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Measuring the level of some trace elements (Zinc, Iron, Lead, Cadmium and Copper) in the serum of acute kidney injury patients in Nineveh Governorate

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Abstract:

Background: Evaluation of the level of trace minerals in blood serum is one of the important things that can give us evidence of acute kidney injury, as the high concentrations of some trace minerals such as (Iron, lead, Cadmium, and Copper) and low concentrations of other minerals such as (zinc) in the blood serum are considered one of the Evidence of acute kidney injury, **Objective:** is to try to Prove that increasing the Concentrations of Some trace minerals can Cause nephrotoxicity and acute kidney failure, while their Presence in normal proportions in blood serum is beneficial to the human body as antioxidants or Cofactor. **Methods and Material:** This cross-sectional study was conducted in (Ibn Sina, Al-Salam, and Al-Jumhuri) Teaching Hospitals and the Central Blood Bank in Mosul, Iraq. Between the period (May 2022 - February 2023), where the study included 124 blood samples collected from men and women who suffer from acute Kidney injury and 108 blood samples collected from control groups, whose ages ranged from (≤35-≥56 years). The levels of Iron, Lead, Cadmium, Zinc, and Copper were determined in the blood serum of both acute kidney injury patients and the control group by atomic absorption spectroscopy technique. **Results:** The results indicated a significant increase in the level of (Iron, Lead, Cadmium and Copper) at ($P \leq 0.05$) compared to the control group, while a significant decrease in the level of Zinc at the probability level ($p \leq 0.05$) compared to the control group. **Conclusion:** We conclude, through our study, that the decrease in the concentration of Zinc in acute kidney injury patients is matched by an increase in the concentration of Copper on the other hand, while an increase in the concentration of minerals (Iron, Lead and Cadmium) occurs in acute kidney injury patients as a result of the accumulation of these minerals in the kidney after reaching toxicity.

Key-words: Acute Kidney Injury, Cadmium, Copper, Iron, Lead, Trace minerals Zinc,

Introduction:

Heavy minerals are defined as those natural minerals in the earth's crust and in living tissue [1]. minerals are of great importance to the human body, as they build cells, send signals

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to nerves and muscles, and help in the vital reactions that take place in the body, in addition to helping body to produce energy. A number of these heavy metals, like Zinc and Copper, are required and crucial to sustain the metabolic process in the human body, in terms of considerable consumption (their existence in high quantities in the body) that is harmful and toxic to the body and results in what is known as "heavy metal poisoning" [1]. For example, drinking water is polluted with Lead because it passes through pipes made of Lead, in addition to the presence of these metals at high quantities in the air near the sources of their distribution, or received through the food chain, the risk of these minerals is reflected by their bio-accumulation inside the human body, some trace minerals have toxic biological effects, while others are beneficial to humans and the environment, depending on their sources and formation oxidation processes [2], at a faster rate than that they are excreted through the metabolism process. Metabolism embodies were the physical and chemical process in the body that create and use energy [1]. The basic process of trace mineral poisoning is the generation of reactive oxygen species, which causes oxidative damage and has a negative impact on health. As a result, water polluted with trace minerals causes high rates of sickness and mortality around the world [3]. Many of the trace minerals have immediate and chronic harmful effects on many organs in the body, including the kidneys, digestive weakness, nervous system abnormalities, skin lesions, and vascular damage. Haematological problems, immune system malfunction, cell abnormalities, and cancer are among the numerous examples of consequences of the harmful effects of trace minerals, and concurrent exposure to two or more minerals often results in cumulative effects [4].

Iron is considered an essential component of blood proteins responsible for a large number of vital functions of the cell, through its role in the processes of transporting oxygen in the respiratory chain [5]. Despite this, excessive iron is hazardous to tissue cells, especially kidneys because it is capable of causing oxidative stress and causing malfunction [6]. In mitochondrial functions, promoting inflammation and cell death it supports the progression of acute to chronic kidney impairment [6]. Transferrin is the protein responsible for transporting Iron in the blood, while ferritin is the protein responsible for strong it in the liver and tissues [7].

Lead is a toxic mineral that it appears in the earth's crust in its natural form, and that the extensive usage of it in industrial and recycling purposes has Led to environmental Pollution, human exposure to it, and health problems [8]. It is not known that there is a safe level of lead in the blood, as Low Concentration of it led to leaning Problems in children [9]. Among the disorders caused by lead in adults is high blood pressure, atrophy of brain cells, disorders in the nervous system, Kidney and stomach problems, as it damages body system [10, 11].

Cadmium, A heavy toxic, and environmentally dangerous mineral that has wide uses in industry, especially dyes, batteries, and tobacco, due to its long half-life, people who are

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opposed to Cadmium a accumulate in their body organs, in clouding the liver, pancreas, lung and kidney [12]. Cadmium has carcinogenic effects because it is absorbed through the skin and the respiratory tract [12, 13]. The kidneys are more susceptible to Cadmium toxicity [14], as Cadmium binds to the protein metalloid thionine, which is easily filtered by the glomerulus and absorbed by the proximal tubules [15], resulting in an imbalance in kidney function.

Zinc is an essential and second most frequent divalent cation in the human body (2-4 gm); It is mostly located in the bones (29%) and in the skeletal muscles by (57%) [16]. Normal Zinc homeostasis is regulated by the actions of transporters such as Zinc-binding protein. Which controls the level of Zinc both inside and outside the cell, It functions as a cofactor for more than 300 enzymes [17]. For example, Superoxide dismutase (SOD), tyrosyl which is considered an enzymatic antioxidant [18]. Plasma Zinc levels decrease gradually with a reduction in the glomerular filtration rate (GFR) [19] as a result of acute renal insufficiency [20] and this in turn is associated with a reduction in serum Zinc levels [21].

Copper is one of the minerals of great importance to humans, due to the many benefits it provides to public health, which requires attention to maintain the balance of natural copper Levels in the body [22]. Copper is present in the body at a rate ranging between (75-100) µg/dl, and it ranks third after iron and Zinc, in the liver and its concentration is lower in the heart, brain, muscles, and kidneys [23]. Where copper participates in many enzymatic reactions, being as cofactor that the body needs in the development of tissues that form bones, joints, and connective tissues [23], and Copper has a crucial part in the synthesis of collagen, maintaining the health of the heart and blood vessels, reducing free radicals, enhancing immunity, and energy production. Iron absorption however, when its rate is higher than the normal limit, more than (140) µg/dl, it will lead to Copper poisoning, causing vomiting and diarrhea, and leading to kidney damage, including acute kidney failure, decreased urine production [24]. The reason is anemia as a result of the breakdown of red blood cells [25]. Also, an increase or decrease in the blood, both of which affect the work of the brain, and these imbalances have been associated with Alzheimer's and Wilson's diseases [26, 27], our aim during this study is to try to prove that increasing the concentrations of some trace minerals can cause nephrotoxicity and acute kidney failure, while their presence in normal proportions in blood serum is beneficial to the human body as antioxidants of cofactor.

Materials and methods:

during the period (May 2022- February 2023) from (Ibn Sina, Al-Salam, and Al-Jumhori) teaching hospitals and the central blood bank in the city of Mosul, Iraq. This investigation was undertaken in the control laboratory/ College of Agriculture/ University of Mosul.

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Patients

The blood samples collected during this study were (232) blood samples from men and women, where the number of blood samples Collected for the group of acute kidney injury Patients was (124), while the samples number of the control group was (108) whose ages ranged within the range (≤35-≥56 years). Ten ml of blood was drawn from each group of acute kidney injury patients and the control group using gel tubes, which were placed in the refrigerator at 4C° for 15 minutes, where the serum was separated and kept in clean and tight tubes covered at -20C° until use.

Exclusion criteria:

The collected samples are free from decomposition and turbidity to avoid any interference with the results, as well as free from viral hepatitis.

Methods:

Concentration of (Iron, Lead, Cadmium, Zinc, and Copper) was estimated, in serum sample using the Atomic Absorption Spectrometry (AAS) technique, due to the specificity, sensitivity and accuracy of this technique in estimating the small quantities of minerals in biological models [28].

1. Determination of Iron concentration in the serum

The concentration of serum Iron is determined using the standard curve prepared as shown in Figure (1).

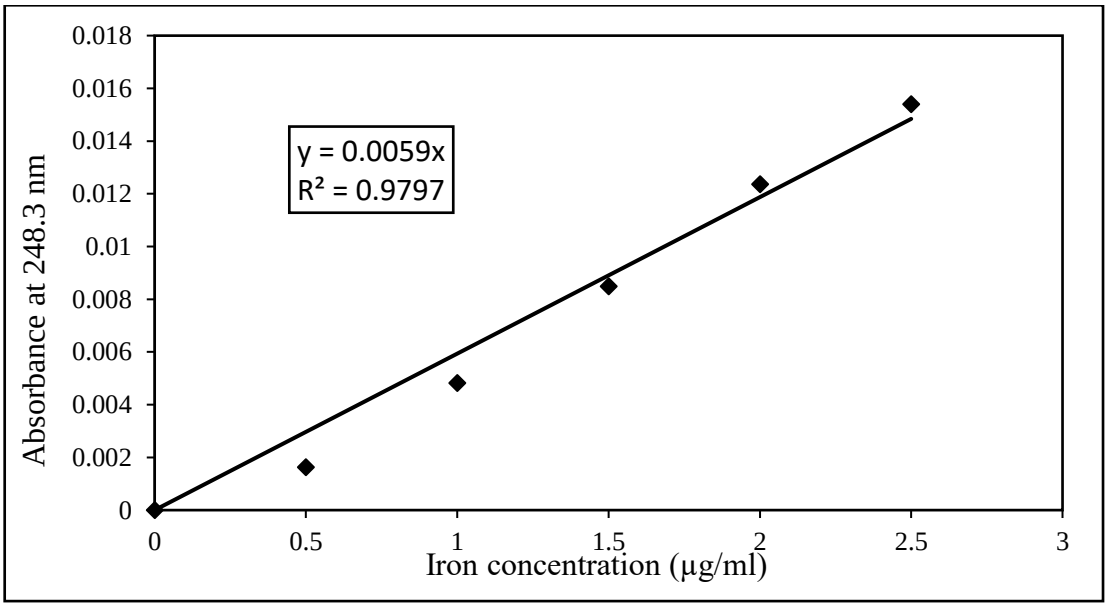

Fig. (1) Standard curve of Iron

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2. Determination of Lead concentration in the serum

The concentration of serum Lead is determined using the standard curve prepared as shown in Figure (2).

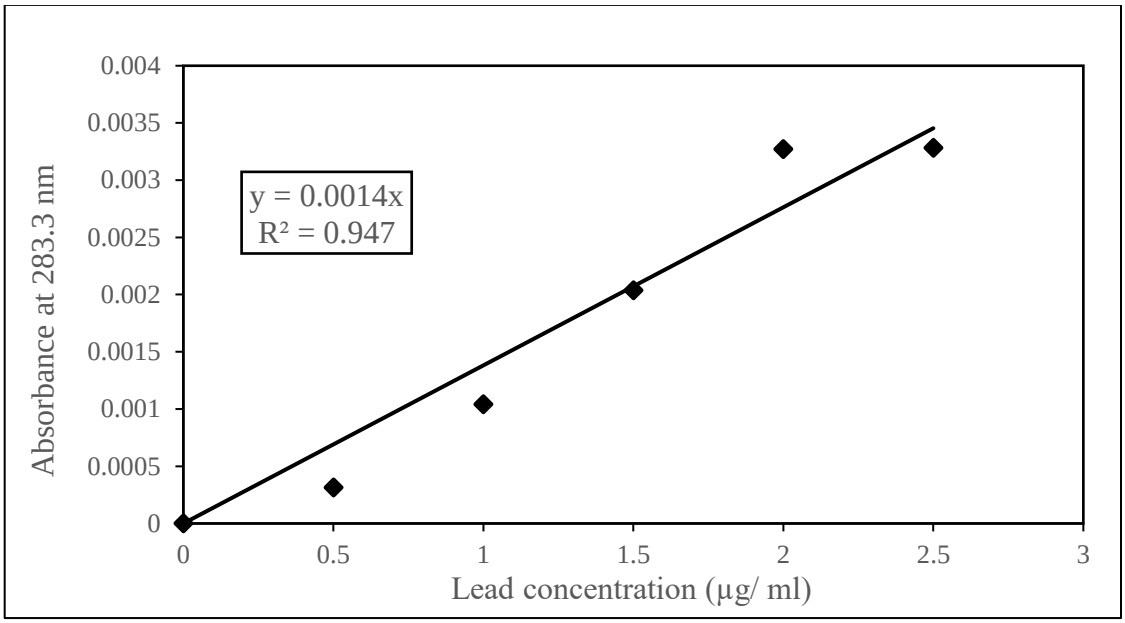

Fig. (2) Standard curve of Lead

3. Determination of Cadmium concentration in the serum

The concentration of serum Cadmium is determined using the standard curve prepared as shown in Figure (3).

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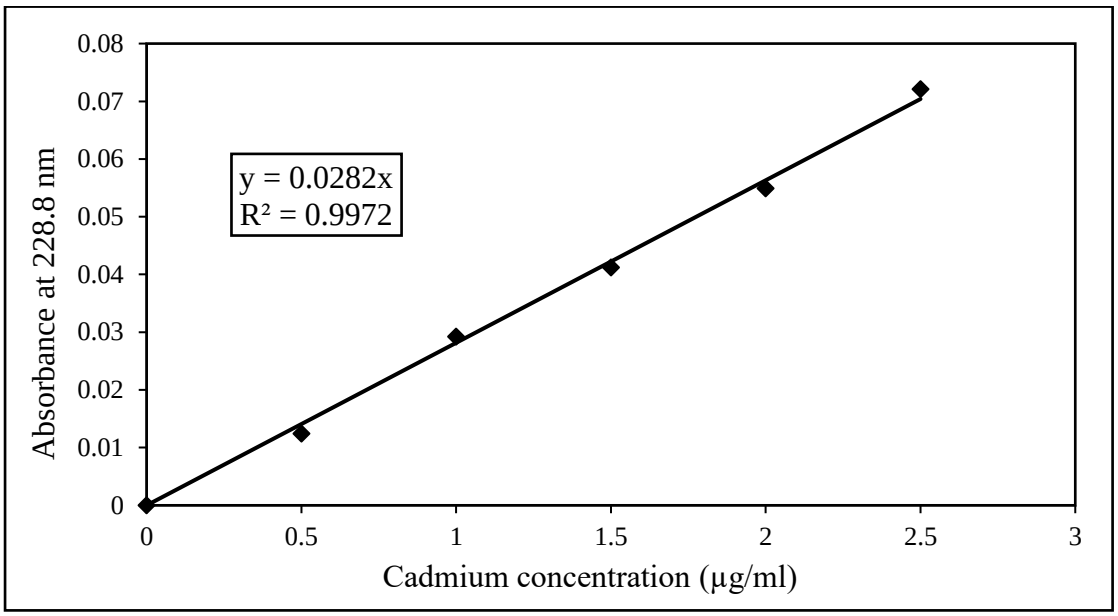

Fig. (3) Standard curve of Cadmium

4. Determination of Zinc concentration in the serum

The concentration of serum Zinc is determined using the standard curve prepared as shown in figure (4).

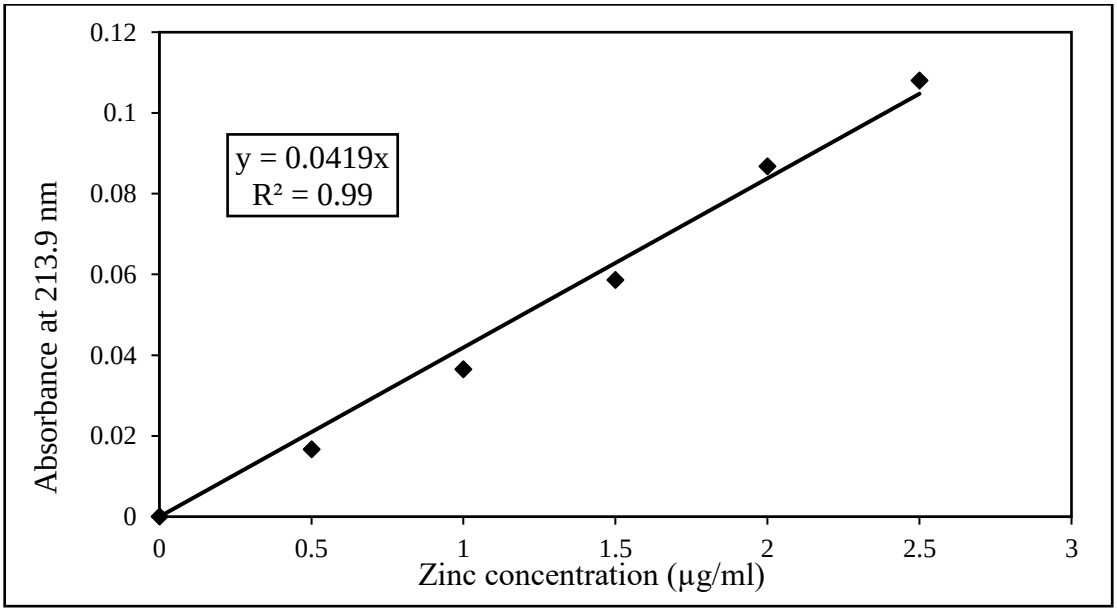

Fig. (4) Standard curve of Zinc

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5. **Determination of Copper concentration in the serum**

The concentration of serum Copper is determined using the standard curve as shown in figure (5).

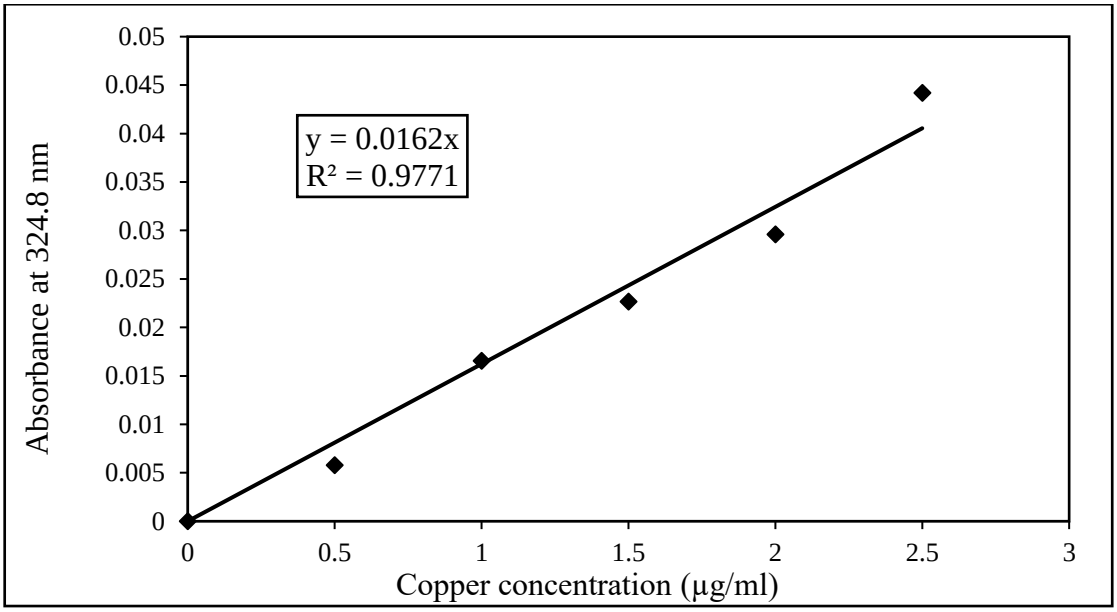

Fig. (5) Standard curve of Copper

Statistical analysis:

The SPSS statistically, as it was used through the independent t-test analysis program to analyze the results of studies that include two variables, While the completely randomized Desing (CRD) was used to analyze the variance of traits that included more than two variables, and that through one way analysis of Variance, as well as extracting the Correlation Coefficient for some of the School Characteristics, and the correlation factor, as well as extracting the means, as well as extracting the Standard error, while using Duncan's multiple range teste in order to find the difference between means and Significant reduction score $p \leq 0.05$ [29].

Ethical approval:

The study was done in accordance with ethical standards derived from the Declaration of Helsinki. Before taking the sample, the patients provided verbal and analytical approval. The study protocol details and permission form were evaluated and authorised by a local ethics committee in accordance with document number 14459 (containing the number and date of (26/4/2022).

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Results

Table (1) indicates that there was a significant decrease in Zinc concentration at the probability (P≤0.05) in acute kidney injury patients (0.091 ± 0.004) µg/dl when compared with the control group (0.83±0.0169) µg/dl, as the level of Zinc is lower in patients with acute kidney injury, we also note that the results in Tablet (1) showed a significant increase in Iron concentration at probability (P≤0.05) in serum acute kidney injury patients (0.943 ± 0.024) µg/dl.

Table (1) Level of trace minerals measured in serum of acute kidney injury patients compared to the control group

Concentration of trace minerals µg/dl	Control group N=108		Patients group N=124		P-Value
	Mean	±SE	Mean	±SE	
Zinc	0.813	0.0169	0.091*	0.004	P≤0.05
Iron	0.588	0.014	0.943*	0.024	P≤0.05
Lead	0.407	0.012	1.461*	0.021	P≤0.05
Cadmium	0.247	0.011	0.584*	0.020	P≤0.05
Copper	0.698	0.014	1.290*	0.023	P≤0.05

*The difference is significant horizontally at P≤0.05.

Table (1) also shows that there was a significant increase in Lead concentration (1.461± 0.021) µg/dl at (P≤ 0.05) and there was a significant increase in the level of Cadmium (0.584 ± 0.020) µg/dl, at (P≤ 0.05), we also note that there was a significant increase in the level of Copper in acute kidney injury patients (1.290±0.023)µg/dl at (P≤0.05).

Correlation between levels of (Zinc, Iron, Lead, Cadmium, and Copper) measured in serum of acute kidney injury patients compared to control group as shown in Table (2), it was studied by finding the linear Correlation Coefficient (Y).

Table (2) Correlation between trace minerals measured in serum patients and compered with control group

Concentration of trace minerals µg/dl	[Control group N=108]	[Patients group N=124]
	r-Value	P-Value
Zinc	-0.065**	0.506
Iron	0.346**	P≤0.05

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Lead	0.361**	P≤0.05
Cadmium	0.378**	P≤0.05
Copper	0.455**	P≤0.05

** The differences are significant horizontally between each two means at P≤0.05.

Significant differences horizontally at a level between each two averages are (P≤ 0.05) as shown in Table (2).

The effect of sex on the level of trace minerals measured in the serum of acute kidney injury patients as shown in the Table (3) and figure (6), which indicate that there was a significant decrease in the level of Zinc in males' patients compared to females' patients, and there is a significant increase in the level of each of the (Iron, Lead, Cadmium) in males patients compared with females patients.

Table (3) also shows a significant increase in the level of Copper in females patients compared to male patients

Table (3) The effect of sex on the level of trace minerals measured in serum of acute kidney injury patients

Concentration of trace minerals (µg/dl)	**Male N=62**		**Female N=62**		**P-Value**
	Mean	**±SE**	**Meam**	**±SE**	
Zinc	0.11*	0.054	0.068	0.049	P≤0.05
Iron	0.98*	0.031	0.90	0.037	P≤0.05
Lead	1.52*	0.028	1.40	0.031	P≤0.05
Cadmium	0.63*	0.029	0.54	0.028	P≤0.05
Copper	1.24*	0.33	1.34	0.31	P≤0.05

*The difference is significant horizontally at P≤0.05.

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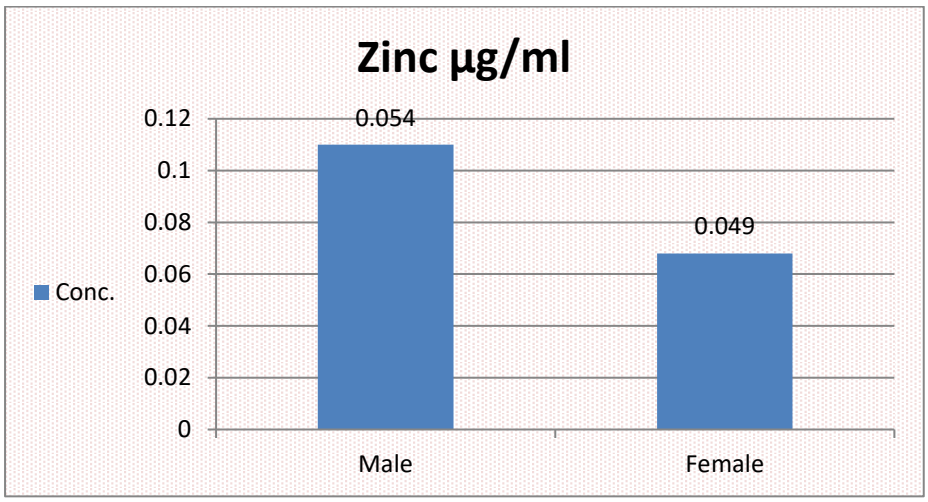

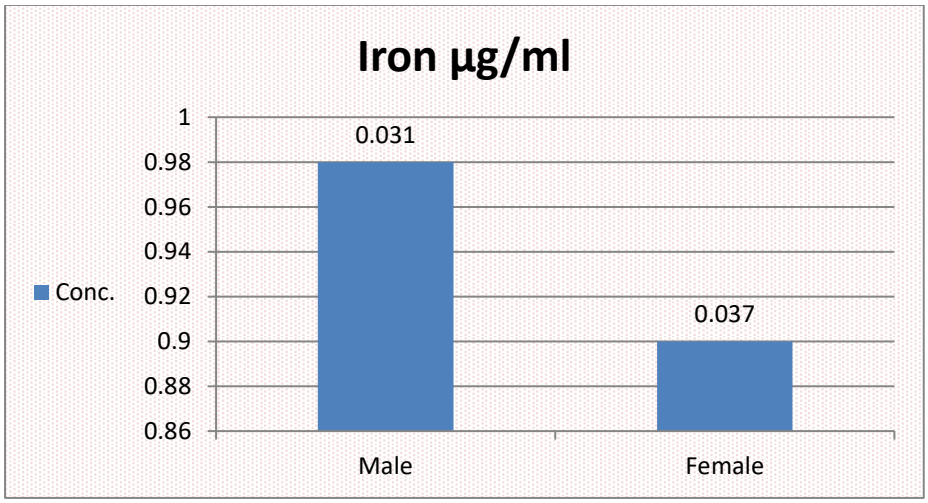

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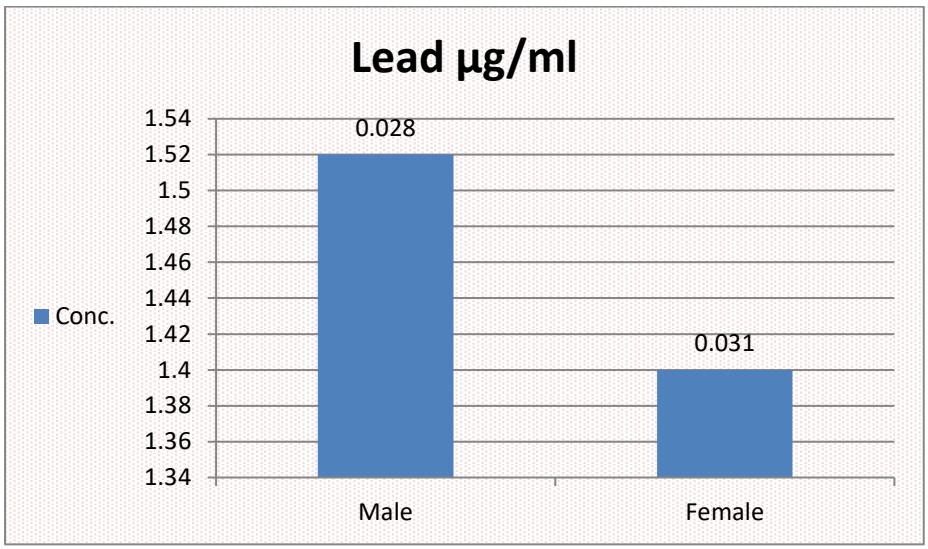

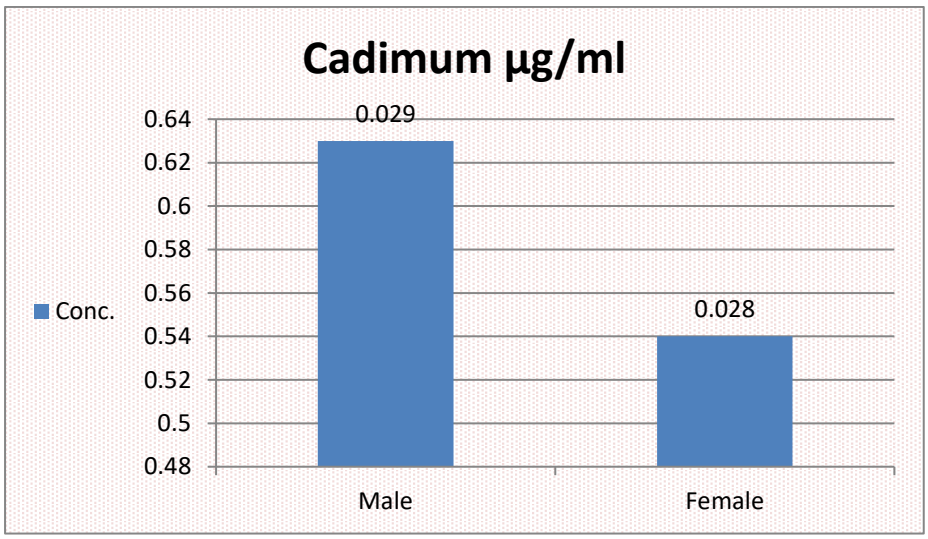

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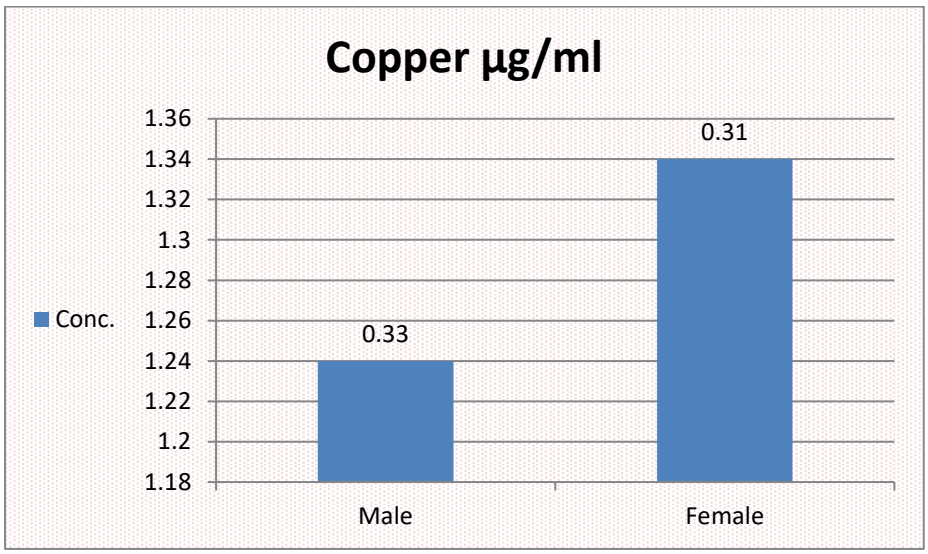

Figure (6): Effect of sex on the level of trace minerals in serum acute kidney injury patients

Discussions

The reasons for the low level of Zinc in the serum of acute kidney injury patients are not fully understood, but it may be the lack of Zinc intake through food, and the use of mineral medicines prescribed by doctors may be one of the reasons, as well as taking Zinc supplements, and eating a certain diet as an attempt to prevent the development of kidney failure, in addition to hypoalbuminemia, is consistent with what the authors stated [30], reduced Zinc absorption in the gastrointestinal tract, increased Zinc excretion in the urine, and redistribution in the intracellular fluid may change the concentration of Zinc in the extracellular fluid and hence impact the total Zinc storage in the body of patients with renal failure [31].

This can explain the cause for the increase in the amount of Iron at ($P \leq 0.05$), in acute kidney injury patients, as stated by the authors, increased glomerular filtration of iron-carrying proteins such as haemoglobin, transferrin, and gelatinase-associated lipoxin (NGAL) exposes the kidney tubules to greater concentrations of iron [32].

The reason for increase the level of Lead at ($P \leq 0.05$) in acute kidney injury patients is often due to its easy of absorption through the intestines as well as the lungs when exposed to Lead pollutants, from the circulatory system. Where Lead is distributed in various tissues, including the kidney, which causes toxic damage to cells, resulting in a decrease in kidney function among individuals especially in middle-aged and elderly people, as indicated by the authors [33].

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The kidney is one of the primary organs for Cadmium accumulation, and thus it is more sensitive to Cadmium toxicity, since the proximal tubule is the main target of Cadmium toxicity, which can be absorbed by the human body through the digestive system or through the skin, as exposure to Cadmium occurs through three main sources (which Converts Cadmium into Cadmium oxides, which leads to absorption more effective through the lung), Exposure during work in industries producing nickel-CD batteries, paints, and dyes, as well as through phosphate names, the use of which led to an increase in the Cadmium content in the soil, in addition to seafood contaminated with Cadmium through water, and this is what indicated to the authors Iu Yan, and Agarwal, 2022, it's shows that there was a significant increase in Cadmium concentration at ($P \leq 0.05$) [34].

In contrast to what we found of a decrease in the level of Zinc, experts also believe that high many pathological conditions [35]. Also, excessive intake of Copper from food may lead to Copper deposition in the kidney and induce nephrotoxicity, characterised by proximal tubule necrosis as a result of oxidative stress and cell damage, which leads to a worsening of kidney function, and this is what the authors indicated Ay, A. *et al.*, 2021 and they show the reason of increase in level of Copper in acute kidney patients at ($P \leq 0.05$) [36].

Results in Table (2) indicate that there was decrease in Zinc concentration in acute kidney injury patients due to ischemia, as mineral accumulates in proximal tubule cells and is released following acute kidney damage, compared to the control group [37]. While we notice a significant increase in minerals (Iron, Lead, Cadmium, and Copper) in acute kidney injury patients, compared to the control group [33-36-38].

Conclusion

We conclude, through our study, that the decrease of Zinc concentration in acute kidney injury patients was matched by an increase in Copper concentration on the other hand, while an increase in the concentration of minerals (Iron, Lead and Cadmium) occurs in acute kidney injury patients as a result of the accumulation of these minerals in the kidney after reaching toxicity.

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