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# The utility of ischemia modified albumin as an oxidative stress biomarker in seborrheic dermatitis

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## Abstract

**Aim:** Seborrheic dermatitis (SD) is a commonly seen chronic inflammatory skin disease that occurs as scaly reddish-brown itchy patches on sebaceous, gland-rich areas of the scalp, face, and trunk. The relation between SD disease and serum IMA (Ischemia modified albumin) levels remains unknown. To investigate the potential role of serum IMA and corrected IMA levels in SD disease.

**Materials and Methods:** Thirty-seven participants who were diagnosed with SD disease and sixty-two healthy subjects (control group) were enrolled in the study. Venous blood samples were collected from each participant, and serum IMA was measured spectrophotometrically using the albumin cobalt binding test.

**Results:** The serum IMA and corrected IMA levels were statistically significant between the groups, and the levels of IMA and corrected IMA were measured as SD patients group 0.70, 0.70 and control group 0.52, 0.51 ABSU (absorbance units), respectively ($p < 0.05$). Moreover, serum IMA and corrected IMA levels were statistically significant between male and female groups in terms of gender as 0.75 and 0.69 ABSU, respectively ($p < 0.05$). Serum albumin levels, age, and BMI (body mass index) were statistically insignificant between these groups.

**Conclusion:** Our results show increased serum IMA and corrected IMA levels in patients with SD. Evaluation of IMA and corrected IMA levels in SD disease may contribute to diagnosis and prognosis. Further and comprehensive studies are needed.



## Introduction

Seborrheic dermatitis (SD) is a commonly seen chronic inflammatory skin disease and it causes scaly reddish-brown itchy patches on sebaceous, gland-rich areas of the scalp, face, and trunk [1]. SD, which is one of the most common diseases in the world, may be seen in all age groups, but it is more common in the adolescent and post-adolescent age group between the ages of 20-50. Disease prevalence in the community varies between 2-8% [2]. Although SD is accepted as a multifactorial disease with endogenous and exogenous, its etiopathogenesis is not fully understood.

Local immune response, especially due to Malassezia species, may be held responsible in the pathogenesis. Moreover, ultraviolet, hormones, some drugs, various environmental and nutritional factors were found to be associated with SD. It also has been suggested that all these factors result in excessive production of reactive oxygen species and hydroxyl radicals or inadequacy of antioxidant mechanisms, and as a result of this, oxidative stress develops and the inflammatory response in the SD beginnings [3, 4].

Albumin is a protein that is synthesized in the liver and has different functions as binding some molecules and substances such as bilirubin, hormones, fatty acids, and drugs in the blood [5]. In the case of conditions such as free iron and copper exposure, acidosis, hypoxia, free radical damage, and oxidative stress, the N-terminal end of albumin are modified, as a carrier part for toxic substances [6]. This new form of albumin is called ischemia modified

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albumin (IMA) and its capacity to bind certain metals such as cobalt and nickel is reduced. The modified shape formed is measured spectrophotometrically by the albumin cobalt binding test (ACB) [7]. In some dermatological diseases, IMA has been studied with oxidative stress in related diseases etiopathogenesis, and it has been shown that the increase of IMA levels is closely related to the etiopathogenesis as a marker of oxidative stress [8]. Oxidative stress plays an important role in the development of psoriasis. In a performed study, Özdemir et al. determined that IMA levels are higher in patients with psoriasis than in the healthy controls [9].

In this present study, it was aimed to investigate IMA levels of patients with seborrheic dermatitis, whose etiology was reported with oxidative stress and to examine the relationship between IMA levels and some parameters such as the duration of the disease and the location.

## Materials and Methods

In this prospective case-control study, thirty-seven participants over the age of 18, who were admitted to the dermatology outpatient clinic and had the diagnosis of seborrheic dermatitis and also sixty-two healthy volunteers without any disease of similar age and characteristics, were enrolled in the current study. Demographic data of the patients and healthy volunteers such as age and gender, disease onset age, disease duration, family history, and recurrence frequency were also recorded on the patient forms. Patients with heart disease, diabetes mellitus and/or any other systemic disease, dermatological diseases other than seborrheic dermatitis, any systemic drug use, smoking, alcohol use, pregnant and breastfeeding patients, and those under 18 years of age were excluded from the study. The blood taken from the subjects during routine examinations was centrifuged at 2500 g for 10 minutes and separated into their serum, and then 4 ml of this serum was stored at -20 degrees.

The levels of IMA were studied (at once) on the same day after all samples were collected. Serum IMA levels were evaluated by a spectrophotometric method using the albumin cobalt binding test. Sigma-Aldrich (Germany) chemicals and Spekol spectrophotometer (Jena, Germany) were used to measure IMA levels. The albumin measurements were performed on Siemens Dimension Expand (Dade Behring, USA) analyzer using a fully compatible Siemens albumin kit. Corrected-IMA (C-IMA) levels according to IMA and albumin of each patient and healthy controls were calculated with the formula [C-IMA = IMA x (albumin/median of albumin of the group)], and were given as absorbance of unit (ABSU). The study was approved by the non-interventional clinical trials ethics committee (Approval no:433). All participants had signed their consents before the study.

### *Statistical analysis*

For the statistical analyses, the SPSS Version 25.0 was used. Mean and standard deviation (X±SD) were used for the quantitative variables and number and percentage (n-%) were used for qualitative variables. The normality test of numerical variables was controlled with the Kolmogorov-Smirnov test. The independent samples t-test was used for the comparison of two independent groups for normally distributed continuous variables, and the Mann-Whitney U test was used for data with non-normal distribution. Categorical variables were evaluated with the Pearson chi-square test and Fisher's exact test. P values $< 0.05$ were considered as statistically significant.

## Results

The serum IMA and corrected IMA levels were statistically significant between the groups, and the levels of IMA and corrected IMA were measured as SD patients group 0.70, 0.70 and control group 0.52, 0.51 ABSU (absorbance units), respectively ($P < 0.005$). Moreover, serum IMA and corrected IMA levels were statistically significant between male and female groups in terms of gender as 0.75 and 0.69 ABSU, respectively ($P < 0.005$) (Table 1).

Serum albumin levels, age, and BMI (body mass index) were statistically insignificant between these groups.

As shown in Table 1, the mean duration of SD disease in 37 patients was 7.8 ± 7.1 years. Family history was found in 10 of the patient group. IMA and corrected IMA were found to be significantly higher in those with a family history. There was no statistically significant difference between the age, weight, height, and BMI values of the patient and control groups. Considering the albumin and IMA values, IMA and corrected IMA values were significantly higher in SD patients (Table 2).

The receiver operating characteristic (ROC) curve was determined (AUC: 0.898) to the status of being patients by IMA level (Figure 1).

The likelihood ratio was determined and the highest value was found as 8.71, and the cut-off value was 0,6535. Sensitivity and specificity were found as 0,703 and 0,919, respectively (Figure 2).

The cut-off values according to the sensitivity and likelihood ratio values are presented in Table 2. The corrected IMA value was the area under the curve (AUC) 0.903 and the highest likelihood ratio as 7.81. The cut-off value of the corrected IMA value was 0.6381, sensitivity as 0.757, and specificity as 0.903 (Table 3).

## Discussion

Seborrheic dermatitis (SD) is a chronic and recurrent endogenous eczema affecting the body, including the scalp, face (nasolabial fold, ear, and eyebrows), and upper trunk (chest/presternal) [9]. SD occurs especially in areas of the skin where the sebaceous glands are active and is often associated with excessive sebum production. While sebum production may be normal in patients with SD, it may not occur in patients with severe sebum production (10). Although the etiopathogenesis of seborrheic dermatitis is not fully known, some endogenous and exogenous factors are held responsible for the development of the disease through different mechanisms [11].

Some studies declared that stress is the main trigger factor in seborrheic dermatitis, and it has also been stated

**Table 1.** The distribution of the group in terms of gender and the comparison of IMA according to the presence of family history

| Group | Gender | | | | |
|---|---|---|---|---|---|
| | Male | | Female | | P value * |
| | n | % | n | % | |
| Patient (SD) | 9 | 24.3 | 28 | 75.7 | 0.019 |
| Control | 31 | 50 | 31 | 50 | |
| | Family History (Yes) (n=10) | | Family History (No) (n=27) | | P value ** |
| | Mean | Std. Deviation | Mean | Std. Deviation | |
| IMA | 0.75 | 0.21 | 0.69 | 0.09 | 0.000 |
| Corrected- IMA | 0.75 | 0.21 | 0.69 | 0.09 | 0.000 |

* Fisher's chi-square test, ** Mann Whitney U test

**Table 2.** Some comparisons of SD patients and healthy control group

| Parameter | Group | N | Minimum | Maximum | Mean | Std. Deviation | P value |
|---|---|---|---|---|---|---|---|
| Age | Patient | 37 | 19 | 62 | 31.56 | 10.32 | 0.306 |
| | Control | 62 | 118 | 62 | 34.12 | 11.85 | |
| Weight, (kg) | Patient | 37 | 45 | 98 | 66.89 | 13.6 | 0.062 |
| | Control | 62 | 42 | 95 | 71.12 | 12.1 | |
| Lenght, (cm) | Patient | 37 | 150 | 190 | 164 | 0.08 | 0.139 |
| | Control | 62 | 143 | 190 | 167 | 0.09 | |
| BMI, (Body mass index) | Patient | 37 | 16.85 | 35.25 | 24.73 | 4.98 | 0.218 |
| | Control | 62 | 13.32 | 38.54 | 25.51 | 4.35 | |
| Albumin, (mg/dL) | Patient | 37 | 3.75 | 4.27 | 4.06 | 0.10 | 0.274 |
| | Control | 62 | 3.81 | 4.29 | 4.08 | 0.11 | |
| Alb-median | Patient | 37 | 0.92 | 1.04 | 0.99 | 0.02 | 0.274 |
| | Control | 62 | 0.93 | 1.05 | 0.99 | 0.02 | |
| IMA, (ABSU) | Patient | 37 | 0.50 | 1.34 | 0.70 | 0.13 | 0.000 |
| | Control | 62 | 0.33 | 1.17 | 0.52 | 0.13 | |
| Corrected-IMA, (ABSU) | Patient | 37 | 0.48 | 1.34 | 0.70 | 0.13 | 0.000 |
| | Control | 62 | 0.33 | 1.11 | 0.51 | 0.12 | |

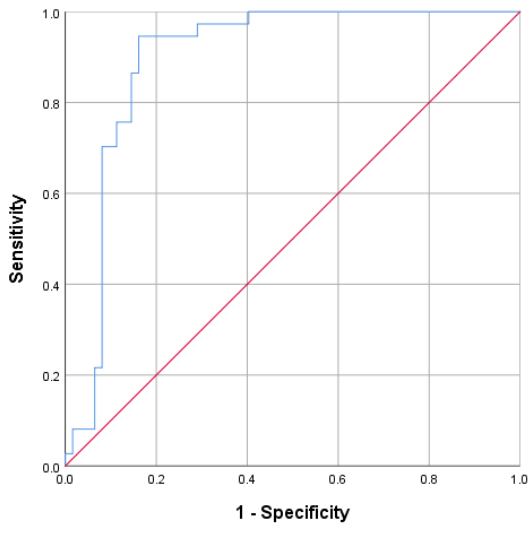


**Figure 1.** The ROC curve for IMA values

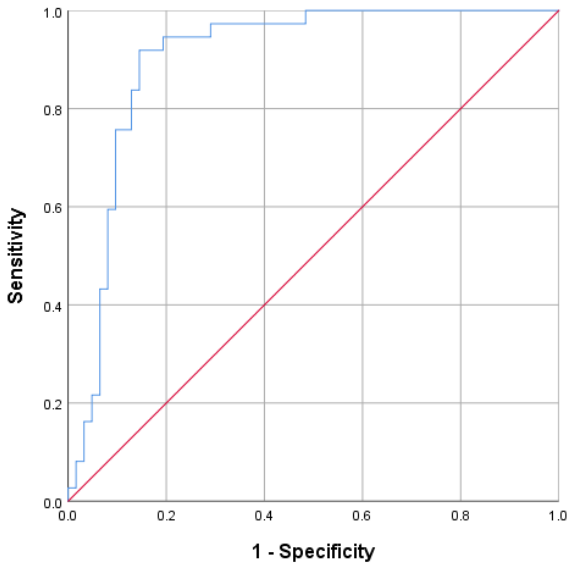


**Figure 2.** The ROC curve for Corrected-IMA values

**Table 3.** Comparison of sensitivity, specificity and likelihood ratio for IMA and Corrected IMA values.

| IMA | Sensitivity | Specificity | Likehood Ratio | Corrected-IMA | Sensitivity | Specificity | Likehood ratio |
|---|---|---|---|---|---|---|---|
| 0.60 | 0.92 | 0.84 | 5.70 | 0.60 | 0.92 | 0.85 | 6.33 |
| 0.60 | 0.86 | 0.84 | 5.36 | 0.60 | 0.89 | 0.85 | 6.14 |
| 0.61 | 0.86 | 0.85 | 5.96 | 0.60 | 0.86 | 0.85 | 5.96 |
| 0.61 | 0.84 | 0.85 | 5.77 | 0.61 | 0.84 | 0.85 | 5.77 |
| 0.62 | 0.81 | 0.85 | 5.59 | 0.61 | 0.84 | 0.87 | 6.49 |
| 0.63 | 0.78 | 0.85 | 5.40 | 0.62 | 0.81 | 0.87 | 6.28 |
| 0.63 | 0.76 | 0.85 | 5.21 | 0.62 | 0.78 | 0.87 | 6.07 |
| 0.64 | 0.76 | 0.87 | 5.86 | 0.63 | 0.76 | 0.87 | 5.86 |
| 0.64 | 0.76 | 0.89 | 6.70 | 0.63 | 0.76 | 0.89 | 6.70 |
| 0.65 | 0.70 | 0.89 | 6.22 | 0.64 | 0.76 | 0.90 | 7.82 |
| 0.65 | 0.70 | 0.92 | 8.71 | 0.64 | 0.73 | 0.90 | 7.54 |
| 0.66 | 0.68 | 0.92 | 8.38 | 0.65 | 0.70 | 0.90 | 7.26 |
| 0.67 | 0.62 | 0.92 | 7.71 | 0.65 | 0.68 | 0.90 | 6.98 |
| 0.67 | 0.59 | 0.92 | 7.37 | 0.66 | 0.65 | 0.90 | 6.70 |
| 0.68 | 0.57 | 0.08 | 7.04 | 0.66 | 0.62 | 0.90 | 6.42 |
| 0.69 | 0.54 | 0.08 | 6.70 | 0.67 | 0.59 | 0.90 | 6.14 |

that stress is an indicator of poor prognosis [12]. In addition, depression and anxiety levels in seborrheic dermatitis patients have also been shown to increase and affect the quality of life [13]. Various neurological diseases and emotional stress can trigger the disease, so it's proposed that neurotransmitters may play a role in the etiology of the disease. The improvement of sebum production and seborrheic dermatitis lesions after L-Dopa treatment in patients with Parkinson's suggests that neurotransmitters play a role in the SD disease [14, 15].

Recently there are studies that have focused on increased oxidative stress (OS) in T cell-mediated skin diseases such as contact dermatitis, psoriasis, and atopic dermatitis (16). As a variant form of human serum albümin, ischemia-modified albumin (IMA) has been exposed to ROS in the condition of oxidative stress and/or ischemia [17]. Regarding the previous studies, IMA is well-known a marker of oxidative stress and an association was determined with some other markers of oxidative stress [18, 19]. Reactive oxygen species (ROS)-mediated oxidative stress is related to neutrophil activation and has an important role in the pathogenesis and severity of Behçet's disease (BD) [20]. Moreover, Altunısık et al. reported that serum total bilirubin, direct bilirubin, indirect bilirubin, uric acid and albumin levels of alopecia areata patients were lower than the control group but there was no statistically significant difference [21].

In a study performed by Keskin et al, it has been determined that levels of IMA in patients with BD was 0.65±0.11 ABSU, and healthy controls were 0.55±0.12 ABSU (P=0.0001). In the study, it's also concluded that elevated IMA levels showed superiority to other markers such as total antioxidative capacity (TAC), total oxidative capacity (TOS), or oxidative stress index (OSI) to evaluate oxidative stress in BD patients as well as in considering disease activity [22]. Another study reported that BD patients had significantly higher levels of IMA, calprotectin, and hsCRP than the healthy control group in both active and inactive patients [23]. As similar to our study, levels of IMA in patients with SD were increased compared to healthy controls as 0.70 ABSU and healthy 0.52 ABSU, respectively (P=0.0001). Moreover, levels of Corrected IMA in patients with SD were increased compared to healthy controls as 0.70 ABSU and healthy 0.51 ABSU, respectively (P=0.0001). As shown in Table 2, serum albumin levels, age and BMI (body mass index) were statistically insignificant between SD and healthy control groups.

As a sensitive marker for ischemia, IMA levels are increased in different diseases such as metabolic syndrome [24], hypercholesterolemia [25], and type 2 diabetes [26]. A very limited number of studies investigate the IMA levels in dermatological diseases, high levels of IMA were detected in dermatological diseases such as vitiligo [27] and psoriasis [8]. So, increased or decreased levels of IMA may contribute to the diagnosis, prognosis, and clinical evaluation of some dermatological diseases.

The limitations of our study were as follows; the locations of the lesions and seborrheic dermatitis severity area index were not evaluated.

## Conclusion

To the best of the authors' knowledge, the present study is the first clinical study that investigates the role of IMA in the SD disease as a biomarker. Regarding the results of the study, a potential role of IMA may be considered in the diagnosis and prognosis for the mentioned disease. To clarify this topic, further and more comprehensive researches are needed.

### *Statement of Ethics*

The current study has been carried out in accordance with The Declaration of Helsinki.

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