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# EVALUATION OF SERUM ZINC LEVEL AMONG HEMODIALYSIS SUDANESE PATIENTS WITH ERYTHROPOIETIN RESISTANT

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**ABSTRACT** **Background: Anemia is principle health problem in patients with chronic renal failure on hemodialysis treatment and erythropoietin is treatment of choice, some patients e, some patients do not respond as expected. Various researches suggest that zinc may play a role in the etiology of erythropoietin resistant anemia. Objectives: To assess serum zinc level in erythropoietin resistant hemodialysis Sudanese patients and its relation to hemoglobin and comparison with apparently non erythropoietin resistant hemodialysis control patients. Materials and methods: Case control study was performed in Khartoum state at kidney disease clinic Khartoum Sudan, during the period from February to October 2018. 50 samples were collected from erythropoietin resistant Hemodialysis patients test group. In addition to other 50 from non-erythropoietin resistant hemodialysis patient's sex and age matched control group. The levels of serum zinc elements were determined in both groups by atomic absorption spectroscopy, and hemoglobin was measured by colorimetric method. Results: Serum zinc level was significantly lower in erythropoietin resistant hemodialysis patients when compared with non-erythropoietin resistant hemodialysis patients control group (0.26 ± 0.08 mg/L versus 0.67 ±0.09 mg/L). Furthermore Hb was significantly decreased (8.56 ± 0.56 gm/L versus 11.34 ± 0.59 gm/dl, p=0.000). In addition the study observed no significant difference in zinc level and hemoglobin across gender (P>0.05) in the test group. Also the study recorded serum zinc level is significantly correlated with Hb (R=0.58, P=0.00) and inversely correlated with age (R=-43, P=0.01). Whereas Hb level is insignificantly correlated with patients age in the study group (R=0.24, p=0.16). Conclusion: Erythropoietin resistant anemia in hemodialysis patients is associated with reduced serum zinc level. Which provide evidence that serum zinc levels should be measure especially in hemodialysis patients resistant to erythropoietin therapy.**

**KEYWORDS** :Chronic renal failure; Hemodialysis erythropoietin resistant; Zinc;

## INTRODUCTION

Anemia is one of the most frequent early complications of chronic renal failure (CKF) [1]. The main cause is lack of erythropoietin due to reduced kidney function. The treatment of anemia in CKF patients is recombinant human erythropoietin (rHuEPO) [2,3]. The main cause of rHuEPO treatment failure is the loss or low iron availability. The prevalence of iron deficiency is very common in CKF, affecting as many as 50% of patients [3-5]. How-ever, despite rHuEPO and intravenous iron in the majority of patients, the prevalence of anemia exist in large numbers of hemolysis patients [4-6]. This rise the existence of other important factors related to rHuEPO resistance, including hyper and hypothyroidism, severe secondary hyperparathyroidism, malnutrition hypoprotienemia malabsorption and exposure to large amount of dialysis solution which does not contain any trace elements might be related to zinc and other trace elements deficiency in hemodialysis patients [7]. Zinc is an essential trace element for human's life, which is part of many enzymes [8]. Zinc plays essential biological functions, including gene expression, protein synthesis, immune responses, and other behavioral functions [9,10]. Serum zinc levels can be decreased by increased expression of intracellular metallothioneins or oxidative stress [8-10]. Zinc deficiency may be associated with some of the uremic symptoms such as anorexia decreased immunologic function hypogeusia and sexual dysfunction [10,11]. The dialysate concentration of other trace elements is not routinely manipulated. Substances that have lower concentrations in dialysate than in blood tend to be removed by dialysis [10-12]. This is true in the case of uremic toxins; it may lead to depletion of biologically essential substances. Besides the potential for ongoing removal of trace elements by dialysis, hemodialysis patients are at risk for low dietary intake of such substances due to uremia-related anorexia and dietary restrictions [11,13]. Nemours researches illustrated strong relationship between zinc deficiency and other disorders, such as inflammation, cardiovascular diseases, oxidative stress, and erythropoietin resistant anemia. Hence this study was conducted to explore the role of serum zinc level in erythropoietin resistant anemia in hemodialysis Sudanese patients.

## Material and Methods

**Study population:** The current study was a case control hospital base study conducted at kidney disease (HD) clinic Khartoum Sudan, during the period from February to October 50 samples were collected from erythropoietin resistant Hemodialysis patients test group (26 male, 24 female with age of 20-80 years). In addition to other 50 from non- erythropoietin resistant hemodialysis patient's sex and age matched control group.

**Inclusion criteria:** Any patients who have maintenance hemodialysis at least for six month having (rhEPO) with age more than 20 years and less than 80 years.

**Exclusion criteria:** Any patients of CRD (HD) with age less than 20 or more than 85 years patients with known malignancy infectious disease endocrine abnormalities gastric problems over drugs alcohol abuse and treatment with steroids or immune suppresser.

**Data collection and clinical examination:** Each site used a standardized questionnaire which collected the demographic and symptom information assessed in this study. Clinical examinations done by clinicians in above mentioned hospital.

**Sample collection:** Blood was taken from each participant by standard procedures. Serum zinc was estimated by atomic absorption spectrometry (AAS) method with Zeeman background correction (Z-2000 instrument, Hitachi, Japan), in the Laboratory of National Center for Research. EDTA container was used for hemoglobin estimation which was measured by standard colorimetric method.

**Ethical consideration:** Informed consent was taken from all participants and ethical approval was obtained from EL Neelain University research committee.

**Quality control:** Samples representing the normal and pathological level of zinc (Zn) hemoglobin were used for assessment of the quality control. Results ± 2 SD of the target values of the control sera were accepted.

**Statistical analysis:** Data was analyzed by computer software by using SPSS program manual master sheet (SPSS version 21), the results expressed as frequency percentage mean and SD. The independent t-test was used to compare the mean level of Hb and zinc in case and control. Correlation between measured variable was

significant at $p \leq 0.05$.

## Result

The study comprised 100 participants divided into two groups. 50 erythropoietin resistant Hemodialysis patients test group, with age range 20–80 years (male 26, female 24) and 50 non erythropoietin resistant hemodialysis patients sex and age matched control group.

As presented in **Table 1**, the level zinc and Hb was significantly decreased in the study group when compared with control group (0.26 ± 0.08 mg/L versus 0.67 ± 0.09 mg/L, p=0.00 and 8.56 ± 0.56 gm/L versus 11.34 ± 0.59 gm/dl, p=0.000) respectively.

**Table 1 Comparison of Zinc and Hb levels in the study group with the control group.**

| Parameters | Case (mean ± SD) | Control (mean ±SD) | P-value |
|---|---|---|---|
| Zinc (mg/L) | 0.26 ±0.08 | 0.67 ± 0.09 | 0 |
| Hb (gm/dl | 8.56 ± 0.56 | 11.34 ± 0.59 | 0 |

Across gender there is insignificant difference in the level of both zinc and Hb in male when compared with female in the study (0.28 ± 0.06 mg/L 0.24 ± 0.17 mg/L, p=0.08 and 8.64 ± 0.66 gm/dl versus 8.47 ± 0.42 gm/dl, p=0.75) respectively depicted in **Table 2**.

**Table 2 Comparison of Zinc and Hb levels across gender in the study group.**

| Parameters | Male (mean ± SD) | Female (mean ±SD) | P-value |
|---|---|---|---|
| Zinc (mg/L) | 0.28 ± 0.06 | 0.24 ± 0.17 | 0.08 |
| Hb (gm/dl | 8.64 ± 0.66 | 8.47 ± 0.42 | 0.75 |

As shown in figure the level of serum zinc is significantly correlated with Hb and inversely with age in the study group (R=0.58, P=0.00, R=-43, P=0.01) **Figures 1 and 2** respectively. Whereas Hb level is insignificantly correlated with patients age in the study group (R=0.24, p=0.16) **Figure 3**.

## Discussion

Erythropoietin resistant anemia is very series since cardiovascular mortality; morbidity and quality of life of patients are related to better control of anemia. Failure of rhEPO to correct anemia for many causes. Iron deficiency is the most important causes [14-16]. Prasad et al. [17] raised relationship between iron deficiency anemia and zinc deficiency. Great number of studies appeared in the literature in the recent years exploring the relationship between zinc deficiency and, general health, cardiovascular diseases, male infertility as well as erythropoietin resistant anemia in maintenance hemodialysis patients [5,6,17].

**Figure 1 Correlation of zinc level with Hb level in the study group.**

**Figure 2 Correlation of zinc level with patient's age in the study group.**

**Figure 3 Correlation of Hb level with patient's age in the study group.**

In the current study there was high statistically difference in the mean zinc and hemoglobin levels between the study group and the control group. The levels zinc and hemoglobin were significantly decreased in erythropoietin resistant group when compared with non-erythropoietin resistant group (P≤0.000) Which agree with the studies performed by Dashti et al. [18], Dvornik et al. [19] and Yegenaga et al. [20], whom reported that the mean serum Zn concentration in patients on maintenance HD was significantly lower than that of the control group. Serum Zn deficiency has been reported in CKD patients due to hypoproteinemia, proteinuria, tubular reabsorption impairment and calcitriol deficiency which has a role in the intestinal absorption of Zn. In addition HD patients are exposed to large amounts of highly purified dialysis solutions, which removed zinc and other essential trace elements that may lead to clinically relevant deficiency [21]. Tonelli et al. [22] performed systemic review and meta-analysis on trace elements in hemodialysis patients, and illustrated that average blood concentrations of biologically important trace elements (selenium, zinc,) were substantially different in hemodialysis patients, compared with healthy controls.

Across gender our study illustrated insignificant difference in the level of both zinc and Hb in male when compared with female in the study group. Although the level of both zinc and hemoglobin is slightly higher in male compared to female in the test group [23,24].

In the present study the level of serum zinc is significantly correlated with Hb and inversely with age in the study group. In accordance to Hiroki et al. who concluded that Zinc supplementation reduces ERI in patients undergoing HD and may be a novel therapeutic strategy for patients with renal anemia and low serum zinc levels. Although no previous studies illustrated an association between zinc concentrations and hemoglobin production, some studies observed that zinc play an essential role in erythroid differentiation and development [17,18]. Fukushima et al. [25] reported that zinc concentration and all anemia parameters showed significant positive correlation, indicating that anemia improves in patients with high serum zinc levels [19].

# CONCLUSION

The study demonstrated that serum zinc level is significantly reduced in hemodialysis patients with erythropoietin resistant anemia.

**Consent:** As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

**Ethical approval:** As per international standard or university standard written approval of ethics committee has been

collected and preserved by the authors.

**Competing interests:** Authors have declared that no competing interests exist.

**Authors contribution:** This work was carried out in collaboration between all authors. Author AEIK designed the study, performed the statistical analysis. Wrote the protocol and wrote the first draft of the manuscript. Authors (AEIK) and (AMA) managed the analysis of the study and the literature searches. All authors read and approved the final manuscript.

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