Evaluation of serum zinc level in patients with Alopecia Areata

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ABSTRACT:

Background: Alopecia areata (AA) is non-scarring telogenic alopecia of autoimmune etiology. Clinically, the disease is characterized by the appearance of alopecic patches or plaques of varying size and number on the scalp with peak incidence 2% in the general population, can involve any age group with higher prevalence in younger patients.

Aim: The purpose of this study is to estimate serum zinc level in patient with alopecia areata comparing to age, sex match healthy controls.

Method: A case-control study was conducted on total number of 120 subjects;60 patients with AA and 60 age- and sex matched healthy controls. Serum zinc levels were assessed in all subjects. Comparison of mean serum zinc levels was done between all patients and controls. A significantly lower serum zinc level was found in patients with AA compared with controls and the significant inverse correlations existed between serum zinc level and severity of AA.

Keywords: alopecia areata, serum zinc level, telogenic alopecia, autoimmune.

تقييم مستوى الزنك في الدم لدى مرضى الثعلبة البقعية

الخلاصة: الثعلبة البقعية (AA)هي ثعلبة تيلو جينبة غير تندب من مسببات المناعه الذاتية ، سريريا يتميز المرض بظهور بقع أو لويجات متفاوتة الحجم والعدد على فروة الرأس مع ذروة حدوث 2% من عامة الناس، ويمكن أن تشمل أي فئة عمرية مع انتشار أعلى لدى المرضى الاصغر سنا.

الهدف : الغاية من الدراسة هو تقدير مستوى الزنك في مصل الدم لدى المرضى الذين يعانون من داء الثعلبة مقارنة بالعمر، والضوابط الصحية المتطابقة مع الجنس.

طريقة العمل: أجريت الدراسة على الحالات والشواهد اجمالي العدد 120 شخصا، 60 مريضا لديهم الثعلبة البقعية و 60 عمرا وجنسا متطابقين مع الضوابط الصحية. تم تقييم مستويات الزنك في الدم في جميع الحالات. تم اجراء مقارنة بين متوسط مستويات الزنك في الدم بين جميع المرضى والضوابط. فوجد ان مستوى منخفض من الزنك في مصل الدم لدى المرضى الذين يعانون من الثعلبة البقعية مقارنع مع الضوابط ووجدت ارتباطات عكسية كبيرة بين مستوى الزنك في الدم وشدة AA.

الكلمات المفتاحية: الثعلبة البقعية ، مستويات الزنك في الدم ، تيوجينبة، مناعية.

INTRODUCTION:

Alopecia Areata (AA); is common non-scarring hair loss that is usually characterized by acute onset with a peak incidence from 1.7% to 2% in the general population, can involve any age group with higher prevalence in younger patients (21-40 years of age)[1]. An autoimmune disease that can affect any hair-bearing area but is mostly noticeable in the scalp, beard area and eyebrow. A single, well-demarcated patch with hair loss or multiple patches is the most clinical presentation[3]. Depending on its acuity

and extent, hair loss is obviously an important cause of anxiety and disability[4]. At any given time, the prevalence of other autoimmune conditions in patients with AA is 16 %[5]. As with other immune-mediated diseases, a complex interaction between environment and genetics is thought to lead to the development of AA. A modifiable risk factor associated with the development of AA may be a deficiency of micronutrients such as vitamins and minerals, given the importance of zinc and micronutrients in the normal growth of hair follicles and the function of immune cells[6]. Zinc is a well-known trace element associated with hair shedding because it may accelerate the regeneration of hair follicles and prevent the regression of hair follicles[7]. A growing number of studies have attempted to ascertain whether serum levels of this zinc can differ in AA patients and whether zinc supplementation can be a therapeutic alternative for AA[8]. Zinc may also affect the biology of hair through its immunomodulatory effects[9,10]. It exerts an indirect antioxidant effect by causing those compounds that function as the ultimate antioxidant, such as metallothionein. In addition, in the hair follicles, zinc exerts major functional activities and it is a potent inhibitor of endonucleases, the key constituents of the apoptotic machine, given the crucial role of keratinocytes apoptosis in HF (hair follicle) regression during the involution phase of the hair cycle catagen. Zinc-mediated inhibition of endonuclease activity was found to be a strong candidate for inhibition of HF regression[8]. Zinc also inhibits the expression or activity of many enzymes important for hair biology, including tyrosine, the HF melanogenesis rate-limiting enzyme. Zinc is important in hair biology for DNA maintenance and repair parameters, as the epithelial hair matrix is one of the most rapidly proliferating and damage-sensitive tissues in the mammalian organism[11]. Al-Jaff et al , reported a significant increase in basal malondialdehyde (MDA) level, as a strong biomarker of lipid peroxidation, and a significant decrease in glutathione (GSH) level, as a major antioxidant, in erythrocytes of alopecic patients compared to their normal control, suggesting the role of oxidative stress in the pathogenesis of alopecia areata.[12]The aim of this study is to evaluate serum zinc level in in patient with alopecia areata comparing to age, sex match healthy controls.

METHODS:

Study design and population:

A case -control study, was conducted on a total number of 120subjects;60 patients with AA and 60 age and sex- matched healthy controls. They were randomly selected from attending outpatient department of Erbil dermatology teaching center in Erbil city Iraq between March 2021 to March 2022. Every participant was subjected to full history taking, general examination, and local scalp examination for assessment of the clinical type and\ or pattern of hair loss. The inclusion criteria for patients with AA were: being over 6 years of age, and willing to participate in the study. Exclusion criteria Patients who taking any supplement, included the use of zinc supplements, Pregnant and lactating females. Patients with a history of any systemic disease e.g. chronic liver or renal diseases, and autoimmune diseases. The control group will be chosen from healthy individuals who did not use any minerals in the last 3 months.3_4 milliliters of fasting (6–8 hours) venous blood were taken from each case participating in this study using plastic disposable syringes, left to clot, then centrifuged to separate serum. Serum was then stored frozen in Eppendorf tubes at -20 °C until used. The serum level of zinc was measured by using the colorimetric method with a spectrophotometer wavelength 560 nm. According to the manufacturer, the serum zinc level was considered normal for values of 68–107 μg/dl. Data were obtained on a specially constructed questionnaire. The statistical analysis was performed by using IBM-SPSS 26. The normality of these data tested by the Shapiro-Wilk test, mean and stander values were calculated. The t-test for independent two means, Chi-square test, Kruskal-Wallis test,

and Mann-Whitney U test were used. The odd ratio was also estimated. P-value ≤ 0.05 is considered as significa

Ethical Consideration:

* Information sheet: (as shown in Appendix II)

* Consent Form: (as shown in Appendix III)

RESULTS:

The present case-control study included 60 patients with alopecia areata and 60 healthy individuals. Table (1) shows the comparison between cases and controls regarding basic characteristics and reveals that the mean age among the cases is lower than that of controls but the difference is statistically insignificant. The male gender forms 61.7% of cases and 63.3% of controls while the female gender is 38.3% and 36.7% of cases and controls respectively, although the male gender is risky, the association of gender with alopecia areata is non-significant. Furthermore, the rural residents are at risk for the disease with OR=1.3 but with non-significant statistical association. Table (2) shows the comparison of S. zinc levels between cases and controls and reveals that the mean of s. zinc among cases 59.43±20.54 µg/dl is lower than the mean among controls 90.71±37.33 µg/dl in a statistically significant way. Moreover, 51.7% of cases have s. zinc level of <60 µg/dl while among the controls no individual has that level, a difference that is statistically significant. Above >80 µg/dl, Serum zinc levels are 13.3% and 41.7% among cases and controls respectively, the difference is statistically significant. Zinc levels between 60-80 µg/dl among the cases 35.0% is significantly lower than that among controls 58.3% with p=0.010. Table (3) demonstrates the S. zinc level among cases according to study parameters Table there is a statistically significant difference is found among different durations of disease (p=0.030) with a real difference presents only between <3 months and>12 months (p=0.004).

Table (1): The comparison between cases and controls regarding basic characteristics.

		Cases	Controls	p-value*	
		Mean±SD	Mean±SD		
Age		25.93±10.80	25.75±10.86	0.926	
		Cases No.(%)	Controls No.(%)	OR	p-value
Gender	Male	37(61.7%)	38(63.3%)	0.931	0.850**
	Female	23(38.3%)	22(36.7%)		
Residence	Rural	10(16.7%)	8(13.3%)	1.3	0.609**
	Urban	50(83.3%)	52(86.7%)		

* t- test for independent two means; **Chi-square test.

Table (2): The comparison of S. zinc level between cases and controls.

Level of S. zinc	Cases	Controls	p-value*
	Mean±SD	Mean±SD	
Serum Zinc	59.43±20.54	90.71±37.33	0.000
	No. (%)	No. (%)	p-value**
<60 µg/dl	31(51.7%)	0(0.0%)	0.000
60-80 µg/dl	21(35.0%)	35(58.3%)	0.010
>80 µg/dl	8(13.3%)	25(41.7%)	0.001

*Mann-Whitney U test; **Chi-square test

Table (3): The S. zinc level among cases according to the duration of disease.

S. zinc level in cases' duration of the disease			Mean ±SD	p-value*
Duration of the disease	<3 month	S. zinc	66.83±18.74	0.030
	3-6 months	S. zinc	57.38±22.57	
	9-12months	S. zinc	68.58±21.99	
	>12 months	S. zinc	48.48±15.60	

DISCUSSION:

Zinc is a trace element. It is an essential cofactor of enzymes and transcription factors that are necessary for human metabolism, reproductive function, immune systems, and wound healing process. Patients with zinc deficiency present with a variety of symptoms including hair loss [13]. However, the effect of zinc on hair follicles is still unknown. The mean age of patients in the present study was 25.93±10.80 years with 75.0% of patients having onset around 16-49 years age interval with 38.3% of cases being female. Different findings were found in the Sellami *et al.*, study where fifty patients with AA were seen in the Department of Dermatology of Hedi Chaker University Hospitals found that the patient's

mean age was 32.92 years. 52% of patients were females [14]. This may be due to difference in sample size between our and this study.

Regarding gender, no significant difference was found in the present work between males and females although the male was predominant which was corresponding to Mirzoyev et al., study [15]. Similarly, studies have shown a male predominance ranging from 2:1 to 1.1:1 [16, 17] The present study found that the mean of s. zinc among cases 59.43 µg/dl is significantly lower than the mean among controls 90.71µg/dl, moreover, 31 cases have zinc levels <60 µg/dl in comparison to the control group which has zinc levels of 60 and higher in a statistically significant way. Similar result was found in a case-control study conducted by Abdel Fattah et al., [18] who reported a significantly lower serum zinc level in patients with AA compared with controls. Additionally, the Aiempanakit et al., [19] cross-sectional study found that the patients with AA showed mean plasma zinc levels lower than those in the controls with statistical significance (61.20±12.00, 67.17±10.04 µg/dL), respectively, p-value = 0.04). Different findings obtained from Dastgheib et al., study [20] conducted in Iran did not detect a significant difference in serum zinc levels between patients and those in the control group. Moreover, Mussalo-Rauhamaa and colleagues 24 reported no differences in zinc levels and other trace elements among Finnish AA and normal subjects [21]. The mean serum zinc level in this study was significantly higher in patients with <3 month in comparison to those with >12 months. Similar findings were found in another study where the mean plasma zinc level in patients who had AA for more than three months was lower than those who had AA for less than three months without statistical significance (58.33±8.59, 62.43±13.19 µg/dL (mean ± SD), respectively, p-value = 0.40). In a linear regression analysis, there was no correlation between plasma zinc levels and the duration of AA (p-value = 0.31) The significant inverse correlations existed between serum zinc level, the severity of AA, and disease duration in all patients as well as in patients with resistant AA [18]. While Saniee et al., found significant correlations between AA duration and zinc levels (r=0.483, p<0.001) [22].

CONCLUSION:

According to the results obtained in the present study, we concluded that serum zinc level is lower in patients with AA compared to age -sex matched heathy controls. More over patients with resistant AA have lower mean serum zinc level compared to patients with newly diagnosed AA. Accordingly, serum zinc level may be useful marker of disease severity and duration in AA.

RECOMMENDATION:

Further studies with large sample size are therefore recommended to evaluate the role of zinc and zinc supplement in patients with AA, especially those with severe, longstanding, or resistant disease.

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Appendix I

Questionnaire Evaluation of serum zinc level in a patient with Alopecia Areata

Code:

Name of patient: **Age**:   **Tel.no**:

Gender: 1. Male   2. Female

Residency: 1. Rural   2. Urban

Occupation:

1. Child   2. Student   3.housewife   4.employee   5.Retired

Economic status: 1. Poor   2.Moderate   3. Good   4.Very good

Social status: 1. single   2.Married   3.Divorced   4.Widow

Weight (kg):   **Height (CM):**   **BMI:**

History:

Age of onset

1. Childhood- onset (1-15)   2.Adulthood -onset (16-49)   3.Late- onset (>50)

Past medical history

1. Atopy   2.DM   3.Thyroid disease   4.Others

Family history:

1. Alopecia areata   2.Atopy   3.Thyroid disease   4.Others

Physical examination:

AA characteristic

1. Localized patchy   2.Multifocal (patch>3)   3.Ophiasis   4.Diffuse (AT)

5. Alopecia universals

Nail involvement

1. Pitting   2.Trachonychia   3.Red spots on the lunula

Body hair involvement

1. None   2.Some   3.100%

Duration of the disease(months):

1.12   2.12-24   3.24-36   4.>36

Treatment:

1. Topical   2. Localized (IL)   3.Systemic therapy