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Sleep disturbance in alopecia areata: A cross-sectional study

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Abstract

Background: Alopecia areata (AA) is a nonscarring hair loss with autoimmune pathophysiology, which is associated with psychiatric disorders including anxiety and depression. Sleep disorders are commonly seen with anxiety and depression. Here we evaluate the sleep quality of AA patients.

Methods: This cross-sectional study involved 51 AA patients and 51 age- and sex-matched healthy controls. The sleep quality and day sleepiness were evaluated by the Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS) questionnaires. The severity of AA was evaluated with the Severity of Alopecia Tool (SALT).

Results: Unlike the ESS score, the mean PSQI score was significantly higher in the AA group compared with the controls (7 ± 4.13 vs. 3.53 ± 1.96, $p < 0.001$). The number of cases with ESS ≥ 11, indicating the excess daytime sleepiness, was significantly higher in the AA group compared with controls (15 vs. 6, $p = 0.02$). There was no significant correlation between PSQI score and age, age of onset of the disease, or SALT score ($p > 0.05$). Anxiety and depression were more common in the AA group versus controls ($p = 0.9$). PSQI score was higher in AA patients who had anxiety and depression compared with those who did not (9.9 ± 5.28 vs. 4.76 ± 3.08, $p = 0.001$).

Conclusion: Sleep quality is impaired in AA patients. As expected, sleep would be more disturbed in AA cases with depression or anxiety. Therefore, attention to sleep quality and concomitant psychiatric diseases is essential in AA clinical management.

KEYWORDS

alopecia areata, daily sleepiness, Epworth Sleepiness Scale, Pittsburgh Sleep Quality Index

1 | INTRODUCTION

Alopecia areata (AA) is a nonscarring hair loss due to T-cell-mediated tissue-restricted autoimmune response in the hair follicles.[1] Progressive hair loss impairs several areas of patients' quality of life that contribute to increased risk of psychological and psychiatric complications.[2] The exact etiologic factors of AA are not fully identified. Inflammation and infectious conditions are suggested to be associated with AA development.[1] Interestingly, a recent retrospective cohort study that included a large population found that sleep disorders, especially in those under age 45 years, could be a predisposition factor for AA and some other comorbid conditions (e.g., rheumatoid arthritis, vitiligo, and autoimmune thyroiditis).[3] AA is commonly associated with psychiatric disorders and low quality of

life, which impair sleep. Psychological conditions could also be a trigger for autoimmune diseases including AA.[4]

However, there are conflicting reports of sleep disturbance in AA patients. A study on 105 AA patients showed that only 11.4% suffer from excessive daytime sleepiness (EDS) measured by the Epworth Sleepiness Scale (ESS).[5] Despite the controversial data on the association between sleep and AA, sleep disturbances are suggested to affect the immune system and raise the risk of other autoimmune disorders such as rheumatoid arthritis, systemic lupus erythematosus, Sjogren's syndrome, and ankylosing spondylitis.[6]

Hence, the interaction between sleep and AA seems to be complex and possibly bidirectional, so further investigations are needed to better identify this potential relationship. Here we aim to determine the sleep quality in AA patients measured by ESS and Pittsburgh Sleep Quality Index (PSQI).

2 | PATIENTS AND METHODS

This cross-sectional study included 51 confirmed adults (age > 18 years) of AA, who were referred to the outpatient dermatology clinics between 2018 and 2019. We used dermoscopy to confirm the diagnosis of AA. An experienced dermatologist confirmed the diagnosis of AA, however, if they had a doubt, we would have used biopsy. Fifty-one age- and sex-matched healthy individuals were enrolled as the control group. Simple random sampling was used for selecting the participants. Patients who overconsumed caffeine-rich beverages, alcohol, stimulants, or energizers, or who had night-shift jobs were excluded. The severity of AA was scored with the Severity of Alopecia Tool (SALT).[7]

ESS was used to evaluate EDS. It is a self-administered questionnaire with eight questions each is rated on a 4-point scale from 0 (no daytime sleepiness) to 3 (the most EDS). The final score is the sum of eight item scores and a score equal to or >11 is considered EDS.[5,8] ESS-IR is a reliable and valid instrument for evaluating daytime sleepiness was used.[9] The Persian version of the ESS-IR has Cronbach's α coefficient of 0.82.[9]

The PSQI is another self-report questionnaire of sleep quality during the past month containing 19 items in 7 parts including subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, sleeping medication use, and daytime dysfunction.

The participants were asked to score each item on a 0–3 interval scale. The global PSQI score is ranging from 0 to 21 calculated by totaling the scores. One of the questions in the PSQI questionnaire asks about the participants' assessment of their sleep quality by a 5-Likert score (1 = very bad, 2 = almost bad, 3 = good, 4 = almost good, and 5 = very good). The Persian version of the PSQI was suitable for the psychometric properties with Cronbach's α coefficient of 0.77.[10,11] A total score > 5 is considered poorer sleep quality with sensitivity and specificity of 94% and 72%, respectively.[10] The sensitivity is decreased to 85% and specificity is increased to 84% for a PSQI cutoff value of 6.[11]

All of the participants signed the informed consent. The study was performed according to the Declaration of Helsinki and the Medical Research Involving Human Subjects Act and ethical approval was provided by our university ethics committee.

After providing a complete explanation of the study and obtaining written consent, a past medical history and previously documented history of psychiatric disorder were taken, and an examination was performed. Data on age, sex, severity, and duration of disease were recorded and then patients filled out PSQI and ESS questionnaires.

G*power software (version: 3.1.9.6) was used by considering a significant level of 0.05 and power of 80% for detecting a medium effect size ($d = 0.565$) under two independent t tests. By considering these settings, 51 samples were calculated for each group.[12]

3 | STATISTICAL ANALYSIS

Statistical analysis was performed with SPSS version 25. Continuous variables were presented as mean ± SD. A one-sample Kolmogorov–Smirnov test was used to estimate the distribution of data. To compare continuous variables between two categorical variables, we used Mann–Whitney U test. Fisher's exact test was performed to evaluate the relationship between categorical variables. The correlation of continuous variables was done using the Spearman's correlation test. A $p < 0.05$ was considered the significant level.

4 | RESULTS

This study included consisting of 102 participants (51 cases with AA and 51 in the control group). The demographic data including age, sex, and smoking status were comparable between the groups (Table 1).

Our data showed that 15.7% of AA patients had simultaneous anxiety or depression disorders, which is significantly more than controls (3.9%, $p = 0.09$; Table 1). Women were more vulnerable to psychological disorders ($p = 0.25$; Table 2).

Of 51 patients with AA disease, 33 (64.7%) of them had a relapse and the rest (18 [35.3%]) did not experience relapse.

The age of onset of the disease is significantly lower (20.27 ± 10.76 vs. 26.61 ± 11.01, $p = 0.02$) in patients who experienced relapse versus those without disease recurrence. A significant relationship was observed between nail involvement and the recurrence of disorder ($p = 0.006$, odds ratio = 5.33, 95% confidence interval [CI]: 1.54–18.5) so that the chance of recurrence in people whose nails are involved is 5.33 times that of other patients.

The mean PSQI score was significantly higher in the AA group than the healthy individuals (7 ± 4.1 vs. 3.5 ± 1.9, $p < 0.001$). One of the questions in the PSQI questionnaire asks about the participants' assessment of their sleep quality. Our analysis of this item showed that AA patients had a significantly lower estimation of their sleep quality versus controls (2.76 ± 0.97 vs. 3.65 ± 1.11, $p < 0.001$;

TABLE 1 Baseline demographics, clinical characteristics of study participants

Characteristic	Patients with AA (*n* = 51)	Healthy controls (*n* = 51)	*p**
Gender, *n* (%)			
Female	27 (52.9%)	27 (52.9%)	1
Male	24 (47.1%)	24 (47.1%)	
Age, y	29.71 ± 10.78	29.88 ± 11.01	0.93
Smoking status, *n* (%)	8 (15.7%)	2 (3.9%)	0.09
Duration of current disease, y, mean ± SD	7.2 ± 7.86	–	
Age of onset of disease, y, mean ± SD	22.5 ± 12.7	–	
Type of AA, *n* (%)			
Patchy	24 (47%)	–	
Ophiasis	4 (8%)	–	
Totalis	2 (4%)	–	
Universalis	21 (41%)	–	
Nail involvement, *n* (%)	30 (58.82%)	–	
SALT Score	71.49 ± 34.42		
S1 (1%–25%)	10 (19.6%)		
S2 (26%–50%)	7 (13.7%)		
S3 (51%–75%)	4 (7.8%)		
S4 (76%–99%)	7 (13.7%)		
S5 (100%, totalis and universalis)	23 (45%)		
Anxiety/depression, *n* (%)	8 (15.7%)	2 (3.9%)	0.09
ESS score, mean ± SD	7.63 ± 4.7	6.82 ± 3.83	0.34
ESS ≥ 11	15 (71.4%)	6 (28.6%)	**0.02**
PSQI score, mean ± SD	7 ± 4.13	3.53 ± 1.96	**<0.001**
Patients' self-assessment	2.76 ± 0.97	3.65 ± 1.11	**0.001**

Abbreviations: AA, alopecia areata; ESS, Epworth Sleepiness Scale; *n*, number; PSQI, Pittsburgh Sleep Quality Index; SALT, Severity of Alopecia Tool; y, years.

*A $p < 0.05$ is considered significant and bold.

TABLE 2 Female and male clinical characteristics of AA participants

Characteristic	Female	Male	*p**
Duration of disease, y	7.41 ± 8.13	6.96 ± 7.74	0.88
Age of onset of disease, y	25.37 ± 12.79	19.29 ± 8.10	**0.04**
Anxiety/depression, *n* (%)	6 (22.2%)	2 (8.3%)	0.25
Smoking, *n* (%)	0	8 (33.3%)	**0.001**
Recurrence, *n* (%)	18 (66.7%)	15 (62.5%)	0.98
PSQI, mean ± SD	8.26 ± 4.63	5.58 ± 2.99	**0.02**
ESS, mean ± SD	6.37 ± 4.79	9.04 ± 4.37	**0.04**
Patients' self-assessment	2.48 ± 0.93	3.08 ± 0.92	**0.02**

Abbreviations: AA, alopecia areata; ESS, Epworth Sleepiness Scale; *n*, number; PSQI, Pittsburgh Sleep Quality Index; y, years.

*A $p < 0.05$ is considered significant and bold.

Table 1). Women also had a higher mean PSQI score and self-assessment of sleep quality than males (Table 2). There was a strong negative relationship between the patient's self-assessment of sleep quality and PSQI score (Spearman's $\rho = -0.762$, $p < 0.001$).

Comparing PSQI scores between patients with or without depression and anxiety showed a higher score in those with depression/anxiety symptoms (11 ± 5.2 vs. 6.26 ± 3.4, $p = .002$; Table 1).

The number of cases with PSQI > 5 (13.7% vs. 4%, $p < 0.001$) was significantly higher in patients with AA compared with the control group. Also, the number of cases with PSQI > 6 (45.1% vs. 5.9%, $p < 0.001$) is higher in AA patients. The PSQI score was significantly higher in AA patients with anxiety or depressive disorders than in the controls (9.9 ± 5.28 vs. 4.76 ± 3.08, $p = 0.001$). The self-assessment of the sleep quality was significantly lower in patients with anxiety or depressive disorders versus those without anxiety/depression

TABLE 3 Correlation between clinical characteristics of AA participants and PSQI and ESS

	PSQI		ESS	
Characteristic	p^*	Correlation coefficient	p^*	Correlation coefficient
Age	0.52	0.09	0.26	−0.15
Duration of disease	0.68	0.05	0.26	−0.15
Type of AA	0.93	0.01	0.83	−0.03
SALT score	0.85	0.02	0.64	−0.06

Abbreviations: AA, alopecia areata; ESS, Epworth Sleepiness Scale; PSQI, Pittsburgh Sleep Quality Index; SALT, Severity of Alopecia Tool.
*A $p < 0.05$ is considered significant.

(2.10 ± 0.99 vs. 3.32 ± 1.08, $p = 0.002$). Comparing PSQI scores between patients with (7.15 ± 3.83) or without (6.72 ± 4.75) recurrence revealed there was no significant difference ($p = 0.74$). Comparing ESS scores between patients with (7.61 ± 4.62) or without (7.67 ± 5.12) recurrence revealed there was no significant difference ($p = 0.74$).

Although the ESS mean score was comparable between both groups (7.6 ± 4.7 vs. 6.8 ± 3.8, $p = 0.34$), the number of cases with ESS ≥ 11 was significantly higher in the AA group compared with controls (15(71.4%) vs. 6 (28.6%), $p = 0.02$). The PSQI and ESS scores were significantly lower in women compared with men (Table 2). There was no significant correlation between SALT score and ESS ($r = -0.06$, $p = 0.64$) or PSQI ($r = 0.02$, $p = 0.85$) scores. There was no significant correlation between nail involvement and ESS ($p = 0.85$) or PSQI ($p = 0.45$) scores. There was no significant correlation between the clinical type of AA and ESS ($p = 0.89$) or PSQI ($p = 0.48$) scores.

The correlation between other clinical characteristics of AA participants and PSQI and ESS scores is explained in Table 3.

5 | DISCUSSION

Our findings revealed that the sleep quality measured by PSQI was impaired in AA patients. The excessive daily sleepiness indicated by the ESS ≥ 11 was also more frequent among AA patients compared with normal subjects. Interestingly, anxiety and depression were both more common in such patients could be the explanation for sleep disturbances. There was no significant correlation between PSQI score and age, age of onset of disease, or the severity of AA scored by SALT.

The association between sleep disturbances and AA seems to be reciprocal.[13] Progressive hair loss could be a major risk factor for anxiety, depression, and even psychiatric disorders, all of which impair sleep quality. Psychological conditions could be a triggering factor for the development and exacerbation of autoimmune disorders, including AA.[4] Stress and depression are associated with high levels of serum interleukin-6 and tumor necrosis factor.[14] These cytokines also are increased in AA and are associated with disease severity.[15] Interestingly, genomic analysis has found common HLA genes among AA and major depressive disorder.[14] Our data showed a higher proportion of anxiety or depression disorders among AA patients (15.7%) versus healthy controls (2%). However, the reported prevalence of anxiety and depression in AA measured by valid and reliable questionnaires is much higher at about 47% and 56%, respectively.[16] Herein, we did not use any measurement tool to assess the simultaneous psychiatric disorder, while we were confined to the self-report of any diagnosed anxiety/depression for which cases receive treatment. This would explain our lower rate of depression/anxiety among AA patients. Also, it seems that a great portion of AA patients with simultaneous psychiatric disorders are missed in routine care while these patients need further evaluation for screening of psychiatric disorders. In addition, the sleep quality was significantly lower in those patients with psychiatric disorders compared with AA patients who did not have anxiety or depression. As expected, their self-report of sleep quality was also lower.

Sleep is suggested to be a triggering factor for autoimmune disorders.[6,17] A nation-wide survey on adult patients with a nonapnea sleep disorder (NSD) and age-, gender-, income-, and urbanization-matched controls reported the significantly higher overall risk for rheumatoid arthritis, systemic lupus erythematosus, Sjogren's syndrome, and ankylosing spondylitis among patients with a NSD.[6] AA is also an autoimmune disease that is known to co-occur with other autoimmune disorders associated with impaired sleep quality such as Hashimoto's thyroiditis, vitiligo, and lichen planus.[3,18,19]

A retrospective cohort study included patients with sleep disorders and controls, demonstrated that patients with sleep disorders are at a significantly increased risk for AA with an adjusted hazard ratio of 1.651 (95% CI: 1.382–1.974). Younger age groups (0–24 and 25–44 years) were more vulnerable to having AA. Additionally, sleep deprivation was associated with autoimmunity.[3] Inui et al.[5] reported that a low number of AA patients (11.4%) suffer from EDS measured by ESS. They excluded those who were using systemic corticosteroids, the most common drug therapy for AA, while this treatment and the following high cortisol levels implicate sleep regulation.[5] In the current study, none of the patients was treated with any systemic corticosteroid. Although the sleep quality measured by PSQI was significantly lower in AA patients, the EDS measured by ESS was comparable between the study groups. Similar to the Inui et al.[5] findings, the proportion of those with ESS was >10, which is an indicator that excess EDS was significantly higher among AA patients than the controls. Also, the PSQI score was significantly lower in AA patients versus controls. PSQI is a standardized self-administered questionnaire. The number of AA cases with either PSQI of >5 or 6 was more than controls confirming the more frequent sleep impairment among AA patients. Consistent with our results, Ghafarpour et al.[12] found that the number of cases with PSQI score > 5 were significantly higher in AA patients (45.7%) compared with healthy individuals (21.7%). The sleep time of AA patients (average 6.73 h) was significantly lower than healthy people (average 7.76 h). They did not find any significant difference in the score of

PSQI between the study groups,[12] whereas they did not assess anxiety/depression in the study population as a confounding factor, which might be the reason for their different results.

The limitation of this study is the cross-sectional design that does not provide assessing causality association between sleep disorders and AA. Additionally, our outpatient clinic is a referral center, and patients present with more serve cases of AA, which could cause a selection bias.

6 | CONCLUSION

The sleep quality is impaired in AA and experiencing excess daytime sleepiness is more prevalent among these patients. Also, they are more vulnerable to anxiety and depression and sleep is more disturbed in such a group. Taking into consideration sleep quality is important when treating patients, as sleep deprivation could be a triggering factor for AA exacerbation.

AUTHOR CONTRIBUTIONS

Safoura Shakoei: Conceptualization, data curation, formal analysis, investigation, methodology, project administration, supervision, validation, writing—original draft, writing—review and editing. **Alireza Torabimirzaee**: Data curation, formal analysis, methodology, software, writing—original draft, writing—review and editing. **Zahra Saffarian**: Investigation, resources, visualization, writing—review and editing. **Robabeh Abedini**: Investigation, resources, validation, writing—review and editing.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article. Due to the nature of this study, participants of this study did not agree for their data to be shared publicly, so additional data are not available upon request.

ETHICS STATEMENT

Ethical approval was obtained from the Ethic Committee of Tehran University of Medical Sciences, and the thesis number is (IR.TUMS.IKHC.REC.1398.081).

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