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Thyroid Dysfunction in Alopecia Areata

Alopesi Areatada Tiroid Disfonksiyonu

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Abstract

Objective: Alopecia areata is commonly associated with autoimmune disorders such as thyroid dysfunction. This paper aims to evaluate thyroid dysfunction in alopecia areata patients among the Iranian population.

Material and Methods: In this case-control study, 80 alopecia areata patients were recruited along with 122 age and sex-matched healthy subjects; serum thyroid stimulating hormone and anti-thyroid peroxidase levels were then compared between the groups.

Results: All alopecia areata patients had similar rate of increased thyroid stimulating hormone (10% vs. 8.2%, p=0.66) and anti-tiroid peroksidaz levels (15.6% vs. 23.8%, p=0.14) as compared to the controls. Patients with disease duration >6 months had significantly higher anti-tiroid peroksidaz levels (42.9% vs. 16.9%, p=0.01), with no difference in thyroid stimulating hormone levels (19% vs. 6.8%, p=0.1). Female patients also had higher abnormal anti-tiroid peroksidaz levels (35% vs. 12.5%, p=0.01) compared to the males.

Conclusion: Thyroid stimulating hormone and thyroid antibodies are not significantly increased in alopecia areata patients when compared to the normal population. Thyroid antibodies, however, were found to be increased in females and with the progression of disease duration. Therefore, thyroid function and antibodies must be evaluated in alopecia areata patients, especially in females, and along different time periods in individuals having the disease for a long time.

Keywords: Alopecia areata; thyroid disorders; disease duration

Özet

Amaç: Alopesi areata, tiroid disfonksiyonu gibi otoimmün bozukluklarla sıklıkla ilişkilidir. Bu çalışmada, İran populasyonunda alopesi areata hastalarındaki tiroid disfonksiyonunun değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Bu vaka kontrol çalışmasına 80 alopesi areata hastası ile yaş ve cinsiyet uyumlu 122 sağlıklı birey alındı, daha sonra da gruplar arasında serum tiroid stimüle edici hormon ve anti-tiroid peroksidaz düzeyleri karşılaştırıldı.

Bulgular: Kontrol grubu ile karşılaştırıldığında, alopesi areata hastalarının hepsinde tiroid stimüle edici hormon (%10'a karşı %8,2; p=0,66) ve anti-tiroid peroksidaz düzeylerinde (%15,6'ya karşı %23,8; p=0,14) benzer oranda artış mevcuttu. Hastalık süresi >6 ay olan hastalarda anti-tiroid peroksidaz düzeyleri (%42,9'a karşı %16,9; p=0,01) anlamlı olarak daha yüksekti, tiroid stimüle edici hormon düzeyleri (%19'a karşı %6,8; p=0,1) arasında ise fark bulunmadı. Kadın hastalarda, erkeklere göre daha yüksek anormal anti-tiroid peroksidaz düzeyleri (%35'e karşı %12,5; p=0,01) mevcuttu.

Sonuç: Tiroid stimüle edici hormon ve tiroid antikorları, alopesi areata hastalarında normal popülasyona göre anlamlı olarak artmamıştır. Bununla birlikte, tiroid antikorlarının, kadınlarda ve hastalık süresinin ilerlemesi ile arttığı bulunmuştur. Bu nedenle, alopesi areata hastalarında tiroid fonksiyonu ve antikorları, özellikle kadınlarda ve uzun süre hastalığı olan bireylerde farklı zaman periyotlarında değerlendirilmelidir.

Anahtar kelimeler: Alopesi areata; tiroid hastalıkları; hastalık süresi

Introduction

Alopecia areata (AA) is a common, localized, non-scarring hair loss that may occur on any hair-bearing skin. It affects 1% of the general population (1-3). Although the pathogenesis of AA is still not completely understood, genetic, environmental and autoimmune factors are considered to play, most possibly, a role in its etiology. AA is a T cell-mediated organ-specific autoimmune disease (4-6).

AA is associated with various autoimmune disorders such as vitiligo, atopy, Hashimoto's thyroiditis, diabetes mellitus, psoriasis, celiac disease, and lupus erythematosus (1, 3, 7, 8). Among all these, thyroid disorders, especially hypothyroidism and vitiligo have the strongest association (1, 5, 9).

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The published data show inconsistency in the overall prevalence of thyroid diseases and thyroid function abnormalities in patients with AA. Nevertheless, the reported prevalence is 8% to 28% in AA patients (3, 10). More case-control studies are warranted in order to better understand the prevalence of thyroid diseases and thyroid dysfunction in AA. This study aims to evaluate the rate of thyroid dysfunction in AA.

Material and Methods

This case-control study included 80 patients with AA and 122 normal individuals who visited the dermatology clinic, Sina Hospital, Tabriz, Iran in 2017. The participants from both groups were age and sex matched. Those with acute diffuse and total alopecia or rapidly progressive AA were excluded from the analysis. Those with other types of alopecia and autoimmune dermatological diseases in the control group and those consuming any immunosuppressive medication or having any chronic systematic diseases, in either of the two groups, as well as pregnant women, were excluded from the study.

Ethics Statement

This study was conducted according to the ethical principles of the Declaration of Helsinki and was approved by the ethics committee of Tabriz University of Medical Sciences (#58197, approve date: March 4, 2017).

Samples

Demographics and laboratory findings of the patients, including thyroid function tests, anemia, and history of vitiligo or diabetes mellitus as well as the duration of AA were recorded and the findings between the patient and control groups were compared.
Fasting blood samples of all participants were collected; the concentration of zinc was determined using flame atomic absorption spectrometry (FAAS) method using the commercially available kits (Biorexfars Co. LTD, Tehran, Iran). Thyroid stimulating hormone (TSH) was estimated using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (Diaplus Inc., Canada) while the anti-thyroid peroxidase (anti-TPO) levels were assayed using ELISA kits (Monobind Inc., USA). The cutoff value of positivity for anti-TPO was 40 IU/mL. The normal range of TSH was found to be 0.5-5.5 mIU/L.

Statistical analysis

All the data were analyzed using SPSS 22 (version 22; SPSS Inc., Chicago, IL). The results were expressed as mean±standard deviation or percentage. Chi-square test, Fisher's exact test, and independent T-test were used to compare data between the groups. The *p*-values of less than 0.05 were considered statistically significant.

Results

Demographic findings of the two groups were observed to be similar (Table 1). Disease du-

Table 1. Demographic findings between the groups.

	Control (n=122)	Case (n=80)	P value
Age (years)	29.33±13.30	28.03±12.31	0.48
Gender			
Male	61 (50%)	40 (50%)	------
Female	61 (50%)	40 (50%)	
Skin type			
Type III	105 (88.5%)	64 (80%)	0.09
Type IV	14 (11.5%)	16 (20%)	
Familial history of DM	50 (41%)	28 (35%)	0.39
Familial history of thyroid disease	31 (25.4%)	24 (30%)	0.47
Familial history of AA	16 (13.1%)	8 (10%)	0.5
Familial history of vitiligo	4 (3.3%)	4 (5%)	0.71**

Fisher's exact test (**). DM: diabetes mellitus; AA: alopecia areata.

ration in the patient group was found to be 6.05 ±1.04 months. Three patients (3.8%) in the patient group were noted to have vitiligo. Laboratory findings are demonstrated in Table 2. Although TSH and anti-TPO levels were established to be higher in the patient group and it had more subjects with abnormal TSH and anti-TPO levels, the difference between the groups was not significant.

The disease duration was observed to be below six months in 59 (73.8%) and above six months in 21 (26.3%) the participants. The laboratory findings were compared according to the disease duration (Table 3) which showed significantly lower hemoglobin, ferritin and anti-TPO levels in those subjects who were affected with the disease for less than six months. Although the TSH levels were also considerably lower in these patients, the difference was not significant.

Among AA patients, females had a significantly higher level of anti-TPO as compared to the males, and more females had increased anti-TPO levels than the males (Table 4).

Discussion

It was observed that the TSH and anti-TPO levels did not differ significantly between the patients with AA and healthy individuals. Similarly, Wang and colleagues (11) did not find any significant difference in TSH, FT3 and FT4 levels between AA patients and

Table 2. Laboratory findings between the groups.

	Control (n=122)	Case (n=80)	P-value
Hemoglobin (mg/dL)	14.10 ±1.37	14.22 ±1.50	0.54
Anemia	5 (4.1%)	3 (3.8%)	0.9**
Fasting blood sugar (mg/dL)	90.45 ±12.34	90.56 ±12.05	0.95
Diabetes mellitus	2 (1.6%)	3 (3.8%)	0.38**
Ferritin	69.26 ±5.46	64.38 ±5.72	0.55
Low ferritin	21 (17.2%)	10 (12.5%)	0.36
B12 levels	384.31 ±216.87	337.94 ±263.77	0.17
Low B12 levels	25 (20.5%)	20 (25%)	0.45
TSH	3.03 ±0.39	3.49 ±0.57	0.11
Abnormal TSH	10 (8.2%)	8 (10%)	0.66
Anti-TPO	60.80 ±15.48	95.30 ±32.58	0.19
High anti-TPO	19 (15.6%)	19 (23.8%)	0.14

Fisher's exact test (**).

Table 3. Laboratory findings between the patients grouped as disease duration <6 and >6 months.

	<6 months (n=59)	<6 months (n=21)	P-value
Hemoglobin (mg/dL)	14.00±1.44	14.84±1.53	0.02
Anemia	2 (3.4%)	1 (4.8%)	----
Fasting blood sugar (mg/dL)	91.44±12.63	88.09±10.12	0.27
Diabetes mellitus	3 (5.1%)	0	0.56**
Ferritin	57.13±6.20	84.76±56.30	0.02
Low ferritin	9 (15.3%)	1 (4.8%)	0.21**
B12 levels	349.90±290.66	304.33±167.96	0.57
Low B12 levels	16 (27.1%)	4 (19%)	0.46
TSH	3.05±0.53	4.70±1.58	0.19
Abnormal TSH	4 (6.8%)	4 (19%)	0.1**
Anti-TPO	92.22±41.06	103.96±47.27	0.03
High anti-TPO	10 (16.9%)	9 (42.9%)	0.01

Fisher's exact test (**).

Table 4. TSH and anti-TPO levels between female and male with AA.

	Male (n=40)	Female (n=40)	P value
TSH	3.30 ±0.84	3.67 ±0.78	0.74
Abnormal TSH	2 (5%)	6 (15%)	0.26**
Anti-TPO	22.82 ±7.58	167.78 ±63.05	0.02
High anti-TPO	5 (12.5%)	14 (35%)	0.01

Fisher's exact test (**).

controls. Also, Rahnama and colleagues (3) found no difference in TSH and anti-TPO levels between AA patients and healthy individuals. These authors presumed that there would be no obvious damage to thyroid function in AA patients. Interestingly, Kaur and colleagues (12) observed that AA patients had significantly lower TSH and anti-TPO levels than normal individuals.

Unlike the findings of the present study, previous studies have shown a significant increase in TSH levels in AA patients (13). Bakry and colleagues (14) also reported significantly higher levels of TSH and abnormal anti-TPO in AA patients as compared to that in the healthy individuals. In one of the largest sample study, Park and colleagues (15) evaluated 1408 patients and observed an increased incidence of thyroid dysfunction and thyroid autoimmunity in AA patients, particularly in those having severe AA. A recent meta-analysis by Lee and colleagues (16) reported that the prevalence of thyroid abnormalities and positive auto-antibodies were higher in patients with AA as compared to that in the normal population.

The rate of elevation of TSH and anti-TPO levels were similar to those found in previously reported data. Seyrafi and colleagues (10) observed thyroid disease and autoimmune antibodies in 8.9% and 51.4% of the individuals. Thyroid abnormalities in AA patients were reported to lie between 8% and 28% (3, 10). Bakry et al. (14) also reported hypothyroidism in 16% of the patients with AA. Previous studies also reported the prevalence of anti-TPO level (high) to be 48% and 23.7% (1, 14). The geographical location where the study was carried out and the prevalence of autoimmune diseases in that area may have considerable effects on TSH and anti-TPO levels. Further, the sample size of the studies was often different, which could be another cause for variations in the results obtained.

The present study also observed that the female patients, as compared to the male patients, had significantly higher levels of anti-TPO; also, the number of female patients had increased anti-TPO levels. The TSH levels were also observed to be insignificantly higher in females. Thyroid dysfunction has been found to affect women more commonly (17). Unlike the findings of the present study, Saylam Kurtipek and colleagues (18) found no significant difference between male and female AA patients in terms of TSH and anti-TPO levels.

The present study observed a significant increase in the levels of anti-TPO antibodies with an increase in the duration of the disease. Gonul et al. (19) also reported that the levels of thyroid antibodies increased with an increase in the duration of the disease.

Yet, not all patients with hypothyroidism have alopecia; thus, it is likely that the magnitude of the effect of thyroid hormone on hair growth is variable and its expression may be conditioned by local factors and other hormonal influences (14).

This study had some limitations. Factors including geographical, environmental and cultural conditions would have an effect on the results. Further, no follow-up study assessing the possible seasonal changes or changes after treatment in AA patients was performed.

Conclusion

This study demonstrated that among all AA patients, 10% had elevated TSH while 23.8% had elevated anti-TPO levels; yet, even with the higher rate of abnormal TSH and anti-TPO in AA patients, the difference is not significant when compared to that in the healthy individuals. Thyroid antibodies were observed to be increased in females and with an increase in disease duration; therefore, thyroid function and antibodies should

be evaluated in AA patients, especially in females and at different intervals, especially in those patients who are affected with the disease since a long time.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Sara Saniee; Design: Sara Saniee, Armaghan Ghareaghaji Zare, Afsaneh Radmehr; Control/Supervision: Sara Saniee; Data Collection and/or Processing: Sara Saniee, Armaghan Ghareaghaji Zare, Afsaneh Radmehr; Analysis and/or Interpretation: Sara Saniee; Literature Review: Sara Saniee, Afsaneh Radmehr, Armaghan Ghareaghaji Zare; Writing the Article: Sara Saniee, Armaghan Ghareaghaji Zare, Afsaneh Radmehr; Critical Review: Radan English Edit Institute; References and Fundings: Tabriz University of Medical Sciences; Materials: Sara Saniee, Armaghan Ghareaghaji Zare, Afsaneh Radmehr.

References

1. Kasumagić-Halilović E. Thyroid autoimmunity in patients with alopecia areata. Acta Dermatovenerol Croat. 2008;16:123-125.
2. Baars MP, Greebe RJ, Pop VJ. High prevalence of thyroid peroxidase antibodies in patients with alopecia areata. J Eur Acad Dermatol Venereol. 2013;27:e137-e139. [Crossref] [PubMed]
3. Rahnama Z, Farajzadeh S, Mohamamdi S, Mqasoudi MA. Prevalence of thyroid disorders in patients with alopecia areata. Journal of Pakistan Association of Dermatology. 2016;24:246-250.
4. Dilas LT, Icin T, Paro JN, Bajkin I. Autoimmune thyroid disease and other non-endocrine autoimmune diseases. Med Pregl. 2011;64:183-187. [Crossref] [PubMed]
5. Alkhalifah A, Alsantali A, Wang E, McElwee KJ, Shapiro J. Alopecia areata update: part I. Clinical picture, histopathology, and pathogenesis. J Am Acad Dermatol. 2010;62:177-188. [Crossref] [PubMed]
6. Guo H, Cheng Y, Shapiro J, McElwee K. The role of lymphocytes in the development and treatment of alopecia areata. Expert Rev Clin Immunol. 2015;11:1335-1351. [Crossref] [PubMed] [PMC]
7. Gilhar A, Etzioni A, Paus R. Alopecia areata. N Engl J Med. 2012;366:1515-1525. [Crossref] [PubMed]
8. Huang KP, Mullangi S, Guo Y, Qureshi AA. Autoimmune, atopic, and mental health comorbid conditions associated with alopecia areata in the United States. JAMA Dermatol. 2013;149:789-794. [Crossref] [PubMed]
9. Dainichi T, Kabashima K. Alopecia areata: what's new in epidemiology, pathogenesis, diagnosis, and therapeutic options? J Dermatol Sci. 2017;86:3-12. [Crossref] [PubMed]
10. Seyrafi H, Akhiani M, Abbasi H, Mirpour S, Gholamrezanezhad A. Evaluation of the profile of alopecia areata and the prevalence of thyroid function test abnormalities and serum autoantibodies in Iranian patients. BMC Dermatol. 2005;5:11. [Crossref] [PubMed] [PMC]
11. Wang H, Gan H, Mei L, Yang G, Fang F. The association between alopecia areata and thyroid autoimmunity in Chinese adult patients: a controlled study. Biomedical Research. 2017;28:3517-3521.
12. Kaur G, Kuldeep CM, Bhargava P, Mathur DK, Sharda S, Chaturvedi P. Insignificant correlation between thyroid hormone and antithyroid peroxidase antibodies in alopecia areata patients in Northern Rajasthan. Int J Trichology. 2017;9:149-153. [Crossref] [PubMed] [PMC]
13. Bin Saif GA. Severe subtype of alopecia areata is highly associated with thyroid autoimmunity. Saudi Med J. 2016;37:656-661. [Crossref] [PubMed] [PMC]
14. Bakry OA, Basha MA, El Shafiee MK, Shehata WA. Thyroid disorders associated with alopecia areata in egyptian patients. Indian J Dermatol. 2014;59:49-55. [Crossref] [PubMed] [PMC]
15. Park SM, Oh YJ, Lew BL, Sim WY. The association between thyroid dysfunction, thyroid autoimmunity, and clinical features of alopecia areata: a retrospective study. J Am Acad Dermatol. 2018 May 9. Doi: 10.1016/j.jaad.2018.04.051. [Epub ahead of print]. [Crossref]
16. Lee S, Lee YB, Kim BJ, Lee WS. Screening of thyroid function and autoantibodies in patients with alopecia areata: a systematic review and meta-analysis. J Am Acad Dermatol. 2018;80:1410-1413.e4. [Crossref] [PubMed]
17. Lazarus JH, Premawardhana LD. Screening for thyroid disease in pregnancy. J Clin Pathol. 2005;58:449-452. [Crossref] [PubMed] [PMC]
18. Saylam Kurtipek G, Cihan FG, Erayman Demirbaş Ş, Ataseven A. The frequency of autoimmune thyroid disease in alopecia areata and vitiligo patients. Biomed Res Int. 2015;2015:435947. [Crossref] [PubMed] [PMC]
19. Gönül M, Gül Ü, Pişkin E, Piskin E, Cakmak SK, Soylu S, Kilic A, Biyikli Z. Alopesi areatali hastaların geriye dönük değerlendirilmesi. Turkish J Dermatol. 2011;5:43-47. [Crossref] [PubMed] [PMC]