Dermatology Practical & Conceptual

Evaluating the Effect of the Demographic, Trichoscopic and Laboratory Characteristics on The Recurrence of Alopecia Areata

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ABSTRACT

Introduction: Alopecia areata (AA) has diverse disease characteristics and multiple factors may interfere with the prognosis of the disease.

Objectives: In this study, the factors affecting the AA recurrence were evaluated.

Methods: A total of a hundred patients diagnosed with AA between June 2022 and March 2023 were included in this retrospective, cross-sectional study. The patients were divided into two groups according to the presence of outbreaks. Both groups were compared in terms of age, gender, disease duration, number of outbreaks, family history of AA, previous medical treatment history for AA, clinical type, disease severity, presence of accompanying nail findings, and trichoscopic and laboratory characteristics.

Results: Among 100 patients, male dominance was found (N = 69). Most of the patients had patchy disease (90/100), mild disease severity (88/100), and a solitary outbreak (65/100). Male gender, longer disease duration, family history, presence of S2 severity of alopecia tool score, trachyonychia, short vellus hairs in trichoscopic examination, hypothyroidism, and folic acid deficiency were factors for AA outbreaks. Male gender and the presence of a family member with AA in the family were defined as the independent prognostic factors for disease recurrence.

Conclusions: While demographic, laboratory, and clinical findings are factors for AA outbreaks in the follow-up, male gender and family history should be considered independent predictors.

Introduction

Alopecia areata (AA) is an autoimmune, organ-specific hair disease that develops as a result of damage to hair follicles by sensitive T lymphocytes and progresses with non-scarring hair loss. Although the pathophysiology of the disease is not fully understood, genetic factors that predispose to autoimmune diseases and environmental factors such as infection and/or emotional stress are blamed. It mostly affects individuals younger than 30. Non-scarring oval patches in 1-3 cm diameter on the scalp are the most common clinical form. In addition, there are other clinical forms such as ophiasis in which hair loss is observed on the temporal and occipital areas of the scalp, and the central area of the scalp is protected, ophiasis inversus with the hair loss on the central area of the scalp, reticular type, and diffuse types, such as totalis (total scalp hair loss) and universalis (total body and scalp hair loss) [1].

Although the clinical examination is often sufficient in the diagnosis of the disease, trichoscopic findings could also help clinicians. These trichoscopic findings are yellow dots, black dots, short vellus hairs, broken hairs, exclamation mark hairs, and pigtail hairs [2].

There are many studies regarding clinical findings and trichoscopic and laboratory features of AA, however, the results are controversial. There is also no comprehensive evaluation examining the demographic, trichoscopic, and laboratory characteristics of patients with AA from our region. Also, to date disease, recurrence is associated with stressful life events, the presence of a family member with AA, COVID-19 infection, and vaccination [3-6]. However, more comprehensive studies are needed on this subject [6].

Objectives

Therefore, in this study, the demographic, trichoscopic, and laboratory characteristics of patients with AA in our region were examined. Also, the relationship between disease characteristics and the recurrence of AA was analyzed.

Methods

Study Design

This study is a descriptive, retrospective, and a cross-sectional study. It was carried out in a tertiary dermatology center after the ethics committees approval (Approval number: 2023/06-17). A hundred patients who were admitted to the dermatology outpatient clinic between June 2022 and March 2023 and diagnosed with AA were included in the study. The patients older than 18 gave an informed patient consent form. The patients under the age of 18 were informed together with their families, and the pediatric patient volunteer form was obtained.

All patients age, gender, disease duration, number of outbreaks, family history of AA, clinical type, disease severity, presence of accompanying nail findings, and trichoscopic and laboratory characteristics were obtained from the hospital registry system and recorded in the case report files. Trichoscopic examination was performed with Plusmed. Disease severity was evaluated by the severity of alopecia tool (SALT) classification based on affected hair loss area of scalp and scored as S0 (0%), S1 (<25%), S2 (25–49%), S3 (50–74%), S4 (75–99%) and S5 (100%) [7]. The patients were divided into two groups according to the number of outbreaks non-recurrent disease and recurrent disease. The patients with the first outbreak were included in the group of non-recurrent disease. The patients with 2 and more outbreaks were included in the group of recurrent disease. In terms of age, gender, disease duration, number of outbreaks, family history of AA, clinical type, disease severity, presence of accompanying nail findings, and trichoscopic and laboratory characteristics, the statistical relationship between the two groups was investigated.

Statical Analysis

Statistical analysis was done with IBM SPSS v20.0 (IBM Corp.). Numerical variables were given as mean ± standard deviation or median (25^{th}-75^{th} percentile). Categorical variables were given as frequency (percentage). Relationship between categorical variables were evaluated using chi-square analysis. Binary logistic regression was performed for univariate and multivariate analysis and P value less than 0.05 was considered as statistically significant.

Comparing the family history rates between the non-recurrent and recurrent alopecia areata groups, we calculated the effect size of W=2.02 using SPSS. A post-hoc test was conducted using G*power version 3.1 for power analysis. With a significance criterion of α= 0.05 and 35 patients in each group. The power of the study was calculated as 0.98.

Results

A total of a hundred patients, 31 (31%) female and 69 (69%) male patients who applied to dermatology clinic due to AA were included in the study. The prevalence of the disease was calculated as 1.5% (100/6600). In terms of outbreaks, the patients were divided into two groups. Sixty-five (65%) patients who had one outbreak were grouped as Group 1 (non-recurrent disease). Other 23 (23%) patients who had two outbreaks, and 12 (12%) patients who had three outbreaks were grouped together as Group 2 (recurrent disease).

Patients' demographic and clinical features were summarized in Table 1. The rate of male gender, long disease

Table 1. Patients demografic and clinic features.

Demographic features	Non-Recurrent Disease (N = 65)	Recurrent Disease (N = 35)	P value
Gender -Female -Male	 25 (38.5%) 40 (61.5%)	 6 (17.1%) 29 (82.9%)	0.028[a]
Age (mean+SD, year)	26.2 + 14.8	31.2 + 11.8	0.096
Disease duration (mean+SD, month)	1.71 + 0.92	2.34 + 1.01	0.002[a]
Number of outbreaks 1 2 3	 65[a] (100%) 0[a] (0%) 0 [a] (0%)	 0[b] (0%) 23 [b] (65.7%) 12 [b] (34.3%)	0.001[a]
The presence of family member with AA Absent Present	 61 (93.8%) 4 (6.2%)	 18 (51.4%) 17 (48.6%)	0.001[a]
Additional dermatological disease Absent Androgenetic alopesia Seborrheic dermatitis Acne vulgaris Telogen effluvium Vitiligo	 52 (80%) 4 (6.2%) 5 (7.7%) 1 (1.5%) 2 (3.1%) 1 (1.5%)	 30 (85.7%) 2 (5.7%) 0 (0%) 2 (5.7%) 0 (0%) 1 (2.9%)	0.370
Previous medical treatment history Topical steroid Topical steroids + topical minoxidil Intralesional steroid Intramuscular steroid	 13 (20%) 37 (56.9%) 8 (12.3%) 7 (10.8%)	 5 (14.3%) 23 (65.7%) 4 (11.4%) 3 (8.6%)	0.842
Additional systemic disease Absent Autoimmune hypothyroidism Type-1 diabetes mellitus	 60[a] (92.3%) 2[a] (3.1%) 3[a] (4.6%)	 27[b] (77.1%) 6[b] (17.1%) 2[a] (5.7%)	0.043[a]
Clinical features			
Clinical type Patchy type Reticular type Ofiasis type Alopecia totalis	 64[a] (98.5%) 0[a] (0%) 0[a] (0%) 1[a] (1.5%)	 26[b] (74.3%) 5[b] (14.3%) 3[b] (8.6%) 1[a] (2.9%)	0.001[a]
Disease severity (SALT score) S1 S2 S3 S4 S5	 62[a] (95.4%) 2[a] (3.1%) 0[a] (0%) 0[a] (0%) 1[a] (1.5%)	 18[b] (51.4%) 6[b] (17.1%) 8[b] (22.9%) 2[a] (5.7%) 1[a] (2.9%)	0.001[a]
Hair pull test Positive Negative	 34 (52.3%) 31 (47.7%)	 17 (48.6%) 18 (51.4%)	0.721
Accompying nail finding Absent Pitting Trachyonychia Beau lines	 52[a] (80%) 9[a] (13.8%) 2[a] (3.1%) 2[a] (3.1%)	 18[b] (51.4%) 6[a] (17.1%) 11[b] (31.4%) 0[a] (0%)	0.015[a]

AA = Alopecia Areata; SALT = severity of alopecia tool; SD = standard deviation.
[a]p<0.05, Chi-square test for categorical, Independent samples t-test for numerical variables.

duration, presence of a family member with AA, accompanying autoimmune hypothyroidism, ophiasis, and reticulary clinical type, presence of S2 and S3 SALT score, and accompanying nail finding (pitting and trachionychia) were higher in Group-2 than Group-1 (P = 0.028, P = 0.002, P = 0.001, P = 0.043, P = 0.001, P = 0.001, and P = 0.015, respectively). There was no significant relationship between groups in terms of previous medical treatment (P = 0.842). The patients trichoscopic and laboratory findings were compiled in Table 2. Short vellus hairs, hypothyroidism, and folic acid deficiency rates were higher in Group 2 than in Group 1 (P = 0.031, P = 0.001, and P = 0.037, respectively).

Univariate and multivariate analysis results were shown in Table 3. According to these results, the female gender was associated with a lower outbreak rate. However, long disease duration, the presence of a family member with AA, the presence of S2 SALT score, accompanying trachyonychia, the presence of short vellus hairs in trichoscopic examination, hypothyroidism, and folic acid deficiency were associated with higher outbreak rate. In multivariate analysis, female gender was found to be an independent prognostic factor in a lower outbreak rate, whereas the presence of a family member with AA was found to be an independent prognostic factor in a higher outbreak rate.

Conclusions

In this study, the characteristics of patients with AA who attended the dermatology clinic were analyzed and the factors affecting disease recurrence were defined. The most important finding of the demographic features of the patients was male dominance. Most of the patients had patchy disease (90/100), mild disease severity (88/100), and a solitary outbreak (65/100). Female gender was found to be an independent prognostic factor in a lower outbreak rate, whereas the presence of a family member with AA was found to be an independent prognostic factor in a higher outbreak rate.

In contrast to recent studies, male dominance (69%) was detected in the study [8,9]. This result may be related to the fact that men notice hair loss earlier than women due to shorter hair. In addition, regular visits to the hairdresser may lead to routine scalp control and earlier awareness of hair loss than women. Furthermore, the fact that women in our region often cover their hair may also cause them to realize hair loss later than men.

Several studies investigated the effect of demographic, clinic, and trichoscopic features on the severity of AA. Kavak et al reported that ophiasis type, onset in childhood, and presence of a family member with AA showed a positive correlation with disease severity [10]. Also, Bhardwaj et al reported that female gender, early onset, accompanying atopy, vitiligo, and thyroid disease had a statistically significant relationship with disease severity [11]. Agre et al also reported that having a first-degree relative with AA was a risk factor for recurrence [12]. In this study, there is a statistically significant relationship between the male gender, long disease duration, the presence of a family member with AA, and accompanying autoimmune hypothyroidism and disease outbreak. Male gender, accompanying autoimmune

Table 2. Patients dermoscopic and laboratory features.

Dermoscopic features	Non-Recurrent Disease	Recurrent Disease	P value
Exclamation mark hairs			0.463
Absent	23 (35.4%)	15 (42.9%)	
Present	42 (64.6%)	20 (57.1%)	
Black dots			0.933
Absent	31 (47.7%)	17 (48.6%)	
Present	34 (52.3%)	18 (51.4%)	
Short vellus hairs			0.031[a]
Absent	48(73.8%)	17 (48.6%)	
Present	17 (26.2%)	18 (51.4%)	
Split hairs			0.630
Absent	32 (49.2%)	19 (54.3%)	
Present	33 (50.8%)	16 (45.7%)	
Yellow dots			0.737
Absent	33(50.8%)	19 (54.3%)	
Present	32 (49.2%)	16 (45.7%)	
Pigtail hairs			0.493
Absent	47 (72.3%)	23 (65.7%)	
Present	18 (27.7%)	12 (34.3%)	
Laboratory findings			
Iron deficiency			0.062
Absent	38 (58.5%)	27 (77.1%)	
Present	27 (41.5%)	8 (22.9%)	
Vitamin B12 deficiency			0.051
Absent	49 (75.4%)	32 (91.4%)	
Present	16 (24.6%)	3 (8.6%)	
25-OH vitamin D deficiency			0.209
Absent	55 (84.6%)	26 (74.3%)	
Present	10 (15.4%)	9 (25.7%)	
Hypothyroiditis			0.001[a]
Absent	64 (98.5%)	27 (77.1%)	
Present	1 (1.5%)	8 (22.9%)	
Folic acid deficiency			0.037[a]
Absent	62 (95.4%)	29 (82.9%)	
Present	3 (4.6%)	6(17.1%)	

[a]p<0.05, Chi-square test for categorical variables

Table 3. The independent prognostic factors of disease recurrence

	Univarite Analysis			Multivariate Analysis		
	OR	C.I.	P value	OR	C.I.	P value
Female gender	0.33	0.120-0.910	0.032	0.14	0.026-0.719	0.019
Disease duration	2.43	1.442-4.110	0.001			
The presence of a family member with AA	14.40	4.297-48.272	0.001	16.3	2.792-95.189	0.002
SALT score S1 S2 S3 S4 S5	 Ref 10.3 5.6 5.6 3.4	 Ref 1.918-55.674 0.0- 0.0- 0.205-57.847	 0.007 0.99 0.99 0.39			
Accompanying trachyonychia	2.22	1.290-3.808	0.004			
Accompaying autoimmune hypothyroiditis	18.96	2.260-159.086	0.007			
Short vellus hairs	2.99	1.261-7.089	0.013			
Folic acid deficiency	4.28	0.999-18.308	0.05			

AA = Alopecia Areata; C.I. = Confidence Interval; OR = Odds Ratio; SALT = severity of alopecia tool.

hypothyroidism, and the presence of a family member with AA can be considered as demographic findings indicating the genetic basis of the disease. Therefore, patients with these demographic characteristics may have more frequent outbreaks. Long disease duration, on the other hand, may cause frequent outbreaks by causing high inflammation levels and the presence of excess memory T cells in the tissue [13].

The SALT score evaluation provides clinicians with great benefits in the evaluation of the treatment response of patients with AA. To date, it has been evaluated in recent studies to show the efficacy of many drugs in the treatment of AA and also to determine the prognosis of the disease [14-16]. However, no other study previously reported the relationship between the SALT score of the patients and disease recurrence. In this study, the rate of S1 was higher in non-recurrent disease group, on the other way both S2 and S3 were higher in recurrent disease group. This result should direct us that patients with S2 and S3 are more prone to frequent outbreaks due to intense inflammation and memory T cell in the tissue [9].

The prevalence of accompanying nail findings in AA has been reported at rates between 7% and 66%. The most frequently described nail findings are trachyonychia and pitting of the nails. Other possible deviations are leukonychia, onycholysis, and onychomadesis. Patients with high SALT scores are more likely to manifest nail alterations [1,17]. In this study, pitting and trachyonychia were the most common nail findings, and beau lines were also detected in 2 patients. Accompanying nail finding was related with disease recurrence in our study. High systemic inflammation in patients with AA could be a reason to have nail involvement and frequent disease recurrence.

Due to its chronic autoimmune nature, low ferritin, vitamin B12, and vitamin D levels could accompany AA. Numerous studies showed that patients with AA have vitamin and mineral deficiencies [18-20]. In this study, folic acid deficiency had a statistically significant relationship with disease recurrence. This result may suggest that vitamin deficiencies that are effective in hair follicle growth may also trigger disease recurrence.

Trichoscopy is a noninvasive diagnostic tool and helps clinicians in the diagnosis of alopecia areata. However, the relationship between AA disease severity and dermoscopy findings is controversial. Abhijet et al reported that yellow dots are the most common trichoscopic finding in AA [21]. They also declared a statistically significant correlation between yellow dots and disease severity, and an inversely proportional between short vellus hairs and disease severity. In this study, the presence of short vellus hairs had a significant relationship with outbreaks. This relationship may be associated with more vellus hairs due to hair regrowth in those patients after outbreaks.

The most important limitation of this study is its retrospective design and having unequal number of patients in each group. The strengths of the study were that it investigated the factors affecting disease recurrence with a high number of patients and showed the effect of clinical, trichoscopic, and laboratory features on disease recurrence. Future studies with a higher number of patients, investigating the genetic background in more detail, will increase our knowledge.

In Conclusion, demographic and clinical findings, vitamin and mineral deficiencies, and trichoscopic findings are essential clues for clinicians in the follow-up of patients

with AA. Presence of family history of AA and male gender are predictors for disease recurrence.

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