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Analyzing the trace elements like serum iron, serum zinc and serum ferritin levels with alopecia within the Indian population

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Abstract

Introduction: Background: The actual a etiology of alopecia Areata is unknown, despite the fact that immunologic processes and hereditary factors are considered to play a role. Iron deficiency has been mentioned as a contributing cause, but its significance is questionable. Patients had higher mean blood iron and ferritin levels and lower mean TIBC levels than control individuals in our case control study, however the differences were not statistically significant.
Aim: To analyze the Trace Elements like Serum Iron, Serum Ferritin & Serum Zincin Alopecia areata and in controls.
Materials and Methods: The current study included 150 A.A patients (cases) and 150 controls who attended the Department of Dermatology at L.N. Medical College and Research Center and J.K Hospital in Bhopal, in collaboration with the Department of Biochemistry. The levels of Iron, Ferritin and Zinc were determined using the colorimetric method.
Results: A total of 300(150 cases of AA +150 controls were included Iron, Ferritin & Zinc 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 in Alopecia patients 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*).
Zinc: Zinc levels in controls is 108.66 $\pm$ 26.23 µg/dl, Zinc levels in Alopecia patients is 31.007 + 12.702 µg/dl. The difference in the values Serum Zinc parameters in respect of these groups was highly statistically significant (P<0.0001*).
Conclusion: The widespread effect of reduced iron storage on a variety of etiologically diverse types of hair loss is explained by a threshold theory. Understanding the function of iron in hair loss might lead to the development of new therapies and the production of hypotheses to better understand the biochemical basis of these disorders. Future AA tests should include ferritin levels as a component.

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Keywords: Fully automated analyzer, T-test, P-Value & SPSS software

Introduction

Alopecia Areata (AA) is a persistent inflammatory hair loss that is non-scarring and can affect any hair-bearing location. In clinical terminology, a discoid patch of alopecia without scaling or inflammatory signs is the prototype lesion. Exclamation mark hair on the lesion's border is diagnostic 2. Despite the fact that immunologic processes and genetic factors are considered to have a role in Alzheimer's disease, the specific a etiology is unknown 1, 2. Infectious, neurological, genetic, and organ-specific autoimmune reasons for the etiopathogenesis of AA have all been offered. There is mounting evidence that AA is a tissue-specific autoimmune disease, as it has been related to a number of autoimmune diseases. (3).
Oxidative stress is described as an increase in free radical production that surpasses the antioxidant defenses inside the cell. Thyroid disease, pernicious anemia, diabetes, vitiligo, and psoriasis are just a few of the autoimmune diseases connected to alopecia areata. 2 One of these explanations 31 is oxidative stress, which is defined as a rise in free radical production that surpasses the antioxidant defenses inside the cell. According to certain study, AA's pathophysiology is connected to lipid peroxidation and antioxidant enzymes. The antioxidative system uses iron, which is sequestered in massive levels as ferritin.
Ferritin expression is influenced by iron levels, cytokines, hormones, and oxidative stress. Ferritin has a number of immunological effects, including decreasing lymphocyte antibody production and delaying type hypersensitivity 29. Ferritin levels are increased by infections, inflammation, and malignancy. Ferritin has recently been identified as a novel marker for autoimmunity, with increased ferritin levels being associated with autoimmune diseases 10.
There have been several studies on the levels of iron and ferritin in AA patients. Iron deficiency anemia has been shown to be on the rise 12. The researchers wanted to discover if there was a relationship between blood ferritin levels and alopecia areata severity in this study.
Zinc is an essential mineral for a number of catalytic enzymes [11]. Alkaline phosphatase and copper/zinc superoxide dismutase are two enzymes that rely on zinc for catalytic function [11]. It also has immunomodulatory and antioxidant properties, as well as preventing keratinocyte death via inhibiting hair follicle endonucleases [12]. Zinc deficiency is thought to be involved in the pathophysiology of AA due to a net imbalance in oxidant/antioxidant activity caused by dysregulation of copper/zinc superoxide dismutase [11, 12]. Several research have looked at trace element levels in AA patients vs healthy controls, but none have looked at the link between blood zinc levels and particular AA characteristics.

Materials and Methods

This was a hospital-based observational prospective study. This observational study was conducted in LN Medical College and Research Center &JK Hospital, Bhopal, India. For the study purpose, the patients admitted to the Department of Dermatology in cooperation with the Department of Biochemistry from November 2019 to November 2020 were taken. Analysis of collected data was done in the months of January 2021 and March 2021. Total patients enrolled for the study was 300 based on the inclusion and exclusion criteria, 150 Alopecia patients (cases) and 150 Normal as (controls). The study was done only after obtaining approval of Institutional Ethics Committee (Ref No: MC/190/2007/Pt-II/DEC-2020/10).
And had their blood samples taken and their serum Iron and serum Ferritin & Serum Zinc levels calculated. The hospital's specialized dermatologist had identified all of the patients with AA.

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Study design

Prospective open label observational research was used in this investigation.

Study period

18-month research project.

Sample size

300 patients made up the sample.

Calculation of sample size

The sample size was calculated using a single proportion design. The population from which we randomly chose our sample was estimated to be around 20,000 people. We assumed a 10-percent confidence interval and a 95-percent confidence level. The exact sample size for this study was 150 Alopecia Areata sufferers and 150 healthy people as controls.

Subject and Selection method

Patients with Alopecia Areata who came to the Department of Dermatology affiliated with LNMC & JK Hospital with Alopecia Areata were taken as population.

- The control group, Group A (N=150), consisted of 150 healthy people (Non-Alopecia).
- 150 individuals with Alopecia Areata made up Group B (N=150).

Inclusion criteria

- Age ≥18 years
- Either sex

Exclusion criteria

1. The lactation period and pregnant women.
2. Females or those on hormonal contraceptives.
3. Patients with endocrine diseases.

Procedure
Methodology for the procedure

After obtaining written informed consent, the data of the selected patients was collected retrospectively using a well-designed questionnaire. The questionnaire asked about age, gender, nationality, height, weight, and consanguineous marriage, as well as physical activity and lifestyle behaviours including smoking and drinking.
Throughout the trial period, the same team of laboratory technicians performed all biochemical assays using the same approach.

- Iron Serum
- Ferritin serum Zinc serum

The Beckman Coulter AU 480 Auto analyser was used to measure these.

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For the biochemical tests, the intra and inter-assay coefficients of variations (CV) varied from 3.1 percent to 7.6 percent.
Demographic and clinical data as regards to signs and symptoms, duration of hospital stay, treatment protocol followed which included final prognosis records were collected from Medical Records Department and noted down in a proforma prepared for the purpose. Laboratory data was collected from the Central Clinical Laboratory. On admission of the patients Serum Iron, Serum Ferritin and Serum Zinc were done to collect the baseline data.

Ethical clearance

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

Results

A total of 300 (150 cases of AA + 150 controls were included Iron and Ferritin 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 A.A 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*).

Zinc

- Zinc levels in controls is 108.66 ± 26.23 µg/dl.
- Zinc levels in Alopecia patients is 31.007 + 12.702 µg/dl.

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

Table 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
Zinc(µg/dl)	108.66 + 26.31	31.007 + 12.745

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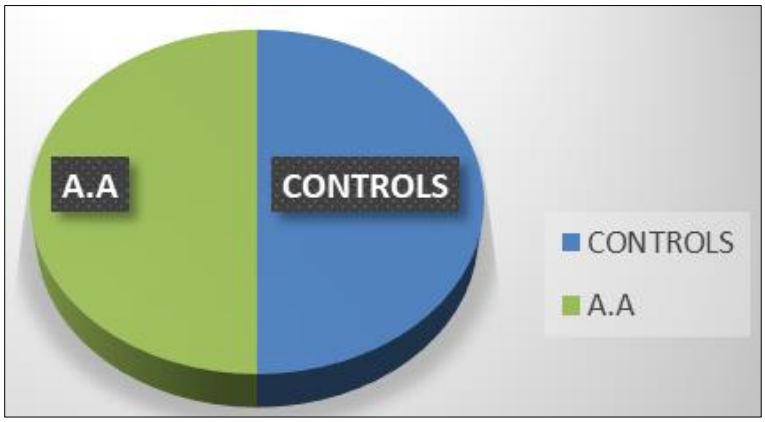

Fig 1: The Pie diagram showing No. of samples in alopecia areata patients and controls

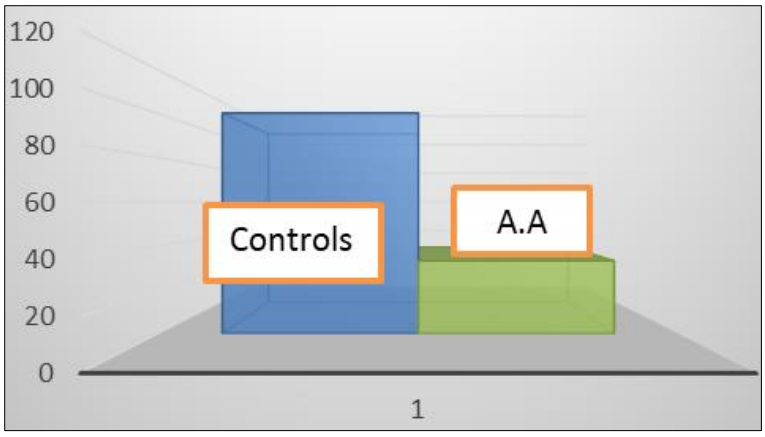

Fig 2: Estimation of iron in controls and alopecia areata patients

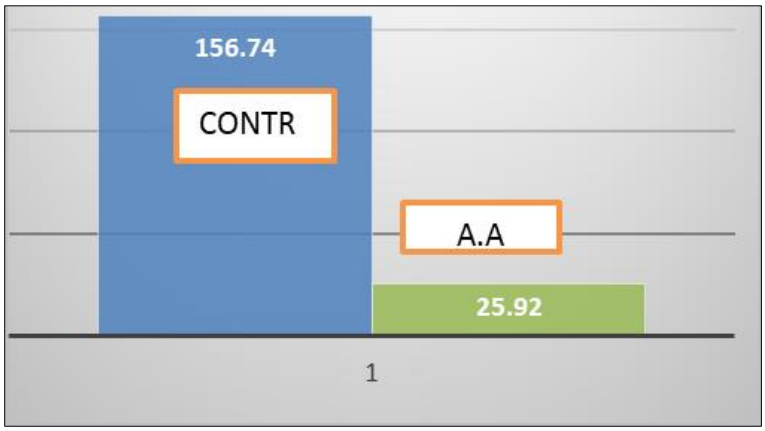

Fig 3: Estimation of ferritin in controls and alopecia areata patients

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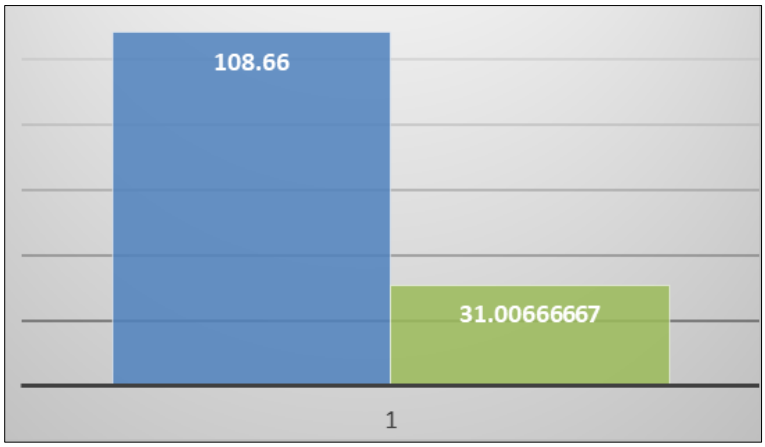

Fig 4: Estimation of zinc in controls and alopecia areata patients

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
Zinc(µg/dl)	1.972	32.5237	P<0.0001*	extremely statistically significant

Discussion

Any area of the body that bears hair may be affected by alopecia areata (AA), a non-scarring, recurring inflammatory hair loss condition. In clinical terminology, the prototype lesion is a discoid alopecia patch without scaling or signs of inflammation. It is diagnostic if there is exclamation point hair around the lesion. 22 Although genetic and immunologic pathways are suspected to have a part in the development of AA, the precise cause is yet understood 1, 2. Ideas for the etiopathogenesis of AA20 include infectious, neurological, genetic, and autoimmune causes that are organ-specific. There is mounting evidence that AA is a tissue-specific autoimmune disease as it has been associated with a number of autoimmune diseases. The zinc, iron, and copper levels in our patients were not substantially different from those in controls, according to Ladan Dastgheib *et al*.

According to a study of the literature, various studies have looked into the mineral and nutritional status of individuals with hair loss, particularly those who have AA.

Naginiene *et al*. [4] discovered that children with alopecia in their hair had lower levels of zinc in their blood and urine than healthy youngsters. The statistical correlation between blood and serum levels of zinc, magnesium, and copper in patients with a variety of dermatological illnesses, including AA, was analysed by Bruske and Salfeld [10]. There were no differences in zinc serum levels between healthy adults and those who were not.

The mean ferritin level in patients with androgenetic alopecia and AA was statistically substantially lower than in normal people without hair loss, according to Kantor et al. [11]. In the Mussalo-Rauhama research [3], the amounts of trace elements Zn, Fe, iron, and Ag in the serum of Finnish alopecia patients were determined. The Cu and Zn content in 24 hour urine, as well as the Zn and Fe amounts in these individuals' hair, were also investigated. The above-mentioned samples had no changes in element concentrations when compared to those of healthy people.

Iron deficiency is more frequent in AA patients, according to our data. According to some studies 16, iron deficiency may be a cause or triggering factor in hair loss. They suggested that if the scalp hairs are at a stage when regeneration is expected, iron deficiency might be a limiting factor [5]. Patients with diffuse androgenic alopecia who had a blood ferritin level more than 40 mg/l respond better to medication, according to a Rushton and Ramsay study [7].

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According to Mussalo & *et al*., there were no statistically significant differences in serum iron levels between AA patients and controls [8]. This study is unrelated to our own findings, and the levels of serum iron are statistically significant (P<0.0001).
Boffa *et al*. investigated the iron status of 32 AA patients in the United Kingdom. They got to the conclusion that the prevalence of iron deficiency in AA patients is not significantly higher [6]. This study has nothing to do with our own results. Our data imply that there is no relationship between AA and iron deficiency since AA is predominantly a (immunogenic) autoimmune disorder with a genetic foundation. It's yet unknown if anaemia improves hair regrowth in AA.
White et al observed that female patients with AA had a greater risk of iron deficiency than the general population in a Danish research. In individuals with AA, serum ferritin should be tested as part of the workup [5].
According to a small number of studies, iron deficiency may be a triggering factor for AA. If the scalp hairs are in a stage when regrowth is possible, iron deficiency might be a limiting factor. Many women with alopecia had lower haemoglobin and ferritin levels than women without alopecia, according to Rushton et al. 10, even though these values were still within the "normal range." As a result, women who are iron deficient physically may be included in "normal" ferritin and haemoglobin levels12.
The absence of lowered ferritin levels in AA patients might be due to the disease's multifarious nature. TE can be caused by a multitude of factors, including drugs, fevers, rapid weight loss, and other factors (Headington, 1993; Harrison and Sinclair, 2002). 24 Because we included all patients with AA, including chronic AA, it's possible that we missed a subset of women with AA who were triggered by low iron body stores. Despite the small patient numbers, our findings suggest that iron deficiency may play a role in the initiation of AA in women under the age of 40. Iron's role in AA has to be investigated more, particularly in women under the age of 40.
Except for hair iron, we found no significant differences in serum iron or serum and hair zinc levels in connection to FAGA grades in the Abdulla A Yacoub & et al research, despite our expectations that zinc and iron levels would correspond with alopecia severity. This might be due to the fact that each group had a tiny sample size. Furthermore, there was no significant link between zinc and iron levels in serum and hair; this might be due to the fact that serum trace elements fluctuate, but hair reflects a depot condition.
AAT/U patients have normal ferritin and haemoglobin levels, indicating that they are genetically distinct from AA patients (Colombe et al, 1995; 1999). 32 These patients may be genetically prone to AAT/U and do not need external triggers to acquire it. Alternatively, our findings might suggest that low body iron levels are more significant in the onset of AA than in its maintenance. To answer this hypothesis' 8, further study will be necessary, notably in the genetics of AA and AAT/U (McDonagh and Messenger, 2001; Tazi-Ahnini et al 2002).

Conclusion

Conclusions on Zinc-Most zinc studies have revealed that persons with AA had higher blood zinc levels than healthy people. Serum levels appear to be associated to the severity of the disease as well. There is a paucity of research on zinc supplementation, highlighting the need for further double-blind, placebo-controlled studies employing this mineral alone. As a result, serum zinc levels should be checked often.

Iron and Ferritin

In order to explain the ubiquity of low iron reserves on a variety of etiologically distinct types of hair loss, we suggest a threshold theory. Understanding the role of iron in hair loss may

help in the development of new therapies as well as the creation of theories to better understand the biochemical basis of these disorders. Every subsequent AA test should include a measurement of ferritin levels.

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