2022 and blood lead levels were estimated using atomic absorption Shimadzu in China, biochemical parameters were measured weight calculated for body mass index divided by height squared in meters, serum creatinine and blood urea by colorimetric methods using Spectrophotometer from Genway company . Results : The average levels of lead in the blood in the group of chronic kidney patients were much higher than it was in the control group ($p \le 0.01$).In addition,compared to the healthy group, the vital indicators such as serum creatinine and blood urea were significantly higher in the patients, while it was There is a significant decrease in the glomerular filtration rate in patients compared to the control group. We also found a significant positive correlation between the levels of lead in the blood, serum creatinine, and blood urea (0.399** , 0.376**) respectively and a significant inverse correlation between blood lead levels and glomerular filtration rate (-0.463**) .

International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.
Manuscript submitted: 09 March 2022, Manuscript revised: 18 April 2022, Accepted for publication: 27 May 2022

***Keywords*---**lead exposure, chronic kidney disease, environmental exposure.

Introduction

Chronic kidney disease (CKD) has become a global public health issue as a result of its rising prevalence, high management costs, and function as a risk factor for cardiovascular disease. The main causes of CKD include diabetes and hypertension. Many other cardiovascular disease risk factors, such as age,obesity,smoking, and hypercholesterolemia, have been related to CKD 1. Heavy metals in the environment, such as lead (Pb) levels have been established nephron toxins at high levels of exposure2 . Long-term exposure to Low levels are common in today's environment, particularly in urban areas. These metals gradually accumulate in the body in industrializing countries 3. Lead (Pb) in the environment, in particular, Exposure can be found in the air,food,cigarettes,gasoline, and other products. crops that have been polluted, and seafood that has been infected4 . However, their significance is debatable.at low-level environmental exposures 5. poisoning has been demonstrated to produce mitochondrial enlargement and impair energy generation in renal tubular cells6 .The loss of nephrons is irreversible in CKD, and the glomerular filtration rate (GFR) eventually decreases 2.In an attempt to compensate for the loss of sick nephrons, these changes are accompanied by structural,functional,and molecular changes in the remaining functional nephrons 7.

Subjects

Study design

The study is case-control study at Adel S' Al-Sabbah Dialysis Center in Al-Hussein Teaching Hospital ,Holy Karbala governorate, Iraq. The study period from December 2021 to May 2022. Included two studied groups patients with DKD and healthy control with retched age and body mass index BIM , their age ranged (17-72) years .

Patient Group

Patient group involved (45) subjects they were diagnosed with CKD . All patients were diagnosed by clinical physicians.

Control Group

The Control group involves (32) appreciates healthy subjects. All subjects do not appear any signs and symptoms of diseases. Controls subjects were matched with patients in gender and age to increase the accuracy of the results.

Methods

Collection of Samples

Disposable syringes and needles are used for blood collection. Blood samples (5 ml) were obtained from Patients and the control group. Blood samples were allowed to clot, and then centrifuged at 4500xg for 10 minutes. Sera are separated and divided into fractions in eppendorf tubes then frozen until use.

Body Mass Index (BMI)

Body mass index was calculated in all subjects according to ratio depend on weight and height obtained by applying a mathematical equation, in which the weight in Kilogram is divided by the square height in Meter, and the results were considered as follows :

BMI (kg/m^2) = weight (kg) / height (m^2)
Underweight ≤ 18.5(kg/m^2)
Normal weight between 18.5 - 24.9(kg/m^2)
Overweight between 25-29.9(kg/m^2).
Obese ≥30(kg/m^2) 8 .

Biochemical measurement

Determination of Creatinine and Urea

Urea and creatinine was measurement by using colorimetric methods by spectrophotometer and using the urea and creatinine kits was being used to assess the serum urea and creatinine.
Calculations :

Creatinine mg/d L = ((A2-A1)SAMPLE)/((A2-A1)STANDARD)*standard concentration

Urea mg/d L = (Asample)/(Astandard)*C standard

Determination of Lead concentration

Preparation of Matrix Modifier , Standards and Sample
In a 100 mL volumetric flask , 5 m L of 10% Triton X-100 , 1 m L of 20% $NH_4H_2PO_4$ and 4 drops of 70% HNO_3 acid were mixed and diluted to volume with deionized water to form the matrix modifier . To prepare a multi-point calibration curve , o , 1oo , 300, and 6oo ppb lead working standard solutions were prepared in 1% HNO_3 . the final standard solutions were prepared by mixing 100 μL each of the working standard solution and 900 μL of matrix modifier in the autosampler vessels to produce o ,10 , 30 and 6o ppb . these standard solutions were set aside until the bubbles were dissipated. The samples were prepared by mixing 100 μL of whole blood (with anti-coagulant) with 900 μL matrix modifier . Measurements were made using a device Graphite Furnace Atomic Absorption Spectrophotometry (GF-AAS) , (AA-6300with GFAX7i2)9,10.

Results

The study's data were examined using the Statistical Package for the Social Sciences (SPSS) model 23 statistic tool. It was created with the intention of making comparisons and highlighting key distinctions. When $p \leq 0.05$ was reported as mean ± SD (standard deviation) , it was judged significant . For parameter comparisons between patients and controls, independent T-test statistics were used.

Table1:- Associations of biochemical parameters between patients with chronic kidney disease and healthy control

Parameters	CKD n = 46 Mean + SD	Control n = 32 Mean + SD	P value
Age (years)	47.40 + 12.63	44.59 + 13.41	NS
BMI (kg/m^2)	26.95 + 6.98	27.39 + 5.05	NS
S Cr (mg/dl)	8.86 + 3.619	0.95 + 0.26	HS
B Ur (mg/dl)	111.10 + 39.32	26.06 + 8.32	HS
e GER ($ml/min/1.73\ m^2$)	7.09 + 8.10	82.78 + 21.87	HS
Blood lead level (mg/dl)	24.38 + 1.35	14.14 + 0.71	HS

SD: standard deviation , BMI : Body mass index , S Cr : Serum creatinine , B Ur: Blood urea , e GFR : Estimated Glomerular Filtration Rate

$$\mathbf{NS: \ t-test\ p-value \geq 0.05, S: p-value \leq 0.05, HS; \ p-value \leq 0.01}$$

According to the data presented, the mean levels of urea (111.1069 + 39.32619 mg/d) in the patient and the control respectively, which increased significantly in the group of chronic kidney patients ($p < 0.001$ compared to the control group) were shown. Presented in Table (1) are the results of our discovery that a significant increase in the measured biomarkers in serum creatinine , BMI and blood lead level in the group of patients compared to the healthy groups while significantly decreased in eGFR. There were non-statistically significant changes in age mean values and BMI between the normal control group and the groups of chronic kidney patients. According to the presented data which explain by Figure :1 showed the mean levels of serum creatinine (mg /ml) increased in CKD patient than controls group .

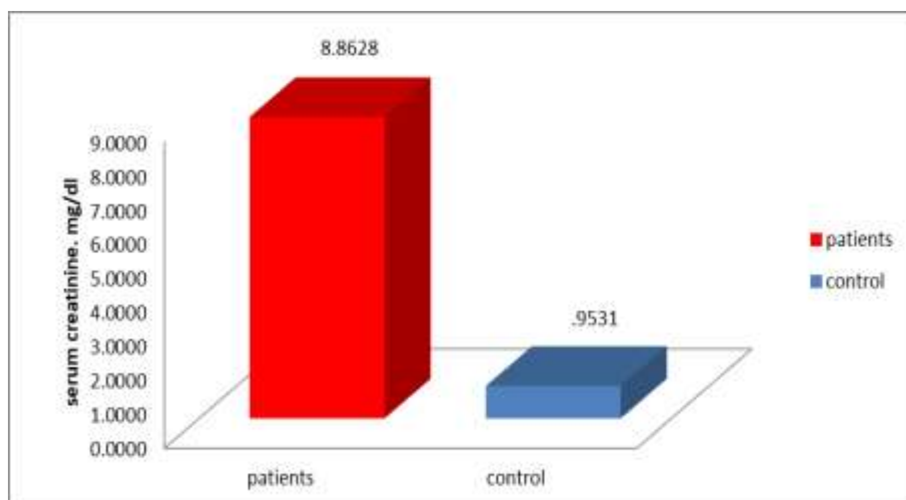

Figure 1 : Mean levels of serum Creatinine (mg/ml) in patients group of CKD compared to controls group.

While figure (2) showed a lower level of e GFR in CKD patients compared to control group

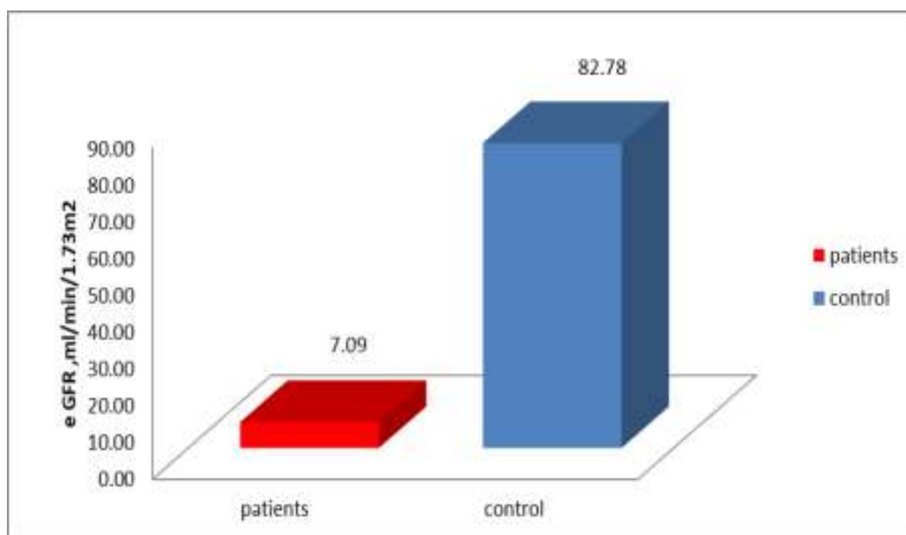

Figure 2 : Mean levels of e GFR ($ml/min/1.73m$ 2) in patients group of CKD compared to controls group

While Figure (3) showed an increase in the mean levels of lead blood in CKD patients compared to the control group.

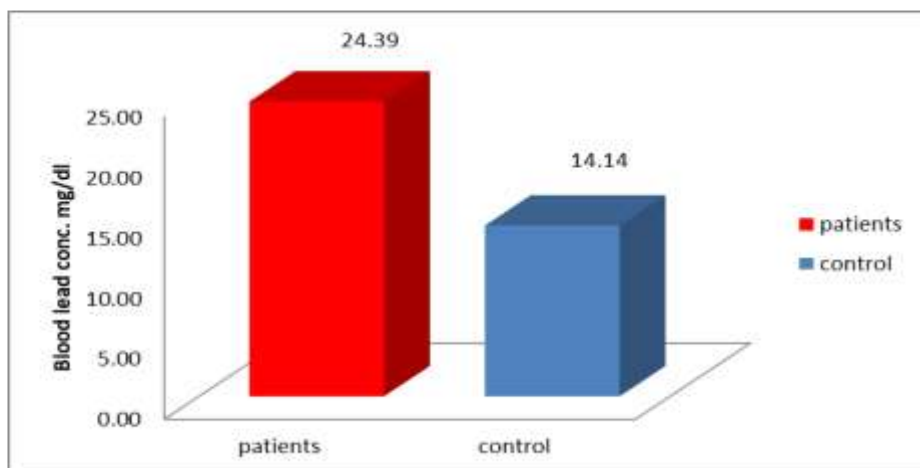

Figure 3 : Mean levels of Blood lead level (mg/dl) in patients group of CKD compared to controls group

Through this study, we found that there was a statistical significance between blood lead level , blood urea and serum creatinine with a direct relationship, while the relationship was inverse between lead and glomerular filtration rate as shown *below in table* 2 .

Table: 2 Correlation *between* B Ur, S Cr and e GFR with Blood lead level

Parameters	*Blood lead level*	
	P – Value	*r*
B Ur	0.001	0.376**
S Cr	0.000	0.399**
e GFR	0.000	-0.463**

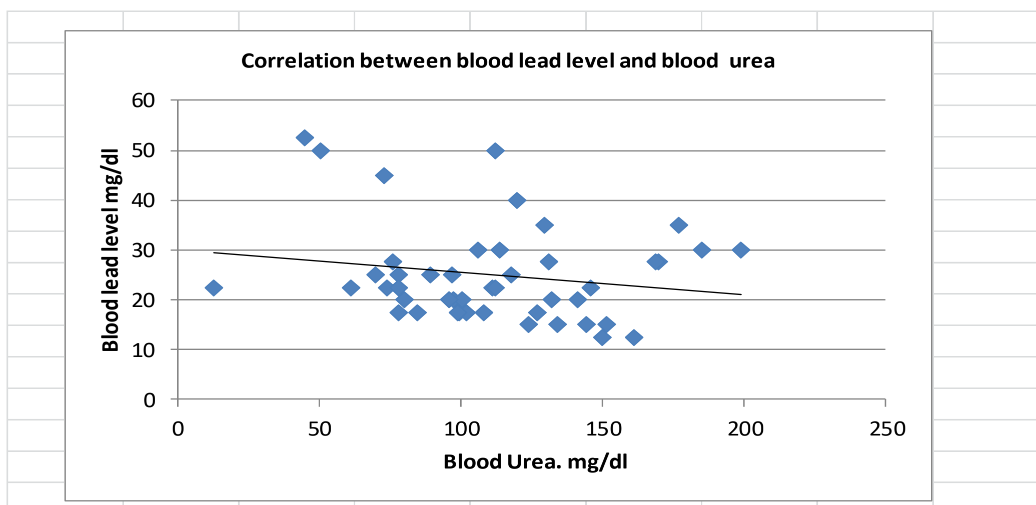

Figure 4 :Correlation between *blood lead level* and blood urea

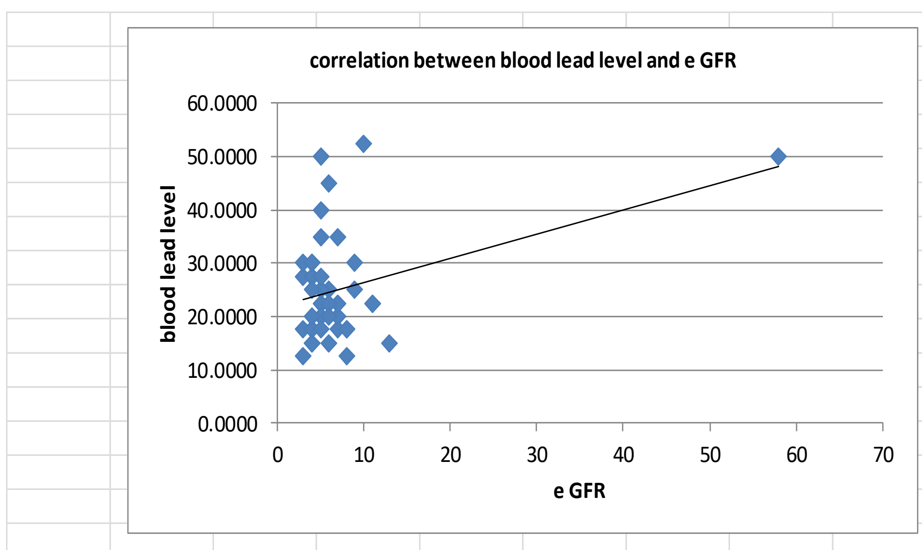

Figure 5 :Correlation between *blood lead level* and e GFR

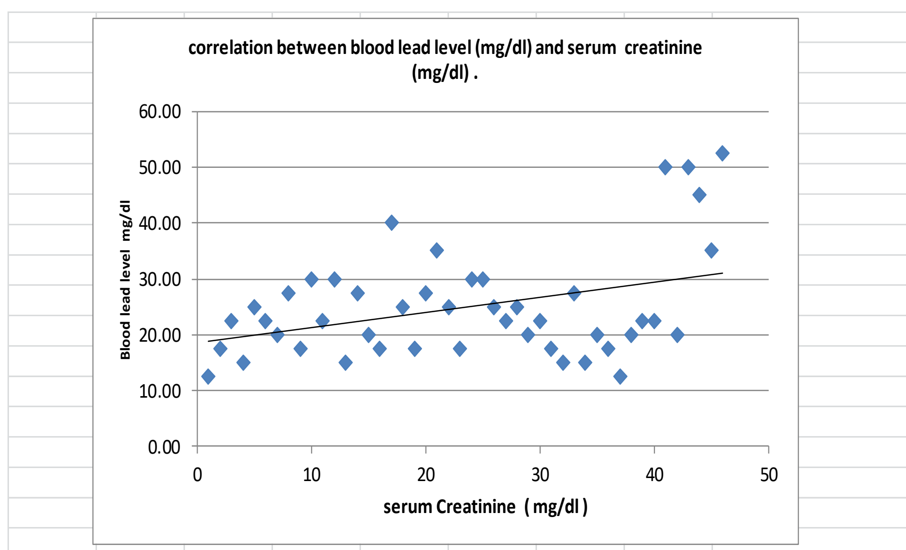

Figure 6 :Correlation between *blood lead level* and serum creatinine

The results of this study it's agree with other studies that have found blood lead level and linked to higher serum creatinine , urea , lower e GFR and progression of CKD 11–13 .

Discussion

Pb is common heavy metal toxins found in the environment. Pb exposure can occur through gasoline,food contamination during processing, and contamination of air,soil,and water in regions near old mines or garages 4,6. These metals have biological half-lives of several decades. Because of the extended half-lives, sustained low-level exposure can create excessive accumulation in specific

organs, particularly the kidney, which can cause physiological dysfunction 3. In cross-sectional and prospective analyses, previous epidemiologic research in vulnerable adult populations, such as those with CKD or hypertension, found that low-level ambient lead exposure was inversely linked with kidney function. Even in the absence of additional comorbidities, lead exposure at levels prevalent in industrialized nations is related with worse kidney function 14. High-level lead exposure damages the proximal tubule in the kidney, and chronic lead exposure is a known cause of kidney interstitial fibrosis, probably due to lead-induced oxidative stress 15.

In a national survey in the United States, cadmium and lead concentrations in red blood cells were found to lower eGFR and increase albuminuria 16. When co-exposed to low levels of cadmium and lead, an epidemiologic research of 14,778 US people (20 years of age) found a combined effect of albuminuria and lowered eGFR 17. Based on our knowledge, this study was the first in Iraq that found a high levels of lead in blood lead to increase risk of CKD by increase level in urea and creatinine with decrease in the glomerular filtration rate and it was recommend to study the combined effect of lead and cadmium in blood of patients with CKD and compared with healthy control .

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