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Original Research Article

A Case-Control Study of the Evaluation of Ischemia-Modified Albumin Level and Metabolic Profile in Alopecia Areata Patients

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Abstract

Background: Alopecia areata (AA) is a dermatological disorder characterized by the autoimmune-mediated impairment of hair follicles, resulting in the manifestation of hair loss in one or multiple circular patches on the scalp or various anatomical regions. The potential association between ischemia-modified albumin (oxidative stress biomarker), and metabolic syndrome remains unexplored in existing scientific literature.

Aim: The goal was to determine whether metabolic syndrome was present in AA patients and ischemia-modified albumin (IMA), visfatin and sd-LDL were raised.

Subjects and Methodology: A cross-sectional study was undertaken within a hospital environment, encompassing AA patients as well as a control group. This study comprised a group of 70 patients diagnosed with AA and an equal number of 70 healthy controls. The participants were carefully selected to ensure matching in terms of sex, age, and body mass index. The evaluation of laboratory and clinical variables related to metabolic syndrome was conducted in all subjects included in the study. Furthermore, the concentrations of visfatin, IMA, and sd-LDL were assessed and subjected to comprehensive analysis in correlation with the disease pattern, severity, and chance of reappearance.

Results: IMA and adjusted IMA levels were found to be significantly elevated in comparison to the control group. Patients presenting with positive pull test findings exhibited significantly increased levels of adjusted IMA concentrations. In the present study conducted within the AA group, a statistically significant positive correlation was identified between adjusted levels of ischemia-modified albumin and waist circumference. Similarly, a significant association was observed between triglyceride and adjusted IMA levels, as well as between adjusted IMA levels and sd-LDL levels. No statistically significant differences were observed in the visfatin, lipid profile, fasting blood glucose, and sd-LDL levels among healthy controls and the patients.

Conclusion: AA patients and the control group showed identical metabolic profiles. Elevated adjusted IMA have been observed to possibly be associated with an imbalance between antioxidants and oxidants, thereby potentially increasing the susceptibility to cardiovascular disease.

Keywords: AA, Visfatin, IMA, sd-LDL, Oxidative Stress, Biomarkers.

Introduction

Alopecia areata (AA), is marked by the abrupt appearance of oval or circular areas of hair loss, is postulated to be an autoimmune disease with an underlying genetic predisposition [1]. In recent times, for the prediction of prognosis of disease, biomarkers such as oxidative stress biomolecules have been proved to be potent [1]. Levels of IMA are found to be elevated in conditions characterized by increased oxidative stress, such as obesity, hypercholesterolemia and type-2 diabetes [2]. It is widely acknowledged that in different systemic inflammatory disorders IMA serves as an indicative marker of oxidative stress. Furthermore, the cholesterol synthesis and other metabolic pathways exert a direct impact on the process of hair growth via specific signaling molecules [3]. AA patient's shows insulin resistance, elevated concentration of

sd-LDL-C represents a prominent constituent of atherogenic dyslipidemia [4].

AA is an immune-mediated disorder characterized by non-scarring alopecia, manifesting as hair loss. It is estimated to have an approximate prevalence of 1 in 1000 individuals. Hair follicles in the anagen phase undergo premature transformation into the catagen and telogen phases due to autoimmune and inflammatory mechanisms, leading to abrupt hair loss in individuals diagnosed with alopecia areata (AA) [5]. While the precise pathophysiological mechanisms underlying AA remain unclear, it is believed that immune dysregulation, genetic predisposition, and raised oxidative stress play significant roles in the development of AA. Oxidative stress and the resultant free radical-induced damage trigger modifications in the chemical composition of albumin, thereby giving rise to the synthesis of IMA [6].

As per our knowledge, no prior research has been done on the visfatin, IMA, and sd-LDL levels of AA patients. In the current investigation, we carried out a case–control study to assess the visfatin, IMA, and sd-LDL levels in AA patients in addition to the laboratory and clinical aspects of metabolic syndrome.

Methods

The study included individuals who sought medical attention for alopecia and received a diagnosis of AA within one year. Seventy patients, consisting of thirty-four females and thirty-six males were included in the study. Additionally, 70 controls, which were matched in terms of age, sex, and body mass index (BMI), were also enrolled. All study participants were of age greater than or equal to 18 years and were subjected to comprehensive systemic and dermatological evaluations.

The inclusion criteria were met by all participants. The control group consisted of individuals who were in good health and sought medical attention for cosmetic concerns. The study did not include patients who exhibited spontaneous hair regrowth upon initial presentation. The exclusion criteria encompassed individuals who met the following conditions: documented history of chronic infection, pregnancy, malignancy, lactation, and hypertension and, ischemic cardiovascular diseases. The two groups were matched based on thyroid and diabetes history. Individuals with a documented familial predisposition to AA were excluded from the pool of healthy control subjects. The demographic characteristics such as daily habits, physical exercises were also studied.

The patients were divided into subclasses based on the SALT scores. These subclasses include S0, indicating no hair loss; S1, indicating less than 20% hair loss; S2, indicating 20% to 45% hair loss; S3, indicating 45% to 70% hair loss; S4, indicating 70% to 99% hair loss; and S5, indicating complete hair loss (100%) [7]. The disease symptoms were studied consisting of duration of disease, age at which disease initially started, pull test presence, scalp hair loss pattern, AA severity. Kavak *et al.,*[8] methodology was followed for the analysis of severity of AA.

Sample collection

Measurements were taken for height (in meters), waist circumference (in centimeters), systolic blood pressure (90–120 mmHg), weight (in kilograms), and diastolic blood pressure (60–80 mmHg), the BMI (kg/m^2), was computed utilizing the Quetelet index [9]. Peripheral venous blood samples, measuring 15 ml each, were obtained from all participants. The study was performed using biochemistry tubes specifically designed for this purpose. The blood samples were collected in the morning (overnight fast). The enzymatic method was employed to measure fasting blood glucose (FBG), HDL-C, and TG and total cholesterol. The nephelometric method was employed to analyze the levels of serum albumin.

LDL-C was analyzed by using the Friedewald formula, which calculates LDL-C as the difference between total cholesterol, HDL, and TG divided by 5.0, (mg/dL). The blood samples were promptly subjected to centrifugation at a relative centrifugal force of 1200 g for duration of 10 minutes. Subsequently, the resulting sera were separated and were stored at a temperature of -80°C. The quantification of serum visfatin levels was performed utilizing ELISA. The measurement of sd-LDL-C levels was conducted using the methodology outlined in the study by Hirano *et al.,*[10].

The rapid colorimetric assay was employed to quantitatively assess the levels of unbound cobalt for the purpose of calculating the IMA. The findings are quantified and presented in terms of absorbance units. The calculation of adjusted IMA levels was performed utilizing the subsequent formula: The individual albumin concentration divided by the median albumin concentration of the population, multiplied by the IMA. For this study laboratory parameters were studied on the basis of normal ranges of TG, LDL-C, FBG, HDL-C and VLDL-C respectively.

Statistical Analysis

Using SPSS software statistical studies were performed. The parametric variables were reported in terms of their means and standard deviations, while the nonparametric, in terms of their IQRs, percentages and frequencies were analyzed. The statistical analysis of the categorical variables

involved the utilization of either the Chi-square test or Fischer's exact test. The normality of the continuous variables was assessed using Kolmogorov-Smirnov and histogram analyses. The analysis was performed using analysis of variance and Student's t-test to examine numeric variables that followed a normal distribution. The Mann-Whitney U and Kruskal-Wallis tests were employed to assess the statistical significance of differences among non-normally numeric variables. The assessment of numeric variables correlations was conducted utilizing the Spearman and Pearson tests. A p-value less than 0.05 were deemed to be statistically significant.

Results

A total of seventy patients diagnosed with AA were enrolled in this study, consisting of 34 females and 36 males. The mean age of the participants was 32.5±10.8 years, as indicated by the standard deviation. The median body mass index (BMI) values observed among the AA patients were 23.5 kg/m^2 for males and 25 kg/m^2 for females. Total of 70 controls consisting of 36 males and 34 females were carefully selected to ensure that BMI, age and sex were analyzed. Study of habits, physical, and demographic characteristics were studied along with blood pressure values.

Both groups showed similarity in physical activity, early cardiovascular disease, comorbid conditions which includes thyroid disease, diabetes mellitus, asthma, and vitiligo exhibited comparable rates. The AA group exhibited a higher prevalence of family history of AA and autoimmune diseases compared to the healthy controls (Table 1). There was no statistically significant disparity in the prevalence of metabolic syndrome between the patient group and the healthy controls.

Table 1: Demographic data and Characteristics of Patients

	Patient (n=70)	**Control (n=70)**	**p-value**
Age (mean±SD, years)	32.5±10.8	32.6±10.8	>0.05
Sex (male/female)	36/34	36/34	>0.05
Habit of cigarette smoking			
Current smoker	28/70	26/70	>0.05
Ex smoker	12/70	4/70	
Never smoked	30/70	26/70	
Alcohol Consumption			
Ever used	62/70	62/70	>0.05
Last week	6/70	2/70	
Last month	2/70	6/70	
Physical activity			
Yes	12/70	20/70	>0.05
No	58/70	50/70	
Premature cardiovascular disease			
Yes	6/70	20/70	>0.05
No	66/70	52/70	
Autoimmune disease			
Yes	22/70	2/70	0.002
No	48/70	68/70	
Alopecia areata			
Yes	16/70	-	0.003
No	54/70	70	
Comorbid disease			
Yes	6/70	6/70	>0.05
No	64/70	64/70	
BMI (Kg/m^2, median IQR)			
Men	23.5	24.6	>0.05
women	25	22	
Waist Circumference (cm, median, IQR)			
Men	95(85-97)	90 (86-97)	>0.05
Women	89 (76-97)	79 (71-87)	
Blood Pressure (mm/Hg, mean±SD)			
Systolic	114±8	114±9	>0.05
Diastolic	71±6	73±9	
Presence of metabolic disorder, n (%)	12(34)	10(28)	>0.05

The median values of ischemia modified albumin showed differences when compared between patients and healthy controls. The adjusted levels of IMA have no significant correlation with disease duration, number of alopecic patches, and age at disease onset, AA severity, total episodes, and SALT score.

In our study, we observed a noteworthy positive association between the adjusted levels of IMA, WCs, and TGlevels in patients AA. Among both female and male AA patients, the levels of IMA and adjusted IMA were found to be comparable.

Discussion

The etiology of AA remains elusive, with the underlying causal mechanisms yet to be fully elucidated. The immune privilege within the hair follicle being disrupted and immunological processes being overexpressed is assumed to be the main mechanisms. Targeting hair follicles with reduced major histocompatibility complex expression, autoreactive CD8+ T-lymphocytes [10]. Keratinocytes within the follicular unit undergo apoptosis as a result of peribulbar lymphocytic invasion. Consequently, alopecia results from the suppression of the cell cycle inside the hair matrix [11, 12].

It is evident from comprehensive genetic and molecular investigations that oxidative stress plays a significant role in the pathogenesis of AA [13]. The patient's medical history includes a diagnosis of conditions. The researchers have additionally exhibited heightened levels of ROS and escalated oxidative stress in individuals diagnosed with AA. An observed elevation in the generation of free radicals is postulated as a plausible etiological element [14-16].

The co-occurrence of AA with various immune disorders, including vitiligo, thyroid disease, atop is of significance, as it suggests a potential involvement of systemic inflammation in the development of AA. The literature presents divergent findings pertaining to the cardiovascular risk and metabolic profile among AA patients [17].

A recent study has reported the association of metabolic syndrome with AA patients. In a study conducted by Lim *et al.,*[18] it was observed that women diagnosed with AA exhibited elevated levels of LDL when compared to a control group of healthy women. Correlation between cholesterol biosynthesis, lipid metabolism and hair disorders were suggested by authors. Whereas the present study showed similar characteristics between the lipid profile of AA patients and the healthy individuals [19].

Elevated sd-LDL was noted in male patients comparatively to female counterparts, suggesting a discernible impact of sex on serum sd-LDL levels. Nevertheless, the current investigation failed to observe comparable elevations in males without any underlying medical conditions [20].

Beyond its basic role of retaining energy, the adipose tissue performs a variety of physiological tasks as a dynamic endocrine tissue. It is essential for the manufacture of many bioactive substances called adipocytokines, which regulate different metabolic processes [21]. The pathophysiology of metabolic disorders, such as insulin resistance, obesity, proinflammatory events and autoimmune disorders is significantly influenced by adipocytokines. Visfatin is a newly discovered adipocytokine that has proinflammatory characteristics. Serum visfatin levels have been found to be elevated in a number of inflammatory illnesses, including cutaneous T-cell lymphoma, psoriasis, atopic dermatitis, and Behçet's disease. These disorders are characterized by Th1- and Th2-mediated immune responses [22, 23].

As anticipated, the current investigation did not produce statistically significant differences in visfatin levels among the groups under investigation. Small sample size became the primary limitation of the study. For the most part, patients' presentations of the disease severity were mild to moderate. As a result, due to small subgroups the statistical analysis was not performed appropriately. Further, the study also not reveals the role of potent biomarkers for metabolic syndrome and insulin resistance.

Conclusion

A steadily increasing amount of research suggests that the pathophysiology of AA disease may be influenced by oxidant and antioxidant imbalance. The literature offers divergent conclusions about patients' metabolic profiles and cardiovascular risk. The current investigation set out to determine the prevalence of metabolic syndrome and clarify the changes seen in IMA and adjusted IMA levels.

Present study postulated that the oxidative process could potentially exhibit an association with disease activity among patients diagnosed with AA. Moreover, the heightened levels of IMA observed in these individuals may potentially indicate an augmented susceptibility to atherosclerosis and cardiovascular ailments. Further investigation is needed to ascertain the precise correlation between AA and the ischemic process through future endeavors involving extensive, prospective studies that effectively control for confounding variables.

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