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Evaluation of Serum Iron and Serum Ferritin levels in the Indian population with Alopecia Areata.

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Abstract:
***Background**: Despite the fact that immunologic mechanisms and genetic factors are thought to have a role in alopecia areata, the exact cause is unknown. Iron deficiency has been cited as a factor; however, its impact is debatable. In our case control research, we discovered that patients had greater mean serum iron and ferritin levels and lower mean TIBC levels than control participants, although the differences were highly significant.*
***Materials and Methods**: This was observational prospective study, The present study included 150 A.A patients(cases) and 150 controls attended to Department of Dermatology in collaboration with Department of Biochemistry, LNMC & J.K Hospital, Bhopal. The levels of Iron and Ferritin was estimated by colorimetric Method*
***Results**: A total of 300(150 cases of AA +150 controls were included T3, T4 & TSH with mean± SD are given in the Table no.1. The two groups were comparable (P<0.0001), (P<0.0001). **Iron:** Iron levels in controls is 100.44 ±32.94 µg/dl, Iron levels in AA is 33.147 ±11.88µg/dl. The difference in the values Serum Iron parameters in respect of these groups was highly statistically significant (P>0.0001*). **Ferritin:** Ferritin levels in controls is 156.74±30.33 ng/dl, Ferritin levels in controls is 25.92 ±12.74 ng/dl. The difference in the values Serum Ferritin parameters in respect of these groups was highly statistically significant (P>0.0001*).*
***Conclusion:** We propose a threshold theory to explain the widespread effect of reduced iron storage on a number of etiologically diverse types of hair loss. Understanding the role of iron in hair loss might aid in the development of novel therapeutics as well as the generation of hypotheses to better understand the biochemical basis of these diseases. Ferritin levels should be assessed as part of future AA examinations.*
Key Word**: **Alopecia Areata, Serum Iron, Serum Ferritin

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I. Introduction

Alopecia Areata (AA) is a non-scarring, recurrent inflammatory hair loss that can affect any hair-bearing region. A discoid patch of alopecia without scaling or symptoms of inflammation is the prototype lesion in clinical terms. The presence of exclamation mark hair on the lesion's perimeter is diagnostic[2]. Despite the fact that immunologic mechanisms and genetic factors are thought to have a role in AA, the exact cause remains unknown 1,2. Infectious, neurological, genetic, and organ-specific autoimmune explanations have all been proposed in the etiopathogenesis of AA. As it has been linked to a variety of autoimmune conditions, there is growing evidence that AA is a tissue-specific autoimmune disease. [3]. Another possible cause is oxidative stress, which is defined as a rise in free radical generation that exceeds the antioxidant defenses inside the cell. Thyroid illness, pernicious anemia, diabetes mellitus, vitiligo, and psoriasis are among autoimmune conditions that are commonly linked to alopecia areata[2] Oxidative stress, which is defined as an increase in free radical generation that exceeds the antioxidant defenses inside the cell, is one such explanation [31]. The pathophysiology of AA may be linked to lipid peroxidation and antioxidant enzymes, according to certain research. Iron is engaged in the antioxidative system, and it is sequestered in the form of ferritin in enormous amounts. Iron levels, cytokines, hormones, and oxidative stress all influence the expression of ferritin. Ferritin has been demonstrated to have a variety of immunological effects, including suppressing lymphocyte antibody production and delayed type hypersensitivity[29]. Infections, inflammation, and cancer all raise ferritin levels. Ferritin has recently been recognized as a new marker for autoimmunity, and higher ferritin levels have been found in autoimmune illnesses [10.] Many research on iron and ferritin levels in AA patients have been undertaken. There has been

evidence of an increase in the incidence of iron deficiency anemia [12]. The goal of this study was to see if there was a link between blood ferritin levels and the severity of alopecia areata.

II. Material And Methods

This was a hospital based observational prospective study conducted at Department of Dermatology in collaboration with Department of Biochemistry LNMC & J.K. Hospital Bhopal, during the study period of Nov 2019 onwards and the study included 150 AA patient (cases) and 150 controls were included in the study. All patients with AA who presented for routine screening in the Department of Dermatology had collected their blood samples and used for the estimation of serum Iron and serum Ferritin levels are measured. All of the patients with AA had been diagnosed by the hospital's specialist dermatologist

Study Design: Prospective open label observational study.

Study Duration: 18 Months.

Sample size: 300 patients.

Sample size calculation: The sample size was estimated on the basis of a single proportion design. The target population from which we randomly selected our sample was considered 20,000. We assumed that the confidence interval of 10% and confidence level of 95%. The sample size actually obtained for this study was 150 patients with Alopecia Areata and 150 normal persons as controls.

Subjects & selection method: The study population was drawn from consecutive Alopecia Areata patients who presented to the Department of Dermatology associated with LNMC &JK Hospital with Alopecia Areata.

Group A(N=150) - included 150 the healthy persons served as a Control group (Non-Alopecia)

Group B (N=150) - included 150patients with Alopecia Areata

Inclusion criteria:
1. Willing to participate in study
2. Either sex
3. Aged ≥ 18 years,
4. Patients agreed to join the study and signed a written consent.

Exclusion criteria:
1. Pregnant women and lactating period.
2. Females or those who were receiving any hormonal contraceptive drugs and
3. Patients suffering from Endocrinal disorders.
4. Hereditary factors are excluded.
5. Participants undergoing any major surgery
6. Participants on medication of iron, folic acid &vitamin B12
7. Patients on medication for systemic disorders and acute inflammatory condition
8. Patients of critical Alopecia**.**
9. Patients with genetic disorders
10. Patients who are physically inactive.
11. Patients with a history of drug or alcohol abuse.

Procedure methodology

After written informed consent was obtained, a well-designed questionnaire was used to collect the data of the recruited patients retrospectively. The questionnaire included socio-demographic characteristics such as age, gender, nationality, height, weight, and consanguineous marriage, physical activity and lifestyle habits like smoking and Alcohol.

All biochemical assays were carried out by the same team of laboratory technicians using the same method, throughout the study period.

- **Serum Iron**
- **Serum Ferritin**

These were measured using the Beckman Coulter AU 480 Auto analyzer.
The intra– and inter-assay coefficients of variants (CV) for the biochemical assays ranged from 3.1% to 7.6%.

Statistical analysis

Data was produced using MS Excel and analyzed using IBM's SPSS software version 20 on a personal computer. All of the biomarkers' diagnostic accuracy was determined. Range, mean, standard deviation (SD), and frequencies (number of occurrences) were used to statistically characterize the data. For comparison between two groups, the Two paired t-test (Independent) was utilized. A statistically significant P value of less than 0.0001 The level $P < 0.0001$ was considered as the cutoff value or significance.

Ethical Clearance

- ❖ Study was approved by the Ethical committee of institutes.
- ❖ Informed consent was obtained from all patients

III. Result

A total of 300(150 cases of AA +150 controls were included T3, T4 & TSH with mean± SD are given in the Table no.1. The two groups were comparable (P<0.0001), (P<0.0001).

Iron

Iron levels in controls is 100.44 ±32.94 µg/dl
Iron levels in AA is 33.147 ±11.88µg/dl

- ❖ The difference in the values Serum Iron parameters in respect of these groups was highly statistically significant (P>0.0001*)

Ferritin

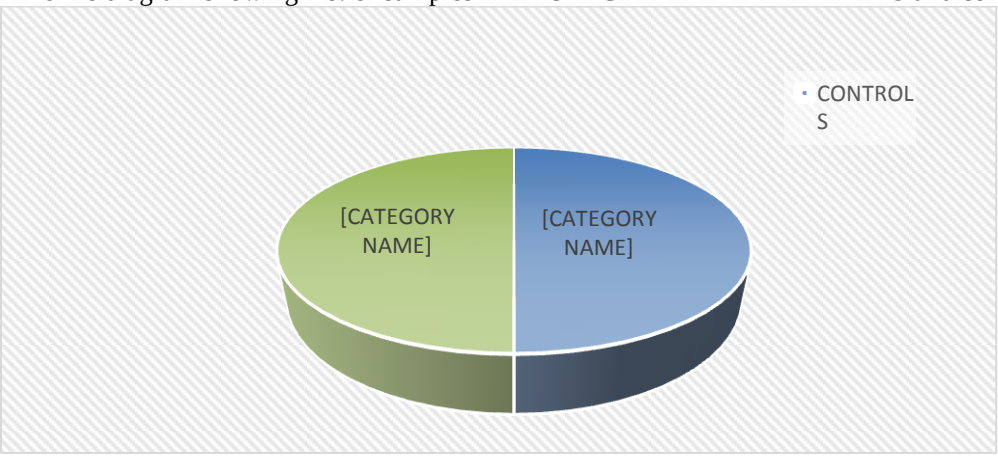
Ferritin levels in controls is 156.74±30.33 ng/dl
Ferritin levels in controls is 25.92 ±12.74 ng/dl

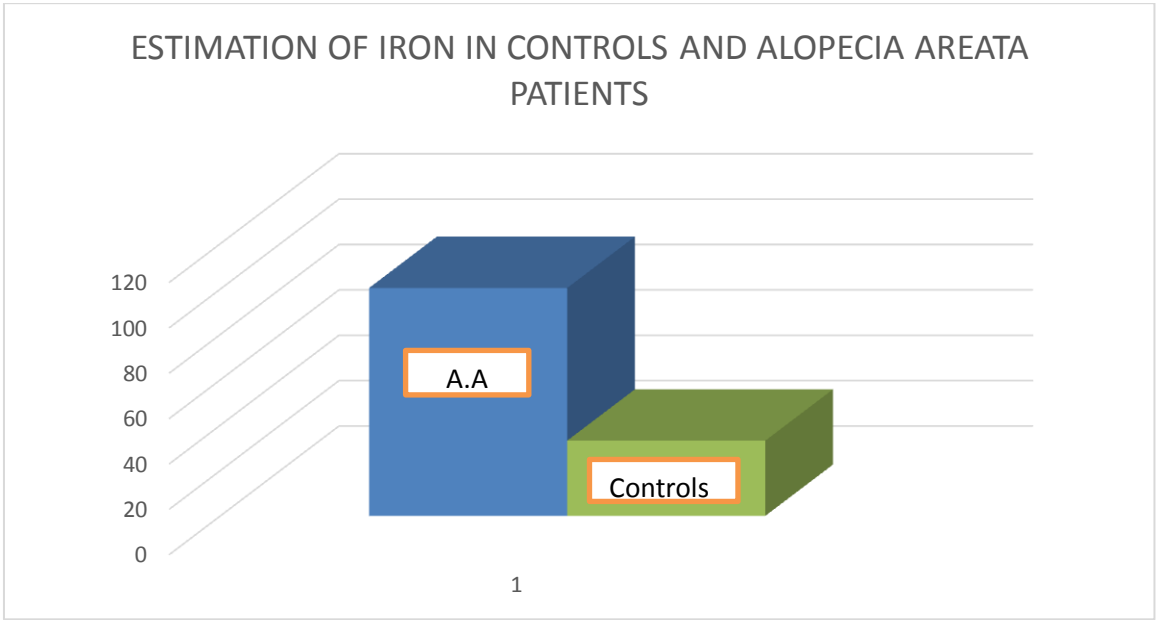
- ❖ The difference in the values Serum Ferritin parameters in respect of these groups was highly statistically significant (P>0.0001*).

Table no 1 Shows metabolic parameters of patients of the 2 groups (Both Controls & AA).

PARAMETERS	CONTROLS	ALOPECIA AREATA PATIENTS
	MEAN ± SD	MEAN ± SD
Iron(µg/dl)	100.44 ± 32.94	33.147 ± 11.88
Ferritin(ng/ml)	156.74 + 30.33	25.92 + 12.74

FIG:1The Pie diagram showing No. of samples in ALOPECIA AREATA PATIENTS and controls





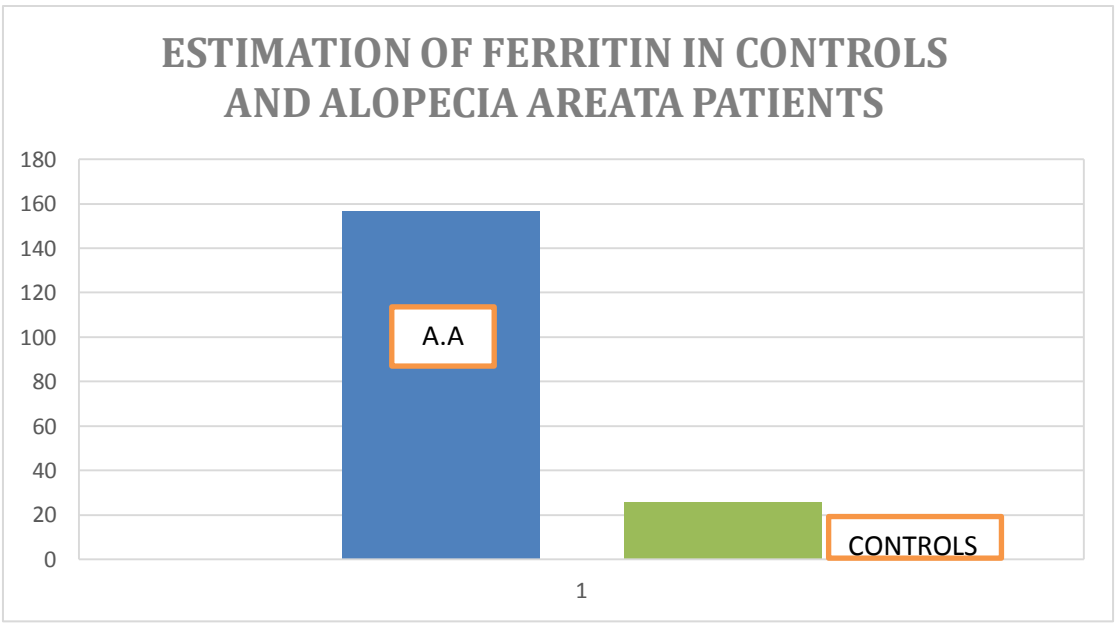


Table-2: This table shows the Critical Value, T-value and P-Value.

Parameter	Critical Value	t-value	P-value	Statistically
Iron(µg/dl)	1.972	23.5344	P<0.0001*	Highly statistically significant
Ferritin(ng/ml)	1.972	48.6975	P<0.0001*	Highly statistically significant

IV. Discussion

Alopecia Areata (AA) is a non-scarring, recurrent inflammatory hair loss that can affect any hair-bearing region. A discoid patch of alopecia without scaling or symptoms of inflammation is the prototype lesion in clinical terms. The presence of exclamation mark hair on the lesion's perimeter is diagnostic[22] Despite the fact that immunologic mechanisms and genetic factors are thought to have a role in AA, the exact cause remains unknown 1,2. Infectious, neurological, genetic, and organ-specific autoimmune explanations have all been proposed as etiopathogenesis ideas for AA[20]. As it has been linked to a variety of autoimmune conditions, there is growing evidence that AA is a tissue-specific autoimmune disease. [3]

Our findings indicate that iron insufficiency is more common in AA patients. Iron deficiency may be a cause or triggering factor in hair loss, according to some researchers [16]. If the scalp hairs are at a phase where regrowth is likely, iron deficiency might be a limiting factor, they claimed [5]. According to a Rushton and

Ramsay research, diffuse androgenic alopecia patients with a blood ferritin level greater than 40 mg/l respond better to therapy [7]. Mussalo & et al. referenced research that found no statistically significant variations in serum iron levels between AA patients and controls (8). This research is not correlated our own findings and Serum Iron levels are statistically significant (P<0.0001)

The iron status of 32 AA patients in the UK was studied by Boffa et al. They came to the conclusion that the frequency of iron insufficiency in patients with AA is not considerably elevated [6]. This research is not correlated to our own findings. Because AA is primarily a (immunogenetic) autoimmune illness with a genetic basis, our findings suggest that there is no link between AA and iron deficiency. It's still unclear if iron deficiency aids hair regrowth in AA.

In a study conducted in Denmark, White et al discovered that female patients with AA had a higher rate of iron insufficiency than the general population. They recommended that serum ferritin be measured as part of the workup in patients with AA [5]. In neither our research nor that of White et al, none of the males with AA exhibited iron deficiency anemia [25]. This ruled out a true link between iron deficiency and AA. According to Kantor et al, the mean ferritin level in AA patients was statistically substantially lower than in healthy people without hair loss (9). This research contradicted our findings. Individuals with various forms of hair loss, including 24 patients with AA, were included in this study. Eleven participants without hair loss make up the control group. This study's conclusion contradicted our findings. It was, however, a small sample size research[31]. Our findings showed Serum Iron levels are statistically significant (P<0.0001)

Iron deficiency may be a triggering factor in AA, according to a small number of studies. If the scalp hairs are in a phase when re-growth is conceivable, they imply that iron shortage might be a limiting factor. According to Rushton et al. 10, many women with alopecia had lower hemoglobin and ferritin levels, while these values are still within the "normal range." As a result, women with physiologically deficient iron may be included in the so-called "normal levels" of ferritin and hemoglobin[12]

The lack of reduced ferritin levels in AA patients might be attributable to the multifaceted character of the disease. TE can be caused by a variety of things, including medications, fevers, fast weight loss, and a variety of other things (Headington, 1993; Harrison and Sinclair, 2002). [24] We may not have recognized a subset of women with AA who were triggered by low iron body reserves since we included all patients with AA, including chronic AA. Our results, for example, imply that iron deficiency may have a role in initiating AA in women under the age of 40, notwithstanding the low patient numbers. More research is needed to determine the function of iron in AA, particularly in women under the age of 40.

Patients with AAT/U have normal ferritin and hemoglobin levels, suggesting that they are genetically separate from those with AA (Colombe et al, 1995;1999).[32] These patients may be genetically predisposed to AAT/U and do not require extrinsic triggering conditions to develop it. Alternatively, our data might imply that low body iron levels are more important in causing AA than in keeping it going. Future research, particularly into the genetics of AA and AAT/U (McDonagh and Messenger, 2001; Tazi-Ahnini et al 2002), will be required to address this hypothesis' [8].

V. Conclusion

We propose a threshold theory to explain the ecumenical effect of low iron reserves on a wide range of etiologically diverse kinds of hair loss. Understanding the role of iron in hair loss might aid in the development of novel therapeutics as well as the development of theories to better understand the biochemical basis of these diseases. Ferritin levels should be assessed as part of any future AA examinations.

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