Oxidant-Antioxidant Status and Chronic Kidney Disease Related to Lead Exposure in a Sample of Iraqi Population

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Abstract

Numerous disease processes, such as chronic kidney disease linked to lead exposure, depend heavily on oxidative stress. This study examined the connection between antioxidant activities and elemental lead in 45 individuals with CKD with the goal of identifying malondialdehyde (MDA) as a marker of lipid peroxide. Subjects and Method: The study included 77 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 2021 to May 2022 and blood lead levels and selenium levels were estimated using atomic absorption, biochemical parameters were measured weight calculated for body mass index divided by height squared in meters, malondialdehyde was determined by competitive ELISA Technique, Where total antioxidant capacity was estimated by colorimetric methods using Spectrophotometer from Genway company. Results: In addition to the biomarkers, such as malondialdehyde, which was significantly higher in the patients compared to the healthy group, there was a significant decrease in the glomerular filtration rate, total antioxidants capacity, and selenium levels in the patients compared to the control group. The mean blood lead levels in the group of chronic kidney disease patients were significantly higher than in the control group ($p \leq 0.01$) as well. Additionally, we discovered a substantial negative link between blood lead levels and glomerular filtration rate (GFR), TAC, and concentration of selenium (-0.463**; -0.722**; -0.559**) respectively, as well as a significant positive correlation between blood lead levels and MDA (0.546**).

Keyword: lead exposure, chronic kidney disease, oxidative stress.

1. Introduction

Renal function loss that occurs gradually and irreversibly over months or years is known as chronic kidney disease (CKD). A glomerular filtration rate (GFR) of around <60 mL/min/1.73 m2 is indicative of CKD. That is unusually low and declining marks various stages of failure (GFR) [1]. Numerous experimental investigations conducted over the past ten years have indicated that oxidative stress, which is a major factor in the development of chronic kidney disease complications, is prevalent in CKD patients [2]. The imbalance of free radicals and antioxidants is what is referred to as oxidative stress. Increased radical generation and/or low antioxidant levels have the ability to modify biomolecules chemically, resulting in a variety of structural and functional changes in the plasma of CKD patients [3].

Changes in the quantities of some important trace elements, like selenium(Se), can affect how much oxidative stress is present [4]. These minor elements work with antioxidant enzymes to catalyze the destruction of free radicals as cofactors or structural elements [5]. Free radicals are challenging to measure because of their short half-lives and reactive nature. Malondialdehyde (MDA) concentration, antioxidant enzymes and non-enzymatic are used as indirect methods of measuring the products of lipid peroxidation [6, 7]. MDA, a short-chain aldehyde, can be employed as a proximate indicator of the oxidation of polyunsaturated fatty acids [8]. The non-enzymatic antioxidant components increase the production of oxygen species, which inhibits the spread of free radical chain reactions and shields tissue from oxidative damage [9].

2. Materials and Methods

Study participants

46 CKD patients were included in the trial, and a specialized physician at Al-Hussein Teaching Hospital in the Holy Karbala Governorate made the diagnosis. The control group included 32 volunteers in good health. Each participant received a brief explanation of the study's objectives. The inquiry was carried out with formal permission. Since the age range of the two groups was (17-72) years, gender and age were matched.

Materials

Ammonium dihydrogen orthophosphate (20%), TitronX-100 (10%), Nitric acid (69%), Standard Selenium solution (1000ppm), Deionized water (DDW), Malondialdehyde (MDA) ELISA KIT, Total Antioxidant capacity (TAC) colorimetric assay KIT, Creatinine colorimetric assay KIT.

Collection of sample

To collect blood, disposable syringes and needles are utilized. Five milliliters of blood were drawn from the control group and the patients. They were split into two equal portions, one of which was immediately frozen after being put in a gel tube. The other half was

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centrifuged at 4500 x g for 10 minutes after allowing the blood samples to coagulate. In Eppendorf tubes, the sera are fractionated and separated before being 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) =weight (kg)/height (m2)
Underweight ≤18.5 (kg/m2)
Normal weight between18.5-24.9(kg/m2)
Overweight between 25-29.9 (kg/m2)
Obese ≥30(kg/m2) [10].

Biochemical analyses

MDA levels was determined using competitive ELISA Technique, UV-Vis Spectrophotometer (JENWAY, 7315) was used to determine TAC capacity by colorimetric method, Blood Selenium level andblood lead level were determined using SHIMADZU model AA-6300 Flameless atomic absorption spectrophotometer, The sample were prepared by mixing 100µL of whole blood with 900µL matrix modifier(in a 100ml volumetric flask, 5ml of 10% TritonX-100, 1ml of NH4H2PO4, and 4 drops of 69% HNO3 were mixed and diluted to volume with deionized water) , and serum creatinine was measurement by using colorimetric method by spectrophotometer (JENWAY, 7315).

Statistical analysis

The study's data were examined using the Statistical Package for the Social Sciences (SPSS) model 21 statistic tool. It was created with the intention of making comparisons and highlighting key distinctions. When p ≤ 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.

3. Results and Discussion

Table 1: Relationships between patients with chronic renal disease and healthy controls for several biochemical markers

Parameters	Patient group N=45 Mean±SD	Control group N=32 Mean±SD	P-value
Age (years)	47.40±12.63	44.59±13.41	NS
BIM (kg/m2)	26.95±6.98	27.39±5.05	NS
e GFR(ml/min/1.73m2)	7.09±8.10	82.78±21.87	HS
MDA (ng/ml)	13.97±1.95	6.55±4.08	HS
TAC (U/ml)	8.75±2.26	15.36±2.93	HS
Conc. Se (mg/dl)	5.00±0.92	14.19±1.23	HS
BLL (mg/dl)	24.38±9.06	14.14±4.04	HS

BIM: Body Mass Index; e GFR: Estimated Glomerular Filtration Rate; MAD: Aalondialdehyde; TAC: Total Antioxidant Capacity; Conc. Se; Concentration of Selenium; BLL; Blood Lead Level; NS: t-test P-value≥0.05; S: P-value≤0.05; HS: P-value≤0.01.

According to the presented data the mean of BLL (24.38±1.35) (14.14±0.71) patients and control groups respectively which is significantly increased in patients group of CKD (P<0.01). And this result agreed with the results of a study that found the kidneys excrete roughly 75% of all lead in a person with normal renal function, while the rest is removed through the gastrointestinal tract. Lead poisoning, on the other hand, can arise when a person's ability to remove the metal is exceeded while , another study it showed that Anemia, renal failure, and brain impairment are all clinical symptoms of lead toxicity that can be assessed clinically and followed up with lab tests [11]. Results of current study was found e GFR (7.09±8.10) ;(82.78±21.87) for patients and control groups respectively were significantly decreased in CKD than in control group (p<0.001) this result agrees with study of Gerhardsson et al that found when Chronic exposure to high lead concentrations damages the glomerulus of the kidney, causing it to lose its capacity to selectively filter high molecular weight proteins. High molecular weight proteins like albumin and macroglobulin are excreted more often in the urine as a result of this [12]. According to results in table 1 there was statistically non-significant changes in (age and BMI) means values between the normal control group and the patients group of CKD this results agrees with study.

In the presented data explained by figure 1 showed the mean of e GFR (ml/min/1.73m2) decreased in CKD patient than control group , while figure 2 showed the mean levels of BLL (mg/dl) increased in CKD patients group than control group.

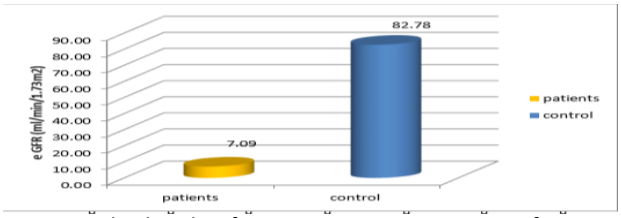

Fig 1: the levels of e GFR in patients group of CKD versus controls subject

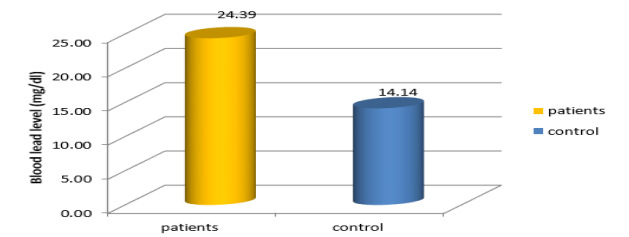

Fig 2: the levels of BLL in patients group of CKD versus controls subject

According to results in table 3.1 The mean of MDA (13.97±1.95);(6.55±4.08) in patients and control groups respectively which is significantly increased in patients

group of CKD when compared with healthy control (P<0.001) and this result agreed with the results of a study by Patil and et al who found the serum MDA content was significantly increased (P<0.001) and the activities of antioxidant enzymes were significantly reduced (P<0.001) in battery manufacturing workers [13].

The results of TAC and conc. Se highly significant decreased in patients with CKD when compared with healthy control, this agreed with the result of other studies that found Pb-induced abnormalities in the antioxidant defense system are to blame for the increased amounts of ROS. Pb decreases the activity of antioxidant enzymes TAC [14, 15]. And it's agreed with the result of a study by Wu and ET. Al who found the red blood cell lead and cadmium were significantly correlated with the increased ROS for CKD. In contrast, the levels of plasma selenium were negatively related to the ROS of CKD [16].

Many epidemiological and animal research have revealed that Pb can generate oxidative stress and alter numerous enzymatic and non-enzymatic components of antioxidant defense. Pb's potential to generate oxidative stress in the blood could be due to a number of ways. Pb, like many other hazardous metals, binds to enzymes' functional –SH groups, rendering them nonfunctional and suppressing their activity by generates the production of H2O2, O2, OH and ROS [17, 18] . The ability of Pb to replace elements that serve as important co-factors of these enzymes can cause increases in their activity as a result of increased ROS production, while their suppression can be explained by the ability of Pb to replace elements that serve as important co-factors of these enzymes In the presented data explained by figure 3 showed the mean of MDA conc. (ng/ml) increased in CKD patient than control group , and so in the case for the mean levels of Se (mg/dl) decreased in CKD patient than control group as shown in the figure 4.

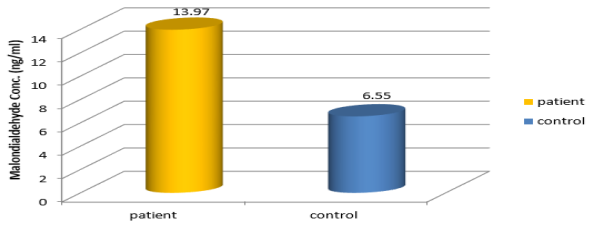

Fig 3: The conc. of MDA in patients of CKD versus control subject

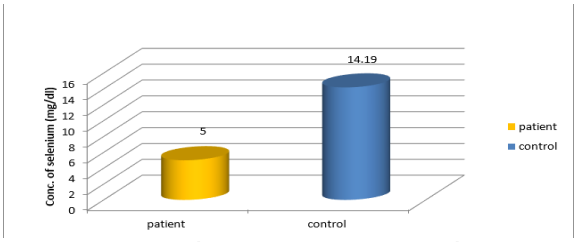

Fig 4: The conc. of selenium in patients of CKD versus control subject

Through this study, as shown below in table 2, we found there is a negative correlation between BLL and e GFR P<0.001. This results agreed with studies [19, 20].

Table 3.2: Correlation between BLL and other clinical characteristics.

Clinical parameters	BLL	
	r	P-value
e GFR	-0.463**	0.000
MDA	0.546**	0.000
TAC	-0.722**	0.000
C Se	-0.559**	0.000

E GFR: Estimated Glomerular Filtration Rate; MDA: Malondialdehyde; TAC: Total Antioxidant Capacity; C Se: concentration of Selenium.
R: Pearson's correlation coefficient *-significant correlation P≤0.05; **-highly significant P<0.01.

As well as, there was a positive correlation between BLL and MDA figure 5 this result agreed with studies by [21-23].

BLL correlated negatively with TAC and selenium conc. P<0.001 as shown in figurer 6. This results agreed with other studies [24, 25].

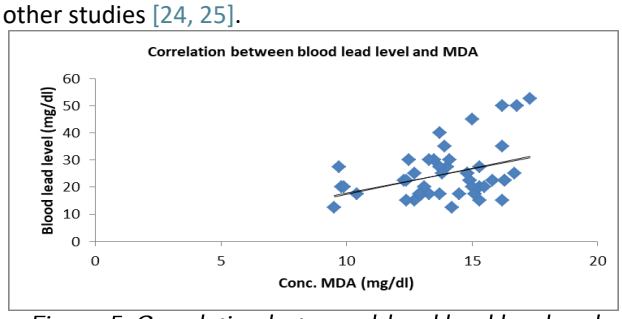

Figure 5: Correlation between blood lead level and malondialdehyde

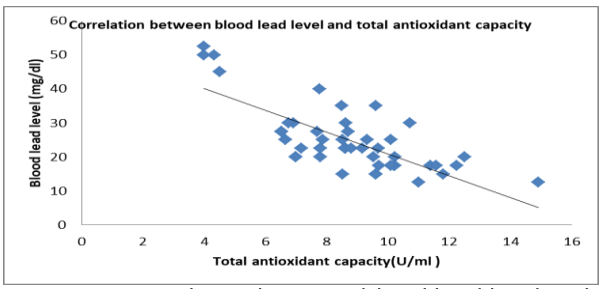

Figure 6: Correlation between blood lead level and total antioxidant capacity

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