

Evaluation of Quality of Life, Anxiety and Depression in Patients with Alopecia Areata: A Prospective Case-Control Study

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Abstract

BACKGROUND/AIMS: Alopecia areata (AA) is an immune response-driven, scarless hair disease specified by the destruction of hair follicles by an inflammatory response resulting from the loss of immune privilege. Apart from posing a cosmetic concern, it is a condition that impacts patients due to its chronic, unpredictable course and the lack of a definitive treatment. This study sought to explore the psychosocial state of patients with AA during its acute phase and compare them with a control group.

MATERIALS AND METHODS: This multicenter, prospective case-control study contained 70 patients with AA and 70 voluntary controls. The AA group included patients with recent onset or recurrent AA with a disease duration of under one year. After the demographic information and clinical traits of the patients were recorded, the study group was asked to complete the hospital anxiety and depression scale (HADS) and the dermatology life quality index (DLQI) to appraise their psychological well-being and quality of life.

RESULTS: In this study, the psychosocial characteristics of 140 participants were evaluated. The AA cohort comprised 70 patients, while the control cohort included 70 individuals matched for age and gender. Of the 70 patients with AA, 45 (64.3%) were men, and 25 (35.7%) were women, with a median age of 29 (interquartile range = 12.25) years. The median anxiety and depression scores according to HADS (HADS-Anxiety and HADS-Depression) were markedly elevated in the patient group compared to controls. Additionally, the median DLQI score of the patient group was substantially greater than that of the control group, which was statistically significant.

CONCLUSION: The outcomes of our study indicated that anxiety and depression scores were elevated in patients with acute AA compared to the controls. Therefore, it is essential for clinicians to recognize and address psychiatric comorbidities in patients with AA, even during the early period of the condition.

Keywords: Alopecia areata, anxiety, depression, quality of life

INTRODUCTION

Alopecia areata (AA) is an immune response-driven, scarless hair disease specified by destruction of hair follicles by an inflammatory response resulting from the loss of immune privilege.¹ It may manifest as one or more alopecic patches on the scalp, as well as alopecia totalis or

alopecia universalis. It can also involve the facial region, leading to hair loss in the eyebrows, eyelashes, and beard.^{2,3} The progression of AA is unpredictable, as it may either resolve spontaneously or persist for a long time, even a lifetime. Given that the duration of the current episode is a key prognostic factor, AA was classified as acute (≤ 12 months) or chronic (> 12 months).⁴ The condition poses a cosmetic concern and impacts

To cite this article: Özdemir Çetinkaya P, Kutlu Ö. Evaluation of quality of life, anxiety and depression in patients with alopecia areata: a prospective case-control study. Cyprus J Med Sci. [Epub Ahead of Print]

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Received: 02.02.2025

Accepted: 21.07.2025

Epub: 29.09.2025



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patients due to its chronic and unpredictable course, compounded by the absence of a curative treatment.

To date, the psychological symptoms and comorbidities associated with AA have been thoroughly investigated, with several meta-analyses conducted on the topic. In their meta-analysis, Lee et al.⁵ assessed all comorbidities associated with AA. According to the findings of 87 studies, an adjusted odds ratio (OR) of 1.72 for anxiety and an adjusted OR of 1.49 for depression were reported. Okhovat et al.⁶ conducted a meta-analysis focused on the link between anxiety, depression, and AA. Analyzing the data from 8 studies, the meta-analysis found pooled ORs of 2.5 for anxiety, and 2.71 for depression. Finally, Lauron et al.⁷ assessed the prevalence of depression and anxiety disorders in a meta-analysis that included 29 studies on depression and 26 studies on anxiety. They reported that the prevalence of depression was 9% (OR:1.38), while the prevalence of depressive symptoms was 37% (OR:2.70). Similarly, the prevalence of unspecified anxiety disorders was 13% (OR:1.51), and the prevalence of anxiety symptoms was 34% (OR:3.07). Overall, it is evident that there are varying levels of association between AA and depression as well as anxiety.

In AA, stressful life events can trigger the onset of the disease, while the condition itself may lead to psychological symptoms, creating a bidirectional relationship. This study aimed to investigate the psychological stress associated with the disease during its acute phase. Given the chronic nature of the condition and the prolonged treatment process, patients experience a disease burden along with associated psychiatric comorbidities. However, in this study, we sought to appraise anxiety and stress symptoms in patients with a disease duration of one year or less who were seeking hospital care for the first time, and to compare these symptoms with a control group.

MATERIALS AND METHODS

This multicenter, prospective case-control study was carried out from March 2020 to March 2021, involving 70 patients with AA and 70 voluntary controls, all recruited from the dermatology outpatient clinics of two state hospitals. The research acquired endorsement from the Erciye University's Ethics Committee (approval number: 2020/119, date: 12.02.2020). Participants were provided with complete information, and written consent was obtained.

The AA group included 70 patients aged 18 to 65 years, diagnosed with AA based on clinical history and dermatological examination. The study included patients with new onset or recurrent AA with a disease duration under one year. Patients with new onset disease were admitted to the outpatient clinic for the first time, while patients with recurrent AA were admitted due to their current relapse. Patients with a diagnosed psychiatric disorder were excluded from the AA group. The control group comprised 70 volunteers who had no history of dermatological or psychiatric conditions. The demographic information, family history, and clinical characteristics of the patients, including disease duration, presence of concomitant autoimmune diseases, pattern of disease involvement, and nail changes, were recorded. The severity of alopecia tool (SALT) was calculated to determine disease severity in patients with AA. The total score of SALT is used to evaluate the extent of hair loss. The scalp is divided into vertex, right lateral side, left lateral side, and the back. The percentage of hair loss in each region is then multiplied by

specific weight factors-0.4 for the vertex, 0.18 for the right and left lateral sides, and 0.24 for the back. The SALT score is calculated by summing the weighted scores from all four regions. Areata Investigational Assessment Guidelines, the SALT score is categorized into the following subgroups: S0 = no hair loss, S1 = <25% hair loss, S2 = 25-49% hair loss, S3 = 50-74% hair loss, S4 = 75-99% hair loss, and S5 = 100% hair loss.

The AA and control group were asked to complete the hospital anxiety and depression scale (HADS) and the dermatology life quality index (DLQI) to assess their mental well-being and quality of life (QoL). The validated Turkish edition of the HADS was used to evaluate manifestations of anxiety/depression. The HADS is a 14-item self-administered inventory, with each item scored on a 4-level Likert scale (0-3 points). It includes subscales of HADS-anxiety (HADS-A) and HADS-depression (HADS-D), with seven questions dedicated to each subscale. The cut-off scores for identifying anxiety and depression were set at 10 and 7, respectively. The QoL of the study groups was evaluated with the Turkish version of the DLQI. The DLQI is a 10-question self-reported instrument with a 4-level Likert scale (0-3), with total scores varying from 0 to 30. Elevated scores reveal a worse QoL, and scores greater than 10 suggest that it is moderately or severely affected.

Statistical Analysis

IBM SPSS Statistics for Windows, version 20.00 (Armonk, New York, USA: IBM Corp) was used to analyze the study, and a p-value of under 0.05 was interpreted as indicating statistical significance. The Shapiro-Wilk test was employed to analyze the normality of the data. The median and interquartile range (IQR) are used to express continuous variables with a non-parametric distribution. Categorical variables were stated as frequencies/percentages. The Mann-Whitney U test was utilized for independent samples. Pearson's chi-square test was applied for categorical variables, and, if any cell contained an expected count below five, Fisher's Exact test was utilized instead.

RESULTS

In this study, the psychosocial characteristics of 140 participants were evaluated. The AA group consisted of 70 patients, and the control group consisted of 70 age- and sex-matched volunteers ($p=0.424$, $p=0.275$, respectively). Of the 70 patients with AA, 45 (64.3%) were men, and 25 (35.7%) were women with a median age of 29 (IQR=12.25) years. Disease duration varied from 10 days to 12 months; and the median duration of AA was 1 month (IQR=1). Ten patients (14.3%) with AA had a family history; and 1 (1.4%) patient also had an accompanying autoimmune disease, Hashimoto's thyroiditis. Clinically, 7 (10%) patients had nail changes that indicated nail involvement, 5 (7.1%) patients had ophiasis, and the SALT scores of all the patients were <25%, categorizing them in the S1 subgroup. Forty-four (62.9%) of the patients stated that they had a history of life stressors before the onset of the disease (Table 1).

The median anxiety and depression scores according to HADS (HADS-A and HADS-D) were statistically significantly higher in the patient group than the control group ($p=0.019$, $p=0.041$, respectively). In addition, the median DLQI scores of the AA group were statistically significantly higher than the scores of the control group ($p<0.001$). The comparison of HADS and DLQI scores between the AA and control groups is given in Table 2.

Table 1. Demographic characteristics and clinical findings of patients with AA

	Patient group (n=70)
Sex (n/%)	
Female	25 (35.7%)
Male	45 (64.3%)
Age [Median, (IQR), years]	29 (12.25)
Duration of AA [Median, (IQR), months]	1 (1)
Family history of AA (n/%)	10 (14.3%)
Accompanying autoimmune diseases (n/%)	
Hashimoto's thyroiditis	1 (1.4%)
Clinical findings of AA (n/%)	
Nail involvement	7 (10%)
Ophiasis	5 (7.1%)
S1 subgroup according to SALT scores	70 (100%)
History of life stressors	44 (62.9%)

AA: Alopecia areata, IQR: Interquartile range, SALT: Severity of alopecia tool data were expressed as the median and the IQR in continuous variables, and the n (%) in categorical variables.

Table 2. Comparison of HADS and DLQI scores between the alopecia areata and control group

	AA group (n=70)	Control group (n=70)	p
HADS [median, (IQR)]			
Anxiety	8 (6.25)	7 (4)	0.019 ^m
Depression	7 (5.25)	4.5 (6)	0.041 ^m
HADS classification (n/%)			
Anxiety			
Absent	40 (57.1%)	58 (82.9%)	0.001 ^x
Present	30 (42.9%)	12 (17.1%)	
Depression			
Absent	33 (47.1%)	44 (62.9%)	0.062 ^x
Present	37 (52.9%)	26 (37.1%)	
Presence of stressful life events (n/%)			
Absent	26 (37.1%)	37 (52.9%)	0.062 ^x
Present	44 (62.9%)	33 (47.1%)	
DLQI [median, (IQR)]	2 (6)	0.5 (2)	<0.001 ^m
DLQI classification (n/%)			
Mildly-moderately affected	63 (90%)	70 (100%)	0.013 ^f
Severely affected	7 (10%)	0	

AA: Alopecia areata, DLQI: Dermatology life quality index, HADS: Hospital anxiety and depression scale, IQR: Interquartile range.
Data were expressed as median (IQR) for continuous variables and n (%) for categorical variables.
Independent samples were compared with the Mann-Whitney U and chi-square tests. If one or more cells had an expected count of less than 5, Fisher's exact test was used.
*p<0.05, ^mMann-Whitney U test, ^xchi-square test, ^fFisher's exact test.

DISCUSSION

An increasing body of evidence suggests a connection between psychiatric comorbidities and inflammatory diseases such as psoriasis, atopic dermatitis, rheumatoid arthritis, and inflammatory bowel disease.⁸⁻¹¹ Among these, AA, an autoimmune condition that results in hair loss, has garnered growing interest due to its potential psychological impact. CD8 + T cells are thought to play a central role in mediating hair loss in AA, and there are higher levels of IL-6, IL-1 β , tumor necrosis factor (TNF), along with cytokines of type 2 and type 17 immune pathways.¹² Several meta-analyses revealed that IL-6, IL-1 β , and TNF have been closely linked to depression.^{13,14} Bain et al.¹² reported that increased levels of IL-17E and IL-22 were positively associated with depression scores of patients with AA.

In our study, we intended to evaluate the psychosocial parameters of patients with AA admitted to outpatient clinics for the first time during the acute phase. While 62.9% of the patients reported a history of significant stress prior to the onset of the disease, the median anxiety and depression scores of the AA group were significantly higher compared to the control group. However, only the frequency of anxiety was significantly higher based on the HADS' defined cut-off values. While the psychosocial effects of AA have been studied in detail in the literature, our study uniquely focuses on the HADS scores in patients at the first hospital admission at disease onset or relapse. Unlike previous studies that may focus on longer disease durations, our focus on early-stage patients offers a unique perspective on the initial emotional challenges faced by individuals with AA. Thus, our findings underscore the importance of addressing mental health early in the course of AA.

The new international classification of psychodermatological disorders categorizes AA as a "primary skin disorder related to mental health," similar to conditions like urticaria, vitiligo, and psoriasis.^{15,16} This implies that AA is a skin condition influenced by stress and linked to secondary psychiatric conditions.¹⁵ It is commonly believed, based on anecdotal evidence, that psychological stress triggers AA. While some case-control studies support this link, other publications have found no evidence to support it.¹⁷⁻²⁰ Kutlu et al.¹⁷ highlighted the increase in AA cases during the coronavirus disease-2019 pandemic compared to the preceding year and proposed that AA may be more closely linked to short-term stress (less than 2 months) rather than long-term stress. Ferentinos et al.¹⁸ conducted a case-control study involving 52 patients with new-onset or recurrent AA and 51 matched controls. They found that patients with AA experienced a significantly higher number of stressful life events in the previous year (number of events: 4 vs. 3) compared to the controls. Although there was no significant difference in HADS scores between the two groups, the study revealed that stressful life events were linked to higher HADS-A scores in patients with AA. Additionally, Taheri et al.¹⁹ investigated the potential role of stressful life events as a trigger for AA in a study involving 61 patients and 61 controls. The results revealed no significant differences in the number or mean scores of physical and sexual stress events between the two groups. However, patients experienced more emotional stress events with higher mean scores compared to the control group. In our study, we found that 62.9% of patients had experienced stressful life events, 52.9% had symptoms of depression, and 42.9% had symptoms of anxiety. Among these, only the prevalence of anxiety was significantly higher than in the control

group. Since no differences were found in stressful life events, it may be concluded that high anxiety may be a comorbidity of the disease rather than a trigger. Although the exact role of stress in triggering AA remains unclear, the possibility that stress could act as a trigger in susceptible individuals still exists and warrants further investigation.

AA often causes cosmetic disfigurement rather than severe physical symptoms, yet it still has a considerable effect on mental well-being. Thus, the psychosocial impact of AA has been studied over an extended period. In their study assessing the psychological profile and QoL in 126 patients (94 adults) with AA, Vélez-Muñiz et al.²¹ found that the majority of patients had patchy alopecia, and 77.6% of the adults had an impaired QoL. Additionally, 71.2% displayed symptoms of depression and anxiety, according to the HADS, and 60% of the referred patients were prescribed pharmacological treatment. The impact of the disease on patients also varies. In a study by Bain et al.¹² involving 39 patients with AA, depression was found in 18% of patients and anxiety in 51% of patients, as measured by the HADS. Interestingly, the frequency of depression and anxiety was higher in patients who had experienced patchy hair loss for less than 10 years compared to those with more advanced stages and longer durations of the condition. Furthermore, Bewley et al.²² conducted a multicenter, cross-sectional survey involving 747 patients with a history of or current hair loss severity of $\geq 50\%$ to assess the disease burden. They reported that 26.1% of patients were diagnosed with anxiety and 18.1% with depression. Additionally, 86.2% of patients had severely affected DLQI scores (>10). Further analysis showed that the DLQI score was lower in patients with less than 50% hair loss compared to those with equal to or more than 50% hair loss, as expected. However, DLQI scores were still lower (but above 10) in patients with a disease duration of >4 years, compared to those with 0-4 years. Improved depression, anxiety, and QoL scores in long-term or severe illness may be attributed to the development of greater disease acceptance and the establishment of effective coping mechanisms. Finally, using several questionnaires, including HADS, Clemmesen et al.²³ studied the psychosocial and mental impact of AA with 376 patients. They reported that Skindex-16 and AA symptom impact scale could distinguish disease severity. They found that moderate to severe disease, female sex, and eyebrow involvement contributed to a higher score and had a detrimental effect on the patient's QoL. They also emphasized that the DLQI is not an ideal tool for evaluating the QoL related to AA, as it mainly focuses on skin symptoms rather than those linked to hair loss.²³ In the studies summarized above, despite variations in disease duration, severity, and the scales used, it is evident that the QoL was impacted, and patients displayed symptoms of depression and anxiety. Although our patient group consisted of individuals with patchy alopecia and a disease duration under one year, 42.9% exhibited symptoms of anxiety, 52.9% exhibited symptoms of depression, and 10% had a severely affected QoL. From these findings, it can be concluded that patients with newly onset disease are more likely to experience psychological impacts, irrespective of the disease's severity. Additionally, it is important to acknowledge that the DLQI may not fully capture the QoL in patients with AA. Moreover, QoL is likely to be more significantly affected in cases of severe disease or during the acute phase, regardless of the disease's overall severity. Therefore, even in cases of mild disease, clinicians should prioritize assessing the psychological well-being and QoL of patients at the onset of the condition.

Study Limitations

Our study has several limitations. While the study design was prospective and the sample size was moderate, it was a case-control study, which limits the ability to draw conclusions about causal relationships. Additionally, the psychological status of the study population was assessed using self-reported questionnaires commonly used in clinical practice. However, neither the patients nor the controls underwent psychiatric evaluations by clinicians. Another limitation of the study was that the patient group consisted of individuals in the S1 group of SALT, with scalp involvement below 25%, despite the inclusion criteria not specifying restrictions based on disease severity. As a result, HADS scores could not be assessed in relation to disease severity. Additionally, because the disease duration was short in this study, we were unable to assess the correlation between disease duration and HADS scores.

CONCLUSION

The findings of our study indicated that anxiety and depression scores were higher in patients with acute AA compared to the control group. Therefore, it is essential for clinicians to recognize and address psychiatric comorbidities in patients with AA, even during the early phase of the condition. In this way, they can ensure a comprehensive approach to the patient's overall well-being and refer them for further evaluation if psychological symptoms are observed.

MAIN POINTS

- Sixty-two point nine percent (62.9%) of the patients reported a history of significant stress before the onset of the disease.
- Although our patient group consisted of individuals with patchy alopecia and a disease duration of under one year, 42.9% exhibited symptoms of anxiety and 52.9% of depression, and 10% had a severely affected quality of life (QoL).
- Even in cases of mild disease, clinicians should prioritize assessing the psychological well-being and QoL patients at the onset of the condition.

ETHICS

Ethics Committee Approval: The research acquired endorsement from the Erciye University's Ethics Committee (approval number: 2020/119, date: 12.02.2020).

Informed Consent: Participants were provided with complete information and written consent was attained.

Acknowledgements: The authors state that they have no relationships that provided financial or editorial assistance for the study, which could potentially lead to a conflict of interest regarding the submission.

Footnotes

Authorship Contributions

Surgical and Medical Practices: P.Ö.Ç., Ö.K., Concept: P.Ö.Ç., Ö.K., Design: P.Ö.Ç., Ö.K., Data Collection and/or Processing: P.Ö.Ç., Ö.M., Analysis and/or Interpretation: P.Ö.Ç., Ö.K., Literature Search: P.Ö.Ç., Ö.K., Writing: P.Ö.Ç., Ö.K.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study had received no financial support.

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