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Original Article

Insulin resistance and metabolic syndrome in Iraqi patients with alopecia areata

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Abstract

Background One of frequent forms of hair loss in humans is alopecia areata; the disease is autoimmune in nature with a clinical course that is often variable with relapse and remission and in some severe cases it may be persistent. A number of skin diseases have been shown to be associated with insulin resistance and the first report that linked alopecia areata with insulin resistance has been described recently by some authors.

Objective Due to the lack of sufficient data in our country about the possible link between alopecia areata and insulin resistance and the high rate of metabolic syndrome and insulin resistance in our society, the planning and conduction of the current study was justified to explore such an association.

Methods The current case control study included 50 patients with alopecia areata randomly selected from the pool of patients visiting dermatology unit at Al-Diwaniyah Teaching Hospital, Al-Diwaniyah province, Iraq. In addition, the study included 40 apparently healthy control subjects with comparable age and gender distribution.

Results There was no significant difference in mean serum triglyceride (p = 0.180) but serum HDL was significantly higher in patients group in comparison with control group (p=0.006). Mean fasting blood sugar (FBS) was higher in patients than in control patients in a significant manner (p=0.032); mean insulin level was also significantly higher in patients than in control group (p=0.019); mean HOMA-IR was additionally higher in patients than in control subjects with a borderline significant value (p=0.054) and the rate of insulin resistance was significantly higher in patients than in control group, 50% versus 25%, respectively.

Conclusion There is significant association between insulin resistance and alopecia areata but the link of this skin disorder to other elements of metabolic syndrome such as obesity and hypertension need further investigations.

Key words
Insulin resistance, metabolic syndrome, alopecia areata.

Introduction

One of the frequent forms of hair loss in humans is alopecia areata; the disease is autoimmune in nature with a clinical course that is often variable with relapse and remission and in some severe cases it may be persistent.[1-3] The rank of the disease among causes of non-scaring hair loss is the second just after female and male pattern of alopecia.[1] The clinical forms of the disease have particular phenotypic patterns including patchy alopecia which is by far the most common form and is characterized by patchy areas of hair loss, the second from is alopecia totalis in which there is complete loss of scalp hair and third form is alopecia

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universalis in which there is total loss of body hair.[4-6] Another form of the disease is called Ophiasis that is characterized by a band like shape of hair loss.[1]

Being an autoimmune disease there must be an interaction between genetic susceptibility and environmental trigger. The inflammtory process in hair follicles has been documented since approximately 100 years[1,7] and the immune basis of the disease has also been established more than 50 years ago by showing role of cytokines and several immune cells.[1,8,9] Several triggers have been proposed such as infection, psychological and physical stress, poisoning with thallium acetate and hormonal disturbance.[1,10-12] Higher susceptibility with positive family history and high concordance rate among monozygotic twins are evidences of genetic susceptibility.[1]

The lifetime incidence of the disease is estimated to be around 2%.[13] The disease can happen at any age, but the incidence is higher with increasing age.[14] There is no gender predilection; however, there may be slight female predilection in some reports due to higher concern expressed to the disease by females in comparison to males.[15]

A number of skin diseases have been shown to be strongly associated with insulin resistance such as acanthosis nigricans, acne and psoriasis and others have been shown to be potentially associated with insulin resistance such as acrochorda, androgenetic alopecia, hidradenitis suppurativa and hirsutism.[16] On the other hand, the association between alopecia areata and insulin resistance is still controversial.[16] The first report that highlighted the possible link between alopecia areata and insulin resistance has been described by Karadag *et al.*[17] There is a recent report about high incidence of insulin resistance in association with alopecia areata.[18]

Due to the lack of sufficient data in our country about the possible link between alopecia areata and insulin resistance and the high rate of metabolic syndrome and insulin resistance in our society, the planning and conduction of the current study was justified to explore such an association.

Methodology

The current case control study included 50 patients with alopecia areata randomly selected from the pool of patients visiting dermatology unit at Al-Diwaniyah teaching hospital, Al-Diwaniyah province, Iraq. In addition, the study included 40 apparently healthy control subjects with comparable age and gender distribution. The study started on August 2019 and ended at December 2020. A questionnaire form was prepared and included information about age, gender, duration of disease and family history of alopecia and also data following examination regarding type of alopecia, body mass index, waist circumference. The following investigations were also done: serum lipid profile, fasting blood sugar and serum insulin levels. The study was approved ethically by ethical approval committee of the college of medicine, University of Al-Qadisiyah and a verbal consent was obtained from all the participants.

The statistical analysis was done with the aid of statistical package for social sciences (SPSS) version 16 (IBM, Chicago, USA) and Microsoft Office Excel 2007. Quantitative variables were expressed as mean, standard deviation and range; whereas, qualitative data were expressed as number and percentage. Independent samples t-test was used to evaluate the difference in mean of quantitative variables between control and patients' groups; where, chi-square test was used to compare variation in proportions of qualitative variables between control and

patients groups. The level of significance was set at $p \leq 0.05$ and the level of high significance was set at $p \leq 0.01$.

Results

The general characteristics of patients and control subjects enrolled in this study are shown in **Table 1**. Mean age of the patients with alopecia areata was 28.56±6.29 years and there was significant difference in mean age between patients and control subjects (p=0.644). There was slight male predilection with 29 (58.0%) male and 21 (42.0%) female patients and the male to female ratio was 1.38:1. There was also no significant difference in frequency distribution according to gender between patients with alopecia areata and control subjects (p=0.848).

The disease duration was in the range of 1 to 9.5 years with a mean of 2.25±2.43 years. The frequency distribution of patients according to pattern of disease was as following: 36 (72.0%), 7 (14.0%), 2 (4.0%) and 5 (10.0%) as alopecia areata, totalis, universalis and ophiasis, respectively. Positive family history was seen in significant proportion of patients accounting for 14 (28.0%).

Data about body mass index (BMI) and waist circumference (WC) in patients and control subjects are shown in **Table 2**.

Table 1 General characteristics of patients and control subjects enrolled in this study.

Characteristic	*Patients* *n = 50*	*Control* *n = 40*	*p value*
Age (years)			
Mean ±SD	28.56±6.29	27.73±10.61	0.644 I
Range	18-42	19-81	NS
Gender			
Male, n (%)	29 (58.0%)	24 (60.0%)	0.848 C
Female, n (%)	21 (42.0%)	16 (40.0%)	NS
Duration of disease (years)			
Range	1-9.5		
Mean ±SD	2.25±2.43		
Type			
Patchy, n (%)	36 (72.0%)		
Totalis, n (%)	7 (14.0%)		
Universalis, n (%)	2 (4.0%)		
Ophiasis, n (%)	5 (10.0%)		
Family history, n (%)	14 (28.0%)		

n: number of cases; SD: standard deviation; I: independent samples *t*-test; C: chi-square test; NS: not significant at $p > 0.05$.

Table 2 Body mass index and waist circumference in patients and control subjects.

Characteristic	*Patients* *n = 50*	*Control* *n = 40*	*P value*
BMI (kg/m^2)			
Mean ±SD	25.49 ±4.51	26.35 ±7.17	0.490 I
Range	19.3 -48.8	19 -54	NS
Normal	27 (54.0 %)	21 (52.5 %)	0.932 C
Overweight	18 (36.0 %)	14 (35.0 %)	NS
Obese	5 (10.0 %)	5 (12.5 %)	
Waist circumference (cm)			
Mean±SD	72.86±23.43	68.90±27.82	0.468 I
Range	31-109	22-136	NS

n: number of cases; SD: standard deviation; I: independent samples *t*-test; C: chi-square test; NS: not significant at $p > 0.05$

Table 3 Comparison of systolic and diastolic blood pressure between patients and control subjects.

Characteristic	*Patients* *n = 50*	*Control* *n = 40*	*P value*
Systolic blood pressure (mmHg)			
Mean ±SD	121.40 ±10.83	115.60 ±27.20	0.171 I
Range	100 -150	12 -145	NS
Diastolic blood pressure (mmHg)			
Mean ±SD	82.10 ±8.40	80.88 ±11.98	0.570 I
Range	70 -95	60 -100	NS

n: number of cases; I: independent samples *t*-test; NS: not significant at $p > 0.05$.

Table 4 Serum lipid profile and insulin resistance in patients and control groups.

Characteristic	*Patients* *n = 50*	*Control* *n = 40*	*P value*
Triglyceride (mg/dl)			
Mean ±SD	109.18±53.21	95.20±42.55	0.180 I
Range	24 -277	45.8-233	NS
HDL (mg/dl)			
Mean ±SD	44.54±15.86	36.90±7.77	0.006 I
Range	18 -93	22-57.97	HS
FBS (mg/dl)			
Mean ±SD	101.76±13.96	95.30±13.99	0.032 I
Range	70.28 -145	67-126	S
Insulin			
Mean ±SD	13.01±14.11	7.26±6.45	0.019 I
Range	0.12-66.5	0.3-26.3	S
HOMA-IR			
Mean ±SD	3.12±4.07	1.78±1.72	0.054 I
Range	0.02-21.55	0.04-7.1	NS
Insulin resistance (IR)			
Negative, *n* (%)	25 (50.0%)	30 (75.0%)	0.016 C
Positive, *n* (%)	25 (50.0%)	10 (25.0%)	S

n: number of cases; I: independent samples *t*-test; C: chi-square test; NS: not significant at $p > 0.05$; S: significant at $p \leq 0.05$.

The mean BMI of patients was 25.49±4.51 kg/m^2 and it was comparable to that of control subjects (p=0.490); the rate of overweight and obesity were also comparable between both groups (p=0.932). The mean WC of patients was 72.86±23.43 cm and it was higher than that of control subjects; however, the difference did not reach statistical significance (p=0.468). Blood pressure readings were also comparables between patients and control subjects (p>0.05), as shown in **Table 3**. Serum lipid profile and insulin resistance in patients and control groups are shown in **Table 4**. There was no significant difference in mean serum triglyceride (p=0.180) but serum HDL was significantly higher in patients group in comparison with control group (p=0.006). Mean fasting blood sugar (FBS) was higher in patients than in control subjects/ group in a significant manner (p=0.032); mean insulin level was also significantly higher in patients than in control group (p=0.019); mean HOMA-IR was additionally higher in patients than in control subjects with a borderline significant value (p=0.054) and the rate of insulin resistance was significantly higher in patients than in control group, 50% versus 25%, respectively.

Discussion

Type 2 diabetes, insulin resistance and metabolic syndrome are among common medical conditions seen in daily clinical practice and in

our country.[19] The mortality and morbidity in association with insulin resistance and metabolic syndrome is high because of the associated ischemic heart diseases and cerebrovascular disorders.[20] The issue of association between some common forms of dermatological disorders and insulin resistance has been raised by a lot of authors in available published medical literatures.[16] However, the link between insulin resistance and alopecia areata is relatively a new issue and little is known about such link in Iraqi patients.[17,18] Therefore, we aimed in the current study to explore the association between alopecia areata and the basic elements of metabolic syndrome, namely obesity, hypertension and insulin resistance. In the current study we fail to establish significant association between obesity and alopecia areata since both control group and patients group showed comparables figures of BMI and WC. On the other hand, we failed to establish a significant association between alopecia areata and hypertension since blood pressure measurements were comparable in both the study groups. Nevertheless, it is obvious in the current study that insulin resistance was strongly associated with alopecia areata as is evident from higher blood sugar readings, higher insulin levels, higher HOMA-IR and higher frequency of insulin resistance rate in patients with alopecia areata in comparison with control group. This linkage has been shown in two previous studies.[17,18] The explanation for such an association or a link can be viewed as some form of common genetic predisposition between insulin resistance and alopecia areata or some common pathogenic inflammatory mechanism; however, further investigations are needed to prove such suggestions.

Conclusion

In conclusion, there is a significant association between insulin resistance and alopecia areata but the link of this skin disorder to other elements of metabolic syndrome such as obesity and hypertension needs further investigations.

References

1. Pratt CH, King LE Jr, Messenger AG, Christiano AM, Sundberg JP. Alopecia areata. *Nat Rev Dis Primers*.2017;**3**:17011.
2. Darwin E, Hirt PA, Fertig R, Doliner B, Delcanto G, Jimenez JJ. Alopecia Areata: Review of Epidemiology, Clinical Features, Pathogenesis, and New Treatment Options. *Int J Trichology*.2018;**10(2)**:51-60.
3. Brzezińska-Wcisło L, Bergler-Czop B, Wcisło-Dziadecka D, Lis-Święty A. New aspects of the treatment of alopecia areata. *Postepy Dermatol Alergol*.2014;**31(4)**:262-5.
4. Kassira S, Korta DZ, Chapman LW, Dann F. Review of treatment for alopecia totalis and alopecia universalis. *Int J Dermatol*.2017;**56(8)**:801-10.
5. Hordinsky MK. Overview of alopecia areata. *J Investig Dermatol Symp Proc*.2013;**16(1)**:S13-5.
6. Hegde SP, Naveen KN, Athanikar SB, Reshme P. Clinical and dermatoscopic patterns of alopecia areata: a tertiary care centre experience. *Int J Trichology*.2013;**5(3)**:132-6.
7. Zhang B, Zhao Y, Cai Z, Caulloo S, McElwee KJ, Li Y, Chen X, Yu M, Yang J, Chen W, Tang X, Zhang X. Early stage alopecia areata is associated with inflammation in the upper dermis and damage to the hair follicle infundibulum. *Australas J Dermatol*.2013;**54(3)**:184-91.
8. Tabara K, Kozłowska M, Jędrowiak A, Bienias W, Kaszuba A. Serum concentrations of selected proinflammatory cytokines in children with alopecia areata. *Postepy Dermatol Alergol*.2019;**36(1)**:63-9.
9. Bain KA, McDonald E, Moffat F, Tutino M, Castelino M, Barton A, Cavanagh J, Ijaz UZ, Siebert S, McInnes IB, Astrand A, Holmes S, Milling SWF. Alopecia areata is characterized by dysregulation in systemic type 17 and type 2 cytokines, which may contribute to disease-associated psychological morbidity. *Br J Dermatol*.2020;**182(1)**:130-7.

10. McElwee KJ, Gilhar A, Tobin DJ, *et al*. What causes alopecia areata?. *Exp Dermatol*.2013;**22(9)**:609-26.
11. Monselise A, Bar-On R, Chan L, Leibushor N, McElwee K, Shapiro J. Examining the relationship between alopecia areata, androgenetic alopecia, and emotional intelligence. *J Cutan Med Surg*.2013;**17(1)**:46-51.
12. Bakry OA, Basha MA, El Shafiee MK, Shehata WA. Thyroid disorders associated with alopecia areata in egyptian patients. *Indian J Dermatol*.2014;**59(1)**:49-55.
13. Villasante Fricke AC, Miteva M. Epidemiology and burden of alopecia areata: A systematic review. *Clin Cosmet Investig Dermatol*.2015;**8**:397–403.
14. Villasante Fricke AC, Miteva M. Epidemiology and burden of alopecia areata: A systematic review. *Clin Cosmet Investig Dermatol*.2015;**8**:397–403.
15. Lundin M, Chawa S, Sachdev A, Bhanusali D, Seiffert-Sinha K, Sinha AA, *et al*. Gender differences in alopecia areata. *J Drugs Dermatol*.2014;**13**:409–13.
16. Napolitano M, Megna M, Monfrecola G. Insulin resistance and skin diseases. Sci World J.2015;**2015**:479354.
17. Karadag A. S., Ertugrul D. T., Bilgili S. G., Takci Z., Tutal E., Yilmaz H. Insulin resistance is increased in alopecia areata patients. *Cutan Ocul Toxicol*.2013;**32(2)**:102–6.
18. Shahidi-Dadras M, Bahraini N, Rajabi F, Younespour S. Patients with alopecia areata show signs of insulin resistance. *Arch Dermatol Res*.2019;**311(7)**:529-33. doi: 10.1007/s00403-019-01929-6.
19. Saklayen MG. The Global Epidemic of the Metabolic Syndrome. *Curr Hypertens Rep*.2018;**20(2)**:12.
20. Mazloomzadeh S, Karami Zarandi F, Shoghli A, Dinmohammadi H. Metabolic syndrome, its components and mortality: A population-based study. *Med J Islam Repub Iran*.2019;**33**:11.