

Correlation between the severity of alopecia areata and its risk factors

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Background: Alopecia Areata (AA) is a recurrent non-scarring type of hair loss that can affect any hair-bearing area. Prognosis of AA is unpredictable and most patients experience more than one episode of hair loss. The purpose of this study was to investigate the relationship between the severity of AA with respect to age of onset, nail involvement, family history, number of recurrences and duration of the disease.

Methods: A total of 239 consecutive patients with AA who were visited in our dermatology clinic from June 2009 to November 2009 were included in this study. The extent of scalp involvement, age of onset, nail involvement, family history, number of recurrences and duration of AA were recorded.

Results: Two hundred and thirty nine (239) patients with AA including 141 males and 98 females entered our analysis (male: female ratio = 1.43:1). The age of the patients at the onset of the disease had a wide range from 1 to 60 years (mean \pm SD = 21.51 \pm 5.4). Two hundred and twelve patients (88.7%) had their first episode of AA before the age of 40 years. Duration of the AA varied from 1 month to 31 years. Ninety six (40.2%) patients experienced only one episode and 25 patients (10.5%) had more than 4 episode of alopecia. Nail changes was reported in 34 patients (14.2%). Forty five patients (18.8%) had a positive family history of alopecia areata. A personal history of atopy and autoimmune diseases was seen in 23 (9.6%) and 27 (11.3%) patients, respectively. The relationship between extensive AA and age of onset, duration, nail changes and positive family history was confirmed ($p < 0.05$). There was no relationship between the severity of AA and sex, recurrences, atopy and autoimmune diseases ($p > 0.05$).

Conclusion: AA occurred at a comparatively younger age. There was a correlation between extensive alopecia areata and age of onset, duration, nail changes, and positive family history as prognostic factors. There were no relationships between the severity of AA and sex, history of atopy and autoimmune diseases.

Keywords: alopecia areata, hair loss, risk factors, prognostic factors

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INTRODUCTION

Alopecia areata (AA) is an autoimmune disease that presents as a recurrent non scarring type of

hair loss. Disease prevalence rates from 0.1% to 0.2% have been estimated for the United States ¹. AA affects all age groups and different ethnics, with an equal sex distribution ^{2,3}. Pediatric AA

constitutes approximately 20% of AA cases, and as many as 60% of patients with AA develop their first episode of alopecia before the age of 20 years^{3,4}. One study suggests that 85.5% of Asian patients with AA have disease onset before the age of 40 years⁵. The disease prevalence peaks between the second and fourth decades of life⁶. AA most often affects the scalp (>90%); however, it can affect any hair-bearing area⁷. Clinically, AA can manifest many different patterns. Hair loss is most often localized and patchy. Recognized subgroups of this disease include alopecia totalis (AT), alopecia universalis (AU), reticular, ophiasis, and band-like hair loss⁸. The prognosis of alopecia areata is unpredictable. Up to 50% of the patients will recover in less than 1 year. However, most of them experience more than one episode of hair loss. In AT/AU, the chance of full recovery is less than 10%^{9,10}. The most important factors indicating a poor prognosis for AA are the extent of hair loss, an ophiasis pattern, a long duration of hair loss, a positive family history, the presence of other autoimmune or atopic diseases, nail abnormalities and onset at childhood or young age⁸. The purpose of this study was to investigate the relationship between the severity of AA with respect to age at onset, nail involvement, family history, number of recurrences and duration of disease.

PATIENTS AND METHODS

This cross sectional study was carried out at the Dermatology Department of Razi Hospital from June 2009 to November 2009. All patients with the scalp involvement of AA were included. Each patient was subjected to a detailed review of clinical history, family history of AA, and personal history of associated diseases such as atopy and auto-immune disorders. Various clinical parameters were studied including age, age of onset, duration of AA, number of recurrences, and extent of alopecia and nail involvement. We classified the extent of hair loss according to the guidelines published by Olsen *et al*⁸ as follows: S1 (<25%), S2 (25-49%), S3 (50-74%), S4 (75-99%) and S5 (100%). The duration of the disease was classified as <3 months, 4-12 months, 13-24 months, 25-60 months and >60 months.

Statistical analysis

Statistical analysis was performed using SPSS version 17 software. Differences in proportions of categorical variables were assessed through the chi-square test and Fisher's exact test. A two-tailed value of $P < 0.05$ was considered significant.

RESULTS

General evaluation

A total of 239 patients with AA were examined during the study period. The age of patients with AA varied from 5 to 67 years (mean = 27.89 ± 11.7). The age at onset varied from 1 to 60 years (mean = 21.51 ± 13.61). There were 141 (59%) male and 98 (41%) female patients; the male to female ratio was 1.43:1. Two hundred and twelve patients (88.7%) experienced their first episode of AA within the first four decades of life, in 133 of whom (54%) the first episode occurred before the age of 20 years. The peak age at onset was in the 11 to 20 year-old age group, as they represented 28% of our study population. There was an extreme variation in the duration of the disease, ranging from 1 month to 31 years with a mean of 6.2 years.

Clinical characteristics of AA

All patients presented with alopecia on the scalp with or without the involvement of other body sites. At the time of presentation, 135 (56.5%) patients had patchy alopecia with less than 25% scalp involvement (S1), 32 (13.4%) patients had S2, 35 (14.6%) patients had S3, 19 (7.9%) patients had S4 and 18 (7.5%) patients had alopecia totalis or universalis S5.

Sex

Alopecia more than 50% was observed in 45 male patients and 27 female patients. There was no significant difference in the severity of disease between sexes ($P = 0.663$).

Age of onset

The severity of AA scalp involvement in

Table 1. Severity of scalp involvement in different age groups

Age at onset	Severity of scalp involvement					Total
	<25%	25-49%	50-74%	75-99%	100%	
<=10	33 (24.4%)	8 (25%)	9 (25.7%)	6 (31.6%)	6 (33.3%)	62 (25.9%)
11-20	32 (23.7%)	10 (31.3%)	12 (34.3%)	6 (31.6%)	7 (38.9%)	67 (28.0%)
21-30	42 (31.1%)	11 (34.3%)	6 (17.1%)	2 (10.5%)	2 (11.1%)	63 (26.4%)
31-40	8 (5.9%)	2 (6.3%)	6 (17.1%)	3 (15.8%)	1 (5.6%)	20 (8.4%)
41-50	14 (10.4%)	1 (3.1%)	1 (2.9%)	0 (0%)	1 (5.6%)	17 (7.1%)
51-60	6 (4.4%)	0 (0%)	1 (2.9%)	2 (10.5%)	1 (5.6%)	10 (4.2%)
Total	135 (100%)	32 (100%)	35 (100%)	19 (100%)	18 (100%)	239 (100%)
P Value<0.001	$\chi^2=275.715$					

different age groups is demonstrated in Table 1. Sixty six (27.6%) patients in whom alopecia had started before the age of 40 years presented with extensive alopecia (S3 and above), compared to 6 (2.5%) who developed alopecia after the age of 40 years. This difference was statistically significant ($P < 0.05$). Alopecia totalis and universalis occurred in 13 (72.2%) patients with the age at onset below 20 years, compared to 3 (16.7) patients with the age at onset between 21 to 40 years and 2 (11.2%) patients with the disease onset after 40 years.

Duration

Severity of scalp involvement of AA in different durations of alopecia is demonstrated in Table 2. Patients with a longer duration of the disease frequently exhibited severe forms of alopecia ($P < 0.001$).

Family history

Only 45 (18.8%) patients had a positive family history of AA and 20 (44.4%) presented with extensive alopecia (S3 and above), compared to 52 patients (26.8%) without any family history of the disease ($P = 0.033$); the difference was statistically significant.

Nail involvement

Nail changes were found in 34 patients (14.2%), but one of them had involvement of all nails. Nail changes were more common in patients with severe forms of alopecia (16/35; 45.7%) as compared to those with mild AA (56/204; 27.4%) ($P = 0.002$). This difference was statistically significant.

The recurrence rate of AA

The severity of the scalp involvement of AA with respect to recurrence is demonstrated in Table 3. Ninety six patients (40.2%) had experienced only one AA episode. Twenty five (10.4%) patients had a history of recurrent episodes (>4). Relapses were more common in patients with severe forms of alopecia (48/72; 66.6%) as compared to those with mild AA (95/167; 56.8%), but the difference was not statistically significant ($P = 0.2$).

The location of alopecia at onset of AA

The scalp was the initial site of involvement in 173 (72.4%) patients. It was the site of onset in a significantly higher proportion of female patients (93/98; 94.8%) than male patients (80/141; 56.7%, $P < 0.001$). In both sexes, temporal and occipital areas of the scalp were common sites of primary lesion. In 49 patients (20.5%), the beard was the

Table 2. Severity of scalp involvement in different duration of alopecia

Duration of alopecia months	Severity of scalp involvement					Total
	<25%	25-49%	50-74%	75-99%	100%	
0-3	38 (28.1%)	1 (3.1%)	1 (2.9%)	0 (0%)	0 (0%)	40 (16.7%)
4-12	24 (17.8%)	10 (31.3%)	6 (17.1%)	4 (21.1%)	2 (11.1%)	46 (19.2%)
13-24	6 (4.4%)	0 (0%)	7 (20%)	1 (5.3%)	0 (0%)	14 (5.9%)
24-60	28 (20.7%)	6 (18.8%)	5 (14.3%)	3 (15.8%)	2 (11.1%)	44 (18.4%)
>60	39 (28.9%)	15 (46.9%)	16 (45.7%)	11 (57.9%)	14 (77.8%)	95 (39.7%)
Total	135 (100%)	32 (100%)	35 (100%)	19 (100%)	18 (100%)	239 (100%)
P Value<0.001	$\chi^2=57.063$					

Table 3. Severity of scalp involvement with respect to recurrence

recurrences	Severity of scalp involvement					Total
	<25%	25-49%	50-74%	75-99%	100%	
0	57 (42.2%)	15 (46.9%)	15 (42.9%)	4 (21.1%)	5 (27.8%)	96 (40.2%)
1	28 (20.7%)	6 (18.8%)	7 (20%)	6 (31.6%)	4 (22.2%)	51 (21.3%)
2	18 (13.3%)	3 (9.4%)	6 (17.1%)	2 (10.5%)	2 (11.1%)	31 (13%)
3	22 (16.3%)	2 (6.3%)	5 (14.3%)	4 (21.1%)	3 (16.7)	36 (15.1%)
≥4	10 (7.4%)	6 (18.8%)	2 (5.8%)	3 (15.8%)	4 (22.3%)	25 (10.4%)
Total	135 (100%)	32 (100%)	35 (100%)	19 (100%)	18 (100%)	239 (100%)
P Value<0.001						$\chi^2=57.063$

first site of hair loss. Eyebrows in 3 patients (1.3%) and the body in 14 patients (5.9%) were the initial site of involvement. The disease had not begun from eye lashes in any patients.

Associated diseases

Twenty three (9.6%) patients were reported to have an atopy history (namely atopic dermatitis, asthma, and allergic rhinitis). Atopy was seen in 20 patients (11.9%) with limited alopecia (S1-S2), compared to 3 patients (4.16%) with severe alopecia (S3 and above) but the difference was not statistically significant ($P = 0.162$). Twenty three (11.3%) patients had at least one autoimmune disease such as thyroid dysfunction or vitiligo. There was no relationship between the occurrence of autoimmune diseases and the severity of alopecia areata ($P = 0.969$).

DISCUSSION

Alopecia Areata (AA) usually presents as a sudden onset of patchy, non scarring alopecia¹¹. In severe cases, hair loss may be diffuse or total. The extent of hair loss (extensive AA/AT/AU) seems to be the most important prognostic factor of alopecia areata. Other factors associated with a poor prognosis include a long duration of hair loss, a positive family history, the presence of other autoimmune or atopic diseases, nail abnormalities, and the first episode in childhood or young ages⁸. Although studies in the past have shown that AA affects both sexes equally, many studies suggest AA is more common in females than males^{3,5,12,13}. This might be due to a heightened awareness of hair loss in women. In our study, there was a slight male preponderance (1.4: 1). Our results were derived from referral clinic application forms, not a field study; therefore, it may not be

indicative of the actual prevalence of the disease in the general population.

The role of gender in the extent of hair loss is unclear. Severe involvement in some studies had a female predominance^{3,13}. In contrast, the present study showed no relationship between sex and severity. Alopecia areata was reported to be total or universal in 8.7% of the patients¹⁴⁻¹⁶. In the present study, the majority of the patients (69.9%) were observed to have a mild disease and totalis or universalis were seen in only 7.5% of the patients. The peak of the onset age was seen between 10 and 20 years but most patients (212 of 239; 88.7%) experienced their first episode of AA within the first four decades of life. These results were similar to those reported earlier^{5,12,13}. There were extreme variations in the duration of the disease, ranging from 1 month to 31 years. The duration of the disease in 36% of the patients was < 12 months. The age at onset and duration of AA were observed to have significant relationships with the severity and extent of the disease in our study ($p < 0.05$).

We found that patients presenting with a childhood onset of AA had a longer disease duration than patients with adult onset of the disease. Early onset of AA and the long duration of the disease are well known poor prognostic factors. In a long-term follow-up study by Tosti, 43% of the children developed AT or AU after presenting with mild AA (S2) at the first visit⁹. Similarly, Goh C noted that longer duration and earlier onset of AA were more seen in AT and AU patients compared to mild and patchy ones¹⁷.

Nail changes have been described in 7–66% of patients with AA⁹. We observed nail changes in 14.2% of our cases. Comparable to earlier reports, nail changes were seen more often in patients with a severe form of the disease (45.7% compared with 27.4%) ($p=0.002$). Similarly, Sharma et al, found

that nail changes was more common in the patients with extensive alopecia¹⁸.

The rate of a positive family history of AA varied widely between the series, from around 10% to 50%^{2,12,13,18-20}. In a previous observation in this center, we studied 123 AA patients and found a positive family history in 24.4%²¹. In the current study, despite increasing the number of the patients, we found a decrease (18.8%) in this rate because in our previous study, most patients had AT and AU. The risk is the highest in the closest relatives, and falls in more distant relatives. Kavak et al, observed a 'decrecendo' rate from 12.8% to 6.5% in the first- to third-degree relatives². In our study, the family history was positive in the first to third degree relatives in 11.2%, 4.2%, and 3.8%, respectively. These results highlighted the role of genetic factors in AA. Some previous studies have revealed that the positive family history was associated with early age at onset and severe AA^{2,12}. Similarly, Yang et al, noted that patients with an early onset of AA had more affected first- and second-degree relatives¹². Our results only corroborate that there is a relationship between the extent of hair loss and a positive family history of AA. We failed to show any relationship between family history and age at onset.

AA most often affects the scalp at onset; however, it can affect any hair-bearing area. Sharma et al, reported 77.6% of patients had onset of hair loss in scalp¹⁸. Similarly, Nanda noted that the scalp was the initial site of hair loss in 95.8% of the patients³. In our study, the scalp was the initial site of alopecia areata in 72.4% of the patients. Onset of hair loss in the scalp was seen more often in patients with a severe form of the disease ($p < 0.001$). However, in previous studies, the pattern of the hair loss such as ophiasis was more important prognostic factor than the site of onset².

Evidence of atopy, including nasal and nasobronchial allergy, bronchial asthma, and atopic dermatitis was detected in 18% of the patients in the study of Sharma¹⁸. In our study, 9.6% of the patients were reported to have an atopic history. Yang et al, observed a higher incidence (36.8%), because their figures also included hypersensitivity detected on intradermal testing¹². We found no correlation between atopic history and more severe alopecia ($p = 0.162$). Van Der Spek in Netherlands found a significant relationship between atopy and

severity of AA¹⁶. There was extreme variation in the association of AA and autoimmune diseases. In a large study from North America, autoimmune diseases were associated in 17.1% of patients²⁰. The corresponding figure was 5% of the patients in the study of Sharma¹⁸. Vitiligo in 1.8% and thyroid dysfunction in 1% of the patients were the most frequent autoimmune diseases¹⁸. Barahmani reported that 5.6% of AA patients had autoimmune diseases. Hypothyroidism was found in 2.5% of the patients²². The frequency of thyroid abnormalities in AA varies from 1% to 2.8%¹⁸. In our study, 11.3% of the AA patients had an autoimmune disease such as thyroid dysfunction, vitiligo and psoriasis. Autoimmune diseases had no association with severe forms of alopecia ($P < 0.969$).

AA occurred at a comparatively younger age and 88% of the patients were below 40 years of age. There was a mild preponderance in men with the M: F ratio being 1.4:1. The correlation between extensive AA and age at onset and duration, nail changes, and positive family history, as prognostic factors, was confirmed. There were no relationships between the severity of AA and sex, recurrences rate and history of atopy and autoimmune diseases. Our results were consistent with previous data obtained from different populations.

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