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Serum Adiponectin and Leptin in Patients with Alopecia Areata

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ABSTRACT

Background: Alopecia areata (AA) is an autoimmune disorder (AID) characterized by transient non-scarring hair loss (HL) with normal hair follicle. Adiponectin (APN) is an endogenous insulin sensitizer. It also plays a main role in glucose uptake upregulation and promoting fatty acid oxidation. Leptin is another adipokine and was found to correlate with insulin, insulin resistance (IR), and glucose.

Aim of the Work: To investigate the relationship between leptin and APN, and alopecia areata (AA) through estimation of their serum levels.

Patients and Methods: This case control study was conducted on 50 patients with AA and 30 healthy controls who matched patients as regard age and sex. Evaluation of AA severity was done by SALT score. Measurement of serum APN and leptin levels was done using Enzyme Linked Immunosorbent Assay (ELISA) method.

Results: The mean fasting insulin and HOMA-IR levels were higher in AA patients. APN levels were significantly lower, and Leptin levels were significantly increased in the patients compared to the control group. Leptin levels showed a significant positive correlation with fasting insulin and HOMA-IR indicating a relationship with insulin resistance markers. Leptin had a negative correlation with HDL cholesterol (r=-0.294, p=0.008), suggesting a potential link between leptin levels and lipid metabolism. **Conclusion**: Both adipokines may be considered as a predictive factor of HL in AA. Our study supports the theory that the impaired secretion of specific adipokines may have an essential and complex role in AA pathogenesis and its continuity.

Keyword: Adiponectin, Leptin, Alopecia Areata, Adipokine.

INTRODUCTION

Alopecia areata (AA) is an AID characterized by transient non-scarring hair loss (HL) with normal hair follicle. HL can manifest in various forms, from well-circumscribed patches to diffuse or total HL, affecting all hair-bearing areas [1]. The prevalence of AA accounts for about 0.15 globally [2]. The pathogenesis of AA hasn't been totally explained. On the other hand, mush research display that AA is accompanied by systemic autoimmune activation implying significantly increased serum levels of Th1 (IL-1β, IL 2, IL-12, TNF-α, and IFN-γ), Th2 (IL-4, IL-10, IL-13, IL-25, IL-31) and Th17 cytokines (e.g. IL-17A) [3].

AA might be accompanied by a higher risk of the development of inflammatory and metabolic co-morbidities. **Conic *et al.*** [4] displayed that dyslipidemia (19.8% versus 6.6%), obesity (18.1% versus three %), diabetes mellitus (DM) (11.4% versus 7.4%) and metabolic syndrome (MetS) (1.4% versus 0.3%) were more often recorded in cases with AA compared with normal subjects. Adipose tissue could act in autocrine, paracrine, or endocrine manner to manage different metabolic processes and play a role in lipid and glucose metabolism. In addition, adipocytes release adipokines comprising hormones (for instance leptin & APN) and cytokines (for instance TNF-alpha and IL-6) [5].

Adiponectin is a serum protein formed primarily by the adipocytes. On the other hand, the fibroblasts, leukocytes, and macrophages can, in addition, synthesize APN [6]. APN has an essential role in terms of insulin sensitization. It also plays a main role in glucose uptake upregulation and promoting fatty acid oxidation [7]. Adiponectin has an anti-inflammatory action and decreases T cell responsiveness, and TNF-alpha synthesis. In addition, it encourages IL-10 formation [8]. The diminished serum values of APN compared with normal subjects were recorded also in cases with psoriasis [8].

Leptin is another adipokine that mostly formed by the white adipose tissue. Its level has a direct correlation with adipose tissue [7]. It causes appetite suppression and body weight regulation. Its level was demonstrated to correlate with insulin, IR, and glucose [5]. It is a pro-inflammatory adipokine, that triggers the release of proinflammatory cytokines. In addition, it activates the formation of chemokines by macrophages and affects Th1/Th2 balance in favor of the Th1 phenotype [9].

The common presence of metabolic abnormalities in patients with AA suggests that dysregulation of adipokines may have a role in AA pathogenesis. In contrast, till now fewer studies has assessed the adipokines role in AA [3, 10].

So, this study aimed to assess the relationship between leptin, APN and alopecia areata (AA) through estimation of their levels in comparison to healthy controls.

PATIENTS AND METHODS

This case control study was conducted at the outpatient clinic of Dermatology, Andrology & STDs Department, Mansoura University Hospitals, Mansoura, Egypt, within duration of one year from September 2022 to September 2023. The present study was conducted on 50 cases with AA and 30 healthy controls who match the patient group as regard age and sex. Patients aged more than 18 years old with clinical

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diagnosis of AA of variable degrees, which was confirmed with dermoscopic examination were included. The cases were classified into three different groups, patchy AA (partial HL), alopecia totalis (full HL in the scalp) and alopecia universalis (complete scalp and body HL).We excluded cases with age less than 18 years old, with a history of systemic therapy for AA within four weeks, with history or clinical evidence of eating disorders, with acute or chronic infection, with chronic renal or liver disease, with other AID of the skin and heavy smoker patients.

Ethical Consideration

The study design was approved by the IRB of Mansoura University, Faculty of Medicine. A written informed consent was obtained from all participants before the study. Confidentiality was respected. Patients felt had the right to leave the study at any time with no consequences. The study followed The Declaration of Helsinki through its execution.

METHODS

All subjects in the study were subjected to history taking comprising personal history (age, gender, occupation, residence, special habits, marital status, systemic diseases which include DM, hypertension, dyslipidemia and management of systemic disorders), history of the current episode of AA (onset, course, duration, precipitating factors and early treatment), past history of previous episodes of AA (number of attacks, history of alopecia totalis or universalis and history of treatment), family history for evidence of relevance of AA and other autoimmune diseases and past history of any accompanying systemic, dermatologic diseases or major surgeries. General clinical examination was done to rule out any systemic diseases and included BMI (weight in kilograms/square of the height in meters= kg/m^2) and blood pressure (BP).

Full Dermatologic examination that included examination of scalp and body hair for clinical diagnosis of AA and determination of hair loss pattern. The clinical diagnosis was confirmed through dermoscopic examination, dermoscopic signs of comprised exclamation mark hairs, black dots, yellow dots, and dystrophic vellus hairs. Hair loss pattern included patchy hair loss, alopecia totalis, alopecia universalis and ophiasis. Nail examination for nail changes which may present in AA patients as nail pitting, trachyonychia, brittle nail, onycholysis or koilonychias.

SALT score was utilized to assess the severity of the disease [11]. Scalp is divided into four areas; vertex included 40% (0.4) of scalp surface area (SSA), right profile of scalp included 18% (0.18) of SSA, left profile of scalp included 18% (0.18) of SSA, posterior aspect of scalp included 24% (0.24) of SSA and percentage of HL in any of such areas is percentage of HL multiplied by percent SSA in that area. SALT score is the sum of percentage of HL in all the aforementioned regions.

Cases are classified as; S0 was no HL, S1 was up to 25% HL from the scalp, S2 was 25% to 49% HL, S3 was 50% to 74% HL, S4a was 75% to 90% HL, S4b was 91% to 99% HL and S5 was 100% HL.

Assessment of the disease activity was done by hair pull test and dermoscopy. Hair pull test is done when 50 to 60 hairs were selected and held between thumb, index and Middle fingers, gentle pulling was done using slow traction. If more than ten percent of the pulled bundle was removed, it was deemed a positive result. It was conducted at the periphery of AA as well as in normal areas. Dermoscopic examination showed the signs of activity as presence of exclamation mark hair, presence of black dots, presence of broken hair or presence of Pohl Pinkus. Signs of inactive long-standing disease included presence of yellow dots or invisible bulbar openings. Signs of hair regrowth include presence of upright regrowing hair, pigtail hair, or vellus hair.

Full laboratory investigations comprised complete blood count (CBC), kidney function tests (blood urea and serum creatinine), liver function tests (ALT and AST), fasting blood sugar, fasting serum insulin, TG, HDL and cholesterol levels. Measurement of serum adiponectin and leptin levels by using ELISA method with commercial kits.

Statistical Analysis

The collected data was revised, and tabulated using SPSS (IBM Corp. Version 25.0. Armonk, NY). Shapiro-Wilk test was conducted to assess the normality of data distribution. Mean± SD, median, and range were utilized for numerical data. Frequency and percentage were utilized for non-numerical data. Student T Test was utilized to assess the difference between two study group means. A non-parametric variable's difference between two study groups was evaluated using the U test. To evaluate the association between two qualitative variables, the chi-square test was utilized. When the predicted count is less than 5 in more than 20% of cells, the Fisher Exact test was utilized to assess the relation between two qualitative variables. If a p value is less than 0.05, it is deemed significant.

RESULTS

Table **(1):** shows insignificant differences between the groups regarding sex age, occupation, marital status, residence, weight, height, BMI, waist circumference, HDL, TG, cholesterol and fasting glucose (p-value>0.05). The mean fasting insulin levels were higher in patients with alopecia areata (16.94 µIU/ml) compared to the control group (11.23 µIU/ml), with a significant p-value of <0.001. This significant difference indicates a potential association between alopecia areata and altered insulin levels. The mean HOMA-IR was also higher in the alopecia areata group (3.36) compared to the control group (2.63) with a significant p-value of 0.006, suggesting a potential link between insulin resistance and alopecia areata.

Table (1): Comparison of demographic data, anthropometric measures, lipid profile, fasting insulin, glucose and HOMA-IR among cases with AA and control group

	Alopecia Areata (n = 50)		**Control (n = 30)**		**Test (p-value)**
	№	**%**	**№**	**%**	
Sex					
Male	37	74.0	22	73.3	Chi-Square=0.004 p-value=0.948
Female	13	26.0	8	26.7	
Age (years)					
Mean ± SD.	33.14 ± 9.63		32.80 ± 10.33		Student-t=0.149 p-value=0.882
Median (Range)	33.5 (18 – 57)		32.5 (18 – 57)		
Occupation					
Housewife	11	22.0	6	20.0	Chi-Square=0.099 p-value=0.992
Office worker	11	22.0	7	23.3	
Outdoor worker	19	38.0	11	36.7	
Student	9	18.0	6	20.0	
Marital Status					
Single	15	30.0	9	30.0	Chi-Square=0.0 p-value=1.000
Married	35	70.0	21	70.0	
Residence					
Urban	31	62.0	19	63.3	Chi-Square=0.014 p-value=0.905
Rural	19	38.0	11	36.7	
Weight (kg)					
Mean ± SD.	87.50 ± 16.08		90.60 ± 14.90		Student- t=0.858 p-value=0.394
Median (Range)	85 (57.0 – 120.0)		86.50 (70.0 – 115.0)		
Height (m)					
Mean ± SD.	1.72 ± 0.10		1.71 ± 0.11		Student- t=0.549 p-value=0.585
Median (Range)	1.71 (1.53 – 1.95)		1.67 (1.53 – 1.88)		
BMI (kg/m^2)					
Mean ± SD.	29.56 ± 5.28		31.27 ± 5.98		Student- t=1.332 p-value=0.187
Median (Range)	28.88 (21.97 – 41.80)		29.60 (23.89 – 41.80)		
Waist circumference (cm)					
Mean ± SD.	98.52 ± 14.03		100.40 ± 13.15		Student- t=0.594 p-value=0.554
Median (Range)	96.50 (72.0 – 125.0)		97.0 (77.0 – 125.0)		
HDL (mg/dl) Mean ± SD.	45.54 ± 11.34		42.93 ± 8.52		Student-t=1.832 p-value=0.071
TG (mg/dl) Mean ± SE.	96.0 ± 4.17		91.90 ± 7.52		U=732.5 p-value=0.862
Cholesterol (mg/dl) Mean ± SE.	173.32 ± 9.93		160.53 ± 9.11		U=671.0 p-value=0.432
Fasting insulin (µIU/ml) Mean ± SD.	16.94 ± 3.37		11.23 ± 2.37		Student-t=4.927 p-value<0.001*
Fasting glucose (mmol/l) Mean ± SD.	5.59 ± 0.82		5.23 ± 1.24		Student-t=1505 p-value=0.116
HOMA-IR Mean ± SE.	3.36 ± 0.17		2.63 ± 0.23		U=472.5 p-value=0.006*

U, Mann Whitney test .

Table **(2):** shows that most of the patients with alopecia areata (90%) reported a sudden onset of the condition, while a smaller proportion experienced a gradual onset (10%). The mean duration of alopecia areata was 80.10 months, with a broad spectrum from 1.0 to 600.0 months. Systemic co-morbidities were present in 66% of cases with alopecia areata, with a variety of conditions reported. The most common comorbidities included psychological issues (39.4%),

Cardiovascular diseases (CVD) (27.3%), and sinusitis (18.2%), 14% of patients with alopecia areata had dermatological comorbidities, with a small percentage reporting conditions such as urticaria, warts, TVC and others.

Table (2): Present history, systemic comorbidities and Dermatological co-morbidities among patients with alopecia areata

	Alopecia Areata n = 50	
	№	**%**
Onset		
Sudden	45	90.0
Gradual	5	10.0
Duration (months)		
Mean ± SE.	80.10 ± 15.96	
Median (Range)	30.0 (1.0 – 600.0)	
Systemic comorbidities		
Absent	17	34.0
Present	33	66.0
Autoimmune	1	3.0
Hypertension	1	3.0
Sinusitis	6	18.2
Dental caries	5	15.2
Refraction errors	8	24.2
Resp. problems	5	15.2
CVS Diseases	9	27.3
Liver	1	3.0
Thyroid	2	6.1
Rh. And bone	6	18.2
Psychological	13	39.4
Operations	3	9.1
Dermatological co-morbidities		
Absent	43	86.0
Present	7	14.0
Urticaria	1	14.3
Warts	1	14.3
TVC	1	14.3
Others	5	71.4

Table **(3):** shows dermatological examination of hair patterns among patients with alopecia areata. The scalp was the commonest site affected (68%), with patchy alopecia being the predominant pattern (70%). Dermatological examination of the skin revealed that 8% of patients with alopecia areata had skin issues present. Among these cases, various types of skin problems were reported, including acne, warts, and others, each representing 25% of the cases, 16% of cases with AA had nail abnormalities. Brittle nails were the most common type reported (50%), followed by longitudinal striations (25%) and other nail conditions.

Table (3): Dermatological examination (hair, skin, nail) among patients with alopecia areata

Dermatological Examination	**Alopecia Areata n = 50**	
	№	**%**
Hair (AA)		
Site		
Scalp	34	68.0
Eyebrow	2	4.0
Beard	7	14.0
Moustache	1	2.0
All	11	22.0
Pattern		
Patchy	35	70.0
Totalis	5	10.0
Universalis	10	20.0
Hair (Others)		
Absent	42	84.0
Present	8	16.0
Type		
AGA	7	87.5
LPP	1	12.5
ttm	1	12.5
Skin		
Absent	46	92.0
Present	4	8.0
Type		
Acne	1	25.0
Urticaria	0	0.0
Warts	1	25.0
TVC	1	25.0
Other	1	25.0
Nail		
Absent	42	84.0
Present	8	16.0
Type		
Brittle nails	4	50.0
Long. Striations	2	25.0
Nail pitting	1	12.5
Onycholysis	1	12.5
Others	2	25.0

Table **(4):** shows that the severity of alopecia areata was evaluated using the SALT score, with most patients falling into S1 (48%) and S5 (16%) categories. The mean SALT score was 36.49 in the population studied. The most prevalent grade is S1 (48%), followed by S3 (14%). The hair pull test activity revealed that 40% of patients with alopecia areata tested positive, 36% tested negative, and 24% couldn't undergo the test. The results of the dermoscopic examination in patients with alopecia areata, showed that 58% had active hair loss, 32% had hair regrowth, and 16% had long-standing inactive disease.

Table (4): SALT Score, Hair pull test, and dermoscopic exam among patients with AA

Severity (SALT Score)	**Alopecia Areata n = 50**	
	№	**%**
Class		
S0	5	10.0
S1	24	48.0
S2	2	4.0
S3	7	14.0
S4a	3	6.0
S4b	1	2.0
S5	8	16.0
%		
Mean ± SE.	36.49 ± 5.51	
Median (Range)	14.2 (0.0 – 100.0)	
Hair Pull Test		
Positive	20	40.0
Negative	18	36.0
Couldn't be done	12	24.0
Dermoscopic Exam		
Evidence of active hair loss	29	58.0
Black dots	23	46
Exclamation marks	23	46
Broken hair	11	22
Pohl Pinkus	6	12
Inactive long standing	8	16.0
Yellow dots	4	8
Bulbar opening not visible	3	6
Hair regrowth	16	32.0
Upright regrowing hair	16	32
Pigtail hair	5	10
Vellus hair	13	26

Table **(5):** shows that there was significant difference between patients with AA, and the control group regarding adiponectin and Leptin levels. Cases with AA had lower mean adiponectin levels compared to the control group (2.83µg/ml vs. 3.19µg/ml) with a significant p-value of 0.006. Leptin levels were significantly higher in patients with AA compared with healthy controls (33.16 ng/ml vs. 21.25 ng/ml) (p <0.001).

Table (5): Comparison of Adiponectin and Leptin among both groups

	Alopecia Areata n = 50	**Control n = 30**	**Test (p)**
Adiponectin (µg/ml)			
Mean ± SD.	2.83 ± 0.73	3.19 ± 0.42	Student-t=2.827 p-value=0.006*
Leptin (ng/ml)			
Mean ± SD.	33.16 ± 4.14	21.25 ± 3.52	Student-t=8.975 p-value<0.001*

SD. Standard deviation, Range: Min. – Max. *: Significant ≤0.05.

Table **(6):** shows the correlation analysis and shows that age, weight, height, BMI, waist circumference, BP (SBP and DBP), triglycerides (TG), HDL cholesterol, total cholesterol, fasting insulin, fasting glucose, HOMA-IR, duration of alopecia areata, do not exhibit significant correlations with adiponectin levels. Adiponectin showed non-significant negative correlation with SALT score (p>0.05). No significant correlations were found between adiponectin levels and studied parameters in control group.

Table (6): Correlation between Adiponectin with different parameters among all studied subjects

	Adiponectin			
	AA		**Control**	
	r	***P-value***	***r***	***P-value***
Age	0.132	0.242	0.156	0.409
BMI	0.071	0.529	-0.151	0.427
SBP	0.013	0.910	0.001	0.996
DBP	-0.021	0.855	-0.160	0.399
HDL	0.167	0.139	0.132	0.486
TG	-0.017	0.879	-0.357	0.053
Cholesterol	0.174	0.124	0.291	0.119
Fasting insulin	-0.128	0.256	0.032	0.867
Fasting glucose	0.129	0.254	0.059	0.756
HOMA-IR	-0.017	0.883	0.105	0.582
Duration	0.045	0.755	-	-
SALT Score	-0.011	0.944	-	-

p<0.05 is considered significant.

Table **(7):** shows that leptin levels displayed a significant positive correlation with fasting insulin (r=0.456, p < 0.001) and HOMA-IR (r=0.321, p=0.004), indicating a relationship with insulin resistance markers. Additionally, leptin had a negative correlation with HDL cholesterol (r=-0.294, p=0.008), recommending a possible link between leptin levels and lipid metabolism. Other parameters like age, weight, height, BMI, waist circumference, BP, lipid profile (TG and cholesterol), fasting glucose, duration of alopecia areata, do not show significant correlations with leptin levels. Leptin displayed non-significant positive correlation with SALT score (p>0.05). Regarding control group, leptin revealed significant negative correlation with HDL (p=0.049), but not with other parameters studied.

Table (7): Correlation between leptin with different parameters among all studied subjects

	Leptin			
	AA		**Control**	
	r	***P-value***	***r***	***P-value***
Age	-0.039	0.732	-0.090	0.636
BMI	-0.036	0.753	0.165	0.383
SBP	0.134	0.237	0.252	0.180
DBP	0.104	0.358	0.244	0.194
HDL	-0.294	**0.008***	-0.361	**0.049***
TG	0.049	0.669	0.213	0.258
Cholesterol	0.119	0.291	0.241	0.199
Fasting insulin	0.456	**<0.001***	0.261	0.164
Fasting glucose	-0.194	0.085	-0.054	0.779
HOMA-IR	0.321	**0.004***	0.173	0.362
Duration	-0.030	0.836	-	-
SALT Score	0.203	0.175	-	-

*, p<0.05 is considered significant.

DISCUSSION

Alopecia areata (AA) is an immune-mediated disease that targets anagen hair follicles and causes non-scarring HL. It arises from an autoimmune disturbance in the normal hair cycle, causing deprivation of the hair follicles from their immunological privilege. [2]**.** It might be accompanied by a higher risk of the development of metabolic co-morbidities including hyperlipidemia, overweight, DM and MetS [4]

A network of several soluble mediators called adipokines connects metabolism with the immune system. These adipokines are actively produced by adipocytes. Adipokines are comprised in the control of glucose and lipid metabolism. In addition, adipokines develop as active regulators of physiological and pathological processes, comprising MetS, and inflammation. Nowadays, the role of adipokines has been defined in the development of AIDs such as rheumatoid arthritis (RA), psoriasis vulgaris, Crohn disease and ulcerative colitis [12, 13].

Adipokines have pro- or anti-inflammatory characteristics. APN is an anti-inflammatory adipokine (good adipokine). It is an endogenous insulin sensitizer. APN has been recorded to be included in certain inflammatory diseases which include DM, atherosclerotic CVD, MetS, and RA by its action on the immune system [7]**.**

Leptin, is a pro-inflammatory cytokine. It causes appetite suppression and body weight regulation. In addition, it has a direct correlation with adipose mass. Its level was demonstrated to correlate with insulin, IR, and glucose. In addition, it raises cytokine formation and T cell proliferation [14]**.**

This work aimed to explain the potential role of APN and leptin in AA pathogenesis, through estimation of their serum levels in AA cases and compare them with levels in healthy controls. This study was a case-control study, conducted on 50 cases with AA and 30 healthy controls who match the patient group as regard age and sex.

The present study revealed male predominance of AA with no significant differences regarding other parameters with control group. Ninety % of AA patients had sudden onset with mean (± SD) duration of the disease was 80.10 ± 15.96 months. This agrees with other authors who found that AA was more common in males [15, 16]. Family history of AA was recorded in 7% of our cases. Nearly similar results of positive family history were recorded by other authors as **Alshahrani *et al.*** [17] who recorded positive family history in 6% and 7% of patients respectively. The present study revealed that 90 % of AA cases had sudden onset, with mean duration of the disease was 80.10 ± 15.96 months. **Mohamed *et al.*** [18] reported similar results with most of their cases having sudden onset and progressive course with disease duration ranging between 0.1–50 months. This study found that the mean fasting insulin and HOMA-IR in AA cases were higher than controls with statistically significant difference, while no significant differences regarding fasting glucose levels in both groups. In agreement **Waśkiel-Burnat *et al.*** [19] who revealed increased values of insulin, and HOMA-IR in cases with AA compared to normal subjects.

It was suggested that alopecia areata, as an autoimmune disease, might be associated with an increased risk of metabolic diseases. The current study found that 66 % of AA cases had various comorbidities which agreed with **Mahmoudi *et al***. [20] who revealed that majority of AA cases had combined comorbidities. While **Augustin *et al.*** [21] had found that those with AA significantly had more other dermatological insults**.**

Regarding hair examination in our study, scalp was the commonest site affected with patchy distribution mostly. While skin in the current study was affected

only in 8% of AA cases, and nails also were affected in 16% of AA cases. Also, active hair loss affected 58% of cases.

While **Bhardwaj *et al.*** [22] revealed that scalp mostly affected by AA with circumscribed patchy pattern. In addition, nails were involved in (38%) patients**.** Discrepancy may contribute to difference in subject's characters as severity and course of the disease.

The current study revealed that mean (± SD) SALT score among patients with AA was 36.49 ± 5.51, with most cases having class S1 (48%) and also most cases had localized SALT score (62%), and Hair Pull Test was positive in 40% of cases which agreed with **Mohamed *et al.*** [18] who revealed that 46% of AA were S1 and Hair Pull Test was positive only in 15% of 126 cases.

The present study found that SALT score had significant correlation with the disease duration, otherwise no significant correlation with other parameters, in agreement with **Mohamed *et al***. [18] who revealed that SALT score had statistically significant difference with the disease duration and non-significant difference was demonstrated regarding the remaining variables including as age and gender.

In this work, statistically significant lower serum levels of APN were displayed in AA patients compared to normal subjects. A negative relationship was recognized between the serum levels of APN and SALT score; however, this correlation was not statistically significant, most probably due to small number of patients.

We found insignificant correlation between the level of serum APN and the patient's sex, age, BMI, BP, serum lipids, fasting glucose, fasting insulin or HOMA-IR, duration or onset of the disease, or disease activity (hair pull test). These results agree with previous reports [3, 23]. One study reported strong negative correlations between APN levels and BMI [10].

Formerly recorded data on APN values in cases with AA are unreliable. In agreement with the current results, two studies revealed a significant reduction in serum APN levels in AA patients compared to control group [10, 23]. **Salman *et al.*** [24] revealed that serum APN was slightly lower in the patient group with insignificant difference between AA and control group. In contrast, preceding study on serum adipokines level conducted by **Serarslan *et al***. [10] didn't display significant differences in APN level in cases with AA compared with healthy controls. Increased serum levels of APN and leptin were demonstrated in cases with scalp HL compared with cases with isolated beard and eyebrow AA.

In this work, statistically significant higher serum values of leptin were detected in AA cases compared with those in healthy control. A positive correlation was recognized between the serum levels of leptin and SALT score; however, this correlation wasn't statistically significant. In agreement with our results, one study showed significantly higher serum leptin concentrations in AA cases compared with healthy controls [10]. In contrast to our results, **Stochmal *et al.*** [3] revealed that serum leptin in AA group did not differ significantly compared to control group.

Our study displayed a significant correlation between leptin level and fasting insulin as well as with HOMA-IR, with no significant differences regarding other parameters, including patient's sex, age, BMI, BP, serum lipids, fasting glucose, duration or onset of the disease, or disease activity (hair pull test). These results agree with previous reports [3, 25]. A positive strong relationship was recorded between TG and leptin levels by **Serarslan *et al.*** [10].

In the present work, no significant correlation was recorded between AA severity as measured by SALT score and serum leptin. These results agree with other authors who reported no significant correlation between the serum levels of leptin and disease severity [3, 10]. The contradictory findings regarding serum leptin in AA may be attributed to differences in study design regarding sample size, racial/ethnic composition, age, gender, and metabolic status. Mush research on large numbers of AA cases with different severities is needed to clarify these conflicting results.

Elevation of serum leptin in our AA may reflect the metabolic status of AA patients. However, this assumption can be excluded because our patients match control subjects regarding metabolic parameters. Leptin is a pro-inflammatory cytokine which may be involved in the pathogenesis of several AIDs comprising AA [12, 13]. This hypothesis may explain our results regarding elevated serum leptin in AA patients.

The study's main limitation is its small sample size. Upcoming studies comprising a higher number of cases will permit the proper re-assessment of the correlation between adipokines and AA.

CONCLUSION

Patients with AA exhibit abnormal serum levels of two adipokines with varying pathophysiological functions. High serum levels were reported with the pro-inflammatory cytokine leptin, while low serum levels were reported with the anti-inflammatory cytokine adiponectin. Both adipokines could be considered as a predictive factor of HL in AA. Our results support the theory that the impaired release of specific adipokines may have an essential and complex role in the pathogenesis of AA and its continuity.

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