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Evaluation of Serum Zinc Levels Among Patient of Chronic Kidney Disease in a Tertiary Care Hospital

Kehkshan Waheed, Zujaja Hina Haroon, Afshan Bibi, Muhammad Aamir, Sobia Irum Kirmani, Muhammad Usman Munir

Department of Chemical Pathology, Armed Forces Institute of Pathology/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

Objective: To evaluate serum zinc levels in various stages of chronic kidney disease and to compare serum zinc levels in patients of chronic kidney disease undergoing and not undergoing hemodialysis.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Chemical Pathology and Endocrinology, Armed Forces Institute of Pathology, in collaboration with Armed Forces Institute of Urology, Rawalpindi, Pakistan from Jan to Jun 2021.

Methodology: Zinc levels of 120 individuals were analyzed on Flame Atomic Absorption Spectrophotometer and creatinine measured in serum samples. Patients were divided into five subgroups, stages 1-5, according to eGFR values. Zinc levels were expressed as Mean±SD. Independent sample t-test was used to compare serum zinc concentration of hemodialysis patients with non-hemodialysis patients and one-way ANOVA was used to compare zinc concentrations in patients with different stages of chronic kidney disease.

Results: Mean age of patients was 58±17 years. Mean value of serum zinc level was 9.03±2.51 µmol/L. The level of serum zinc showed a statistically significant difference (p=0.005) at different stages of disease, with significant decreasing trend in late-stage chronic kidney disease. We found a significant difference in mean serum zinc level among hemodialysis and non-hemodialysis individuals.

Conclusion: Patients of chronic kidney disease showed significant difference in serum levels of zinc across different stages. We found an increasing trend of zinc deficiency as the disease progressed, as well as with hemodialysis dependency.

Keywords: Atomic Absorption Spectrometry, Chronic Kidney Disease, Zinc Deficiency.

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INTRODUCTION

Zinc deficiency has emerged as a major micronutrient deficiency in last few decades.[1] A zinc level of <10.6 µmol/L is labelled as deficient.[2] Zinc deficiency negatively impacts cutaneous, gastro-intestinal, nervous, immunological, musculoskeletal and reproductive systems because zinc is an important cofactor in the expression and function of several enzymes, transcription factors and regulatory proteins.[2] In patients of chronic kidney disease (CKD), zinc metabolism is altered, and zinc deficiency may lead to advancement of complications, especially in later stages.[3,4]

The last resort to managing CKD is hemodialysis, which can cause zinc deficiency in approximately 40-78% patients.[6-8] One meta-analysis mentions that by supplementing zinc, the nutritional condition of patients on maintenance haemodialysis is benefitted because of zinc's anti-inflammatory and anti-oxidant activity.[9]

The aim of this study was to assess the relevance between chronic renal disease and zinc deficiency, with a focus on advanced stages of chronic kidney disease, and to identify any potential link between zinc deficiency and maintenance hemodialysis.

METHODOLOGY

This cross-sectional study was carried out at the Department of Chemical Pathology and Endocrinology, Armed Forces Institute of Pathology (AFIP) Rawalpindi, Pakistan in collaboration with Armed Forces Institute of Urology (AFIU) Rawalpindi, Pakistan from Jan 2020 to June 2020 after approval from the Institutional Ethical Review Committee (Letter no. FC-CHP-3/READ-IRB/21/147).

Inclusion Criteria: Patients of either gender aged between 30 to 90 years, diagnosed with chronic kidney disease, those who were or were not undergoing hemodialysis were included.

Exclusion Criteria: Patients taking zinc supplements or having chronic illnesses other than CKD that affect serum zinc levels like chronic liver disease (CLD),

Correspondence: Dr Kehkshan Waheed, Department of Chemical Pathology, Armed Forces Institute of Pathology, Rawalpindi Pakistan

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malignancies and ischemic heart disease (IHD) were excluded.

World Health Organization (WHO) calculator was used for sample size calculation, based on prevalence of chronic kidney disease in Pakistan 12.5%, which came to 120. Patients were inducted by consecutive non-probability sampling, after taking written informed consent.

Chronic kidney disease subjects were categorized into five groups corresponding to the estimated Glomerular Filtration Rate (eGFR), which was assessed by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation.2 Stage 1 CKD: eGFR 90 ml/min/1.73m or greater, Stage 2 CKD: eGFR between 60 and 89 ml/min/1.73m, Stage 3 CKD: eGFR between 30 and 59 ml/min/1.73m, Stage 4 CKD: eGFR between 15 and 29 ml/min/1.73m and Stage 5 CKD: eGFR less than 15 ml/min/1.73m. Subjects were also classified into the following six age groups, 30-40 years, 41-50 years, 51-60 years, 61-70 years, 71-80 years and 81-90 years. About 5ml Blood sample was collected in gel tube with clot activator from each patient for serum creatinine and zinc levels. Within two hours following sample collection, gel tubes were allowed to clot at room temperature, and serum was separated by centrifugation at 3000 RPM for three minutes. Serum was frozen at -20ºC until analysis to maintain its integrity. Serum creatinine was analyzed on automated chemistry analyzer using principle of homogenous enzymatic colorimetric test. Serum zinc levels were measured on Flame Atomic Absorption Spectrophotometer. Each batch of samples was subjected to two levels of quality control by ClinChek. For evaluating the deficiency of zinc among the study population, serum zinc levels 10.7-18.4umol/l were considered as optimal, while <10.7µmol/l were considered as zinc deficient.

Statistical Package for Social Sciences (SPSS) version 21 was used for analysis. Kolmogorov-Smirnov test was used to check for normality of data and normal distribution result was obtained. To compare serum zinc levels of hemodialysis patients in relation to non-hemodialysis patients, independent sample t-test was applied. For quantitative data, mean and standard deviation were computed, while for qualitative variables, frequencies and percentages were calculated. Serum zinc concentration in patients with various stages of chronic kidney disease were compared using one-way ANOVA. A *p*-value ≤0.05 was deemed statistically significant.

RESULTS

Out of total 120 patients 36(30%) were females and 84(70%) were males. Mean zinc level in males (CKD) was 9.16±2.64 (µmol/L) while mean zinc level in females (CKD) was 8.68±2.08 (µmol/L). The mean age was 58±17 years. According to their eGFR values, the patients were divided into five categories, stages 1-5. Mean serum zinc level in chronic kidney disease patients equated to be 9.03±2.51 µmol/L while reference range in our study age group was 10.7-18.4 µmol/L. Table-I shows some descriptive parameters.

Table-I: Descriptive Statistics of Quantitative Parameters (n=120)

Parameters	Mean±SD
Age	58.00 ± 17.00 years
Serum Creatinine	229.7 ± 216.3(µmol/L)
eGFR	62.2±38.5 ml/min/1.73m²
Mean zinc level in males (CKD)	9.16 ± 2.64 (µmol/L)
Mean zinc level in females (CKD)	8.68 ± 2.08 (µmol/L)

Serum zinc levels differed significantly (p<0.005) across different stages of chronic kidney disease, with a substantial downward trend in late-stage disease. Statistically significant difference was seen across stages, as shown in Table-II.

Table-II: Serum Zinc Levels across stages of Chronic Kidney Disease (n=120)

CKD stage	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5	*p*-value
	(n=60)	(n=10)	(n=10)	(n=10)	(n=30)	
Zinc Mean±SD (µmol/L)	10.94± 2.0	8.35±0.87	8.41±0.76	8.20±0.69	6.49±0.83	< 0.001

Out of 120 patients, 60(50%) were of stage 5 chronic kidney disease, out of those 30(25%) were on maintenance hemodialysis and 30(25%) were not on maintenance hemodialysis. Average serum zinc content in individuals on maintenance was substantially lower than the non-maintenance hemodialysis category (7.91 vs 7.60; p=0.001), however, individuals of both the groups had zinc deficiency, below the cut-off point of 10.6 µmol/L as recommended by IFCC.

DISCUSSION

Out of 120 patients 36(30%) were female and 84(70%) were male. Mean zinc levels in males was 9.16±2.64 (µmol/L) while in females it was 8.68±2.08

(µmol/L). Other studies have found gender differences in serum zinc in elderly, with males exhibiting elevated levels as compared to females of age-matched geriatric patients.[9,10]

Table-III: Comparison of Serum Zinc Levels Between Hemodialysis Dependent and Non-Hemodialysis Dependent Patients (n=60)

	No. of Patients	Zinc levels (Mean±SD)	*p*-value
CKD patients on Dialysis	30	7.6±1.3 µmol/L	0.005
CKD patients not on Dialysis	30	7.9±1.2 µmol/L	

**CKD: Chronic Kidney Disease*

Patients with CKD enrolled in this study had significantly decreased zinc levels in the blood as compared to the reference values of our population (10.7-18.4umol/l). This finding could be explained by several factors, including changes in zinc stores in the body due to lower absorption through the gastrointestinal tract, and a drop in oral zinc ingestion due to dietary limitations for these (CKD) patients, that restrict the utilization of zinc-rich food items.[11,12] We found that as CKD stages progressed, deficiency of serum zinc became more severe, with stage 5 CKD patients being most zinc-deficient. These findings are consistent with a study done in Switzerland by Damianaki *et al*.[13]

Those undergoing maintenance hemodialysis accounted for 25% of the 120 CKD patients included in our study. The dialysate composition was the main cause of zinc deficiency in patients subjected to maintenance hemodialysis, as it promoted zinc excretion due to the difference in osmolality of two fluid compartments.[14] Both in hemodialysis and non-hemodialysis CKD patients, inverse relationship of Zinc level were noted in some studies with older patients.[15,16] In contrast to prior publications, the frequency of hemodialysis and the duration since it began did not show any link with serum zinc levels in these patients. One study indicated that patients on maintenance hemodialysis who were given zinc supplementation had improved overall health and nutritional condition.[17]

Manifestation of zinc deficiency may be the result of hyperproteinemia, poor overall health, impairment in the formation of 1,25 dihydroxy-cholecalciferol, which plays a role in the absorption of zinc from intestines, or consumption of a diet that is low in zinc.

A study done in Bangladesh by Barman *et al*., showed descending zinc values with ascending age.18 Deficiency of zinc could be a reversible cause of depression in hemodialysis patients, which could be due to positive correlation of zinc deficiency and the possibility of depression and the inverse relation of zinc supplementation and signs of depression.[18]

Zinc abnormalities in chronic kidney disease can lead to development of cardiovascular atherosclerotic disease, decreased immunity and depressive symptoms. In order to avoid these consequences, monitoring and correction of serum zinc levels is indicated in all patients with chronic kidney disease. Zinc is mainly excreted through faeces and there are no body stores of zinc, hence supplementation may be a useful intervention for patients with chronic kidney disease. More research is needed to better understand Zinc deficiency and its consequences on hemodialysis patients with greater sample size and a multi-centric approach.

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LIMITATIONS OF STUDY

Zinc levels may differ with individual's diet and medications. Still there are some possible limitations that must be focused upon. Because the sample size in this cohort is small and not illustrative of the actual population of CKD patients, the generalizability of the current findings may be limited. Furthermore, serum values might not be the best predictor of total body reserves of trace elements.

CONCLUSION

Patients of chronic kidney disease showed significant difference in serum levels of zinc across different stages. We found an increasing trend of zinc deficiency as the disease progressed, as well as with hemodialysis dependency.

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Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

KW & ZHH: Conception, study design, drafting the manuscript, approval of the final version to be published.

AB & MA: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

SIK & MUM: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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