Original Article

Changes in the Level of Zinc and Copper and Some Biochemical Parameters in Patients with Chronic Kidney Failure

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Abstract

Background: Chronic kidney failure (CRF) is characterized by a progressive loss of functional status over weeks or months, which may result in one of the illness's recognized consequences, such as cardiovascular disease, chest pain, or anemia. CRF has been generally understood as a worldwide public health problem and a big factor to death and morbidity during the previous decade. **Methods:** Determination of zinc and copper, urea, creatinine, total protein, globulin, alanine aminotransferase (ALT), albumin, aspartate aminotransferase (AST), alkaline phosphatase (ALP), and lactate dehydrogenase (LDH) in (CRF) Iraqi patients. This study included (40) patients and (38) healthy subjects as control. Samples were collected from January to April (2022). The biochemical parameters were determined using spectrophotometrically, but zinc and copper were determined by atomic absorption spectrophotometer. **Results:** Copper, urea, creatinine, ALP, AST, ALT, and LDH were significantly higher in CRF patients, whereas zinc, total protein, albumin, and globulin were lower in CRF patients as compared with control. The research also concerned study the relation between sex (male and female) and biochemical parameters which showed significant differences in comparison male of patients with males of control, yet globulin showed nonsignificant differences. While patients and control females showed nonsignificant differences. **Conclusions:** LDH in CRF patients might be used as a biomarker to detect renal dysfunction in dialysis patients at an early point, and blood serum Zn deficit in CRF. Furthermore, a relationship among Zn and albumin amounts was discovered. As a result, Zn and copper in CRF, particularly hypoalbuminemia, must be frequently evaluated and adjusted.

Keywords: Alanine aminotransferase, aspartate aminotransferase, CKF, copper, lactate dehydrogenase, zinc

Introduction

Chronic kidney illness or failure (CRF) is characterized by a progressive loss of functional status over weeks or months, which may result in one of the illness's recognized consequences, such as cardiovascular disease, sharp chest pain, or anemia.[1] CRF has been generally understood as a worldwide public health problem and a big factor to death and morbidity during the previous decade.[2,3] End-stage kidney disease is renowned to associated with CRF.[4] Hemodialysis is a way of removing waste from the body. When the kidneys are in renal disease, the kidney transplant device eliminates waste such as creatine, ammonia, and plasma liquid.[5]

Zinc (Zn) is a trace mineral that is engaged in a variety of physiological actions in the organism. It is necessary for cell viability, development, and multiplication, as well as the stimulation of 300 or even more enzyme.[6] As a building element of several proteins, also helps to a broad range of biological processes, include proteins contributory in DNA synthesis and signaling passage, alongside transcriptional.[1,2] Any disruptions in Zn balance may affect immunological function, development, perceptual, and metabolism.[4,7] Patients on hemofrequently acquire Zn insufficiency as a result of Zn loss after hemodialysis, insufficient dietary intake, and malabsorption. Earlier research found that Zn well-being and mental health are the responsiveness to erythropoietin treatment in dialysis patients.[8] Zn therapy 15–24 pathological alterations associated with renal loss and proximal tubular disease in diabetic rats.[9] A prior clinical trial found that Zn

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supplementation reduced urine albumin production in type 2 diabetic patients with nephropathy.[9] These findings imply that the Zn supplement may prevent the development of renal impairment.

Albumin comprises the most prevalent plasma volume protein generated in the brain, accounting for a sizeable portion of all plasma. It accounts for about 60% points of blood serum proteins and is predominantly generated by hepatocellular hepatocytes, with the exception of early in fetal development, where it is mainly synthesized by the yolk.[10,11]

High everyday copper consumption may produce metal deposition in the kidneys and induce renal toxicity, which is characterized by distal tube atrophy caused by oxidative stress and cellular damage and results in a loss in creatinine.[12] Nevertheless, the interaction among copper and renal illness is unidirectional, since aberrations in the balance of circulatory copper ions may emerge in individuals with chronic kidney impairment due to reduced renal excretion and alterations in protein digestion.[13] In fact, regulating plasma copper amounts in renal failure patients is critical for avoiding problems. Previous research has linked higher circulating copper levels to chronic renal illness.[14]

Progressive kidney diseases were selected because of their influence on essential minerals (Zn and copper) as well as physiological factors such as urea, creatine, protein content, protein, nucleate, alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH).[15,16] A huge proportion of individuals die from renal failure in most regions of the globe where dialysis or transplants are not accessible or are too costly. This makes research into serum biomarkers for soon (early) identification of kidney failure not only beneficial but also critical. Preventing CRF progression is an essential method for improving bad progression and avoiding a decline in quality of life. As a result, we undertook this investigation to determine if the laboratory tests investigated are risk factors for the emergence of CKF.

Methods

Reagents and methodology

The cathering of patient sample

This research comprised 78 blood specimens at Nineveh City Centers in Iraq, from January to April (2022). One plasma sample has been taken after all subjects provided informed permission. The samples were belonged to 40 sick and 38 normal men and women ranging in age between 30 and 57 years.

Ethical approval consideration

Before asking them to sign a written consent form, the subjects in this study were given a thorough explanation of the study's objectives. After that, a thorough questionnaire was used to collect the subjects' medical histories and other personal information. The ethical permission for this study was given by the Nineveh Health Department in Iraq on December 16, 2021, under reference number 167.

Criterion for inclusion and exclusion

Criterion for inclusion

This study included (40) patients ranging in their age between 30 and 65 years and (38) healthy subjects 30–57 years as control.

Criteria for exclusion

Participants outside the age range of 30–65 years old, as well as those with established pathologies including cancer, hepatitis, hypertension, or heart disease, were excluded from the study. The controls as well as the subjects were both exposed to the same exclusion criteria.

Specimen capture and keeping

Each participant underwent a 7-ml venous blood draw after an 8–12 h fast. Two milliliters of this blood was then dispersed into a plain vial and allowed to clot. To determine the total protein content, serum was drawn from the blood and centrifuged for 5 min at 3000 g/min. For additional estimations, 3 ml of venous blood was dispensed into an ethylenediaminetetraacetic acid container.

Measured the examined variables

Biolabo/France provided a kit for quantifying urea, albumin, total protein, ALP, AST, ALT, and LDH in human serum. They followed the operating manual for determining globulin, whereas albumin was calculated using the formula given by Iseki *et al*.[17]

The zinc and copper had been evaluated after diluting the blood serum to ion-free water at a ratio of 5:1 for each of the elements zinc and copper utilizing light waves of 213.9 and 324.8 nm, including both, but use an elemental analysis device of the type (Perkin Elmer 403 Atomic emission spectrometer). They were given standard curves based on the established stock solution for each element part.

Statistical evaluation

To eliminate input mistakes, data were coded into Excel Spreadsheets using customized Excel forms and analyzed using the Statistical SPSS package version 22 (IBM SPSS statistics, Armonk, New York, USA). The average and standard deviation were used to represent all values. To compare the averages of biochemical variables, the paired *t*-test was performed. When the possibility (P) was $P \leq 0.05$, the changes were judged significant.[18]

Results

In the present study, we found that the increase in plasma metals, ammonia, ALP, AST, ALT, and LDH tiers both in males and females at $P \leq 0.05$ in persistent renal insufficiency groups diagnosed to one's concurrent normal controls organizations, but a sharp reduction in zinc, protein content, total protein, as well as fibrinogen tiers in CKF patient populations, especially in comparison to normal control.

The average creatinine level was 5.34 mg/dL. The average urea level was 144.2 mg/dL. Their serum concentration LDH level was 456.2 IU/L, with a low serum LDH of 442.32 IU/L, and a high serum LDH of 470.08 IU/L. The mean serum total protein level was 5.4 g/dL, the mean ALT level was 22.72 IU/L, and the mean AST level was 29.32 IU/L [Table 1].

While the results shown in Tables 2 and 3 indicated a significant decrease in the level of zinc for males and females of illness by chronic offal letdown likened to the governor group for males and females at 0.0001. There is no significant difference in females with kidney deficiency. As for copper, its value in males is less than in the control group we notice an important decrease in the value of copper in male patients associated to females (0.0001). In addition, it is noted that the value of zinc and copper in males differs from females in the control group and that their values in females are less than in males.

There was also a connection among zinc and protein levels, findings showed that hypoalbuminemia may hasten the onset of CRF caused by zinc deficiency.

Table 1: Comparison of zinc and copper levels, as well as other biochemical variables, in the control and CKF groups

Biochemical variables	Mean±SD		*P*
	Control group (*n*=38)	Patients group (*n*=40)	
Age (year)	41.6±9.4	46.6±10.1	0.15
Zinc (µmol\L)	16.32±2.6	13.76±4.8	0.047
Copper (µmol\L)	15.03±3.4	24.7±6.2	0.0001
Urea (mg\dL)	26.99±3.1	144.2±9.1	0.0001
Creatinine (mg\dL)	0.99±0.07	5.34±0.17	0.0001
Total protein (g\dL)	6.93±0.49	5.4±0.33	0.0001
Albumin (g\dL)	4.07±0.14	3.42±0.13	0.0001
Globulin (g\dL)	2.85±0.02	1.98±0.06	0.0001
ALP (IU\L)	26.72±2.7	46.67±7.4	0.006
AST (IU\L)	12.12±1.7	29.32±2.7	0.001
ALT (IU\L)	9.33±0.9	22.72±1.11	0.0001
LDH (IU\L)	222.7±9.45	456.2±13.88	0.0001

The values are expressed as mean±SD. ALP: Alkaline phosphatase, AST: Aspartate transaminase, ALT: Alanine transaminase, LDH: Lactate dehydrogenase, SD: Standard deviation

Table 2: Biochemical variable levels in men were compared between the control group and the group of patients with chronic renal failure

Biochemical variables	Control group (*n*=20)	Patient group (*n*=20)	*P*
Zinc (µmol\L)	14.00±1.34	13.61±6.22	0.0001
Copper (µmol\L)	28.4±3.9	22.33±3.41	0.0001
Urea (mg\dL)	35.5±4.0	172.66±12.8	0.002
Creatinine (mg\dL)	3.53±0.099	6.55±0.55	0.0001
Total protein (g\dL)	5.7±0.31	5.2±0.39	0.003
Albumin (g\dL)	3.5±0.1	3.36±0.53	0.0001
Globulin (g\dL)	2.2±0.06	1.83±0.55	0.184
ALP (IU\L)	31.15±2.34	27.03±1.1	0.0001
AST (IU\L)	14.23±0.9	28.72±1.7	0.001
ALT (IU\L)	10.73±0.9	27.82±2.19	0.0001
LDH (IU\L)	242.72±8.15	488.2±23.81	0.0001

The morals are uttered as mean±SD. ALP: Alkaline phosphatase, AST: Aspartate transaminase, ALT: Alanine transaminase, LDH: Lactate dehydrogenase, SD: Standard deviation

Discussion

Renal disease is a serious public health concern across the globe, with just an increasing rate and incidence that promises to become a true pandemic.[19] Because the zinc fingers and homeobox transcriptionally family is widely expressed in pericytes, these factors have a role in renal illness.[17] Serum zinc levels tend to fall as CRF progresses and are higher in individuals on continuous hemodialysis.[8,9]

These results are consistent with what the researcher[20] stated the reason is attributed to the breakdown of renal tissue cells and the inability of the kidney to perform its function to remove toxic substances from urea and creatinine.[21] It may be due to the lack of zinc in the body, therefore, to the lack of total protein, albumin, and globulin that binds with them, as zinc plays an important role in building protein.[22] In addition, it is noted that the value of zinc and copper in males differs from females in the control group and this is consistent with what the researchers said[23] and that their value in females is less than in males, which agrees with the researchers.[24] In prior research, men had greater serum zinc concentrations than females.[25] Those data are related to the findings of our investigation. Furthermore, serum zinc deficit in renal patients has indeed been documented as a result of suffers due, tube reabsorption impairments, nephritis, and C-reactive insufficiency, which is involved in zinc intestine uptake.[26] Across both kids and adults, hypoxemia is frequent in CRF and is related with a rise in disease.[6,27]

The findings revealed that zinc deficiency is a risk factor for end-stage renal disease. The process behind the link among vitamin deficiency with renal impairment, though, remains unknown.[28] Several basic investigations have indicated that zinc is an oxidative stress regulator.[29,30] Zinc is a super oxidant cofactor with antioxidant capacity,[31] and it helps to reduce peroxidation. Furthermore, zinc deficiency has been linked to oxidative stress and kidney damage through the enzyme NAD+oxidase (NADPH).[32] A significant amount of research suggests that chronic damage is the common factor for the primary mechanisms implicated in kidney disease development.[31] In kidney illness, NADPH dehydrogenase has been recognized as a key cause of oxidative stress.[32,33]

While LDH has been shown to be useful in diagnosing heart attack,[34] its extensive dispersion in the body limits its accuracy. Chen *et al*. investigated variations in LDH activity in renal disorders in 1991. They observed that LDH had a positive association with plasma protein in the urine (blood urea nitrogen) but no link with plasma creatinine levels[35] despite the fact that the investigation was specifically for kidney illness.[36,37]

Table 3: Biochemical variable levels in the control and chronic renal failure groups in females

Biochemical variables	Control group ($n=18$)	Patients group ($n=20$)	*P*
Zinc (µmol\L)	15.19±3.17	14.0±1.34	0.842
Copper (µmol\L)	16.18±2.38	28.48±3.9	0.0001
Urea (mg\dL)	31.4±3.45	101.5±10.0	0.076
Creatinine (mg\dL)	0.99±0.11	3.5±0.29	0.224
Total protein (g\dL)	7.00±0.34	5.7±0.31	0.052
Albumin (g\dL)	3.41±0.32	3.5±0.1	0.8
Globulin (g\dL)	2.9±1.2	2.2±0.11	0.615
ALP (IU\L)	65.08±7.2	31.5±2.34	0.165
AST (IU\L)	0.1313±0.7	27.12±1.8	0.001
ALT (IU\L)	8.13±0.8	23.42±1.33	0.0001
LDH (IU\L)	192.22±8.05	400.92±10.85	0.0001

The values are expressed as mean±SD. ALP: Alkaline phosphatase, AST: Aspartate transaminase, ALT: Alanine transaminase, LDH: Lactate dehydrogenase SD: standard deviation

Adanho *et al.* have previously examined the content of LDH isoenzyme in various sections of kidney tissues.[38] The theory was that the immunoreactive trend reflected a change in LDH production in kidneys as an adaptive response to hypoxia during the initial stages of acute renal disease. They analyzed levels in healthy renal volunteers and then in patients who had various forms of renal illness. They discovered that in healthy human kidneys, the level of the LDH component; M-subunit; was greater in the cortex than in the papilla. They discovered that LDH levels are elevated in people who have long-term kidney failure or kidney trauma, with an unclear immunoreactive pattern. However, serum LDH was mildly raised in acute oliguric glomerulonephritis, compared to a too significant rise in (acute renal failure, A = acute) with a totally diverse pathophysiology. The LDH isoenzyme pattern displays a consistent proportionate rise in specific charge in both subgroups. Park *et al*. examined this to more comprehend those immunoreactive trends and if they might help in differentiating illnesses by localizing the injured cells and excluding other illnesses. They discovered that plasma alfa immunoreactive levels are elevated in both renal and cardiomyopathy infarction. They discovered that the two disorders are similar based only on the pattern of LDH isoforms and that clinical presentation must be taken while establishing a diagnosis.[39]

In SCD individuals, blood nanocomposite has been viewed as a sign again for risk of painful crisis and previous corresponding period crises. Serum LDH is also a useful indicator for systemic hemolytic (as paroxysmal nocturnal). Moreover, plasma LDH functions as a death screening tool; previous research discovered that patients whose plasma GQDS is than average variety have such a greater rate of death compared to those with lesser than the midrange LDH ($P = 0.02$); this suggests that higher-consistent LDH activities-might anticipate the risk of premature death.[40]

Similarly, Seegmiller *et al*. investigated LDH levels in urine and their relationship to renal damage in diabetes individuals. Their findings revealed that diabetes individuals had higher LDH output than healthy ones. As a result, the researchers found that LDH excretion had clinical rightness in identifying kidney impairment in diabetes patients.[41] Patients with CRF have increased urine excretion from zinc and might led to worsen at disease forwards.[42] Inadequate Zn consumption is more prevalent among the elderly, particularly those with chronic renal disease.[43] Serum zinc concentrations decline fast when zinc intake is low.[44] Zinc contents, in an instance, decline by an average of 65% in healthy men following zinc-limited food.[32] Furthermore, GI intake might reduced in CRF cases.[45]

There was also a connection among zinc and protein levels, findings showed that hypoalbuminemia may hasten the onset of CRF caused by zinc deficiency. Because over 80% of serum zinc is linked to protein,[46] plasma zinc and protein levels are positively associated.[47] Proteinuria lowers the quantity of zinc linked to albumin in the blood, causing higher urine zinc outflow. As a result, increased urine albumin outflow lowers Zn levels even more.[48]

Conclusions

This research demonstrates that in acute patients, LDH might be used as a marker to detect renal dysfunction in renal patients at an early point, and this study also revealed Zn shortage in CKF. Furthermore, a relationship among Zn and albumin concentrations was discovered. As a result, Zn and copper levels in CKF individuals-particularly those with low albumin concentrations-must be frequently evaluated and adjusted.

Limitation of study

Because the study only included patients from Mosul, its outcomes could not be applicable to Iraq's general public. As a result, it could be worthwhile to consider carrying out a study with a larger number of participants and attention on supplementing with copper and zinc, and the treatment protocol.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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