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Role of Insulin Resistance and Oxidative Stress in Hair Loss

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ABSTRACT
Background: Alopecia is a common cosmetic problem that affects over 50% of adults at some stage in their life, and It can lead to various psychological and social difficulties, especially in young people.Recent studies have suggested that insulin resistance and oxidative stress have a pathological role in hair loss.
Objective: Despite the wide range of physiological variables that contribute to hair loss, there have been few studies that completely cover these problems. The current study directed to highlight the effect of insulin resistance(HOMA IR), oxidative stress (MDA nmol/ml and H2O2 μmol/L), and antioxidant marker(superoxide dismutase SOD) on diffuse hair loss in males and females in Basra Governorate.
Methods:ninety-six patients with diffuse hair loss between the age of 16 and 42 years old as cases and fifty-three normal controlwere measured with serum concentrations of HOMA-IR, MDA,H2O2and SOD.
Results: The statistical analysis revealed no significant difference between the groups in terms of HbA1C, fasting insulin, and HOMA IR (P value >0.05). Additionally, there was a statistically significant difference seen in oxidative marker H2O2, MDA and antioxidant marker SOD P value $P < 0.05$.
Conclusion: The study found that an oxidative stress marker (MDA and H2O2), together with reduced SOD activity, is critical in developing diffuse hair loss. More studies are needed to validate these findings, evaluate the potential links between oxidative stress and insulin resistance, and look into other oxidative stress indicators in the pathology of diffuse hair loss.

Keywords: Hair loss, diffuse hair loss, HOMA IR, MDA, H2O2

INTRODUCTION

Hair is an ectodermal structure that has high aesthetic value. It allows an individual to maintain their self-image and carry on healthy and meaningful social connections[(1)] .Alopecia is a prevalent cosmetic issue that impacts more than 50% of adults at some point in their lives.[(2)] It can lead to various psychological and social difficulties, especially in young people[(3).]Excessive hair loss and thinning are significant symptoms that are commonly presented during medical consultations, sometimes accompanied by feelings of depression, anxiety, and fear. Baldness is commonly linked to the process of ageing, as well as the loss of attractiveness [(4).]
Hair loss disorders are commonly divided into two categories: scarring and nonscarring alopecia. The choice of treatment depends on the underlying cause and is established through a dermatological evaluation.[(2).]A typically healthy scalp has more than 100,000 hairs, with 86% in the anagen stage, 1% in the catagen stage, and 13% in the telogen stage. Hair loss is typically up to 100 telogen hairs per day, and the normal hair cycle lasts 3-5 years. [(1,5,6)] .Diffuse hair loss is nonscarring, diffuse hair loss from the scalp, and it is a common complaint seen by dermatologists in their everyday clinical work[(7).]Whether acute or chronic, Telogen effluvium (TE) is the primary cause of diffuse hair loss.[(5)] That occurs when there is a disturbance in one phase of the hair cycle, leading to the shedding of more than 200 hairs from the scalp daily[(8).]While diffuse hair loss is a widely observed issue, there is just a little research exploring the underlying causes of this health problem [(7).] To determine the cause of diffuse hair loss, it is necessary to obtain relevant information about the patient's medical history and do suitable laboratory tests to rule out any hormonal, nutritional, or immunological diseases. A diverse range of possible factors have been associated with the development of DHL[(1,9)] .Several recent studies have shown that insulin resistance is implicated as the causative factor of several modern disorders, including Psoriasis, Androgenetic Alopecia, and Alopecia Areata. [(10,11)] .Hair follicles are essential parts of the body, and as a highly active organ, they require a complex regulatory micro-environment with enough oxygen and

nutrients. As a result, prolonged deficits in oxygen and food supply caused by hyperglycemia might cause follicular damage, altering normal hair growth[12] .Insulin resistance is a physiological state characterized by decreased responsiveness of insulin-targeting tissues to a high level of physiological insulin. It is well recognized as the causative factor for several modern disorders [13] .Oxidative stress is a prevalent issue in redox biology and medicine [14]. characterized by an imbalance between reactive oxygen/nitrogen byproduct generation and antioxidant protection. These byproducts are essential for maintaining physiological activities in low quantity, but excessive production can damage vital biomolecules like DNA, proteins, and membranes, This damage is implicated in the development of several diseases [15,16,17] .A growing body of data also suggests that it plays a part in the development of one of the factors that causes hair to grey and fall out [18] The mitochondria create the majority of reactive oxygen species (ROS), which include superoxide anion, hydrogen peroxide, and hydroxyl radicals.[19] Lipid peroxidation an oxidative breakdown process of polyunsaturated fatty acids driven by ROS and resulting in themembrane damage malondialdehyde[20,16] .Superoxide dismuta formation of highly reactive aldehydes such as malondialdehyde (MDA), is another marker of oxidative stress, it may be one of the reasons for cellular se (SOD), catalase (CAT), and glutathione peroxidase (GPX) are the primary enzymes implicated in antioxidant defence functions[19]. These enzymes govern ROS formation to maintain a healthy cellular redox balance. Changes in this redox balance, such as increased ROS levels and/or reduced antioxidant levels, can cause oxidative stress[16,21]

MATERIALS AND METHODS

Sample collection

A case-control study was carried out from the privet dermatology clinic of Doctor FirasFakhirAltameemi at AL Basra City. The research was carried out between November 2023 and April 2024 .The current research comprised a case-control study involving 149 samples: (96) patient samples with diffuse non-scarring hair loss (50 females and 46 males) with ages between 16-42, mean of age was (27.145±7.572) and (53) healthy control samples. (26 females and 27 males) aged between 17-41 years with a Mean of age (26.849±6.171) was taken for control had no exclusion criteria and healthy individuals. As insulin resistance cannot be determined by a single definitive test, the diagnosis was made using the homeostasis model assessment of insulin resistance (HOMA-IR) using the following formula:

IR = (Fasting insulin level [μIU/mL] × fasting glucose level [mg/dL]/405) [22] .

Blood sampling

Aseptically A 5 mL venous blood sample was collected from every participant in the studyan overnight fast of >8 h,1ml of blood was transported to the Clinical Biochemistry Laboratory in a tube containing ethylene diamine tetra acetic acid (EDTA) tube for assay HbA1c by used ichromaII device and 4ml of venous blood in basic test tubes with no anticoagulant (gel tube). After coagulation, samples were centrifuged (at 2000 g for 10min). Each serum sample was divided and then transferred into separate Eppendorf tubes for analysis using ELISA for assay of oxidative stress (H2O2 and MAD), spectrophotometer V1100 DIGITAL was used for assay of antioxidative markersSOD also used ARCHITECT i1000SR for assay of fasting insulin, photoelectric colorimeter AP-101 was used for assay fasting glucose. To limit the number of freezing-thawing cycles. one part was used immediately at the time of the blood sample for assay of Fasting glucose and fasting insulin. In contrast, the other part of the serum samples was frozen deep freeze at a temperature of -80 degrees Celsius until the start of the investigation for subsequent assay ofH2O2 and MDA measure by using ELIZA technique,SOD assay by using spectrophotometer V1100 DIGITAL.At the time of the study, after several samples were complete, plasma from both the patients and control groups was taken out from deep freeze and kept in a laboratory room until they reached room temperature. Afterwards, they were mixed thoroughly using vortex techniques and made ready for analysis. The assays were carried out using an enzyme-linked immunosorbent assay (ELISA) technique for assay MDA and H2O2.

RESULT

A total of 149 individuals who met both the criteria for inclusion and exclusion were included in the study. Among them, 96 individuals were classified as the case group, exhibiting diffuse non-scarring hair loss, while the remaining 53 individuals were healthy control subjects. The case and control groups were matched based on age and gender. The main characteristics of descriptively analysed study samples are listed below in Tables 1 and 2

The independent samples' parametric data was analysed using a t-test to examine the differences in quantitative variables between two groups, including controls and patients.

Table 1: Comparison between HbA1c, fasting insulin, and HOMA IR in patients with diffuse hair loss and healthy control

Parameters	**Control Mean ± SD N=53**	**Patients Mean± SD N=96**	**P value**
HbA1c	4.926±0.551	4.934±0.582	0.934
Fasting insulin	12.466±6.0861	13.221±9.273	0.595
HOMA.IR	2.583±1.470	2.641 ±1.846	0.844

P-value ≤ 0.05 is considered significant; N: number; Mean ±SD is the mean value and standard deviation,HOMA-IR, homeostasis model assessment of insulin resistance.
The statistical analysis showed no statistically significant difference between the groups in terms of HbA1C, fasting insulin, and HOMA IR, as shown by the P value>0.05.

Table 2: Comparison between MDA, H2O2, and SOD in patients with diffuse hair loss and normal control.
According to the table-2 found there was a statistically significant difference in MDA, H2O2and the antioxidant marker SOD between the groups, P < 0.01.

Parameters	**Control Mean ± SD N=53**	**Patients Mean± SD N=96**	**P value**
MDA	1.512±0.451	1.907±0.724	0.001*
H2O2	12.33± 4.854	15.63± 6.341	0.001*
SOD	1.372±0.86	1.056±0.60	0.010

DISCUSSION

There is a limited amount of epidemiological research available in the literature regarding the connections between diffuse hair loss and other disorders. The study of hair loss focuses on two main areas: the biological aspect of hair loss, which includes microscopic, biochemical (hormonal, enzymatic), and molecular changes in the hair follicle's "secret life" within the skin's depth, and aesthetic problems and management of ageing hair, which happen outside the skin.[23,24].In our study, we focus on biological problems (biochemical part) by studying the effect of insulin resistance and oxidative stress markers on diffuse hair loss because both IR and oxidative stress have been found to link pathological mechanisms in different diseases in humans.Insulin is present in hair follicles and has the potential to impact the hair growth cycle.[25]. Insulin and the effects of insulin resistance may play a pathogenic role in the miniaturisation of hair follicles. Vasoactive chemicals associated with endothelial dysfunction in insulin resistance disrupt microcirculation, induce perifollicular vasoconstriction, and enhance smooth muscle cell proliferation within the vascular wall. This syndrome leads to microvascular insufficiency, localized tissue hypoxia, and the progressive miniaturisation of hair follicles. [26,27] .The measurement of HbA1c excludes individuals from both groups who do not have diabetes mellitus, the Mean± SD of the HbA1c value was below 5 (patient=4.934±0.582 and control= 4.926±0.551), the comparison between the DHL group and the control group was not statistically significant (P=0.934). HbA1c is an important biomarker of long-term glycemic management since it reflects total blood glucose levels over three months. It is critical in diagnosing diabetes and determining the likelihood of complications. Understanding the implications of glycemic control through HbA1c measurements can provide insights into potential metabolic factors contributing to hair loss in individuals.This study involved measuring and comparing fasting insulin levels in patients with diffuse hair loss and a healthy control group. The analysis indicated no statistically significant difference in fasting insulin levels between the two groups (P = 0.595). This indicates that insulin levels, a marker typically linked to insulin resistance, may not be significant in the pathogenesis of diffuse hair loss in this specific. Analyzed the average HOMA-IR of diffuse hair loss patients and healthy individuals to determine if insulin resistance is a causative factor. Results showed a mean HOMA-IR of 2.64 in patients with diffuse hair loss, which is close to healthy control values. However, the statistical analysis showed this minor difference is not statistically significant and may not significantly impact insulin resistance's relationship with diffuse hair loss development among all subjects. Insulin resistance has a role in the pathology of different diseases, including hair loss. Many studies have been done to measure the effect of insulin resistance on androgenic alopecia and areata alopecia. Still, there are limited studies on the role of insulin resistance in diffuse hair loss. Some studies support the hypothesis that insulin resistance has a markedly increased risk for developing different types of hair loss like androgen hair loss and alopecia areata[28,29,30,26] but also studies showed no role of IR in androgenic hair loss and alopecia areata.[31,22,32] .The pathophysiology of this condition is multifaceted, and current research has discovered that oxidative stress, a complex pathophysiology, is connected to a variety

of human disorders. UV radiation, inflammation, and elevated ROS levels damage DNA, proteins, and lipids, resulting in premature skin and hair ageing. This causes impaired melanocyte activity, greying, decreased hair production, and hair loss [33].The current investigation found a significant increase in serum lipid peroxide (MAD) concentration in Table 2 with values of 1.512±0.451 and 1.907±0.724 (p=0.001) in DHL when compared to healthy controls. The elevated level of MDA can be due to many forms of exposure to environmental causes and/or psychological stress[34]. High MDA levels indicate oxidative stress, which may cause cellular damage in hair follicles. This damage disturbs the normal hair development cycle and may cause hair follicles to reach the telogen (resting) phase prematurely, resulting in increased hair loss. In contrast, the activities of plasma SOD antioxidant capacity were found to be considerably lower in DHL patients than in healthy persons with measurements of 1.372±0.86 and 1.056±0.60 (p=0.010), that shown to be adversely linked between MDA and SOD activity in DHL patients, A reduction in SOD activity suggests a weakened antioxidant defence mechanism cause accumulation of ROS, which exacerbating oxidative stress and may provoke inflammatory reactions that might damage hair follicles. These results were also approved by Jabbar B. Kareem[33].Hydrogen peroxide (H2O2), is an indicator of oxidative stress. It influences biological behaviour via various mechanisms, such as alterations in cellular redox balance, modifications in membrane potential, and the synthesis of new molecules that regulate signal transduction pathways [33]. The hydrogen peroxide levels were significantly higher DHL as compared to control, recorded at 12.33±4.854 and 15.63±6.341 (p=0.001), the elevated H2O2 levels further confirm the existence of oxidative stress. Hydrogen peroxide can trigger apoptosis in dermal papilla cells, which are essential for regulating hair development. This apoptotic impact may result in decreased hair density and subsequent hair loss [35,34].

CONCLUSION

This study supports the concept that certain substances in the blood and hair can cause hair loss. The results of this investigation indicate significant increases in MDA and H2O2 levels, together with reduced SOD activity, highlighting the contribution of oxidative stress to the development of diffuse hair loss. Future research should focus on investigating therapeutic strategies that attack oxidative stress pathways to develop effective treatments for patients experiencing hair loss, antioxidants may be useful in controlling disorders linked to diffuse hair loss, oxidative damageand restoring cellular health. While statistical analysis suggests insulin resistance does not likely have a significant impact on diffuse hair loss, additional research is required to confirm these results, and examine the possible effects of insulin resistance on the development of diffuse hair loss.

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