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ORIGINAL RESEARCH

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Effects of age and sex on the comorbidities of alopecia areata: A cross-sectional hospital-based study

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Abstract

Background and Aims: Alopecia areata (AA) is a common autoimmune nonscarring hair disorder with strong genetic links. It seems to be associated with several comorbidities affecting the AA treatment plan. On the other hand, the prevalence of comorbidities in different populations can be different based on genetic differences. This study aimed to clarify the association between age and sex with various comorbidities in AA patients.

Methods: This cross-sectional study was conducted on 402 patients suffering from AA referred to our hospitals between 2018 and 2021. The clinical records of the patients were reviewed, including demographic and clinical information.

Results: The most common diseases associated with AA were anxiety (36%), dermatitis (30%), hypothyroidism (9%), hyperlipidemia (5%), and vitamin D deficiency (4%). The most common comorbidities in AA patients over 18 years were allergic rhinitis, psychological problems, diabetes, hypertension, and hypothyroidism ($p < 0.05$). Hypothyroidism was more common in female patients than in male patients ($p = 0.002$). In contrast, hyperlipidemia was more common in male patients than in female patients ($p = 0.024$). There was a significant association between the severity of AA and hyperlipidemia and vitiligo ($p = 0.003$ and 0.045).

Conclusion: Sex and age could affect comorbidities. The prevalence of hypothyroidism was higher in our study; it was higher in women than in men. Thyroid function tests were recommended for AA patients.

KEYWORDS

alopecia areata, comorbidities, cross-sectional, hypothyroidism

1 | INTRODUCTION

Alopecia areata (AA) is a chronic inflammatory disease, which is the second most common hair loss disorder after androgenetic alopecia. Its lifetime risk is about 2% globally.[1] Although its early onset is most common in the third and fourth decades of life, it may occur at any age and is associated with an increased risk of a widespread disease throughout life.[2] The pathogenesis of AA is related to a systemic autoimmune disorder, in which the body attacks the anagen hair follicles and suppresses them.[3] The role of genetic factors, oxidative stress, atopy, and gut microbiota in the development of AA has been discussed in the literature.[4] Several comorbidities are associated with

AA, including cardiovascular disease, atopic dermatitis, thyroid disease, lupus erythematosus, vitiligo, psoriasis, inflammatory bowel disease, and rheumatoid arthritis.[4]

Psychiatric disorders are more common in people with AA than in the general population, suggesting that people with alopecia may be at greater risk of developing a major depressive episode, anxiety disorder, social phobia, or paranoid disorder.[5,6]

Considering the destructive effects of AA on the appearance and quality of life, it is necessary to know more about this disease, as well as the diseases and conditions that accompany it. Along with providing basic medical services to AA patients for hair regrowth, it is very important to evaluate the possible comorbid conditions and provide the necessary care to improve the outcome. In addition, it is challenging to predict which patients will have the most severe form of the disease. Accordingly, this study aimed to investigate AA to choose the best treatment to achieve the best results.

Keypoints

- The prevalence of comorbidities in different populations can be different based on genetic differences.
- Sex and age could affect comorbidities. The prevalence of hypothyroidism was higher in our study; it was higher in women than in men.

2 | MATERIALS AND METHODS

This cross-sectional hospital-based study was conducted on 402 patients with AA referred to our hospitals between April 2018 and September 2021. The study was approved by the ethics committee (IR.TUMS.MEDICINE.REC.1400.1493). All patients signed the informed consent form and entered the study.

The clinical records of the patients were reviewed, including demographic and clinical information such as age, sex, location of the lesions, onset time of the disorder, and so forth. All AA diagnoses were established by dermatologists. AA patients were examined for medical comorbidities, including diabetes mellitus, thyroid diseases, inflammatory bowel disease, systemic lupus erythematosus, rheumatoid arthritis, *Helicobacter pylori* infection, hyperlipidemia, high blood pressure, iron deficiency anemia, vitamin D deficiency, depression, and anxiety.

First, the data distribution was evaluated using the Shapiro–Wilk test. All continuous variables were expressed as mean with standard deviation and median with 25th percentile and 75th percentile. Also, categorical variables were presented with frequency and %. *T*-test or Wilcoxon–Mann–Whitney test was used to compare quantitative data and χ^2 or Fisher's exact statistical test was used to compare qualitative data between two groups after the checking of the assumptions. All the analyses were performed using Stata (Version 16; Stata Corp.). *p*-Value less than 0.05 was considered statistically significant.

3 | RESULTS

A total of 402 AA patients referred to the Razi Alopecia Clinic were enrolled in this study. Patient characteristics and investigated comorbidities are shown in Table 1. The average age of patients was 27.2 ± 13.4 years old. There were 192 females (47.8%) and 210 males (52.2%). Patchy alopecia, universalis, totalis, and ophiasis were the most common forms of AA. The mean duration of the disease was 1.93 ± 2.15 years.

Of the 402 patients, 38 patients (9.5%; 18 women [47.3%] and 20 men [52.7%]) had a history of AA in their first-degree relatives. In addition, 125 patients were under 18 years old (31.09%), and 277 patients (68.91%) were over 18 years old. The recurrence rate, allergic rhinitis, anxiety, depression, diabetes, hypertension, and hypothyroidism were more common in patients over 18 years old (Table 2).

Fifty-three patients (13.2%; 25 women and 28 men) had nail involvement. In addition, 21 (39.6%) patients had alopecia universalis, 21 had alopecia totalis (39.6%), 21 had patchy type alopecia (39.6%), and 2 had alopecia ophiasis (3.77%).

There was a significant association between the type of alopecia and sex ($p = 0.016$). we found that SALT score, and age did not have any association with sex ($p = 0.193$ and 0.118). There was no significant association between the relapses and the type of AA ($p = 0.111$), as well as the severity of disease ($p = 0.125$); however, there was a significant association between the recurrences and age over 18 years ($p = 0.024$).

Based on the results (Table 1), the most common comorbidities in AA patients were anxiety and dermatitis. There was a significant association between sex and hypothyroidism and hyperlipidemia ($p = 0.002$ and 0.024). There was no significant association between the severity of AA and the onset of disease and hypothyroidism ($p = 0.975$ and 0.665).

There was a significant association between age and hypothyroidism, hypertension, hyperlipidemia, and DM ($p = 0.005$, 0.000, 0.008, and 0.001). There was a significant association between the severity of AA and hyperlipidemia and vitiligo ($p = 0.003$ and 0.045). There was no significant association between the type of alopecia and the prevalence of dermatitis, anxiety, and allergic rhinitis ($p = 0.645$, 0.127, 0.810).

A significant association was found between the prevalence of allergic rhinitis and age over 18 years old ($p = 0.037$). Regarding AA patients with asthma ($n = 7$), there was no significant association between asthma and age, type of disorder, and SALT score ($p = 0.843$, 0.102, and 0.340).

4 | DISCUSSION

The most common diseases associated with AA in our study were anxiety, dermatitis, hypothyroidism, hyperlipidemia, and vitamin D deficiency, respectively. In addition, the most common diseases were hypothyroidism and hyperlipidemia in women and men, respectively.

TABLE 1 Baseline demographics, clinical characteristics, and laboratory findings of patients with AA.

Characteristic	Patients with AA (*n* = 402)	Female (*n* = 192)	Male (*n* = 210)	*p* Value
Age (years), mean ± SD	27.2 ± 13.4	28.61 ± 14.38	25.89 ± 12.31	0.118
Onset of disease (years), mean ± SD	1.93 ± 2.15	1.68 ± 0.46	1.69 ± 0.46	0.398
Salt score, median (p25–p75)	68 (40–100)	58.5 (34.5–98.5)	70 (40–100)	0.193
Family history, *N* (%)	38 (10)	18 (47)	20 (53)	0.950
Type of AA, *N* (%)				
Patchy	204 (51)	101 (49)	103 (51)	0.016
Ophiasis	19 (5)	15 (79)	4 (21)	
Totalis	81 (22)	39 (45)	47 (55)	
Universalis	93 (23)	37 (40)	56 (60)	
Nail involvement, *N* (%)	53 (13)	25 (47)	28 (53)	0.390
Recurrence, *N* (%)	73 (18)	41 (56)	32 (44)	0.112
Comorbidities, *N* (%)				
Anxiety	145 (36)	77 (53)	68 (47)	0.107
Depression	4 (1)	4 (100)	0 (0)	0.016
Dermatitis	119 (30)	67 (56)	52 (44)	0.095
Hypothyroidism	34 (9)	25 (74)	9 (26)	0.002
Hyperlipidemia	21 (5)	5 (24)	16 (76)	0.024
Hypovitaminosis D	16 (4)	7 (44)	9 (56)	0.744
Allergic rhinitis	15 (4)	8 (53)	7 (47)	0.661
Hypertension	14 (4)	7 (50)	7 (50)	0.865
Diabetes	13 (3)	4 (31)	9 (69)	0.213
Iron deficiency	9 (2)	4 (44)	5 (56)	0.841
Vitiligo	9 (2)	3 (33)	6 (67)	0.382
Asthma	7 (2)	3 (43)	4 (57)	0.794
IBD	3 (1)	2 (67)	1 (33)	0.577
IBS	3 (1)	1 (33)	2 (67)	0.616
Psoriasis	1 (0.2)	1 (100)	0 (0)	0.478

Abbreviations: AA, alopecia areata; IBD, inflammatory bowel disease IBS, irritable bowel syndrome; SALT, severity of alopecia tool.

The rates of allergic rhinitis, anxiety, depression, diabetes, hypertension, and hypothyroidism were influenced by patients' age.

In a recent systematic review and meta-analysis conducted by Lee et al. The results of 87 studies indicated that atopic diseases, metabolic syndrome, *H. pylori* infection, lupus erythematosus, iron deficiency anemia, thyroid diseases, mental diseases, vitamin D deficiency, and hearing and eye abnormalities were more common in AA patients. In addition, these patients had a higher risk of developing autoimmune diseases.[1] In our study, *H. pylori* infection and hearing and eye abnormalities were not reported.

Anxiety and dermatitis under the age of 18 compared to other associated disorders with AA are seen more. Approximately half of the psychiatric disorders presented earlier than AA.[7] The use of antidepressants and anti-anxiety drugs was more often started before the diagnosis of AA.[8] Depression, generalized anxiety disorder, social phobia, and paranoid disorder were significantly higher in AA patients than in the general population.[6] AA causes morphological deformity and has a significant negative effect on the quality of life of patients. Therefore, psychological and emotional support is of great importance in AA treatment.[1] The prevalence rate of anxiety was higher in our study than in a previous study (36.1% vs. 18.8%).[6] It was higher in women (53.1%) than in men (46.8%); in addition, the highest prevalence was in patchy and universalis types, respectively. Also, 1% of patients had depression, which was lower than in previous studies.[6]

Wang et al. investigated the prevalence of various chronic diseases in 517 people with AA and 2969 of their first-degree relatives, showing an association between the prevalence of type 1 and type 2 diabetes in patients and their relatives.[9] In their study, only 1 patient had type 1 diabetes, but 14 sisters of the patients had

TABLE 2 Comparison of the clinical characteristic of AA patients between patients under and over 18 years.

Characteristic	Patients with AA <18 years-old (n = 125)	Patients with AA >18 years-old (n = 277)	p Value
Sex, *N* (%)			0.950
Female	60 (48)	132 (48)	
Male	65 (52)	145 (52)	
Type of AA, *N* (%)			
Patchy	61 (49)	143 (52)	0.017
Ophiasis	9 (7)	10 (4)	
Totalis	35 (28)	51 (18)	
Universalis	20 (16)	73 (26)	
Nail involvement, *N* (%)	15 (28)	38 (72)	0.637
Recurrence, *N* (%)	20 (16)	73 (26)	0.024
Atopy, *N* (%)			
Asthma	2 (29)	5 (71)	0.885
Allergic rhinitis	1 (7)	14 (93)	0.037
Dermatitis	41 (34)	78 (66)	0.447
Psychological problem, *N* (%)			
Anxiety	36 (25)	109 (75)	0.041
Depression	1 (25)	3 (75)	0.040
Metabolic syndrome, *N* (%)			
Diabetes	0 (0)	13 (100)	0.014
Hyperlipidemia	3 (14)	18 (86)	0.087
Hypertension	0 (0)	14 (100)	0.011
Deficiency, *N* (%)			
Hypovitaminosis D	3 (18)	13 (82)	0.277
Iron deficiency	2 (22)	7 (78)	0.560
Gastrointestinal disease, *N* (%)			
IBS	1 (33)	2 (67)	0.933
Autoimmune disorders, *N* (%)			
Vitiligo	2 (22)	7 (78)	0.560
Psoriasis	1 (100)	0 (0)	0.136
IBD	1 (33)	2 (67)	0.680
Hypothyroidism	3 (9)	31 (91)	0.003

Abbreviations: AA, alopecia areata; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome.

type 1 diabetes. Thus, type 1 diabetes was significantly more common in siblings (1.2%) than in patients with alopecia (0.2%) or the general population (0.12%–0.25%; $p < 0.05$).[9] In the current study, 3.2% of patients had diabetes type 2, which was higher in men than in women. Totalis and patchy alopecia had the highest prevalence, respectively, which is similar to the study by Wang et al.[9] Similar to our study, the prevalence of diabetes in alopecia patients is 3.3%, which is not the most common comorbidity.[1] In addition, in our study, no significant association was found between the prevalence of diabetes and the type of alopecia and sex, but a significant association was found between the prevalence of diabetes and age over 18 years ($p = 0.014$).

The prevalence of hypothyroidism was higher in our study than in a previous study [1]; it was higher in women than in men. In this regard, a study in Iran evaluated the prevalence of thyroid disorders in AA patients and showed that thyroid function disorders were observed in 8.9% of patients, which is similar to our study. In addition, Seyrafi showed no significant association between the severity or onset of the disease and hypothyroidism, which is similar to our study.[10] However, unlike Seyrafi's study, hypothyroidism was detected after the first 2 decades of life in the majority of our patients. In a systematic study, Kinoshita et al. also showed that AA was significantly associated with both TPO-Ab and TG-Ab; however, it did not support routine screening of thyroid function tests for asymptomatic AA patients but highlighted the potential future risk of autoimmune thyroid disorders, particularly in severe and refractory AA.[11]

AA is associated with atopic dermatitis, allergic rhinitis, and asthma. The study by Ibrahim et al. in 2015 showed that AA was associated with atopy in 10%–38.2% of patients, which is twice the prevalence found in the general population.[12] In many cases, the severity and prevalence of flare-ups of atopic diseases are related to the severity of AA, especially in patients with alopecia totalis or alopecia universalis, unlike our study.[12-14] A large meta-analysis found that patients with AA had a higher odds ratio (OR) of having allergic rhinitis (OR: 1.33) compared with controls; the prevalence of allergic rhinitis was higher in this meta-analysis study than in our study (17.7% vs. 3.7%), as well as the prevalence of asthma (9.9% vs. 1.7%).[1]

In the current study, 5.2% of patients had dyslipidemia, which was higher in men than in women. As mentioned earlier, the study by Huang et al. in 2013 also showed a higher prevalence of hyperlipidemia (24.5%) and high blood pressure (21.9%)[15]; however, a recent meta-analysis showed the same prevalence as our study.[1] Also, in our study, 3.5% of patients had high blood pressure, and its prevalence was the same between men and women as in a recent meta-analysis.[1]

The serum level of vitamin D was significantly lower in AA patients than in healthy subjects.[16] There is an inverse association between its level and the severity of AA.[17] In our study, 4% of patients had vitamin D deficiency. In addition, patients with vitamin D deficiency had high SALT scores but it was not statistically significant.

Iron deficiency is the most common nutritional deficiency in the world and is associated with growth retardation, poor behavior, decreased intellectual function, and decreased resistance to infection. Iron deficiency may be associated with AA, androgenetic alopecia, telogen effluvium, and diffuse hair loss.[18] Patients with iron deficiency had high SALT scores but it was not statistically significant.

The immune attack on the melanocyte was seen in vitiligo and AA. There is an association between AA and vitiligo, and its incidence in AA is between 1.8% and 7.0% (2.2% in our study).[1,2] In our study, patients with vitiligo had higher SALT scores ($p = 0.045$).

AA is an autoimmune disease with strong genetic links. It seems to be associated with several comorbidities affecting the AA treatment plan.[19] On the other hand, the prevalence of comorbidities in different populations can be different based on genetic differences.

Although one of the strengths of our study is the large sample size, this study used retrospective data and we suggest prospective studies with high-quality data such as cohort studies. Our study did not have a control group. Comparing results between AA patients and healthy subjects leads to more accurate results.

5 | CONCLUSION

Anxiety, dermatitis, and hypothyroidism were the most common diseases associated with AA. Sex, age, and severity of the disorder can affect the associated disorders. Thyroid function tests and psychiatric support are recommended for AA patients.

AUTHOR CONTRIBUTIONS

Elham Hamidpour: Data curation; formal analysis; writing—original draft. **Safoura Shakoei**: Project administration; supervision; writing—review and editing. **Maryam Nasimi**: Data curation; supervision; writing—review and editing. **Narges Ghandi**: Data curation.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data of this study are not publicly available due to ethical restrictions but are available upon request from the corresponding author upon reasonable request.

TRANSPARENCY STATEMENT

The lead author Safoura Shakoei affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

ETHICS STATEMENT

This study protocol was reviewed and approved by the Research Ethics Committee of the Tehran University of Medical Sciences, approval number IR.TUMS.MEDICINE.REC.1400.1493. Written informed consent was obtained from participants in our study.

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