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ROLE OF SERUM ZINC LEVEL IN VITILIGO

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ABSTRACT

Background: Melanocyte apoptosis associated with vitiligo has been related to an imbalance in the oxidants-antioxidants system. Melanogenesis depends upon zinc, as a cofactor in the antioxidant defense system. Published researches reviewing the zinc level in vitiligo has yield inconsistent results. **Aim**: to calculate the variations in serum zinc levels between Vitiligo patients and healthy control individuals. To assess the link between zinc level and Vitiligo severity. **Patients and Methods:** The study was conducted as case-controlled study to investigate 98 Vitiligo patients and 50 healthy age-gender matched participants recruited from dermatology outpatient clinic at Mosul General Hospital. Five ml blood was taken for estimating zinc level in both groups of the study. **Results**: The average age of vitiligo patients were 23.32±15.63 years, composed of 52% (n=51) females and 48% (n=47) males with a duration vary from 1 month to 21 years (mean & SD = 4.56±5.17 years). Serum zinc levels in vitiligo and control group were 86.36± 12.05 mg/dl and 92.94±10.36 mg/dl respectively (p=0.001). The serum Zinc level of vitiligio patients was significantly low in extreme age and female patient. In Vitiligo patients, results reveal Inversely significant relationship (r = -0.26, r2 = 0.06, P = 0.01) between the patient's age-serum zinc level and between serum Zinc level-severity of vitiligio (r=-0.28, r2 = 0.08, P= 0.006). **Conclusions**: The study offer a new prof that low zinc level is a contributor in initiation and continuation of vitiligo. Zinc level is inversely linked to extent and tensity of Vitiligo rather than its duration.

KEYWORDS: Vitiligo, Serum zinc, hair loss, case-controlled study, Vitiligo Extent Tensity Index (VETI) score, Vitiligo Disease Activity Score (VIDA).

INTRODUCTION

Vitiligo is a common multifactorial acquired depigmenting cutaneous illness result from localized destruction of melanocytes.[1] Their cosmetic impact is tremendous and its psychological impact is devastating, particularly in colored people.[2] Various etiopathogenesis theories have been postulated to clarify the absence of lesional melanocytes[3], among them are: build-up of toxic compounds, alterations in the cellular environment, and the imbalance in the oxidant-antioxidant system.[4]

Molecular studies reveal that vitriliginous skin lacks antioxidants. Based on this, research conclude that environmental stressors exposure like UV-produced reactive oxygen will trigger apoptosis of vulnerable melanocytes.[5] Inamadar et al. reported two siblings with acrodermatitis entropathica who exhibit Vitiligo lesions after sessation of taking supplemental zinc.[6] This shed the light on a possible role of zinc in stopping apoptosis by overcoming the harmful effect of accumulated toxic free radicals.[7] So, zinc may play important role in prevent or even manage Vitiligo.[8] Animal study show that zinc plays a part in the production and secretion of α-melanocyte stimulating hormone and melanogenesis. Furthermore, it catalyze dopachrome and enhance melanin polymer formation from monomers.[9] Review of literatures revealed that some investigators link Vitiligo to low serum zinc[10], others fail to show such a relation.[11] Does zinc levels vary with predominate site of lesions (covered versus sun-exposed), and how strongly zinc levels correlate with the severity of vitiligo? The goal of the ongoing investigation is to resolve this dispute and close some knowledge gaps.

The goals of this study are

1. To estimate the differences in serum zinc levels in different health status, site of lesions, degree of disease activity.

2. To assess the correlation of zinc level with (age of patient, duration and severity of Vitiligo).

PATIENTS AND METHODS

This a case-control Study investigating 98 Vitiligo patients recruited from dermatology outpatient clinic at Mosul General Hospital between January 2023 and December 2023. Further 50 age and gender-matched, healthy subjects were requested to participate as a control group. The study excluded individuals with systemic disorders such as mal-absorption or those using nutritional supplements, as these conditions may cause erroneous interference with the measurement of serum zinc levels. Three ml venous blood sample was taken to estimate Serum zinc levels using atomic absorption spectrophotometry. The zinc level less than 70mg/dl was considered low.

The Vitiligo Extent Tensity Index (VETI) score[12] was used to quantitatively evaluate the severity of vitiligo by multiply percentage of extension involvement (p) by illness tensity (T) (0: Normal skin; 1: Hypopigmentation; 2: Complete depigmentation with Black hair; 3 complete depigmentation with mixed White and black; 4: Complete depigmentation and hair whitening). Based on patient's opinion and using Vitiligo Disease Activity Score (VIDA)[13], disease activity was graded as +4 (<6 weeks), +3 (6 weeks to 3 months), +2 (3 - 6 months), +1 (6 to12 months), 0 (stable at least for 1 year), −1 (Stable at least for 1 year with spontaneous repigmentation).

Edit, summarize and examine the data was performed using statistical software SPSS (version 26.0). While continuous variables like age, serum zinc levels, duration and severity of Vitiligo were expressed as range, mean, and standard deviations, categorical data like gender, site of lesion and disease activity grade were expressed as percentages. The normality of the data was evaluated using the Kolmagrov-Simirnov test prior to proceeding with additional analysis. The study applied the bivariate Student's t-test to assess the significance of Zinc variations between two groups of the study and in between both gender of the patients. ANOVA test was used to determine the significance of variations in zinc across various age groups, location of lesions, and disease activity scores. Using the Pearson correlation coefficient, the strength of relationship between the Zinc level and other parameters like age, duration and severity of Vitiligo was determined. Furthermore, linear regression was utilized to produce best fit line and construct prediction equation. A p-value smaller than 0.05 was considered significant.

RESULTS

Figure 1 display the age distribution of the investigated sample. The age of Vitiligo patients were ranged from 4-66 years with mean±SD of 23.32±15.63, while healthy control group was ranged from 9-69 years, with mean±SD of 25.54±12.35 years. The difference was not statistically significant (p=0.09). Patients group included 52% (n=51) females and 48% (n=47) males with male to female ratio of 1:1.08. The controls group sample divided equally between both genders 50% (n=25). Duration of sampled Vitiligo patients last anywhere from one month to twenty-one years, with a mean ± standard deviation of 4.56±5.17 years. The lesions were predominantly located in covered area in 49 (50.0%) of patients, 28 (28.6%) had lesions in sun-exposed areas, and 21 (21.4%) had mixed lesions. The severity of vitiligo estimated by VETI score range from 1-22 with mean±SD of 7.48±3.53. Patient grade the activity of their Vitiligo lesion to grade (+4) in 8 (8.2%) of patients, grade (+3) in 4 (4.1%) patients, grade (+2) in 10 (10.2%), zero grade in 67 (68.4%) and grade (−1) in 9 (9.2%) of patients.

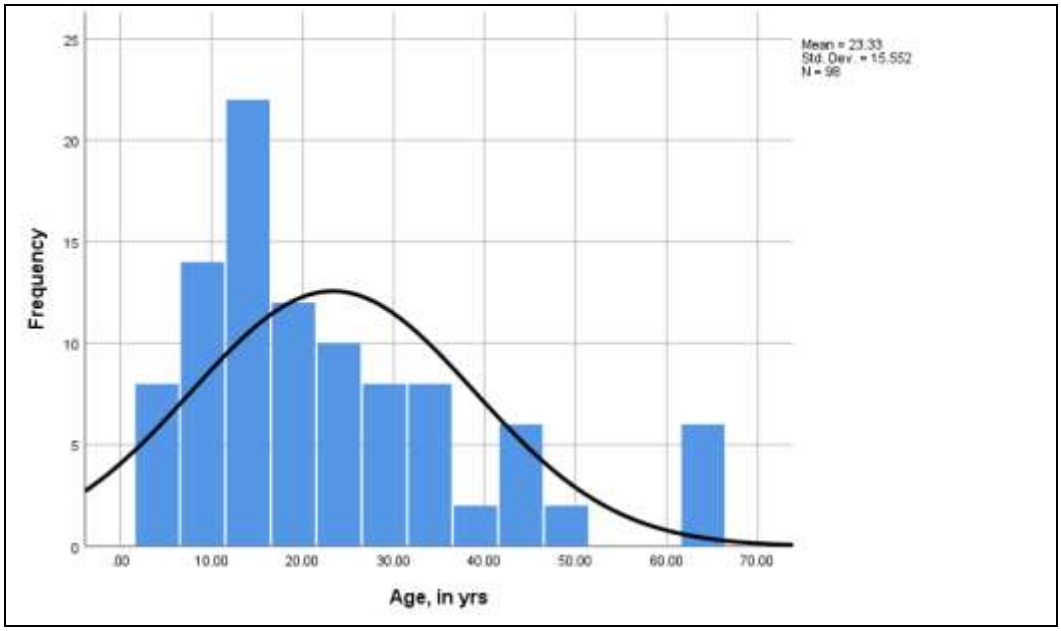

Fig. 1: Age distribution of the studied Vitiligo patients.

Table 1 displays the serum zinc level of Vitiligo patients based on various parameters. The findings show that the extreme age groups (less than 10 years and older than 50 years) had significantly lower zinc levels. The zinc levels in females were significantly lower than those in males. The findings showed no statistically significant differences between the zinc levels in the various disease activity and lesion site subgroups.

Table 1: Comparison of S. Zinc level in different demographic and clinical characteristics.

Demographic and clinical characteristics.		Mean	SD	p-value
Age group				0.0001
	1-9	79.87	5.73	
	10-19	91.38	11.68	
	20-29	88.33	5.61	
	30-39	90.33	11.73	
	40-49	80.75	3.49	
	50+	72.00	20.11	
Gender				0.02
	Male	89.21	16.06	
	Female	83.74	5.25	
***Disease activity score**				0.5
	Grade +4	84.00	4.84	
	Grade +2	91.00	16.16	
	Grade +1	88.60	13.10	
	Grade 0	85.37	12.74	
	Grade -1	91.33	6.06	
Site of lesions				0.4
	Covered areas	84.81	14.63	
	Sun-exposed areas	88.07	9.51	
	Mixed areas	87.71	7.11	

*Disease activity grade: +4 (<6 weeks), +3 (6 weeks to 3 months), +2 (3 - 6 months), +1 (6 to12 months), 0 (stable at least for 1 year), −1(Stable at least for 1 year with spontaneous repigmentation).

The distribution of serum zinc levels in the two study groups is shown in Figure 2. In the studied vitiligo patients sample, the zinc levels varied between 40 and 113 mg/dl, with a mean±SD of 86.36±12.05 mg/dl (95% CI for mean 83.96-88.77), while. The control group's zinc level ranged from 75-116 gm/dl with mean±SD 92.94±10.36 mg/dl (95% CI for mean 89.99-95.88). In contrast, the average zinc level in the vitiligo patients was 6.57 gm/dl lower than in the healthy group (95% CI of the Difference 5.98-10.51), and this difference was statistically significant (p=0.001). After breakdown zinc level, result reveal that 8 (%) were considered low, in contrast, all control group have a normal level, and the difference was statistically significant (p=0.03).

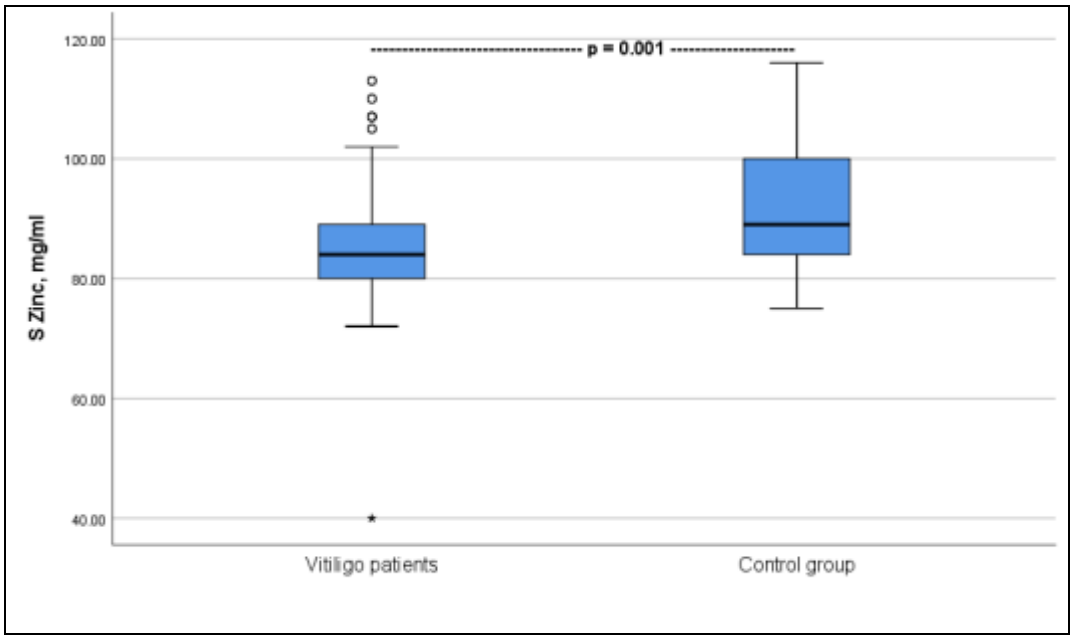

Figure 2: Box blot comparison of serum Zinc between Vitiligo patient and healthy control group.

The findings of a series of correlation and linear regression between serum zinc as a "dependent outcome" and a number of independent predictors (vitiligo severity, age, and duration), respectively, are shown in Figures 3 a, b, and c. The results show that: the patient's age and serum zinc level have an inversely significant relationship (r = -0.26, r2 = 0.06, P = 0.01); the serum zinc level and the duration of vitiligo have a non-significant relationship (r = 0.02, r2 = 0.001, P = 0.8); and, finally, there is a significant inverse relationship (r = -0.28, r2 = 0.08, P = 0.006) between the serum zinc level and the severity of vitiligio.

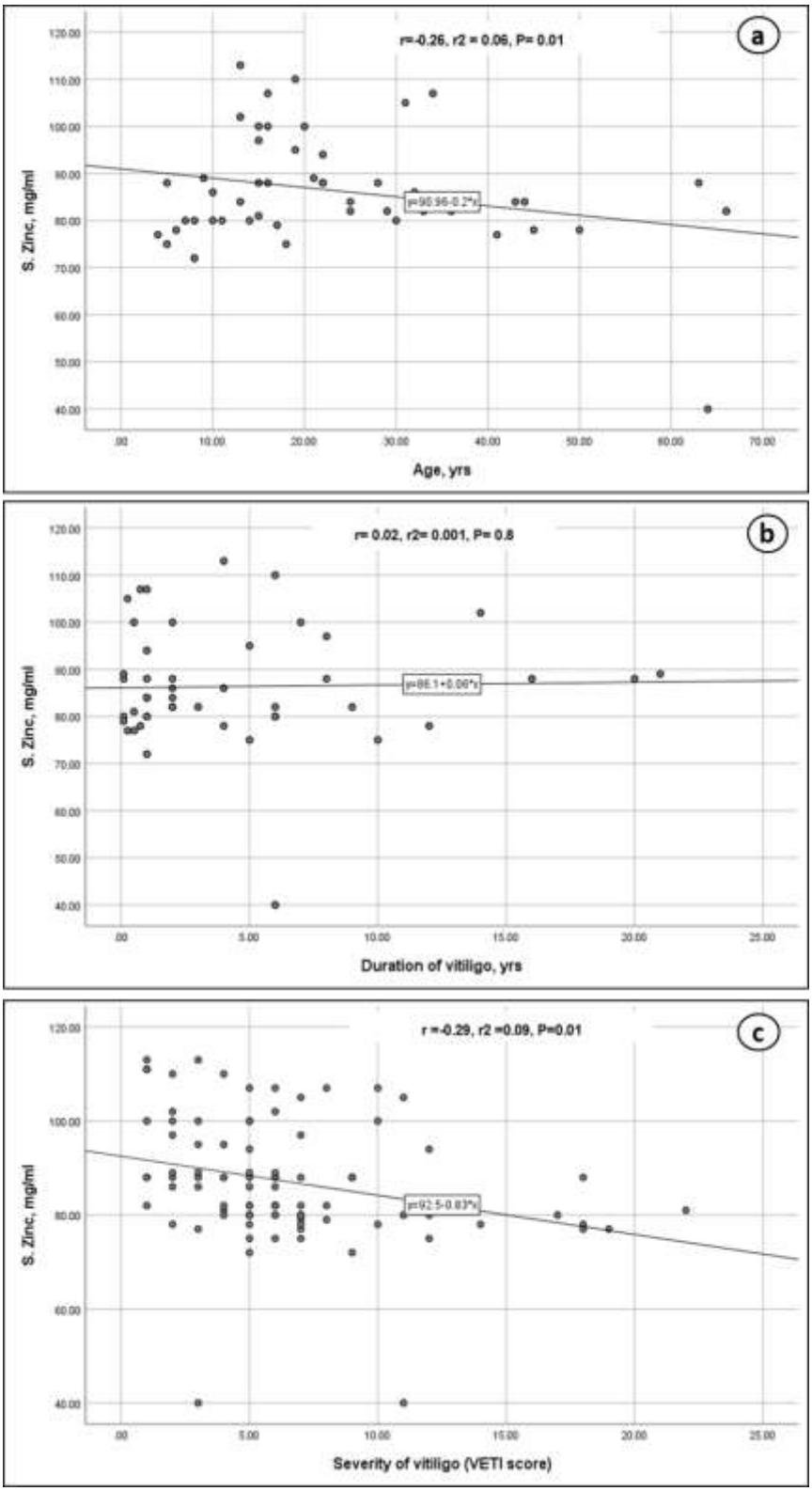

Figure 3: Correlation between serum Zinc as a depended outcome and different independent predictors (a: age, b: duration of disease and c: severity of Vitiligo).

DISCUSSION

Zinc is one of the most crucial micronutrients for healthy skin because it regulates a variety of processes, including melanocyte development, maturation, and differentiation.[14] Unfortunately, technical document published by the International Zinc Nutrition Consultative Group (IZiNCG) show that 33% of people globally do not get enough zinc from their daily diets.[15]

The findings of this study provide additional support for role of zinc in the etiopathogens of vitiligo. The results indicate that serum zinc levels are lower in vitiligo patients (86.36±12.05 versus 92.94±10.36) compared to controls. This result is largely in line with a local study carried out at Tikrit Teaching Hospital by Ahmed et al.[16], but it differs in that the zinc level estimated in our study was higher than that of their study (86.36±12.05 Vs. 73.14+19.32). The lower zinc level in patients compared to control is also in line with earlier research findings published from different countries by Shameer et al.[10] (21.6% of patient show reduced zinc level), Mogaddam et al.[17] (80.11 ±17.10 µg/dl Vs. 96.10 ±16.16 µg/dl), and Mirnezami et al[18] (81.3 mcg/dl Vs. 91.8 mcg/dl in the control group). Furthermore, Zeng et al.[19] in their meta-analysis study conclude that decreased levels of serum Zn are generally present in Chinese vitiligo patients ($Z = 4.88$, $P < 0.00001$; SMD, -1.09; 95% CI, -1.51 to -0.64). They recommend administration of oral Cu and Zn in the management of Vitiligo. However, Arora et al. [20] found that the zinc level in Vitiligo patients was 97.3 ± 26.6 µgm/100 ml, but they came to the conclusion that there was no discernible difference between that level and the control group. Additionally, Dogan et al.[21] measure intraerythrocyte zinc concentration in vitiligo patients revealed no appreciable variations between the patient and control groups. On the other hand, Azzam et al.[22], and Witasari etal[23]., demonstrated greater serum levels of zinc in vitilgo compared to controls. They attributed this raise to increased cell death and release of large amount of intracellular zinc in disease condition. The possible factors behind contradictories and variation in reported zinc level may be attributed to sampling variation regarding age span, disease severity, and activities.

Zinc level changes was not linearly related to age or duration of Vitiligo in the current series. This contrary to observation of Mirnezami and Rahimi [18], who they conclude that there is negative correlation between serum zinc level and age in patients with vitiligo ($R = -0.67$, and $R = 0.73$ respectivly). A reason behind failure to demonstrate linear relation between age and zinc in the current study is that zinc level start low in first, later raised with then it drop again in the 6th decade. The correlation between severity Vitiligo and zinc leve is consistent with Zaki et al study [24]. The report A high statistically significant negative correlation between serum zinc levels and the extension of vitiligo (P value = .0001 and R value = − 0.835).

CONCLUSIONS

The role of zinc in the pathophysiology of vitiligo was highlighted by a relative decrease in the serum zinc level in vitiligo patients compared to general population. Zinc level has a negative impact on the extent and tensity of Vitiligo. Zinc supplement incorporated as part of management of Vitiligo patient is still questionable.

Statement of Ethics: The Ethical Committee of the Ninevah directorate of health verified the project. Participants provide consent before enrollment.

Conflict of Interest: No conflicts of interest exist, according to the conflict-of-interest statement.

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