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Original Article

Assessment of the Relation of Serum Adiponectin Level with Alopecia Areata

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ABSTRACT

Background: Decreased serum levels of adiponectin are associated with chronic inflammation of metabolic disorders. Limited data regarding the relationship among metabolic conditions, cardiovascular diseases and Alopecia Areata (AA) is available. This study aimed to clarify the possible participation of adiponectin in the pathogenesis of AA.

Methods: This case-control study has been conducted in Dermatology, Venereology and Andrology Department at Zagazig University Hospitals. It included 48 participants, 24 AA patients and 24 apparently healthy control subjects of matched age, sex and body mass index (BMI). Serum adiponectin level was measured from each subject using quantitative ELISA kits. **Results:** We revealed that serum adiponectin was slightly lower in the patient group, but no significant difference was found between the alopecia group and the control group regarding serum adiponectin (p=.563) or HbA1c (p=.403). While serum adiponectin had no correlation with Hb A1c in the alopecia group (r=.190, p=.375), it had a significantly positive correlation with Hb A1c in the control group (r=.411, p=.046). Serum adiponectin showed a significantly strong negative correlation with the SALT score and the mean size of patches (r=-.602, p=.002) and (r=-.650, p=.001), respectively. A cut-off of 302.06 ng/ml of serum adiponectin for the prediction of AA had 50% sensitivity, 50% specificity, 50% positive predictive value (PPV), 50% negative predictive value (NPV), 1.00 positive likelihood ratio (+LR), and 1.00 negative likely hood ratio (-LR).

Conclusion: Adiponectin may be involved in part in the pathogenesis of AA. The strong negative correlation between serum adiponectin level and SALT score suggests that adiponectin serum concentration can be considered a severity marker of hair loss in AA.

Keywords: Adiponectin Level, Alopecia Areata, hair loss

INTRODUCTION

With a lifetime incidence of 2% and a prevalence of 1 in 1000, autoimmune alopecia areata (AA) is the second most frequent kind of non-scarring hair loss, behind androgenetic alopecia. The majority of patients are under the age of 30 and just 20% are 40 or older [1]. Sudden, localized hair loss in clearly defined places is the most common symptom of alopecia areata. Typically, the lesion appears as a single or many circular or oval patches of alopecia. Normal hair typically demarcates the perimeter of the alopecia patch, giving it a characteristic boundary. The majority of AA cases manifest on the scalp. Alopecia totalis can impact only the hair on the scalp, but alopecia universalis can affect all hair on the body (including the beard, eyebrows, eyelashes, underarms and pubic hair) [2]. Genetics, immunology, oxidative stress, the microbiome, allergies, microbiota, epigenetics and other factors have recently been uncovered as

contributing to the etiopathogenesis of AA. As a result of these breakthroughs, several effective therapies for AA have been developed [3]. There is evidence that alopecia areata is associated with several comorbidities, including vitiligo, lupus erythematosus, atopic dermatitis, thyroid disease, allergic rhinitis and atopic dermatitis. Recent research has shown a strong correlation between alcohol use disorder (AA) and mental health issues such as anxiety and sadness [4].

Fat tissue is not an inert tissue. Adipokines are actively produced by it.These adipokines control insulin sensitivity and energy expenditure and regulate inflammation and immunity, among many other physiologic and pathologic processes [5]. Secreted mostly by white adipose tissue (WAT), adiponectin is the most abundant adipokine in human plasma. Three different isoforms of adiponectin—high-molecular-weight (HMW), middle-molecular-weight (MMW) and low-molecular-weight (LMW), are found in the bloodstream. Type 2 diabetes, obesity and atherosclerosis are metabolic diseases characterized by chronic inflammation and low serum adiponectin levels are related to these conditions. However, some studies suggest adiponectin may promote inflammation in autoimmune disease patients [6].

The correlation between metabolic disorders, cardiovascular illnesses and AA is poorly understood. Also, several studies have revealed that people with AA have impaired antioxidant activity and higher levels of lipid peroxidation. This is when it becomes useful to look at a few indicators linked to inflammation, atherosclerotic hyperlipidemia, ischemia and oxidative stress and how these relate to AA disease features [7]. This study aimed to clarify the possible participation of adiponectin in the pathogenesis of AA.

METHODS

This was a case-control study. All the patients had been recruited from the Outpatient Clinic of Dermatology, Venereology and Andrology Department at Zagazig University Hospitals. It included 48 participants, 24 AA patients and 24 apparently healthy control subjects of matched age, sex, and body mass index (BMI). Written informed consent was obtained from all participants; the research ethical committee of the Faculty of Medicine, Zagazig University, approved the study. The study was conducted according to the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. This study was carried out after the approval of the Institutional Review Board (ZU-IRP#9532/17-5-2022).

The present study was carried out on 48 individuals. Participants were divided into 2 groups, a diseased group and a control group, as follows: Group A: 24 patients with AA, 13 males and 11 females, from both sexes, aged more than 18 years old. Group B: 24 apparently healthy individuals, 13 males and 11 females. Cases with the following characteristics were excluded: cases who were receiving systemic or topical therapy for 4 weeks before they visited our clinic, patients with chronic systemic diseases such as diabetes mellitus, hypertension, liver, renal or cardiac disease, patients with other autoimmune diseases, cicatricial alopecia as well as pregnant and lactating females were also excluded.

All patients and controls were subjected to the following assessments before collecting the blood samples: complete history taking, general examination and clinical assessment. In addition, dermatological examination of Alopecia areata patients included Calculation of BMI by weight (in kilograms) divided by square of height (in meters) as a measure of total adiposity [8]. Evaluation of AA by trichoscopy and photography taking. The severity of hair loss was assessed using the severity of the alopecia tool (SALT). The SALT score is computed by measuring the percentage of hair loss in each of 4 areas of the scalp vertex (40%), right profile (18%), left profile (18%) and posterior (24%) and adding the total to achieve a composite score [9].

Laboratory investigation included Evaluation of HbA1c: a venous blood sample was taken from both AA patients and the healthy group.

For measurement of serum Adiponectin five milliliters of venous blood was withdrawn from each subject in clot activator vacutainers to separate serum. In (HITACHI himac CT6E® centrifuge), the blood samples were centrifuged at 3000 rpm for 15 minutes to separate serum and then stored in Eppendorf tubes at -80°C before assaying. In samples, serum adiponectin was measured using a human adiponectin immunoassay using quantitative sandwich enzyme-linked immunosorbent assay (ELISA) serum kits by Wuhan Fine Biotech Co., Ltd, catalog No.: EH2593 The standard assay Range: 1.563-100ng/ml and the sensitivity is 0.938ng/ml.

Statistical analysis: The data were analyzed using IBM SPSS 23 (SPSS Inc., Chicago, IL, USA) and NCSS 11 for Windows (NCSS LCC., Kaysville, UT, USA). Quantitative data were presented as mean, standard deviation and range, while categorical data

were presented as numbers and percentages. The differences among groups were assessed using an independent sample t-test and Chi-square test. The influence of variables on adiponectin was analyzed using Pearson's correlation coefficient (r). The diagnostic performance of adiponectin in AA was assessed using receiver operating characteristic (ROC) curves. The optimal cut-off values for the prediction of the control group were chosen to maximize the sum of sensitivity and specificity. Statistical analysis was performed on the data collected, and P <0.05 was defined as statistically significant.

RESULTS

Table 1: show that the studied groups had the same sex distribution of thirteen males and eleven females. Age and BMI showed no significant difference between the groups (p=.128) and (p= 0.555). Nineteen alopecia patients had no family history, while five patients had a positive family history.

Table 2: show that the mean number of the examined patches was 1.33±0.64, and the mean size was 5.53±4.58 cm2. Nineteen (79.2%) patients had black dots, and thirteen (54.2%) had yellow dots.

Table 3 show that there was no significant difference was found between the alopecia group and the control group regarding serum adiponectin (p=.563) or HbA1c (p=.403).

Table 4: show that serum adiponectin showed no significant correlation with age or BMI in both groups. It also showed no significant correlation with disease duration or the number of patches in the alopecia group. While serum adiponectin had no correlation with Hb A1c in the alopecia group (r=.190, p=.375), it had a significantly positive correlation with Hb A1c in the control group (r=.411, p=.046).

Tables 5: Eighteen (75%) patients had acute onset and six (25%) patients had gradual onset. Eleven (45.8%) patients showed a progressive course, while thirteen (54.2%) showed a stationary course. The mean duration of the disease was 0.97±0.60 years and the mean SALT score was 7.63±4.49 %; twenty-two patients had scalp distribution; nine (37.5%) of them showed posterior predominance, six (25%) showed vertex predominance, two (8.3%) showed left-side predominance and five (20.8%) showed right-side predominance. Only two patients showed barbae distribution: one (4.2%) with right side and one (4.2%) with left side predominance.

There was no significant relation between the serum adiponectin level according to the patient's sex or the clinical presentation of the disease in alopecia patients (Table 5).

The ROC curve for Serum adiponectin showed a 0.535 (AUC) Area under the curve with p=.680. A cut-off of 302.06 ng/ml of serum adiponectin had 50% sensitivity, 50% specificity, 50% positive predictive value (PPV), 50% negative predictive value (NPV), 1.00 positive likelihood ratio (+LR), and 1.00 negative likely hood ratio (-LR) (Figure 1).

Table (1) : Comparison between the studied groups regarding demographic characteristics

Demographic characteristics		Groups		P
		Alopecia Areata Group	Control group	
		N=24	N=24	
Sex	Male	13 (54.2 %)	13 (54.2%)	1.00# (NS)
	Female	11 (45.8%)	11 (45.8%)	
Age (years)	Mean±SD.	34.63±10.47	30.33±8.65	.128* (NS)
BMI	Mean±SD.	26.04±4.58	25.23±4.88	.555* (NS)
Family history	Negative	19 (79.2%)	-	-
	Positive	5 (20.8%)	-	

#chi square test & *independent samples t-test are used to analyze the difference between the groups. (NS): not significant.

Table (2): Distribution of patients according to the clinical presentation:

Clinical presentation		**Alopecia Areata (N=24)**
Onset	Acute	18 (75.0%)
	Gradual	6 (25.0%)
Course	Progressive	11 (45.8%)
	Stationary	13 (54.2%)
Duration (years)	Mean±SD	0.97±0.60
	Range	(0.25-2)
SALT score (%)	Mean±SD	7.63±4.49
	Range	(1-17)
Site	Posterior	9 (37.5%)
	Vertex	6 (25.0%)
	Left side of scalp	2 (8.3%)
	Right side of scalp	5 (20.8%)
	Left side of face	1 (4.2%)
	Right side of face	1 (4.2%)
Number	Mean±SD	1.33±0.64
	Range	(1-3)
Clinical presentation		**Alopecia Areata (N=24)**
Size (cm^2)	Mean±SD	5.53±4.58
	Range	(1.5-24.5)
Black dots	Present	19 (79.2%)
	Absent	5 (20.8%)
Yellow dots	Present	13 (54.2%)
	Absent	11 (45.8%)

Table (3): Comparison between the studied groups regarding serum adiponectin and HbA1c

		Groups		**P**
		Alopecia	**Control group**	
		N=24	**N=24**	
Serum adiponectin (ng/ml)	Mean ± SD.	279.79±61.23	289.02±47.73	.563* (NS)
Hb A1c (%)	Mean ± SD.	5.38±0.20	5.32±0.27	.403* (NS)

*Independent samples t-test is used to analyze the difference between the groups. (NS) not significant.

Table (4): Correlation of serum adiponectin with demographic data and SALT score

	Groups			
	Alopecia		Control	
	r	p	r	p
Age	-.015	.945	.026	.905
BMI	.101	.638	-.087	.685
Duration of the disease	-.331	.114	-	-
Number of patches	.019	.930	-	-
Size of patches	-.650	.001(S)	-	-
Hb A1c	.190	.375	.411	.046(S)
SALT	-.602	.002(S)	-	-

Correlations between Serum adiponectin and variables are analyzed using the Pearson correlation coefficient. P <0.05 was defined as statistically significant. (S): significan.

Table (5): Effect of clinical data on serum adiponectin:

Serum Adiponectin			
		Alopecia N=24	p
Sex	Males	264.19±69.84	.180 (NS)
	Females	298.24±45.59	
Onset	Acute	284.04±61.97	.568 (NS)
	Chronic	267.06±62.69	
Course	Progressive	295.65±45.43	.236 (NS)
	Stationary	266.38±70.99	
Family history	Absent	281.81±67.15	.761 (NS)
	Present	272.14±34.26	
Yellow dots	Absent	256.12±69.78	.081 (NS)
	Present	299.82±46.68	
Black dots	Absent	288.29±65.13	.736 (NS)
	Present	277.56±61.83	
Site of patches	Scalp	277.71±63.61	.591 (NS)
	Face	302.77±9.78	

Independent samples t-test is used to analyze the difference between the two groups. P <0.05 was defined as statistically significant

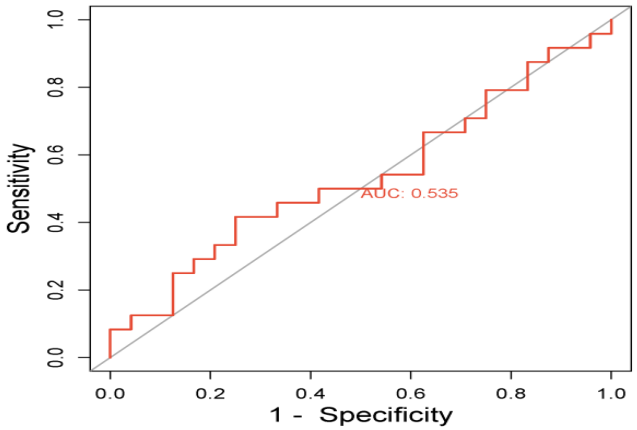

Figure (1): ROC of serum adiponectin to predict alopecia areata.

DISCUSSION

The pathophysiology of AA is not fully understood and no single concept could be universally accepted. AA is mostly considered an autoimmune disease in which the collapse of hair follicle IP plays a key role. Therefore, immunosuppressive treatments such as corticosteroids, ultraviolet irradiation and cyclosporine A have been tried on AA patients, but the responses are not definite [10].

Several lines of evidence point to adiponectin as a key player in developing and maintaining inflammation. Proliferation, flexibility, and polarization of macrophages, representative of the innate immune system , are essential features of inflammatory reactions. According to some studies, adiponectin prevents inflammation by controlling the polarization of macrophages, the generation of cytokines that promote inflammation and the proliferation of these cells [10]. This work aimed to clarify the possible participation of adiponectin in the pathogenesis of AA. This case-control study has been conducted in the Dermatology, Venereology and Andrology Department at Zagazig University Hospitals. It included 48 participants, 24 AA patients, and 24 apparently healthy control subjects of matched age, sex and BMI. Serum adiponectin level was measured from each subject using quantitative ELISA kits.The present study results revealed that serum adiponectin was slightly lower in the patient group, but there was no significant difference between both groups. No significant difference was found between the alopecia and control groups regarding serum Hb A1c. While serum adiponectin had no correlation with Hb A1c in the alopecia group, it had a significantly positive correlation with Hb A1c in the control group.

We found no significant correlation between the level of serum adiponectin and the patient's sex, age, BMI or clinical presentation of the disease. In the patient group, serum adiponectin showed a significantly strong negative correlation with the SALT score and the mean size of patches. To our knowledge, only very few studies were made to assess the role of adiponectin in AA.

Seralasan et al. [11] examined 70 persons in all: 36 (25 male, 11 female) patients with AA ranging in age from 18 to 55, and 34 (18 male, 16 female) healthy controls ranging in age from 18 to 51. Three of the AA patients and two of the healthy volunteers were found to have metabolic syndrome. In terms of gender, age, and body mass index (BMI), there was no discernible difference between the two data sets. They split the patients into two groups, with subgroup 1 consisting of those experiencing hair loss on the scalp (AA1). Part 2 (AA2) included patients who had thinning hair on their beards and eyebrows. The adiponectin levels were noticeably greater in the AA1 subgroup when contrasted with the control group. Regarding all other measures, there was no statistically significant difference between the control group and the AA1 subgroup. Adiponectin levels and body mass index (BMI) had a strong negative connection ($r = -0.645$; $p = 0.032$), while subgroup AA2 showed a statistically significant rise in fasting glucose levels but no differences in other parameters compared to the control group.

According to Stochmal et al. [12], who researched 65 AA patients and 71 healthy controls who were matched for age, sex, and body mass index, the SALT score ranged from 2 to 100% (mean: 30%). In 51 individuals, AA was found in patches; 7 patients had total alopecia totalis, and 7 had universalis. One person in the control group and two people with AA were found to have metabolic syndrome; one person with AA also had type 1 diabetes, while none of the healthy controls had a family history of the disease. Patients with AA did not differ significantly from healthy controls concerning their mean fasting glucose concentrations. Patients with AA had considerably reduced mean adiponectin concentrations in their plasma compared to healthy controls. A negative association between adiponectin serum concentrations and SALT score was also statistically significant. Adiponectin concentration was also significantly lower in universalis patients than in patchy alopecia AA patients. Patients with AA did not show any associations between age, body mass index and blood adiponectin levels.

Farag et al. [5] compared 75 individuals with AA with 75 healthy controls who were similar in age and gender. The age range of the patients was 22–53 years, and there were 36 men and 39 females. With ages ranging from eighteen to fifty-four, the control group consisted of forty-three men and thirty-two females. Regarding age, sex and body mass index, there were no statistically significant differences between the control group and the cases. Patients with AA had considerably lower serum adiponectin levels than controls. However, patients experiencing hair loss on the scalp had higher levels than those with isolated AA in the beard and eyebrow. Patients with alopecia totalis had considerably decreased serum adiponectin levels compared to those with patchy AA. The same robust inverse relationship was

also seen between adiponectin serum levels and SALT score.

There are many potential explanations for the contradictory findings in our and other investigations, including differences in sample size, racial/ethnic composition, age, gender, and metabolic status. Other forms of AA, such as alopecia universalis and totalis, have also been the subject of studies into adiponectin levels. Additionally, instead of using HbA1c, they relied on fasting blood glucose to gauge metabolic status. To our knowledge, serum adiponectin levels can be influenced by various factors in many autoimmune and inflammatory diseases. Until now, almost all research that has attempted to assess the role of adiponectin in AA has indicated a substantial negative connection between the two variables and the SALT score. This suggests that adiponectin could be utilized as a severity marker in patients with AA, but the results of these studies have been controversial.

Limitations of this study : Several limitations should be acknowledged in our study. Firstly, the relatively small sample size of 48 participants may limit the generalizability of our findings. A larger and more diverse cohort could provide a more comprehensive understanding of the predictive capabilities of Adiponectin Level in Alopecia Areata. The absence of long-term follow-up data prevents us from assessing the enduring possible effects and correlations of thoracoscopic Adiponectin level and alopecia areata.

CONCLUSION

Adiponectin may be involved in part in the pathogenesis of AA. The strong negative correlation between serum adiponectin level and SALT score suggests that adiponectin serum concentration can be considered a severity marker of hair loss in AA. Studying the role of the remaining members of adipokines in the pathogenesis of AA is advisable. Adiponectin needs to be studied in different patterns and grades of AA.

No potential conflict of interest was reported by the authors.

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