Effects of anxiety and depression symptoms on oxidative stress in patients with alopecia areata

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Abstract

Introduction: Increased oxidative stress (OXS) and a high prevalence of psychiatric disorders are seen in alopecia areata (AA). However, OXS and psychiatric disorders have been studied separately in AA patients.
Aim: To determine the effects of anxiety and depression symptoms on OXS in AA patients.
Material and methods: The anxiety and depression levels of 33 AA patients and 33 normal controls (NC) were determined using the Hospital Anxiety and Depression Scale. The oxidative stress index (OSI) was calculated by measuring serum total antioxidant status (TAS) and total oxidant status (TOS) levels in AA patients and NC.
Results: The AA patients had higher anxiety and depression scores than NC ($p < 0.001$ for both). Total oxidant status ($p = 0.002$) and OSI ($p < 0.001$) values were higher, and TAS ($p < 0.001$) levels were lower, in patients with AA compared to NC. However, patients' anxiety and depression scores were not correlated with the TAS, TOS, or OSI values ($p > 0.05$). There was no significant difference in TAS, TOS, or OSI values between patients with high and low anxiety or depression scores ($p > 0.05$).
Conclusions: These results show that OXS, anxiety, and depression scores were higher in patients with AA compared to NC. However, anxiety and depression scores were not associated with OXS in AA patients. More extensive studies should be performed to investigate the relationship between psychological status and OXS in patients with AA.

Key words: alopecia areata, oxidative stress, anxiety, depression.

Introduction

Alopecia areata (AA) is an autoimmune and inflammatory disease characterized by recurrent hair loss without scarring on the scalp and/or body. AA, which can occur in all age groups, commonly affects men and women equally [1]. Although the etiopathogenesis of AA has not been fully elucidated, genetic predisposition, T-cell-mediated immunological reactions, and environmental factors such as hormones, diet, vaccinations, and stress are considered to play a role in the development of this disease [2, 3].

The skin, which protects the body from external factors, is continuously exposed to endogenous and environmental pro-oxidant agents, leading to the overproduction of reactive oxygen species (ROS). Reactive oxygen species are thought to activate proliferative and cell signaling pathways, which can in turn alter apoptotic pathways that may play a pivotal role in the pathogenesis of many dermatological diseases [4]. The tissue damage caused by increased ROS is prevented by enzymatic and non-enzymatic antioxidant agents [5]. Oxidative stress (OXS) caused by deterioration of the balance between ROS and the antioxidant defense system may play a role in the pathogenesis of AA [6, 7].

Hair loss, especially on the scalp, has a negative effect on the esthetic appearance and self-esteem of individuals. Therefore, patients suffering from AA may be prone to various psychiatric illnesses, such as anxiety and depression [8]. Some researchers also emphasized that stressful life events may play an important role in the onset or progression of the disease [9, 10]. Studies have shown that the prevalence of psychiatric disorders such as depression and anxiety is higher in AA patients than in healthy controls [11, 12].

Although psychiatric disorders and OXS status have been investigated independently in AA patients, the relationship between psychiatric disorders and OXS was not evaluated in these patients.

Aim

In this study, we aimed to determine the effects of depressive and anxiety symptoms on OXS in patients with AA.

Material and methods

Participants

Thirty-three AA patients and 33 normal controls (NC) were included in this study. The AA patients were enrolled from the dermatology outpatient clinic of Sanliurfa Mehmet Akif İnan Training and Research Hospital (Turkey), between March and December 2017. The demographic characteristics of the patients (age and gender, disease duration, recurrences, family history, presence of stress, and pattern of AA) were recorded. The Severity of Alopecia Tool score for AA was used to determine the degree of hair loss based on the percentage of scalp surface area involved. Exclusion criteria were concomitant systemic diseases, acute/chronic infection, use of any treatment including antioxidant vitamins and systemic or topical medications over the last 3 months, smoking, and alcohol intake. Ethical approval for this study was obtained from the local ethics committee.

Measurement of oxidative stress parameters

Venous blood was obtained from AA patients and NC to measure the total antioxidant status (TAS) and total oxidant status (TOS) after 8–12 h of fasting. The collected blood samples were centrifuged and the serum was stored in Eppendorf tubes at –80°C until needed. Serum levels of TOS and TAS were measured using the fully automated colorimetric method described by Erel [13, 14]. After determination of TOS and TAS levels, oxidative stress index (OSI) was calculated. The ratio of TOS to TAS yields the OSI, an indicator reflecting the severity of OXS.

Hospital Anxiety and Depression Scale (HADS)

The HADS, which is used to evaluate patients' anxiety (HADS-A; 7 items) and depression (HADS-D; 7 items) scores, consists of 14 items. HADS subscale scores range from 0 to 21 [15]. In a study on the validity and reliability of the Turkish version of HADS by Aydemir *et al.*, cut-off scores were determined as 10 for the HADS-A subscale and 7 for the HADS-D subscale [16]. In this study, we used the Turkish version of the scale to evaluate the anxiety and depression symptoms of patients with AA.

Statistical analysis

Statistical calculations were carried out using IBM SPSS Statistics 22 (IBM Corp., Armonk, NY). A p-value < 0.05 was considered to indicate statistical significance. The normality of the variables was assessed by the Kolmogorov-Smirnov test. Differences between the groups were determined using Student's t-test, the Mann-Whitney U-test or the χ^2 test. The relationship between HADS subscale scores and OXS markers in AA patients was evaluated by Pearson's correlation test.

Results

This study included 33 patients with AA (25 males/ 8 females) with a mean age of 26.33 ±6.08 years, and 33 NC (22 males/11 females) with a mean age of 27.30 ±7.84 years. There was no difference in age and sex distribution between the two groups ($p = 0.588$ and $p = 0.415$, respectively). Demographic features of patients are summarized in Table 1.

As illustrated in Table 2, compared to NC, the TOS ($p = 0.002$) and OSI values ($p < 0.001$) were higher, while the TAS level ($p < 0.001$) was lower, in patients with AA.

Table 1. Demographic characteristics in patients with alopecia areata

Parameter	Value
Gender (male)	25 (75.8%)
Disease duration [months]	3 (1–48)
Family history	6 (18.2%)
Recurrence	7 (21.2%)
Stress	24 (72.7%)
Pattern:	
Patch	31 (93.9%)
Patch + ophiasis	2 (6.1%)
SALT score:	
S1	27 (81.8%)
S2	5 (15.2%)
S3	1 (3%)

Table 2. Hospital Anxiety and Depression Scale scores and oxidative stress markers in patients with alopecia areata and controls

Parameter	Patients ($n = 33$)	Controls ($n = 33$)	P-value
HADS-A score	9.45 ±3.40	6.18 ±3.30	< 0.001
HADS-D score	8.67 ±3.11	4.73 ±2.76	< 0.001
TAS [μmol Trolox Eq/l]	1.24 ±0.33	1.58 ±0.42	< 0.001
TOS [μmol H2O2 Eq/l]	19.64 ±4.54	15.55 ±5.46	0.002
OSI [arbitrary units]	1.69 ±0.55	1.05 ±0.46	< 0.001

HADS – Hospital Anxiety and Depression Scale, HADS-A – HADS-Anxiety, HADS-D – HADS-Depression, TAS – total antioxidant status, TOS – total oxidant status, OSI – oxidative stress index.

Table 3. Effects of anxiety and depressive scores on oxidative stress markers in patients with alopecia areata

Parameter	Patients with anxiety HADS-A > 10 (n = 12)	Patients without anxiety HADS-A ≤ 10 (n = 21)	P-value	Patients with depression HADS-D > 7 (n = 19)	Patients without depression HADS-D ≤ 7 (n = 14)	P-value
TAS [μmol Trolox Eq/l]	1.32 (0.71–1.98)	1.14 (0.74–1.86)	0.359	1.15 (0.71–1.98)	1.27 (0.74–1.86)	0.913
TOS [μmol H2O2 Eq/l]	21.13 (12.5–25.25)	20.75 (12.25–29.25)	0.627	21.88 (12.5–29.25)	20.32 (12.25–23.13)	0.126
OSI [arbitrary units]	1.59 (0.64–2.57)	1.6 (0.94–2.72)	0.681	1.77 (0.64–2.71)	1.51 (0.98–2.72)	0.362

TAS – total antioxidant status, TOS – total oxidant status, OSI – oxidative stress index.

Table 4. Correlation between Hospital Anxiety and Depression Scale scores and oxidative stress markers in patients with alopecia areata

Parameter	HADS-A score		HADS-D score	
	r	p	r	p
TAS	0.178	0.321	0.132	0.464
TOS	0.071	0.693	0.189	0.293
OSI	−0.148	0.412	0.021	0.909

HADS – Hospital Anxiety and Depression Scale, HADS-A – HADS-Anxiety, HADS-D – HADS-Depression, TAS – total antioxidant status, TOS – total oxidant status, OSI – oxidative stress index.

According to the cut-off values, anxiety symptoms (HADS-A > 10) were present in 12 (36.4%) patients and 5 (15.2%) NC, while depression symptoms (HADS-D > 7) were present in 19 (57.6%) patients and 6 (18.2%) NC. HADS-A (9.45 ±3.40 vs. 6.18 ±3.30; $p < 0.001$) and HADS-D (8.67 ±3.11 vs. 4.73 ±2.76; $p < 0.001$) scores were higher in AA patients compared to NC (Table 2).

There was no significant difference in TAS, TOS, or OSI levels between patients with high anxiety scores (HADS-A > 10) and low anxiety scores (HADS-A ≤ 10). Similarly, patients with high (HADS-D > 7) and low (HADS-D ≤ 7) depression scores did not differ in terms of TAS, TOS, or OSI values (Table 3).

Patients' HADS-A and HADS-D scores did not correlate with TAS, TOS, or OSI values ($p > 0.05$) (Table 4).

Discussion

The skin is the target of OXS due to ROS produced by exposure to physical and chemical agents [4]. Researchers have shown that OXS plays an important role in skin aging [17], as well as various skin diseases such as psoriasis [18], lichen planus [19], and AA [6, 7].

Oxidative stress, which is an imbalance between ROS production and detoxification, may cause cellular damage by interacting with macromolecules such as protein, lipid, and DNA. Levels of ROS in the organism are maintained in a normal range through antioxidant agents such as superoxide dismutase (SOD), glutathione peroxidase (GPx), glutathione, and vitamins C and E [5].

To date, many studies have been conducted to assess the OXS status of patients with AA, and contradictory results have been obtained. Abdel Fattah et al. [20] and Naziroglu et al. [21] found higher levels of lipid peroxidation products and lower levels of antioxidant enzyme activities in patients with AA than in NC. Similarly, Yenin et al. [7] reported high levels of malondialdehyde, a lipid peroxidation product, and low GPx and SOD activities in AA patients compared to NC, indicating that AA patients are in a state of enhanced OXS. In our study, TOS and OSI values were higher, and the TAS level was lower, in AA patients compared to NC, as reported previously [6, 22].

Contrary to the above observations, Akar et al. [23] observed that SOD and GPx activities in the scalps of AA patients were significantly higher than in the NC. The authors also found that SOD and GPx activities were increased in the early stages of the disease compared to the late stage. Another study revealed higher levels of SOD and GPx in patients with AA than in NC. In the same study, no significant increase in plasma malondialdehyde level was observed in the patient group [24]. Interestingly, Motor et al. [25] reported that TAS, TOS, and OSI values were similar in the AA patients and NC. The discrepancy in the results of these studies may be due to differences in the sample size, disease duration, and extent of hair loss, as well as the use of different samples in each study. Collectively, these results suggest that increased OXS and impaired antioxidant capacity may be related to the pathogenesis of AA.

Since AA can seriously affect individuals' self-esteem and cosmetic appearance, these patients may be prone to psychiatric disorders such as depression, anxiety, and social phobia [8]. Another approach that explains the relationship between AA and psychological disorders is that stressful life events may play an important role in the onset and/or exacerbation of the disease [9, 10].

Sellami et al. [11] reported that 38% of patients with AA had depression and 62% had anxiety symptoms. In addition, many studies have shown high rates of depression and anxiety in AA patients compared to the general population [12, 26]. Consistent with these studies, we found that depression and anxiety scores were higher in patients with AA compared to NC, which indicates a relationship between AA and psychological disorders.

Moreover, some studies indicated that antidepressants may have beneficial effects on AA in AA sufferers with psychiatric disorders [27, 28].

On the other hand, Güleç *et al*. [29] reported that the scores for stressful life events, anxiety, and depression were not significantly different between AA patients and NC. These contradictory results can be attributed to differences in the scales used to screen for psychiatric disorders, and to differences in population size among these studies.

The brain, which shows high oxygen utilization and has a lipid-rich environment, is susceptible to the harmful effects of ROS [30]. Studies have shown that OXS may play a role in the pathophysiology of various psychiatric diseases, including anxiety and depressive disorders [31, 32]. To our knowledge, no study has investigated the effects of psychiatric disorders on OXS in AA patients. In the current study, we evaluated the relationship between HADS subscale scores and OXS markers in patients with AA. Our findings showed that there was no difference in terms of TAS, TOS, or OSI values between patients with and without anxiety or between patients with and without depression. Moreover, HADS scores did not correlate with TAS, TOS, or OSI values in patients with AA. Similarly, Karababa *et al*. [33], using the HADS scale, did not find an association between OXS and psychological status in psoriasis patients. In another study, the relationship between OXS and HADS scores was investigated in acne patients, and it was found that higher HADS subscale scores did not lead to a further increase in OXS [34]. In our opinion, these results may be attributed to the use of the HADS rather than clinical psychiatric evaluations of AA patients, and to the small numbers of cases included.

The main limitation of this study was the small number of AA cases. Another limitation was the use of the HADS rather than clinical psychiatric assessments for determining the anxiety and depression status of AA patients.

Conclusions

Consequently, both the HADS subscale scores and OXS were higher in AA patients compared to NC. However, OXS was unrelated to the anxiety or depression scores of the AA patients. In addition, in patients with AA who are at risk of depression or anxiety, psychological intervention may be part of the treatment. To better understand the effect of psychiatric disorders on OXS in AA patients, further studies should be performed with large patient populations.

Conflict of interest

The authors declare no conflict of interest.

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