The Relationship Between Depression Levels and Suicide Risk in Pediatric Patients with Alopecia Areata and the Oxidant-**Antioxidant Balance**

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Abstract

Aim: This research aimed to investigate oxidative stress (OS) markers and their relation to depressive symptoms and suicide tendencies in children diagnosed with alopecia areata (AA) compared to a healthy cohort.

Materials and Methods: A cross-sectional design was implemented, enrolling 30 children with AA and 30 healthy peers. The biomarkers evaluated included malondialdehyde (MDA), superoxide dismutase (SOD), total antioxidant status (TAS), total oxidant status (TOS), OS index (OSI), asymmetric dimethylarginine (ADMA), and homocysteine. Receiver operating characteristic curve analysis was used to determine their diagnostic potential. Psychiatric conditions were assessed using Diagnostic and Statistical Manual of Mental Disorders, fifth edition based interviews, while depressive severity and suicide risk were measured through the Beck Depression Inventory and the Suicide Probability Scale, respectively.

Results: Children with AA displayed significantly elevated levels of MDA, TOS, OSI, ADMA, and homocysteine, while TAS and SOD values were notably reduced (P < 0.001), Depression and suicide scores did not differ significantly between groups, Diagnostic accuracy for TAS, TOS, OSI, and SOD reached 96.7% sensitivity and 93.3% specificity. Homocysteine, MDA, and ADMA also showed acceptable predictive power.

Conclusion: The findings support a possible etiological contribution of OS in the development of AA.

Keywords: Child psychiatry, alopecia areata, oxidative stress, depression, suicide

INTRODUCTION

Alopecia areata (AA) is a relatively common, non-scarring, immune-mediated disorder that causes abrupt hair loss in welldefined patches. It affects individuals across all age groups, demographics, and impacts roughly 2% of the population.1 Hair loss can remain localized or progress to involve the entire scalp (alopecia totalis) or the whole body (alopecia universalis).2

Despite extensive research, the exact pathogenesis of AA remains elusive. However, current evidence points toward an interplay of hereditary factors, immune system dysfunction, psychological triggers, and environmental influences.³⁻⁵ Many AA patients also experience psychiatric disturbances, particularly anxiety and depression.⁶ A subset of patients has been identified as being even at increased risk for suicidal thoughts or behaviors, with one study reporting this in nearly 13% of individuals with AA.7

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The skin acts as a vital barrier against environmental aggressors and is continuously exposed to oxidative elements. Such prooxidant exposure promotes excessive production of reactive oxygen species (ROS), which are known to interfere with cellular signaling and proliferation, as well as modulate apoptotic mechanisms. These disruptions in programmed cell death have been implicated in various dermatological disorders.^{8,9} Oxidative stress (OS) arises from a disruption in the balance between the generation of ROS and the body's antioxidant defenses. Elevated ROS levels or insufficient antioxidant protection can trigger cellular injury and inflammation, mechanisms suspected to be involved in AA. OS emerges when endogenous antioxidant defenses fail to neutralize an overabundance of oxidants, creating a redox imbalance. This imbalance has been associated with the pathophysiology of AA. 10-12 Although the underlying mechanisms of AA remain partly unknown, the condition is widely regarded as autoimmune in origin. OS is believed to contribute to autoimmune processes by promoting inflammatory responses and impairing immune regulation through apoptotic induction.¹³

OS is also implicated in psychiatric conditions, but whether it is a cause or a consequence of such disorders remains unclear.¹⁴

This study was designed to assess and compare the OS parameters, depression severity, and suicide probability between AA patients and healthy controls; and to explore potential correlations among them.

MATERIALS AND METHODS

Study Groups

The sample size for the study was calculated with the GPower 3.1 program. The required sample size for this study was determined using an a priori power analysis based on a two-tailed Wilcoxon-Mann-Whitney test comparing two groups' distributions. The effect size was derived from the study by Yıldız Miniksar and Göçmen¹⁵ in which the mean and standard deviation (SD) of malondialdehyde (MDA) levels were reported as 0.29 ± 0.003 in the major depressive disorder (MDD) group and 0.33 ± 0.04 in the control group. Based on these values, the calculated effect size was d=1.13. Using this effect size, with a significance level of $\alpha=0.05$ and statistical power of $1-\beta=0.95$, the power analysis indicated that 23 participants per group, or 46 in total, would be required.

This research used a cross-sectional methodology and included a total of 60 individuals: 30 adolescents aged between 12 and 18 years diagnosed with AA and 30 agematched healthy controls. Participants in the AA group were

recruited from the Department of Dermatology, Yozgat Bozok University Medical Faculty over a five-month period from January to May 2021. Inclusion criteria were based on clinical diagnosis, and participants were excluded if they had chronic systemic conditions, cognitive impairments, were undergoing psychiatric or systemic treatment, or had other visible dermatological disorders unrelated to AA.

Disease severity in the AA group was assessed using the Severity of Alopecia Tool (SALT), categorizing individuals into mild (< 50% scalp involvement, S1-S2) and severe ($\ge 50\%$ involvement, S3-S5) groups. All dermatological assessments were conducted by a single experienced dermatologist to ensure consistency. 16 Subsequently, participants from both groups underwent psychiatric evaluation by a certified child and adolescent psychiatrist. A structured clinical interview based on the Diagnostic and Statistical Manual of Mental Disorders, fifth edition, was used to diagnose any co-existing psychiatric conditions.¹⁷ Depression levels were determined through the Beck Depression Inventory (BDI), while suicide risk was assessed using the Suicide Probability Scale (SPS). This study was approved by the Clinical Research Ethics Committee of Yozgat Bozok University (approval number: 2017-KAEK-189, date: 16.12.2020). Written informed consent was obtained from all participants.

Biochemical Analysis

Following an overnight fast of 12 hours, 3 to 5 mL of venous blood was collected from each participant. The blood samples were transferred to biochemistry tubes and centrifuged at 4000 rpm for ten minutes to separate the serum. These serum samples were stored at -80 °C until they were analyzed.

Serum total antioxidant status (TAS) and total oxidant status (TOS) were measured using Erel's commercial kits (Rel Assay Diagnostics, Mega Tip, Gaziantep, Türkiye). The OS index (OSI) was computed by dividing TOS by TAS and expressed in arbitrary units as OSI = TOS (μ mol H₂O₂/L)/TAS (mmol Trolox equivalent/L).

TAS was measured via a method based on the suppression of the 2,2'-azinobis-(3-ethylbenzothiazoline-6-sulfonate) radical cation. TOS was determined through the oxidation of a ferrous ion-o-dianisidine complex to ferric ion, which forms a colored compound with xylene orange in acidic medium. The intensity of the color, measured spectrophotometrically, correlated with the amount of oxidant in the serum. All readings were calibrated using hydrogen peroxide as a reference standard.

Superoxide dismutase (SOD) activity was quantified using a SOD assay kit (Rel Assay Diagnostics, Mega Tip, Türkiye), while MDA concentrations were determined via a colorimetric kit from Cayman Chemical (Michigan, United States of

America). Levels of asymmetric dimethylarginine (ADMA) and homocysteine were evaluated using commercial ELISA kits provided by Elabscience (Wuhan, China). All laboratory analyses were performed in the same lab using a BioTek EL × 800 microplate reader, following the protocols and wavelengths specified by the respective kit manufacturers.

Psychological Measurement Tools

Beck Depression Inventory (BDI): Originally developed by Beck et al.¹⁸ this 21-item self-assessment scale uses a 4-point Likert format to quantify depressive symptoms. Score categories are as follows: 0-9 (minimal), 10-16 (mild), 17-29 (moderate), and 30-63 (severe). The Turkish validation was carried out by Hisli.¹⁹

Suicide Probability Scale (SPS): The SPS comprises 36 self-report items across four domains-hopelessness, suicidal ideation, negative self-image, and hostility.²⁰ Responses are rated from 1 (never/rarely) to 4 (almost/always). Higher total scores reflect increased suicide risk. The Turkish adaptation was validated by Atlı et al.²¹

Statistical Analysis

All statistical analyses were performed using an appropriate software package. Descriptive statistics were presented in tabular form. The independent samples t-test was used to compare means between groups, while non-parametric tests were applied where assumptions of normality were not met. The chi-square test assessed categorical data. Pearson correlation was employed to explore relationships between variables such as age, disease duration, and severity, OS markers, depression scores, and suicide risk. Receiver operating characteristic (ROC) analysis was used to determine the sensitivity and specificity of biochemical markers in predicting AA. A *P* value < 0.05 was accepted as statistically significant.

RESULTS

This study included 60 participants: 30 individuals diagnosed with AA and 30 healthy controls. Among those with AA, 53.3% were female, with a mean age of 14.9 years (SD: 1.77), whereas the control group had a slightly higher proportion of females (66.7%) and a mean age of 16.0 years (SD: 1.70), yielding a statistically significant age difference (P = 0.017). In terms of disease characteristics, over half of the AA group (53.3%, n = 16) reported a disease duration of less than 6 months. A smaller portion (26.7%, n = 8) had lived with the condition for over one year. The majority (80%) presented with a mild severity level, based on SALT scores categorized as S1 or S2 (Table 1).

Oxidative Stress Biomarkers

Evaluation of OS-related biomarkers revealed that patients in the AA group exhibited higher mean values of MDA, TOS, OSI, ADMA, and homocysteine, compared to their healthy counterparts. Conversely, levels of SOD and TAS were significantly reduced in the AA group. All of these differences were statistically significant (P < 0.001), supporting increased oxidative imbalance in the patient group (Table 1, Figure 1).

Psychiatric Evaluation

From a psychiatric standpoint, four children in the AA group met criteria for MDD, while three were diagnosed with generalized anxiety disorder. In comparison, two individuals in the control group were found to have major depression. However, the prevalence of psychiatric comorbidities did not differ significantly between the two groups. The average BDI scores also showed no significant difference between AA patients and controls. Additionally, no group differences were observed in the distribution of depression severity categories (minimal, mild, moderate, or severe). Regarding suicide risk, the mean SPS score was higher in the control group (67.6%) than in the AA group (60.4%), but the difference did not reach statistical significance (P = 0.079). Subscale analysis of the SPS showed that the control group scored significantly higher in hopelessness and hostility domains (P < 0.05), whereas no significant variation was detected in the suicide ideation and negative self-evaluation subscales (Table 1).

ROC Curve Analysis

ROC analysis demonstrated that the OS indicators SOD, TAS, TOS, and OSI had high diagnostic value in differentiating AA patients from controls, each with 96.7% sensitivity and 93.3% specificity. Similarly, homocysteine (96.7% sensitivity; 83.3% specificity), MDA (93.3%; 83.3%), and ADMA (73.3%; 70.0%) also showed acceptable predictive power, although ADMA had the lowest discriminatory capability among the markers analyzed (Table 2, Figure 2).

Correlation Findings

In the AA group, a moderately strong positive correlation (r = 0.667) was identified between disease duration and disease severity. However, no statistically significant relationship was found between disease duration or severity and OS biomarkers, except for ADMA. Notably, weak positive correlations were observed between disease duration and the following variables: ADMA (r = 0.368), BDI scores (r = 0.368), suicide ideation (r = 0.408), and hostility (r = 0.436). In both AA and control groups, age was moderately associated with higher BDI scores: AA group (r = 0.420), control group

| | | | G | roups | | | |
|-----------------------------|---|---------|----------|-------------|---------------|--------|---------|
| | | Control | (n = 30) | Alopecia ar | eata (n = 30) | | |
| | | Mean | SD | Mean | SD | t | P |
| Gender | Male (n,%) | 10 | 33.3 | 14 | 46.7 | 1.111ª | 0.202 |
| Gender | Female (n,%) | 20 | 66.7 | 16 | 53.3 | 1.111" | 0.292 |
| | Age (year) | 16.0 | 1.70 | 14.9 | 1.77 | 2.455 | 0.017 |
| | 0-6 months | | | 16 | 53.3 | | |
| Alopecia areata duration | 7-12 months | | | 6 | 20.0 | | |
| aui ation | ≥ 13 months | | | 8 | 26.7 | | |
| | S1-S2 | | | 24 | 80.0 | | |
| | S3-S5 | | | 6 | 20.0 | | |
| SALT score | MDA (μmol/L) | 0.70 | 0.09 | 0.88 | 0.06 | 8.842 | < 0.001 |
| | SOD (U/mL) | 19.06 | 1.19 | 15.99 | 1.15 | 10.185 | < 0.001 |
| | TAS (μmol Trolox Eq/L) | 0.86 | 0.04 | 0.73 | 0.04 | 13.070 | < 0.001 |
| | TOS (μmol H ₂ O ₂ Eq/L) | 10.90 | 0.71 | 13.08 | 0.94 | 10.120 | < 0.001 |
| | OSI (arbitrary unit) | 1.27 | 0.14 | 1.80 | 0.23 | 10.963 | < 0.001 |
| | ADMA (μmol/L) | 0.80 | 0.07 | 0.91 | 0.10 | 4.667 | < 0.001 |
| | Homocysteine (mcmol/L) | 3.94 | 0.21 | 4.54 | 0.30 | 9.075 | < 0.001 |
| | BDI scores | 12.00 | 8.55 | 11.03 | 9.65 | 0.411 | 0.683 |
| OPS | Minimal (0-9) (n,%) | 15 | 50.0 | 17 | 56.7 | 0.258b | 1.000 |
| | Mild (10-16) (n,%) | 5 | 16.7 | 4 | 13.3 | | |
| | Moderate (17-29) (n,%) | 9 | 30.0 | 7 | 23.3 | | |
| | Severe (30-63) (n,%) | 1 | 3.3 | 2 | 6.7 | | |
| | SPS total | 67.60 | 15.40 | 60.40 | 15.81 | 1.786 | 0.079 |
| | Hopelessness | 25.43 | 6.38 | 21.60 | 6.04 | 2.390 | 0.020 |
| | Suicide ideation | 11.90 | 2.95 | 10.47 | 3.88 | 1.612 | 0.112 |
| | Negative self-evaluation | 17.97 | 5.54 | 18.23 | 5.00 | 0.196 | 0.845 |
| | Hostility | 12.30 | 3.50 | 10.10 | 4.12 | 2.230 | 0.030 |
| | Total | 30 | 100.0 | 30 | 1.00 | | |
| | | | | | | | |

^aChi-square test, ^bKolmogorov-Smirnov test, SALT: Severity of Alopecia Tool, BDI: Beck Depression Inventory, SPS: Suicide Probability Scale, OPS: Oxidative stress parameters, MDA: Malondialdehyde, SOD: Superoxide dismutase, TAS: Total antioxidant status, TOS: Total oxidant status, OSI Index: Oxygen saturation index, ADMA: Asymmetric dimethyl arginine, SD: Standard deviation

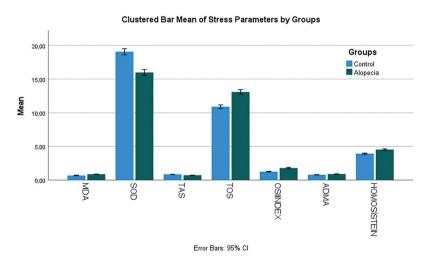


Figure 1. Mean oxidative stress parameters in alopecia areata and control groups MDA: Malondialdehyde, SOD: Superoxide dismutase, TAS: Total antioxidant status, TOS: Total oxidant status, OSI index: Oxygen saturation index, ADMA: Asymmetric dimethyl arginine

(r = 0.478) (Table 3). ANCOVA ruled out a significant association between disease duration and BDI score (P = 0.472); rather, it identified participant age as a significant predictor of depressive symptoms (P < 0.001).

In the control group, no significant links were found between oxidative markers and either psychiatric status or age. As expected, moderate correlations were identified between depression severity and suicide risk, along with significant associations between SPS subscales across both groups (Tables 3, 4).

DISCUSSION

The present study set out to examine OS markers in relation to psychological outcomes-specifically depression and suicide risk-in pediatric patients with AA, compared to a healthy control group. Our results show a distinct biochemical profile in AA patients, with significantly increased levels of MDA, TOS, OSI, ADMA, and homocysteine, and markedly reduced levels of TAS and SOD, consistent with previous findings linking oxidative imbalance to AA pathophysiology.

Numerous studies have investigated redox disturbances in AA. with many reporting heightened levels of lipid peroxidation products and diminished activity of antioxidant enzymes in affected individuals compared to healthy controls.²² Our study corroborates these findings, showing significantly elevated MDA, TOS, OSI, ADMA, and homocysteine in AA patients, alongside reduced TAS and SOD activity. These observations suggest a tilt in the oxidative-antioxidative balance toward a prooxidant state. For instance, MDA, a terminal product of lipid peroxidation, has been shown to accumulate both in plasma and scalp tissues in AA patients.²³ Furthermore, reductions in SOD activity have been noted in previous research, with evidence linking declining SOD levels to increasing disease severity.24,25 A systematic review and meta-analysis by Acharya and Mathur²⁴ highlighted similar trends: namely, increases in oxidative indicators like MDA, nitric oxide, and TOS, and decreases in antioxidants such as SOD, paraoxonase, glutathione peroxidase, and TAS. This study also found a connection between oxidative levels and the extent of hair loss in AA. However, our own analysis did not identify a statistically significant relationship between OS

| Table 2. Sensitivity and specificity of oxidative stress parameters in alopecia areata based on ROC curve analysis | | | | | | | | | | |
|--|-------|-------|---------------|---------------|---------------|--|--|--|--|--|
| Test result variable (s) | Area | Sig. | Cut-off point | Sensitivity % | Specificity % | | | | | |
| MDA | 0.932 | 0.000 | < 0.785 | 93.3 | 83.3 | | | | | |
| SOD | 0.022 | 0.000 | > 17.705 | 96.7 | 93.3 | | | | | |
| TAS | 0.007 | 0.000 | > 0.795 | 96.7 | 93.3 | | | | | |
| TOS | 0.979 | 0.000 | < 11.93 | 96.7 | 93.3 | | | | | |
| OSI | 0.986 | 0.000 | < 1.485 | 96.7 | 93.3 | | | | | |
| ADMA | 0.804 | 0.000 | < 0.855 | 73.3 | 70.0 | | | | | |
| Homocysteine | 0.971 | 0.000 | < 4.170 | 96.7 | 83.3 | | | | | |

MDA: Malondialdehyde, SOD: Superoxide dismutase, TAS: Total antioxidant status, TOS: Total oxidant status, OSI index: Oxygen saturation index, ADMA: Asymmetric dimethyl arginine, ROC: Receiver operating characteristic

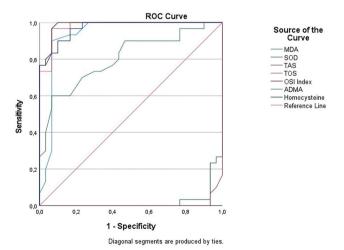


Figure 2. Discriminatory power of oxidative stress markers for alopecia areata using ROC analysis ROC: Receiver operating characteristic, MDA: Malondialdehyde, SOD: Superoxide dismutase, TAS: Total antioxidant status, TOS: Total oxidant status, OSI index: Oxidative stress index, ADMA: Asymmetric dimethylarginine

| | | | | | | | | | | | | • | | | |
|--|---------------------|---------------|---------|----------|----------|----------|---------|---------|---------|-------------------|--------------|--------------|-------------------|---------------------|------------------------------|
| | Disease duration | SALT | Age | MDA | SOD | TAS | 108 | IS0 | ADMA | Homo- cysteine | BDI score | SPS total | Hope- lessness | Suicide ideation | Negative self- evaluation |
| Alopecia severity | 0.657** | - | | | | | | | | | | | | | |
| Age (year) | -0.187 | 0.030 | 1 | | | | | | | | | | | | |
| MDA | -0.175 | 0.047 | 0.203 | - | | | | | | | | | | | |
| SOD | -0.171 | -0.224 | -0.079 | -0.664** | П | | | | | | | | | | |
| TAS | -0.118 | -0.185 | -0.105 | -0.683** | 0.962** | 1 | | | | | | | | | |
| TOS | 0.183 | .0225 | 0.111 | 0.684** | **686.0- | -0.928** | - | | | | | | | | |
| ISO | 0.207 | 0.226 | 0.149 | 869'0 | -0.967** | -0.926** | 0.980** | П | | | | | | | |
| ADMA | 0.396 | 0.277 | 0.080 | 0.317 | -0.844** | -0.794** | 0.847** | 0.891** | 1 | | | | | | |
| Homocysteine | 0.242 | 0.246 | 0.144 | 0.628** | -0.965** | -0.913** | 0.980** | 0.994** | 0.920** | - | | | | | |
| BDI score | 0.368* | 0.260 | 0.420* | -0.199 | 0.093 | 0.068 | -0.092 | -0.071 | 0.032 | -0.057 | 1 | | | | |
| SPS score total | 0.296 | 0.058 | 0.243 | -0.250 | 090.0 | 0.030 | -0.059 | -0.023 | 0.135 | 0.001 | 0.739** | 1 | | | |
| Hopelessness | 0.079 | -0.092 | 0.296 | -0.172 | 0.041 | -0.014 | -0.046 | 0.001 | 0.123 | 0.013 | 0.617** | 0.894** | 1 | | |
| Suicide ideation | 0.408 | 0.141 | 0.183 | -0.217 | 0.080 | 0.016 | -0.093 | -0.047 | 0.101 | -0.030 | 0.721** | 0.849** | 0.719** | | |
| Negative self- evaluation | 0.165 | -0.004 | 0.190 | -0.192 | 0.078 | 0.012 | -0.091 | -0.079 | 0.008 | -0.064 | 0.600** | 0.811** | 0.615** | 0.585** | - |
| Hostility | 0.436 | 0.229 | 960.0 | -0.270 | -0.001 | 0.104 | 0.040 | 0.050 | 0.232 | 680.0 | 0.528** | 0.745** | 0.543** | 0.554** | 0.447* |
| *Correlation is significant at the 0.05 level (2-tailed) | ficant at the 0 (| 75 level (2-t | 'ailed) | | | | | | | | | | | | |

^{*}Correlation is significant at the 0.05 level (2-tailed)
**Correlation is significant at the 0.01 level (2-tailed)
**MDA: Malondialdehyde, SOD: Superoxide dismutase, TAS: Total antioxidant status, Total oxidant status, OSI index: Oxygen saturation index, ADMA: Asymmetric, BDI: Beck Depression Inventory, SPS: Suicide Probability Scale

| | | | | _ | | | | Homo- | BDI | SPS | Hope- | Suicide | Negative self- |
|------------------------------|---------|----------|----------|----------|---------|---------|---------|----------|---------|---------|----------|----------|----------------|
| | Age | MDA | SOD | TAS | TOS | OSI | ADMA | cysteine | Score | Total | lessness | ideation | evaluation |
| MDA | 0.072 | 1 | | | | | | | | | | | |
| SOD | -0.040 | -0.575** | 1 | | | | | | | | | | |
| TAS | -0.181 | -0.631** | 0.932** | 1 | | | | | | | | | |
| TOS | 0.096 | 0.430* | -0.827** | -0.809** | 1 | | | | | | | | |
| OSI | 0.161 | 0.536** | -0.831** | 0894** | 0.868** | 1 | | | | | | | |
| ADMA | 0.250 | -0.455* | -0.303 | -0.292 | 0.367* | 0.339 | 1 | | | | | | |
| Homocysteine | 0.157 | 0.211 | -0.768** | -0.773** | 0.882** | 0.804** | 0.591** | 1 | | | | | |
| BDI score | 0.478** | 0.239 | -0.213 | -0.251 | 0.008 | 0.053 | 0.017 | 0.067 | 1 | | | | |
| SPS total | 0.505** | 0.000 | 0.041 | -0.049 | -0.125 | -0.054 | -0.043 | -0.083 | 0.743** | 1 | | | |
| Hopelessness | 0.441* | 0.145 | 0.084 | -0.011 | -0.192 | -0.122 | -0.281 | -0.198 | 0.650** | 0.924** | 1 | | |
| Suicide ideation | 0.151 | -0.055 | -0.173 | -0.219 | 0.109 | 0.174 | 0.101 | 0.243 | 0.523** | 0.662** | 0.511** | 1 | |
| Negative self- evaluation | 0.542** | -0.083 | 0.054 | -0.037 | -0.104 | -0.008 | 0.118 | -0.050 | 0.649** | 0.889** | 0.763** | 0.462* | 1 |
| Hostility | 0.435* | -0.088 | 0.086 | 0.047 | -0.129 | -0.150 | 0.054 | -0.130 | 0.618** | 0.754** | 0.605** | 0.407* | 0.551** |

^{*}Correlation is significant at the 0.05 level (2-tailed)

parameters and AA severity. Mild cases accounted for 80% of AA patients. The significantly lower number of severe AA cases may explain the lack of a significant difference between disease severity and OS.

Hair loss in pediatric AA patients often causes distress, contributing to reduced self-image and emotional wellbeing. These psychosocial factors may predispose individuals to anxiety or depressive disorders.6 Conversely, chronic psychological stress has been suggested as a potential initiating factor for AA, indicating a possible bidirectional relationship.²⁶ In our study, although psychiatric diagnoses were more frequent in the AA group, the difference was not statistically significant. Similarly, BDI scores and depression severity classifications did not differ meaningfully between the AA and control groups. While the control group had a higher mean SPS score, along with greater hopelessness and hostility subscale scores, these differences lacked statistical significance. Notably, the control group was older and included a higher proportion of females-both factors previously linked to elevated suicide risk during adolescence. 26 Literature suggests that suicidal behavior becomes more prevalent with increasing age and is more common in girls.²⁷ These demographic differences, along with the fact that 80% of AA cases in our sample were mild, may explain the similar psychiatric outcomes across groups.

Given the dual role of OS and psychological stress in AA etiology, we further assessed whether psychiatric conditions

were associated with oxidative changes in AA patients.^{6,25} Previous research has implicated OS in psychiatric illnesses, particularly mood and anxiety disorders.^{28,29} A systematic review of 10 studies also found that AA has significant psychosocial effects on pediatric and adolescent populations, with deterioration in quality of life, increased anxiety levels, and higher rates of depression. 30 A meta-analysis examining both adult and pediatric AA patients found that depression and anxiety were significantly higher in adult patients than in children. This suggests that appearance and body image may be more important in adolescents and adults than in childhood.³¹ However, our results showed no significant relationship between OS biomarkers and psychiatric measures, including BDI and SPS scores. A recent case-control study by Cakirca et al.32 also explored this topic and, despite finding elevated TOS and TAS values alongside higher anxiety and depression scores in AA patients, reported no direct correlation between oxidative markers and psychological symptoms.

While a subset of studies supports the idea that mental health disorders are more prevalent in AA populations, others emphasize the role of psychological stress in the initial onset and worsening of AA. 5,6,33 In our case, the limited sample size and predominance of mild AA could have weakened these associations. Importantly, OS is not only implicated in disease pathogenesis but may also serve as a therapeutic target. Antioxidant agents, particularly in mild to moderate cases, may offer a complementary approach to standard treatments.

^{**}Correlation is significant at the 0.01 level (2-tailed)

MDA: Malondialdehyde, SOD: Superoxide dismutase, TAS: Total antioxidant status, TOS: Total oxidant status, OSI index: Oxygen saturation index, ADMA: Asymmetric dimethyl arginine, BDI: Beck Depression Inventory, SPS: Suicide Probability Scale

In our ROC analysis, OS markers such as SOD, TAS, TOS, and OSI demonstrated high sensitivity (96.7%) and specificity (93.3%) in distinguishing AA patients from healthy controls. Other markers, including homocysteine (96.7% sensitivity, 83.3% specificity), MDA (93.3%, 83.3%), and ADMA (73.3%, 70.0%), also showed diagnostic potential, though to varying degrees. These results reinforce the utility of redox biomarkers in understanding the disease and potentially tracking its course.

Study Limitations

Despite its contributions, this study has certain limitations. The sample size was relatively modest, and group imbalances in age and gender could have influenced both clinical and psychological outcomes. Additionally, the predominance of mild AA cases may have limited our ability to detect associations with disease severity.

CONCLUSION

The present findings reinforce the involvement of OS in the development of AA. Although psychiatric parameters did not differ significantly between groups, the clear oxidative imbalance in AA patients suggests a biochemical role in the disease's underlying mechanisms. Antioxidant-based interventions may provide a valuable adjunct to standard therapy, especially in less severe cases. Further studies involving larger, more diverse samples are warranted to better understand these relationships and to evaluate antioxidant treatments more comprehensively.

Ethics

Ethics Committee Approval: This study was approved by the Clinical Research Ethics Committee of Yozgat Bozok University (approval number: 2017-KAEK-189, date: 16.12.2020).

Informed Consent: Written informed consent was obtained from all participants.

Footnotes

Authorship Contributions

Surgical and Medical Practices: D.Y.M., E.Ç., Concept: D.Y.M., E.Ç., Design: D.Y.M., E.Ç., Data Collection or Processing: D.Y.M., E.Ç., Analysis or Interpretation: A.Y.G., M.K., Literature Search: D.Y.M., E.Ç., A.Y.G., Writing: D.Y.M., E.Ç., M.K.

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