The Egyptian Journal of Hospital Medicine (April 2022) Vol. 87, Page 2207-2211

Evaluation of Serum Zinc levels in Patients on Regular Hemodialysis in Zagazig University Hospitals

Ashraf Naged Ismael*, Amir Mohammed Elokily, Mahmoud Hosny Zahran
Internal Medicine Department, Faculty of Medicine, Zagazig University, Egypt.
***Corresponding author:** Ashraf Naged Ismael, **Email:** ashrafnaged8@gmail.com

ABSTRACT

Background: Due to fecal excretion or a decrease in zinc absorption, chronic kidney disease (CKD) patients may have a zinc deficit. **Objective:** The aim of the work was to study levels of serum zinc in patients on regular hemodialysis and to detect the relationship between serum zinc levels and CRP levels among Zagazig university hospital patients.
Patients and Methods: From July 2021 to November 2021, our cross-sectional trial was conducted on ninety-two End-Stage Renal Disease (ESRD) patients on regular hemodialysis admitted to hemodialysis unit, Department of Internal Medicine, Zagazig University Hospitals. All patients were subjected to laboratory investigations to assess serum levels of Zinc and CRP. **Results:** Findings showed that there were statistically non-significant correlation between zinc level and either total leukocyte count (TLC), platelet count, hematocrit, serum ferritin or plasma iron. Our finding regarding the correlation between serum zinc and C reactive protein among the studied patients revealed statistically significant negative correlation between zinc level and C reactive protein (r=-0.227, p=0.029). **Conclusion**: It could be concluded that zinc concentrations are lower in chronic kidney disease patients undergoing hemodialysis (HD) and there is a moderate negative correlation between C-reactive protein (CRP) as an inflammatory marker and serum zinc level.
Keywords: Hemodialysis, Chronic Kidney Disease, Serum Zinc

INTRODUCTION

Hemodialysis patients often have shortages in trace elements, such as zinc (Zn), iron, and perhaps selenium. Patients with Chronic Kidney Disease (CKD) who undergo hemodialysis (HD) see a dramatic shift in trace element metabolism. Decreased absorption or fecal excretion may be to blame for zinc deficiency in patients with chronic kidney disease (CKD) [(1)].

Anorexia, hypogeusia, sexual dysfunction, and reduced immunologic function may all be indications of Zn insufficiency [(2)]. In Zn deficient rats, erythropoietin (EPO) concentrations were found to be low, resulting in a decrease in hematopoiesis [(3)]. The increase in parathyroid hormone (PTH) was restricted by Zn deficiency in another rat renal ablation paradigm that produced uremia [(4)]. Some researchers have suggested that Zn deficiency may have a role in the development of uremic pruritus in HD patients [(5)]. In hemodialysis patients (HPs), zinc supplementation failed to improve taste perception. After dialysis is completed, zinc levels in the blood rise significantly [(6)]. Circulating levels of CRP, a pentameric protein that is annular (ring-shaped), increase in response to inflammation. It is a hepatic acute-phase protein that increases after macrophages and T cells secrete interleukin-6. C1q is responsible for activating complement by attaching to lysophosphatidylcholine, which is expressed by dead or dying cells (and some microorganisms) [(7)].

The liver is responsible for producing CRP [(8)]. In reaction to macrophage and fat cell-released factors (adipocytes). It has nothing to do with insulin or the C-peptide or protein C. (blood coagulation). The first pattern recognition receptor (PRR) discovered was C-reactive protein [(9)]. The aim of the current work was to study levels of serum zinc in patients on regular hemodialysis and to detect the relationship between serum zinc levels and CRP levels among Zagazig University Hospital patients.

PATIENTS AND METHODS

This cross-sectional trial study included a total of ninety-two patients with ESRD on regular hemodialysis, attending at hemodialysis Unit, Department of Internal Medicine, Zagazig University Hospitals. This study was conducted between July 2021 to November 2021.

Ethical Consideration:

This study was ethically approved by Zagazig University's Research Ethics Committee. Written informed consent of all the participants' parents was obtained and submitted them to Zagazig University (ZU-IRB#6852). The study protocol conformed to the Helsinki Declaration, the ethical norm of the World Medical Association for human testing.

Inclusion Criteria: Age range 18-80 years, both sexes (male and female), and patients on regular hemodialysis.

All participants were subjected to:

a. **Full history taking and thorough physical examination** with emphasis on demographic and clinical data.
b. R**outine and specific investigations** including complete blood count CBC) before any interventional measures and fluid administration, prothrombin time (PT), INR, Liver function tests (LFTs), Kidney function tests (KFTs), random blood sugar (RBS), serum calcium and phosphorus, serum zinc, CRP and ESR.

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal

Received: 01/12/2021
Accepted: 30/01/2022

distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Fisher's Exact or Monte Carlo correction, Student t-test, as well as Mann Whitney test were used. Chi square test ($\chi 2$) to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value < 0.05 was considered significant.

RESULTS

Table (1) shows that age of patients ranged from 20 to 77 years with mean 48.33 (± 14.09) years. Males represented 46.7% of them. BMI ranged from 17 to 29 kg/m^2 with mean 23.83 (± 3.12) kg/m^2.

Table (1): Distribution of the studied patients according to demographic data:

	N=92	%
Age (year): Mean ± SD Range	 48.33 ± 14.09 20 – 77	
Gender: Female Male	 49 43	 53.3% 46.7%
BMI (kg/m^2): Mean ± SD Range	 23.83 ± 3.12 17 – 29	

Table (2) shows that plasma zinc level ranged from 1.26 to 12.2 µmol/L with mean 5.82 µmol/L with zinc deficiency occurred in 53.3% of the studied patients.

Table (2): Distribution of the studied patients according to zinc level:

	Mean ± SD	Range
Zinc (µmol/L)	5.82 ± 2.49	1.26 – 12.3
Zinc deficiency Present Absent	 49 43	 53.3% 46.7%

Table (3) shows that there was statistically non-significant relation between the studied patients regarding gender. Female gender represented 46.9% and 60.5% of those with and zinc deficiency respectively. There was statistically significant relation between zinc deficiency and unknown cause of renal failure (all patients with unknown renal failure had zinc deficiency).

There was statistically non-significant relation between zinc deficiency and other causes of renal failure, frequency, duration of sessions or presence of urine output. Zinc deficiency non-significantly associated with presence of congenital kidney disease, and PIH. Zinc deficiency was lower among those with diabetes, hypertension, drug induced renal failure, immune disorder, renal stones, polycystic kidney, and lymphoma.

Table (3): Relation between zinc deficiency and disease specific data

Parameter	Zinc deficiency		Test	
	Present	Absent	χ^2	p
	N=49 (%)	N=43 (%)		
Cause of RF:				
Unknown	6 (12.2%)	0 (0%)	Fisher	0.028*
Congenital	3 (6.1%)	1 (2.3%)	Fisher	0.62
DM	3 (6.1%)	6 (14%)	Fisher	0.296
Hypertension	23 (46.9%)	23 (53.5%)	2.32	0.198
Drug induced	5 (8.2%)	4 (9.3%)	Fisher	>0.999
FMF	1 (2%)	0 (0%)	Fisher	>0.999
Immune disorder	1 (2%)	3 (7%)	Fisher	0.336
Renal stones	4 (8.2%)	4 (9.3%)	Fisher	>0.999
Polycystic kidney	1 (2%)	1 (2.3%)	Fisher	>0.999
PIH	3 (6.1%)	1 (2.3%)	Fisher	0.62
Lymphoma	0 (0%)	1 (2.3%)	Fisher	0.467
Sessions/week:				
1 / week	1 (2%)	0 (0%)		
2 / week	0 (0%)	1 (2.3%)	1.987¥	0.159
3 / week	48 (98%)	42 (97.7%)		
Duration of session:				
4.5 hours	1 (2%)	0 (0%)	Fisher	>0.999
4 hours	48 (98%)	43 (100%)		
UOP:				
No	47 (95.5%)	39 (90.7%)	Fisher	0.413
Yes	2 (4.5%)	4 (9.3%)		

Table (4) shows that there was statistically non-significant correlation between zinc level and either hemoglobin, TLC, platelet count, hematocrit, serum ferritin or plasma iron.

Table (4): Correlation between serum zinc and hematological data among the studied patients

	Serum zinc	
	r	p
Hemoglobin (g/dL)	0.109	0.301
TLC	-0.017	0.875
Platelet count (mcL)	-0.032	0.761
Hematocrit (g/dl)	0.086	0.416
S. ferritin (ug/L)	0.135¥	0.201
S. iron (mg/dL)	0.118¥	0.261
TIBC (mcg/dL)	0.014¥	0.895
Transferrin saturation (%)	0.076¥	0.469

Table (5) and Figure (1) shows that there was statistically significant negative correlation between zinc level and C reactive protein.

Table (5): Correlation between serum zinc and C reactive data among the studied patients:

	Serum zinc	
	r	p
CRP (mg/dL)	-0.227	0.029*

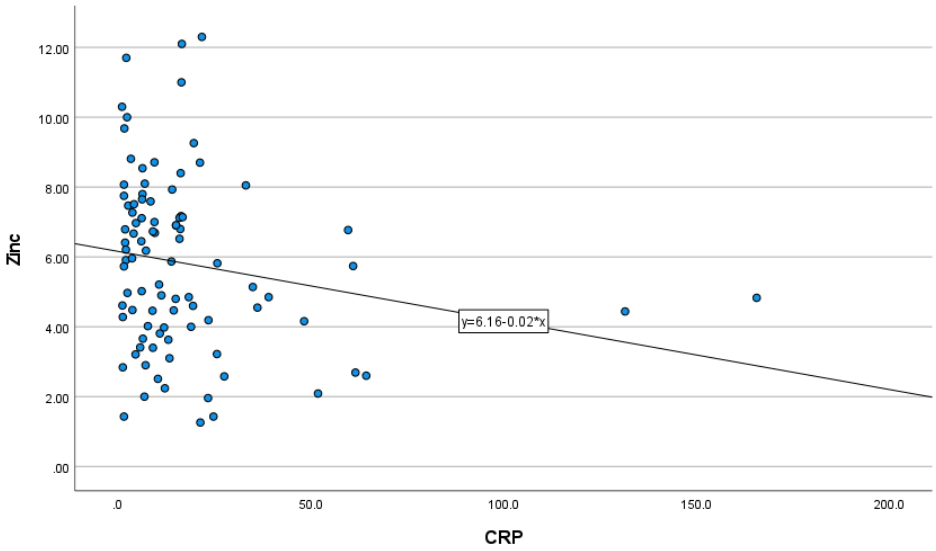

Figure (1): Scatter dot plot showing significant negative correlation between CRP and zinc level among the studied patients.

Table (6) shows that that there was statistically non-significant correlation between zinc level and either phosphorus, calcium, parathyroid hormone, blood urea nitrogen, serum creatinine or serum albumin.

Table (6): **Correlation between serum zinc and both electrolytes and kidney and liver function tests among the studied patients:**

	Serum zinc	
	r	p
Phosphorus (mmol/L)	0.057	0.586
Calcium (mmol/L)	-0.013	0.904
PTH (ng/L)	-0.133¥	0.206
S. creatinine (µmol/L)	0.005	0.961
BUN (mg/dL)	-0.018	0.866
Serum albumin (g/dl)	0.024	0.823

DISCUSSION

Chronic kidney disease (CKD) has become a serious public health issue in the last two decades, affecting approximately one in ten persons globally. A persistent loss of kidney function eventually necessitates renal replacement therapy as a result of chronic kidney disease (CKD), which is a condition in which the kidneys fail to function normally (dialysis or transplantation) [10].

An HD machine utilizes a semi-permeable membrane to extract uremic toxins from the blood plasma. If the dialysate concentration is lower than the blood concentration, it is possible that important substances will be lost. HD patients can have both deficiency and metal poisoning, depending on their remaining renal function, diet, and HD treatment quality [11].

Patients on maintenance dialysis had lower serum zinc (Zn) levels than those with more advanced stages of chronic renal disease. Zinc insufficiency is a common problem among dialysis patients due to zinc loss during hemodialysis, poor nutritional intake, and malabsorptive bowel movements [12].

The age of the included patients ranged from 20 to 77 years with mean 48.33 years. The females represented the majority with 53.3% and males represented 46.7% of them. BMI ranged from 17 to 29 kg/m^2 with mean 23.83 kg/m^2.

Previous studies have shown that individuals who have been on dialysis for a longer period are more likely to die. In study of **Okechukwu *et al.*** [13],12 687 HD patients were examined, ranging in age from one to twenty-six years, and the mean age was found to be 4.4 years. According to their findings, increasing adjusted mortality was linked to older dialysis patients' ages until 6 to 8 years into their treatment, but after that point the death rate began to decline.

Zinc deficiency has been seen in 40% to 78% of patients with chronic kidney disease (CKD). There are three possible explanations for this finding: reduced absorption via the gastrointestinal tract and lower zinc intake due to severe dietary restrictions for these patients are among the factors that affect zinc levels in these patients [14]. The dialysate composition, which allows for excessive zinc excretion due to the osmolarity differential, is a fourth factor contributing to zinc insufficiency in hemodialysis patients [15].

In the present study, plasma zinc level ranged from 1.26 to 12.2 µmol/L with mean level 5.82 µmol/L with zinc deficiency occurred in 53.3% of the studied patients. Other studies by **Dashti-Khavidaki *et al.*** [16] **and Lee *et al.*** [17] revealed that 58% of patients had Zn deficiency.

Hemodialysis patients in our study have lower serum zinc concentrations, was nearly agreed with which is in line with earlier research [16, 18].

We found no statistically significant differences in zinc levels between men and women in our study sample, which included 46.9% of women and 53.1% of men with zinc insufficiency. There was also no statistically significant connection between the analyzed patients and the genders. This is in accordance to **Elbadri *et al.*** [19].

Regarding the etiology of the renal failure and zinc status, our finding showed that all patients with unknown renal failure had zinc deficiency with statistically significant relation between zinc deficiency and unknown cause of renal failure. Otherwise, there was statistically non-significant relation between zinc deficiency and other causes of renal failure, frequency, duration of sessions or presence of urine output. Unlike **Stojsavljević *et al.*** [20], it was found that end-stage kidney disease and hemodialysis among Zn deficiency were reported to be hypertension (52.38 percent), diabetic nephropathy (23.71%), glomerulonephritis (14.29%), as well as polycystic kidney disease (9.52 percent).

Zinc deficiency tended to be lower among those with diabetes, hypertension, drug induced renal failure, immune disorder, renal stones, polycystic kidney, and lymphoma.

Our finding were similar to that of **Tokuyama *et al.*** [12] who revealed that the prevalence of DM, hypertension, and cardiovascular diseases were lower in low zinc level groups in comparison to high zinc group.

Our research found no link between serum Zn levels and any of the clinical or laboratory metrics.

Hemoglobin levels were shown to be positively correlated with serum zinc levels in the patients who had their hematological data examined, however this was not statistically significant. **Elbadri *et al.*** [19] reported that the level of serum zinc in the study group is strongly connected with Hb levels and negatively correlated with age.

Our finding showed that there was statistically non-significant correlation between zinc level and either total leukocytes count (TLC), platelet count, hematocrit, serum ferritin or plasma iron. Unlike to **Fukushima *et al.*** [21] who found that zinc concentration and anemia parameters showed a substantial positive connection, showing that anemia improves in patients with high zinc levels.

Regarding the link between serum zinc and Ca, phosphorus, parathyroid hormone, blood urea nitrogen, serum creatinine, and albumin in the individuals tested, statistically non-significant correlation was found between zinc level and any of these substances. However **Takic *et al.*** [22] investigated the serum zinc concentrations and the biochemical parameters found no significant relationships, they concurred with our findings. However, significant inverse correlations between the serum Zn and serum albumin ($r = -0.404$, $p = 0.009$).

Our finding regarding the correlation between serum zinc and C reactive data among the studied patients revealed statistically significant negative correlation between zinc level and C reactive protein (r=-0.227, p=0.029). These results were similar to several studies as **Trendafilov *et al.*** [23] reported that

level of zinc in the body was found to be negatively associated with inflammatory indicators (CRP and IL-6) .

CONCLUSION

It could be concluded that zinc concentrations are lower in chronic kidney disease patients undergoing hemodialysis (HD) and there is a moderate negative correlation between C-reactive protein (CRP) as an inflammatory marker and serum zinc level.

REFERENCES

1. **Skarupskiene I, Kuzminskis V, Abdrachmanovas O *et al.* (2005):** Zinc and alumi-num concentrations in blood of hemodialysis patients and its impact on the frequency of infections. Medicina (Kaunas), 41(1):65-8.
2. **Cabral P, Diniz A, Arrruda L (2005):** Vitamin A and zinc status in patients on maintenance haemodialysis. Nephrology, 10:459-63.
3. **Konomi A, Yokoi K (2005):** Zinc deficiency decreases plasma erythropoietin concentration in rats. Biol Trace Elem Res., 107(3): 289-292.
4. **Kimmel P, Langman C, Bognar B *et al.* (2001):** Zinc Nutritional Status Modifies Renal Osteodystrophy in Uremic Rats. Clinical Nephrology, 56(6):445–58.
5. **Sanada S, Kuze M, Yoshida O (1987):** Beneficial Effect of Zinc Supplementation on Pruritus in Hemodialysis Patients with Special Reference to Changes in Serum Histamine Levels. Hinyokika Kiyo., 33(12):1955–60.
6. **Navarro-Alarcon M, Reyes-Pérez A, Lopez-Garcia H *et al.* (2006):** Longitudinal Study of Serum Zinc and Copper Levels in Hemodialysis Patients and Their Relation to Biochemical Markers. Biological Trace Element Research, 113(3):209–22.
7. **Thompson D, Mark B, Wood S (1999):** The Physiological Structure of Human C-Reactive Protein and Its Complex with Phosphocholine. Structure, 7(2):169–77.
8. **Pepys M, Hirschfield G (2003):** C-reactive protein: a critical update. J Clin Invest., 111: 1805-1812.
9. **Mantovani A, Cecilia G, Andrea D *et al.* (2008):** Pentraxins in Innate Immunity: From C-Reactive Protein to the Long Pentraxin PTX3. Journal of Clinical Immunology, 28(1):1–13.
10. **Vaidya S, Aeddula N (2021):** Chronic Renal Failure. In: StatPearls Publishing, Treasure Island (FL): StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK535404/
11. **Almeida A, Gajewska K, Duro M *et al.* (2020):** Trace element imbalances in patients undergoing chronic hemodialysis therapy - Report of an observational study in a cohort of Portuguese patients. J Trace Elem Med Biol., 62, 580-85.
12. **Tokuyama A, Kanda E, Itano S *et al.* (2021):** Effect of zinc deficiency on chronic kidney disease progression and effect modification by hypoalbuminemia. PLOS One, 16(5): 554-60.
13. **Okechukwu C, Lopes A, Stack A *et al.* (2002):** Impact of years of dialysis therapy on mortality risk and the characteristics of longer-term dialysis survivors. Am J Kidney Dis., 39(3): 533-538.
14. **Rahimi-Ardabili B, Argani H, Ghorbanihaghjo A *et al.* (2012):** Paraoxonase enzyme activity is enhanced by zinc supplementation in hemodialysis patients. Ren Fail., 34(9): 1123-1128.
15. **Neto L, Bacci M, Sverzutt L *et al.* (2016):** The role of zinc in chronic kidney disease patients on hemodialysis: A systematic review. Health, 8(04): 344-49.
16. **Dashti-Khavidaki S, Khalili H, Vahedi S *et al.* (2010):** Serum zinc concentrations in patients on maintenance hemodialysis and its relationship with anemia, parathyroid hormone concentrations and pruritus severity. Saudi J Kidney Dis Transpl., 21(4): 641-645.
17. **Lee S, Huang J, Hung K *et al.* (2000):** Trace Metals' abnormalities in hemodialysis patients: relationship with medications. Artif Organs, 24(11): 841-844.
18. **Choi S, Liu X, Pan Z (2018):** Zinc deficiency and cellular oxidative stress: prognostic implications in cardiovascular diseases. Acta pharmacologica Sinica, 39(7): 1120-1132.
19. **Elbadri A, Kheiri I, Abdalla A (2018):** Evaluation of Serum Zinc Level among Hemodialysis Sudanese Patients with Erythropoietin Resistant. Health Science Journal, 12(6): 1-4.
20. **Stojsavljević A, Ristić-Medić D, Krstić Đ *et al.* (2021):** Circulatory Imbalance of Essential and Toxic Trace Elements in Pre-dialysis and Hemodialysis Patients. Biol Trace Elem Res., 21: 1-9.
21. **Fukushima T, Horike H, Fujiki S *et al.* (2009):** Zinc deficiency anemia and effects of zinc therapy in maintenance hemodialysis patients. Ther Apher Dial., 13(3): 213-219.
22. **Takic M, Zekovic M, Terzic B *et al.* (2021):** Zinc Deficiency, Plasma Fatty Acid Profile and Desaturase Activities in Hemodialysis Patients: Is Supplementation Necessary? Frontiers in Nutrition, 8: 688-93.
23. **Trendafilov I, Georgieva I, Manolov V *et al.* (2018):** Status and relation to inflammation of some serum trace elements (TE) in hemodialysis (HD) patients. Nephrology Renal Diseases, 3(3): 1-4.