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# The Role of Ischemia-modified Albumin and Ischemia-Modified Albumin to Albumin Ratios in Patients with Alopecia Areata

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## ABSTRACT

**Introduction:**

**Objective:** To investigate the role of ischemia-modified albumin (IMA) and IMA/albumin levels in patients with AA.

**Methods:** The present prospective crossectional study includes patients ≥18 who were admitted to the Dermatology and Venerology Department of Hitit University Hospital between April 1, 2021, and September 30, 2021. 70 patients participated in the study (n=34 for the study group and n=36 for the control group). Demographic features, clinical characteristics, IMA, and IMA/albumin levels were compared between the groups. The study group was divided into subgroups based on the number of patches, disease duration, and the number of disease attacks. IMA and IMA/albumin levels were compared between each subgroup.

**Results:** The study and control groups were similar with regard to demographic features and clinical characteristics. Significant differences were observed between the mean IMA and IMA/albumin ratio (p=0.004 and 0.012, respectively). The study subgroups were comparable in the number of patches, disease duration, and number of disease attacks.

**Conclusion:** Although oxidative stress is an important component in the etiology of AA, IMA and IMA/albumin may not be useful in the prediction of disease severity in patients with AA.

## Introduction

Alopecia areata (AA) is a chronic, immune-mediated disease resulting in non-scarring hair loss with an approximate prevalence of 1/1000 [1]. Hair follicles in the anagen phase prematurely transform into catagen and telogen phases by autoimmune and inflammatory mechanisms resulting in a sudden hair loss in patients with AA [2]. Although the pathophysiological mechanisms behind AA have not been clearly revealed yet, immune dysregulation, genetic predisposition, and excessive oxidative stress seem to be the main predisposing factors behind the development of AA [3].

Oxidative stress and free radical damage alter the chemical structure of albumin, leading to the production of ischemia-modified albumin (IMA) [4]. Hence, the utility of IMA and IMA/albumin were investigated in various studies for revealing the oxidative stress-related events behind the etiology of autoimmune and inflammatory diseases [5, 6].

The role of IMA was also investigated in several dermatologic diseases like psoriasis, Behçet's disease, and alopecia areata [7-9]. However, no consensus has been reached on the utility of IMA in daily dermatology practice. For this reason, more data is necessary to reach more precise results.

The aim of the present study is to investigate the role of IMA and IMA/albumin levels in patients with AA.

## Material and Methods

The present prospective crossectional study consisted of patients ≥18 who were admitted to the Dermatology and Venerology Department of Hitit University Hospital between April 1, 2021, and September 30, 2021. Seventy patients participated in the study (n=34 for the study group and n=36 for the control group). Patients with alopecia areata served as the study group. Thirty-six gender and age-matched patients with dermatologic complaints other than inflammatory skin diseases were used as the control group. Cases with pregnancy, lactation, history of malignancy, and active or chronic infection were excluded from the study. Written informed consent was signed by all participants. The institutional ethics committee approved the study protocol with reference number 449. Firstly, the clinical characteristics of AA patients were evaluated. Gender, pattern of alopecia area, duration of disease, family history with AA, involved area (scalp, beard, eyebrow) and the number of disease attacks were evaluated for each AA patient. Both study and control groups were evaluated for gender, age, height (m), weight (kg), Body mass index (BMI), smoking and alcohol consumption, IMA, and albumin levels. The IMA/albumin ratio of all participants was calculated. Afterwards, the study group was divided into subgroups based on number of patches, disease duration, and number of disease attacks. IMA and IMA/albumin levels were compared between each subgroup. All the blood samples (peripheral venous blood) from all participants were collected after overnight fast. Statistical analyses were performed by Statistical Package for the Social Sciences (SPSS.22, IBM SPSS Statistics for Windows, Version 22.0 Armonk, NY: IBM Corp.).

Student t-test was used for comparing the mean values between the groups as the data was normally distributed. Chi-square test was conducted to compare the categorical variables. Pearson correlation test was performed for correlation analyses. A two-tailed P value < 0.05 was regarded as statistically significant.

## Results

The clinical characteristics of the patients with Alopecia Areata were shown in Table 1. In the alopecia areata group, most of the participants were male. Approximately 60% of the patients had a single patch. Disease duration was less than one year in 19 patients. Only three patients had a family history of alopecia areata.

**Table 1. Demographic features and Disease Characteristics of the patients with Alopecia Areata.**

| | N | % |
|---|---|---|
| Gender | | |
| Female | 12 | 35.3% |
| Male | 22 | 64.7% |
| Patern of AA | | |
| Single patch | 20 | 58.8% |
| Multiple patch | 14 | 41.2% |
| Duration of illnes | | |
| < 1 year | 19 | 55.9% |
| 1-4 years | 9 | 26.5% |
| ≥5 years | 6 | 17.6% |
| Family history of AA | | |
| Yes | 3 | 8.8% |
| No | 31 | 91.2% |
| Involvement area | | |
| Scalp | 22 | 64.7% |
| Beard | 8 | 23.5% |
| Eyebrow | 2 | 5.9% |
| ≥2 | 2 | 5.9% |
| Number of attacks | | |
| 1 | 20 | 58.8% |
| 2 | 10 | 29.4% |
| 3 | 4 | 11.8% |

The patients' most common areas of disease involvement were scalp, beard, and eyebrows, respectively. In addition, 58.8% of the patients had an alopecia attack for the first time, while the other 4 in 10 patients had an alopecia attack for the third time.

Comparison of the gender distribution, mean age, height, weight, BMI, smoking, alcohol consumption, IMA, and albümin levels between the study and control groups are shown in Table 2.

Significant differences were observed between the mean IMA and IMA/albumin ratio (p=0.004 and 0.012, respectively). The study subgroups were comparable for the number of patches, disease duration, and number of disease attacks, as shown in Table 3.

## Discussion

The pathogenetic mechanisms of AA have still not been clarified. Impaired immune system activation and genetic predisposition seem to be the main events behind AA. Destruction of hair follicles by immune-mediated cells and inflammatory products results in reversible hair loss in a specific pattern [1]. Excessive oxidative stress is considered to be another triggering event in the development of AA. There are many studies showing the effect of oxidative stress on AA and many other dermatological diseases [10-17]. Degradation products resulting from oxidative stress may damage hair follicles and they may alter the balance between the anagen, telogen and catagen phases. Furthermore, some of these products may be used as biological markers of oxidative stress [18-20].

IMA (ischemic modified albumin) is produced by the modification of albumin due to the reactive oxygen species (ROS). A higher level of IMA was observed in various diseases like ischemic heart disease, pulmonary embolism, cancer, and stroke [21-24]. The role of IMA was also evaluated in dermatological diseases. Elevated levels of IMA were shown in psoriasis, hair diseases, and vitiligo. In recent years, some studies have addressed the risk of thrombosis, acute myocardial infarction, and stroke in AA with various results [25-28]. Shakoei et al. found elevated D- Dimer levels and increased risk of thromboembolism in AA. Kang et al. defined that patients with AA were associated with a higher risk of stroke in the 3-year follow-up period. However, some data do not support the risk of heart attack and stroke in alopecia

**Table 2. Comparison of the gender distribution, mean age, height, weight, BMI, smoking, alcohol consumption, IMA, and albümin levels between the study and control groups.**

| | Patients (n=34) | Controls (n=36) | P value |
|---|---|---|---|
| Gender | | | |
| Female | 12 | 13 | 0.57 |
| Male | 22 | 23 | |
| Mean age | 31.56±8.5 | 31±8.5 | 0.78 |
| Height | 170.8±9.5 | 169.7±9.9 | 0.72 |
| Weight | 72.6±12.8 | 72.2±10.04 | 0.86 |
| BMI | 24.79±3.3 | 25.05±2.8 | 0.72 |
| Smoking | 0 | 0 | N/A |
| Alcohol consumption | 0 | 0 | N/A |
| Family history of AA | 3 | 0 | N/A |
| IMA | 0.71±0.17 | 0.50±0.14 | **0.04** |
| Albumin | 4.09±0.10 | 4.08±0.11 | 0.62 |
| IMA/Albumin | 0.17±0.04 | 0.12±0.03 | **0.012** |

**Table 3. Comparison of IMA, Albumin, and IMA/Albumin according to number of patches, disease duration, and number of disease attacks.**

| | Single patch (n=20) | Multiple patch (n=14) | P value | <6 months (n=19) | >6 months (n=15) | P value | Number of attack 1 (n=20) | Number of attack ≥2 (n=14) | P value |
|---|---|---|---|---|---|---|---|---|---|
| IMA | 0.70±0.20 | 0.72±0.10 | 0.76 | 0.75±0.21 | 0.66±0.09 | 0.13 | 0.73±0.21 | 0.68±0.08 | 0.39 |
| Albumin | 4.09±0.11 | 4.10±0.09 | 0.65 | 4.05±0.10 | 4.13±0.09 | **0.04** | 4.08±0.13 | 4.11±0.05 | 0.38 |
| IMA/Albumin | 0.17±0.05 | 0.17±0.02 | 0.81 | 0.18±0.05 | 0.16±0.02 | 0.11 | 0.18±0.05 | 0.16±0.02 | 0.35 |

areata [27, 28]. On the other hand, recently, in alopecia areata, literature data show a tendency to thrombosis and an increased risk of heart attack and stroke. In addition, studies have found elevated levels of cardiac biomarker troponin I and congestive heart disease biomarker BNP in patients with alopecia areata [29, 30].

There are publications in the literature indicating the association of IMA with the severity and deterioration of AA [9, 31]. These reports focused on the pathophysiological pathways related to increased oxidative stress in patients with AA. As excessive oxidative stress was reported to be an important triggering event in the development of AA, markers associated with oxidative stress might increase with disease severity [32]. Moreover, although the utility of IMA/albumin was investigated in various conditions like chronic liver disease and hemorrhagic shock, to the best of our knowledge, it has not been studied in cases with AA [6, 33]. However, similar to other autoimmune and inflammatory diseases, the etiology of AA is complex, and using a single oxidative biomarker may be insufficient to predict the severe course of the disease [34]. In the present study, no significant differences were observed for IMA and IMA/albumin between the cases with regard to patch characteristics, duration of the disease and number of attacks per year. In our opinion, more studies, including a larger number of cases and many more study parameters, are necessary to reach more reliable results for the role of IMA in the prognosis of AA.

The main strengths of the present study were its prospective design and investigation of IMA/albumin levels in patients with AA. On the other hand, the relatively low number of cases and single-center experience were the main limitations.

In conclusion, although oxidative stress seems to play an important role in the etiology of AA, IMA and IMA/albumin may not be useful in the prediction of disease severity in patients with AA.

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